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ABSTRACTS FOR JOURNAL

FROM PREVENTION TO INTERVENTION

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OPENING LECTURE

When standard options fail: management of advanced CAD

M. Simons[1]

[1]*Cardiology, Yale University, New Haven, USA*

Despite dramatic advances in the treatment of coronary heart disease, a significant minority of patients still cannot be effectively managed with available therapeutic options. It is this group of patients that requires alternative approaches. The presentation will review available options including potential for growth of new arteries (therapeutic arteriogenesis), use of stem cells, and metabolic manipulation of the heart. Both basic science foundations of these approaches and clinical applications will be considered.

No conflict of interest

INTERVENTIONAL CARDIOLOGY: TOPICAL ISSUES

Management of left main disease with PCI

Document not received

INTERVENTIONAL CARDIOLOGY: TOPICAL ISSUES

Can drug eluting balloons be used in de-novo lesions?

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INTERVENTIONAL CARDIOLOGY: TOPICAL ISSUES

The ABSORB bioresorbable vascular scaffold

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INTERVENTIONAL CARDIOLOGY: TOPICAL ISSUES

Intracoronary MRI-guided local agent delivery into coronary artery walls/plaques

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INTERVENTIONAL CARDIOLOGY: TOPICAL ISSUES

Management of aortic stenosis: added value for biomarkers?

J. Bergler-Klein[1]
[1]*Cardiology, Med. Univ. of Vienna, Vienna, Austria*

In severe aortic stenosis (AS) development of symptoms presents a Class I indication in current guidelines for valve replacement. However, symptoms are frequently unspecific such as dyspnea or are reported by the patient with delay. Increased myocardial wall stress in left ventricular pressure overload induces the expression of B-type natriuretic peptide and its N-terminal pro-form (BNP, NT-proBNP). In AS, BNP has been shown to relate to the aortic valve area, symptoms onset and severity, as well as LV function (EF). BNP is also related to longitudinal systolic strain in speckle tracking echocardiography, which may be impaired even in preserved ejection fraction as an early sign of LV deterioration. Importantly, BNP can predict symptom-free survival and mid-term outcome in severe AS. A recent risk score combining AV-velocity and BNP together with gender has been validated, integrating the interplay of AS severity and LV function. The clinical outcome of AS is also determined by accompanying cardiac diseases, as in coronary artery disease or myocardial hypertrophy further aggravated by arterial hypertension, reflected by rising BNP levels. In low flow low gradient AS with reduced LV function BNP is also related to valve area and outcome. In asymptomatic severe AS increasing serial levels of BNP may point towards LV deterioration and should prompt close follow-up of patients. Biomarkers are easy to perform and readily available, and may help in optimal timing of intervention together with clinical findings and echocardiography.

No conflict of interest

INTERVENTIONAL CARDIOLOGY: TOPICAL ISSUES

Valve prosthesis - patient mismatch (VP-PM)

S.H. Rahimtoola[1]
[1]*Cardiology, University of Southern California, Los Angeles, USA*

VALVE PROSTHESIS-PATIENT MISMATCH (VP-PM): A LONG-TERM PERSPECTIVE

S.D. Daneshvar, S.H. Rahimtoola
University of Southern California, Los Angeles, CA, USA

VP-PM was first described in 1978 by Rahimtoola. From that time to 2011, aortic VP-PM has received a great deal of attention but studies have come to varying conclusions especially with regard to its effect on mortality. This is because prosthetic heart valve (PHV) area [effective orifice area index (EOAi)] has been predicted rather than measured. To better assess the outcomes of VP-PM, EOAi should be measured at hospital discharge which provides information of actual PHV after insertion into the patient. It should also be measured at 6-12 months of follow-up at which time the 4 phases of physiological healing and morphological changes are complete; EOAi at this time determines the long-term impact of VP-PM on patients' outcomes. Mild, severe and critical VP-PM should be defined as EOAi of > 0.9 cm^2/m^2, ≤ 0.6 cm^2/m^2 and ≤ 0.4 cm^2/m^2. One needs to focus especially on severe/critical degrees of VP-PM and determine if death was actually due to VP-PM and/or was VP-PM an important determinant of cardiac related cause of death by multivariate analysis?

No conflict of interest

INTERVENTIONAL CARDIOLOGY: TOPICAL ISSUES

Percutaneous valve replacement: the future is here

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INTERVENTIONAL CARDIOLOGY

COMPARISON OF TRANSRADIAL VERSUS TRANSFEMORAL APPROACH FOR PATIENTS WITH ACUTE ST ELEVATION MYOCARDIAL INFARCTION WHO UNDERWENT PRIMARY PERCUTANEOUS CORONARY INTERVENTION

K. Villena[1], R. Ramboyong[1], J.P. Prado[1], M. Sabas[1], E. Dolores[1]
[1]Adult Cardiology, The Medical City, Pasig, Philippines

Background and Objectives: *In cases of acute ST elevation myocardial infarction (STEMI), where there is strong correlation between door-to-balloon time (D2B) and mortality rate, hesitation in using transradial approach (TRA) is common. The study aims to compare the efficacy and safety of transradial intervention (TRI) versus transfemoral intervention (TFI) in patients with acute STEMI undergoing primary percutaneous coronary intervention (PCI)*

Design: *Retrospective cohort study*

Setting: *Tertiary hospital in the Philippines*

Patients: *Chart review of all patients who underwent primary PCI for acute STEMI from October 2010 to December 2012.*

Main Outcome Measure: *Compare TRI vs TFI in terms of: cardiac catheterization laboratory (Cathlab) D2B, total procedural time, total intensive care unit (ICU), and hospital length of stay, incidence of in-hospital major adverse cardiovascular events (MACE) including death, re-infarction, repeat target vessel revascularization (TVR).*

Result: *No significant difference in cathlab D2B (TFI 52.3 $\pm$ 21.3 TRI 50.8 $\pm$ 20.4 min P= 0.77), total procedural time (TFI 71.2 $\pm$ 26.3 vs TRI 65.4 $\pm$ 32.9 min P=0.44), incidence of death (P= 0.24), re-infarction (P= 0.55) and TVR (P= 0.1).TRI has significantly shorter length of ICU (P= 0.0001), hospital stay (P= 0.0002), with significantly lower incidence of TIMI major bleeding (P=0.02), TIMI minor bleeding (P=0.03), and incidence of hematoma (P=0.03).*

Conclusion: *The study showed that TRA can be done safely and effectively in acute STEMI patients undergoing primary PCI, with lower vascular access site bleeding, shorter ICU and hospital stay, and comparable to TFA in cathlab D2B and total procedural time.*

No conflict of interest

ACUTE MYOCARDIAL INFARCTION

The universal definition of MI

J.S. Albert[1]
[1]*Professor of Medicine and Editor in Chief, The American Journal of Medicine*

Clinicians and clinical scientists have often defined myocardial infarction in different ways thereby leading to confusion both in daily practice and in clinical investigation. In an attempt to alleviate some of this confusion and arrive at an internationally agreed upon definition of myocardial infarction, the European Society of Cardiology and the American College of Cardiology completed consensus processes in 2000, 2007 and 2012 that sought to define myocardial infarction in a universally acceptable manner. The consensus process led to documents that were published simultaneously in the *European Heart Journal*, the *Journal of the American College of Cardiology* and *Circulation.* Central to the universal definition of myocardial infarction is the use of the highly sensitive and specific biomarker, troponin, in the identification of ischemic myocardial necrosis. Clinical identifiers such as an appropriate history and typical ischemic ECG changes are also a required part of the definition.

Several new features were added to the 2012 definition based on scientific advances of the last seven years. Nevertheless, a number of features of the first definition were retained or were amplified. The new definition is still based on a patient history involving an appropriate clinical syndrome with chest discomfort or its equivalent together with ischemic ECG changes and a rise in blood troponin values. Troponin assays must be carefully done and shown to be highly reproducible.

No conflict of interest

ACUTE MYOCARDIAL INFARCTION

Infarct size as a surrogate endpoint in STEMI – what do we know and how does it affect therapy?

S.J. Brener[1], A. Maehara[2], J.M. Dizon[3], B. Witzenbichler[4], H. Parise[2], M. El-Omar[5], J.H. Dambrink[6], R. Mehran[7], K. Oldroyd[8], C.M. Gibson[9], G.W. Stone[3]
[1]Medicine, NY Methodist Hospital, Brooklyn, USA
[2]CTC, Cardiovascular Research Foundation, New York, USA
[3]Medicine, Columbia University Medical Center, New York, USA
[4]Medicine, Charité Campus Benjamin Franklin, Berlin, Germany
[5]Medicine, Manchester Heart Centre, Manchester, United Kingdom
[6]Medicine, Isala Klinieken, Zwolle, Netherlands
[7]Medicine, Mount Sinai Medical Center, New York, USA
[8]Medicine, University of Glasgow, Glasgow, United Kingdom
[9]Medicine, Beth Israel Deaconess Medical Center, Boston, USA

Background: Successful microcirculatory reperfusion, defined angiographically by myocardial blush grade (MBG 2 or 3), is associated with improved outcomes in patients with ST-elevation myocardial infarction (STEMI). The precise mechanism underlying this association is not well defined.

Objective: To compare infarct size (IS) measured by MRI in patients with successful (MBG 2/3) vs. unsuccessful (MBG 0/1) microcirculatory reperfusion in the INFUSE-AMI trial.

Methods: The INFUSE-AMI trial randomized 452 patients with anterior STEMI to intracoronary (IC) bolus abciximab delivered locally at the infarct lesion vs. no abciximab, and to manual thrombus aspiration vs. no aspiration. The primary endpoint was IS (% of left ventricular mass) at 30 days.

Results: MBG 2/3 was achieved in 367 patients (81.4%). IS was significantly lower in patients with MBG 2/3 than in those with MBG 0/1 (16.7% [7.0, 22.7] vs. 19.5% [11.1, 29.2], P=0.002). IC abciximab further reduced IS in patients with MBG 2/3 (14.4% [5.4, 20.9] vs. 17.4% [10.5, 23.8], P=0.01). MBG 2/3 was associated with ~30% reduction in infarct mass (P=0.002) and ~90% reduction in microvascular obstruction (MVO) on day 5. Ejection fraction was higher with MBG 2/3 at 30 days: 50.3% [43.8, 57.8] vs. 46.9% [37.5, 54.0], P=0.004. At 30 days, the rate of death was significantly lower (1.7% vs. 8.3%, P=0.0008) in the MBG 2/3 group.

Conclusions: MBG 2/3 occurs in 80% of STEMI patients treated with primary PCI, and is associated with smaller infarct size, less MVO, improved ejection fraction and significantly lower 30-day mortality

No conflict of interest

ACUTE MYOCARDIAL INFARCTION

Angina pectoris in women: focus on microvascular disease

G. Ambrosio[1]
[1]*Cardiology, University of Perugia School of Medicine, Perugia, Italy*

Contrary to the common vision that considers ischemic heart disease (IHD) a typically “male” condition, IHD actually is the leading cause of death among women in Western countries, and it is even associated with higher morbidity and mortality than in men. Nevertheless, IHD in women remains underdiagnosed and undertreated, and the misperception that females are “protected” against cardiovascular disease leads to underestimation of their cardiovascular risk. Instead, women with chest pain have a high risk of cardiovascular events.

Women suffering from angina pectoris tend to have different characteristics compared to men, with a high prevalence of non-significant coronary artery disease. Importantly, angina in women is more often microvascular in origin than in men, and therefore standard diagnostic algorithms commonly employed may be suboptimal for women.

This different pathophysiology impacts clinical management of IHD in women. While response to medical therapy may differ in women, they tend to be scarcely represented in clinical trials. Therefore, solid data in terms of gender efficacy of antianginal drugs are lacking, and particularly when angina is microvascular in origin, women often continue to be symptomatic despite maximal therapy with classical antianginal drugs.

In conclusion, women with angina are a group of patients in whom it seems appropriate to concentrate efforts aimed at improving cardiovascular risk profile, reducing morbidity, and improving quality of life.

Conflict of interest

ACUTE MYOCARDIAL INFARCTION

Performance indicators in a large Italian STEMI network

G. Di Pasquale[1], L. Riva[1], R. De Palma[2], P. Guastaroba[2], E. Berti[2], P.C. Pavesi[1], G. Casella[1], R. Grilli[2]
[1]Unità Operativa di Cardiologia, Ospedale Maggiore, Bologna, Italy
[2]Agenzia Sanitaria e Sociale Regionale, Regione Emilia-Romagna, Bologna, Italy

The organization of a regional system of care (RSC) for STEMI has been implemented in the northern Italian Region Emilia-Romagna (approx. 4.5 million inhabitants) since 2003.

The routes of STEMI pts during the year 2011 were analyzed from hospital discharge charts and Emergency Room (ER) records along with a regional web-based primary PCI (PPCI) registry (REAL registry). 3105 STEMI pts were admitted in 28 CCU (12 Hub CCU with h/24/7 days cath lab and 16 Spoke CCU without cath lab): 60.7% had a 118 EMS ambulance transport to hospital and 39.3% had a direct access to ER by personal initiative.

Out of the 1884 pts calling 118 EMS, 31.2% had a fast track route from the ambulance directly to the Hub hospital CCU cath lab, through ECG transmission and telephone consulting, bypassing ER (PPCI 88%; in-hospital mortality 8%), 17.8% had an ambulance transport to the Hub hospital ER (PPCI 73%; in-hospital mortality 18%) and 11.7% a transport to a Spoke hospital ER (PPCI 76%; in-hospital mortality 18% in case of transport to a Hub CCU). Out of the 1221 pts not calling 118 EMS, 16.3% had a spontaneous access to the Hub hospital ER (PPCI 80%; in-hospital mortality 3%) and 23.1% to a Spoke hospital ER (PPCI 85%; in-hospital mortality 3% in case of transport to a Hub CCU).

The implementation of a RSC for the treatment of STEMI in Emilia-Romagna was associated with high rates of reperfusion by PPCI and reduction of in-hospital mortality, in comparison with the pre-RSC period.

No conflict of interest

ACUTE MYOCARDIAL INFARCTION

Acute myocardial infarction: the ESC Stent for Life Initiative in Europe and beyond

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ACUTE MYOCARDIAL INFARCTION

Low molecular weight heparin in ST-elevation myocardial infarction: new data and practical implications

I.B.A. Menown[1]
[1]*Cardiology, Craigavon Cardiac Centre, Craigavon, United Kingdom*

Culprit artery reperfusion, ideally with timely percutaneous coronary intervention (PCI), or otherwise with fibrinolytic therapy, is the established treatment for ST-elevation myocardial infarction (STEMI). Given the limitations of unfractionated heparin (UFH) both in the cath lab and coronary care unit alternative anticoagulants have been investigated. Clinical trial data for fondaparinux suggest advantages for medical management but not in the cath lab, whereas the main evidence base for bivalirudin is in the cath lab.
The low molecular weight heparin enoxaparin possesses several potential mechanistic advantages over UFH. Several studies have shown enoxaparin to provide superior net clinical benefit to UFH as an adjunct to fibrinolytic therapy. In recent analysis we have shown this to be cost-effective with the cost per life year saved being £12,353 (€14,250) and cost per quality-adjusted life years between £13,556 to £15,413 (€17,780) depending on use of abbreviated or conventional therapy durations.
In the setting of primary PCI, randomised data from a contemporary study of 910 patients, showed that pre-procedural IV enoxaparin (0.5mg/kg) compared with standard IV UFH (50-70U/kg with IIb/IIIa inhibitors or 70-100U/kg without IIb/IIIa inhibitors) was associated with a strong trend to reduction in the primary composite endpoint (death, complication of myocardial infarction, procedural failure, or non-bypass major bleeding at 30 days) and significant reduction in the main secondary endpoint of death, recurrent MI/acute coronary syndrome (ACS) or urgent revascularization.
Given these data, practical aspects of using IV enoxaparin in the cath lab during primary PCI or when transitioning from the coronary care unit will be discussed.

Conflict of interest

ACUTE MYOCARDIAL INFARCTION

Effect of therapeutic heart rate slowing on recurring hospitalizations for worsening heart failure in CAD patients

J. Borer[1], M. Böhm[2], I. Ford[3], M. Komajda[4], L. Tavazzi[5], J. Lopez-Sendon[6], M. Alings[7], E. Lopez-de-Sa[6], K. Swedberg[8]
[1]Cardiovascular Diseases, State University of New York Downstate Medical Center, Brooklyn NY, USA
[2]Klinik fur Innere Medizin III, Universitatskliniken des Saarlandes, Homburg/Saar, Germany
[3]Robertson Centre for Biostatistics, University of Glasgow, Glasgow, United Kingdom
[4]Cardiology, University Pierre et Marie Curie Paris VI, Paris, France
[5]Maria Cecilia Hospital—GVM Care and Research, Ettore Sansavini Health Science Foundation, Cotignola, Italy
[6]Cardiology, Hospital Universitario La Paz, Madrid, Spain
[7]Cardiology, Hospital Amphia Ziekenhuis, Breda, Netherlands
[8]Emergency and Cardiovascular Medicine, University of Gothenburg-Sahlgrenska Academy, Gothenberg, Sweden

Heart rate influences outcomes in patients with heart failure (HF), with or without CAD. In the ***Systolic Heart failure treatment with the I_f inhibitor ivabradine Trial*** (SHIFT), ivabradine, a pure heart rate–slowing agent, substantially reduced rate of either cardiovascular death or first HF hospitalization irrespective of HFetiology. More recently we demonstrated reduction of all events, not only first events, throughout the trial (median 22.9 mos, max approx 3.5 yrs). In SHIFT, 6505 patients with moderate-to-severe HF and left ventricular systolic dysfunction, all hospitalized for HF during the preceding year, were randomized to ivabradine or placebo on background of guidelines-based HF therapy (including maximized beta-blockade). HF etiology was ischemic in 68%. After randomization, 1186 patients experienced further HF hospitalizations, 472 suffered at least two, and 218 suffered at least three. Patients with additional HF hospitalizations during study had more severe disease than those without. Ivabradine was associated with fewer total HF hospitalizations (902 events versus 1211 events with placebo; incidence rate ratio, 0.75, 95% CI, 0.65 to 0.87, p=0.0002) during follow-up. Ivabradine-treated patients also evidenced fewer second or third additional HF hospitalizations (HR, 0.66, 95% CI, 0.55 to 0.79, p<0.001 and HR, 0.71, 95% CI, 0.54 to 0.93, p=0.012, respectively). Ivabradine also reduced cardiovascular and all-cause hospitalizations throughout the duration of the study. Thus, treatment with ivabradine, on a background of guideline recommended HF therapy, is associated with a substantial reduction in the likelihood of recurrent hospitalizations for worsening HF. This benefit has potentially important implications for quality of life and health care costs.

Conflict of interest

ACUTE MYOCARDIAL INFARCTION

EFFECT OF INTRACORONARY THROMBUS BURDEN ON MICROVACULAR DYSFUNCTION AFTER PRIMARY PCI; DEMONSTRATION OF WORSE OUTCOME WITH INDEX OF MICROCIRCULATORY RESISTANCE

B. Kim[1], H. Lee[1], J. Kim[1], C. Goh[1], K. Rhee[1], J. Chang[2], E. Chung[2], C.H.U.L. Kim[3], H. Choi[3]
[1]Cardiology, Sanggye Paik hospital, Seoul, Korea
[2]chest surgery, Sanggye Paik hospital, Seoul, Korea
[3]Cardiac rehabilitation, Sanggye Paik hospital, Seoul, Korea

INTRODUCTION:

Aspiration thrombectomy (AT) has been advocated for ST-segment-elevation myocardial infarction (STEMI) and known to improve myocardial dysfunction after percutaneous coronary intervention (PCI), but it is not evaluated how a large thrombus affects post procedural results. We aimed to quantify the intracoronary thrombus in STEMI and to correlate it with post-procedural myocardial perfusion.

METHODS:

In consecutive 73 STEMI patients who underwent primary PCI with aspiration thrombectomy, intracoronary thrombus burden was angiographically categorized as 2 groups; large thrombus burden (LTB), defined as ≥ 2 vessel diameter and small thrombus burden (STB). Main outcome measures were post-procedural TIMI flow, myocardial blush grade (MBG), and index of microcirculatory resistance (IMR) measured with a pressure sensor/thermistor-tipped guidewire.

RESULTS:

History of hypertension, diabetes and smoking status were not difference between groups. Door to balloon time and left ventricular ejection fraction were similar between two groups. Patients with high thrombus burden had higher peak CK-MB and peak TroponinI and worse baseline TIMI flow grade. Post procedural TIMI flows and MBG were similar between groups. IMR was higher in patients with larger thrombus burden. In correlation analysis, large thrombus burden was positively correlated with peak CKMB, peak TnI and IMR (r=0.3, 0.4, 0.34; p=0.006, <0.001, 0.009; respectively). In multivariate analysis, LTB was an independent predictor of unfavorable IMR (>32 mmHg·sec, OR: 1.1, 95% CI: 1.002-1.106, P = 0.04).

CONCLUSION:

Large thrombus burden was associated with poor postprocedural microvascular dysfunction even after aspiration thrombectomy.

No conflict of interest

BASIC RESEARCH AND MOLECULAR BIOLOGY

PROTECTIVE EFFECTS OF APELIN-12AND ITS STRUCTURAL ANALOGUES IN EXPERIMENTAL MYOCARDIAL ISCHEMIA-REPERFUSIONINJURY

V.S.,L.S.,I.S. O. Pisarenko[1]
[1]*Institute of Experimental Cardiology*
[2]*Institute of Clinical Cardiology, Russian Cardiology Research-and-Production Complex, Moscow, Russia*

Background. This study was designed to explore efficacy of the adipokineapelin-12 (A12) and itsstructural analogues [MeArg[1],NLe[10]]-A12 (I) and [MeArg[1],NLe[10]]-A12amide(II) as cardioprotective agents in ex vivo and invivo models of myocardial ischemia/reperfusion (I/R) injury. Effects ofthese peptides were examined in comparison with [d-Ala[12]]-A12 (III),a putative antagonist of APJ receptor.

Methods. Peptides A12, I, II and III were synthesized by theautomatic solid phase method using Fmoc technology and identified by [1]H-NMRspectroscopy and mass spectrometry. Isolated rat hearts were subjected to35-min global ischemia and 30-min reperfusion. Anaesthetized open-chest rats were subjected to 40-min LAD coronaryartery occlusion and 1-h coronary reperfusion.

Results. Infusion of A12, I or II before orafter ischemia increased recovery of cardiac function and energy metabolism ofisolated rat heart during reperfusion. These effects were combined with adecreased ROS formation and increased antioxidant capacity of reperfused heart.Coadministration of A12 and L-NAME aggravated metabolic and functional recoveryof isolated rat heart. Intravenous injection of A12, I or II afterregional ischemia in anesthetized rats decreased infarctsize (IS), improved preservation of myocardialhigh energy phosphates and reduced LDH and CK-MB activities in plasma at the end of reperfusion. Subsequentadministration of L-NAME and A12 or its analogues substantially increased ISand CK-MB and LDH activities in plasma compared with these peptides alone. Protectiveeffects of analogue III were poor in bothmodels.

Conclusions. The resultssubstantiate the use of apelin peptides as adjunctive therapy in the treatment of acute coronary syndrome.

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BASIC RESEARCH AND MOLECULAR BIOLOGY

ANGIOPOIETIN-2 PROMOTES INFLAMMATORY LYMPHANGIOGENESIS AND ITS EFFECT CAN BE BLOCKED BY THE SPECIFIC INHIBITOR L1-10

Z.-X. Yan[2], Z.-H. Jiang[1], N.-F. Liu[1]
[1]Lymphology Center, Department of Plastic and Reconstructive Surgery, Shanghai 9th People's Hospital, Shanghai Jiao Tong University, School of Medicine, Shanghai, China
[2]Department of Plastic Surgery, Affiliated Hospital of Jiangsu University, Zhengjiang, China

"**Aims** Angiopoietin-2 (Ang-2) is a ligand of the receptor tyrosine kinase Tie2. Ang-2 is involved in regulating embryonic lymphangiogenesis, but its role in postnatal pathological lymphangiogenesis, such as inflammation, is largely unknown. We therefore investigated whether Ang-2 regulates inflammatory lymphangiogenesis.

Methods and results Using a combination of imaging, molecular, and cellular approaches, we observed strong expression of Ang-2 on newly generated lymphatic vessels in sutured corneas of BALB/C mice. The expression of Ang-2 continued to increase for 2 weeks after suture. The content of Ang-2 was increased with the growth of lymphatic vessels in cornea models. In the mean time, the expression of tumour necrosis factor (TNF)-α was also increased, which reached peak before that of Ang-2 expression and declined on day 7 after suture. In vitro cellular study showed that TNF-α stimulates Ang-2 and Tie2 as well as ICAM expression on human lymphatic endothelial cells (LECs) and blood endothelial cells (BECs). Ang-2 alone did not affect the biological behaviour of LEC, while Ang-2 combined with TNF-α significantly promoted proliferation of LECs but not BECs. In mouse models, blocking of Ang-2 with L1-10, an Ang-2 specific inhibitor, significantly inhibited lymphangiogenesis but promoted angiogenesis.

Conclusion Ang-2 acts as a crucial regulator of inflammatory lymphangiogenesis. Ang-2 sensitises lymphatic vasculature to inflammatory stimuli and dominates lymphangiogenesis."

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BASIC RESEARCH AND MOLECULAR BIOLOGY

ACTIVATION OF VEGFR-2 IN ADVENTITIAL STEM CELLS TRIGGERS VASCULAR REMODELLING

C. Chang[1], C. Lin[1], C. Lin[1], J. Lehrer[1], G. Krampitz[1], F. Ikeno[1], Z. Ali[1], R. Wang[1], E. Ashley[1], M. Rabinovitch[1]
[1]Cardiology, Stanford University, Stanford, USA

Coronary artery obstruction is the leading cause of morbidity and mortality in the developed world. Obstructed arteries are opened by percutaneous coronary intervention (PCI) with angioplasty and stenting[1]. A major complication of PCI is re-narrowing (restenosis) of treated vessels, caused by adverse tissue remodelling with neointimal hyperplasia- a process characterized by the formation of a new intima layer (neointima) that protrudes into the lumen and obstructs blood flow[2]. Mechanisms that govern neointimal hyperplasia during vascular remodelling, however, are poorly understood. Here we show that Vegfr-2, the receptor 2 of vascular endothelial growth factor, is required in adventitial stem cells to control neointimal formation in arteries stressed with pressure overload or wounded by angioplasty and stenting. Mechanical stress of vascular injury activates Vegfr-2 in a subset of cells resident in the adventitial layer of arteries. These adventitial cells are slow cycling, label-retaining cells in the arterial wall and display features of tissue stem cells. Soon after injury, a pulse of Vegfr-2 signaling triggers those adventitial stem cells to differentiate into adventitial and neointimal cells, an event that initiates the restenosis process. Inhibition of such spatial and temporal Vegfr-2 actions in mice prohibits stem cell activation, adventitial expansion, and neointimal hyperplasia in injured arteries. Similarly, VEGFR-2 is activated in the adventitia of human arteries with neointimal hyperplasia, suggesting a role of VEGFR-2 in human arterial disease. Our studies thus demonstrate a new mechanism by which Vegfr-2 dynamically controls adventitial stem cells to remodel injured arteries.

No conflict of interest

BASIC RESEARCH AND MOLECULAR BIOLOGY

CONSTRUCION OF AN IN-VITRO HEART MODEL TO STUDY VALVULAR FUNCTION IN CT, MRT, AND ULTRASOUND

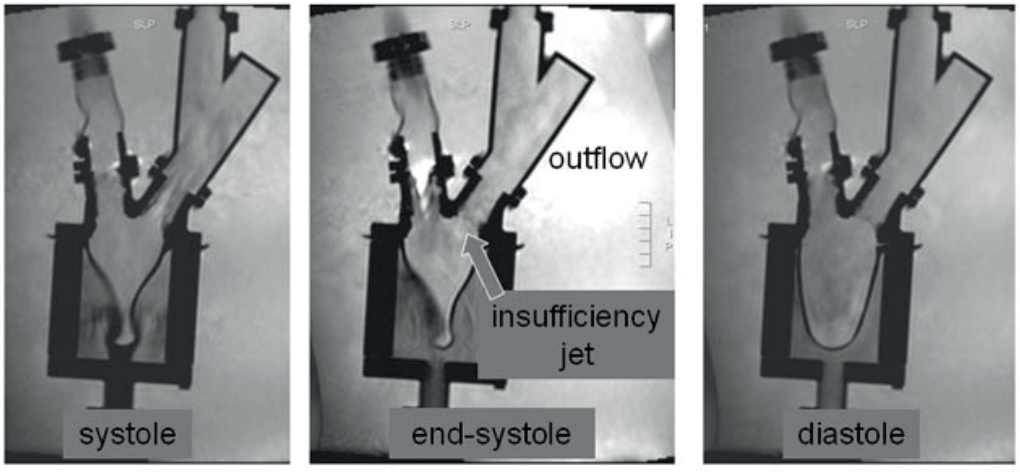
M. Funovics[1], R. Borny[1], W. Schima[2]
[1]Cardiovascular and Interventional Radiology, Medical University of Vienna, Vienna, Austria
[2]Biomedicl Research, Medical University of Vienna, Vienna, Austria

Background: Imaging modalities to quantify valvular function (insufficiency and stenosis) in vivo are rapidly evolving. A heart model to study the accuracy of these methods and to compare them to an accurately known gold standard suitable for CT, MRI, and ultrasound imaging with interchangeable human or artificial valves was constructed and characterized.

Methods: A polyurethane bag representing a single ventricle was placed in an acrylic chamber. The ventricle was filled by passive hydrostatic pressure from an elevated reservoir and periodically compressed by pumping fluid into the acrylic chamber outside of the ventricle. The ventricle and its inflow and outflow tubes were filled with diluted CT or MRI contrast agent. The flow was directed by artificial or human heart valves in the inflow and outflow. The afterload was controlled by a spring mechanism. The employed materials were metal-free except for the valves, which made the assembly fully CT and MRI compatible.

Results: The electronically controlled injection pump provided constant and adjustable stroke volume and frequency within physiologic range. The flow could be calculated from stroke volume and frequency, but also be measured by CT-Angiography after the injection of contrast agent into the ventricle, and by MR-Angiography TIme-of-Flight sequences. The correlation between the methods depended on flow conditions. After creating an insufficiency in the outflow valve by cutting a 5mm hole in one leaflet, the regurgitation volume could be both exactly determined by physically measuring stroke volume minus outflow, but also be assessed ba quantifying the regurgitation jet in MR-Angiography (Figure 1), and by measuring the difference between ejected ventricular volume and aortic flow in CT-Angiography.

Conclusion: The described model is suitable to assess the accuracies of CT, MRI, and potentially ultrasound in quantifying valvular insufficiencies in a realistic environment.



No conflict of interest

BASIC RESEARCH AND MOLECULAR BIOLOGY

SPECIFIC INTERFERENCE WITH NUCLEAR ERK1/2 SIGNALING PREVENTS PATHOLOGICAL CARDIAC HYPERTROPHY

C. Ruppert[1,2], K. Deiss[1], S. Herrmann[2,3], M. Vidal[1], M. Oezkur[2,4], A. Gorski[2,4], F. Weidemann[2,3], M.J. Lohse[1,2], K. Lorenz[1,2]
[1]Institute of Pharmacology and Toxicology, University of Würzburg, Würzburg, Germany
[2]Comprehensive Heart Failure Center, University Hospital Würzburg, Würzburg, Germany
[3]Department of Internal Medicine I, University Hospital Würzburg, Würzburg, Germany
[4]Department of Thoracic Cardiac and Thoracic Vascular Surgery, University Hospital Würzburg, Würzburg, Germany

Background: Extracellular signal-regulated kinases 1 and 2 (ERK1/2) are central mediators of cardiac hypertrophy and have been discussed as potential therapeutic targets. However, direct inhibition of ERK1/2 leads to exacerbated cardiomyocyte death and impaired heart function.

Objectives: Here, we investigated whether interference with the recently identified ERK-autophosphorylation at Thr188 (in ERK2) permits to impair ERK1/2-mediated cardiac hypertrophy without increasing cardiomyocyte death.

Methods and Results: To this end, we overexpressed in isolated cardiomyocytes and in transgenic mice an ERK2^{T188A}-mutant, which dominant-negatively inhibits ERK^{Thr188}-phosphorylation. ERK2^{T188A} efficiently attenuated cardiomyocyte hypertrophy in response to phenylephrine and to chronic pressure overload, but it affected neither anti-apoptotic ERK1/2-signaling nor overall physiological cardiac function. In contrast, ERK2^{T188A} did not interfere with *physiological* cardiac growth occurring with age or upon voluntary exercise. Interestingly, ERK2^{T188A} selectively attenuated the activation of the nuclear, hypertrophic ERK1/2 target (Elk1), without affecting the cytosolic, anti-apoptotic ERK1/2 targets (p90RSK and BIM). In patients with aortic valve stenosis, ERK^{Thr188}-phosphorylation was 8.5±1.3-fold increased in high-gradient cases (≥40mmHg gradient) with rapidly progressing hypertrophy, whereas in low-gradient, slowly progressing cases ERK^{Thr188}-phosphorylation was not significantly increased.

Conclusion: These data indicate that interference with ERK^{Thr188}-phosphorylation may selectively allow to address pathological cardiac hypertrophy without affecting physiological cardiac growth and cardiomyocyte survival. Therefore, inhibition of ERK^{Thr188}- phosphorylation might be a potential therapeutic strategy in the treatment of pathological cardiac hypertrophy.

No conflict of interest

BASIC RESEARCH AND MOLECULAR BIOLOGY

CARDIOPROTECTIVE EFFECT OF CORM2 AND DITPA DURING MYOCARDIAL ISCHAEMIA / REPERFUSION

N. Hadi[1], F.G. AL-amran[2], K. Hassan[1]
[1]Pharmacology and Therapeutics, kufa college of medicine, kufa, Iraq
[2]Cardiovascular surgery, kufa college of medicine, kufa, Iraq

Background: the process of restoring blood flow to ischemic myocardium, can induce myocardial reperfusion injury.Additionally, Prolonged periods of myocardial ischemia and reperfusion leads to an enhancement in apoptosis.

Objectives: This study was undertaken to assess the possible protective potential of CORM2(carbone monoxide releasing molecule) and 3,5-Diiodothyropropionic Acid (DITPA) against regional myocardial ischemia reperfusion injury and apoptosis during ischemia via interfering with inflammatory markers

Materials and Methods:1. sham group: rats underwent the same anesthetic and time of surgical procedure (but no ischemia)**2.control group:** rats underwent 30 min of regional myocardial ischemia(LAD ligation) followed by 3hr of reperfusion.**3.control vehicle (1):** rats pretreated with DITPA vehicle {0.1 N NaOH diluted with 0.9% saline (pH 9)} s.c.**4.control vehicle (2):** Rats underwent 30 min of LAD ligation and 3hr reperfusion and received 0.5%DMSO at reperfusion time.**5.DITPA treated group:** rats pretreated with DITPA (3.75 mg/kg)s.c before ligation 30min and another dose before reperfusion**6.CORM2 treated group:** rats treated with CORM2 (8mg/kg via tailvien) at reperfusion time.

Results: Compared with sham group, the levels of cardiac TNF-α, IL-1β, IL-6,ssDNA and plasma level of cardiac troponin I (cTnI) were increased in control group ($p<0.05$). Histologically all rats in control group showed significant ($p<0.05$) cardiac injury.Both CORM2 and DITPA significantly counteract the increase in the levels of cardiac TNF-α, IL-1β, IL-6,ssDNA and plasma level of (cTnI) ($p<0.05$). Morphologic analysis showed that both CORM2 and DITPA markedly improved ($p<0.05$) the severity of cardiac injury.

Conclusions: CORM2 and DITPA may ameliorate regional myocardial ischemia reperfusion injury and apoptosis during ischemia via interfering with inflammatory pathway.

No conflict of interest

BASIC RESEARCH AND MOLECULAR BIOLOGY

MUTATIONAL ANALYSIS OF THE PORTUGUESE COHORT WITH CLINICAL DIAGNOSIS OF FAMILIAL HYPERCHOLESTEROLEMIA

A.M. Medeiros[1,2], A.C. Alves[1,2], M. Bourbon[1,2],
P.F.H.S. on behalf of the investigators of the Portuguese FH Study
[1]Unidade de I&D, Grupo de Investigação Cardiovascular,
Departamento de Promoção da Saúde e Doenças Crónicas,
Instituto Nacional de Saúde Dr. Ricardo Jorge, Lisboa, Portugal
[2]Center for Biodiversity, Functional & Integrative Genomics (BioFIG), Universidade de Lisboa,
Faculdade de Ciências, Lisboa, Portugal

Background: Familial hypercholesterolemia (FH) is a common autosomal dominant disorder of lipid metabolism (1:500 frequency), caused by mutations in genes involved in cholesterol's clearance. FH patients present high levels of plasma cholesterol since birth, and if untreated, develop premature coronary heart disease (pCHD). The aim of the Portuguese FH Study is to promote the early identification and characterization of FH patients in order to decrease their cardiovascular risk by the implementation of correct and early counselling/treatment.

Methods: The clinical criteria of FH were adapted from the Simon Broome Register (UK) and genetic diagnosis was performed by the analysis of *LDLR* (18 fragments), *APOB* (2 fragments) and *PCSK9* (5 fragments), using PCR and Sanger sequencing techniques; MLPA was also performed in *LDLR*.

Results: A genetic defect was identified in 549 patients: 90 children, 143 adults (index-cases) and 81 children, 235 adults (relatives), representing 2.75% of the FH cases estimated to exist in Portugal. We also identified 3 true homozygous and 5 compounds heterozygous. FH patients presented 88 different mutations in *LDLR*, 30 being exclusive of the Portuguese population; 12 patients had a mutation in *APOB* and 3 in *PCSK9*. CHD was present in 92 adults with clinical diagnosis of FH (1st event: 46.6±11.9years), however, a genetic defect was only found in 34 of these cases.

Conclusion: The genetic diagnosis of FH provides an unequivocal diagnosis and early identification of relatives at risk, allowing the implementation of appropriate treatment in early ages to decrease avoidable deaths.

No conflict of interest

BASIC RESEARCH AND MOLECULAR BIOLOGY

LEVOSIMENDAN PROTECTION AGAINST KIDNEY ISCHEMIA/REPERFUSION INJURIES IN ANESTHETIZED PIGS.

E. Grossini[1], C. Molinari[1], P. Pollesello[1], G. Bellomo[1], G. Valente[1], D. Mary[1], P. Caimmi[1], G. Vacca[1]
[1]Translational Medicine, "A. Avogadro" University of Eastern Piedmont, Novara, Italy

Ischemia/reperfusion (I/R) injury is an important cause of acute renal failure because of oxidative, inflammatory, and apoptotic mechanisms. The aim of the present study was to examine any possible protective effects of levosimendan in an in vivo pig model of renal I/R injury. In 40 anesthetized pigs (eight groups of five pigs each), I/R was induced by clamping-reopening the left renal artery. During ischemia, in three groups of pigs, levosimendan and the multiorgan preservation solution Custodiol, alone or in combination with levosimendan, were infused in the renal artery. In two other groups of animals, levosimendan in combination with Custodiol was administered after the intrarenal nitric-oxide (NO) synthase blocker N(ω)-nitro-L-arginine methyl ester (L-NAME) or the mitochondrial ATP-sensitive K(+) channel (K(ATP) channel) inhibitor 5-hydroxydecanoate (5-HD). In the other animals, saline, L-NAME, or 5-HD were administered alone. Throughout the experiments, urinary N-acetyl-β-glucosaminidase (NAG) release was measured, and renal function was assessed. Moreover, renal biopsy samples were taken for the detection of apoptosis and tissue peroxidation. In pigs treated with levosimendan or the combination of levosimendan and Custodiol, NAG, peroxidation, and apoptotic markers were lower than in animals treated with Custodiol alone. In addition, renal function was better preserved, and cell survival and antioxidant systems were more activated. All beneficial effects were prevented by L-NAME and 5-HD. In conclusion, levosimendan alone or in combination with Custodiol exerted better protection against renal I/R injuries than Custodiol alone through antioxidant, antiapoptotic, and prosurvival actions depending on mitochondrial K(ATP) channels and NO-related mechanisms.

No conflict of interest

BASIC RESEARCH AND MOLECULAR BIOLOGY

STUDY OF THE SIGNALLING MECHANISMS OF CARDIOPROTECTION INDUCED BY CONSECUTIVE ACTIVATION OF PROTEIN KINASES A AND C

I. Khaliulin[1], A.P. Halestrap[2], M.S. Suleiman[1]
[1]School of Clinical Sciences, University of Bristol, Bristol, United Kingdom
[2]School of Biochemistry, University of Bristol, Bristol, United Kingdom

We have recently shown that consecutive activation of protein kinase A (PKA) and protein Kinase C (PKC) induced by perfusing rat heart with 200 nM isoprenaline (Isop) and 30 μM adenosine (Aden) confers marked protection against ischemia/reperfusion injury. In the present work, we studied the mechanisms of this cardioprotective effect using a clinically relevant (5nM) dose of Isop or a cAMP analogue 8-Br-cAMP-AM in combination with Aden. Langendorff-perfused rat hearts were subjected to 30 min global normothermic ischemia followed by 2 hrs reperfusion. During pre-ischemia, hearts were perfused consecutively with 5 nM Isop or 5 μM 8-Br-cAMP-AM and 30 μM Aden (Isop/Aden or cAMP/Aden), with the mitochondrial permeability transition pore (MPTP) inhibitor cyclosporine A (CsA), Erk inhibitor PD98059 (PD) or PI3K inhibitor wortmannin (Wort) in combination with Isop/Aden. Glycogen content, Erk, Akt and GSK3 phosphorylation were determined at the end of preischemia. Hexokinase II (HKII) expression in mitochondria was assessed in Isop treated hearts. A significant protection was seen in Isop/Aden, CsA and cAMP/Aden groups. However, the protection was not additive in the presence of CsA. Prior to ischemia, phosphorylation of Erk 1/2 and GSK3α were increased whilst glycogen content was depleted in the Isop/Aden group. But neither PD nor Wort reduced Isop/Aden-induced cardioprotective effect. Isop induced HKII translocation to mitochondrial membrane. Thus, clinically relevant concentration of isoprenaline or 8-Br-cAMP-AM in the consecutive treatment with adenosine protects the heart by triggering mechanisms which inhibit MPTP including glycogen depletion and HKII translocation to mitochondria but do not involve PI3K-GSK3 pathway.

No conflict of interest

INTERVENTIONAL CARDIOVASCULAR MEDICINE: A NEW SPECIALTY ON THE HORIZON?

PCI - Latest news on drug eluting stents (DES)

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INTERVENTIONAL CARDIOVASCULAR MEDICINE: A NEW SPECIALTY ON THE HORIZON?

Contemporary coronary revascularization using the Hybrid approach

A. Repossini[1]
[1]*Cardiac Surgery, University of Brescia Medical School, Brescia, Italy*

Conventional Coronary Artery By-pass (CABG) or multi-vessel PCI stenting alone have been considered the only chance to treat Multivessel Disease (MVD) to date, although nowadays a new hybrid strategy is rising as a safe and viable strategy for MVD patients. Hybrid Coronary Revascularization (HCR) combines Left Internal Mammary Artery (LIMA) on Left Anterior Descending Artery (LAD) Minimally Invasive Direct Coronary Artery By-pass (MIDCAB) and PCI stenting with new generation Drug Eluting Stent (DES) on other vessels. This technique should be considered a valid alternative to achieve an anatomically and/or functionally complete revascularization. HCR, avoiding cardiopulmonary by-pass (CPB) and median sternotomy, reduces the invasiveness compared to conventional on/off-pump surgical approach, achieving an arterial revascularization through a 5cm left anterior thoracotomy with the advantages of the LIMA-LAD by-pass on DES in terms of graft patency and repeated revascularization. Hybrid approach has shorter in hospital stay and lower post-operative comorbidities (bleeding, acute kidney failure, pleural-pericardial effusion), mostly in high risk patients for conventional CABG. Up to date HCR hasn't been widely adopted in clinical practice, lacking randomized trials and clinical guidelines. Although conventional CABG should be still considered the gold-standard treatment for complex MVD lesions, according to five–year SYNTAX Trial results, further experiences on HCR are needed to provide clear indications and to facilitate a widespread adoption of this technique, that can be considered the future for coronary revascularization, not only in high risk patients or patients with LAD residual ostial lesion after primary PCI stenting on other vessels.

No conflict of interest

ABSTRACT WITHDRAWN

TAVI and PCI: To do or not to do

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INTERVENTIONAL CARDIOVASCULAR MEDICINE: A NEW SPECIALTY ON THE HORIZON?

Tips and tricks in TAVI

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INTERVENTIONAL CARDIOVASCULAR MEDICINE: A NEW SPECIALTY ON THE HORIZON?

How to set up an interventional medicine practice

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INTERVENTIONAL CARDIOVASCULAR MEDICINE: A NEW SPECIALTY ON THE HORIZON?

Treating Resistant Hypertension with Renal Denervation

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EPIDEMIOLOGY AND PREVENTION

New approaches to risk assessment in cardiovascular disease

P. Greenland[1]
[1]*Preventive Medicine, Northwestern University, Chicago Illinois, USA*

Standard cardiovascular risk assessments involve either single risk markers) or the use of logistic equations that utilize multiple measures to estimate "global" cardiovascular risk. Commonly used global risk scores are the Framingham Risk Score (USA), SCORE (Europe), and QRISK2 (England and Wales). While global risk scores are often recommended in clinical practice guidelines, they are also criticized for being neither adequately sensitive nor specific. Therefore, the quest for more accurate risk assessment approaches continues as an active area of research. Circulating blood markers, such as C-reactive protein, BNP, or genetic polymorphisms have been widely studied. Imaging tests such as carotid IMT and coronary artery calcium are also well-studied for risk assessment. Additional newer tests, such as metabolomics-based profiles, are emerging as new areas of research. Published evidence (net-reclassification index - NRI) suggests that coronary artery calcium score adds substantially to improved risk assessment while other measures of risk contribute little to traditional risk factors in scores such as the Framingham Risk Score (see table, Rotterdam Study and MESA Study). These data will be discussed as well as novel information emerging from metabolomics research.

Marker	NRI – versus traditional risk factors (Rotterdam) – entire population	NRI – versus Framingham Score (MESA)-Intermediate risk only
Coronary artery calcium score	0.193	0.659
N-terminal pro-BNP	0.076	-
Fibrinogen	0.029	-
Chronic Kidney Disease	0.027	-
C-reactive protein	0.020	0.079
Carotid intima-media thickness	0.016	0.102
Leukocyte Count	0.015	-
Uric Acid	0.008	-
Peripheral Artery Disease (ABI)	0.006	0.036
Brachial Flow-mediated dilation	-	0.024
Family History	-	0.160
Pulse Wave Velocity	0.000	-

No conflict of interest

EPIDEMIOLOGY AND PREVENTION

The current scientific status of alcohol and coronary artery disease

The current scientific status of alcohol and coronary artery disease

Ellison RC

Boston University School of Medicine, Boston, MA, USA

For more than four decades, epidemiologic studies have consistently shown that the risk of developing coronary artery disease (CAD) is significantly lower among light-to-moderate drinkers than it is for non-drinkers, including lifetime abstainers. Reports from prospective, cohort studies in the past few years have continued to confirm such a relation.

During the past few decades, a huge number of basic scientific experiments have been carried out attempting to discover the underlying biologic mechanisms that may underlie an inverse relation between alcohol and CAD. Confirmation of earlier results as well as new mechanisms have been shown for lipids, including higher HDL cholesterol, and a tendency for lower LDL and LP(a). Many studies have shown lower levels of inflammatory markers, and improved endothelial function among moderate drinkers. A number of metabolic factors have been identified, and moderate drinkers have consistently been found to have about 30% lower risk of developing diabetes mellitus. Similar beneficial effects have been shown for factors leading to the metabolic syndrome.

The focus of this presentation will be on epidemiologic and basic scientific data that have been published within the past two years. Such data have confirmed what has been shown for many years, and have especially helped identify the mechanisms of such an effect. The conclusion is that, in 2013, we have very strong scientific evidence that regular, moderate alcohol consumption is associated with less CAD.

Conflict of interest

EPIDEMIOLOGY AND PREVENTION

Healthy ageing and the role of cardiovascular prevention

U. Keil[1]
[1]*University of Muenster, Institue of Epidemiology and Social Medicine, Muenster, Germany*

Healthy Aging and the Role of Cardiovascular Prevention
U. Keil
University of Muenster, Germany

Since 1840 life expectancy (LE) in the record holding countries has increased by 2,5 years per decade in women (slightly less in men). In 1840 Swedish women held the LE record with 45 years, while in 2010 Japanese women reached a LE of more than 86 years.

In Germany LE from 1962-2008 increased by 10,3 years in men and by 9,5 years in women, with major gains in the age groups 65+ in both men (+3,9 years) and women (+4,7 years). The decline in CVD mortality contributed to LE by 3,7 and 3,9 years in men and women, respectively.

In 1990 the gap in LE between East and West Germany was 3 years for men and 2,6 years for women, today the differences are negligable. Improvements in social conditions are responsible for closing this gap.

The WHO MONICA project showed that 2/3 of the decline in CHD mortality was due to a decline in event rate and 1/3 to a decline in case fatality.(2/3 prevention, 1/3 improvements in acute coronary care). The decline in CVD incidence means that CVD events have been shifted to higher age groups, producing declining age specific incidence rates and thus gaining healthy life years.

Stroke, CHD and Type 2 diabetes can be prevented through life-style modifications by 70%, 80% and 90% respectively, mainly by consuming a mediterranean diet, engaging in light to moderate physical activity, refraining from smoking and consuming only small amounts of alcohol.

No conflict of interest

EPIDEMIOLOGY AND PREVENTION

Novel lipid-lowering therapies and cardiovascular risk management

M. Rizzo[1]
[1]*Biomedical Department of Internal Medicine and Medical Specialties, University of Palermo and Euro-Mediterranean Institute of Science and Technology, Palermo, Italy*

In the last few years most of the international scientific guidelines as well as several expert panels have confirmed that low-density lipoproteins (LDL)-cholesterol represents the primary or even the only target of therapy. Yet, increasing evidence suggests to abandon the paradigm of treating dyslipidemic patients to LDL-cholesterol targets only, moving away from a target-based approach to a more tailored treatment approach. In this context, atherogenic dyslipidemia and its associated risk would become the main target of tailored therapy. Atherogenic dyslipidemia is typically characterized by elevations in LDL-C and triglyceride levels, often accompanied by decreased high-density lipoprotein cholesterol (HDL-C) concentrations and increased levels of small, dense LDL. Indeed, most studies suggest that measuring LDL particle size, small, dense LDL cholesterol content, and LDL particle number provides additional assessment of cardiovascular risk risk. There are a number of novel lipid-lowering drugs that may play a significant role in atherogenic dyslipidemia, and increasing data are available from the drugs inhibiting microsomal transfer protein (MTP) and proprotein convertase subtilisin/kexin 9 (PCSK9).

No conflict of interest

EPIDEMIOLOGY AND PREVENTION

Residual risk: an approach to understand and management in diabetic patients

J.M. Núñez-Cortés[1]
[1]*Internal medicine, School of Medicine, Madrid, Spain*

Residual Risk: an approach to understand and management in diabetic patients

Guidelines emphasize the relevance of considering all factors that contribute to vascular risk. For this reason, dyslipidemia was not defined only by LDL cholesterol. Atherogenic dyslipidemia, characterized by elevated trilglycerides levels and low HDL syndrome, often with elevated non-HDL cholesterol, elevated apoB, and LDL small and dense particles play an important role in the burden of cardiovascular diseases and is prevalent in patients with a metabolic cluster of cardiovascular risk factors: type 2 diabetes, metabolic syndrome, visceral obesity.In the major trials with statins as therapeutic lipid-lowering drugs, the presence of atherogenic dyslipidemia contribute in a significant manner to Residual Cardiovascular Risk. Patients with low HDL cholesterol and elevated triglycerides shown a significative increase of major coronary events in relation with those patients with isolated elevated LDL cholesterol. So, statin therapy incompletely addresses vascular risk attributable to elevated triglycerides and low HDL cholesterol. This is a common feature in different trials at “standard” or intensive statin treatment and other lipid modifying therapies are usually needed for the treatment of higher triglycerides concentrations and low HDL cholesterol. Current guidelines recommend the addition of a fibrate, niacin, or omega-3 fatty acids in patients with atherogenic dyslipidemia. Clinical data from large prospective studies show that fibrate treatment offers improved cardiovascular risk reduction in patients with atherogenic dyslipidemia. Based on this feature, the combination of a fibrate and statin would be a logical approach to improving achievement of lipid targets in statin-treated patients with residual atherogenic dyslipidemia.

No conflict of interest

EPIDEMIOLOGY AND PREVENTION

Understanding the mechanisms of diabetic cardiomyopathy and its counter-regulation

R. Ritchie[1]
[1]*Baker IDI Heart and Diabetes Institute, Melbourne, Australia*

Cardiovascular disease is the primary cause of morbidity and mortality amongst the diabetic population. Both experimental and clinical evidence suggest that diabetic subjects are predisposed to a distinct cardiomyopathy, independent of concomitant macro- and microvascular disorders. 'Diabetic cardiomyopathy' is characterized by early impairments in left ventricular (LV) diastolic function, accompanied by the development of cardiomyocyte hypertrophy, myocardial fibrosis and cardiomyocyte apoptosis. The pathophysiology underlying diabetes-induced cardiac damage is complex and multifactorial, with elevated oxidative stress a key contributor, in addition to a number of other molecular disturbances that are present in the diabetic heart, which also affect the development of diabetes-induced impairments in myocardial function and structure. Contributions from increased reactive oxygen species production and reduced antioxidant defenses to diabetic cardiomyopathy, together with modulation of novel protein signaling pathways and post-translational modifications, to the progression of diabetic heart disease may be differentially regulated by conventional and novel therapeutic approaches for the treatment of LV dysfunction in diabetic patients. Targeting redox stress and protective protein signaling pathways may represent a future strategy for combating the ever-increasing incidence of heart failure in the diabetic population.

No conflict of interest

EPIDEMIOLOGY AND PREVENTION

WOMEN WITH EARLY MENOPAUSE ARE AT HIGHER RISK OF ANGINA AFTER MYOCARDIAL INFARCTION

S. Parashar[1], K.J. Reid[2], J.A. Spertus[2], L.J. Shaw[1], V. Vaccarino[3]
[1]Department of Medicine, Emory University, Atlanta, USA
[2]Department of Medicine, Mid America Heart Institute, Kansas City, USA
[3]Department of Epidemiology Rollins School of Public Health, Emory University, Atlanta, USA

Objective: In population studies, younger age at menopause (AAM) predicts coronary heart disease. It is unknown whether early menopause predicts angina after myocardial infarction (MI). We examined whether younger AAM increases risk of angina after an AMI.

Design: In a prospective longitudinal multicenter MI registry (PREMIER), 493 post-menopausal women were enrolled (mean age 65.4 ± 11.3 years and mean AAM 45.2 (± 7.8) years) We categorized AAM into ≤40 years, 41-49 years and ≥50 years. In multivariable analysis, we examined whether AAM predicted 1-year post-MI angina and severity of angina after adjusting for angina prior to MI, demographics, comorbidities, MI severity and quality of care (QOC).

Results: Women with early AAM (≤40 years; N=132, 26.8%) were younger and more often smokers but were as likely to have comorbidities compared with women with AAM ≥50 years. Although there were no differences in pre-MI angina, MI severity, obstructive coronary disease and QOC based on AAM, the rate of 1-year angina was higher in women with AAM ≤40 (32.4%) than in women with AAM ≥50 (12.2%). In multivariable analysis, women with AAM ≤40 years had more than twice the risk of angina (RR 2.09; 95% CI 1.38, 3.17) and a higher severity of angina (OR 2.65; 95% CI 1.34, 5.22 for a higher severity level) compared with women with AAM ≥50.

Conclusions: Women with early age at menopause are at higher risk of angina after MI, independent of comorbidities, severity of MI and quality of CHD care. The use of a simple question regarding AAM may help in the identification of women who need closer follow-up, careful evaluation and intervention to improve their symptoms and quality of life after MI.

No conflict of interest

MOLECULAR BIOLOGY AND BASIC SIGNALING MECHANISMS

Cardiac remodeling via transcriptional modulation regulated by P-TEFb/CLP-1 activity

M.A.Q. Siddiqui[1], E. Mascareno[1], I. Rozenberg[1]
[1]Cell Biology, State University of New York Downstate Medical Center, Brooklyn NY, USA

The response of the heart hypertrophic stress is designed to normalize heart function that itself is responsive to activation of signal transduction pathway(s). The ability to link distress signals to genomic response is critical to understand how heart responds to stress. We have been investigating the molecular events involved in the hypertrophic network of adaptive linkage. A variety of stimuli, among them the renin angiotensin system (RAS), contribute to ventricular hypertrophy and fibrosis which are the major determinants of myocardial stiffness. It has been shown that the RAS signaling alters the fibroblast phenotype by promoting its differentiation into morphologically distinct pathological fibroblast which, in turn, potentiate collagen synthesis and its deposition into extracellular matrix. Interestingly, the atrial natriurretic peptide that is also induced during the left ventricular hypertrophy plays an anti-fibrotic and an anti-hypertrophic role by blocking the TGF-beta-induced nuclear localization of Smads. Despite this knowledge, it is not clear how the underlying event specific transcriptional changes are triggered and regulated. We have recently shown that Hexim1, aka CLP-1, regulate the activity of transcription elongation complex (P-TEFb) causing inhibition of CDK 9 mediated serine-2 phosphorylation in RNA polymerase II. The serine kinase activity of CDK 9 not only targets RNA polymerase II but also the conserved serine residue of the polylinker region in Smad3. We have evaluated the role of CLP-1 in vivo in the induction of left ventricular hypertrophy by using the angiotensin overexpressing transgenic mice harboring CLP-1 heterozygosity. We observed that the introduction of CLP-1 haplodeficiency in transgenic alpha-MHC-angiotensin mouse causes prominent changes in hypertrophic and fibrotic responses. Concomitantly this also is accompanied by activation of Smad3/Stat3 signaling. Thus, by acting at the nexus of signaling and transcriptional responses by activation of Smad/Stat/CLP-1 linked network controls the stress responsive mechanism and how it could be maintained in order to avert progression to the compensatory hypertrophy.

No conflict of interest

MOLECULAR BIOLOGY AND BASIC SIGNALING MECHANISMS

Ontogenetic aspect of cardiac protection

I. Ostadalova[1], Z. Charvatova[1], M. Milerova[1], Z. Drahota[1]
[1]Developmental cardiology, Institute of Physiology Academy of Sciences of the Czech Republic, Prague, Czech Republic

ONTOGENETIC ASPECTS OF CARDIAC PROTECTION

B. Ostadal, I. Ostadalova, Z.Charvatova, M. Milerova. Z. Drahota

Institute of Physiology, Academy of Sciences of the Czech Republic, Prague

The mechanisms of the high resistance of the immature heart to oxygen deprivation have not yet been clarified; still unclear is the role of mitochondria. Mitochondrial oxidative phosphorylation is not completely developed in rat heart at birth; cardiac maturation during the first postnatal week is characterized by increasing content and specific activity of cytochrome ***c*** oxidase and enhanced flux of adenine nucleotides across the inner mitochondrial membrane. Moreover, in newborn animals, a single population of mitochondria with high mitochondrial membrane potential was observed. Moreover, we have found significant ontogenetic differences in the role of mitochondrial pore (MPTP) in the I/R injury. Whereas the blockade of MPTP by sanglifehrin had a protective effect on I/R damage in the adult myocardium, it had no effect in the neonatal heart. Furthermore, the Ca-induced swelling of mitochondria from neonatal rats is significantly lower than that from adult animals. All these results support the hypothesis that cardiac mitochondria are involved in the regulation of cardiac tolerance to oxygen deprivation during ontogeny. The neonatal period seems to be critical also for the development of cardiac protection against ischemia: ischemic preconditioning or adaptation to chronic hypoxia failed to increase hypoxic tolerance to oxygen deprivation in the newborn rat heart; their protective effect develops only during the early postnatal period. It seems, therefore, that the decreasing tolerance to oxygen deprivation is counteracted by the development of endogenous protection. It may be concluded that the cardiac effect of ischemia is markedly influenced by the age of experimental animals.

No conflict of interest

MOLECULAR BIOLOGY AND BASIC SIGNALING MECHANISMS

Circulating cell populations for cardiovascular risk prediction

I. Hoefer[1]
[1]*Experimental Cardiology, UMC Utrecht, Utrecht, Netherlands*

Cardiovascular risk prediction still relies mostly on traditional risk factors or derivatives hereof like the Framingham Risk Score (FRS). While their predictive value on the population level is undeniable, their ability to predict individual remains low. Hence, numerous searches have been undertaken to identify new biomarkers. Most studies focused on easily available sources such as serum or plasma, but the majority of these markers have only marginal added value on top of traditional risk factors. Circulating blood cells are crucially involved in plaque development, progression and destabilization and can be retrieved from the peripheral circulation for biomarker assessment. This encompasses various –omics approaches (proteomics, genomics, transcriptomics including miRNA) and specific marker measurements by flow-cytometry that can further be combined with functional assays like cell activation tests. Moreover, such measurements can be performed in various blood cell fractions ranging from whole blood assays to tightly defined cell subfractions related to disease. This presentation will give an overview of known cell-based cardiovascular risk biomarkers, available platforms and our approaches integrating markers from different cell populations and different assays to provide novel markers for individual risk prediction.

No conflict of interest

MOLECULAR BIOLOGY AND BASIC SIGNALING MECHANISMS

Lipogems® - new device, method and human fat tissue product highly enriched in pericytes/mesenchymal stem cells ready for autologous use: Implications in cardiovascular regenerative medicine

C. Ventura[1], F. Bianchi[1], E. Olivi[1], M. Maioli[1], C. Tremolada[1], S. Rinaldi[2], C. Ricordi[3]
[1]Laboratory of Molecular Biology and Stem Cell Engineering, National Institute of Biostructures and Biosystems (NIBB), Bologna, Italy
[2]Department of Regenerative Medicine, Rinaldi Fontani Institute, Florence, Italy
[3]Cell Transplant Center and Diabetes Research Institute, University of Miami, Miami, USA

The human adipose tissue has been regarded as an attractive source for cell therapy, owing to the presence of cells with phenotypic/transcriptional profiles of human mesenchymal stem cells (hMSCs) and pericytes. Clinical translation of their multilineage potential is hampered by poor/negligible cell survival in cryopreserved lipoaspirates, the difficulty of ***ex vivo*** expansion, and complexity of the current Good Manufacturing Practice (cGMP) requirements for expanded cells. The availability of a minimally manipulated, hMSC/pericyte-containing fat product would have remarkable biomedical and clinical relevance.
We present an innovative method and device, named Lipogems, yielding a stromal vascular fraction (SVF) highly enriched in pericytes and hMSCs from human lipoaspirates, using mild mechanical forces in a completely closed system, avoiding enzymes, additives, and other manipulations. The non-expanded Lipogems product shows a remarkably preserved SVF, with slit-like capillaries wedged between adipocytes and stromal stalks with evident vascular lumina. Immunohistochemistry and flow cytometry showed that Lipogems-derived SVF (LD-SVF) harbored a significantly higher percentage of mature pericytes and hMSCs, and lower amount of hematopoietic elements, than enzymatically-digested lipoaspirates. Differently from lipoaspirate, the distinctive traits of fresh LD-SVF were not altered by cryopreservation. Noteworthy, the features of the fresh product were retained in the Lipogems product from human cadavers, even after cryopreservation. In culture, the Lipogems product yielded a highly homogeneous hMSC population, committable to osteogenic, chondrogenic and adipogenic lineages. Moreover, vasculogenic transcription in LD-hMSCs was enhanced at a significantly greater extent by a mixture of natural pro-vasculogenic molecules, as compared to hMSCs from enzymatically-digested lipoaspirates. Xenotransplantation of non-expanded human LD-SVF in rats with chronic hindlimb ischemia, completely rescued the ischemic limb, without immune rejection, in the absence of immunesupressant agents.

These findings suggest that Lipogems-harbored stem cells may be amenable for further optimization of their pluripotency. Within this context, we have recently shown that exposure to radio electric fields asymmetrically conveyed with an innovative device named Radio Electric Asymmetric Conveyer (REAC) was able to remarkably enhance the cardiovascular commitment in mouse embryonic stem cells (Cell Transplant 2012;21(6): 1225-33), and even afford a direct reprogramming in human dermal skin fibroblasts, leading to a high-throughput of commitment towards myocardial, neuronal, and skeletal muscle lineages (Cell Transplant, 2012 Oct 2. doi: 10.3727/096368912X657297).

Here, we show that REAC exposure of LD-hMSCs remarkably enhanced the transcription of prodynorphin, GATA4, Nkx2.5, VEGF, HGF, vWF, neurogenin1, and myoD, indicating the commitment towards cardiac, vascular, neuronal and skeletal muscle lineages, as inferred by the overexpression of a program of targeted marker proteins. REAC exposure also finely tuned the expression of pluripotency genes, including Nanog, Sox2, and Oct4. Noteworthy, the REAC-induced responses were fashioned at a significantly higher extent in Lipogems-derived than in enzymatically-dissociated hMSCs.

In conclusion, the interplay between radio electric asymmetrically conveyed fields and Lipogems-derived hMSCs appears to involve the generation of an ideal “milieau” to optimize a cardiovascular commitment within a multi- to pluri-potency cell switch reprogramming. Hopefully, these findings may pave the way to unprecedented cell therapy perspectives.

Conflict of interest

MOLECULAR BIOLOGY AND BASIC SIGNALING MECHANISMS

Role of adenosine receptor subtypes in coronary reactive hyperemia and its signaling

S. Mustafa[1]
[1]*Physiology and Pharmacology, School of Medicine, Morgantown, USA*

Adenosine mediates reactive hyperemia (RH), in part, by activating ATP-dependent K^+ (K_{ATP}) channels in coronary smooth muscle cells (CSMC). We investigated the roles of all four adenosine receptors (A_1, A_{2A}, A_{2B} and A_3) and their signaling in RH using A_1, A_{2A}, A_{2B} and A_3 KO and A_1/A_3 and A_{2A}/A_{2B} double KO (DKO) mice. We used Langendorff setup for these experiments. Flow debt for a 15 s occlusion was reduced in hearts from A_{2A} KO and $A_{2A}/_{2B}$ DKO but not in A_{2B} KO compared to WT mice. On the other hand, A_1 KO and A_1/A_3 DKO, but not A_3 KO showed a higher flow debt repayment than WT mice. Catalase reduced the repayment of flow debt in hearts from WT but had no effect on the already diminished repayment in hearts from A_{2A} KO and abolished the enhanced RH in A_1 KO mice. Glibenclamide (K_{ATP} channel blocker) reduced the flow debt in A_{2B} and abolished the enhanced RH in A_1 KO mice. The data suggest that A_1 but not A_3 AR counteracts the A_{2A} AR-mediated CF increase and deletion of A_1 AR results in an up-regulation of A_{2A} AR and/or removal of the negative modulatory effect of A_1 AR, thus leading to an enhanced A_{2A} AR-mediated H_2O_2 production. Finally, our data suggest that adenosine A_{2A} receptors are coupled to CSMC K_{ATP} channels in RH via the production of H_2O_2 as a signaling intermediate. These data can lead to better understanding of the role of adenosine receptor(s) in RH and ultimately in coronary artery disease

No conflict of interest

MOLECULAR BIOLOGY AND BASIC SIGNALING MECHANISMS

NRF2 as a cardiac protective gene

Q. Chen[1]
[1]*Department of Pharmacology, University of Arizona, Tucson, USA*

Nrf2 is a bZIP transcription factor regulating the expression of a cluster of antioxidant and detoxification genes containing the Antioxidant Response Element in the promoter. Recent genome-wide studies indicate that Nrf2 also controls the expression of several signaling molecules, transcription factors and growth factors. While Nrf2 has been heavily studied in the etiology of cancer and inflammation among various organ systems, little is known about the role of Nrf2 in the myocardium. We have found that knocking out Nrf2 gene in mice results in a reduced degree of cardiac protection by means of ischemic preconditioning, an increased infarction size in response to regional ischemic reperfusion, and accelerated development of heart failure. Interestingly, brief cycles of ischemic reperfusion induce Nrf2 protein by ***de novo*** protein translation, an event contributing to cardiac protection by preconditioning. With isolated cardiomyocytes, low to mild dose of oxidants cause ***de novo*** Nrf2 protein translation and therefore increased levels of Nrf2 protein. Using LC-MS/MS based proteomics, we have found that RNA binding protein La plays an important role in binding to Nrf2 mRNA, allowing Nrf2 mRNA being selectively translated into protein under oxidative stress. In addition, Nrf2 mRNA forms G-quadruplex in the 5' Untranslated Region (5'UTR). Such 3-D structure recruits a unique protein to mediate Nrf2 protein translation in cells responding to oxidative stress. Our works point out a novel mechanism of cardiac protection by ***de novo*** Nrf2 protein translation involving interactions of RNA binding proteins with 5'UTR of Nrf2 mRNA in cardiomyocytes.

No conflict of interest

MOLECULAR BIOLOGY AND BASIC SIGNALING MECHANISMS

ROLES OF HTRA1 IN NON-HYPERTENSIVE ARTERIOSCLEROSIS OF SMALL VESSELS

M. Ikawati[1], A.P. Hadi[1], C. Oka[1], M. Kawaichi[1]
[1]Division of Gene Function in Animals, Nara Institute of Science and Technology (NAIST), Nara, Japan

HtrA, a family of serine proteases, is highly conserved in various species from bacteria, plants to humans. HtrA1, one of four family members in mammals, is expressed in skeletal elements, blood vessels, the eye, and the placenta during pre- and post-natal stages. HtrA1 digests various extracellular matrix proteins and inhibits transforming growth factor (TGF)-β signaling in a proteolytic activity dependent manner.

Loss of function mutations of human ***HtrA1*** causes a non-hypertensive ischemic cerebral small-vessel disease called CARASIL (cerebral autosomal recessive arteriopathy with subcortical infarcts and leukoencelopathy) which accompanies alopecia, spondylosis, and dementia in early adulthood. CARASIL is histopathologically characterized by severe arteriosclerosis accompanying intimal proliferation, splitting of the internal elastic lamina, thinning of media and adventitia, loss of smooth muscle cells, and alteration in arterial extracellular matrix. Enhanced TGF-β signaling is also observed in the arterial wall.

We generated HtrA1 knock-out mice to analyze the function of HtrA1 in CARASIL. The knock-out mice do not show abnormalities in brain arteries even 52 weeks after birth. In contrast, the aorta of knock-out mice of 37 and 52 week old showed markedly decreased medial smooth muscle cells. Enhancement of TGF-β signaling as indicated by the increase in phosporylated-SMAD2 is observed in the aortic wall. Our result indicates that HtrA1 knock-out mice can serve as the model of human CARASIL or other arteriosclerotic diseases, and the pathogenesis of CARASIL depends not on the tissues but on the size and structure of the vessel.

No conflict of interest

MOLECULAR BIOLOGY AND BASIC SIGNALING MECHANISMS

CARDIAC LINEAGE PROTEIN (CLP-1), AKA HEXIM-1, CONTROLS SATELLITE CELL EXPANSION AND SKELETAL MUSCLE CELL REGENERATION

M.A.Q. Siddiqui[1], *P. Hong*[1]
[1]*Cell Biology, State University of New York Downstate Medical Center, Brooklyn NY, USA*

An attribute of skeletal muscle, distinct from cardiac muscle, is the native capacity of skeletal muscle cells to undergo regeneration after physical injuries and in dystrophic diseases. Therefore, the understanding of the skeletal muscle cell regeneration process is likely to provide valuable insights into the design of therapeutic intervention of cardiac cell regeneration. We, among others, have established that HEXIM1 (aka CLP-1), an inhibitory component of the positive transcription complex P-TEFb, regulates the transcriptional elongation of Pol-II genes via its association with and dissociation from P-TEFb. We have also shown that HEXIM1 regulates the process of skeletal myoblast differentiation and cardiac myocyte hypertrophic growth in culture. In this study, we have used a skeletal muscle acute injury model of mice to demonstrate that HEXIM1 plays a pivotal role in regulation of cell regeneration. HEXIM1 haplo-deficient muscle exhibit greater mass and enhanced contractile function compared to wild type muscle after injury.

The enhanced function was attributable to rapid proliferation of muscle stem cells, the satellite cells. Transplanted HEXIM1 haplo-deficient satellite cells expanded and improved muscle regeneration more effectively than the wild type satellite cells. Conversely, HEXIM1 over-expression restrained satellite cell proliferation and impeded its regeneration. Mechanistically, signal-induced dissociation of HEXIM1 from P-TEFb and its subsequent activation is the hallmark of satellite cell proliferation and inhibition of myogenic differentiation, whereas blockade of P-TEFb activation reduced satellite cell proliferation both in vivo and in vitro. These data thus offer the potential of HEXIM1 as a therapeutic target for degenerative muscular disease.

No conflict of interest

RISK FACTORS AND DIABETES

PREDICTORS OF MORTALITY, MYOCARDIAL INFARCTION AND STROKE AMONG BARI 2D PATIENTS WITH TYPE 2 DIABETES AND STABLE ISCHEMIC HEART DISEASE

M. Brooks[1], M. Singh[2], R.M. Hardison[1], B.R. Chaitman[3]
[1]Epidemiology, University of Pittsburgh, Pittsburgh, USA
[2]Cardiology, Mayo Clinic, Rochester, USA
[3]Cardiology, Saint Louis University Health Sciences Center, St. Louis, USA

Background: Patients with both type 2 diabetes and stable ischemic heart disease have a high risk of death and death, myocardial infarction and stroke (D/MI/S). We sought to develop risk scores for these outcomes from the BARI 2D trial data.
Methods: Using a 2x2 factorial design, 2368 BARI 2D patients with type 2 diabetes and angiographically documented coronary artery disease were randomized to prompt revascularization with medical therapy versus medical therapy alone and to one of two glycemic control strategies. Patients were actively treated and followed for an average of 5.4 years. Multivariable Cox proportional hazards regression models were created, and Harrell c-statistics were used to evaluate model discrimination.
Results: At five years, the cumulative risk of mortality was 11.9% and the risk of D/MI/S was 23.5%. Older age, history of CHF, low ejection fraction, history of COPD, low ankle brachial index, non-compressible arteries, high creatinine, albuminuria, number of diseased coronary vessels (≥50% stenosis), C-reactive protein (CRP) and D-dimer were independently associated with mortality. Many of the same factors were predictive of D/MI/S along with a history of TIA/stroke and ST depression on the baseline ECG. C-statistics for the multivariable risk models were c=0.744 for mortality and c=0.676 for D/MI/S indicating very good and good discrimination respectively.
Conclusion: Risk of mortality and major cardiovascular outcomes in this large cohort of patients with diabetes and stable ischemic heart disease was best predicted by combination of factors including clinical history, angiographic and ECG variables, the presence of diabetes complications, and biochemical markers.

No conflict of interest

RISK FACTORS AND DIABETES

CHILDHOOD DETERMINANTS OF ADULT IDEAL CARDIOVASCULAR HEALTH

T.T. Laitinen[1], K. Pahkala[2], A. Venn[3], J.G. Woo[4], M. Oikonen[1], T. Dwyer[5], V. Mikkilä[6], N. Hutri-Kähönen[7], K.J. Smith[3], S.L. Gall[3], J.A. Morrison[8], J.S.A. Viikari[9], O.T. Raitakari[10], C.G. Magnussen[1], M. Juonala[9]
[1]The Research Centre of Applied and Preventive Cardiovascular Medicine, University of Turku, Turku, Finland [2]The Research Centre of Applied and Preventive Cardiovascular Medicine and Paavo Nurmi Centre Sports & Exercise Medicine Unit, University of Turku, Turku, Finland
[3]Menzies Research Institute Tasmania, University of Tasmania, Hobart, Australia
[4]The Heart Institute and Division of Biostatistics and Epidemiology Department of Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati OH, USA
[5]Murdoch Childrens Research Institute, The Royal Children's Hospital, Melbourne, Australia
[6]Department of Food and Environmental Sciences, University of Helsinki, Helsinki, Finland
[7]Department of Pediatrics, University of Tampere and Tampere University Hospital, Tampere, Finland
[8]The Heart Institute Department of Pediatrics, Cincinnati Children's Hospital Medical Center, Cincinnati OH, USA [9]The Research Centre of Applied and Preventive Cardiovascular Medicine and Department of Medicine, University of Turku and Turku University Hospital, Turku, Finland
[10]The Research Centre of Applied and Preventive Cardiovascular Medicine and Department of Clinical Physiology and Nuclear Medicine, University of Turku and Turku University Hospital, Turku, Finland

Background

The American Heart Association recently defined ideal cardiovascular health by the simultaneous presence of seven health behaviors and factors. The concept is associated with cardiovascular disease incidence, and cardiovascular disease and all-cause mortality. To effectively promote ideal cardiovascular health already early in life, childhood factors predicting future ideal cardiovascular health should be investigated. Our aim was thus to comprehensively explore childhood determinants of adult ideal cardiovascular health in population based cohorts from three continents.

Methods

The sample comprised a total of 4409 participants aged 3-19 years at baseline from the Cardiovascular Risk in Young Finns Study (YFS; N=1883) from Finland, Childhood Determinants of Adult Health Study (CDAH; N=1803) from Australia and Princeton Follow-up Study (PFS; N=723) from the United States. Participants were re-examined 19-31 years later when aged 30-48 years.

Results

In multivariable analyses, independent childhood predictors of adult ideal cardiovascular health were family socioeconomic status (P<0.01; direct association) and BMI (P<0.001; inverse association) in all cohorts. In addition, blood pressure (P=0.007), LDL-cholesterol (P<0.001) and parental smoking (P=0.006) in the YFS, and own smoking (P=0.001) in CDAH were inversely associated with future ideal cardiovascular health.

Conclusions

Among several lifestyle and clinical indicators studied, higher family socioeconomic status and non-smoking (parental/own) in childhood predict ideal cardiovascular health in adulthood. As atherosclerotic cardiovascular diseases are rooted in childhood, our findings suggest that special attention could be paid to children who are from low socioeconomic status families, and who smoke or whose parents smoke, to prevent cardiovascular disease morbidity and mortality.

No conflict of interest

RISK FACTORS AND DIABETES

CELLULAR ADHESION MOLECULES: EARLY INDICATORS OF SUBCLINICAL AND CLINICAL CARDIOVASCULAR DISEASE RISK IN A YOUNG ADULT POPULATION

M. Gross[1], S. Bielinski[2], J. Suarez-Lopez[3], A. Reiner[4], J. Carr[5], D. Duprez[6], A. Odegaard[3], C. Lewis[7], D. Jacobs[8]
[1]Laboratory of Medicine and Pathology, University of Minnesota, Minneapolis, USA
[2]Health Sciences Research, Mayo Clinic, Rochester, USA
[3]School of Public Health, University of Minnesota, Minneapolis, USA
[4]Epidemiology, University of Washington, Seattle, USA
[5]School of Medicine, Wake Forest University, Winston-Salem, USA
[6]School of Medicine, University of Minnesota, Minneapolis, USA
[7]School of Medicine, University of Alabama, Birmingham, USA
[8]Nutrition, University of Oslo, Oslo, Norway

Cellular adhesion molecules have an important role in the accumulation of circulating leukocytes at sites of injury, infection and/ inflammation, and have been associated with the development of atherosclerotic plaque in coronary artery disease. We have studied the prospective relationship between circulating CAMs and the risk of cardiovascular disease in a young adult human population (mean age=32). Circulating CAM molecules (ICAM-1, p-selectin, e-selectin and VCAM) were associated in a Cox proportional hazard analysis with incident cardiovascular disease, with the strongest association occurring for ICAM-1 (HR and (CLs) of 1.92 (0.91-4.04)). Combination of the 4 CAMs and their quartile levels in a rank sum analysis indicated an enhancement of the cardiovascular disease association (HR and (CL) of 2.16 (1.12-4.17)). This finding indicates cumulative effects with multiple CAMs. ICAM-1 also had a strong association with measures of subclinical atherosclerosis including coronary artery calcium (CAC), and stenosis and intima media thickness (IMT) of the carotid arteries. The analysis was performed in minimally- (age, race, sex, and clinic) and/or fully- adjusted (smoking, exercise, body mass index, waist, education, systolic and diastolic blood pressures, antihypertensive medication, plasma cholesterol, HDL-c, triglycerides, and cholesterol lowering medication) models. ICAM-1 was significantly associated with stenosis (OR per SD=1.23, CL=1.11-1.36, p=0.001) and progression of CAC from years over 5years (OR per SD=1.33, CL=1.20-1.46, p<0.001). ICAM-1 concentrations may be an early biomarker that indicates the presence of advanced plaque in coronary and carotid arteries, even in young adults with low atherosclerosis burden and decades prior to the development of clinical CVD.

No conflict of interest

RISK FACTORS AND DIABETES

GENETIC POLYMORPHISMS ASSOCIATED WITH THE DEVELOPMENT OF TYPE 2 DIABETES MELLITUS.

M. Mendonca[1], S. Gomes[1], A. Pereira[1], R. Rodrigues[1], A. Sousa[1], G. Guerra[1], S. Borges[1], M. Rodrigues[1], D. Pereira[1], R. Palma dos Reis[1]
[1]Unit Research, Funchal Central Hospital, Funchal, Portugal

Type 2 diabetes mellitus (T2DM) constitutes a worldwide health problem associated with strong cardiovascular risk. There are environmental factors that contribute for the development of this disease, such as obesity or sedentary life. However, individuals with normal weight can have T2DM and, on the other hand, many of the obese individuals will not develop diabetes, suggesting that it is compelling. the evaluation of other variables, such as genetic factors.

Objective: Our study aims to investigate genetic polymorphisms associated with the T2DM onset in a Portuguese population.

Methods: We performed a case-control study with 1938 Caucasians which 548 were diabetic type 2 patients (classified as diabetic according to the European Association for the Study of Diabetes) and 1390 were controls, with no significant difference in age. Blood samples for genetic analysis were collected, from both groups, in order to evaluate 18 genetic variants previously described as being associated to hypertension, obesity, diabetes or coronary disease as PON1 Q192R and PON1 L55M, KIF6 T/A, HNF4A C/G, FTO A/C, TAS2R50 A/G, PCSK9 G/A, GJA4 C/T, TCF7L2 C/T, ACE I/D, AGT M235T, AT1R A1166C, MTHFR C677T e MTHFR A1298C, 9P21 locus (rs1333049 G/C) and APOE (ε2,ε3,ε4). Data are presented by mean ± SD. Continuous variables are evaluated by Student t test and categorical variables by Chi Square tests. The power of the association was expressed by the Odds Ratio (OR) and 95% confidence intervals. Multivariate logistic regression is performed to determinate which polymorphic variants were significantly and independently associated with T2DM. A p-value less than 0.05 was considered statistically significant.

Results: The polymorphisms that showed association with T2DM, in the univariate analysis were: TCF7L2 TT (OR=1.69; p=0.0002) and AT1R CC (OR=1.58; p=0.021). After logistic regression, with all the genetic variants investigated and the environmental factors, only the TCF7L2 TT (OR=1.99; p<0.0001) remained in the equation showing to be significantly and independently associated with T2DM emergence.

Conclusions: This study suggests that there is in our population a genetic polymorphism that independently contributes to the development of T2DM. Since diabetes is associated with a very strong cardiovascular risk, the patients carrying this polymorphism should be approached with early preventive measures, in order to counteract their genetic tendency to develop diabetes.

No conflict of interest

RISK FACTORS AND DIABETES

TRENDS IN AGE-SPECIFIC CORONARY HEART DISEASE MORTALITY IN THE EUROPEAN UNION OVER THREE DECADES: 1980 TO 2009

M. Nichols[1], N. Townsend[2], P. Scarborough[2], M. Rayner[2]
[1]Population Health Strategic Research Centre Faculty of Health, Deakin University, Geelong, Australia
[2]British Heart Foundation Health Promotion Research Group Department of Public Health, University of Oxford, Oxford, United Kingdom

Background: It has been hypothesised that reductions in CHD mortality rates in recent years have occurred largely within older age groups, and that rates in younger groups may be plateauing or even increasing. The aim of this study was to examine sex-specific trends in CHD mortality between 1980 and 2009 in the European Union (EU) and compare trends between adult age groups.

Methods: Joinpoint analysis of sex-specific trends in age-standardised mortality rates. The number and location of significant joinpoints for each country by sex and age group was determined (maximum of 3) using a log-linear model, and the annual percentage change within each segment calculated.

Results: Fifteen countries showed evidence of a recent plateauing of trends in at least one age group for men, as did twelve countries for women. This did not, however, appear to be any more common in younger age groups compared to older adults. There was little evidence to support the hypothesis that mortality rates have recently begun to plateau in younger age groups in the EU as a whole, although such plateaus and even a small number of increases in CHD mortality in younger sub-populations were observed in a minority of countries.

Conclusions: There is limited evidence to support the hypothesis that CHD mortality rates in younger age groups in the member states of the EU have been more likely to plateau than in older age groups. There are, however substantial and persistent inequalities between countries.

No conflict of interest

RISK FACTORS AND DIABETES

EUROPEAN CARDIOVASCULAR DISEASE STATISTICS: THE EUROPEAN HEART HEALTH II (EUROHEART II) PROJECT

N. Townsend[1], M. Nichols[2], P. Scarborough[1], M. Rayner[1]
[1]Public Health, University of Oxford, Oxford, United Kingdom
[2]Faculty of Health, Deakin University, Geelong, Australia

Background: *European Cardiovascular Disease Statistics 2012,* part of the EuroHeart II project, is the most recent update in a series of comprehensive Europe-wide reports on the mortality, morbidity, treatment, risk factors and costs of cardiovascular disease (CVD) in Europe.

Methods: The report draws on international data sources that provide comparable data across the greatest number of European countries. The 53 member states of the WHO European region were included in the definition of Europe. In addition, a new cost of disease study was carried out to estimate the total costs (direct and indirect) of CVD in the EU.

Results: Every year, CVD causes over 4 million deaths in Europe (47% of all deaths), and 1.9 million in the EU (40%). There are important inequalities between countries in mortality, morbidity, and in many risk factors that indicate the possible extent of the future burden. CVD is estimated to cost the EU almost €196 billion per year, of which 54% is due to direct costs to the health care system. Comparable data on incidence and prevalence of CVD are very limited, as are high quality data on important contributing risk factors, particularly diet and obesity.

Conclusions: CVD remains the leading cause of death in Europe, and places a considerable burden on the health systems and economies of Europe. Further, the report highlights that there remain substantial gaps in the quality of data available to monitor and evaluate efforts to reduce CVD and CHD in Europe.

No conflict of interest

RISK FACTORS AND DIABETES

EFFECT OF FACTOR XIII POLYMORPHISMS ON THE RISK OF MYOCARDIAL INFARCTION

Z. Bereczky[1], Z.A. Mezei[1], L. Balogh[2], E. Katona[1], E. Balogh[2], I. Czuriga[2], I. Édes[2], L. Muszbek[3]
[1]Clinical Research Center, University of Debrecen Medical and Health Science Center, Debrecen, Hungary
[2]Institute of Cardiology, University of Debrecen Medical and Health Science Center, Debrecen, Hungary
[3]Clinical Research Center and Vascular Biology Thrombosis and Haemostasis Research Group of the Hungarian Academy of Sciences, University of Debrecen Medical and Health Science Center, Debrecen, Hungary

Elevated factor XIII (FXIII) levels were demonstrated to be associated with increased risk of myocardial infarction (MI) in females, but not in males. Moreover, in our population FXIII-A Val34Leu polymorphism was protective against MI in patients with elevated fibrinogen levels. The role of FXIII-B subunit His95Arg and IntronK (nt29756C>G) polymorphisms in cardiovascular diseases has not been investigated, yet. In this study the above-mentioned polymorphisms were determined in 882 consecutive patients admitted for coronary angiography and in 1000 individuals representing the general Hungarian population. The rare allele frequencies of the His95Arg and IntronK (nt29756C>G) polymorphisms in the population were 0.08 and 0.15, respectively, which are similar to the results for Caucasians available in the HapMap database. The allele frequencies in the clinical controls (without MI and no significant coronary stenosis, n=276) did not differ significantly from the respective values in the general population. Individuals carrying the rare allele of FXIII-B IntronK polymorphism had significantly ($p<0.0001$) lower FXIII activity (94±21% vs. 103±21%) and $FXIIIA_2B_2$ antigen (20.7±4.7 mg/L vs. 23.1±5.0 mg/L) levels compared to individuals homozygous for the frequent allele. FXIII-B IntronK polymorphism decreased the risk of MI by 60% in patients with elevated fibrinogen level (OR:0.37, 95% CI:0.17-0.84, $p=0.017$). Moreover, an interactive effect was demonstrated between FXIII-B IntronK and FXIII-A Val34Leu polymorphisms; OR for MI in the case of double carriers with elevated fibrinogen was 0.031 (95% CI:0.01-0.21, $p<0.0001$).

Our results confirm that the well-known effect of high fibrinogen level as a risk factor of MI is considerably modified by FXIII polymorphisms.

No conflict of interest

VASCULAR BIOLOGY AND ENDOTHELIAL FUNCTION

Mitochondrial dynamics and mitophagy in the diabetic endothelium

J.A. Vita[1]
[1]*Medicine/Cardiology, Boston University, Boston, USA*

There is growing recognition that the vascular endothelium plays a central role in the regulation of vascular homeostasis. Abnormalities of endothelium-dependent vasodilation are detectable at all stages of atherosclerosis. In addition to loss of the bioactivity of endothelium-derived nitric oxide, these conditions are also associated with abnormalities of many other aspects of “endothelial function” including control of thrombosis, inflammation, and intimal growth. Patients with type 2 diabetes mellitus, obesity, and the metabolic syndrome, have increased risk for cardiovascular disease, and such patients also display endothelial dysfunction. Recent studies suggest links between mitochondria dysfunction and endothelial dysfunction in patients with type 2 diabetes mellitus. In particular, endothelial cells show evidence of increased mitochondrial fission and impaired autophagy compared to cells from age-matched healthy control subjects. Interventions that reduce excess fission under diabetic conditions tend to restore endothelial function, while inhibiting autophagy in healthy cells has a detrimental effect. Overall, these studies suggest that altered mitochondrial dynamics and loss of mitochondrial quality control contribute to endothelial dysfunction in patients with diabetes mellitus. These findings may suggest new approaches for patient management.

No conflict of interest

VASCULAR BIOLOGY AND ENDOTHELIAL FUNCTION

EFFECT OF DPP4-INHIBITOR ON VASCULAR FUNCTION IN PATIENTS WITH ISCHEMIC HEART DISEASE

H. Adachi[1], *H. Kan*[1], *J. Tomono*[1]
[1]*Dep. of Cardiology, Gunma Prefectural Cardiovascular Center, Maebashi Gunma, Japan*

Background and Purpose: It is well documented that vascular function is attenuated in patients with diabetes mellitus, and vascular dysfunction is the first step of coronary arteriosclerosis. Therefore, treatment for diabetes mellitus is important to prevent heart disease, however, it is not well studied what kind of pharmaceutical agent is optimal. Recently, DPP4 inhibitor can be used and many favorable effects on glycemic control are reported. Hereby, we planned to investigate the effect of DPP4 inhibitor on vascular function in ischemic heart disease (IHD) patients with diabetes mellitus.
Method: Twenty-two IHD patients with mild diabetes mellitus were prescribed DPP4 inhibitor and assigned to Group D, and seventeen control patients without DPP4 inhibitor were to Group C. Flow mediated dilatation(FMD) and cardio-ankle vascular index(CAVI) were measured before administration and 6 months later.
Results: HbA1c improved from 6.7±0.5% to 6.1±0.5 ($p<0.01$) in Group D, 6.3±0.6 to 6.5±0.5 (n.s.) in Group C. FMD and CAVI improved in Group D from 3.8±1.5 to 4.4±1,7($P<0.05$), 9.3±0.9 to 8.9±0.8($P<0.05$), respectively, while they failed to improve in Group C (3.9±2.3 to 4.2±2.1, 9.2±0.9 to 9.3 ±1.1, respectively). Even if we compared Group D with patients who showed improvement of glycemic control in Group C, neither FMD nor CAVI had shown any improvement.
Conclusion: DPP4 inhibitor was revealed to improve vascular function regardless of glycemic control.

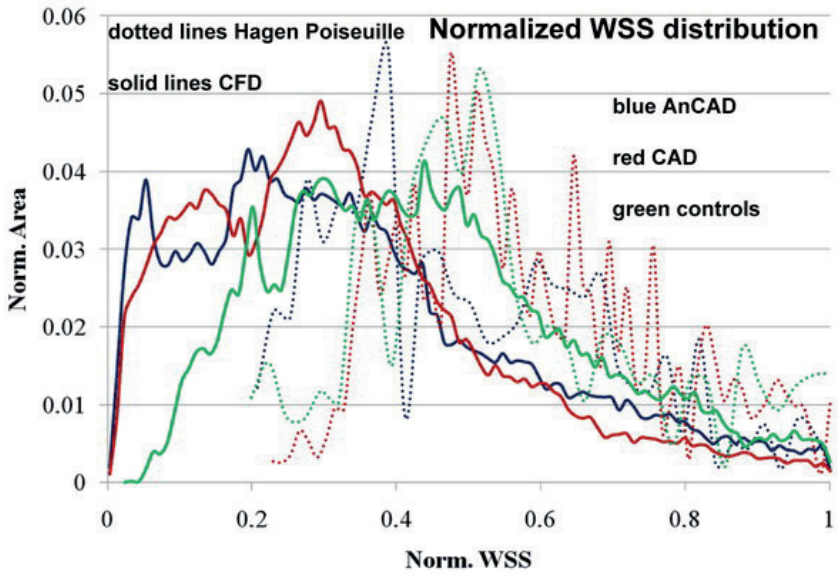
No conflict of interest

VASCULAR BIOLOGY AND ENDOTHELIAL FUNCTION

VALUE AND LIMITATIONS OF HAGEN-POISEUILLE'S LAW IN THE ESTIMATION OF CORONARY WALL SHEAR STRESS.

E. Wellnhofer[1], J. Osman[2], R. Mevert[2], U. Kertzscher[2], K. Affeld[2], L. Goubergrits[2]
[1]Internal Medicine/Cardiology, German Heart Center Berlin, Berlin, Germany
[2]Biofluidmechanics laboratory, Charité Universitätsmedizin Berlin, Berlin, Germany

Background: Hagen-Poiseuille's law (HP) is widely used to estimate wall shear stress (WSS, WSS_HP) in medicine. Only flow rate and local vessel diameter are needed as input data. This advantage is achieved at the cost of accuracy due to simplified assumptions concerning vessel shape. Calculation of WSS by numerical integration of the Navier-Stokes differential equations for incompressible fluids (CFD, WSS_CFD) in three-dimensional finite element vessel reconstructions is more accurate, but also more demanding and time-consuming.
Methods: Vascular trees from 17 right (RCA) and 15 left (LCA) coronary arteries stratified with respect to luminal remodeling (controls (C), aneurysmatic (AnCAD) and non-aneurysmatic coronary artery disease (CAD)) were reconstructed from biplane angiograms. Patient specific flow simulations were performed by CFD. Results for WSS_ CFD and WSS_HP were compared.
Results: Mean WSS_CFD was 2.6±2.6 Pa and WSS_HP was 2.4±2.6 Pa. The mean difference was 0.23 (-0.09-0.58) was not significant and correlation was 0.942. There were major differences in distribution particularly in the low WSS range (minimum (min) WSS (r=0.494), percent area <0.4 Pa (A_.4) (r=0.811)), however. Min WSS is over-estimated (p=0.01) and A_0.4 WSS is under-estimated (p=0.01) significantly by HP. The estimation of maximum (max) WSS can be improved (r=0.933; r=0.816 with max WSS_HP) by estimation from mean WSS_HP using a factor of 2 in RCA and 3 in LCA due to a strong trend of max WSS_CFD with mean WSS_CFD (different slopes in RCA/LCA).



Conclusion:
Estimation of WSS by Hagen Poiseuille's law performs well for mean and maximum values, but is a poor estimate in low WSS areas.

No conflict of interest

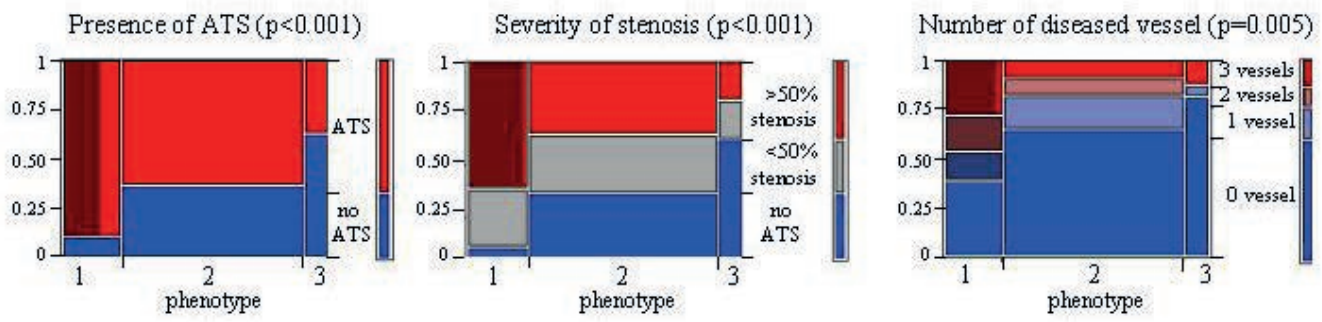
VASCULAR BIOLOGY AND ENDOTHELIAL FUNCTION

ADIPONECTIN AND CARDIOVASCULAR RISK PREDICTION: STRATIFICATION OF CHEST PAIN PATIENTS BY A CLUSTER ANALYSIS

C. Caselli[1], M. Coceani[1], T. Prescimone[1], M. Cabiati[1], A. Mazzarisi[1], M. Schlueter[1], S. Del Ry[1], F. Cocci[1], D. Giannessi[1], P. Marraccini[1]
[1]CNR, Institute of Clinical Physiology Pisa, Pisa, Italy

The new European guidelines on cardiovascular disease (CVD) prevention report the need to a better identification of population at high risk of CVD, the major cause of premature death in Europe.
With an unbiased statistical approach, we sought to identify clusters of patients with chest pain in order to better stratify their CVD risk.
We prospectively included 202 consecutive patients with chest pain (63% males, age 62±12 yr) undergone to CT coronary angiography (CTCA). Patients were classified using K-means cluster analysis of clinical, imaging and bio-humoral data, selected for their relevance to CVD.
The relevance of this classification was validated using presence of atherosclerosis (ATS) and significant stenosis (>50%) as assessed by CTCA.
The most relevant patient classification resulted in three phenotypes distinguished according to Framingham Risk Score (FRS) and high molecular weigth (HMW) adiponectin plasma levels: Phenotype 1 (n=39) included subjects at very high CVD risk (FRS 34.6±9.7%) and very low HMW adiponectin (1.6±1.3 mg/mL); Phenotype 2 (n=124) subjects with lower FRS (11.8±5.4%) and higher HMW (1.9±1.1); Phenotype 3 (n=16) the less severe patients (FRS 8.1±4.5%) with high levels of HMW (7.8±2.8).
Presence and severity of ATS (existence of significant stenosis and number of diseased vessels) were significantly identified trough these phenotypes (Figure).

By K-means cluster analysis, we identified three different CVD phenotypes allowing to stratify chest pain patients. Subjects within these phenotypes may required different diagnostic and therapeutic approach to improve their outcome.



Mosaic plot illustrating the results of the cluster analysis in 202 chest pain subjects.
Pathological conditions (presence of ATS, severity of stenosis and number of diseased vessels) are reported on vertical lines and are distinguished by different colours. Phenotypes are reported on orixontal lines. In each phatological condition, cluster analysis significantly stratified patients allowing their distribution in three groups: phenotyphe 1 group contained pathological subjects, while phenotyphe 3 group contained healthy subjects.

No conflict of interest

VASCULAR BIOLOGY AND ENDOTHELIAL FUNCTION

THE INFLUENCE OF HEMODYNAMIC FORCES AND INTERCELLULAR INTERACTIONS ON ENDOTHELIAL CELL MIGRATION

J.A. Brennan[1], E.J. Su[1], A. Babataheri[1], A.I. Barakat[1]
[1]Laboratoire d'Hydrodynamique de l'X, Ecole Polytechnique, Palaiseau, France

Endothelial cell (EC) migration plays a fundamental role in a number of vascular scenarios including angiogenesis, wound healing, and re-endothelialization of vascular grafts. Hemodynamic forces from blood flow are known to mechanically regulate the migration of ECs by applying shear stresses to their apical surfaces. Much research has shown that cell migration is correlated to the level of applied shear stress, yet little has been studied on the specific effects of shear rate in modulating cell mobility. It was the aim of this study to characterize the individual contribution of these two factors on subconfluent bovine aortic ECs under steady laminar flow. Shear stress and shear rate were independently controlled by adjusting the viscosity of the culture medium, and resulting cell velocities and overall net displacements were observed. We demonstrate that cell mobility is not only modulated by shear stress but is rather a result of a combination of hemodynamic factors. More specifically, shear stress tends to regulate cell velocity, whereas shear rate guides cell movement in the direction of flow. Implications for this research are vast, as the failure of the endothelium to adapt to flow can lead to atherosclerosis or abnormal vessel repair. To understand if these trends hold true in a more physiologically-relevant environment, we also performed flow experiments on EC-smooth muscle cell co-cultures and elucidated the interplay of these cell-cell interactions in regulating flow-induced EC migration. Taken together, these findings provide insight into the contributions of the mechanical environment on vascular function and dysfunction.

No conflict of interest

SURGICAL ASPECTS: NEW CHALLENGES IN CARDIAC SURGERY

Ischemic mitral regurgitation: best treated by intervention (Mitra-Clip) or surgery?

H. Reichenspurner[1], L. Conradi[1], H. Treede[1], B. Goldmann[2], E. Lubos[2], J. Schirmer[1], S. Baldus[3], P. Diemert[2], S. Blankenberg[2]
[1]Department of Cardiovascular Surgery, University Heart Center Hamburg, Hamburg, Germany
[2]Department of Cardiology, University Heart Center Hamburg, Hamburg, Germany
[3]Department of Cardiology, Heart Center Cologne, Cologne, Germany

Functional mitral regurgitation: Best treated by intervention (Mitra-Clip) or surgery?

Objectives

Corrective surgery for functional mitral regurgitation (MR) by restrictive annuloplasty has proven beneficial in that it improves New York Heart Association (NYHA) functional class and induces reverse left ventricular remodeling. However, proof of a survival benefit for these patients is still pending. Percutaneous techniques of mitral valve repair (MVR) have become a viable treatment alternative for selected high-risk patients with severe functional MR.

Methods

We retrospectively analyzed our prospective hospital database of patients with severe functional MR undergoing either surgical MVR or percutaneous treatment using the MitraClip device. Patient characteristics and 6-month clinical and effectiveness outcomes are reported.

Results

From March 2002 trough June 2010, 76 patients with functional MR underwent isolated surgical MVR while 95 patients were treated using the MitraClip device at our center. Patients undergoing MitraClip treatment were significantly older (mean 72.8±8.2 vs. 64.5±11.4 years, p<0.001), had a lower left ventricular ejection fraction (mean 36.2±12.5% vs. 42.1±16.2%, p=0.014), and were generally more high-risk, with a significantly higher mean logEuroSCORE I compared to surgical candidates (33.7±18.7 vs. 10.1±8.7%, p<0.001). Procedural success was 98.7% (75/76) for MVR and 95.8% (91/95) for MitraClip treatment (p=0.383). 30-day mortality was 4.2% (4/95) and 2.6% (2/76; p=0.557) and mean grade of residual MR was 1.4±0.8 and 0.2±0.4 (p<0.001) after MitraClip treatment and surgical MVR respectively. Six-months survival rates after adjustment for baseline differences were not significantly different in the respective groups (p=0.642).

Conclusions

In our experience, characteristics and risk factors of patients with severe functional MR undergoing surgery differ significantly from those considered for percutaneous therapy. Surgery was more effective compared to MitraClip in reducing MR. However, a large proportion of patients benefits from percutaneous intervention with sustained MR < 2+ and improvement in NYHA functional class at 6 months. Especially for elderly patients with reduced left ventricular function and relevant comorbidities, MitraClip therapy seems to be an adequate alternative to surgery. Assessment, treatment and postprocedural care of patients by an interdisciplinary team is of paramount importance for clinical success.

No conflict of interest

SURGICAL ASPECTS: NEW CHALLENGES IN CARDIAC SURGERY

Robotic mitral valve repair

A. Trento[1]
[1]*Division of Cardiothoracic Surgery, Cedars-Sinai Heart Institute, Los Angeles, USA*

Objective: To review our first 300 consecutive robotic mitral valve repairs (R-MVr) from June, 2005 to October 2012 comparing our previously reported initial 120 with the subsequent 180 procedures.
Methods: Our initial 120 R-MVr were compared to our recent 180 consecutive cases. All patients received an annuloplasty band and one or more of the following: leaflet resection, secondary chordal transposition and/or neochordal replacement and edge-to-edge repair.
Results: All 300 patients had preoperative severe mitral regurgitation (MR). There were no differences in preoperative characteristics between the initial and recent cohorts. The incidence of anterior and posterior leaflet prolapse was similar in both groups while Barlow syndrome was higher in group 2. There was 1 hospital mortality (none in the last 180). Eight patients required MV replacement via sternotomy (6/120, 2/180). One patient in each group had MV re-repair via right mini-thoracotomy and one in the first group required MV replacement during the original procedure. Two of the 180 patients had CVA, both recovered (none in last 120). Cross clamp times decreased from 116 to 91 minutes. Post-pump echocardiograms showed none/trace MR in 86.1% of the last 180 cases and mild MR in 11.1%. Follow-up echo from 1 month to more than 1 year showed none/trace MR in 70.7% and mild in 21.7%. Ten patients (6.0%) had moderated MR and 1 patient (0.6%) had severe.
Conclusions: Most complications occurred in the early experience using the first generation daVinci robot. The newer daVinci Si HD system has made R-MVr of all types of degenerative MV pathology reproducible.

No conflict of interest

SURGICAL ASPECTS: NEW CHALLENGES IN CARDIAC SURGERY

Ischemic cardiomyopathy: cardiac transplant or rotary blood pump?

S. Westaby[1]
[1]*Cardiothoracic Surgery, Oxford University Hospitals NHS Trust, Oxford, United Kingdom*

In Western countries prevalence of heart failure exceeds 5% in the over 60s. The majority comprises patients with ischaemic heart disease. In severe heart failure, 10% of the last year of life is spent in hospital with 59% dying after at least 3 re-admissions. At the ceiling of symptomatic relief through medical therapy only cardiac transplantation, mechanical circulatory support or palliative care remain. Rotary blood pumps (LVADs) are increasingly recognised as main stream therapy for severely symptomatic heart failure. Carefully targetted refinements in postoperative care have substantially reduced the adverse event burden. These improvements translate into better survival and quality of life in comparison with medical managment. Evidence based outcome data indicate that transplant and lifetime LVAD candidates are fundamentally different. Transplantation predominantly benefits UNOS Status I patients <55 years with low pulmonary vascular resistance, BMI <30 kg/m^2 without metabolic risk factors. In contrast LVADs can be deployed in patients of any age in the presence of elevated pulmonary vascular resistance and other factors which contraindicate transplantation. 3-4 year survival now rivals cardiac transplantation. Challenges remain in relation to neurological injury and right heart failure.

The debate is now rarely between cardiac transplant or lifetime LVAD. It should focus on the choice between pump versus palliative care for the thousands of patients of all age groups who are ineligible for transplantation. Comprehensive healthcare systems must consider contemporary evidence and provide the most symptomatic of heart failure patients with effective care. Cardiac resynchronisation therapy is no longer the ceiling for this.

Conflict of interest

SURGICAL ASPECTS: NEW CHALLENGES IN CARDIAC SURGERY

Surgical options and decision making in end-stage coronary artery disease

Document not received

SURGICAL ASPECTS: NEW CHALLENGES IN CARDIAC SURGERY

Heart transplantation in patients with aortic stenosis and left ventricular dysfunction

R. Kass[1]
[1]*Cardiothoracic Surgery, Cedars-Sinai Heart Institute, Los Angeles, USA*

Introduction. Decisions to perform aortic valve replacement (AVR) or heart transplantation (HTx) for aortic stenosis (AS) with severe left ventricular dysfunction is difficult and may be affected by prior myocardial infarction (MI) and coronary artery disease (CAD).

Methods. Patients who underwent AVR from 1988 to 2001 with left ventricular ejection fraction (LVEF) <30% and severe AS (aortic valve area [AVA] <1.0cm2; *n*=51) were assessed for operative mortality, late survival, and predictors of outcome, and compared with HTx. Subsequently, 131 patients with LVEF ≤35% who underwent AVR for critical AS (AVA <0.8cm2) were evaluated.

Results. In the first 51 patients, 3-year survival was 100% with no CAD, and 45%±10% with CAD (*P*<.05); 3-year survival was 88%±12% with no bypass, 73%±12% with one or two grafts, and 18%±11% with three grafts (*P*<.01). Survival with HTx was 78% at 3 years. In the subsequent analysis of 131 patients, 90-day survivors were followed for 4.6±3.5 years. Advanced age (*P*<.001) was the only predictor of long-term mortality. LVEF improved from 28.5%±5.2% before AVR to 45.4%±13.2% at 1-month postoperatively (*P*<.0001). New York Heart Association class III/IV decreased from 94.2% pre-AVR to 12.8% at 1 year (*P*<.0001). Predictors of LVEF recovery were no previous MI (*P* =.007) and higher AS gradient (*P* =.03).

Conclusions. In severe AS and LVEF ≤30% with no CAD or CAD requiring one or two bypass grafts, AVR has survival equal or exceeds HTx. Patients with CAD requiring more than two bypass grafts, survival is significantly reduced, and HTx can be considered.

No conflict of interest

SURGICAL ASPECTS: NEW CHALLENGES IN CARDIAC SURGERY

TOTAL ARTERIAL REVASCULARISATION: A SUITABLE TREATMENT OPTION IN ELDERLY PATIENTS LACKING VEIN GRAFTS

H. Khan[1], S. Chaubey[1], O. Wendler[1]
[1]Cardiothoracic, King's College London, London, United Kingdom

Objectives: Total arterial coronary artery bypass grafting (TACABG) is a surgical treatment option to improve long-term results in younger patients. However, less is known on its value in the treatment of elderly patients lacking adequate vein conduits. We report on our experience with TACABG in elderly patients.

Methods: Outcomes of patients undergoing isolated CABG by a single surgeon were analysed and three groups compared: TA-1: patients ≥70 underwent TACABG. TA-2: patients <70 underwent TACABG. VG: patients ≥70 underwent CABG using vein grafts. TACABG was performed using a maximum of two grafts and "T-grafts" if needed. Vein grafts were used in sequential technique as needed.

Results: TA-1 (n=53:male=81%,age 75years) had a significantly higher logistic EuroSCORE compared to TA-2 (n=218: male=83%,age 59years) (5.2±3.4 vs 2±1.7,p<0.001). TA-1 patients were also more likely to have peripheral vascular disease (p=0.002), respiratory disease (p=0.048), hypertension (p=0.02), or a previous neurovascular event (p=0.003). No significant differences between TA-1 and VG (n=91:male=78%,age 76years) were found. Number of coronary bypasses/patient (TA-1:n=3.4±1.0,TA-2:n=3.3±1.1,VG:n=3.8±0.9), bypass-times (TA-1:70±24min,TA-2:68±22min,VG:68±23min) and ischemic-times (TA-1:40±17min,TA-2:43±19min,VG:40±16min) were similar for the three groups.

Post-operatively TA-1 and VG patients were longer intubated (TA-1:6.7±6.6h,VG:6.9±6.9h vs TA-2:4.9±2.9h,p=0.02), suffered more often from atrial fibrillation (TA-1:32%,VG:24% vs TA-2:12%,p=0.001) and had a longer post-op stay (TA-1:9±11d,VG:8±7d vs TA-2:7±6d,p=0.04). In-hospital or thirty-day mortality was not different between TA-1 (4%) and VG (6%) but significantly higher compared to the younger group (TA-2:1%,p=0.02).

Conclusions: Although patients ≥70y face higher risk for CABG in general, TACABG is a safe and effective alternative for elderly patients lacking adequate vein grafts.

No conflict of interest

SURGICAL ASPECTS: NEW CHALLENGES IN CARDIAC SURGERY

LOGISTIC RISK MODEL PREDICTING SIGNIFICANT CORONARY ARTERY DISEASE IN PATIENTS WITH DEGENERATIVE AORTIC VALVE DISEASE

D. Gilmanov[1], M. Murzi[1], M. Solinas[1], M. Baroni[2], M. Glauber[1], S. Berti[2], R. De Caterina[3], A. Mazzone[2]
[1]Adult Cardiac surgery, G. Pasquinucci Heart Hospital - FTGM, Massa, Italy
[2]Adult Cardiology, G. Pasquinucci Heart Hospital - FTGM, Massa, Italy
[3]Laboratory for Thrombosis and Vascular Research, CNR Institute of Clinical Physiology - FTGM, Pisa, Italy

Purpose:
Contemporary research data affirm that degenerative aortic valve disease (DAVD) shares many features of active atherosclerosis-like process, but no study has linked yet coronary artery disease (CAD) and DAVD like two forms of systemic atherosclerosis. We aimed to develop a logistic regression model and a simple score system for the prediction of significant CAD in patients with DAVD.

Methods:
A total of 1392 consecutive patients with DAVD (727 males (52%), mean age 73±8 years, range 45-89), who underwent routine coronary angiography (CAG) before aortic valve replacement between 2001 and 2012, was retrospectively analysed. A bootstrap refined logistic regression model was developed on the basis of preoperative clinical risk factors, and an additive model was derived from the former. Receiver operating characteristic (ROC) curves (c-statistic) were used to compare discrimination, and precision was quantified by the Hosmer-Lemeshow statistic. Significant coronary atherosclerosis was defined as 50% or more luminal narrowing in one or more major epicardial vessels by means of CAG.

Results:
Five hundred eighty-eight (42%) patients had significant coronary atherosclerosis. Multivariate analysis revealed male gender (odds ratio (OR) 2.09, 95% confidence interval 1.548-2.816, p=0.0000), age (OR 1.361 (1.156-1.60) for every additional 5 years, p=0.0002), dialysis for chronic renal failure (OR 2.851 (1.029-7.90), p=0.044), dyslipidemia (OR 1.354 (1.024-1.792), p=0.033), type II diabetes mellitus (OR 1.853 (1.365-2.514), p=0.0000), family history of CAD (OR 1.323 (1.008-1.736), p=0.043), peripheral artery disease (OR 2.718 (1.885-3.920), p=0.0000), previous acute myocardial infarction (OR 13.462 (5.098-35.553), p=0.0000), and angina pectoris (OR 4.763 (3.579-6.338), p<0.0000) as independent predictors of significant CAD. There was the only protective factor for CAD – transvalvular aortic pressure gradient (OR 0.988 (0.982-0.994), p=0.0000). A logistic equation including the coefficients of the regression analysis accurately predicted individual patient's risk for the presence of significant CAD (area under the ROC curve: 0.815, 95% confidence interval 0.79-0.83). Similar discriminating ability was achieved by the simple additive model (area under ROC curve of 0.794). Goodness of fit tested by the Hosmer-Lemeshow statistic was satisfactory for both models (chi-square 4.157, p=0.843 and chi-square 4.431, p= 0.816).

Conclusions:
Higher atherosclerotic burden is associated with the presence of significant CAD in patients with DAVD. Our logistic regression model may be used with simplicity and accuracy as a predictive scoring system to estimate the risk of significant CAD in patients with DAVD, based on the individual presentation of risk factors.

No conflict of interest

ACUTE ISCHEMIA, ACUTE CORONARY SYNDROMES AND MYOCARDIAL INFARCTION

THE USE OF MECHANICAL RONARY ARTERY BYPASS GRAFT MIGHT REDUCE MYOCARDIAL INJURY EARLY AFTER ACUTE MYOCARDIAL INFARCTION

T. Takano[1], Y. Ohtsu[1], T. Seto[1], T. Terasaki[1], H. Tanaka[2], J. Amano[1]
[1]Cardiovascular Surgery, Shinshu University, Matsumoto, Japan
[2]Surgery, Okaya City Hospital, Matsumoto, Japan

On-pump beating-heart coronary artery bypass graft (OPBH) unloads left ventricle and avoids cardioplegic arrest during surgery for AMI and would reduce injury to non-infarcted myocardium. We evaluated myocardial injury of OPHB comparing conventional CABG with cardiac arrest (OPCA) within 24 hours after the onset of AMI.

We performed 31 solitary CABG for AMI from March of 2007 to April of 2013 in our institution. Of 31 cases, skin incision was started within 24 hours after the symptom of AMI started in 23 patients, and OPHB was done in 11 cases whereas OPCA in 12 cases.

Patients' basic characteristics, operative procedure, in-hospital mortality, morbidity, duration of IABP support, intubation period, ICU and hospital stay after the surgery, changes in creatinine phosphokinase (CK) and myocardial subset of CK (CK-MB) were retrospectively evaluated.

Pre-operative characteristics were not significantly different in 2 groups. Time interval between the onset of AMI symptom and skin incision was 14.7±8.0 and 15.4 ±6.7 hours in OPCA and OPBH group, respectively.

No significant difference was observed in the mortality and morbidity between 2 groups.

CK and CK-MB increased in 9 of 12 patients of OPCA and decreased in 9 of 11 patients of OPHB group after the surgery (p=0.01). CK and CK-MB significantly increased after the surgery (852±936 v.s. 1647±1532 IU and 88±113 v.s. 139±159 IU) in OPCA group although they did not significantly increase in OPBH group (2064±2203 v.s. 1830±1390 IU and 210±194 v.s. 165±117 IU).

OPBH might reduce myocardial injury during CABG early after AMI and would improve outcomes.

No conflict of interest

BASIC RESEARCH, MOLECULAR BIOLOGY

Document not received

BASIC RESEARCH, MOLECULAR BIOLOGY

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BASIC RESEARCH, MOLECULAR BIOLOGY

LEFT VENTRICULAR ASSIST DEVICE ACTIVATES THE TRANSCRIPTIONAL APOPTOTIC PROFILE IN HUMAN HEART

T. Prescimone[1], S. Masotti[1], A. D'Amico[1], R. Caruso[2], M. Cabiati[1], C. Caselli[1], F. Viglione[1], A. Verde[2], S. Del Ry[1], D. Giannessi[1]
[1]CNR, Istituto di Fisiologia Clinica-CNR, Pisa, Italy
[2]CNR, Istituto di Fisiologia Clinica-CNR, Milano, Italy

Background. To assess whether Left Ventricular Assist Device (LVAD) implantation modifies the expression of pro- and anti-apoptotic biomarkers in the human heart.

Methods. Cardiac tissue biopsies were collected from different sites in both left (LV) and right ventricles (RV) of severe HF patients with LVAD and from patients undergoing cardiac transplantation (HTx).

Results. At the mRNA level, higher expression of both anti-apoptotic Hsp72 and Bcl-2 and pro-apoptotic Casp-3 and Bax was observed in LVAD compared to HTx, both in LV and RV (LV, Hsp72: 3.38 ± 0.76 vs 0.86 ± 0.15, p = 0.0004; Bcl-2: 0.72 ± 0.17 vs 0.36 ± 0.08, p = 0.048; Bax: 2.20 ± 0.66 vs 0.57 ± 0.07, p = 0.014; Casp-3: 0.68 ± 0.03 vs 0.34 ± 0.06, p = 0.003). The increase in pro- and anti-apoptotic factors in LVAD samples was confirmed by WB and immunohistological analysis, (LV, WB of Hsp72: 4.10 ± 0.47 vs 2.76 ± 0.32, p = 0.03).

Conclusions. The increase in apoptotic factors induced by LVAD was an unexpected finding, while the up-regulation of the anti-apoptotic factors was in line with the expected ability of the LVAD to reverse apoptosis and offer the cells a new viable state, in tune with the potential activation of the reverse remodeling process. This study suggests that with appropriate therapies such as LVAD, cardiac apoptosis could be modulated, possibly contributing to improvement of failing hearts.

No conflict of interest

BASIC RESEARCH, MOLECULAR BIOLOGY

TRANSGENIC OVEREXPRESSION OF THE NRF2 IN THE SPONTANEOUSLY HYPERTENSIVE RATS AMELIORATES OXIDATIVE STRESS IN MYOCARDIUM AND AORTA.

O. Oliyarnyk[1], H. Malinska[1], L. Kazdova[1], M. Pravenec[2]
[1]Center for Experimental Medicine, Institute for Clinical and Experimental Medicine, Prague 4, Czech Republic
[2]Institute of Physiology, Academy of Sciences, Prague 4, Czech Republic

Aims

Nuclear factor-erythroid 2-related factor-2 (***Nrf2***) is a key transcription factor responsible for regulation of antioxidant enzymes such glutathione peroxidase (GSH-Px), glutathione transferase (GST) etc. We investigated the effect of Nrf2 transgenic expression on the activity of these enzymes, reduced glutathione concentration (GSH), and lipid peroxidation in myocardium and aorta in the spontaneously hypertensive rats (SHR).

Methods

We derived a transgenic line of SHR rats (SHR-***Nrf2)*** by microinjecting zygotes with the construct containing Nfe2l2 cDNA under control of the universal promoter.

Results Expression of Nrf2 significantly increased activities of GSH-Px and GST in myocardium and aorta compared to nontransgenic controls (Table). In SHR-***Nrf2*** thioredoxin activity was increased in myocardium (0.802±0.062 vs 0.0559±0.028 nM NADPH/min/mg protein, $p<0.05$). Concentration of enzymes cofactor, GSH, was increased only in aorta (5.16±0.16 vs 4.43±0.22 mM/g protein, $p<0.05$) as well as catalase activity.

Increased antioxidant defense in SHR-***Nrf2*** was associated with reduced level of lipid peroxidation products-TBARS. Triglycerides concentration in aorta were decreased in transgenic rats compared to controls (1.41±0.14 vs 2.10±0.19mmol/l, $p<0.02$), whereas serum triglyceride levels were not different.

Conclusion Transgenic expression of ***Nrf2*** ameliorate oxidative stress in myocardium and aorta in experimental model of metabolic syndrome. Given the role of Nrf2 as a regulator of antioxidant system, pharmacological manipulation of Nrf2 might be beneficial in treating metabolic disorders related to insulin resistance.

	SHR	SHR- *Nrf2*
GSH-Px, μM NADPH min/mg protein		
Myocardium	101±9	132±84*
Aorta	48±3	63±5*
GST, nM CDNB min/mg protein		
Myocardium	49±2	64±2***
Aorta	2.027±0.181	2.664±0.161*
TBARS, nM/mg protein		
Myocardium	0.835±0.040	0.713±0.029*
Aorta	0.752±0,047	0.413±0.028***

***p<0.001. *p<0.05

Grant P303/13-04420S

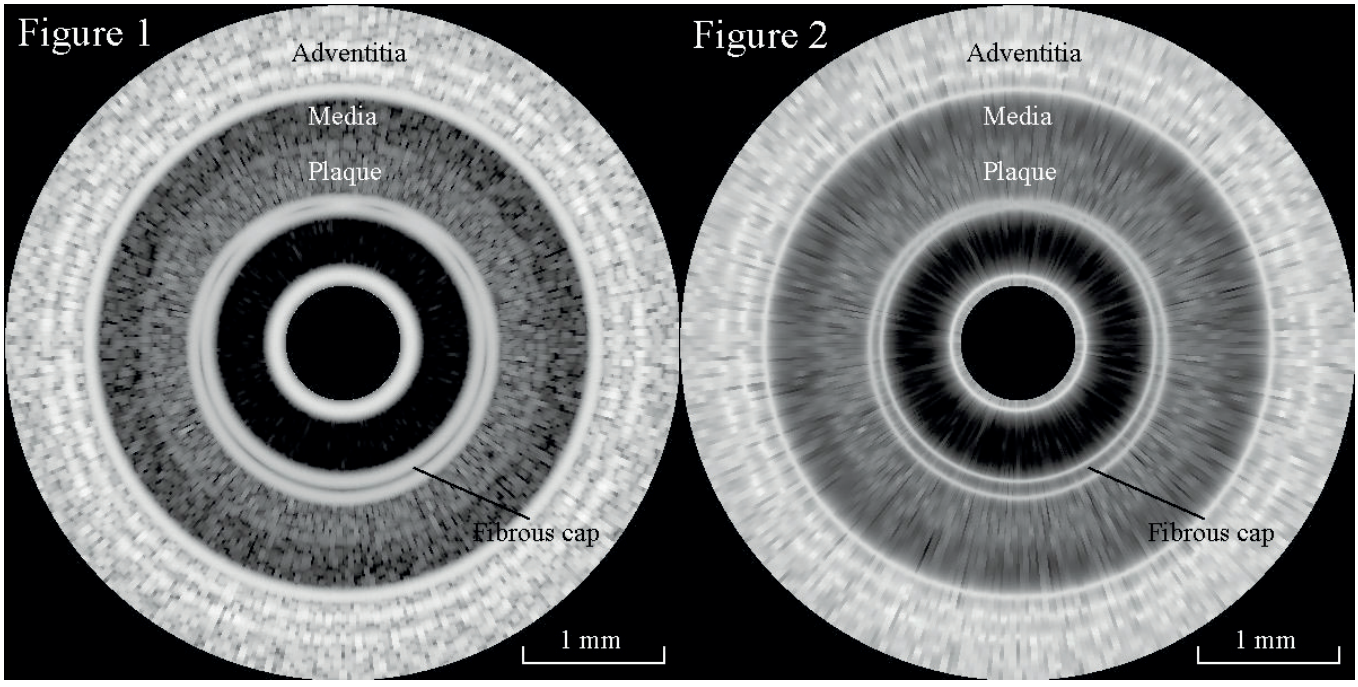
No conflict of interest

BASIC RESEARCH, MOLECULAR BIOLOGY

APPLICATION OF OPTICAL COHERENT TOMOGRAPHY TECHNIQUE TO INTRAVASCULAR ULTRASOUND FOR HIGH-AXIAL-RESOLUTION: BASIC STUDY

H. Taki[1], M. Kudo[2], T. Shiina[3], K. Taki[2], T. Sato[1]
[1]Graduate School of Informatics, Kyoto University, Kyoto, Japan
[2]Department of Anatomy, Shiga University of Medical Science, Otsu City, Japan
[3]Graduate School of Medicine, Kyoto University, Kyoto, Japan

Intravascular ultrasound (IVUS) becomes a common procedure in cardiology, because it provides valuable information about coronary vessel walls. However, the inherent limitation of the axial resolution prevents accurate diagnosis of fibrous caps. Our aim is to approach the axial resolution of IVUS to that of intravascular optical coherence tomography (OCT) for the assessment of fibrous caps by using IVUS. This study is based on frequency domain interferometry (FDI), where the method is employed for intravascular OCT. Since the method can construct foci at all depth from each transmit event, the method achieves high spatial resolution without the deterioration of temporal resolution. Figure 1 shows the conventional IVUS image of an artery in the simulation study, where the artery has a plaque layer with a fibrous cap. Because the thickness of the fibrous cap is from 40 to 120 μm, Conventional IVUS failed to acquire a clear image of the fibrous cap. In contrast, IVUS with OCT technique succeeded to depict the fibrous cap clearly, as shown in Figure 2. This result indicates the potential that the application of the proposed method to IVUS improves its range resolution to 40 μm.



No conflict of interest

BASIC RESEARCH, MOLECULAR BIOLOGY

ERYTHROPOIETIN PROTECTS AGAINST DOXORUBICIN-INDUCED HEART FAILURE

H. Ammar[1], S. Saba[2], R.I. Ammar[3], L.A. Elsayed[1], W.B. Abu-Alyamin Ghaly[1], S. Dhingra[4]
[1]Department of physiology, Cairo University, Cairo, Egypt
[2]Department of pathology, Cairo University, Cairo, Egypt
[3]Department of pediatric cardiology, Cairo University, Cairo, Egypt
[4]Toronto General Research Institute, University Health Network, Toronto, Canada

The hormone erythropoietin (EPO) has been demonstrated to have cardioprotective properties. The present study investigates the role of EPO to prevent heart failure following cancer treatment with doxorubicin [adriamycin (AD)]. Male Wistar rats (150 g) were

treated with saline (vehicle control group); with EPO, subcutaneously at 1,000 IU/kg body wt, three times per week for 4 wk (EPO group); with adriamycin, intraperitoneally at 2.5 mg/kg body wt, three times per week for 2 wk (AD group); and with adriamycin and EPO

(EPO-AD group). Echocardiographic measurements showed that EPO-AD treatment prevented the AD-induced decline in cardiac function. Each of the hearts was then exposed to ischemia and reperfusion during Langendorff perfusion. The percentage of recovery

after ischemia-reperfusion was significantly greater in EPO-AD than the AD-treated group for left ventricular developed pressure, maximal increase in pressure, and rate pressure product. The level of oxidative stress was significantly higher in AD (5 uM for 24 h) -exposed

isolated cardiomyocytes; EPO (5 U/ml for 48 h) treatment prevented this. EPO treatment also decreased AD-induced cardiomyocyte apoptosis, which was associated with the decrease in the Bax-to-Bcl2 ratio and caspase-3 activation. Immunostaining of myocardial tissue for CD31 showed a significant decrease in the number of capillaries inAD-treated animals. EPO-AD treatment restored the number of capillaries. In conclusion, EPO treatment effectively prevented AD induced heart failure. The protective effect of EPO was associated with a decreased level of oxidative stress and apoptosis in cardiomyocytes as well as improved myocardial angiogenesis.

No conflict of interest

BASIC RESEARCH, MOLECULAR BIOLOGY

QUANTITATIVE TRAIT LOCI FOR ATHEROSCLEROSIS IDENTIFIED IN AN EXTREMELY ATHEROSCLEROSIS-RESISTANT MOUSE STRAIN

W. Shi[1]
[1]*Radiology, University of Virginia Health Systems, Charlottesville, USA*

Background- C3H/HeJ (C3H) mice are extremely resistant to atherosclerosis, especially males. To understand the underlying genetic basis, we performed quantitative trait locus (QTL) analysis on a male F_2 cohort derived from an intercross between C3H and C57BL/6 (B6) apolipoprotein E-deficient ($Apoe^{-/-}$) mice. **Methods and Results-** 246 male F_2 mice were started on a Western diet at 8 weeks of age and kept on the diet for 5 weeks. Atherosclerosis in the aortic root and fasting plasma lipid levels were measured. 134 microsatellite markers across the entire genome were genotyped. 4 significant QTLs on chromosomes (Chr) 2, 4, 9 and 15, and 4 suggestive loci on Chr1, 4 and 7 were identified for atherosclerotic lesions. Unexpectedly, the C3H allele was associated with increased lesion formation for 2 of the 4 significant QTLs. 6 loci for HDL, 6 for non-HDL cholesterol, and 3 for triglyceride were also identified. The QTL for atherosclerosis on Chr9 coincided with a QTL for HDL, and there was a moderate, but statistically significant, correlation between atherosclerotic lesion sizes and plasma HDL cholesterol levels in F_2 mice. **Conclusions**- These data indicate that most atherosclerosis susceptibility loci are distinct from those for plasma lipids except for the Chr9 locus which exerts effect through interactions with HDL.

No conflict of interest

BASIC RESEARCH, MOLECULAR BIOLOGY

EFFECT OF INTERMITTENT FASTING ON CYTOKINE (IL-6 AND TNF-?) LEVELS IN KNOCKOUT MICE LDL -/-

F. Reis de Azevedo[1], E. Sant'anna Melo[1], M.C. Jurado[1], A.F. Pastana[1], B. Caramelli[1]
[1]Heart Insititute, University of São Paulo Medical School, São Paulo, Brazil

Purpose: To investigate the effects of intermittent fasting (IF) on variables related to atherosclerosis development, such as cytokines levels.

Methods: Six weeks old LDL -/- Knockout mice were divided into three groups, receiving daily 5 grams of each diet: Atherogenic (AT) – rich in cholesterol, saturated fatty acids and low in fibers; DASH (Dietary Approaches to Stop Hypertension) – rich in mono and polyunsaturated fatty acids and low in sodium and Intermittent Fasting (IF) – Standard chow supplemented with micronutrients, every other day. By the end of fifteen weeks, blood was collected and analyzed for cytokine IL6 and TNFα, using REAL-TIME and ELISA.

Results: IF group showed an enhanced expression of IL6 RNAm when compared to DASH group. However there was no increase in protein synthesis. In AT group the opposite happened, reduced expression of IL6 RNAm with increase in protein synthesis. Figure 1 shows the values of RNAm expression for each group: 1,2 in IF group, 0,2 in DASH group and 0,1 in AT, p<0,05 between IF and DASH. Protein expression of IL6 was 50,10pg/ml in IF group, 60,31pg/ml in DASH and 230,54pg/ml, as shown in figure 2, p<0,05 between IF and AT. TNFα analysis showed an increased protein expression in AT group when compared to IF group. Values were 70,49pg/ml in IF group, 50,36pg/ml in DASH group and 250,90pg/ml in AT group, p<0,05 between IF and AT. We performed Student's t-test and all values ??were expressed as mean ± standard error of the media.

Conclusion: These results suggest that, in animal model, Intermittent fasting has a reduced atherogenesis effect than DASH or AT diet, represented by the lower protein expression of IL-6 and TNF-α.

Figure 1. IL6 RNAm Expression

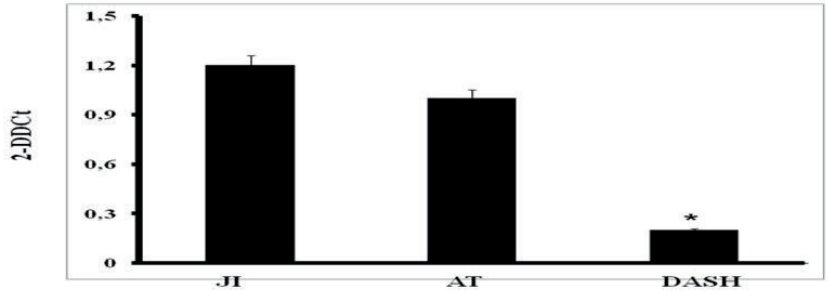
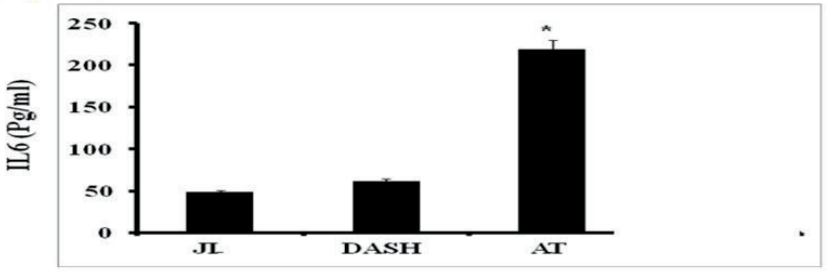


Figure 2. IL6 Protein expression



*** p<0.05 (IF)**
n=12

No conflict of interest

INTERVENTIONAL CARDIOLOGY AND STENTING

LONG-TERM CLINICAL RESULTS OF SEQUENT PLEASE PACLITAXEL-COATED BALLOON ANGIOPLASTY FOR THE TREATMENT OF IN-STENT RESTENOSIS

J. Benezet[1], I. Sanchez-Perez[1], F. Lozano[1], F. Higuera[1], N. Pinilla[1], Y. Hessein[1], J.M. Arizon[2]
[1]Interventional Cardiology, Hospital General Universitario de Ciudad Real, Ciudad Real, Spain
[2]Cardiology, Hospital General Universitario de Ciudad Real, Ciudad Real, Spain

Background: Paclitaxel-coated balloons (PCB) have been proven to be effective for the treatment of coronary in-stent restenosis (ISR) after bare-metal stent (BMS) or drug-eluting stent (DES) implantation. This study aims to evaluate the long-term safety and efficacy of the second-generation SeQuent Please PCB in coronary ISR in routine real-world practice.

Methods: Between May 2009 and April 2011, all consecutive patients with ISR lesions treated with the SeQuent Please PCB at our institution were prospectively included. Patients were followed up for 24 months by clinical observation. The primary endpoint was the clinically driven target lesion revascularization (TLR) rate at 24 months. The secondary endpoint was the rate of major adverse cardiac events (MACE: defined as a composite of cardiac death, myocardial infarction, and TLR) at 24 months.

Results:48 patients with 52 ISR lesions (30 BMS, 22 DES) were included. Mean age was 66.2±12.3 years. 75 % were male and 50 % were diabetics. The majority of patients presented with stable angina (63.5%). The target lesion was mainly located in the right coronary artery (46.1%) and the left anterior descending coronary artery (42.3%). The mean reference vessel diameter was 3.0±0.5 mm and the mean target lesion length was 21.4±6.8 mm.Procedural success was 100 %. Coronary dissection occurred in 1 patient (1.9 %), requiring additional stent implantation. Follow-up rate was 94.2 %. The TLR rate was 5.8 % after 24 months. Cumulative MACE at 24 months was 9.6 %, with 1.9 % cardiac death and 1.9 % myocardial infarction. No vessel thrombosis was documented. The TLR rate did not differ for PCB angioplasty for BMS-ISR compared with DES-ISR (3.3% vs. 9.1%, p=0.38). Baseline lesion characteristics and procedural data did not differ except for a longer lesion length for BMS-ISR compared with DES-ISR (25.4 ±5.1 mm vs. 19.7±6.9 mm, p=0.008).

Conclusions: Treatment of coronary ISR with the second-generation SeQuent Please PCB provides good clinical outcomes demonstrated by the low TLR rate and low MACE rates at long-term follow-up.

No conflict of interest

INTERVENTIONAL CARDIOLOGY AND STENTING

WHICH IS THE OPTIMUM STENT TO THE CORONARY ARTERY LESION WITH CALCIFICATION?

H. Hara[1], M. Yamamoto[1], N. Ikeda[1], S. Ito[1], Y. Hiroi[1]
[1]Cardiology Division, National Center for Global Health and Medicine, Tokyo, Japan

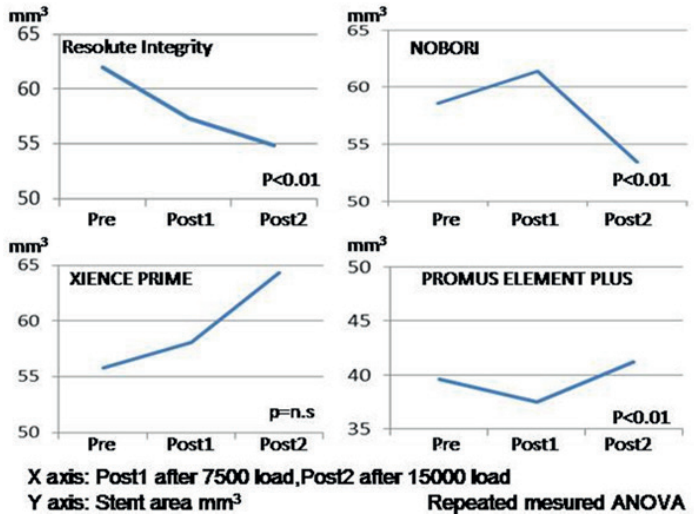
Objectives: To investigate stent deformation by torsional, sterch and bent stress after implantation at the right ostium with calcification of a coronary artery model.

Background: The restenosis decreased sharply by second generation DES. However, it did not disappear at all. Little is known about coronary stent deformation, especially the association between stent design and deformation at the coronary ostium with calcification. Recent reports have suggested that mechanical factors are important for stent restenosis.

Methods: A coronary ostium model was constructed and four different stents (XiencePrime, Promus Element Plus, Nobori and Resolute Integrity, n=2 each) were implanted at the aorto-ostial junction. Differences of stent deformation were assessed after exposure to torsional, sterch and bent stress. After time attainment and the number of times 15,000 of a load, the volume change after time attainment was measured by Intravascular ultrasound. Then the extent and pattern of plastic deformation were compared between the four stent types.

Result: Nobori caused the stent cell fracture. Xience and Promus change to which volume increases and decreases by a load was obtained. Only Resolute Integrity caused the volume decrease gradually. By experiment, the stent cannot become large. Only Resolute Integrity was change in assumption. Show the fig.

Conclusion: The possibility which needs the stent selection based on coronary artery morphology on the occasion of stent placement was suggested.



No conflict of interest

INTERVENTIONAL CARDIOLOGY AND STENTING

NEOINTIMAL RESPONSE TO THE SECOND GENERATION DES IN DIABETIC PATIENTS WITH DE NOVO CORONARY LESIONS: INTRAVASCULAR ULTRASOUND STUDY

B. Hong[1], Y. Yoon[1], H. Won[1], T. Kang[2], S. Lee[3], D. Jeon[4], S. Ryu[5], P. Min[6], H. Kwon[6], B. Lee[6], Y. Jang[6]
[1]Internal Medicine, Yonsei University College of Medicine, Seoul, Korea
[2]Internal Medicine, Dankook University College of Medicine, Cheonan, Korea
[3]Internal Medicine, Yonsei University Wonju College of Medicine, Wonju, Korea
[4]Internal Medicine, National Health Insurance Corporation Ilsan Hospital, Ilsan, Korea
[5]Internal Medicine, Eulji University, Seoul, Korea
[6]Internal Medicine, Yonsei University Wonju College of Medicine, Seoul, Korea

AIMS

Diabetic population is still challenging for percutaneous coronary intervention (PCI) using drug-eluting stents (DES). This study evaluated the extent of neointimal response with intravascular ultrasound (IVUS) after implantation of second-generation DES, zotarolimus-eluting (Endeavor Resolute) or everolimus-eluting (Xience V) stents, for de novo coronary lesions in diabetic patients.

METHODS AND RESULTS

154 diabetic patients with de novo coronary lesions were randomized to zotarolimus-eluting stent or everolimus-eluting stent implantation, and angiographic 9-months follow-up combined with complete IVUS study was available in 98 patients with 101 lesions. The primary end point was in-stent neointimal volume obstruction on follow-up IVUS.
Baseline demographic and lesion parameters were similar in both groups at index PCI. On follow-up angiography, in-stent late lumen loss (0.12±0.43 vs. 0.13±0.70mm, p=0.967) and minimal lumen diameter (3.05±0.39 vs. 3.18±0.35mm, p=0.087) were not different between zotarolimus-eluting stent and everolimus-eluting stent. On IVUS study, neointimal hyperplasia volume (median [interquartile range]: 2.25 [0.57 to 6.25] vs. 1.59mm3[0.45 to 8.37], p=0.849) and in-stent percentage of volume obstruction (median [interquartile range]: 1.16 [0.33 to 3.61] vs. 0.77% [0.29 to 4.01], p=0.663) were similar between groups. Serial quantitative IVUS analysis is shown in table. For two years after index PCI, one cardiac death and one target vessel revascularization occurred only in zotarolimus-eluting stent group, which was not statistically significant as compared with everolimus-eluting stent group.

Table. Quantitative intravascular ultrasound analysis in stented segment

Variable	Endeavor Resolute (n=53)		P-value	Xience V (n=48)		P-value
	After Procedure	Follow-up		After Procedure	Follow-up	
Vessel volume index (mm^3/mm)	15.1 ± 3.7	15.0 ± 4.1	0.536	16.0 ± 5.3	16.4 ± 5.2	0.080
Peri-stent plaque volume index (mm^3/mm)	8.0 ± 2.5	8.0 ± 2.6	0.947	8.6 ± 3.4	8.7 ± 3.6	0.811
Lumen volume index (mm^3/mm)	7.1 ± 1.7	7.0 ± 1.9	0.191	7.4 ± 2.2	7.5 ± 2.2	0.546
Stent volume index (mm^3/mm)	7.0 ± 2.0	7.2 ± 1.8	0.094	7.5 ± 2.1	7.7 ± 2.4	0.036
Minimum lumen area (mm^2)	5.8 ± 1.5	5.7 ± 1.7	0.571	6.3 ± 2.0	6.1 ± 2.1	0.147
Neointimal volume index (mm^3/mm)		0.2 ± 0.4			0.2 ± 0.5	
Percent neointimal obstruction (%)		2.7 ± 4.8			2.6 ± 3.7	

Data are presented as mean ± SD
The volume index was calculated as the volume data divided by the length
All p-value > 0.05 for Endeavor Resolute versus Xience V.

CONCLUSIONS

In diabetic patients, both second-generation DES were comparable in inhibiting neointimal proliferation as well as 2-year clinical outcome.

No conflict of interest

INTERVENTIONAL CARDIOLOGY AND STENTING

FIVE-YEAR CLINICAL OUTCOMES AFTER IMPLANTATION OF SIROLIMUS-ELUTING STENT IN PATIENTS WITH AND WITHOUT DIABETES MELLITUS

T. Sato[1], T. Ono[1], K. Hatanaka[1], M. Tanaka[1], S. Fuke[1], T. Ikeda[1], H. Saito[1]
[1]Cardiovascular Medicine, Japanese Red Cross Okayama Hospital, Okayama, Japan

Percutaneous coronary intervention in patients with diabetes mellitus (DM) is associated with worse clinical outcomes; however, the long-term efficacy of sirolimus-eluting stents (SES) in diabetic patients remains uncertain. We evaluated 5-year clinical outcomes after SES implantation in 201 consecutive patients (87 in the DM group and 114 in the non-DM group), and 250 lesions (108 and 142, respectively). The primary end point was major adverse cardiac events (MACE) defined as cardiac death, nonfatal myocardial infarction, target lesion revascularization (TLR), stent thrombosis or admission for congestive heart failure. The risk of congestive heart failure was significantly higher (19.5% vs 5.3%, odds ratio [OR]: 4.327, 95% confidence interval [CI]: 1.641 to 11.643, p=0.003) in the DM group compared with the non-DM group; however, MACE did not occur significantly more often (26.4% vs 15.8%, p=0.072). Multivariate logistic regression analysis showed that diabetes was associated with congestive heart failure (OR: 4.706, 95% CI: 1.723 to 12.640, p=0.002) and multivessel disease was associated with MACE (OR: 2.682, 95% CI: 1.051 to 6.842, p=0.037). The cumulative rates (%) of TLR were as follows: after 1 year; 5.7 vs 5.3, 2 years; 6.9 vs 5.3, 3 years; 9.2 vs 7.0, 4 years; 9.2 vs 8.8, 5 years; 9.2 vs 8.8 (p=0.642) in the DM group and the non-DM group, respectively. Diabetic patients had worse long-term prognosis in terms of congestive heart failure than non-diabetic patients. TLR was performed steadily for up to 5 years of follow-up following the late catch-up phenomenon both in diabetic and non-diabetic patients.

Conflict of interest

INTERVENTIONAL CARDIOLOGY AND STENTING

RESTENOTIC STENTED VERSUS DE NOVO CHRONIC TOTAL OCCLUSION OUTCOMES FOLLOWING SUCCESSFUL INTERVENTION WITH DRUG-ELUTING STENTS

W.Y. Shin[1], U. Jeon[1], S.H. Park[1], S.J. Lee[1], D.K. Jin[1], B.G. Choi[2], J.O. Na[2], C.U. Choi[2], H.S. Seo[2], D.J. Oh[2]
[1]Cardiology, Soonchunhyang University Cheonan Hospital, Cheonan, Korea
[2]Cardiovascular center, Korea University Guro Hospital, Seoul, Korea

Background: There are limited data comparing angiographic and clinical outcomes of re-stenotic stented chronic total occlusive (CTO) lesion successfully revascularized with drug-eluting stents (DESs) with those of de novo CTO lesion.

Methods: The study population consisted of consecutive 269 CTO patients (pts) who successfully treated with DESs between January 2004 and June 2010. A total 249 pts with de novo CTO lesion and 20 pts with re-stenotic stented CTO lesion were included for analysis. The 6-to-9 month angiographic and 2-year clinical outcomes were compared between the 2 groups.

Results: The baseline clinical characteristics were similar between the two groups except prior myocardial infarction, LDL-cholesterol level, number of total implanted stent and use of cilostazol. Angiographic outcomes at 6-to-9 months were similar between the two groups. At 2-year follow-up, the incidence of major clinical outcomes including all death, any myocardial infarction, any revascularization, target lesion and vessel revascularization (TLR and TVR) and major adverse cardiac events (MACEs) were similar between the two groups (Table). Further, even after adjustment of baseline differences with multivariate analysis adjusted by age, gender, dyslipidemia, LVEF, Lefevre classification, all the major clinical outcomes were similar between the two groups.

Conclusions: In our study, there were no difference in 6-to-9 month angiographic and 2-year clinical outcomes between pts with stented and de novo CTO lesions once the CTO pts were successfully treated with DESs

No conflict of interest

INTERVENTIONAL CARDIOLOGY AND STENTING

PRONE POSITION CORONARY ANGIOGRAPHY DUE TO INTRACTABLE BACK PAIN: ANOTHER MERIT OF TRANSRADIAL APPROACH COMPARED TO TRANSFEMORAL APPROACH

S. Kwon[1], J.H. Rhee[1]
[1]Division of Cardiology Department of Internal Medicine, Yongin Severance Hospital Yonsei University College of Medicine, Yongin-si, Korea

We report a case of prone position coronary angiography due to intractable back pain via left transradial approach. When a patient can not lie down on a supine position, prone position coronary angiography can be performed alternatively. This may be another merit of transradial approach compared to transfemoral approach on the evaluation of patients with suspected coronary artery disease.

Keywords: Transradial coronary angiography, Prone position

No conflict of interest

ALEGLITAZAR PROTECTS CARDIOMYOCYTES AGAINST THE ADVERSE EFFECTS OF HYPERGLYCEMIA

Y. Birnbaum[1], *S. Ling*[2], *M.K. Manhwan*[2], *B. Thomas*[2], *Y. Ye*[2]
[1]*Medicine/ Cardiology, Baylor College of Medicine, Houston, USA*
[2]*BMB, University of Texas Medical Branch, Galveston, USA*

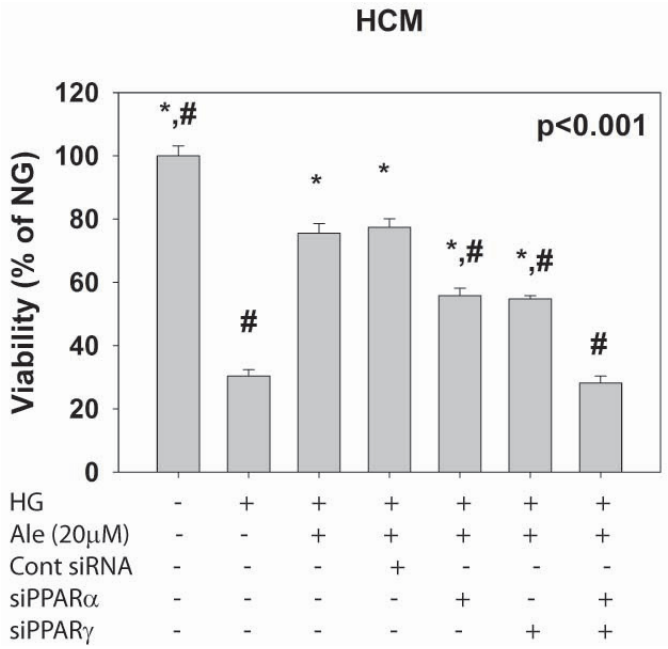
Background: Aleglitazar (ALE) is a balanced dual peroxisome proliferator-activated receptor (PPAR) agonist, activating both PPARα and PPARγ. Both fibrates (PPARα agonists) and thiazolidinediones (PPARγ agonists) protect cardiomyocytes against various insults. The protective effects of the thiazolidinediones; however, are partially PPARγ-independent.

Purpose: We assessed whether ALE protects human cardiomyocytes (HCM) *in vitro* against the effects of hyperglycemia (HG).

Methods: HCM [ScienCell Research Laboratories] were incubated for 48h at normoglycemic (NG, glucose 5.5mM) or HG (glucose 25mM) conditions with escalating concentrations of ALE. Cell viability (MTT), DNA fragmentation, caspase-3 activity and cytochrome-C release were measured. The effects of PPARα and PPARγ silencing to dissect their roles on the effects of ALE were assessed.

Results: HG reduced HCM viability and increased apoptosis which were dose-dependently attenuated by ALE. HG reduced antioxidant capacity and increased reactive oxygen species generation, which were both significantly blunted by ALE treatment. Promoter studies showed ALE increased PPARα and PPARγ activation in HCM which could be opposed by siRNA selectively targeting their mRNAs. The effects of ALE to counter the HG induced hypertrophy and increase in ANP and β-myosin heavy chain mRNA expression could be partially blocked by siRNA against PPARα or PPARγ, and completely blocked by combined siPPARα and siPPARγ. These data show that ALE protects HCM via mechanisms mediated by activation of both PPARα and PPARγ and suggest no off-target effects.

Conclusions: ALE protects HCM in vitro against the adverse effects of HG by activation of both PPARα and PPARγ.

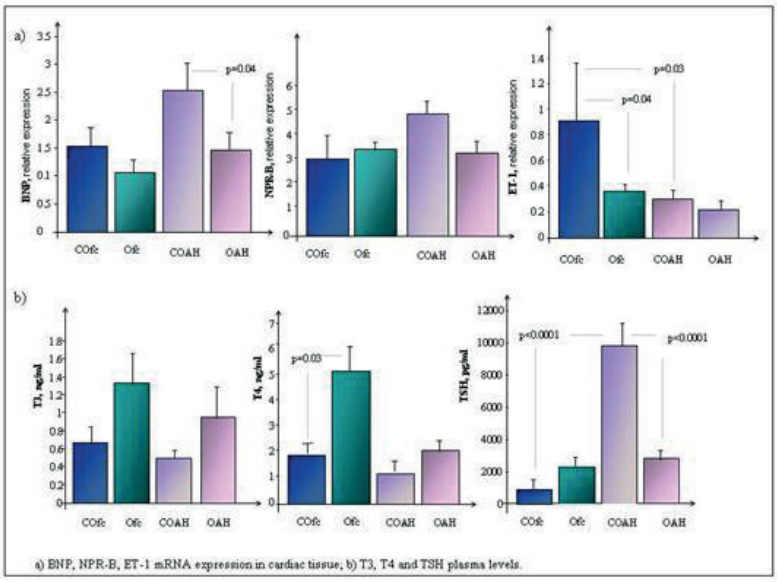


No conflict of interest

OBESITY MODULATES THE TRANSCRIPTIONAL ALTERATIONS OF THE NATRIURETIC PEPTIDE AND ENDOTHELIN SYSTEMS

M. Cabiati[1], E. Belcastro[1], C. Caselli[1], T. Prescimone[1], M.A. Guzzardi[1], P. Iozzo[1], D. Giannessi[1], S. Del Ry[1]
[1]CNR, Istituto di Fisiologia Clinica, Pisa, Italy

Natriuretic peptides (NPs) and endothelin (ET)-1 system appear to be associated with the development and progression of many cardiovascular disease (CD) linked to obesity. Aim of this study was to evaluate their transcriptional alterations by Real Time-PCR in cardiac tissues of Zucker rats subdivided in obese rats (O, n=20), and controls (CO, n=20): half under fasting conditions (CO_{fc}-O_{fc}) and the remainders after the induction of acute hyperglycemia (CO_{AH}-O_{AH}). Thyroid function was also determined using MagPix system.Lower BNP and ANP mRNA were observed in O with respect to CO while CNP expression resulted higher probably for its endothelial role. A down-regulation of NPR-B and NPR-C and an up-regulation of NPR-A was observed in O. Lower pre-proET-1 and ECE-1 mRNA levels were observed in O with respect to CO (p=0.02). ET-A and ET-B mRNA showed no significant differences between CO and O. Significantly higher plasma levels of T3 (p=0.01), T4 (p=0.02) and lower levels of TSH (p=0.005) in O with respect to CO, were found. The more relevant pathway observed subdividing into fasting and hyperglycemic rats are reported in Fig1.The results of this study suggest a reduced release of NPs by cardiac cells as well as of its counter-regulatory ET-1 system and could be a useful starting point for future studies aimed to identify new therapeutic strategies for the treatment of cardiometabolic syndrome.



a) BNP, NPR-B, ET-1 mRNA expression in cardiac tissue; b) T3, T4 and TSH plasma levels.

No conflict of interest

C-TYPE NATRIURETIC PEPTIDE TRANSCRIPTOMIC PROFILING INCREASES IN LEUKOCYTES OF PATIENTS WITH CHRONIC HEART FAILURE AS A FUNCTION OF CLINICAL SEVERITY

M. Cabiati[1], L. Sabatino[1], R. Caruso[2], A. Verde[3], C. Caselli[4], T. Prescimone[4], D. Giannessi[4], S. Del Ry[4]
[1]CNR, Istituto di Fisiologia Clinica-CNR, pisa, Italy
[2]CNR, Istituto di Fisiologia Clinica-CNR, Milano, Italy
[3]Cardiovascular Department, Niguarda Ca' Granda Hospital, Milano, Italy
[4]CNR, Istituto di Fisiologia Clinica, Pisa, Italy

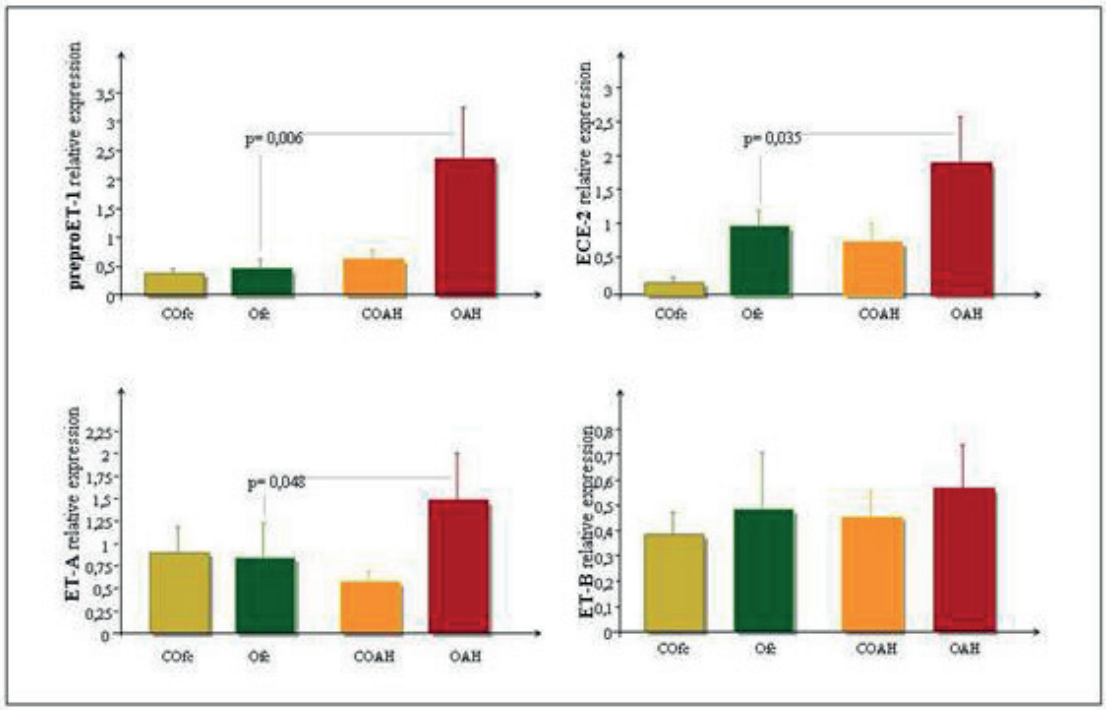
After the isolation of C-type natriuretic peptide (CNP) from porcine brain tissue, both CNP and CNP mRNA have been identified in vascular endothelium and in cardiac, renal, skeletal, and reproductive tissues as well as in organs of the immune system and in a variety of blood cells. The aim of this study was to evaluate the transcriptomic profiling of CNP and of its specific receptor, NPR-B in human leukocytes of heart failure (HF) patients as a function of clinical severity, assessing the possible changes with respect to healthy subjects (C). mRNA expression was evaluated by Real-time PCR and total RNA was extracted from leukocytes of C (n=8) and of HF patients (NYHA I-II n=7; NYHA III-IV n=13) with PAXgene Blood RNA Kit. Significantly higher levels of CNP mRNA expression were found in HF patients as a function of clinical severity (C: 0.23±0.058, NYHA I-II=0.47±0.18, NYHA III-IV=2.58±0.71, p=0.005 C vs NYHA III-IV, p=0.017 NYHA I-II vs N YHA III-IV) and NPR-B transcript levels resulted down-regulated in HF patients with higher NYHA class (C: 2.2± 0.61, NYHA I-II=2.76±0.46, NYHA III-IV=0.29±0.13, p=0.001 C vs NYHA III-IV, p<0.0001 NYHA I-II vs. NYHA III-IV). A significant negative correlation between CNP and NPR-B mRNA expression (r=-0.5, p=0.03) was also observed. These results suggest a co-regulation of NPR-B and CNP expression supporting the relevance of this receptor in human disease characterized by a marked inflammatory/immune component and suggesting the possibility of manipulating inflammation via pharmacological agents selective for this receptor.

No conflict of interest

TRANSCRIPTIONAL ALTERATIONS OF THE ENDOTHELIN-1 SYSTEM IN LUNG TISSUE OF OBESE ZUCKER RAT.

M. Cabiati[1], C. Salvadori[1], C. Caselli[1], T. Prescimone[1], A. Bartoli[1], L. Guiducci[1], D. Giannessi[1], S. Del Ry[1]
[1]CNR, Institute of Clinical Physiology, Pisa, Italy

Obesity has been implicated in the development of many carcinomas, and its prevalence is reaching epidemic proportions in children and teenagers. Recently the endothelin (ET) axis has been shown to have a role in the growth and progression of several tumour types including lung cancer. Aim of this study was to evaluate the ET-1 system transcriptional alterations in lung tissue of Zucker rats by Real Time-PCR subdivided in obese rats (O, n=20), and controls (CO, n=20): half were studied under fasting conditions (CO_{fc}-O_{fc}) and the remainders after the induction of acute hyperglycemia (CO_{AH}-O_{AH}). Significantly higher prepro-ET-1 (p=0.05) and ECE-2 mRNA expression was observed in O with respect to CO. ECE-1 mRNA expression resulted undetectable in the lung tissue of zucker rats while ET-A and ET-B resulted to be expressed at similar levels both in CO than in O. The more relevant pathway observed subdividing into fasting and hyperglycemic rats are reported in Fig1. A significantly correlation was observed between ET-A and ET-B (p=0.04) as well as between prepro-ET-1 and ET-A (p=0.009). ET-1 overexpression, together with the ET-A and ET-B upregulation observed in O_{AH}, are in line with previous studies on solid tumors. The study of ET axis may provide an important tool to modulate the inappropriate secretion of this peptide in pathological conditions providing the key to a new generation of chemotherapeutic agents.



No conflict of interest

ASSOCIATION BETWEEN COMMON VARIANTS IN THE SLCO1B1 GENE AND STATIN-INDUCED MYOPATHY.

D. Dlouha[1], J. Hubacek[1], V. Adamkova[1], M. Snejderlova[2], R. Ceska[2], M. Vrablik[2]
[1]CEM, Institute for Clinical and Experimental Medicine, Prague, Czech Republic
[2]3rd Department of Internal Medicine, 1st Faculty of Medicine Charles University, Prague, Czech Republic

Introduction: Statins belong to drugs of first choice in patients with increased cardiovascular risk. Gene for SCLO1B1 (codes for organic anion transporter, regulates the hepatic uptake of statins) belongs to the candidates with potential to influence the statin treatment efficacy. A genomewide scan among 85 individuals with myopathy identified a noncoding SNP in intron 11 of the SLCO1B1 gene (rs4363657).

Materials and methods: SCLO1B1 rs4363657 (T>C) polymorphism was analysed on group of 85 patients with dyslipidemia treated by statins with myopathy and 752 control individuals. Polymorphism was analysed using PCR-RFLP.

Results: Distribution of the individual genotypes in Czech patients with myopathy (TT=61%, CT=32%, CC=7%) was similar (P=0.095) to the controls (TT=65%, CT=32%, CC=3%).

Conclusions: We didn´t identified a significant association between rs4363657 variant in the SLCO1B1 gene and statin-induced myopathy in our pilot study. Because of the low frequency of the potentially advantageous genotype, it is necessary to analyse larger group of patients.

Funding sources: This study was supported by the project No. NT/11307-5 (IGA MH CR).

No conflict of interest

VARIANTS WITHIN HNF1-A AND ANGPTL4 GENES AND ACUTE CORONARY SYNDROME IN CZECH POPULATION. THE GENDEMIP STUDY.

D. Dlouha[1], J. Pitha[1], V. Adamkova[1], V. Lanska[1], J. Hubacek[1]
[1]CEM, Institute for Clinical and Experimental Medicine, Prague, Czech Republic

BACKGROUND: Atherosclerosis is a complex arterial disease involving interactions of multiple genetic and environmental factors. Large number of genetic polymorphisms associated with atherosclerotic diseases was identified in recent years. We investigated the possible association between hepatic nuclear factor (*HNF1-α*) and angiopoietin-like 4 (*ANGPTL4*) single nucleotide polymorphisms and risk of acute coronary syndrome (ACS) in the Czech population.

MATERIALS AND METHODS: 1,182 patients (835 males and 347 females) with ACS and 1,200 healthy controls (827 males and 373 females) in both groups younger than 65 years were included in the study. Rs7310409 (A>G within the *HNF1-α* gene) and rs116843064 (G>A within the *ANGPTL4* gene) were genotyped using TaqMan genotyping assays.

RESULTS: The frequency of genotypes in patients with ACS did not significantly differ (AA=17.1%, AG=46.6%, GG=36.2%) from the control group (AA=14.4%, AG=50.3%, GG = 35.3%, P = 0.12) neither for rs7310409 nor for rs116843064 (AA=0.1%, AG=3.5%, GG =96.4% vs. controls AA=0.1%, AG=4.2%, GG=95.7%, P = 0.69) polymorphism. There was no interaction with gender. In addition, gene variants were not associated with common cardiovascular risk factors (dyslipidemia, hypertension, smoking, obesity and diabetes).

CONCLUSIONS: We didn´t find any association between polymorphisms within *HNF1-α* and *ANGPTL4* genes and risk of ACS in the Czech populations.

Supported by the project (Ministry of Health, Czech Republic) for development of research organization 00023001 (IKEM, Prague, Czech Republic) – Institutional support

No conflict of interest

SURFACE MODIFIED POLYTETRAFLUOROETHYLENE PROMOTES ENDOTHELIAL CELL ADHESION AND SIMULTANEOUSLY INHIBITS THE ATTACHMENT OF PLATELETS AND BACTERIA

M. Gabriel[1], K. Niederer[2], C.F. Vahl[3], H. Frey[4]
[1]Cardiothoracic and Vascular Surgery, University Medical Center of the Johannes Gutenberg University of Mainz, Mainz, Germany
[2]Johannes Gutenberg-University Mainz, Department of Organic Chemistry, Mainz, Germany
[3]Johannes Gutenberg-University School of Medicine, Department of Cardiothoracic and Vascular Surgery, Mainz, Germany
[4]Johannes Gutenberg-University School of Medicine, Department of Organic Chemistry, Mainz, Germany

Introduction

Synthetic vascular grafts generally suffer from inherent thrombogenicity and fail to promote endothelialization. Commonly used materials - e.g. polytetrafluoroethylene (PTFE) - are also prone to bacterial biofilm formation. We modified PTFE, creating antifouling as well as cell-adhesive properties using polyethyleneglycol (PEG) as a spacer to immobilize the endothelial-cell (EC) specific adhesion peptide REDV.

Experimental

PTFE was surface activated by a wet-chemical procedure [1], followed by direct (PTFE-REDV) or PEG-mediated (PTFE-PEG-REDV) peptide immobilization. Modified and untreated samples were seeded with ECs and monitored up to 2w. In addition, specimen were tested with thrombocytes and *Staph. aureus*. Fluorescent-stained samples were analyzed using ImageJ software and results were expressed as percent coverage.

Results & Discussion

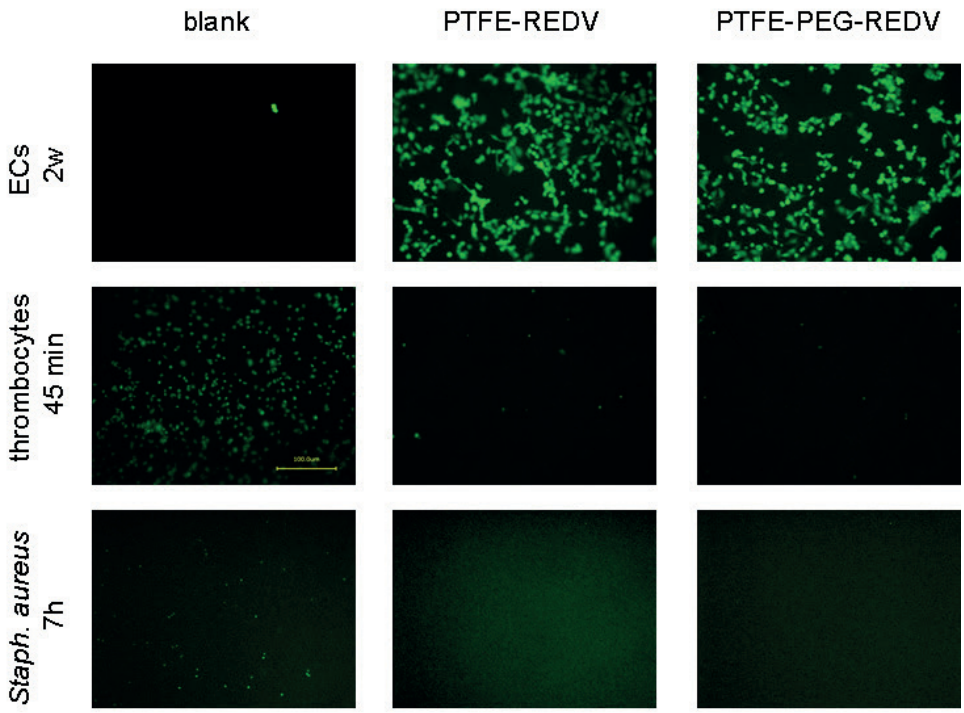
REDV-conjugation with or without a PEG-spacer converts PTFE into an excellent substrate for cell-growth. Colonization of ECs on modified substrates reached 21% (PTFE-REDV) and 18% coverage (PTFE-PEG-REDV) respectively after 2w. Thrombocyte attachment was reduced 35-fold (PTFE-PEG-REDV) and 26-fold on PTFE-REDV. The latter result may be explained by the mere hydrophilicity of this surface. In addition, the modification largely prevented bacterial attachment.

Conclusion

Thrombogenicity and device-associated contamination can effectively be reduced by an appropriate functionalization. For vascular prosthesis, where endothelialization is desirable, the combination of cell-specific adhesiveness and antifouling properties may provide a basis for novel vascular grafts.

Reference

[1] Gabriel et al. Biomed Mater. 2011;6(3):035007



No conflict of interest

IRBESARTAN AMELIORATES APOPTOSIS AND PROTECTS FROM ISCHAEMIA/REPERFUSION INJURY

F.G. Al-Amran[1], N.R. Hadi[2], S.T. Zamil[2]
[1]Cardiovascular surgery, kufa college of medicine, kufa, Iraq
[2]PHARMACOLOGY AND tHERAPEUTICS, kufa college of medicine, kufa, Iraq

This Objective: This study was undertaken to investigate the potential role of Irbesartan in amelioration of myocardiall/R injury.

Material and Methods: The rats were randomized into 4 equal groups each of 6. Group 1 sham group, rat underwent the same anesthetic and surgical procedure as the control group except for ligation of LAD, group 2 control group, rats underwent ligation for LAD and subjected to regional ischemia for 25 min and reperfusion for 2 hours, group 3 control vehicle, rats underwent ligation for LAD and received Irbesartan vehicle (normal saline), group 4 rat pretreated with Irbesartan 3mg/kg i.p.30 minuts before LAD ligation,. At the end of experiment (2 hr of reperfusion), blood samples were collected from the heart for measurement of plasma level of cardiac troponin I(cTn I). The heart were harvested, the apical side was fixed in 10% formalin for histological examination and ssDNA (apoptosis marker), the basal side was homogenized for the measurement of TNF-α,IL-1β,IL-6,MCP-1 and MIP-1alpha..

Results:

Compared with sham group, levels of myocardial TNF-α & IL-1β, IL-6,MCP-1.MIP-1alpha ; plasma cTn I were increased ($p<0.05$), Histologically,all rats in control group showed significant ($p<0.05$) cardiac injury and significant ($p<0.05$) apoptosis. Irbesartan significantly counteracted the increase in myocardium level of TNF-α, IL-1B,IL-6,MCP-1,MIP-1alpha,plasma cTnI & ssDNA ($P < 0.05$). histological analysis revealed that Irbesartan markedly reduced ($P < 0.05$) the severity of heart injury in the rats underwent LAD ligation.

Conclusion:

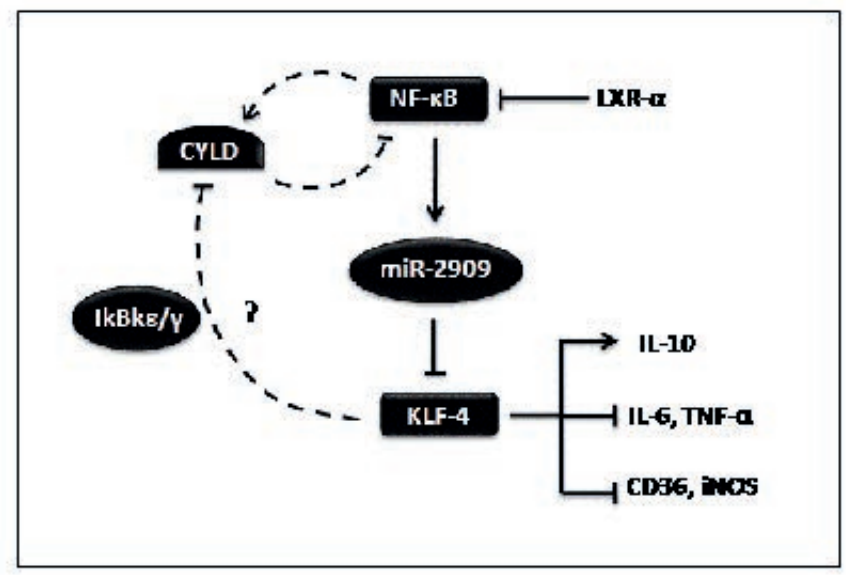
Irbesartan may ameliorate myocardial I/R injury in rats via interfering with inflammatory reactions & apoptosis induced by I/R injury.

No conflict of interest

ATHEROGENIC POTENTIAL OF BLOOD CELLULAR MIR-2909 IN HUMAN CORONARY HEART DISEASE SUBJECTS

M. Arora[1], D. Kaul[1], Y.P. Sharma[2]
[1]Experimental Medicine and Biotechnology, Post Graduate Institute of Medical Education and Research, Chandigarh, India
[2]Cardiology, Post Graduate Institute of Medical Education and Research, Chandigarh, India

NF-κB activation is a pivotal pro-inflammatory pathway in atherogenesis. Thus, uncovering its intracellular signaling cascades is indispensable to identify novel targets for therapeutic intervention. Our earlier observation had revealed that blood mononuclear cells from human Coronary Heart Disease (CHD) patients harbor a mutant LXR-α protein responsible for sustained NF-κB activation in these cells, contributing thereby to chronic inflammation involved in the initiation of CHD. In the present study, we show for the first time that NF-κB induces the expression of miR-2909 and that its expression increases with the severity of coronary occlusion. Further, we provide evidence that miR-2909 targets vasoprotective Kruppel like factor 4 (KLF4), thus tipping the balance towards a pro-inflammatory milieu. Elevated expression of miR-2909 also results in limited proliferation accompanied by increase in apoptosis and ROS production. Interestingly, miR-2909 expression also induces a significant increase in T regulatory ($CD4^+/CD25^+/FOXP3^+$) cell population. Collectively, our findings provide significant insights into the complex regulatory network governing the patho-physiology of atherosclerosis and can add a new dimension both to non-invasive early diagnosis of the disease as well as treatment at the epigenomic level.



No conflict of interest

INTEGRIN, ALLROUNDER MEDIATOR AT IN-STENT RESTENOSE

L. Li[1], M. Joner[1]
[1]Adult experimental cardiology, German Heart Centre, Munich, Germany

Purpose: Integrins are ubiquitous transmembrane receptors, which play a crucial role as a intermediator between cell and extracellular matrix in the proliferation, migration, spreading, survival and adhesion of cells. In the current project, we aimed to develop a new stent system with improved biocompatibility utilizing specific peptides or peptidomimetics targeted at integrin receptor subtypes..

Method: In the first step the differential expression of integrin subtypes present on human coronary smooth muscle - and endothelial cells (SMC and EC) was first examined *in vitro* by flow cytometry analysis. Subsequently, highly selective peptides or peptidomimetics were synthesized and functionally evaluated *in vitro*. In a second step optimized RGD peptides were coated on stents and implanted bilaterally into the iliac arteries of New Zealand White rabbits. After 28 days the RGD peptide coated stents were evaluated for vascular healing.

Results: *In vitro* assessment of differential integrin expression showed upregulation of integrin alpha 5 beta 1 on SMCs, while alpha v beta 3 integrin was found to be of utmost importance on quiescent ECs, which was confirmed by flow cytometry analysis. Coating of bare metal stents with peptides selective for alpha v beta 3 integrin resulted in a balanced attenutation of neointimal growth in the presence of complete endothelialization of stent surfaces.

Conclusions: Vascular SMCs and ECs displayed a differential expression of integrin receptors. The release of peptide specific for integrin alpha v beta 3 resulted in reduced neointimal growth in the absence of delayed vascular healing after stent implantation. Considering a substantial degree of delayed vascular healing in contemporary drug eluting stents, the currently applied coating technology may serve an innovative tool for stent coating in the future.

Conflict of interest

ROLE OF PPAR-ALPHA ACTIVATING CARDIOPROTECTIVE MECHANISMS IN A RAT MODEL OF TYPE-2 DIABETES AND MYOCARDIAL INFARCTION.

V. Oidor Chan[1], E. Hong Chong[1], M.A. Sánchez Mendoza[2]
[1]Pharmacobiology, CINVESTAV-Sede Sur, Mexico City, Mexico
[2]Pharmacology, Instituto Nacional de Cardiología "Ignacio Chávez"., Mexico City, Mexico

Type 2 diabetes (DM-2) increases oxidative stress and endothelial dysfunction. The lack of tetrahydrobiopterin (BH4), a key cofactor for nitric oxide (NO) production, has been related to endothelial dysfunction and DM-2.The aim of this work was to study if the activation of peroxisome proliferator-activated receptors α (PPAR-α) promotes a decrease in oxidative stress and increases BH4, eliciting a cardioprotective response in rats with DM-2 and myocardial ischemia followed by reperfusion (I/R). Neonate male Wistar rats (3-4 days old) were administered with vehicle (CT) or streptozotocin (DB) (STZ) (70 mg/kg, i.p.) to generate DM-2. Eight weeks after STZ administration both experimental groups were treated (14 days) with: 1.-Vehicle (0.9% saline); 2.-Fenofibrate (100 mg/Kg); or 3.-Metformin (100 mg/Kg). After treatment, rats underwent acute myocardial infarction (30min) followed by reperfusion (120 min.). Our results show that I/R increased coronary vascular resistance (CVR) and decreased cardiac work, fenofibrate and metformin decreased CVR and increased cardiac work in CT and DB rats. The antioxidant capacity of the organism decreased in DB rats with I/R, fenofibrate and metformin increased antioxidant capacity. BH4 production and NO bioavailability were lower in DB-I/R rats, fenofibrate and metformin increased BH4 and NO production. We conclude that the stimulation of PPAR-α by fenofibrate and metformin promotes an increase in the antioxidant capacity and normalizes NOS functioning leading to an improvement in the cardiac function of DM-I/R rats.

No conflict of interest

EFFECT OF INTERMITTENT FASTING ON CYTOKINE (IL-6 AND TNF-ALFA) LEVELS IN KNOCKOUT MICE LDL -/-

F. Reis de Azevedo[1], E. Sant'anna Melo[1], M.C. Jurado[1], A.F. Pastana[1], B. Caramelli[1]
[1]Heart Insititute, University of São Paulo Medical School, São Paulo, Brazil

Purpose: To investigate the effects of intermittent fasting (IF) on variables related to atherosclerosis development, such as cytokines levels.

Methods: Six weeks old LDL -/- Knockout mice were divided into three groups, receiving daily 5 grams of each diet: Atherogenic (AT) – rich in cholesterol, saturated fatty acids and low in fibers; DASH (Dietary Approaches to Stop Hypertension) – rich in mono and polyunsaturated fatty acids and low in sodium and Intermittent Fasting (IF) – Standard chow supplemented with micronutrients, every other day. By the end of fifteen weeks, blood was collected and analyzed for cytokine IL6 and TNFα, using REAL-TIME and ELISA.

Results: IF group showed an enhanced expression of IL6 RNAm when compared to DASH group. However there was no increase in protein synthesis. In AT group the opposite happened, reduced expression of IL6 RNAm with increase in protein synthesis. Figure 1 shows the values of RNAm expression for each group: 1,2 in IF group, 0,2 in DASH group and 0,1 in AT, $p<0,05$ between IF and DASH. Protein expression of IL6 was 50,10pg/ml in IF group, 60,31pg/ml in DASH and 230,54pg/ml, as shown in figure 2, $p<0,05$ between IF and AT. TNFα analysis showed an increased protein expression in AT group when compared to IF group. Values were 70,49pg/ml in IF group, 50,36pg/ml in DASH group and 250,90pg/ml in AT group, $p<0,05$ between IF and AT. We performed Student's t-test and all values were expressed as mean ± standard error of the media.

Conclusion: These results suggest that, in animal model, Intermittent fasting has a reduced atherogenesis effect than DASH or AT diet, represented by the lower protein expression of IL-6 and TNF-α.

Figure 1. IL6 RNAm Expression

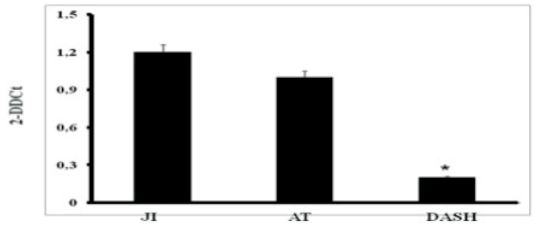
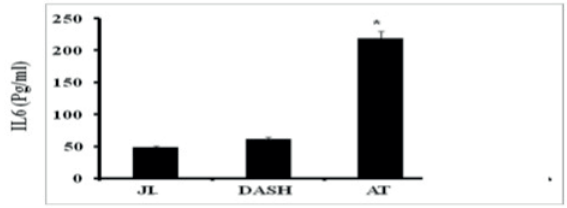


Figure 2. IL6 Protein expression



*** p<0.05 (IF)**
n=12

No conflict of interest

CORONARY ARTERY PREDICAMENT: DIFFERENT MALADIES OF SAME CONDUIT. CAN OCCAM'S RAZOR HELP?

V. Subbotin[1]
[1]*Vladimir M Subbotin, Vladimir M Subbotin, Madison, USA*

BACKGROUND:
Coronary artery conduit is vulnerable to maladies of different etiologies: atherosclerosis; spastic angina; Hurler's syndrome; post-transplant vasculopathy; restenosis following PCIs, or venous, arterial and prosthetic bypass grafting.

ANALYSIS:

A variety of etiology-aimed treatments were implemented: altering levels of blood lipids, vasodilatation, anti-rejection therapies, modulation of stents' or grafts' properties, etc. However, cure remains illusive. Nevertheless, all agree that the crucial event is cell proliferation in coronary tunica intima, i.e. in diffuse intima thickening (DIT), as an initiator or a major accomplice. Specific signals inducing DIT proliferation were suggested for each disease, or, alternatively, invoking principle of parsimony, different triggering non-specific stimuli were suggested unbalancing preexisted regulations. However, all pathogenesis models fall apart, if neointimal pathology of prosthetic coronary grafts is added. None of aforementioned models can incorporate prosthetic neointimal pathology.

HYPOTHESIS:

The arterial blood-tissue interface is sufficient for inducing arterial intimal phenotypes, which explains all facts. The model suggests that any cells capable of colonizing the interface (i.e. attaching and surviving), acquire the ability to form intimal phenotype. The hypothesis suggests that the vessel can be a residual artery, natural or prosthetic grafts. Intimal phenotype is expressed as one cell-layered endothelium or as normal variant – DIT. Both phenotypes always occur in a variety of species and are wildtype. Both phenotypes retain controlled proliferative capacity, which could be unbalanced by non-specific signals. Instead of studying non-specific signals, investigation of what controls switches of single cell-layer phenotype into normal DIT, and normal DIT into pathologic DIT could be useful.

No conflict of interest

PATHOGENESIS OF ABDOMINAL AORTIC ANEURYSMS: THE ROLE OF METALLOPROTEINASES AND THEIR INHIBITORS

C. Tefé-Silva[1], K.M. Mata[1], C.R. Fernandes[1], P.S. Prudente[1], C.M. Prado[1], M.A. Rossi[1], S.G. Ramos[1]
[1]Pathology, Faculty of Medicine of Ribeirao Preto - University of Sao Paulo, Ribeirão Preto, Brazil

Abdominal aortic aneurysm (AAA) represents a pathophysiological process of weakening and dilatation of the aortic wall, which is associated with atherosclerosis, inflammatory response and hemodynamic alterations. Degradation of the extracellular matrix by the matrix metalloproteinases (MMPs) and an imbalance between MMPs and their tissue inhibitors (TIMPs), have fundamental roles in the development of AAA. In this study, we used an experimental model developed in our laboratory to induce AAA by combining two potential causes of MMP secretion: inflammation and turbulent blood flow. Rats were divided into a control group (C) and aneurysm group (A). The group A received both an injury and extrinsic stenosis of the wall of aorta. The group C received a sham operation. The rats were euthanized at 3, 7 or 15 days post-surgery. Sections of the aorta including the aneurysm were collected for morphological studies and MMP-2 and -9 and TIMP-1 and -2 assays. Dilatation to more than 300% of the normal aortic diameter was observed in 65% of the group A. The AAA wall underwent an intense remodeling process characterized by a severe inflammatory response (neutrophils, macrophages and lymphocytes), considerable destruction of elastin fibers and deposition of collagen as well as an increase in the myofibroblast population and neovascularization. These alterations were directly related to the dramatic increase of the levels of MMP-2 and -9 and TIMP-1 and -2 throughout the study period. The MMPs cause massive destruction of elastin fibers which significantly remodels the arterial wall, resulting in dilatation and AAA formation.

No conflict of interest

SEARCHING OF CORRELATION BETWEEN GENOTYPE AND PHENOTYPE OF PATIENTS WITH NONSENSE SEQUENCE VARIANT GLN1233* IN GENE MYBPC3

P. Vanickova[1], J. Januska[2], I. Grochova[3], L. Badurova[1], V. Krhutova[1], A. Boday[1]
[1]Laboratory of medical genetic deptartment of molecular biology,
AGEL Research and Training Institute – Nov? Jicín Branch AGEL Laboratories, Nov? Jicín,
Czech Republic
[2]Department of cardiology, Hospital Podlesí, Trinec, Czech Republic
[3]Department of Internal Medicine-Cardiac Angiology I, St Ann Teaching Hospital, Brno,
Czech Republic

Familial hypertrophic cardiomyopathy (HCM) is autosomal dominant genetic disease of myocardium with frequence 1/500 in world population. HCM is heterogenic disease with variant expressivity, age of onset and symptoms severity. Penetrance is highly incomplete, patients can be without any clinical symptoms for many years. HCM is characterized by progressive hypertrophy of left and right ventricle and interventricular septum of any degree. Abnormal structure of cardiac muscle results to malfunction of heart rhythm, arrythmia which leads to palpitations and syncope, diastolic dysfunction responsible for dyspnea. All these heart defects can leads up to sudden cardiac death and heart failure in any age category also in asymptomatic patients.

Genetic heterogeneity is caused by mutations in approximately 29 genes that encode sarcomeric protein complex and Z-band proteins and other non-sarcomeric proteins. Mutations in 3 genes: *MYH7* (gene encodes heavy chain of β-myosin), *TNNT2* (gene encodes troponin T), and *MyBPC3* (gene encodes myosin binding protein C) cause 2/3 of all cases of HCM.

In group of selected 211 patients with diagnosis HCM we identified nonsense mutation p.Gln1233* c.3697C>T in 6 patients in unrelated families in *MyBPC3* gene. Next analysis confirm this variation in 3 relatives. This nonsense mutation p.Gln1233* causing development of premature termination signal in exon 33 at codon 1233, which was previously described as causal mutation, but in other sources it was found in control group of patients and reported as polymorphism.

In this work we try to compare phenotype and posssible causality of this variation in these possitive family members.

No conflict of interest

ALEGLITAZAR, A NEW BALANCED DUAL PPAR? AND PPAR? AGONIST, PROTECTS CARDIOMYOCYTES AGAINST SIMULATED ISCHEMIA-REPERFUSION INJURY

Y. Ye[1], S. Ling[1], M. Manhwan[1], T. Thomas[1], Y. Birmbaum[1]
[1]Biochemistry & Molecular Bio, University of Texas Medical Branch, Galveston, USA

Background: Peroxisome proliferator-activated receptor (PPAR) γ and α agonists attenuate ischemia-reperfusion injury and reduce myocardial infarct size. The protective effects of the thiazolidinediones (TZDs); however, are partially PPARγ-independent. Aleglitazar (ALE) is a new balanced non-TZD dual PPAR agonist, activating both PPARα and PPARγ.

Purpose: We assessed whether ALE protects cardiomyocytes aganst simulated ischemia-reperfusion injury (SIR).

Methods: Primary human cardiomyocytes (HCMs**)** and cardiomyocytes from PPARγ deficient (mCM^{PPARgKO}) or wild type (mCM^{WT}) mice were incubated for 24h with ALE at different concentrations and then subjected to SIR (2h hypoxia and 4h reoxygenation). Cell viability (MTT), apoptosis, caspase-3 activity, and the activation of the PI3K/AKT/eNOS survival pathway were determined.

Results: SIR decreased viability and increased apoptosis, caspase-3 activity and P-AKT and P-eNOS levels. ALE dose-dependently increased cell viability after exposure to SIR. Higher concentrations were needed in mCM^{WT} and mCM^{PPARgKO} than in HCMs to show an effect, consistent with lower affinity of ALE for rodent vs. human PPARα. ALE attenuated SIR-induced apoptosis and caspase-3 activity dose-dependently in all cell types. The effect of ALE on cell viability and apoptosis was partially blocked by siRNA against PPARα or PPARγ and completely blocked when siPPARα and siPPARγ were combined. ALE further increased AKT and eNOS phosphorylation. The effect of ALE on AKT and eNOS phosphorylation was partially blocked by siRNA to PPARα or PPARγ and completely blocked when siPPARα and siPPARγ were combined.

Conclusions: ALE protects cardiomyocytes from SIR. The effect is explained by dual activation of PPARα and PPARγ with downstream activation of the PI3K/AKT/eNOS survival signaling pathway.

No conflict of interest

INFLUENCE OF CO-CULTURING ADIPOCYTES AND AORTIC SMOOTH MUSCLE CELLS ON PROLIFERATION AND GENE EXPRESSION

J. Zdychova[1], I. Kralova Lesna[1], J. Maluskova[2], L. Janousek[3], S. Cejkova[1], L. Kazdova[1]
[1]Center for Experimental Medicine, Institute for Clinical and Experimental Medicine, Prague 4, Czech Republic
[2]Department of Pathology, Institute for Clinical and Experimental Medicine, Prague 4, Czech Republic
[3]Department of Transplant Surgery, Institute for Clinical and Experimental Medicine, Prague 4, Czech Republic

Background: Abnormal vascular smooth muscle cell (VSMC) proliferation is thought to play an important role in the pathogenesis of atherosclerosis. VSMC migration from the media to intima together with phenotypic modulations defined as switch from the „contractile“ to a „proliferation“ phenotype are involved in neointimal formation. Adipocytes produce several paracrine bioactive substances that could affect VSMC growth and migration and finally could contribute to development of proliferative vascular disease. Our study was focused on the effect of bioactive substances produced by epicardial adipocytes and visceral adipocytes on the VSMC proliferation level and gene expression.

Material and methods: The gene expression of cytokines interleukin-6 (IL-6), interleukin-8 (IL-8) and monocyte chemoattractant protein 1 (MCP1) together with cell proliferation were measured in primary cell cultures of human aortic smooth muscle cells after co-culturing with a conditioned medium obtained from primary cell cultures of epicardial and visceral adipocytes.

Results: VSMC co-cultivated with epicardial preadipocytes conditioned medium showed an increased expression of IL-6 (10.6-fold, $p<0.05$) and IL-8 (4.7-fold, $p<0.05$) compared with co-cultivating with matured epicardial adipocytes conditioned medium. Moreover, co-culturing with epicardial preadipocytes conditioned medium also affected VSMC proliferation level. We observed an increased VSMC proliferation in above mentioned group compared to control made up of VSMC with adding of non-conditioned medium.

Conclusion: Our results suggest that epicardial preadipocytes produced bioactive substances having a potentially stimulating effect on VSMC proliferation and gene expression that might locally contribute to development of proliferative vascular disease.

This study was supported by grant no NT 13188 from IGA MHC

No conflict of interest

CLINICAL OUTCOMES OF MULTIPLE STENT IMPLANTATION IN PATIENTS WITH ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION UNDERGOING PRIMARY PERCUTANEOUS CORONARY INTERVENTION

J. Ahn[1], T.J. Hong[1], J.H. Kim[1], J.S. Park[1], H.W. Lee[1], J.H. Oh[1], J.H. Choi[1], H.C. Lee[1], K.S. Cha[1]
[1]Internal Medicine, Pusan National University Hospital, Busan, Korea

Background: Percutaneous coronary intervention (PCI) with adoption of coronary stents since 1994, is an established managements for ST-segment elevation myocardial infarction (STEMI) and has been known relatively safe and effective resulting in better acute angiographic outcomes, reduction in the frequency of repeated stenosis or revascularization with proper antiplatelet agents. However, stent itself is related with major adverse cardiac events (MACE) depending on stent parameters such as length, diameter or structure materials under various clinical circumstances. In cases of long lesion, implantation of multiple stents is common in daily practice and the relationship between multiple stent implantation and MACE in acute MI is shown by a few studies but data is lack in the setting of STEMI. The aim of this study is to compare clinical outcomes between single and multiple-stent implanted groups in Korean patients with STEMI undergoing primary PCI.

Methods and results: Using data from Korea Acute Myocardial Infarction Registry, total of 1,668 patients with STEMI who proven to have single culprit vessel disease on primary PCI were enrolled in this study. The patients were divided into two groups: single (n=1,391, 83.4%) and multiple stent group (277, 16.6%). The primary outcome, 12-month cumulative MACE defined as composition of death, repeated MI or revascularization was significantly higher in the multiple stent group (10.4% versus 16.7%, p=0.010), which was mainly due to increased target lesion revascularization (3.9% versus 9.4%, p=0.001). By multivariate logistic regression analysis, multiple stent implantation was remained as a prognostic factor for MACE (OR=1.590, p=0.037). Cox-proportional hazard model also showed implanted stent number is associated with MACE significantly (HR=1.900, p=0.011).

Conclusion: This study demonstrated that multiple stent implantation is associated with increased 12-month cumulative MACE and is a predictor for clinical outcomes independent of stent length, diameter or type in Korean populations with STEMI undergoing primary PCI.

No conflict of interest

PREDICTIVE VALUE OF GLYCOSYLATED HEMOGLOBIN ON CARDIOVASCULAR OUTCOMES IN PREDIABETICS WITH ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION UNDERGOING PRIMARY PERCUTANEOUS CORONARY INTERVENTION

J. Ahn[1], T.J. Hong[1], J.H. Kim[1], J.S. Park[1], H.W. Lee[1], J.H. Oh[1], J.H. Choi[1], H.C. Lee[1], K.S. Cha[1]
[1]Internal Medicine, Pusan National University Hospital, Busan, Korea

Background: Prediabetes is well known to have a substantially greater cardiovascular risk as a result of insulin resistance, dysglycemia, dyslipidemia, hypertension, endothelial dysfunction or inflammation shown as in diabetes mellitus. Previous studies demonstrated impaired glucose tolerance and/or impaired fasting glucose are strong predictors of adverse outcome in acute coronary syndrome. However, the prognostic value of glycemic controlled level, determined by glycosylated hemoglobin (HbA1c), in prediabetic patients with ACS is still undefined. The aim of this study was to demonstrate the role of HbA1c at admission on major adverse cardiac events (MACE) in prediabetic patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI).

Methods: Using data from Korea Working Group on Myocardial Infarction (Kormi; February 2008-December 2011), this observational study included 1,536 patients who had not been diagnosed with DM before or after admission (HbA1c at admission less than 6.5%) with STEMI undergoing primary PCI. Patients were divided into two groups based on HbA1c at admission: non-diabetic (HbA1c≤5.6%, n=607, 39.5%) and pre-diabetic group (5.7%≤HbA1c≤6.4%, n=929, 60.5%).

Results: One-year cumulative MACE which was defined as a composite of mortality, nonfatal MI, repeated PCI or coronary artery bypass graft, was not different between two groups (7.4% vs 9.4%, p=0.182). After multivariate logistic analysis, HbA1c was not associated with occurrence of MACE (OR 1.009, 95% CI 0.579-1.759, p=0.975). We conducted subgroup analysis and divided pre-diabetic patients into two groups by the HbA1c level of 6.0%. Both of one-year cumulative MACE (11.1% versus 7.5%) and OR for MACE were lower (OR 0.586) in patients with higher HbA1c level, but did not show any statistical significances, either.

Conclusion: This study demonstrated HbA1c level at admission was not significantly associated with cardiovascular outcomes in prediabetic Korean populations with STEMI undergoing primary PCI.

Key words: glycosylated hemoglobin; ST-segment elevation myocardial infarction; prediabetes mellitus; major adverse cardiac events

No conflict of interest

EFFECTS OF COMBINATION THERAPY ON ISOPROTERNOL-INDUCED MYOCARDIAL INFARCTION IN A RAT MODEL

N.M. Alrasheed[1], N.M.I. Alrasheed[1], H. Attia[1], R. Ahmed[2], M. AL-Amin[1]
[1]Pharmacology and Toxicology, King Saud University, Riyadh, Saudi Arabia
[2]Anatomy, King Saud University, Riyadh, Saudi Arabia

In this study, we sought to investigate whether selenium, zinc, chromium and their combination offers a protective effect against myocardial infarction (MI) induced by isoproternol (ISO) in rats. To achieve this aim, rats were pretreated daily with oral zinc sulfate (30 mg kg^{-1}), chromium picolinate (400 µg kg^{-1}), selenium (0.1 mg kg^{-1}) and their combination for 28 days. At days 27 and 28, MI was induced by subcutaneous injection of ISO (85 mg kg^{-1}). Cardiac biomarkers, lipid profile, oxidative stress markers, tumor necrosis factor (TNF-α, inflammatory mediator) and vascular endothelial growth factor (VEGF, angiogenic marker) were measured. The results of this study demonstrated that ISO-induced MI was indicated by elevation of cardiac biomarkers, oxidative stress, hyperlipidemia, inflammatory response and impaired angiogenesis. Pretreatment with selenium normalized cardiac enzymes, troponine-I (11.5±0.4 Vs 18.66±0.6 pg/ml), TNF-α (25.05±2.3 Vs 45.37±2.3 pg/ml), VEGF (128.2±13.1 Vs 52.8±2.5 pg/ml) as well as reduced oxidative stress ($P < 0.001$). Selenium failed to correct dyslipidemia. Lipid profile significantly improved by chromium (Triglycerides: 99.5±5.4 Vs 137.3±10.8 mg/dl ($P<0.05$), Cholesterol: 80.9±1.8 Vs 94.4±3.8 mg/dl ($P<0.05$), HDL: 37.8±1.2 Vs 23.7±1.7 ($P<0.001$), LDL: 23.3±0.52 Vs 43±1.6 ($P<0.001$). Chromium also improved all other biochemical deviations except for VEGF. Zinc significantly reduced oxidative damage ($P<0.001$), triglycerides ($P<0.05$), cholesterol ($P<0.01$) and TNF-α ($P<0.001$) in addition to improved angiogenesis ($P<0.01$). Although showed improvement, combination therapy exhibited less prominent protection as compared to individual minerals. In conclusion, daily supplementation with microminerals may be promising for improving myocardial performance via preventing oxidative damage, induction of angiogenesis anti-inflammatory and/or anti-hyperlipidemic mechanisms.

No conflict of interest

IMPACT OF AN EXERCISE-BASED REHABILITATION PROGRAM ON THE SEXUAL FUNCTION OF MEN AFTER ACUTE MYOCARDIAL INFARCTION: RANDOMIZED CONTROLLED TRIAL

I. Begot[1], T.C.A. Peixoto[1], L.M. Duarte[1], R.S.L. Moreira[1], A.C.C. Carvalho[1], W.J. Gomes[1], S. Guizilini[1]
[1]Cardilogia, Universidade Federal de São Paulo, São Paulo, Brazil

Objetive: to evaluate the influence of exercise capacity in sexual function after a cardiovascular rehabilitation program based on unsupervised exercise (phase ii rehabilitation) in men who suffered acute myocardial infarction (ami).

Methods: 547 men with ami were eligible, at discharge were randomly allocated into two groups: **control group-gc** (n=45) received only a booklet with guidelines and weekly connections emphasizing the importance of maintaining daily life activites and correct intake of medication; **rehabilitation group-rg** (n=41) received a booklet with guidelines and underwent a rehabilitation program based on unsupervised cardiovascular exercise (progressive walking) for 30 days after discharge and received weekly calls to stimulate the implementation of the program and correct intake of medication. All patients underwent an evaluation at discharge and 30 days after hospital discharge. This evaluation consisted of a six-minute walk test (6mwt) and an evaluation of sexual function using the international index of erectile function questionnaire.

Results: erectile dysfunction was found in 89% of patients in the cg compared with 12% od rg after the exercise protocol ($p<0,05$). Regarding the functional capacity both groups showed an increase in 6mwt after the implementation of the program, though the rg had greater increase when compared to the cg ($p=0.01$).

Conclusion: an unsupervised exercise-basead cardiovascular rehabilitation program (phase ii rehabilitation) determined increased exercise capacity end improved sexual function in men after recent ami.

no conflict of interest

THE IMPACT OF GLYCEMIC VARIABILITY ON LOCAL CONTRACTILITY OF THE LEFT VENTRICULAR IN ACUTE PERIOD OF MYOCARDIAL INFARCTION

N. Beliaeva[1], L. Strongin[1], E. Baranov[2]
[1]Endocrinology and Internal disease, State Medical Academy, Nishny Novgorod, Russia
[2]ICU, State Medical Academy, Nishny Novgorod, Russia

Aims: To evaluate the influence of glycemic variability on wall motion index score (WMIS) and mortality withing 6 month in patients with acute period of myocardial infarction (MI) and type 2 diabetes mellitus.
Methods: Of 65 intensive care unit (ICU) patients with acute MI,30 were assigned to a 24 hours insulin infusion of short acting insulin, 35 were randomized as controls receiving subcutaneous injections of insulin to maintain the blood glucose level between 5 and 7,5 mmol/l.The baselin characteristics of the patients were comparable at randomisation. WMIS was measured by echocardiography in dynamic: on admission and after 21 days. The mean amplitude of glycemic excursions (MAGE) was used as a marker of glycemic variability.
Results: Daily bllood glucose variability during the first 24 hours of admission measured by MAGE was significantly higher in patients with the worst dynamic of WMIS, (p=0,0003). MAGE was highly correlated with the increased risk of six month-mortality,(p=0,006). In insulin infusion group MAGE was statistically lower 0,95 (0-3), than in the group with subcutaneous injections 3,8 (1,9-5,8),(p=0,045). Six month-mortality was 14,3% in the infusion group and 44,1% in the control group (p=0,04).
Conclusions: Wide glucose fluctuations have a deleterious effect on local contractility of the left ventricular in patients with MI. Maintaining the level of glycemia under very strict control using permanent insulin infusion resulted in significant reduction of glycemic variability and improves prognosis.

No conflict of interest

THE RIGHT VENTRICLE IN PATIENTS WITH ACUTE ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION. CHARACTERIZATION WITH CARDIOVASCULAR MAGNETIC RESONANCE.

C. Bonanad[1], M.P. López-Lereu[2], J.V. Monmeneu[2], S. García-Blas[1], F. Chaustre[1], V. Bodi[1], F.J. Chorro[1]
[1]Cardiology, Hospital Clinico Universitario de Valencia-INCLIVA, Valencia, Spain
[2]Cardiology, Hospital Clinico Universitario de Valencia-ERESA, Valencia, Spain

Objectives: We sought to characterize the right ventricular repercussion in patients with inferior ST-segment elevation myocardial infarction (STEMI) using cardiac magnetic resonance (CMR) and its correlation with clinical data at admission and at 6 months of follow-up.

Methods: We included 62 consecutive patients with a first STEMI and reperfused right proximal or medium coronary artery occlusion. We collected clinical and ECG data of RV involvement. CMR was performed at baseline and at 6-month follow-up, quantifying volumes, systolic function, wall motion abnormalities, myocardial edema and late gadolinium enhancement (LGE), a week and follow-up at 6 months. We used a 7-segment model to analyze the RV.

Results: Mean age was 62±11 years and 82% were male. 17 (27%) had hypotension. 40% had ST elevation in VR4. Half of the patients (31) showed wall motion abnormalities in the RV, 42% edema and 33% late enhancement in at least one segment. In 37% of the patients we observed depressed right ventricular ejection fraction (RVEF), although only in 5 cases it was moderate. ST elevation in VR4 showed high specificity (74%) but poor sensitivity (59%) for wall motion abnormalities (p=0.04). The presence of hypotension did not correlate with RV ischemic damage. CMR was performed in 34 patients at 6.7 ± 3.1 months of follow-up, showing significant improvement in RVEF in those who was previously depressed (47 ± 5 vs. 60 ± 8%, p <0.001), and in the wall motion abnormalities (dysfunctional segments: 3.1 ± 1.6 vs. 1.4 ± 1.7, p = 0.01), but no significant change in the number of segments with late gadolinium enhancement (LGE) (1.9 ± 1.6 vs. 1.4 ± 0.5, p = 0.14). Depressed RVEF was present only in 4 patients (12%) during follow-up.

Conclusions: RV ischemic injury in inferior STEMI occurs in half of the cases, but only compromises systolic function in 31% of them, being frequently slight grade. ST segment elevation in VR4 is a non-sensitive but more specific marker of RV injury. Severe hypotension is not associated with ischemic right ventricular involvement. At follow-up at 6 months there is an improvement in RVEF and contractility without significant changes in the extent of LGE.

No conflict of interest

TRENDS AND RESULTS OF STENT SELECTION IN A PROGRAM OF PRIMARY ANGIOPLASTY AS THE REPERFUSION TREATMENT FOR ACUTE MYOCARDIAL INFARCTION.

F. Cambronero[1], J. Nieto Tolosa[2], A. Fernandez Fernandez[2], A. Lopez Cuenca[3], A. Vidal[4], D. Lopez Cuenca[5], J.R. Gimeno-Blanes[5], J.A. Hurtado Martinez[5], M. Valdes Chavarri[5], E. Pinar Bermudez[5]
[1]Cardiology, Hospital Morales Meseguer, Murcia, Spain
[2]Cardiology, Hospital del Noroeste, Caravaca, Spain
[3]Cardiology, Hospital de Cieza, Cieza, Spain
[4]Cardiology, Hospital de Lorca, Lorca, Spain
[5]Cardiology, Hospital Virgen de la Arrixaca, Murcia, Spain

Use of drug-eluting stents in patients with acute myocardial infarction (AMI) remains an “off label” indication due to concerns regarding their performance in this patient subset. We present descriptive data from our population of patients with acute ST-segment elevation myocardial infarction treated with a drug eluting stent (DES) or bare metal stent (BMS).
Retrospective study in a cohort of 491 consecutive patients in a hospital with a primary angioplasty program. Data of clinical characteristics, procedure until the end of hospitalization and follow up were collected.
Between January 2006 and December 2010, 491 primary coronary intervention (PCIp) with the implantation of stents were performed, 257 with a DES and 234 with a BMS. Prevalence of HTA, DLP, Diabetes Mellitus and smoking was high and similar between both groups. Two of the comorbidities that influence the type of stent implanted was atrial fibrillation (3,9% in DES and 8,5% BMS) and severe valvulopathy (0,4% DES vs 2,6% BMS). The anterior descendant artery (AD) was more frequently affected in patients treated with DES (52.5%) compared with BMS (33,3%). Characteristic related to the procedure and complications were similar in both goups except that there was a tendency to implant a DES in patients with thrombosis of a stent previously implanted (5,4% vs 3%). Short and long term results are summarized in the attached table.

%	DES	BMS
Total mortality 30 days	5	9,4
Total mortality 1 year	6,6	12,4
Cardiac mortality 30 days	4	7
Cardiac mortality 1 year	5	8,5
AMI 30 days	1	1
AMI 1 year	3	3,4

Conclusions: Patients treated with a DES present with better short and long term results. Thrombosis of stents previously implanted and descendent anterior artery lesions are treated more frequently with DES. On the contrary, patients with comorbidities are treated more frequently with BMS.

No conflict of interest

18F-FDG PET/CT IN A TRANSGENIC MURINE MODEL OF MYOCARDIAL INFARCTION

S. Gargiulo[1,3], M.P. Petretta[2], M. Gramanzini[1,3], A. Greco[2,3], A. Cuocolo[1,2], A. Brunetti[1,2,3], M. Salvatore[1,2]
[1]Institute of Biostructures and Bioimages of National Council of Research,Naples, Italy
[2]Department of Advanced BioMedical Sciences, University Federico II, Naples, Italy
[3]CEINGE scarl, Naples, Italy

Aim: to investigate by molecular imaging the role of UCP3 protein in cardiac remodelling in a transgenic murine model of myocardial infarction.

Methods: 20 control, and 15 wild type and 5 UCP3 knockout infartuated C57Bl/6J mice, 9-16 weeks aged, were analyzed with ^{18}F-FDG PET/CT (eXplore VISTA GE, spatial resolution PET 1.4 mm FWHM, CT 200 µm). Left ventricle mean uptake values (SUV, MBq/ml) have been measured with eXplore VISTA analysis tool in a representative axial slice; surface area and volume have been calculated in vivo with MunichHeart software from polar maps.

Results:

Left ventricle ^{18}F-FDG mean uptake in healthy mice resulted 2.018±0.979 SUV/ 0.505±0.235 MBq/ml, whereas mean surface area and volume were 72.37 mm^2 and 56.62 µl respectively. ^{18}F-FDG uptake in infartuated mice resulted 2.57±0.73 SUV/0.66±0.38 MBq/ml for wild type, 4.48±1.21 SUV/1.12±0.37 MBq/ml for UCP3 knockout mice (p 0.0031 and 0.002, Wilcoxon test, respectively). Mean values of surface area and volume in infartuated mice were 91.87 mm^2 and 75 µl, more than 20.5% (p 0.0034), and 17.7% (p 0.18, Wald test) of healthy mice, respectively, without significative changes over time (p>0,05).

Conclusions:

UCP3 play a crucial role in mitochondrial energy metabolism and reactive oxygen species (ROS) generation. ^{18}F-FDG PET in genetically engineered mice have emerged as important research tool to understand myocardial ischemic disease processes and to evaluate potential target of therapies.

No conflict of interest

MARKERS ON CHROMOSOME 2 AND 9 AND RISK OF THE MYOCARDIAL INFARCTION IN CZECH POPULATION. GENDEMIP STUDY.

J. Hubacek[1], V. Adamkova[2], V. Stanek[3], J. Pitha[1]
[1]DEM, Institute for Clinical and Experimental Medicine, Prague, Czech Republic
[2]DPC, Institute for Clinical and Experimental Medicine, Prague, Czech Republic
[3]CC, Institute for Clinical and Experimental Medicine, Prague, Czech Republic

Background: Myocardial infarction (MI) is the leading cause of death in industrialized countries. The traditional cardiovascular risk factors (dyslipidemia, hypertension, obesity, smoking and diabetes) for myocardial infarction are responsible for approximately 50 % of MI cases. Attention is recently focused on those genetic variants that are not associated with these conventional risk factors. Among them are the rs2943634 and rs1075974 markers within the “gene-free” areas of chromosomes 2 and 9, recognised as risk factors for MI in Western European populations. We analyzed the relationship between rs2943634 and rs1075974 variant and the risk of acute coronary syndrome (ACS) in the Czech population.

Methods: Both rs2943634 (C?A) and rs1075974 (A?G) variants were successfully analyzed by PCR-RFLP in 1,144 control men (aged under 65 years, post MONICA study) and in 467 consecutive patients, with ACS (men, up to age 65 years). ANOVA and chi-square were used for statistical analysis.

Results: Polymorphisms were not associated with the plasma lipids, blood pressure, obesity, smoking or diabetes. We confirmed, however, both rs2943634 and rs1075974 are significantly associated with development of ACS (P = 0.025 for marker on chromosome 9 and P = 0.007 for marker on chromosome 2). Detailed analysis of the combinations of the individual genotypes revealed, that the carriers of the rs2943634 G allele and rs1075974 AA genotype were represented less likely among patients with ACS than in the control group (6.6% vs. 12.7%, P = 0.0001, OR 0.49, 95% CI 0.33–0.73).

Conclusion: Variants on chromosome 2 and 9 are important risk factors for ACS development also in the Czech Slavonic population. The causal relationship remains to be elucidated.

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No conflict of interest

COMPARISON OF 1-YEAR CLINICAL OUTCOMES BETWEEN INVASIVE AND CONSERVATIVE TREATMENT STRATEGIES FOR STEMI COMPLICATED BY CARDIOGENIC SHOCK IN ELDERLY PATIENTS

K. Jung[1], K.H. Kang[1], S.C. Park[1], Y.J. Choi[1]
[1]Cardiology, Eulji University Hospital, Daejeon city, Korea

Objectives: We investigated the benefit of an invasive strategy for elderly (≥75-year-old) patients with acute ST-segment elevation myocardial infarction (STEMI) complicated by cardiogenic shock (CS). **Background:** The benefit of an invasive strategy for elderly patients with STEMI complicated by CS is controversial. **Method:** Data from 409 elderly patients with CS out of a total of 6,132 acute STEMI cases enrolled in the Korea Acute Myocardial Infarction Registry between January 2008 and June 2011 were collected and analyzed. In-hospital deaths and 1-month and 1-year survival rates free from major adverse cardiac events (MACE; defined as death, myocardial infarction, and target vessel revascularization) were compared between patients who had received invasive (n = 310) and conservative (n = 56) treatment strategies. **Result:** Baseline clinical characteristics were not significantly different between the 2 groups. There were fewer in-hospital deaths in the invasive treatment strategy group (46.4% vs. 23.5%, p < 0.001). In addition, the 1-year MACE-free survival rate after invasive treatment was significantly lower compared to the conservative group (51% vs. 66%, p = 0.001). **Conclusion:** In elderly patients with acute STEMI complicated by CS, an invasive strategy is superior to a conservative one at the 1-year follow-up.

No conflict of interest

CHARACTERIZATION OF PHARMACOLOGICALLY INDUCED TAKOTSUBO SYNDROME: IMPLICATIONS FOR TREATMENT AND MECHANISMS

M.D.M. David Murdock[1], D.O. Robert Murdock[2], M.T.C. Jeffrey Kaliebe[2], M.T. Emmalee Nichols[2], B.S. Anna Drewry[2], M.A. Rita Murdock[3], R.N. Karen Olson[2]
[1]Cardiology, Aspirus Heart & Vascular Institute, Wausau, USA
[2]Research & Education, Aspirus Heart & Vascular Institute, Wausau, USA
[3]Resarch & Education, Academic Enterprise, Wausau, USA

Background: Takotsubo Syndrome (TS), is characterized by sudden onset of localized left ventricular (LV) dysfunction in the setting of clinical features suggesting an acute coronary syndrome. It occurs much more commonly in women and is frequently associated with emotional or physical stress. Sporadic cases of pharmacologically induced TS (PITS) have been reported but full characterization of PITS has not occurred. Such investigation may provide insight into mechanisms and treatment of TS.

Purpose: Characterize PITS with respect to presentation, outcome, and instigating agents.

Methods: Local cases were combined with literature review of PITS cases. For each case, sex, age, presentation, presumed causal agent, electrocardiography, ejection fraction (EF), LV contraction abnormalities, and outcome were compiled.

Results: Ninety four patients (90% female) were identified. Direct or indirect beta adrenergic agonist accounted for 82% of PITS which includes epinephrine (EPI) alone (30%) or in combination with other catecholamines (6.4%), dobutamine (DOB) (17%), or any other beta-adrenergic enhancing agents (24%). Primary vasoconstrictors caused 12% of PITS. Administration errors caused 20% of PITS but 43% of PITS due to EPI. All DOB induced PITS occurred during stress echocardiography. ST segment elevation (45%) was common. Apical ballooning occurred in 64%. The mean EF was 32±11%. 38% developed congestive heart failure (CHF) and 29% required hemodynamic support. Mortality was infrequent (1.1%). All survivors normalized their EF.

Conclusions: The strong female preponderance mirrors spontaneous TS and suggests an increased female susceptibility at the myocardial level. EPI is the most frequent causal agent for PITS and was commonly associated with dosing errors. PITS was frequently associated with CHF and severe LV dysfunction requiring hemodynamic support. Vasoconstrictors caused a small minority of PITS. Patients with a TS history should avoid DOB stress testing or agents known to cause PITS. Beta agonists for hemodynamic support should be avoided if possible.

No conflict of interest

RESCUE ANGIOPLASTY ANT FARMACOINVASIVE STRATEGY POR STEMI TREATMENT IN NON PCI CAPABLES

HOSPITALS IN REGIÓN DE MURCIA (SPAIN)

J. Nieto Tolosa[1], F. Cambronero Sanchez[2], J.R. Gimeno Blanes[3], J. Hurtado Martinez[3], A. Lopez Cuenca[3], A. Fernandez Fernandez[1], J. García de Lara[3], J. Lacunza Ruiz[3], R. Valdesuso Aguilar[3], E. Pinar Bermudez[3]

[1]Cardiology, Hospital Comarcal Noroeste, Caravaca de la Cruz, Spain

[2]Cardiology, Hospital Morales Meseguer, Murcia, Spain

[3]Cardiology, Hospital Clínico Universitario Virgen de la Arrixaca, Murcia, Spain

Introduction.- Primary angioplasty (PCIp) has demonstrated its superiority in terms of efficacy and security in the treatment of STEMI. Nowadays it is the recommended option, although its main limitation is still the geographical availability. In hospitals without PCIp availability 24/7, a valid option is the pharmacologic reperfusion (thrombolysis, TL). In our region an Integral Plan for the Treatment of Ischemic Heart Disease consider this reperfusion option as an alternative to those patients that can not receive prompt PCIp. Methods: Retrospective analysis of patients diagnosed with STEMI between 2006-2010 in two second level hospitals, more than 70 km from PCI capable hospital (third level). After a STEMI diagnosis was made, those patients without contraindication received thrombolysis (TL) and were sent to a third level hospital. If reperfusion was not achieved, rescue angioplasty was performed. Otherwise an elective coronariography was scheduled (farmacoinvasive strategy, FI). Results: We included 147 patients with STEMI treated with TL. 36.7% of them required rescue PCI. Coronariography was performed in 88.2% of patients with successfull TL (FI). Table 1 shows angiographic features. Mean follow-up: 1210 (± 523) days. There were no significant differences in total mortality (4 FI vs 4% rescue PCI), cardiac mortality (4 vs 2%), AMI incidence (2 vs 0%), stroke (2 vs 2%) or reestenosis (1 vs 0%) at 30 days (previous data) and at 1 year follow-up (8 vs 6%, 6 vs 2%, 4 vs 0%, 2 vs 2%, 1 vs 4%, respectively). Conclusion: Farmacoinvasive strategy achieves good clinical results in STEMI patients with long distances to PCI-capable hospitals, even in patients without reperfusion criteria and need of rescue PCI.

	Farmacoinvasive	Rescue
Evolution time (h)	2,51 (± 2,1)	2,1 (± 1,51)
% <3 horas	82	86,8
Time to PCI (h)	68,71 (±68.9)	3,59 (±2.2)
Responsible vessel: (%)	44,3	51,92
DA	16,4	9,6
CX	39,2	38,46
CD	0	0
LM		

Nº vessels with lessiones (%) 0 1 2 3	17,1 54,9 17,1 11	0 66 24,5 9,4
Trombectomy (%)	3,2	18,5 (70% éxito)
Predilatacion (%)	38,2	40,7
GpIIb/IIIa inhibitor (Abciximab) (%)	15,2	35,2
TIMI flow 3 final (%)	97,4	90,6
Nº stents	1,34 (± 1,17)	1,38 (± 0,99)
DES (%)	71	38,8
Length stents (mm)	28,63 (± 20,09)	25,52 (± 16,94)
Diameter máx. stents (mm)	3,21 (± 0,52)	3,33 (± 0,46)
Procedure success (%)	86,3	94,4
2nd time revascularization (%)	10,8	20,4
Complete revascularización (%)	77,8	71,7
Procedure complications (%)	0	0

No conflict of interest

PRIMARY ANGIOPLASTY OF STENT THROMBOSIS: CLINICAL PROFILE AND OUTCOMES

J. Nieto Tolosa[1], F. Cambronero Sanchez[2], J.R. Gimeno Blanes[3], A. Lopez Cuenca[4], J. Hurtado Martinez[3], J. García de Lara[3], F.J. Lacunza Ruiz[3], R. Valdesuso Aguilar[3], E. Pinar Bermudez[3], M. Valdés Chávarri[3]
[1]Cardiology, Hospital Comarcal del Noroeste, Caravaca de la Cruz, Spain
[2]Cardiology, Hospital Morales Meseguer, Murcia, Spain
[3]Cardiology, Hospital Clínico Universitario Virgen de la Arrixaca, Murcia, Spain
[4]Cardiology, Hospital de la Vega Lorenzo Guirao, Cieza, Spain

Introduction: Stent thrombosis is an uncommon but serious complication of PCI with stenting, usually presented as STEMI. Death and myocardial infarction are frequent complications of stent thrombosis, and outcomes appear to be worse than in individuals with ACS due to plaque rupture in a native coronary artery. *Objective*: Analyze the clinical profile and outcomes of a population of STEMI patients caused by definite stent thrombosis (ST) (according to ARC criteria) treated with primary PCI.*Methods*: Retrospective study of consecutive STEMI patients caused by a definite stent thrombosis in a reference hospital with primary PCI 24/7 between 2006-2010.*Results*: We included 25 definite ST patients (4.3% of total primary-PCI performed in the same period), 40% BMS. The distribution of early, late and very late stent thrombosis is shown in table 1. The anterior descendant artery (52%) was the more frecuently affected, followed by right coronary artery (32%). All cases of early ST except one were on dual antiplatelet therapy, and the rest of cases were en single antiplatelet therapy (mainly AAS). Final TIMI 3 flow was achieved in 96% of cases. Thrombus aspiration performed in 46 % (successfull 73%). A new stent was used in 84% patients (66% DES). Outcomes are shown in table 2.*Conclusion*: ST is a not very rare cause of primary PCI, that affects both previous BMS and DES use, even years after its implantation. Angioplasty gets high degree of success, and in the majority of cases a new stent is used (mainly DES), with good short and long-term outcomes.

Clasification	Early	Late	Very late
BMS	4	0	6
DES	5	1	9

Outcomes (%)	30 days	1 year	5 years
CV dead, AMI, stroke, reestenosis	8	20	40
Cardiovasc dead	4	4	12
AMI	0	4	16
Stent thrombosis	0	0	8 (very late)

No conflict of interest

CLINICAL PROFILE AND OUTCOMES OF STEMI PATIENTS WITH NEAR-NORMAL CORONARY ARTERIES

J. Nieto Tolosa[1], F. Cambronero Sanchez[2], J.R. Gimeno Blanes[3], J.R. Hurtado Martinez[3], M. Bru Cartagena[4], R. Zoyo Lopez-Navarro[5], F. Celdran Gil[5], A.L. Valcarcel Ruiz[6], N. Martinez Jimenez de Cisneros[6], E. Pinar Bermudez[3]
[1]Cardiology, Hospital Comarcal del Noroeste, Caravaca de la Cruz, Spain
[2]Cardiology, Hospital Morales Meseguer, Murcia, Spain
[3]Cardiology, Hospital Virgen de la Arrixaca, Murcia, Spain
[4]Emergency Service, Hospital Virgen del Castillo, Yecla, Spain
[5]Emergency Service, Servicio Murciano Salud, Murcia, Spain
[6]Internal Medicine, Hospital Virgen del Castillo, Yecla, Spain

Introduction: Obstructive coronary artery disease is not detected in up to 14% of patients who present with acute coronary syndrome, typically young women and with fewer cardiovascular risk factors (CVRF). Its prognosis has typically been excellent. However, different recent results show that these conditions are not always so benign. ***Objetive***: Analyze the clinical profile and outcomes of a population with STEMI and near-normal coronary arteries. ***Methods***: Retrospective study of STEMI patients treated with medical or mecanical reperfusion in a PCI-capable hospital between 2006-2010. STEMI diagnosis confirmed with analysis, clinical y ecocardiography evolution. Data of clinical characteristics and follow up were collected. ***Results***: 24 (3.6%) of 667 STEMI patients did not present significant coronary disease in coronariography and did not receive angioplasty nor stent placement. They were more often women (42 vs 21%), younger (53.08 vs 64.12 yr), and with a trend toward less traditional risk factors (n.s.). The size of infarction (estimated by CK-MB) was smaller (95.27 vs 179.9 (mean); p=0.024) and LVEF was higher (57.05% vs 52.46%; p=0.052) in patients without lesions. Mean follow up 989 (±574,9) days. Outcomes during the follow up are shown in table 1. ***Conclusion***: STEMI patients without significant coronary lesions, have a different clinical profile (younger, more often women) and a lower risk of cardiovascular dead or stroke than pacients with stent placement, but the same risk of reinfaction.

Outcomes (%)	**No lesions**	**Lesions**
CV dead, AMI, stroke (1 yr)	4	13
AMI (1 yr)	4	3
CV dead (1 year)	0	7

No conflict of interest

NURSE-LED INTERPERSONAL COUNSELING FOR DEPRESSIVE SYMPTOMS IN PATIENTS WITH MYOCARDIAL INFARCTION

O. Oranta[1], S. Luutonen[2], R.K.R. Salokangas[2], T. Vahlberg[3], H. Leino-Kilpi[1]
[1]Nursing Science, University of Turku, Turku, Finland
[2]Department of Psychiatry, University of Turku, Turku, Finland
[3]Biostatistician, University of Turku, Turku, Finland

Depression is not always treated adequately after myocardial infarction (MI). Interpersonal counseling (IPC) is a brief and easy-to-adopt treatment for depressive symptoms designed for non-psychiatric patients. This study examined the outcomes of IPC on depressive symptoms, distress, health-related quality of life (HRQOL) and recovery experienced by the patients after MI.

Acute MI patients (n=103) were randomized into the IPC-intervention group (n=51) and the control group (n=52) with standard care. We studied patients in hospital and at 6 and as well as 18 months after discharge from hospital using validated questionnaires: Beck's Depression inventory, Symptoms Checklist-25 and EuroQol-5D. The patients in both groups (n=40) kept diaries for 6 months and were interviewed (n=91) at 18 months regarding their experiences of MI.

During the follow-up, depressive symptoms and distress decreased statistically significantly (p=0.009) in the intervention group compared with the control group. No differences in the changes of HRQOL were found between the groups during the follow-up. However, considering patients under 60 years, the effect of IPC was significant in the intervention group compared with the control group. Five main categories with supporting and inhibiting factors in recovery were identified: clinical and physical, psychological, social, functional and professional categories.

These results justify adopting depression screening and IPC as part of routine care after MI. Recovery after MI seems to consist of many supporting and inhibiting factors regardless of IPC. The result is important in developing treatment after MI, and indicates more specific topics for further studies.

No conflict of interest

THE EFFECTIVENESS OF THE ACUTE TREATMENT OF INFARCTING MYOCARDIUM IN THE ELDERLY

J.R. Siles Rubio[1], A. Ramirez Moreno[1], J.C. Salas Serantes[2], C. Pera Rojas[3], F.J. Martínez García[4], R. Bravo Marqués[4], L. Iñigo García[4], J. Muñoz Bellido[4], M. Pombo Jiménez[4], L. Fernández López[4]
[1]CARDIOLOGY, HOSPITEN ESTEPONA, Málaga, Spain
[2]INTENSIVE CARE, HOSPITEN ESTEPONA, Málaga, Spain
[3]ANESTHESIOLOGY, HOSPITEN ESTEPONA, Málaga, Spain
[4]CARDIOLOGY, Hospital Costa del Sol. Marbella, Málaga, Spain

BACKGROUND: Elderly patients presenting with STEMI are recognized as a high-risk sub-group, and are increasingly prevalent. Primary PCI is sometimes delayed or withheld from such patients due to perceived risks. There is limited data on the relative efficacy and safety of Primary PCI in the elderly. The goal of this study was to compare differences and outcomes between elderly and younger patients with STEMI treated with Primary PCI, with respect to time to treatment, procedural success, clinical outcomes, and complications.

METHODS: We evaluated consecutive patients over a 48-month period who presented with STEMI undergoing primary PCI. Patients aged 75 or greater were defined as elderly. Intra-procedural and post-procedural data was derived from existing databases that included mode of patient presentation, time to treatment, procedural success, length of stay, and complications including in-hospital mortality. Symptom onset-to-1st medical contact and 1st medical contact-to-balloon times were sub-categorized according to mode of presentation (EMS to cath lab or ED, self-presentation to ED). Primary endpoint was a composite of in-hospital mortality and stroke. Patients with non-obstructive CAD were excluded from analysis.

RESULTS: A total of 85 consecutive patients were analyzed, 20 (23%) of whom were elderly. 1st medical contact-toballoon times were only significantly longer for elderly patients who were taken directly to the cath lab by EMS (75 vs. 93 mins, p=0.02). Procedural success rate was similar for elderly (92.3%) and younger (93.6%) patients. Median length of stay was similar between elderly (4) and younger (3) patients (p_ns). A composite of in-hospital mortality and stroke was significantly higher in the elderly (11.5% vs 3.0%, p= 0.005). All other complication rates were statistically similar.

CONCLUSIONS: Compared with younger patients, major inhospital complication rates are higher among the elderly who undergo Primary PCI, although procedural success rates are similar. When compared to historical STEMI mortality and complication rates, these data suggest that Primary PCI in the elderly is an effective and timely treatment option that may reduce mortality and morbidity in patients with this condition.

No conflict of interest

COMPARISON OF REPERFUSION EFFICACY OF THROMBUS BETWEEN WITH AND WITHOUT DISTAL PROTECTION DURING PRIMARY PCI IN ACUTE STEMI PATIENTS

H. Inoue[1], S. Omura[1], E. Ejima[1], T. Mori[1], K. Takenaka[1], N. Kawamura[1], K. Numaguchi[1], E. Mori[1], A. Asoh[1], T. Nakamura[1], K. Hiyamuta[1], S. Satoh[1]

[1]Cardiology and Clinical Research Institute, NHO Kyushu medical Center, Fukuoka, Japan

Group (n)	A (104)	A + DP (72)	p
TIMI flow grade 2-3, n (%)	77 (74)	68 (94)	0.0005
MBG 2-3, n (%)	74 (71)	63 (88)	0.0103

	A	A + DP	p
Follow-up study, n (%)	62 (60)	52 (72)	0.1085
LVEF at PCI (%)	56 [48-62]	52 [46-59]	0.1161
Post-LVEF (%)	57 [49-64]	55 [47-59]	0.1876
LVEDVI at PCI, mL/m^2	57 [51-71]	62 [50-71]	0.7219
Post-LVEDVI, mL/m^2	65 [54-74]	66 [56-74]	0.9682
LVESVI at PCI, mL/m^2	26 [20-35]	27 [22-38]	0.1621
Post-LVESVI at PCI, mL/m^2	28 [21-38]	29 [23-35]	0.4506

Purpose: We inspected a hypothesis that thrombus aspiration with distal protection is superior to simple thrombus aspiration in primary PCI.

Methods: Consecutive 176 STEMI patients were enrolled prospectively and were assigned to thrombus aspiration group (A, n=104) or thrombus aspiration with distal protection group using a filter-device system (A+DP, n=72). We compared angiographic reperfusion grades, LV function, and clinical outcomes between the two groups.

Results: There were no significant differences in age, sex distribution, the onset-to-reperfusion time, the peak levels of creatine kinase, or 6-month mortality between the two groups. The achievement rate of TIMI flow grade 2-3 and myocardial blush grade (MBG) 2-3 was higher in A+DP than in A. In patients who underwent the follow-up catheterization 6 months after PCI, there were no significant differences in LVEDVI, LVESV, or LVEF between the two groups at the time of PCI and 6 months after PCI, respectively.

Conclusions: Thrombus aspiration with distal protection may be more effective in the initial restoration of coronary blood flow than thrombus aspiration alone, but it may not be superior to thrombus aspiration in preventing LV remodeling or preserving LV function in STEMI patients.

No conflict of interest

INDICATION OF COUNTERPULSATION TREATMENT IN ACUTE CORONARY SYNDROME ON THE BASIS OF THE EXTENSION OF THE MYOCARDIAL AREA AT RISK

G. Szabó[1], I. Rácz[1], G. Vajda[1], I. Edes[1], Z.S. Koszegi[1]
[1]Department of Cardiology, Univesity of Debrecen, Debrecen, Hungary

Background

In the last years there are many unclear statements and clinical evidences in the use of intra-aortic balloon pump (IABP) during high risk percutaneous coronary intervention (PCI). One reason for the uncertainty can be the lack of determination and consideration of the left ventricular area at risk with decent power.

Aim and Method

Holistic Coronary Care (HCC) software was developed in our department. In this program an algorithm was generated to correlate the epicardial coronary arteries and the left ventricular segments on the basis of the coronary angiogram. We aimed to retrospectively study the data of patients in ACS treated with IABP in our department in 2009. The extension of the left ventricular area at risk was calculated with the HCC. Occurrence of death, urgent coronary artery bypass graft operation (CABG) were analyzed. The cases were study separately when the IABP therapy was started on the basis of the clinical status but later than the PCI (rescue IABP). The duration of IABP – use was also analyzed in all subgroups.

Results

53 patients were treated with ABPM in acut coronary syndrome. Adverse events (death, CABG and rescue IABP) were detected in 29 cases. According to the Receiver Operating Curve (ROC) analysis, the left ventricular area at risk determined with the HCC showed the occurrence of adverse events with 9.99 segments (58.8%) cut off value (p=0.024). Analyzing the duration of the IABP treatment in different subgroups, significantly longer time was detected in the rescue IABP subgroup than in the subgroup with elective IABP treatment without adverse event: 6.6$\pm$ 1.5 vs. 4.5$\pm$ 2.8 days (p<0.04).

Conclusion

The precise determination of ventricular area at risk helps the correct indication of IABP counterpulsation started in optimal time. The correct evaluation of patients decreases the mortality and the duration of IABP use.

No conflict of interest

TWO YEAR CLINICAL OUTCOMES AFTER SIROLIMUS-ELUTING STENT IMPLANTATION FOR THE TREATMENT OF CORONARY ARTERY DISEASE

J. Adam[1], A. Harrypaul[1], R. Dyer[2], W. Rmaih[1]
[1]Biomedical and Clinical Technology, Durban University of Technology, Durban, South Africa
[2]Cardiology, Ethekwini Hospital and Heart Centre, Durban, South Africa

Background:

Coronary artery stents are known to reduce rates of restenosis after coronary stenting, but it is uncertain how long this benefit is maintained. Clinical data has raised concerns that drug-eluting stents are associated with increased rates of late stent thrombosis, death or myocardial infarction.

Objectives:

To evaluate the safety and reliability of sirolimus-eluting stents in real-world practice in South Africa out to two years.

Methods:

From January 2008 to June 2008, 30 patients were enrolled in the study after implantation of one or more sirolimus-eluting stents. We evaluated clinical follow-up information for up to two years after the implantation of Cypher® Select stents in 30 patients with 35 lesions.

Results:

Mean patient age was 62.33 +/- 10.99 years, 7 percent were diabetic and 30 percent presented with acute myocardial infarctions. The procedure's success rate was 100 percent for the sirolimus-eluting stent implantation, and follow-up rates were 100 percent. Mean total stent length was 22.32 +/- 6.63 mm, with 13 percent receiving more than one stent. Two year freedom from mortality, myocardial infarction, target vessel revascularization and stent thrombosis was 100 percent. Dual antiplatelet therapy was taken by 100 percent at 1 month, 53 percent at 6 months, 40 percent at 1 year and 0 percent of patients at 2 years. The rate of survival free of myocardial infarction, bypass surgery and repeated angioplasty for stented lesions was 100% at two years.

Conclusions:

Treatment of lesions with sirolimus-eluting stents is associated with a sustained clinical benefit two years after device implantation.

No conflict of interest

SEQUENT PLEASE PACLITAXEL-COATED BALLOON ANGIOPLASTY FOR DE NOVO CORONARY LESIONS: A LONG-TERM FOLLOW-UP STUDY

J. Benezet[1], I. Sanchez-Perez[1], F. Lozano[1], N. Pinilla[1], F. Higuera[1], Y. Hessein[1], J.M. Arizon[2]
[1]Interventional Cardiology, Hospital General Universitario de Ciudad Real, Ciudad Real, Spain
[2]Cardiology, Hospital General Universitario de Ciudad Real, Ciudad Real, Spain

Background: Paclitaxel-coated balloons (PCB) have been demonstrated to be successful for the treatment of in-stent restenosis; however, their role in the treatment of de novo lesions is unclear. This study aimed to evaluate the long-term safety and efficacy of the second-generation SeQuent Please PCB for the treatment of de novo coronary lesions.
Methods: Between May 2009 and April 2011, all consecutive patients with de novo coronary lesions treated with the SeQuent Please PCB at our institution were prospectively included. Bare-metal stent (BMS) were implanted if the result after PCB therapy alone was not satisfactory because of recoil, residual stenosis or dissections. Patients were followed up for 24 months by clinical observation. The primary endpoint was the clinically driven target lesion revascularization (TLR) rate at 24 months. The secondary endpoint was the rate of major adverse cardiac events (MACE: defined as a composite of cardiac death, myocardial infarction, and TLR) at 24 months.
Results: 53 patients with 56 lesions were included. Mean age was 66.1±11.9 years. 62.5 % were male and 50 % were diabetics. The majority of patients presented with unstable angina (44.6%). The target lesion was mainly located in the left anterior descending coronary artery (60.7%) and 23.2 % were bifurcation lesions. The mean reference vessel diameter was 2.4± 0.4 mm and the mean target lesion length was 18.1±6.2 mm.Procedural success was 98.2%. Coronary dissection occurred in 7 patients (12.5 %) and no vessel thrombosis was documented. Additional BMS was implanted in 14 target lesions (25 %). Follow-up rate was 94.3 %. The TLR rate at 24 months was 5.4 %. The MACE rate at 24 months was 8.9 %, with 1.8 % cardiac death and 3.6 % myocardial infarction.Baseline and procedural data for patients with PCBs versus PCBs plus BMS did not differ. The TLR and MACE rates did not differ between PCB angioplasty with and without additional BMS implantation (TLR: 0% vs.7.1%, p=0.56; MACE: 7.1 % vs. 9.5 %, p = 0.78).
Conclusions: Treatment of de novo coronary lesions with the second-generation SeQuent Please PCB provides good clinical outcomes demonstrated by the low TLR rate and low MACE rates at long-term follow-up.

No conflict of interest

CLINICAL PROFILE AND OUTCOMES OF PATIENTS WITH VERY LATE THROMBOSIS AFTER BARE-METAL STENT IMPLANTATION

I. Gomez Blazquez[1], S. Fernandez Barbeira[1], G. Bastos Fernandez[1], A.A. De Miguel Castro[1], V.A. Jimenez Diaz[1], A. Ortiz Saez[1], J.A. Baz Alonso[1], A. Iñiguez Romo[1]
[1]Interventional Cardiology, Hospital Meixoeiro, Vigo, Spain

Purpose: Stent thrombosis (ST) occurring beyond 1 year after bare-metal stent (BMS) implantation is a rare complication, and there are few data on clinical characteristics and prognosis of patients Our aim was to evaluate the profile and outcome in patients with very late ST after BMS implantation. Methods: A total of 11,266 coronary angiographies in patients with acute coronary syndromes were performed at our center, from 2006 to 2012. During this period we identified 34 consecutive patients with angiographically confirmed very late ST related to BMS. Follow-up period of 1 year and 2 years was available in 34 and 28 patients, respectively. Results: Mean age of patients with very late ST of a BMS was 62±14 years, 94% were male, 55% smokers, 26% diabetics, 79% had hyperlipidemia and 71% hypertension. Clinical presentation was STEMI in 31 patients (91%) and non-STEMI in 3 patients (9%). Median period from BMS implantation to very late ST was 7.5 years and most of the patients (72%) were receiving oral antiplatelet therapy at the time of ST. All patients were treated with a new PCI and a significant deterioration of LVEF occurred after very late ST related to BMS (62±10% to 50±11%; p<0.001). MACE (cardiovascular death and myocardial infarction) rates were 14%, 26% and 43% at 30 days, 1-year and 2-year follow-up, respectively. During the 2-year follow-up period, 6 patients died and 6 patients had a non-fatal STEMI. Conclusions: Very late ST after BMS implantation is an uncommon phenomenon, mainly presented as STEMI, and its treatment with a new PCI is feasible. Nevertheless, MACE occur frequently in this group of patients at short- and mid-term follow-up.

No conflict of interest

COMPARISON OF ZOTAROLIMUS- VS. EVEROLIMUS-ELUTING STENTS IN THE TREATMENT OF CORONARY BIFURCATION LESIONS

J. Herrador[1], V. Aragon[1], J.C. Fernandez[1], M. Guzman[1]
[1]Cardiologia, Complejo hospitalario Jaen, Jaen, Spain

Objectives: To compare zotarolimus-eluting stent (Endeavor Sprint®; ZES-S) and the everolimus-eluting stent (Xience V®; EES) in the treatment of coronary bifurcation lesions

Background: Both these stents have demonstrated good outcomes in the treatment of coronary lesions. However, the outcomes with respect to treatment of bifurcation lesions have yet to be conclusively demonstrated.

Methods: In this single centered, non-randomized, open label study, we treated, between August 2006 and December 2008, 110 bifurcations with ZES-S and, in a second stage of the study, 129 bifurcations with EES. The primary end point was to compare the rate of major adverse cardiac events (MACE; death, myocardial infarction and new target lesion revascularization) in-hospital and at 12 months of follow-up. Provisional T stenting was the strategy used in the majority of cases. Angiographic follow-up was performed only in patients who presented signs or symptoms suggestive of angina or ischemia.

Results: There were no significant differences in in-hospital MACE between the groups (ZES-S: 8.1%; EES: 6.2%; p = 0.5). At 12 months, the ZES-S group had significantly more MACE than the EES group (23.1% vs. 4.5%; p<0.001) and an elevated index of new revascularization of the bifurcation (17.5% ***vs***. 3.2 %; p<0.001). There were no significant differences in mortality (4 patients in ZES-S ***vs***. 1 in EES; p=0.14).

Conclusion: The treatment of coronary bifurcation lesions using everolimus-eluting stents results in better outcomes at 12 months of follow-up than zotarolimus-eluting stents.

No conflict of interest

LONG-TERM PROGNOSIS OF CORONARY ARTERY ANEURYSM DEVELOPING AFTER IN DRUG-ELUTING STENT IMPLANTATION

B. Hong[1], Y. Yoon[1], H. Won[1], C. Ahn[2], J. Jung[3], P. Min[1], B. Lee[1], M. Hong[1], H. Kwon[1], Y. Jang[1]
[1]Internal Medicine, Yonsei University College of Medicine, Seoul, Korea
[2]Internal Medicine, Korea University College of Medicine, Seoul, Korea
[3]Internal Medicine, Hanllym University College of Medicine, Seoul, Korea

Background: The occurrence of coronary artery aneurysms (CAAs) after drug-eluting stent (DES) implantation is rare, but can be fatal. However, long-term prognosis of CAA remains unclear. This study sought to investigate long-term outcome of DES-associated CAA

Method: We investigated clinical and angiographic outcome in 29 patients (34 CAAs).

Results: Angiographically, maximal CAA diameter measured 5.6±0.4 mm at diagnosis of CAA. Among these patients, 11 patients (12 lesions) were performed follow up angiography at a median 36 months (interquartile 17-68 months) after CAA diagnosis. The size of CAAs increased by more than 1 mm in four lesions, but the size of CAAs increased or decreased within 0.3mm in five lesions. In 2 lesions, CAAs disappeared at follow up angiography. During a median 58 months (interquartile 52–69 months) of median follow up duration from CAA diagnosis, ST elevation myocardial infarction (STEMI) due to stent thrombosis occurred in one patients on aspirin without clopidogrel. Non-STEMI not associated with CAA occurred in two patients.

Conclusion: Although CAAs rarely develop after DES implantation and show mostly favorable clinical courses over 3 years, long-term maintenance of clopidogrel therapy might be required to minimize occurrence of adverse clinical events resulting from stent thrombosis.

No conflict of interest

DIRECT ASPIRATION OF LARGE THROMBI IN ACUTE MYOCARDIAL INFARCTION USING A STANDARD 6 FR GUIDE CATHETER VIA THE TRANSRADIAL APPROACH

K. ITO[1], Y. Shimada[1], K. Yano[1], D. Tonomura[1], K. Takehara[1], N. Kino[1], K. Furubayashi[1], T. Kurotobi[1], T. Tsuchida[1], H. Fukumoto[1]
[1]Cardiovascular Center, Shiroyama Hospital, Habikino-City, Japan

Aims

A large thrombus load in the culprit coronary artery in patients with acute myocardial infarction (AMI) is generally associated with increased procedural complications and adverse coronary events following angioplasty. Currently available aspiration catheters are insufficient for removing large thrombi because of their small inner lumen diameter. We describe three clinical cases in which the large gross thrombi burdens were successfully aspirated by direct intracoronary insertion of a standard 6Fr guide catheter (GC).

Methods and Results

Direct GC thrombosuction was performed successfully in three patients with AMI. All culprit vessels were right coronary arteries, and all procedures were performed using the transradial approach. Commercially available aspiration catheters were ineffective for removing the intracoronary thrombi. A standard 6Fr GC was advanced deeply into the targeted lesion, which allowed successful removal of the gross thrombi burden almost completely by direct aspiration using only GC. After definitive treatment with balloon angioplasty and/or stenting, TIMI 3 flow was restored in all target vessels. There was no angiographic evidence of distal branch losses or vessel injuries. No major procedural or device-related complications occurred in any patient.

Conclusion

Direct GC aspiration with a standard 6Fr guide catheter may offer a simple, rapid, and effective method for thrombus burden reduction in AMI patients at a low cost. This technique can be performed using a transradial approach and could be a simple alternative in cases of failure of thrombus aspiration with the currently used thrombectomy catheters for patients with challenging thrombus-containing coronary lesions.

No conflict of interest

PATIENTS WITH ADVANCED ATHEROSCLEROSIS PRESENTED HIGH INCIDENCE OF BOTH CARDIAC AND NON-CARDIAC DEATH FOLLOWING DRUG-ELUTING STENT IMPLANTATION

J. Kotani[1], Y. Ikari[2], E. Kyo[3], M. Nakamura[4], H. Yokoi[5]
[1]Cardiovascular Medicine, Osaka University, Suita Osaka, Japan
[2]Cardiovascular Medicine, Tokai University, Isehara, Japan
[3]Cardiovascular Medicine, Kusatsu Heart Center, Kusatsu, Japan
[4]Cardiovascular Center, Toho Uniuversity, Tokyo, Japan
[5]Cardiovascular division, Kokura Memorial Hospital, Kokura, Japan

Background: It is well known that poly-vascular disease (PVD: prior cerebral artery disease, peripheral artery disease and coronary bypass surgery) having coronary artery disease (CAD) shows poor clinical outcomes. However, the cause of death is still under debate. The aim of this study was to clarify the long-term clinical outcomes of PVD in whom CAD was treated by drug-eluting stent (DES).

Method and Results: We used J-PMS (multicenter registry for post marketing surveillance of sirolimus-eluting stent; SES) database. The 1923 patients who underwent complete 5-year follow up (94.5%) were divided into PVD (n=375) and control group (n=1548). The profiles of PVD were more likely to be elder (age>75yrs; 29.1% vs 23.1%), suffer from multi-vessel disease (50.4% vs 38.8%), and suffer from diabetes (49.1% vs 42.1%; p<0.05). However, there was no difference in LVEF<30% (4.5% vs 3.5%) and lesion characteristics assessed by qualitative coronary angiography of both pre- and post-procedure. Five-year follow-up showed that PVD presented higher frequency of in cardiac death (7.5% vs 4.1%), non-cardiac death (15.7 vs 6.9%), non-QMI (2.9% vs 1.3%) and stent thrombosis (2.4% vs 1.0%) than the control group (P<0.05). In PVD, frequency of non-cardiac vascular event was approximately 3 times higher (2.7% vs 0.9%) than the control group. On the other hand, target lesion revascularization rate was similar (11.7% vs 8.9%), but frequency of revascularization for de novo lesion of target vessel (remote from target lesion: non TL-TVR) was different between the two groups (12.0 vs 8.5%: P<0.05). Duration of dual-antiplatelet therapy was similar in two groups.

Conclusion: Patient with poly-vascular disease does not reveal only high frequency of cardiac events but also non-cardiac vascular events including non-cardiac death. Strict optimal medical therapy should be required for this population for improvement of prognosis.

No conflict of interest

TREATMENT OF CORONARY CHRONIC TOTAL OCCLUSIONS: WHAT INFLUENCE OUR DECISION-MAKING?

V. Martin-Yuste[1], L. Alvarez Contreras[1], Y. Azpeitia[1], A. Santos[1], S. Brugaletta[1]
[1]Cardiology, ITC, Barcelona, Spain

Chronic total coronary occlusions (CTO) are a common finding among patients with coronary heart disease. CTO are as high as 30% among those patients referred for a coronary angiography and who had coronary disease. However only less than 10% of all diagnosed are treated.

OBJETIVE: to analyze which factors influence the decision-making about therapy in this patients: medical, surgical or percutaneous therapy.

METHODS. June 2010 - September 2011 all consecutive patients admitted to our institution for a coronary angiography who had a CTO were included in a registry. 7 demography factors, 5 cardiac history data, ACEF (age/Left ventricular ejection fraction (LVEF)(+1 if creatinine>2) y SYNTAX score were registered.

RESULTS: 350 patients were included Clinical and angiographycal characteristics: table 1. Bivariate analysis showed: doctor's advice, age, creatinine clearance, ACEF score, to have conducted a test of ischemia and it's result and Syntax score were the most important factors in making decisions on the type of treatment offered. On multivariate analysis age OR 0,96 (0,93-0,98) p=0,002, acute myocardial infarction OR0,32 (0,12-0,89) p=0,03, and Syntax score OR 0,97 (0,94-0,99) p=0,012 were associated significantly to not refer the patient for percutaneous treatment. On the other hand one positive ischemic test was associated to percutaneous revascularization OR 3,45 (2-6) p<0,001.

CONCLUSIONS. The type of treatment chosen in the CTO patients is mainly determined by doctor's advice. Is more likely to perform a percutaneous treatment in stable patients with better clinical and angiographic profile

No conflict of interest

EFFICACY OF USING NON SLIP ELEMENT BALLOON (LACROSSE NSE) TO TREATMENT FOR IN-STENT RESTENOSIS LESION. ~ OPTICAL COHERENCE TOMOGRAPHY ANALYSIS ~

N. Miyai[1], K. Oota[1], R. Nakamura[1], T. Sawanishi[1], N. Kinoshita[1], K. Matsumoto[1]
[1]Cardiology, Kouseikai Takeda Hospital, Kyoto, Japan

Background: Drug-eluting stents (DES) have been shown to reduce restenosis rates. However, restenosis after DES implantation is still observed. In this study, we evaluated the efficacy of non slip element balloon (NSE) for target lesion revascularization (TLR) of in-stent restenosis (ISR). Methods: We enrolled 71 patients who underwent TLR for ISR using NSE. We succeeded in performing angiographic follow-up in 58 patients. We classified these patients into a re-restenosis group and a non re-restenosis group. We compared OCT images of pre-procedure with images of post-procedure. Results: Recurrent restenosis was angiographically documented in 18 patients (31%), and TLR was in 17patients (29%). There were no difference in gender, age, and coronary risk factor between a re-restenosis group and a non re-restenosis group. QCA data before and after procedure were not difference between two groups. Tissue coverage structures in stent, for example homogeneous, heterogeneous, and layered, were not difference between two groups. However, peri-stent low signal area had a tendency to be more detected in re-restenosis group compared with non re-restenosis group (73% vs. 32%, p=0.072). After NSE angioplasty, we detected fissures in 73% of patients. Irregular lumen shape had tendency to be more detected in re-resteosis group (55% vs. 16%, p=0.069). Stent area change after using NSE was bigger in non re-restenosis group than re-restenosis group (1.67±0.66mm2 vs. 0.52±0.38mm2, p=0.0039). Conclusion: A treatment with NSE for ISR lesion may be more effective compared with plain old balloon angioplasty.

No conflict of interest

THE FEASIBILITY AND USEFULNESS OF OPTICAL COHERENCE TOMOGRAPHY USING 5-FRENCH GUIDING CATHETER

R. NAKAMURA[1], K. Ota[1], N. Miyai[1], T. Sawanishi[1], N. Kinoshita[1], K. Matsumoto[1]
[1]Cardiovascular center, Kouseikai Takeda Hospital, Kyoto city, Japan

“Background: Optical coherence tomography (OCT) is a recently developed optical imaging technique that provides high resolusion cross-sectional images of vessels. The OCT system have switched from time domain OCT to frequency domain OCT, In either case, in order to use both devices are needed more than 6Fr guiding chatheter. The present study was designed to assess the feasibility of optical coherence tomography (OCT) analysis using 5French (5F) guiding catheter.
Methods and Results: We evaluated the initial feasibility and safety of 10 patients treated with 5F guiding catheter using OCT guidance. The OCT was performed with contrast injection or low-molecular-weight-dextran L (LMD-L) through the guiding catheter to acquire pullback images. Both contrast media and LMD-L were infused at a rate of 3ml/sec for RCA lesions, and infused at a rate of 3ml/sec for LCA lesions by an autoinjector. Among the 10 patients in this study, 9 patients had a high quality imaging of OCT to evaluate the lesion. OCT catheter could not be advance in one patient because of the calcificated lesion. However there were no adverse events related to the OCT procedure in any patients.
Conclusions: FD-OCT image acquisition using 5F guiding catheter is safe and useful for less invasive percutaneous coronary intervention.

Document not received

PERCUTANEOUS CORONARY INTERVENTION TO CHRONIC TOTAL OCCLUSIONS CAN BE SAFELY AND EFFECTIVELY PERFORMED IN STANDALONE PCI CENTRES

A. Ramirez Moreno[1], J.R. Siles Rubio[1], J. Muñoz Bellido[2], L. Iñigo García[2], P. Chinchurreta Capote[2], J.C. Salas Serantes[3], C. Pera Rojas[4], L. Fernández López[2], M. Pombo Jiménez[2], R. Bravo Marqués[2], F.J. Martínez García[2]
[1]CARDIOLOGY, HOSPITEN ESTEPONA, Málaga, Spain
[2]CARDIOLOGY, Hospital Costa del Sol. Marbella, Málaga, Spain
[3]INTENSIVE CARE, HOSPITEN ESTEPONA, Málaga, Spain
[4]ANESTHESIOLOGY, HOSPITEN ESTEPONA, Málaga, Spain

BACKGROUND: Successful percutaneous coronary intervention (PCI) for chronic total occlusions (CTO) has been shown to reduce angina symptoms, reduce the need for coronary bypass surgery and may improve survival. With the development of retrograde and contemporary anterograde approaches the success rates of CTO PCI continues to improve. There remains much debate whether CTO PCI can be performed safely and effectively in high volume stand alone PCI centres.

METHODS: We identified all patients undergoing CTO PCI between January 2008 and March 2012. Patient demographics, angiographic features, procedure details and clinical outcomes were collected from local medical database.

RESULTS: 42 patients (85.8% male; 63.15 years) underwent PCI to 43 CTO lesions. Clinical presentations of the patients were stable angina (91.78%), non ST elevation MI (7.05%) and left ventricular failure ((LVF) 1.17%). The overall PCI success rate was 74.41%.Success rates of ad hoc, elective first, and subsequent reattempts were 59.1%, 68% and 69.7% respectively. Arterial access used was radial only in 21%, femoral only in 79%. Bilateral injections were used in 15% of cases. Mean procedure time was 75.2 minutes. Mean radiation dose was 3.4+/-0.2 Gy/cm2. Mean contrast volume used was 297+/-10 ml. Complications of coronary perforation and coronary dissection occurred in 2% and 3% respectively with no occurrence of cardiac tamponade. Periprocedural myocardial infarction occurred in 1%. There were no periprocedural deaths and no patients required emergency cardiac surgery. The mean hospital stay in patients presenting with the stable angina, NSTEMI and LVF were 1.5, 9 and 4 days respectively. At mean follow up of 285 days, target vessel revascularisation (TVR) was only 3.1%. After successful CTO PCI, patient's CCS angina class decreased significantly from 2.2 to 0.5 (p=0.0001).

CONCLUSION: Successful CTO PCI significantly improves angina symptoms with overall low rates of periprocedural complications. CTO PCI can be safely and effectively performed in experienced stand alone PCI centres

No conflict of interest

UNUSUAL TREATMENT OF POSTOPERATIVE BLEEDING AFTER CARDIAC SURGERY: RIGHT CORONARY ARTERY STENTING WITH COVERED STENTS.

J.S.Q.,B.A.N.,D.O. J. Rubio Alvarez[1]
[1]Cardiac Surgery
[2]Cardiology, Universitary Hospital Santiago de Compostela, Santiago de Compostela
[3]Vascular Surgery, Universitary Hospital de Elche, Elche, Spain

Angiosarcomas, are the most common primary malignantneoplasms of the heart. Coronary perforation is a rare but seriouscomplication of percutaneous coronary intervention with important bleeding into de pericardium, however, thiscomplication can be tackle successfully by covered stents.
A 50-year-old man visited theemergency service because of palpitations and left chest pain. A transthoracic echocardiogram was performed and detected a right atrial(RA) mass that infiltrated the RAfree wall and that protruded into the RA. For further evaluation of this mass, magnetic resonance imaging and computed tomography were performed. These explorations showed alarge excentric tumor in the RA free wall, protruding into the RA. The tumorextended into the right atrioventricular groove. Coronary angiography showed a right coronary artery withcolateral circulation to a big mass. The surgery was performed under standard extracorporeal circulation. The RA was excised and the tumour could only be partially resectedbecause it extended rightventricle free wall and tricuspid valve annulus. The RA wasreconstructed using bovine pericardium and after declamp a persistent bleeding wasobserved. Because the bleedingcontrol was no possible, we decided to close the chest and to perform a rightcoronary angiography which had revealed an important free extravasation ofcontrast into the pericardium throught the colateral circulation. Thesebranches were tackled successfullyby covered stents and post-covered stent angiogram showed complete cessation ofcontrast extravasation. The postoperative course was uneventful and after asymptom-free survival of six months the patient presented with bone metastases.

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PSEUDOANEURYSM OF THE ASCENDING AORTA FOLLOWING RIGHT CORONARY STENTING

J.S.Q.,B.A.N.,J.G. J. Rubio Alvarez[1]
[1]*Cardiac Surgery, Universitary Hospital Santiago de Compostela, Santiago de Compostela*
[2]*Vascular Surgery, Universitary Hospital de Elche, Elche, Spain*

Ascending aortic pseudoaneurysm (AAP) following priorcardiac procedures is a rare but serious complication. Disruption of atherosclerotic plaques couldplay an important role in the pathogenesis of dissection and Pseudoaneurysms occurring after coronary stenting. Currently,there are no established guidelines regarding the management of AAP, but mostauthors recommend surgical treatment even in asymptomatic patients.

We report the caseof a 46-year-old man with risk factors for coronary artery disease ofex-smoking, obesity, hyperlipidemia and peripheral arterial disease. His past medical history was remarkable fora non-ST elevation myocardial infarction, treated four months previously withpercutaneous coronary intervention (PCI) and four sirolimus-eluting stent implanted to treat stenosis of the right coronaryartery. Two months laterhe was referred to our hospitalbecause of persistent fever. Computed tomography angiography was performed and revealed the presence ofa pseudoaneurysm of the ascending aorta involving the right coronary sinus ofValsalva. The patient underwent surgical intervention under extracorporealcirculation, At surgery the aorta was not dilated and in the aortic wall Atherosclerotic fragments were predominantly seen. The entry of the Pseudoaneurysm was closed withbovine pericardial patch. Surgical intervention was successful and he wasdischarged home without significant issues. At the two-month follow-upvisit the patient was asymptomatic. A follow-up visit and a computed tomography has been recommended at 6 months.

The forceful manipulation of the guide catheter seemed to be the Pathophysiologic mechanism of the Pseudoaneurysm involving the right coronary sinus of Valsalva.

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PREDICTORS AND OUTCOMES ASSOCIATED WITH RADIAL VERSUS FEMORAL ACCESS FOR INTERVENTION IN PATIENTS WITH ACUTE CORONARY SYNDROME IN A REAL WORLD SETTING

P. Fefer[1], S. Matetzky[1], S. Gannot[1], S. Gottlieb[2], D. Meerkin[2], N. Gavrielov-Yosim[1], I. Goldenberg[1], R. Kornowski[3], A. Segev[1]
[1]The Heart Center, Chaim Sheba Medical Center, Tel Hashomer, Israel
[2]Cardiology, Shaarei-Tzedek Hospital, Jerusalem, Israel
[3]The Heart Center, Rabin Medical Center, Petach-Tikva, Israel

Objective: To describe current utilization of trans-radial intervention (TRI) in real world patients presenting with acute coronary syndromes (ACS).

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Background: Use of TRI is becoming more popular, and recent studies suggest an advantage for TRI in high-risk ACS patients.

Use of TRI is becoming more popular, and recent studies suggest an advantage for TRI in high-risk ACS patients.**Methods: Data was derived from the ACS Israeli Survey (ACSIS 2010), a nationwide prospective survey of patients presenting with ACS over a two-month period. Followup was continued for up to one year**

Results:

Of 1815 ACS patients undergoing coronary angiography, 613 (34%) underwent TRI which was more likely to be employed among patients with lower risk characteristics. Patients undergoing TRI had significantly lower 30-day mortality and in-hospital bleeding. On multivariate analysis the risk of in-hospital major bleeding was reduced by 60% in patients undergoing TRI (p=0.045). However, no significant differences in other components of major adverse cardiac events (MACE) or mortality were demonstrated at 30-days. All-cause mortality at 1-year was significantly lower among patients who underwent TRI. However, after multivariate adjustment this effect was no longer significant.

Conclusions: Use of TRI seems to be associated with improved outcomes in high-risk ACS patients. Our data suggest that in a real world setting this approach is underutilized in this population. A more widespread adoption of TRI may reduce major bleeding events and improve outcomes in high-risk ACS patients.

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No conflict of interest

THE IMPACT OF ARTERIAL STIFFNESS ON THE PERFORMANCE OF PERCUTANEOUS CORONARY INTERVENTION

J. Seo[1], H.L. Kim[1], S.H. Kim[1], W.Y. Chung[1]
[1]Internal Medicine, Boramae Medical Center, Seoul, Korea

Background and objectives: Increased arterial stiffness is an accepted cardiovascular risk factor. However, the effect of arterial stiffness on the performance of percutaneous coronary intervention (PCI) is not well known. The aim of this study was to evaluate the impact of arterial stiffness measured by pulse wave velocity (PWV) on acute gain and late loss after PCI.

Subjects and Methods: Data from 242 consecutive patients who underwent PCI using drug eluting stents and pulse wave velocity study were analyzed.

Results: Mean PWV, acute gain and late loss were 1675 ± 391 cm s(-1), 1.48 ± 0.55 mm and 0.13± 0.51mm. There was negative relation between PWV and acute gain (correlation coefficient = -0.153 ; p=0.017). However, there was no relation between PWV and late loss (correlation coefficient = 0.009 ; p=0.887)

Conclusions: Increased arterial stiffness is unfavorable for acute gain of the patients undergoing PCI. However, this is not prognostic factor for late loss.

No conflict of interest

ANEMIA IS A STRONG PREDICTOR OF PERSISTENT RENAL DYSFUNCTION IN PATIENTS WITH CONTRAST-INDUCED ACUTE KIDNEY INJURY UNDERGOING PERCUTANEOUS CORONARY INTERVENTION

J. Sugioka[1], M. Inagaki[1], S. Fukuzawa[1], A. Ikeda[1], S. Okino[1], J. Maekawa[1], S. Maekawa[1], S. Ichikawa[1], T. Uchiyama[1], N. Kuroiwa[1]
[1]Division of Cardiology, Funabashi Municipal medical Center, Funabashi, Japan

<Background> The incidence and predictor of persistent renal dysfunction in patients with contrast-induced acute kidney injury (CIAKI) treated with primary PCI (percutaneous coronary intervention) are not well characterized. The aim of this study was to determine the clinical predictors of persistent renal dysfunction in patients with CIAKI undergoing primary PCI for AMI (acute myocardial infarction). <Methods > 367 consecutive AMI patients undergoing primary PCI were enrolled in this study. We examined renal function for these patients at the 6 month follow-up after PCI. <Results> Overall, CIAKI occurred in 101(27.5%) patients. Of the 101 patients with CIAKI, impaired renal function was not restored to baseline in 54(53.5%) patients. Patients with persistent renal dysfunction were older (65.7±9.3 vs 61.7±13.0, p=0.015) and had higher baseline creatinine levels (0.87±0.43 vs 0.83±0.22, p=0.006). The incidence of anemia (baseline hemoglobin<=13.0mg/dl) was significantly higher in patients with persistent renal dysfunction (37.0% vs 14.9%, p=0.010). In multivariate analysis, anemia (OR 2.92, 95%CI 1.07-7.98, p=0.037) was independent predictor of persistent renal dysfunction. <Conclusion> We found out that persistent renal dysfunction frequently occurred in patients with CIAKI undergoing primary PCI for AMI and the presence of anemia was associated with persistent serum creatinine level elevation. Improvement of anemia might be needed to prevent persistent renal dysfunction in patients with CIAKI.

No conflict of interest

AVANTGARDE™ CARBOSTENT IMPLANTATION AND SHORT DAPT IN HIGH BLEEDING RISK PATIENTS

D. Trabattoni[1], F. Fabbiocchi[1], P. Montorsi[1], G. Calligaris[1], L. Grancini[1], A. Lualdi[1], G. Teruzzi[1], S. Galli[1], P. Ravagnani[1], S. De Martini[1], A. Bartorelli[1]
[1]Invasive Cardiology, Centro Cardiologico Monzino IRCCS, Milano, Italy

Background. Coronary stenting in patients with undelayable surgery or at high risk of bleeding is challenging.

Aim: To evaluate safety and efficacy of a short dual antiplatelet therapy (DAPT) after AvantgardeTM Carbofilm-coated stent (CID Vascular, Saluggia, Italy) implantation in this high-risk patients.

Methods. Patients with contraindications to standard DAPT duration (anemia 20%, thrombocytopenia 15%, scheduled surgery for cancer 30%, cardiac surgery for severe aortic valve stenosis 20% and intracranial hemorrhage 15%) received AvantgardeTM stenting and were followed-up at 1 and 9 months.

Results. Seventy-five patients (70% male, mean age 72±11 years) with 97 coronary lesions (5 LM; 43 LAD; 16 LCx-oM; 30 RCA; 3 SVGs) received AvantgardeTM Carbofilm-coated stents (mean stent n°/ pt 1.25±0.61). Multivessel stenting was performed in 53% of cases with long lesions (31%; mean stented segment length 28.8±19 mm; stents >25 mm: 41%) and small vessels (<2.5mm: 12%) treated. High pressure postdilation (17.1±2.4 atm) was performed in all cases. Procedural success was 100%. Average DAPT treatment lasted 18±4.7 days. In-hospital cumulative MACE rate was 5.3%. Major bleeding occurred in two (2.5%) patients without clinical sequelae. At follow-up (>6 mos), currently available in 48/75 (64%) patients, a low (10.9%) cumulative rate of death, MI, angina and target lesion/vessel revascularization was observed. In-stent restenosis occurred in four (8.3%) patients so far and was treated with drug-eluting stent (n=2) or balloon (n=2). No early or late stent thrombosis occurred.

Conclusions: Short DAPT after AvantgardeTM Carbofilm-coated stent in high bleeding risk patients is safe and associated with excellent mid-term outcomes.

No conflict of interest

THE WAR-STENT (WARFARIN AND CORONARY STENTING) REGISTRY: IN-HOSPITAL MANAGEMENT AND OUTCOME OF PATIENTS AGED < 75 VS = 75 YEARS.

S. Zagnoni[1], M. Colletta[1], L. Steffanon[2], P. Magnavacchi[3], L. Vignali[4], S. Boarin[5], M. Dallago[6], G. Di Pasquale[1], A. Rubboli[1]
[1]Cardiology, Maggiore Hospital, Bologna, Italy
[2]Cardiology, Hesperia Hospital, Modena, Italy
[3]Cardiology, Ospedale Civile, Baggiovara, Italy
[4]Cardiology, Azienda Ospedaliera Universitaria, Parma, Italy
[5]Cardiology, Ospedale G.B. Morgagni, Forlì, Italy
[6]Cardiology, Ospedale S. Chiara, Trento, Italy

Background: In-hospital incidence of major adverse cardiac events (MACE) in patients on warfarin undergoing coronary stent implantation (PCI-S) has been shown to be affected by procedural and patient-related variables. As elderly patients are a more frail population, we aimed at evaluating whether the in-hospital management and outcome were different compared to younger patients.

Methods: The WARfarin and coronary STENTing (WAR-STENT) registry is a prospective, multicenter, observational study and included 411 consecutive patients on chronic warfarin undergoing PCI-S at 37 Italian centres between November 2008 and June 2010. The outcome measures were MACE, including death, myocardial infarction, need for urgent revascularization, stroke and venous thromboembolism, and major and minor TIMI bleeding.

Results: Patients undergoing PCI-S ≥ 75 years showed a higher prevalence of acute coronary syndrome (ACS) (74% vs 63%, p = 0.014) and chronic kidney disease (CKD) (35% vs 21%, p = 0.002). No significant differences regarding peri-procedural management were observed, except the preferred use of bare metal stent in older patients (64% vs 53%, p = 0.034). MACE rate was similar, however an excess of major bleeding in patients ≥ 75 years was observed (3,5% vs 0,5%, p = 0.045).

Conclusions: In a real-world population of warfarin treated patients undergoing PCI-S, patients ≥ 75 years are slightly more frequent, and are at higher overall risk, as shown by the higher prevalence of ACS and CKD. In-hospital management is generally carried out according to current recommendations, with no differences in the two groups, except for the preferred use of bare metal stent in older patients. Nonetheless, a significantly higher incidence of in-hospital major bleeding was observed in patients ≥ 75 years, thereby confirming the greater frailty of such subgroup also among patients on chronic warfarin.

No conflict of interest

THE WAR-STENT (WARFARIN AND CORONARY STENTING) REGISTRY: COMPARISON OF IN-HOSPITAL MANAGEMENT AND OUTCOME OF ACUTE CORONARY SYNDROME VS. ELECTIVE PATIENTS.

S. Zagnoni[1], M. Colletta[1], A. Sciahbasi[2], F. Saia[3], P. Calabrò[4], M. Valgimigli[5], M. Margheri[6], M. Santi[7], A. Capecchi[8], A.M. Leone[9], G. Di Pasquale[1], A. Rubboli[1]
[1]Cardiology, Maggiore Hospital, Bologna, Italy
[2]Cardiology, Policlinico Casilino, Rome, Italy
[3]Cardiology, Institute of Cardiology S. Orsola-Malpighi, Bologna, Italy
[4]Cardiology, Seconda Università, Naples, Italy
[5]Cardiology, Azienda Ospedaliera Universitaria, Ferrara, Italy
[6]Cardiology, Ospedale S. Maria delle Croci, Ravenna, Italy
[7]Cardiology, Ospedale Civile, Lugo, Italy
[8]Cardiology, Ospedale Civile, Bentivoglio, Italy
[9]Cardiology, Policlinico Gemelli, Rome, Italy

Background: The in-hospital management of patients on warfarin undergoing coronary stent implantation (PCI-S) is variable and the in-hospital outcome incompletely defined.
Methods: The WARfarin and coronary STENTing (WAR-STENT) is a prospective, multicenter, observational registry. Between November 2008 and June 2010, 411 consecutive patients on chronic warfarin undergoing PCI-S were included at 37 Italian centers. The outcome measures were major adverse cardiac events (MACE) and major and minor TIMI bleeding. Outcomes were compared between patients undergoing PCI-S for an acute coronary syndrome (ACS) and elective patients.
Results: Baseline and peri-procedural characteristics are summarized in Table 1.

	Overall	ACS	Elective
Patients (%)	**411 (100%)**	**284 (69%)**	**127 (31%)**
Age (years, mean±SD) 73.9 ± 9.1		75 ± 8,9	72 ± 9,5
Female (%)	302 (73)	197 (69)	105 (83)
Diabetes (%)	144 (35)	100 (35)	44 (35)
Renal Failure (%)	116 (28)	77 (27)	39 (31)
Indication for warfarin:			
AF (%)	323 (78,6)	222 (78)	103 (81)
Mechanical heart valve (%)	27 (6,6)	18 (6,3)	8 (6,3)
Venous thromboembolism (%)	26 (6,3)	16 (5,6)	4 (3,1)
Other (%)	35 (5,5)	28 (9,9)	12 (9,5)
Intra-procedural management			
Warfarin uninterrupted (%)	176 (43)	128 (45)	48 (38)

GP IIb/IIIa inhibitors (%)	48 (12)	42 (15) *	6 (5)
Bivalirudin (%)	7 (1,7)	5 (1,8)	2 (1,6)
Radial approach (%)	262 (64)	187 (65)	75 (59)
Bare metal stent implantation (%)	244 (59)	171 (60)	73 (57)

* p = 0.003 vs. elective

The MACE and major bleeding rates were 2.7% and 2.1% respectively, with no differences in the two subgroups.

Conclusions: The in-hospital management of warfarin patients undergoing PCI-S is generally carried out according to current recommendations, namely extensive adoption of the radial approach, limited use of glycoprotein IIb/IIIa inhibitors, and preferred use of bare metal stents, thereby contributing to the observed limited incidence of in-hospital adverse events including MACE and especially bleedings. No differences in in-hospital outcome were observed in the two groups, although the small population size and the low absolute incidence of adverse events must be acknowledged.

No conflict of interest

EPIDEMIOLOGY OF ABDOMINAL AORTIC ANEURYSMS AND CARDIOVASCULAR ASSOCIATIONS IN QATAR

H. Al-Thani[1], A. El-Menyar[2]
[1]vascular surgery, Hamad general hospital, Doha, Qatar
[2]cardiology, Hamad general hospital & Weill Cornell medical school, Doha, Qatar

Screening programs for abdominal aortic aneurysm (AAA) are lacking in the developing countries. Qatar is a rapidly developing country that characterizes with high prevalence of cardiovascular risk burden. We aimed to evaluate the frequency, clinical profiles and outcomes of AAA and its cardiovascular association in Qatar.

Methods: Data were collected from March 2004 to March 2008 for all adult patients who underwent abdominal computed tomography scans at Hamad general hospital in Qatar. **Results**: out of 13,115 screened patients for various reasons, 61 patients (0.5%) had abdominal aneurysms. Most AAA patients were male (82%) with a mean age of 67±12. The incidence of AAA substantially increased with age reaching up to 5% in patients >80 yrs. The main location of AAA was infra-renal (67%), followed by Thoracoabdominal (23%). The mean AAA diameter was 5.3±2.5 cm with a range of 3 to 14 cm. AAA of diameter ≥5.5 and ≥7 cm comprised 41% and 26% of cases, respectively. The rate of AAA rupture was 8 %, whereas overall mortality was 33%. Among ruptured AAA, 100% of them were of age >60yrs, 80% were infrarenal, 80% had diameter ≥5.5cm and 60% of cases died. Cardiovascular risk factors were prevalent among AAA patients in terms of hypertension (66%), smoking (60%), dyslipidemia (51%), renal impairment (46%) and diabetes mellitus (41%). Coronary artery disease and peripheral arterial disease were observed in 36% and 13% of AAA patients, respectively. There were no significant correlations between CAD or PAD and site and size of AAA.

Conclusion: This is the largest study in our region that describes the epidemiology of Abdominal aneurysm. Although there is high prevalence of CAD and PAD, this association does not reflect site, size or severity of AAA. The impact of population-based screening for AAA warrants researchers' attention.

No conflict of interest

IMMUNE CORRECTION IN PREPARATION OF PATIENTS FOR CORONARY INTERVENTION

I. Andrievskih[1], O.P. Lukin[1], A.A. Grafov[1]
[1]Surgery Department, South Ural State Medical University, Chelyabinsk, Russia

At present, more attention is focused on study of immune inflammation in cases of coronary pathology as a predictor of acute coronary disorder. It primarily concerns the patients with ischemic heart disease in terms of co-morbidity and clinical-laboratory symptoms of the coronary arteries inflammation.

During the last 12 years for this category of coronary disease patients we include cytoflowmetry into the diagnostic algorithm for more precise evaluation of individual characteristics of immune status on cellular-molecular level. Analysis of clinical-laboratory indices of all these patients (277) has revealed the secondary combined structured immunodeficiency with individual peculiarities in all the cases.

In order to reduce intra- and postoperative thrombohemorrhagic and reparative complications all these patients (277) in the preoperative period have undergone immune correction on individual basis, including various combinations: immunomodulators, plasmapheresis and intravenous immunoglobulin therapy. All these measures have been taken in addition to common basic therapy in preoperative period.

We have carried out a comparative analysis in an identical group of patients (group II) who have undergone only standard preoperative preparation. It turned out that in group with additional individual immune correction the patients have suffered thrombohemorrhagic inflammation and pyoinflammatory complications 2.5 times less in intra- and postoperative period as compared to group II.

Thus, immune correction of severely ill patients with ischemic heart disease can be considered as a reasonable and effective instrument in prevention of thrombohemorrhagic and reparative complications and surgical intervention that enables safer surgical interventions.

No conflict of interest

NT-PROBNP AND HS-CRP BUT NOT CYSTATIN C PREDICTS CARDIOVASCULAR EVENTS IN PATIENTS WITH PAD INDEPENDENTLY OF AMBULATORY PULSE PRESSURE

J. Arpegård[1], P.H. Skoglund[1], J. Östergren[1], P. Svensson[1]
[1]Department of Emergency Medicine, Karolinska University Hospital, Stockholm, Sweden

Background: Patients with peripheral artery disease (PAD) are at high risk for cardiovascular (CV) events. We have previously shown that ambulatory pulse pressure (PP) predicts CV events in PAD patients. The biomarkers NT-proBNP, hs-CRP and Cystatin C are related to a worse outcome in patients with CV-disease but their predictive value have not been studied in relation to ambulatory PP.

Method: Blood samples and 24-hour measurements of ambulatory blood pressure were examined in 98 males referred for evaluation of PAD during 1998-2001. Patients were followed for a median of 71 months. The outcome variable was CV events defined as either CV mortality or any hospitalization for myocardial infarction, stroke or coronary revascularization. The predictive value of log(NT-proBNP), log(hs-CRP) and log(Cystatin C) alone and together with ambulatory PP was assessed by Cox regression. Hazard ratios (HR) with 95% confidence intervals were calculated for an increase in one SD.

Results: During follow up, 36 of the 98 patients had at least one CV event. Ambulatory PP (HR 1.63 (1.18-2.24)), log(NT-proBNP) (HR 2.12 (1.49-3.00)), log(hs-CRP) (HR 1.61 (1.20-2.16)), all predicted CV events in univariate analysis, whereas log(Cystatin C) did not. In multivariate analysis both log(NT-proBNP) (HR 1.74 (1.12-2.71)), and log(hs-CRP) (HR 1.76 (1.27-2.45)) predicted events independently of ambulatory PP. The combination of ambulatory PP, log(NT-proBNP) and log(hs-CRP) improved risk discrimination when added to a traditional risk factor model (AUC 0.825 vs 0.746, $p<0.05$).

Conclusion: NT-proBNP and hs-CRP predict CV-risk independently of ambulatory PP and the combination improve risk discrimination in PAD-patients.

No conflict of interest

RISK OF CORONARY HEART DISEASE AND RISK OF STROKE IN WOMEN WITH POLYCYSTIC OVARY SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS

J.A. Barry[1], S. Anderson[1], P. Hardiman[1]
[1]Hampstead Campus Medical School, UCL, London, United Kingdom

BACKGROUND: Polycystic ovary syndrome (PCOS) is a common condition affecting around eight percent of women. Although the syndrome is associated with numerous cardiovascular risk factors, the specific effects on the risk of (a) stroke and (b) coronary heart have never been reported.

METHODS: A systematic review and meta-analysis of observational studies. Studies were eligible for inclusion if they compared PCOS to non-PCOS groups for fatal or non-fatal coronary heart disease and stroke. The main data sources searched were PubMed, EMBASE, and Web of Knowledge.

RESULTS: From 489 references, eight studies that examined separately non-fatal CHD and non-fatal stroke met the inclusion criteria for the meta-analysis (1292 women with PCOS and 3862 non-PCOS controls). In the five studies where the average age was more than 45 years old, the risk in PCOS was significantly increased for non-fatal stroke (OR, 1.94; 95% CI, 1.19 – 3.17) and slightly increased in the six studies of CHD (OR, 1.70; 95% CI, 0.92 – 3.11). In the three studies where BMI was similar in the PCOS and control group, the risk of stroke was similar in the groups (OR, 0.95; 95% CI, 0.24 – 3.77), but the risk of stroke was significantly higher in the PCOS group in the three studies that did not control for BMI (OR, 2.14; 95% confidence interval, 1.04 – 4.39).

CONCLUSIONS: This is the first meta-analysis to show an increased risk of stroke in women with PCOS. This risk is almost doubled in subjects aged over 45 years, but was reduced to being statistically non-significant in those studies where BMI was similar in PCOS and controls. The risk of CHD was also doubled in these women. These results highlight the important cardiovascular morbidities associated with PCOS, and suggest that strategies to manage obesity may reduce the burden of disease in this vulnerable population.

No conflict of interest

CLINICAL EPIDEMIOLOGY SURVEY OF THE TRADITIONAL CHINESE MEDICINE ETIOLOGY AND SYNDROME OF CORONARY ARTERY DISEASE: STUDY PROTOCOL OF A MULTICENTER TRIAL

Y. Bi[1], J. Mao[1]
[1]Cardiovascular Department,
First Teaching Hospital of Tianjin University of Traditional Chinese Medicine, Tianjin, China

BACKGROUD:Coronary artery disease (CAD), a common disease, with high incidence and mortality rate, has seriously threatened the health and life of the masses. Traditional Chinese medicine (TCM) has an important role to play in the prevention and treatment of the disease. Through clinical epidemiological survey, deeper understanding on TCM etiology and syndromes characteristics of CAD would further improve the clinical efficacy of the disease.

METHODS/DESIGN: The preliminary clinical questionnaire for TCM etiology and syndrome of CAD was designed after literature reviews and analysis. Through a series of clinical pre-survey, expert consultation and demonstration, the formal TCM clinical epidemiology questionnaire on the etiology and syndromes of CAD was finalised, after which, the study protocol, inclusive and exclusive criteria and related quality control measures were prepared. The multi-regional clinical epidemiological survey with more than 5, 000 CAD cases will be carried out in 41 TCM hospitals of China for investigating the etiology and syndromes of CAD.

DISCUSSION: Multiregion large sample size clinical epidemiology survey on TCM etiology and syndrome of CAD (CHIMES-CAD) will provide further evidence in preventing CAD and improving the standardizationg of syndrome research.

No conflict of interest

CHARACTERISTICS AND ADVANTAGES OF TRADITIONAL CHINESE MEDICINE IN THE TREATMENT OF ACUTE MYOCARDIAL INFARCTION

H.X. Liu[1], J.J. Shang[1], F.Y. Chu[1], Z.H. Zhang[1], D.W. Zhang[1]
[1]cardiology, Beijing Hospital of Traditional Chinese Medicine, Beijing, China

OBJECTIVE:

To obtain epidemiological data on Traditional Chinese Medicine (TCM) therapeutic status of acute myocardial infarction (AMI) and to determine TCM characteristics and advantages to improve the level of TCM prevention and treatment of AMI.

METHODS:

From 2001 to 2011, a 10-year-long register survey on hospitalized AMI patients in Third-grade A-Level TCM hospitals in Beijing was carried out to obtain authoritative data on the therapeutic status of AMI patients in TCM hospitals in China.

RESULTS:

We found that Chinese herbal intravenous preparations may be beneficial in reducing the mortality of AMI. Major complications of AMI, such as heart failure and arrhythmia, were significantly less during the 10-year survey period. The mortality of hospitalized AMI patients showed a decline. TCM treatment was helpful for AMI patients in improving their quality of life. Ten-year dynamic monitoring showed that the ability to perform reperfusion and to use drugs appropriately, as well as an effort to carry out the Clinical Guidelines has made great progress in TCM hospitals. However, TCM hospitals still have some problems in treating AMI, including a lack of standardized TCM syndrome diagnosis, the need for syndrome differentiation and treatment standardization, and clinical skills in reperfusion and standardized drug treatment still need to be further improved. Compared with AMI patients in Western medicine hospitals during the same period, those in TCM hospitals had the following characteristics: they were admitted to hospital later; they were older when they had a heart attack; there were more females, they had more problems in their medical history, and they had more concomitant illnesses and complications. Therefore, the demographic baseline data were significantly different between AMI patients in TCM hospitals and those in Western medicine hospitals. This indicated that patients in TCM hospitals were more critical than those in Western medicine hospitals.

CONCLUSIONS:

TCM has special advantages in treating AMI. TCM hospitals are making continuous progress in standardized treatment of AMI, but further improvement is still required. AMI patients in TCM hospitals have some special characteristics, and their condition may be more critical. Further clinical research on TCM treatment of AMI is required.

No conflict of interest

A COMPARISON OF OUTCOMES IN THE POST CARDIAC SURGERY PATIENT POPULATION

T.J.F. Colella[1], M. Calouro[1], B.S. Goldman[1], P. Oh[1]
[1]Cardiovascular Prevention and Rehabilitation, UHN/Toronto Rehab, Toronto, Canada

The early transition period after coronary artery bypass graft (CABG) surgery is one associated with intense physiological and psychosocial adjustment which requires that patients make sustainable long-term lifestyle changes. Cardiac rehabilitation (CR) is an evidence-based, multidimensional program aimed at enhancing physical activity, psychosocial well being and quality of life in patients with cardiac disease. Participation in a CR program can reduce the associated risk of mortality by 50% within the first three years following a cardiac event. The development of strategies to bridge the gap from acute care into community secondary prevention through early follow up for cardiac surgery patients is essential. The early post surgical clinic is an interdisciplinary CR model where the patient visit includes: medical assessment, screening for program suitability, reinforcement of post operative education, normalizing of symptoms, early identification of post operative complications and individualized streamlining into a CR program that best suits the patient's needs at an earlier time point in recovery. This retrospective study will examine the profile and outcomes of patients (N=100) referred to the early post surgical follow up clinic in comparison to an age matched cohort (N=100) of non-clinic attenders. It is anticipated that the clinic patients will exhibit higher levels of self efficacy and activity, improved access, adherence and utilization of CR services, as well reduced morbidity and mortality outcomes across the continuum of care. This type of intervention may have the potential to significantly impact health system efficiencies through interdisciplinary collaboration while enhancing quality outcomes.

No conflict of interest

TARGETTING CLINICAL SAFETY AND LIFESTYLE RISKS IN DISCHARGE PLANNING SESSIONS FOLLOWING ACUTE CORONARY SYNDROME

S. Cossette[1], N. Frasure-Smith[2], J. Dupuis[3], A. Nigam[3], J.F. Tanguay[3], J. Coté[4], S. Heppell[3], T. Mailhot[1]
[1]Research Center, Montreal Heart Institute/Faculty of Nursing University of Montreal, Montreal, Canada
[2]Research Center, Montreal Heart Institute/CHUM/McGill University, Montreal, Canada
[3]Research Center, Montreal Heart Institute, Montreal, Canada
[4]Research Center, CHUM/Faculty of Nursing University of montreal, Montreal, Canada

Introduction: Results of the CCU-TRANSIT randomized trial (Cossette et al., 2011; 2012) testing the efficacy of a novel Hospital Discharge Nursing Practice Model (HD-NPM) for risk factor reduction following acute coronary syndrome were presented previously. HD-NPM resulted in greater CR intake (45%) in the experimental group than in the controls (24%; p =.001). We sought to implement HD-NPM in clinical practice in a knowledge transfer (KT) project at the CCU (coronary care unit) of the Montreal Heart Institute. This presentation will describe 1) usual care nursing practices before implementing HD-NPN and 2) patients' lifestyle risks one month post-discharge.

Results: Nurses discussed lifestyle risks with 83% of patients, and Mediterranean diet with 73%. They gave CR program pamphlets to 70%. One month post-discharge, 63% of patients reported exercising ≥ 2-3 times a week and 90% reported eating fast food only occasionally (vs regularly). Of the 8 smokers before hospitalisation, three continued smoking at one month. The chronicity of ACS was discussed with 67% of patients. Barriers to risk factor discussion included lack of time before discharge because nurses had to focus on short term clinical safety (taking medications including clopidogrel, monitoring symptoms).

Conclusions: Lifestyle risk-related topics were discussed with only two-thirds of ACS patients despite their high risk for cardiac re-events. Life style risk factor issues are life-threatening in the mid-long term, but may be lower in priority in acute care settings. Increasing awareness about cardiac life style risk factor modification in both cardiac patients and nurses remains a challenge.

No conflict of interest

DECREASED ANTIOXIDANT STATUS AND INCREASED THROMBOTIC AND INFLAMMATORY FACTORS IN OBESE ADOLESCENTS AND YOUTH-RISK OF EARLY ATHEROSCLEROTIC DISEASES

V. Dimitrijevic-Sreckovic[1], B. Sreckovic[2], P. Djordjevic[3], H. Janeski[4], E. Colak[5], I. Soldatovic[6]
[1]Dpt. for nutrition and prevention of metabolic disorders,
Clinic for endocrinology diabetes and metabolic diseases Medical Faculty University of Belgrade, Belgrade, Serbia
[2]Cardiology, Clinical Center Bezanijska Kosa, Belgrade, Serbia
[3]Endocrionology, Medical Faculty University of Belgrade, Belgrade, Serbia
[4]Dpt. for nutrition and prevention of metabolic disorders,
Clinic for endocrinology diabetes and metabolic diseases, Belgrade, Serbia
[5]Medical Biochemistry, Institute of Medical Biochemistry Clinical Center of Serbia, Belgrade, Serbia
[6]Medical Statistics and Informatics,
Institute for Medical Statistics and Informatics Faculty of Medicine University of Belgrade, Belgrade, Serbia

Background: In obesity and metabolic syndrome (MS) abdominal obesity is accompanied with hyperinsulinism and insulin resistance (IR). Abdominal obesity correlates with increased thrombotic and inflammatory factors supporting the progression of atherosclerotic complications. This study analyzes IR, thrombotic, inflammatory factors and antioxidant status in obese youth.

Methods: The study included 115 obese individuals (age 16-26 years). We used ATP III classification for MS diagnosis. Patients with increased waist circumference (WC) only or WC with one additional criterion were indicated as patients with pre-MS. IR was determined by HOMA IR. Serum CRP was measured by immunometric assay. Plasminogen activator inhibitor (PAI-1) was determined by plasminogen substrate essay. Activities of markers of antioxidant defense, superoxide dismutase (SOD) and glutation peroxidase (GPX) were determined in erythrocytes with Randox Lab (UK) commercial kit.

Results: Patients with MS had increased WC (115.7±17.7cm), blood pressure (132.6±16.4/86.1±11.2mmHg), mean insulinemia (88.8±24.6mU/l), HOMA IR (15.0±19.8), triglycerides (2.5±2.3mmol/l), CRP (8.5±8.1mg/l), PAI-1 (6.1±1.0U/ml) and decreased HDL (0.96±0.16mmol/l), SOD (1046.4±167.3U/gHb), GPX (25.0±17.1U/gHb). Patients with pre-MS had increased WC (100.7±14.4cm), mean insulinemia (52.8±21.6mU/l), HOMA IR (5.1±3.2) and PAI-1 (6.0±1.3U/ml). Patients with MS had a positive family history for obesity (45.6%), diabetes (50.8%), hyperlipoproteinemia (43.2%), hypertension (39.6%), angina pectoris (36,5%), myocardial infarction (40.4%) and stroke (39,5%).

Conclusion: In obese patients, abdominal obesity is accompanied with hyperinsulinism, IR, decreased antioxidant status. Correlations of HOMA IR with WC, PAI-1 and CRP explain connection between IR and abdominal obesity, increased levels of thrombotic and inflammatory factors and early risks of atherosclerosis.

No conflict of interest

BODY MASS DISTRIBUTION IN RELATION TO 5-YEAR RISK (2001-2006) OF CARDIOVASCULAR DISEASE, DIABETES, HYPERTENSION AND HYPERCHOLESTEROLEMIA:THE ATTICA STUDY.

E.N. Georgousopoulou[1], D.B. Panagiotakos[1], C. Pitsavos[2], C. Chrysohoou[2], J. Skoumas[2], C. Stefanadis[2]
[1]Nutrition and Dietetics, Harokopio University, Athens, Greece
[2]School of Medicine, First Department of Cardiology Hippokration Hospital, Athens, Greece

Introduction: overweight, obesity and abnormal waist circumference have been considered as major risk factors for developing cardiovascular disease (CVD) and various cardiometabolic disorders. However, the interaction of overweight/obese subjects with normal waist circumference has rarely been studied.

Methodology: 3042 subjects were recruited at baseline in the ATTICA study; 2101 of them were followed-up for 5-years (2001-2006). Subjects were categorized based on their body mass index and waist circumference values as: normal-weight-normal-waist, overweight/obese with normal waist, abnormal waist circumference with normal weight and with overweight/obese and abnormal waist.

Results: the 5-year incidence of CVD was 4.8% among normal-weight subjects, 7.7% among overweight/obese, 7.5%% among those with abnormal waist circumference and 11.6% among overweight/obese and with abnormal waist ($p<0.001$); however, after adjusting for potential confounders, the specific phenotype was not independently associated with risk for diabetes. Moreover, overweight/obese and with abnormal waist had similar 5-year incidence of hypercholesterolemia and hypertension as compared with the other categories (all $p>0.05$). The 5-year incidence of diabetes was 2.6% among normal-weight subjects, 4.3% among overweight/obese, 4.3% among abnormal waist circumference and 8.4% among with overweight/obese and abnormal waist ($p<0.001$); however, only those who were overweight/obese and with abnormal waist had significantly higher risk for diabetes as compared with the other categories. Moreover, The previous observation was confirmed even after adjusting for potential confounders, such as sex, age, physical activity level and adherence to Mediterranean diet (MedDietScore).

Conclusion: only the interaction of overweight/obesity with abnormal waist circumference seems to have an effect on the risk for diabetes.

No conflict of interest

PARAMETERS FOR ASSESSMENT OF LATE HOSPITAL ADMISSION OF PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

K. Novak[1], D. Glavas[1]
[1]Cardiology, University Hospital Split, Split, Croatia

The aim of this investigation was to analyze the total time from the onset of chest pain to the time of hospitalization in patients with acute myocardial infarction (AMI), and to estimate the parameters that could influence on late hospital admission.

Results: A total of 1314 patients with diagnosis of AMI were adimitted to CCU of University Hospital Split during the 1999, 2003 and 2005. The measurement included the time from the onset of chest pain to admission to CCU. During three investigated years, median period from the onset of chest pain to hospitalization was significantly decreased (5.2 h : 6 h : 4.3 h; $p<0.001$). More than half of male patients were admitted to the CCU more than 12 h after the onset of cardiac pain. On the other hand, almost half of females were hospitalized within 90 min. Older patients were admitted later than younger. The rapidity of hospitalization in patients with AMI significantly differences according to gender ($p=0.018$), age ($p<0.001$), location of myocardial infarction ($p<0.001$), arrhythmias and conduction disturbances ($p<0.001$). Patients with AMI and ST elevation of anterior or inferior location were approached faster to the hospital in comparison with AMI without ST elevation ($p<0.001$). Of 436 patients with anterior and anteroseptal location, 37 patients were arrivaled to the hospital in 90 min from the onset of pain, and only 29 of 442 patients with inferoposterior and inferior AMI. Patients with AMI who had arrhythmias or conduction disturbances, were approached significant faster to the hospital ($p<0.001$). Of 81 patients with AMI who were arrivaled in 90 min from the onset of pain, arrhythmias were recorded in 65.4%. Only 34.6% of patients without recorded arrhythmias were arrivaled to the hospital in 90 min from onset of pain.

Conclusions: During investigated years, median period from the onset of chest pain to hospitalization was significantly decreased. More than half of male patients were admitted to the CCU more than 12 h after the onset of cardiac pain. The rapidity of hospitalization significantly differences according to gender, age, location of infarction, arrhythmias and conduction disturbances.

No conflict of interest

IMPROVED RISK PREDICTION WITH CORONARY ARTERY CALCIUM(CAC)SCORE IN LOW-RISK WOMEN: A META-ANALYSIS OF FOUR COHORTS

P. Greenland[1], C.S. Desai[1], C.R. Ayers[2], M. Budoff[3], R. Erbel[4], M. Kavousi[5], A. Khera[2], N. Lehmann[6], K. Liu[1], S. Mohlenkamp[4], H. Ning[1], J. Witteman[7]
[1]Preventive Medicine, Northwestern University, Chicago Illinois, USA
[2]Cardiology, University of Texas Southwestern Medical Center, Dallas Texas, USA
[3]Cardiology, Harbor UCLA, Torrence California, USA
[4]Cardiology, Universität Duisburg, Essen, Germany
[5]Statistics, Erasmus MC University Medical Center, Rotterdam, Netherlands
[6]Statistics, Universität Duisburg, Essen, Germany
[7]Epidemiology, Erasmus MC University Medical Center, Rotterdam, Netherlands

OBJECTIVE: To determine prognostic significance and added predictive value of CAC for coronary heart disease (CHD) in "low risk" women.

METHODS: We included women without diabetes with 10-year Framingham risk score (FRS) for CHD < 10% from the Multi-Ethnic Study of Atherosclerosis (MESA), Dallas Heart Study (DHS), Heinz Nixdorf Recall (HNR) study, and the Rotterdam Study. CAC score was classified as 0, 1-10, 11-100, 101-300, or > 300. CHD outcomes included nonfatal myocardial infarction and CHD death. Measures included multivariable-adjusted hazards ratios (HR) for CHD and category-free net reclassification improvement (NRI) for addition of CAC to a traditional risk model. We used fixed-effects meta-analysis to combine effect measures.

RESULTS: In 6970 low-risk women (mean age 58 years), prevalence of CAC was: MESA, 32% (N = 880); DHS, 42% (N = 496); HNR, 50% (N = 908); Rotterdam, 73% (N = 949). Over 8 years of follow up, CHD event rate for CAC=0 ranged from 0.3% (DHS) to 1.2% (Rotterdam); event rate for CAC > 0 ranged from 1.0% (DHS) to 3.3% (Rotterdam). Multivariable-adjusted HR for CHD from meta-analysis was 1.84 (1.18-3.00). HR from meta-analysis for CAC > 300 compared to CAC=0 was 6.39 (3.08-13.26). NRI with addition of prevalent CAC to the baseline model ranged from 0.27 (Rotterdam) to 0.49 (MESA), and was 0.36 (P < 0.001) for the meta-analysis. NRI for addition of CAC strata from meta-analysis was 0.45 (P < 0.001).

CONCLUSION: In low-risk women, CAC>0 was associated with incident CHD and improved risk classification for CHD.

No conflict of interest

A STUDY COMPARING QUALITY OF LIFE IN POST MI PATIENTS WITH AND WITHOUT LIFESTYLE INTERVENTION THERAPY

I. gupta[1]
[1]*biomedical engineering, amity school of engineering and technology, gurgaon, India*

Quality of life is determined by various factors like life satisfaction, subjective well being, positive psychology and positive mental health. All these factors and personality traits are measured by the subjective well being inventory. Subjective well being has been widely researched in the past few decades and in practice it encompasses the various ways people evaluate their lives including concepts such as life satisfaction, work and health etc. Since it is well known that psychological factors including stress, anxiety and inadequate social contacts etc are known to be important causes of life style disorders like myocardial infarction, we started with the hypothesis that subjective well being of post acute MI patients is poor. A study was undertaken in which post MI patients were divided into 2 groups (50 subjects in each group)- Group A (on lifestyle interventions and medication) and Goup B (on medication alone).All subjects were administered a self report assessment inventory on subjective well being (WHO- Sell and Nagpal-1992).Both the groups were comparable demographically as well as history of smoking, drinking and family history of diabetes, hypertension etc.The 40 item questionnaire included questions which gave scores for 6 positive (well being factors) and 5 negative (ill being factors).Lifestyle intervention included yoga exercises under supervision, meditation techniques like pranayama (4-5 times a week), diet advice and cessation of smoking and drinking.Our results showed that while total positive scores were comparable at the time of registration into the study in the two groups, there was a significant difference ($p< 0.05$) at the end of one year – total positivity being higher in group A. Similarly total negative scores showed a significant difference at the end of one year of study period (total negativity being lower in group A).A factor wise analysis showed significant improvement in general well being (positive affect), family group support and social support and negative factors like deficiency in social contacts and perceived ill health including disturbed sleep.Thus, a positive well being reported in our study after a year of yoga may be beneficial because of a prudent lifestyle or may be acting through psychological processes like autonomic or neuroendocrine responses.Lot of studies on yoga within the broad category of mind body medicine have shown a reduction in negativity like stress, anxiety and depression as also reported in our study which may go a long way in reducing cardiac stress after MI.

No conflict of interest

SEX-SPECIFIC ASSOCIATIONS OF SERUM PROLACTINCONCENTRATIONS WITH CARDIAC REMODELING: LONGITUDINAL RESULTS FROM THE STUDY OF HEALTH POMERANIA (SHIP)

H.V. "R. Haring[1], R.S.V.,S.B.F.,M.N.,M.D. Izke[2], H.W. rr[4]
[1]Institute of Clinical Chemistry and Laboratory Medicine
[2]Institute for Community Medicine, University Medicine Greifswald, Greifswald, Germany
[3]Preventive Medicine and Epidemiology Section, Boston University School of Medicine, Boston, MA, USA
[4]Department of Cardiology, University Medicine Greifswald, Greifswald, Germany

>Background: Previousexperimental and patient-based studies suggest that prolactin (PRL) and its 16kDa fragment influence cardiovascular phenotypes by modulating angiogenesis.The association between serum PRL and cardiac remodeling in the general population is unknown.

Methods: We evaluated804 individuals (441 women) from the population-based Study ofHealth in Pomerania, aged ≥45 years, with available baseline serumPRL who underwent serial echocardiography at baseline and five-year follow-up.Left ventricular mass (LVM) was calculated and left ventricular hypertrophy(LVH) defined by sex-specific distributions of LVM. LV geometry was defined onthe basis of relative wall thickness (RWT) and LVH. Sex-specific multivariable regression analyses were performed relatingPRL (independent variable modelled as a continuous variable and as sex-specificquartiles) to change in LVM, RWT, and to incident LVH and abnormal geometry.

Results: BaselinePRL concentrations were inversely associated with LVM change in men, but not inwomen (ß per 10% decrease in PRL: 0.37; 95% CI, 0.13 to 0.60 in men and -0.02;95% CI, -0.21 to 0.17 in women, respectively). In men, baseline PRL concentrations were also inversely associated with incident LVH [first vs. fourth PRL quartile: relative risk (RR) 2.26 (95% CI,1.20 to 4.24)] andaltered LV geometry on follow-up [RR for incidentconcentric hypertrophy per 10% decrease in PRL: 1.20 (95% CI, 1.06 to 1.37)]. None of the longitudinal associations wereobserved in women.

Conclusion: Weobserved inverse associations of PRL with LVM change, incident LVH, and alteredLV geometry in men, but not in women.

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ASSOCIATION OF CORONARY ARTERY DISEASE RISK FACTORS WITH LIPID RATIOS ACROSS BODY MASS INDEX CATEGORIES IN 28566 HEALTHY ADULTS

M.m.-m.,N.j. Z.N. hatmi[1]
[1]TUMS, tehran
[2]KUMS, kermanshah, Iran

Background: Algorithm of the distribution of coronary artery disease (CAD) risk factors based on body mass index (BMI) categories remains nontransparent. It has been recognized a varying threshold of obesity for incrementing cardiovascular event risk across populations.
Accordingly detection and treatment of obesity and overweight can guide effective management of CAD epidemic at national and international level.

Objectives: To discover the discrepancy in the pattern of CAD risk factors across five groups of BMI

Methods: A population based cross sectional survey involving 28566 healthy participants was designed. Based on a standardized protocol data regarding multiple CAD risk factors were obtained by taking complete medical history, physical examination and 12 hours overnight fasting blood samples for laboratory tests.

Results: Fully adjustment regarding age, gender, literacy, cigarette smoking, systolic blood pressure, fasting blood sugar, and LDL-C/HDL-C ratio, revealed statistically significant increment of diastolic blood pressure >90 mmHg, high triglyceride level, high level of triglyceride/ HDL-C ratio, hypercholesterolemia, and high level of the ratio of cholesterol/HDL-C, across five groups of BMI.

Conclusions: Risk factors including diastolic blood pressure> 90 mmHg, high triglyceride level, hyper cholesterolemia, elevated ratios of cholesterol/ HDL-C and TG/HDL-C demonstrate a significantly increment across five categories of BMI. These findings are different from former published evidences. We believe present study has endorsed more features of the relationship between CAD risk factors and precisely categorized BMI."

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AMBULANCE PATIENT INFORMATION CLOUD SYSTEM FOR MANAGING ACUTE CORONARY EMERGENCIES IN COMMUNITY MEDICINE

H. Imagawa[1], T. Hatakeyama[1], N. Shinohara[1], K. Nishimura[1]
[1]Regeneration of Community Medicine, Ehime University, To-on, Japan

Background

Obtaining pre-hospital information including 12-lead ECG is becoming the standard of treatment for acute coronary syndrome. It remains a challenge to construct effective ambulance patient information network system in community medicine.

Methods

Pre-hospital 12-lead ECG as well as clinical conditions such as blood pressure, respiratory rate and pulse oximetry O_2 saturation is recorded in ambulance. The data is transtelephonically uploaded to cloud as a jpeg file among community medical institutions and out-of-community cardiologists. Emergency medical technicians, remotely located physicians and cardiologists interoperably interpret data by sharing records in the cloud via internet.

Results

The patients were 27% in mild, 38% in moderate, and 35% in serious condition. Acute coronary revascularization was recommended in 16.7% of total cases. Arrhythmias were found in 20%, congestive cardiac failure 23%, and aortic dissection 7%. Overall valuable ratio in clinical diagnosis was 97 %.

Conclusions

Useful information on myocardial ischemia, arrhythmia, and other cardio-vascular diseases could be obtained by ambulance patient information. The transtelephonic patient information cloud system made it possible to interpret 12-lead ECG among local hospitals as well as by out-of-community cardiologists. The pre-hospital patient information cloud system should be fully integrated into emergency practice in community medicine.

No conflict of interest

MEASUREMENT OF HIGH-MOLECULAR-WEIGHT ADIPONECTIN IS NOT USEFUL IN ASSESSING CORONARY STENOSIS IN JAPANESE MALE

T. Imatoh[1], M. Miyazaki[2], K. Kadowaki[3], S. Tanihara[1], H. Une[4]
[1]Preventive medicine and Public health, Fukuoka University, Fukuoka, Japan
[2]Director of center, Saitama city Institute of Health Science and Research, Saitama, Japan
[3]Division of Cardiology, Akita Medical Center, Akita, Japan
[4]General Medical Research Center, Fukuoka university, Fukuoka, Japan

Background: In many studies, high-molecular-weight (HMW) adiponectin has been considered the active form of adiponectin. However, whether HMW is a good surrogate marker for coronary artery disease still needs to be elucidated.

Methods: We conducted a hospital-based cross-sectional study to examine the relationship between total, HMW or non-HMW adiponectin levels and coronary stenosis in 83 male patients and 138 male controls.

Results: Subjects with coronary stenosis had significantly lower total adiponectin levels compared with controls. However, there were no significantly differences between cases and controls in HMW adiponectin levels. After adjusted for potential confounding factors, non-HMW adiponectin levels in cases were significantly lower than controls. From receiver operating characteristic (ROC) analysis, the area under the curve (AUC) for total and non-HMW adiponectin was significantly larger than that for HMW adiponectin levels. Of the three models, that for non-HMW adiponectin showed the largest AUC (Total adiponectin 0.74, HMW adiponectin 0.54, and non-HMW adiponectin 0.79).

Conclusions: Despite associations between total adiponectin levels and coronary stenosis, our data go against any apparent association between HMW adiponectin levels and coronary stenosis.

No conflict of interest

PREVALENCE OF SUBCLINICAL CORONARY ARTERY DISEASE IN ISCHEMIC STROKE PATIENTS

K. Iwasaki[1], K. Haraoka[2], T. Hamaguchi[1], T. Imamura[1], S. Kawada[1], M. Oono[1], K. Kashihara[1]
[1]Neurology, Okayama Kyokuto Hospital, Okayama, Japan
[2]Cardiology, Okayama Kyokuto Hospital, Okayama, Japan

Background and Purpose;

Recently ischemic stroke patients have emerged as a new coronary artery disease (CAD) risk equivalents. Our purpose is to study the prevalence of CAD in ischemic stroke patients compared with non-stroke patients.

Methods;

We measured coronary calcium score (CCS) in 151 ischemic stroke patients without known CAD (stroke group) and compared it with 151 age- and sex-matched non-stroke patients (control group).

Results;

CCS was significantly higher in stroke group than that in control group (median 64, interquartile range 3 to 382 in stroke group vs. 3, 0 to 65 in control group, $p<0.0001$). No coronary calcium was detected in 23.2% of stroke group compared with 47.7% of control group. High-risk CAD defined as CCS≥400 was detected in 24.5% of stroke group compared with 9.3% of control group ($p<0.0001$). Agreement between Framingham risk score and CCS was found in only 62 patients (41.1%). In multiple logistic regression analysis, age (HR 1.09, 95%CI 1.03-1.14), diabetes (HR 2.97, 95%CI 1.52-5.78), stroke (HR 3.85, 95%CI 1.89-7.81) and male (HR 4.41, 95%CI 1.82-10.75) were significantly associated with high-risk CAD ($p<0.001$).

Conclusions;

Our results showed that the prevalence of subclinical CAD in ischemic stroke patients was very high and a quarter of them had high-risk CAD. The age, diabetes, stroke, and male were independent predictors of high-risk CAD.

No conflict of interest

CRITICAL LIMB ISCHAEMIA: INITIAL TREATMENT AND PREDICTORS OF AMPUTATION-FREE SURVIVAL

J. Karja[1], J. Boos[2], H. Bruijnen[2], K. Woelfle[2], M. Engelhardt[1]
[1]Department of Vascular and Endovascular Surgery, Military Hospital Ulm, Ulm, Germany
[2]Department of Vascular Surgery, Klinikum Augsburg, Department of Vascular Surgery, Germany

In a prospective clinical cohort study the initial treatment and risk factors for amputation-free survival in patients with critical limb ischaemia (CLI) were evaluated at a single vascular surgical centre in Germany.
Patients and methods: Records of 104 consecutive patients (115 limbs) presenting with their first episode of CLI were collected prospectively over a 3-years period. Initial treatment was classified as conservative therapy, catheter-based intervention, surgical arterial reconstruction and primary major amputation. Patient co-morbidities were assessed by uni- and multivariate analysis to determine risk factors for limb-salvage, survival and amputation-free survival.
Results: Indications for treatment were rest pain in 27 (23.5%) limbs and tissue loss in 88 (76.5%) limbs. Revascularisation was attempted in 65% of all limbs: 45% by intervention and 55% by surgery. In 9% primary amputation was performed and 22% received conservative therapy. Median follow-up was 28 months (range, 1 - 42). The 3-years limb-salvage, patient survival, and amputation-free survival rates were 73%, 41%, and 31%, respectively. Diabetes mellitus, major cardiac disease and renal insufficiency were associated with poor survival. A combination of cardiac disease and renal insufficiency adversely affected amputation-free survival rate (HR, 3.68; 95% CI, 1.52-8.95; P< 0.01).
Conclusions: At least two third of all patients presenting with CLI can be offered some type of revascularisation. In less than 10% primary amputation is required. In patients with major cardiac disease and renal insufficiency, a poor outcome in terms of amputation-free survival is to be anticipated.

Keywords: critical limb ischaemia, risk factors, amputation-free survival, diabetes mellitus, renal insufficiency, revascularisation

No conflict of interest

ASSOCIATION BETWEEN HDL CHOLESTEROL AND THE SEVERITY OF CORONARY ARTERY DISEASE IN ASIAN PEOPLE

S.H. Kim[1], H.R. Kim[1], J.B. Seo[1], W.Y. Chung[1], J.H. Zo[1], M.A. Kim[1], H.L. Lee[2], G.J. Ahn[3], D.G. Park[4], Y.J. Seong[1]

[1]Cardiology, Seoul Boramae Medical Center, Seoul, Korea
[2]Internal Medicine, Seoul Bukbu Hospital, Seoul, Korea
[3]Cardiology, Hanjeon Hospital, Seoul, Korea
[4]Cardiology, Gangdong Sacred Hospital, Seoul, Korea

Objective: Low level of low density lipoprotein cholesterol (LDL cholesterol) is the strong predictor for coronary artery disease (CAD). The aim of this study was to investigate impact of HDL cholesterol on prevalence and severity of CAD by coronary angiography.
Methods: The subjects were 1884 Korean patients received a successful coronary angiography. The severity was determined by the number of involved vessels and Friesinger Score on angiography. The evaluation was done on risk of CAD prevalence according to stratified HDL cholesterol and mean HDL cholesterol level according to severity.
Results: As HDL cholesterol has decreased, the odd ratio of CAD prevalence has increased gradually. The patients with HDL cholesterol < 30mg/dL had 3.4 times more risky than patients with HDL cholesterol ≥ 60mg/dL. The mean HDL cholesterol level was 43.5mg/dL, 41.0mg/dL, 38.5mg/dL, 37.5mg/dL respectively for the control group, 1-vessel disease (VD), 2VD, 3VD. Even the subgroup analysis among patients with LDL cholesterol < 100mg/dL showed the correlation between HDL cholesterol level and the severity of coronary artery disease. The HDL cholesterol level was found to have a significant negative association with Friesinger score (r=-0.201, P<0.001).
Conclusion: HDL cholesterol level is significantly associated with the prevalence and severity of CAD on coronary angiography in Korean people.

No conflict of interest

RELATION BETWEEN KIDNEY FUNCTION (SERUM CREATININE, E-GFR& PROTEINURIA) AND SYNTAX SCORE IN NON DIABETIC CKD PATIENTS.

M. Koriem[1], M. Aziz[1], S. Dimitry[1]
[1]Cardiology, Assiut University Hospital, Assiut, Egypt

Background: Chronic kidney disease (CKD) is highly prevalent with significant morbidity and mortality rates among patients with coronary artery disease (CAD).1-3 The SYNTAX Score (Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery) predicts the outcomes of patients undergoing percutaneous coronary intervention. Our aim was to evaluate the correlation between CKD and severity of coronary artery stenosis by calculating SYNTAX Score in non diabetic CKD patients.
Patients and Methods: SYNTAX Score was calculated for 180 non diabetic patients with CKD scheduled for coronary angiography. Serum creatinine and 24 hour proteinuria prior to CAG were assessed in all patients. Patients were divided into 2 groups according to their estimated glomelular filteration rate, (group 1 with eGFR ≥15 to < 30 ml/min per 1.73 m^2) and (group 2 with eGFR ≥ 30 ml/min per 1.73 m^2).
Results: coronary arteries lesions complexity increased progressively with decreasing kidney function as there were significant negative correlation between e-GFR and SYNTAX Score (r = -0.5, P = 0.0004) and significant positive correlation between 24 hr proteinuria and SYNTAX Score (r = 0.6, p = 0.0001).
Conclusion: Serum creatinine, estimated glomerular filtration rate and 24 hours proteinuria were predictors of higher SYNTAX Score.

No conflict of interest

THE LOW LEVEL OF TESTOSTERONE INDIPENDENT RISK FACTOR FOR CORONARY ARTERY DISEASE

M. Lezha[1], L. Bica[1]
[1]Cardiology, University Hospital Center "Mother Theresa" Tirana Albania, Tirana, Albania

Background: The strongest independent risk factors for coronary artery disease (CAD) are increasing age and male gender. Despite regional variations in the prevalence of coronary artery disease (CAD), men are consistently more at risk of developing and dying from CAD than women, and the gender-specific effects of sex hormones are implicated in this inequality.

Aim: To evaluate the relationship between testosterone level and presence and severity of CAD in patients undergoing coronary angiography and in matched controls.

Methods: 933 men, aged of range 27-74y, with chest pain and with or without ECG changes, without recent myocardial infarction, valve disease, cancer prostate, no treatment with androgens, nizoral and corticosteroids, who were admitted in the clinic of cardiology of the UHC in Tirana, were included in the study. They underwent coronaryangiography for the diagnosis of CAD. In the same day with angiography, a blood sample for testosterone (T)level's value was done with radioimmunoessay method. Fasting plasma total cholesterol, low-density lipoprotein cholesterol(LDL-C), high-density lipoprotein cholesterol(HDL-C), triglyceride, glucose levels were measured. The evaluation of risk factors for CAD was made for every subject.
Results: Based on the results of coronaryangiography, our subjects were divided in two groups: patients group(PGR) (n = 689) and control group(CGR) without CAD (n = 244).
There was no significant difference between two GR in the age, (p = NS), in the total level of cholesterol, triglycerides, LDL-C, diabetes mellitus. In the PGR the T level was significantly lower than in CGR: 4.99±2,25 nmol/ml vs 7.196±2,22 nmol /ml, respectively, (p = 0,00005). In the PGR, 217 patients(pts) had 1 vessel disease(VD), 176 pts had 2VD and 296 pts has 3VD. The T levels were respectively 5.61 ± 1.74nmol/ml vs, 5.014 ± 1.6nmol/ml vs 4.44 ± 1.48nmol/ml (r = - 0,08, p = 0,000). The multivariate logistic regression analysis of all risk factors for CAD in the pts of our study, revealed that besides diabetes mellitus (p = 0,062), HBP (p = 0,085), smoking (p = 0,000), BMI (p = 0,165), HDL-C(p=0,088), LDL-C(p=0,063), low free testosterone level (p = 0,000; odds ratio = 0,57; 95% confidence interval = 0,52 – 0,63) was an indipendent risk factor for CAD.

Conclusions: The low level of testosterone is an independent risk factor for CAD and may be involved with the increased risk of CAD in men.

No conflict of interest

DETERMINANTS OF RENIN-ANGIOTENSIN SYSTEM INHIBITORS UNDERUSE IN PATIENTS WITH ACUTE CORONARY SYNDROME.

A. López-Cuenca[1], M.J. Sánchez-Galián[1], F. Cambronero[2], P.J. Flores-Blanco[1], M. Sánchez-Martínez[1], J.M. Andreu-Cayuelas[1], A. García-Narbón[1], I. De las Heras Gómez[1], M. Valdés[1], S. Manzano-Fernández[1]

[1]Cardiology, Hospital Universitario Virgen de la Arrixaca, Murcia, Spain

[2]Cardiology, Hospital Universitario Morales Meseguer, Murcia, Spain

Background: The use of renin-angiotensin system inhibitors (RASI) in patients with acute coronary syndrome (ACS) is associated with a better prognosis. The evaluation of factors related to RASI underuse in ACS patients could help us to improve the clinical management of these patients.

Methods and Results: From January 2012 to January 2013, we enrolled all patients with ACS discharged from two tertiary hospitals in Spain. Patients with intolerance or allergy to RASI were excluded. To identify determinants of RASI underuse we performed a multivariate logistic regression analysis.

Results: The study population consisted of 644 patients (67 ± 13 years, 73% men). Of them, 559 (87%) were discharged on RASI. Patients discharged on RASI were older (68 ± 12 years vs 63 ± 13 years, p=0.01) and had more frequently other comorbidities including diabetes mellitus (93% vs 83%, p<0.001), hypertension (91% vs 75%, p<0.001) and lower left ventricular ejection fraction (LVEF) (57% [45-62] vs 60% [55-62], p<0.001). By contrast, renal function was similar both treatment groups (p>0.05). After multivariate adjustment, preserved LVEF (LVEF>50%, OR 0.21 [0.09-0.51], p=0.001) and absence of hypertension (OR 0.34 [0.20-0.59], p<0.001) were identified as the independent predictors of RASI underuse.

Conclusion: According to current clinical guidelines, there is a high RASI use among the wide spectrum of our ACS patients. Preserved LVEF and absence of hypertension were lined to a RASI uderuse. The lack of strong clinical evidence supporting the benefits of these agents in these subgroups of patients could be implicated on these findings.

No conflict of interest

RELATIONSHIP BETWEEN THE CALCIUM SCORE AND THE CLASSICAL CARDIOVASCULAR RISK FACTORS

A. Mamede[1], L. Bronze[1], R. Fernandes[2], A. Anão[3], A. Oliveira[4], J. Baptista[4], M. Rodrigues[4], M. Figueira[4], J. Pires[4], M. Pinheiro[4]

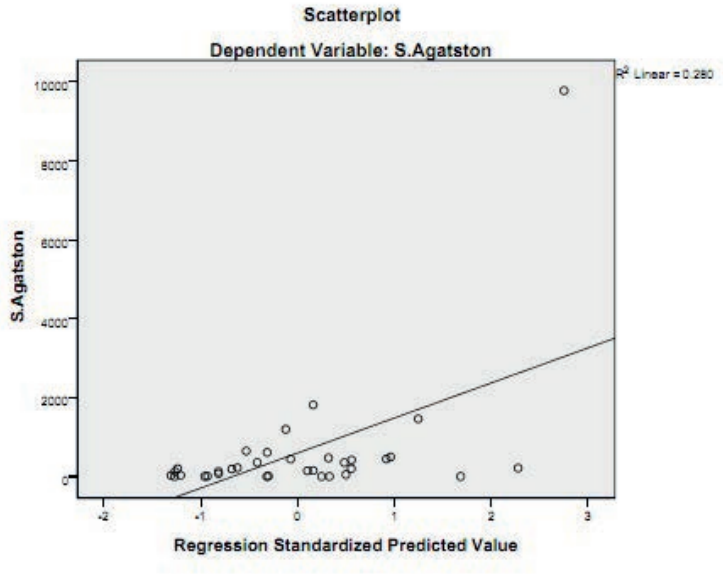
[1]Saúde Naval - Cardiologia, Centro de Investigação Naval, Lisbon, Portugal

[2]Cardiologia, Centro de Medicina Naval, Lisbon, Portugal

[3]Cardiologia, Hospital das Forças Armadas, Lisbon, Portugal

[4]Radiologia, Hospital das Forças Armadas, Lisbon, Portugal

The coronary calcium score (CS) has been used increasingly as a method for assessing the cardiovascular risk. **Objective:** To study the relationship between the CS and the classical cardiovascular risk factors (CVRF). Methods: We studied, prospectively, a population of 62 patients with a mean age of 54.27 ± 10.16 (37-79) years, 4 (4/62 = 6.45%) women, followed in cardiology appointment, without any previous cardiovascular event. Proceeded to quantify elective CS (amount of calcium expressed as an Agatston Score - AS) via computerized axial tomography equipment Toshiba Aquilion 16. They are deemed to CVRF the following parameters: hypertension (HT), diabetes mellitus (DM), smoking (S), family history of coronary heart disease (FH) and dyslipidemia (DYS). Appreciated yet the levels of serum glucose, HbA1c, and low density lipoprotein cholesterol (LDLC) as well as age and biometric values: body mass index (BMI) and waist circumference (WC). We studied the relationship (linear regression) between the values of SA with age and serum values and biometrics referred to the entire population. Proceeded to the multiple linear regression between the SA and the values for WC, LDLC and HbA1c. Finally, we compared the prevalence of cardiovascular risk factors in two groups, according to the SA was above or below the 50th percentile in the study population (chi-square). Results: The prevalence of cardiovascular risk factors in this population were: hypertension (53/62 = 85.48%), S (29/62 = 46.77%), DYS (44/62 = 70.96%), DM (17 / 62 = 27.41%), FH (13/62 = 20.96%). Two groups were found for SA: Group 1 <52 and Group 2 ≥ 52, the comparison of CVRF according to these groups (chi-square) is presented in the table below. The linear regression for SA was age R = 0.33, WC R = 0.20; BMI R = 0.15, LDLC R = 0.19; Glycemia R = 0.12, HbA1C R = 0.12. Multiple linear regression study is presented in the graph (R = 0.53, p = 0.018). Conclusions: The CS seems to be influenced by the presence of DM and FH. Age, WC and LDLC are the factors that, in this population, better relate to CS. Through a model that includes CLDL, HbA1C and WC there is a reasonable relationship to the SC.



	GROUP 1 (N=31)	GROUP 2 (N=31)	P (Qui-quadrado)
DYS	23 (74,19%)	21 (67,74%)	0,390
DM	3 (9,68%)	14 (45,16%)	0,002
FH	3 (9,68%)	10 (32,26%)	0,029
S	15 (48,39%)	14 (45,16%)	0,500
HT	25 (80,65%)	28 (90,32%)	0,236

No conflict of interest

BODY MASS INDEX AND SEVERITY OF CORONARY ARTERY DISEASE IN ACUTE MYOCARDIAL INFARCTION PATIENTS

P.S. Mateus[1], C. Ferreira[1], A. Baptista[1], P. Magalhães[1], S. Leao[1], J.I. Moreira[1]
[1]Cardiology, C.H. Trás-os-Montes e Alto Douro, Vila Real, Portugal

Background

The relationship of excess weight with severity of coronary artery disease (CAD) isn't clear.

The aim of this study was to compare the and severity of CAD in patients admitted for acute myocardial infarction (AMI).

Methods

Patients admitted for a first AMI with information on height and weight were selected. Body mass index (BMI) was available in 486 patients and 389 (80.0%) of them had a coronary angiography (CAT) during hospital stay. Patients were classified as having normal weight (NW) when BMI was 20.0-24.9, overweight when BMI was 25.0-29.9 and obese when BMI was 30Kg/m2 or greater. A coronary stenosis of 50% or more was considered to be significant. Median number of diseased vessels and proportion of patients with left main (LM) disease and 3 vessel disease (3VD) were compared between BMI classes.

Results

Most patients in every BMI class had a CAT and of these 110(28.3%) had NW, 194(50.8%) were overweight and 78(20.4%) were obese. Overweight and obese patients were younger (mean age 64.3+/-13.2 and 63.7+/-12.1 vs. 67.8+/-14.2 years in NW, p=0.02) and more frequently diabetic (23.7% and 40.2% vs. 22.6%, p=0.005) and hypertensive (64.1% and 74.2% vs. 48.1%, p<0.001). Median number of vessels with significant stenosis was not different in overweight, obese and NW patients (median=1.0 in all classes, p=0.74). No differences were found in the proportion of patients with 3VD (17.6% in overweight, 20.6% in obese and 18.8% in NW, p=0.80) or LM stenosis (4.5%, 4.1% and 4.5%, p=0.99). Adjusting for age, diabetes and hypertension, risk of 3VD was not increased in overweight (0.92, 95%CI:0.52-1.62) nor in obese patients (0.94, 95%CI:0.47-1.90). Risk of LM disease was also not different in overweight (OR:1.19, 95%CI:0.42-3.39) and obese (OR:1.17, 95%CI:0.30-4.57).

Conclusions

Overweight and obesity, as measured by BMI, were not related to severity of CAD in AMI patients.

No conflict of interest

ASSESSMENT OF THE TEACHING-LEARNING PROCESS IN EMERGENCY SITUATIONS FOR UNDERGRADUATE STUDENTS: HEALTH PROMOTION AND DAMAGE PREVENTION

S. Meneguin[1], D.G. Santana[1]
[1]Enfermagem, Faculdade de Medicina de Botucatu-Unesp, Botucatu, Brazil

Introduction: Emergency situations come up unexpectedly in people's lives, demanding rapid, objective and effective action. These include basic life support (BLS) fundamental to save lives and prevent sequelae. This study was aimed at analyzing the knowledge (theoretical) and skills (practical) of undergraduate students at a public university in the interior of Brazil, before and after a course/training on BLS. **Methods:** A descriptive and comparative study was undertaken, involving the School of Agronomic Sciences, Veterinary Medicine/Zootechnics, the Institute of Biosciences and the Nursing Program at Unesp – Botucatu/Brasil. Students regularly enrolled in the first year of the respective undergraduate programs and who agreed to participate were considered eligible. Data collection was divided in two phases. The first served to individually assess the knowledge (theoretical) and skills (practical) before the course/training on BLS. In the second phase, cardiopulmonary resuscitation knowledge and skills were assessed after the students had participated in the course/training. **Results:** Between April and June 2013, 97 students participated in the course/training, with a mean age of 18,6 years, mostly female and who had never participated in BLS training. When comparing BLS maneuver skills in the nursing program, performance levels improved between the first and second phase for all items (p=0,000008). **Conclusion:** The nursing students' performance improved with regard to basic life support maneuver skills.

No conflict of interest

QUALITY OF LIFE IN PREGNANT PATIENTS SUFFERING FROM HEART DISEASE: PRE AND POSTPARTUM

S. Meneguin[1], C.L. Xavier[1], D.G. Santana[1]
[1]Enfermagem, Faculdade de Medicina de Botucatu-Unesp, Botucatu, Brazil

Introduction: The association between cardiac illness and pregnancy is an acknowledged obstetric and fetal risk factor during the pregnancy-postpartum cycle. This study aimed to describe the perceptions of pregnant women with heart disease concerning their quality of life pre and postpartum. **Methods:** In this descriptive and exploratory research, the Short-Form Health Survey (SF-36) Questionnaire was applied to pregnant women with heart disease after the second term of pregnancy and 40 days after giving birth. To establish the correlations, Spearman's correlation coefficient was used and significance was set at 5% for the tests.**Results:** Between November 2011 and May 2013, 33 pregnant women with heart disease were interviewed, 81.8% married, with a mean age of 27.2 years (±SD 8.29), and the majority with an unplanned pregnancy (69.6%). In addition, 33.3% reported at least one case of previous abortion and 87.8% did not participate in family planning groups. Quality of life assessment showed significant improvements in the functional capacity, physical, social and A positive correlation was found between planning the pregnancy and the mental health domain (p=0.0277), as well as a negative correlation with emotional aspects (p=0.0202).**Conclusion:** In all patients, a significant improvement was observed in postpartum quality of life, except in the general health status and mental health domains. When the pregnancy was planned, however, this contributed to improve the participants' mental health, although it aggravated emotional aspects.

No conflict of interest

THE SURVIVAL OF PATIENTS WITH DEGENERATIVE AORTIC STENOSIS CORRELATED WITH POSTERIOR MITRAL ANNULAR CALCIFICATION AND INTIMA- MEDIA THICKNESS. A PROSPECTIVE STUDY

D. Mercea[1], C. Pop[1]
[1]Cardiology, Emergency County Hospital Dr Constantin Opris, Baia Mare, Romania

Introduction: Degenerative aortic stenosis (AS) represents 43% of the degenerative valvulopathies. The mortality of patients with asymptomatic aortic stenosis is below 1% per year.
Method and Results: We have studied prospectively 196 patients with degenerative AS over a period of time of 5 years by echocardiography and Doppler echocardiography and we have analyzed the survival rates.
We have identified 106 patients with mild AS (54.1%), 28 patients with moderate AS (14.3%) and 62 patients with severe AS (31.6%). Mitral annular calcification (MAC) was found at 140 patients (71%) and intima- media thickness (IMT) over 1 was discovered at 143 patients (73%). Survival rates were processed with Kaplan-Meier method and Log Rank test. During follow-up period, 61 of our patients have died (31%), with a mortality rate greater than in the general population. Out of the 140 patients associating MAC to AS, 36,4% have died during five year follow-up, compared to only 17,4% of those without MAC associated to AS. The difference between survival rates at 1 year was 6,4% and enhanced at 5 years to 20,3% (HR 2.28, 95% CI 1.16 - 4.49; p=0.01). Regarding the 143 patients with IMT exceeding 1, 33,5% were deceased after 5 years, compared to 24,5% of the subjects with normal IMT. The difference between survival rates at 1 year was 5,4% and enhanced at 5 years to 11,7%, without statistical significance.
Conclusion: The presence of MAC in patients with AS represents an independent predictor of mortality, compared to IMT >1 which does not influence the prognosis of these patients.

No conflict of interest

DOES INACCURATE DEATH CERTIFICATION CONTRIBUTE TO THE REPORTED HIGH RISK OF CARDIOVASCULAR DISEASE AMONGST INDIAN ASIANS?

R.K. Mills[1], S.T. Tan[2], M. Loh[3], V. Panoulas[4], U. Afzal[2], J. Scott[2], P. Elliott[3], J.S. Kooner[2], J.C. Chambers[2]
[1]Cardiology, Ealing Hospital NHS Trust, London, United Kingdom
[2]National Heart and Lung Institute, Imperial College London, London, United Kingdom
[3]Epidemiology and Biostatistics, Imperial College London, London, United Kingdom
[4]Cardiology, Imperial College Healthcare NHS Trust, London, United Kingdom

Background

National mortality statistics report that UK Indian Asians are at ~2 fold higher risk of cardiovascular disease mortality compared with European descendants. However, previous studies in North Americans and Europeans suggest errors in up to 40% of death certificates, leading to cardiovascular disease mortality overestimation. Validity of routine death certification amongst Indian Asians is unknown.

Aims and methods

We investigated the accuracy of routine death certification amongst UK Indian Asians, to determine whether incorrect certification contributes to reported higher cardiovascular disease rates. We reviewed all available medical records for a representative sample of 200 Indian Asians and Europeans who died in London between 2003-11. Deaths were independently coded as cardiovascular or non-cardiovascular according to published international diagnostic criteria by 2 cardiologists; where there was disagreement, a third adjudicated.

Results

Age of death was lower amongst Indian Asians than Europeans (67.1 ± 9.9 vs. 70.0 ± 8.8, P=0.04). Compared to review of records, routine death certification overestimated cardiovascular disease as underlying cause of death amongst Indian Asians (33.1 vs. 27.3%, P<0.001) and Europeans (29.0% vs. 25.8%, P<0.001). Routine death certification showed similar accuracy for the diagnosis of cardiovascular disease amongst both Indian Asians and Europeans (sensitivity: 87.8% vs. 87.5%, P=1.00; specificity: 87.5% vs. 91.3%, P=0.58; positive predictive value: 72.5% vs. 77.8%, P=0.76, respectively).

Conclusion

Although routine death certification overestimates cardiovascular deaths by ~20% amongst UK Indian Asians and Europeans, the accuracy of death certification is similar in both populations. Inaccurate death certification does not contribute to higher reported cardiovascular disease mortality amongst Indian Asians compared to Europeans.

No conflict of interest

TOBACCO SMOKING ASSOCIATED WITH REDUCED LEFT VENTRICULAR EJECTION FRACTION BY 64-MDCT INDEPENDENT OF CORONARY ARTERY DISEASE

R. Mitsutake[1], H. Urata[1], K. Okamura[1], S. Miura[2], K. Saku[2]
[1]cardiovascular disease, Fukuoka University Chikushi Hospital, Chikushino, Japan
[2]Cardiology, Fukuoka University, Fukuoka, Japan

Background Previous studies have demonstrated that tobacco smoking is a major risk factor for coronary artery disease (CAD), hypertension (HTN), chronic obstructive pulmonary disease, oral, nasopharyngeal, bronchial and other visceral malignancies.

Methods and Results Subjects were included 513 consecutive patients who underwent coronary angiography using 64-MDCT. We assessed the presence of CAD, and quantified coronary artery calcification score on MDCT. We also analyzed conventional risk factors, and subcutaneous and visceral fat area (SFA and VFA). Furthermore, we calculated LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), LVEF and LV mass using MDCT. Of the total of 513 subjects, 165 (32%) were smokers, and 209 (41%) were diagnosed as MetS. The number of metabolic factors in subjects with smokers was higher than that in other subjects. LVEF after adjusting for body surface area in MetS group was significantly lower than that in non-MetS group. When all subjects were divided into five groups (0-4) according to the number of metabolic factors, LVEF were significantly decreased as the number increased. In a multivariate logistic regression analysis, age, systolic blood pressure, VFA, and the presence of CAD (in only female) were significantly associated with reduced LVEF in non-smoker group.

Conclusion This study suggested that tobacco smoking or MetS contributed to reduced LV systolic function independent of CAD.

No conflict of interest

DIETARY CHANGE AS A VIRTUOUS CIRCLE? AN ETHNOGRAPHIC STUDY ON THE STEP BY STEP TAKING CARE PROCESS FOR CHOLESTEROL MANAGEMENT

G. naelten[1], T. fournier[2], E. bruckert[3], C. alamowitch[4], N. boireau[5]
[1]cardiovascular department, danone research, palaiseau, France
[2]laboratoire CERTOP UMR CNRS 5044, Université de Toulouse II-Maison de la Recherche, toulouse, France
[3]service endocrinologie et erévention des maladies cardiovasculaires, hôpital pitié salpêtrière, paris, France
[4]-, -, livry-gargan, France
[5]sensory and behavior science department, danone research, palaiseau, France

Background and Aims: Set-up of sustainable lifestyle changes among hypercholesterolemic patients is a challenge. Our study aimed at retracing patient's story in order to identify the steps leading either to successful lifestyle change or failure.

Methods: A three steps qualitative survey was conducted in 25 subjects: a) interview at home (1h30) to identify feelings and steps of cholesterol management, b) auto-ethnography period using photo and video (10 days) to illustrate barriers and levers of cholesterol management, c) interview at home (2h) to build lifestyle habits change model.

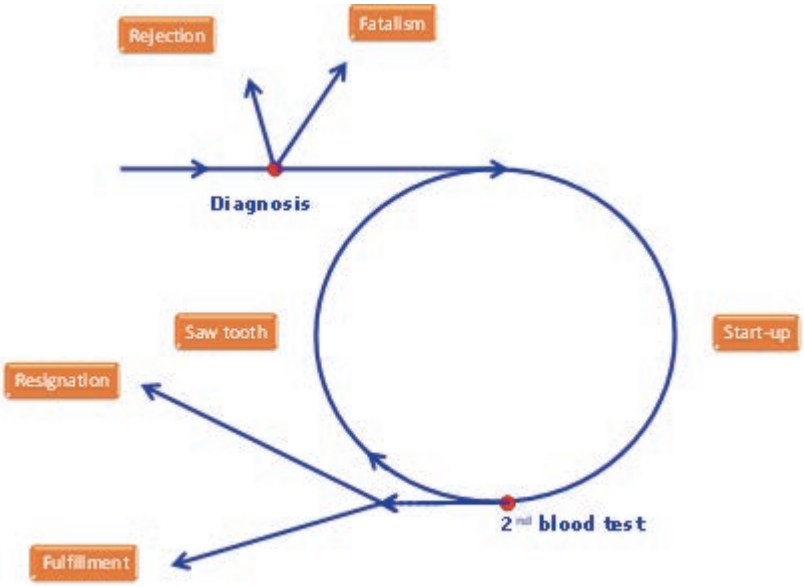
Results: The taking care process for cholesterol management is made of six dynamic stages (table 1)

Table 1. The stages of change

No change	
Rejection	*"I do not want to change my lifestyle habits"*
Fatalism	*"Cholesterol is not my main concern"*
Transitional change	
Start-up	*"I feel suspended, waiting for the second blood test"*
Saw tooth	*"I always alternate between restriction and dietary lapses"*
Stabilized change	
Resignation	*" I have changed my lifestyle habits but it doesn't make me satisfied"*
Fulfillment	*"Even if I was told that my cholesterol was not a problem anymore, I would not change anything in my new life"*

This dynamic process of change corresponds to a virtuous circle with the hypercholesterolemia diagnosis as the starting point (Graph 1). Among people reaching a stabilized lifestyle change, the "resignation" stage depends on an external support such as GP and entourage. The "fulfillment" one feels he is the real owner of his lifestyle change with positive physical and psychological impact.

Graph 1. The virtuous circle for cholesterol management



Conclusion & perspectives:

Diagnosis of hypercholesterolemia, GP's speech and close entourage are the main triggers of sustainable lifestyle changes for cholesterol reduction. The identification of patient's profile inside this dynamic process should allow to better guide him towards compliance to therapeutic lifestyle changes.

Conflict of interest

THE RELATION OF FATIGUE RELATED PSYCHOLOGICAL FACTORS TO ERGOMETRIC CAPACITY IN PATIENTS WITH CARDIOVASCULAR DISEASE

A. Nagy[1], B. Mezey[2], B. Sándor[2], E. Szabados[2], K. Tóth[2], A. Csathó[1]
[1]Institute of Behavioral Sciences, University of Pécs, Pécs, Hungary
[2]1st Department of Internal Medicine, University of Pécs, Pécs, Hungary

Vital exhaustion and chronic fatigue are highly predictive psychological risk-factors of myocardiac infarction and sudden cardiac death. Very little is known, however, how these factors relate to overall cardiorespiratory fitness indicated, for example, by ergometric capacity. Therefore, the present study was aimed to investigate the relationship between cardiovascular reactivity to ergometric exercise and various psychological factors with a special emphasis on chronic fatigue. ***Methods.*** Patients (N = 79; aged between 59-71, with a mean of 65.38) with cardiovascular disease completed the Shortened 9-item Vital Exhaustion Questionnaire, FIS Fatigue Questionnaire, SF-36 Health Survey, as well as they performed a Psychomotor Vigilance Test (PVT). In addition, each participants underwent an ergometric exercise test. ***Results and Conclusions***. The results indicate strong associations between the ergometric and psychological factors. More specifically, the fatigue related psychological parameters were found to show significant association with maximum systolic blood pressure, maximum heart rate, RAC%, METs and T-waves/min.

No conflict of interest

INCREASED INCIDENCE OF SUDDEN DEATH AFTER 2011 EARTHQUAKE AND TSUNAMI DISASTER IN NORTHEAST JAPAN: A POPULATION-BASED STUDY

M. Niiyama[1], F. Tanaka[1], T. Segawa[1], T. Takahashi[1], K. Sato[1], S. Watanabe[1], M. Honma[1], T. Onoda[1], K. Sakata[1], M. Nakamura[1]

[1]Medicine, Iwate Medical University Hospital, Morioka Iwate, Japan

BACKGROUND: A catastrophic earthquake followed by a huge tsunami impacted the northeastern coast of Japan on 11 March 2011. No reports have demonstrated the effect of the disasters on the population-based incidence of sudden death (SD).

METHODS: We surveyed death certificates of all decedents between February 2011 and May 2011 (4 weeks before and 8 weeks after the disaster) in Iwate prefecture including the east coast area also affected by the huge tsunami. For comparison with the previous year's-case numbers, the same survey was conducted in the corresponding area during 2009 and 2010. SD was defined as unexpected death occurred within 24 hours after the onset and was defined by the ICD-10 codes. The standardized incidence ratio of SD and its 95% confidence interval (CI) were determined from the numbers of observed case and expected case calculated by age-adjusted incidence rate of the previous two years.

RESULTS: The crude incidence rate (per 10,000 person-year) after the disaster was significantly increased to compare the previous two years-rate (29.1 vs 21.2; $p < 0.05$). The standardized incidence ratio (95%CI) was tripled at 1st week after the initial quake (3.64, 95%CI = 2.38 – 5.33: $p < 0.001$) and again at 4th week just after the second quake (2.88, 95%CI = 1.78 – 4.41: $p < 0.001$). The direct relationship was observed between the incidence ratio and the seismic intensity ($r = 0.74$, $p < 0.01$). The standardized incidence ratio was significantly elevated in the tsunami area (1.49, 95%CI = 1.18 – 1.86: $p < 0.001$), but not in the control area that was not impacted by the tsunami (1.15, 95%CI = 0.86 – 1.52).

CONCLUSIONS: The population-based incidence of SD was rapidly increased after the disaster especially in the area attacked by catastrophic earthquake and devastating tsunami.

No conflict of interest

WHAT DO WE REALLY KNOW? EVALUATION OF CORONARY HEART DISEASE DATA AVAILABILITY AND ADEQUACY IN AUSTRALIA

M. Nichols[1], *S. Allender*[1]
[1]*Population Health Strategic Research Centre Faculty of Health, Deakin University, Geelong, Australia*

Background: Coronary heart disease (CHD) remains a leading cause of death in Australia and around the world. A range of efforts are underway in many countries to quantify and track over time the morbidity, mortality, treatment, and contributing risk and protective factors for CHD. High quality, representative, and regularly or routinely collected data are a crucial foundation for understanding and informing action, policy and advocacy to address the burden of CHD. The aim of this study was to conduct a national audit of existing data sources relevant to CHD and related risk factors in Australia.

Methods: Data sources were identified and obtained through a variety of methods, including scientific literature searches, grey literature, online searches and contact with key stakeholders. Identified datasets were assessed for content, quality, coverage, collection frequency and availability.

Results: Data sources varied widely in their coverage and accessibility for research. Mortality and morbidity (hospital episodes) data have comparatively very high coverage, quality and detail, and are accessible for epidemiological research. A major issue for many other types of data, particularly for risk factors, was the reliance on semi-regular or ad hoc surveys, rather than data that are routinely collated as part of regular practice.

Conclusions: It remains difficult to form a clear picture or international comparison for many aspects of heart health in Australia. The upcoming release of results from the Australian Health Survey will answer many questions, but will do little to address the ad hoc nature and limited comparability of existing data sources.

No conflict of interest

DEPRESSION AND 16 YEARS RISK OF STROKE IN FEMALE POPULATION AGED 25-64 YEARS IN RUSSIA: EPIDEMIOLOGICAL PROGRAM WHO "MONICA-PSYCHOSOCIAL"

V. Gafarov[1], D. Panov[2], E. Gromova[2], I. Gagulin[1], A. Gafarova[1]
[1]Collaborative laboratory of cardiovascular diseases epidemiology, SB RAMS, Novosibirsk, Russia
[2]Laboratory of psychological and sociological issues of internal diseases,
FSBI Institute of Internal Medicine SB RAMS, Novosibirsk, Russia

The aim: To study the influence of depression (D) on relative risk of stroke and its relation with awareness and attitude towards the health in female population of 25-64 years in Russia.

Material and methods: Under the third screening of the WHO "MONICA-psychosocial" (MOPSY) program random representative sample of women aged 25-64 years (n=870) were surveyed in Novosibirsk. D was measured at the baseline examination by means of test "MOPSY". From 1995 to 2010 women were followed for 16 years for the incidence of stroke.

Results: The prevalence of D in women aged 25-64 years was 55.2% (major D was 12%). With growth of D levels positive self-rated health reduced and almost 100% of those women have health complaints. Women with major D significantly extended negative behavioral habits: smoking and unsuccessful attempts to give it up, low physical activity, reduced motivation in following diet plan. Major D associated with high job strain and family stress.
Risk of stroke development in women with D during 16 years of study was higher in 4.63 times (95%CI=1.03–20.89; $p<0.05$) compared to those without D. Stroke rates were more likely higher in married women having D with incomplete higher/secondary vocational education who being in "physical labor" social classes.

Conclusions: The prevalence of D in women aged 25-64 years more than 50%. High D levels associate with poor self-rated health, unhealthy lifestyle and high level of job and family stress. Women with D had 4.63-fold risk of stroke over 16 years of follow-up.

No conflict of interest

EXCESS WEIGHT AND VISCERAL OBESITY AMONG FIRST-YEAR AND FINAL-YEAR NURSING GRADUATE STUDENTS

C. Pires[1], *F. Mussi*[1]
[1]*Departamento de Enfermagem Médico Cirúrgica e Administração em Enfermagem, Escola de Enfermagem, Salvador Bahia, Brazil*

Excess weight and visceral obesity are underlying factors in pediatric and adult populations for hypertension, resistance to insulin, diabetes mellitus and dyslipidemia.Compare the excess weight and visceral obesity among first year and final year nursing graduate students.A cross-sectional, descriptive study. The sample was made up of 91 students from the first year and 63 from the last year. The anthropometric measures were evaluated by weight, height and circumference of the waist. The presentation and analysis of the information consisted in the socio-demographical and anthropometric characterization with the use of graphs, frequency distributions, averages and standard deviation.The bivariate analysis were performed to describe and verify proportional differences between first-year and final-year students. For variables of the ordinal measure, the Chi-square test of linear tendency was applied.The statistical significance level adopted was of 5%. An average age of 22.4 years (dp=4.5) characterized predominantly by the female sex (89.6%) and civil status single (51.3%), black (78.6%), social class B (80.5%), family income of 3 to 5 minimus wages (40.3%). A high prevalence and homogeneity was observed among the groups (60.3% of the final vs. 58.2% of the first year) in relation to an elevated waist circumference (p= 0.80). The prevalence of excess weight/ obesity for final-year wer, 30.8%, and for first-year 30.2%. There was no tendency for increase or reduction of the body mass index values among the groups.The study points out to the necessity of encouraging the adoption of healthy habits with students and investigate the association of these results with modifiable cardiovascular risk factors.

No conflict of interest

COMPARISON BETWEEN THE PRACTICE OF PHYSICAL ACTIVITIES AMONG THE NEW STUDENTS AND GRADUATE STUDENTS AT A NURSING GRADUATION COURSE

C. Pires[1], F. Mussi[1]
[1]Departamento de Enfermagem Médico Cirúrgica e Administração em Enfermagem, Escola de Enfermagem, Salvador Bahia, Brazil

Despite the recognition of the importance of physical activities as a factor for promoting health and prevention of diseases, the prevalence of sedentary lifestyles in Brazil is high and seems to affect people of all ages. The objective is to compare the practice of physical activities among nursing graduation students, fist-year students and graduate students. This is a cross-section study. A convenience sample was obtained, established by means of 154 students. Both socio-demographic and academic information were collected using questionnaires and information regarding the practice of physical activities was obtained through interviews using the long-version International Physical Activity Questionnaire (IPAQ). For analysis of the information, descriptive analysis was used and for bivariate analysis the Pearson's chi-squared and Fischer's exact tests were used. The level of statistic significance adopted was of 5%. A high predominance was identified of first-year students (59.1%), women (89.6 %), ages between 20 and 24 years (52.6 %), single (93.5 %), race/color black (78.5%), social-economic class C (45.5%). A sedentary lifestyle prevailed for all sections of the IPAQ. There was a significant statistical difference only for the time spent sitting down and year of course (p=0.010), with a higher percentage for first-year students (63.8 % vs. 36.2%). It is necessary for preventive measures to be taken towards the group under study, as well as to associate these results to other cardiovascular risk factors.

No conflict of interest

EVOLUTIONOF ANTIPLATELET THERAPY COMPLIANCE DURING THE FIRST YEAR AFTER PCI: A 100PATIENTS MONOCENTRIC COHORT

A.P.,F.P.,F.B.,T.C. R. POYET[1]
[1]"Cardiology department, Hô
pital Sainte Anne, TOULON
[2]Cardiology department, CHU Timone, MARSEILLE, France"

Background : Non compliance to antiplatelet therapy (APT) after percutaneous coronary intervention (PCI) is associated with higher cardiovascular mortality. Previous studies about APT discontinuation only analysed non compliance during short periods, generally less than three months and focused exclusively on self-willed discontinuation. APT oversight is generally not studied. The purpose of this monocentric prospective study was to analyse all types of APT cessation during a one-year follow-up after PCI in real-life patients.

Methods : We prospectively included 100 consecutive patients who underwent PCI. They received a phone questionnaire focused on antiplatelet therapy compliance every three months on a one-year follow-up. They were considered as non-compliant if they had stopped their medication on their own (self-willed discontinuation) or had forgotten APT more than once a week (oversight).

Results: Global non-compliance to APT (self-willed discontinuation and/or oversight) was 33% at one year. Self-willed APT discontinuation occurred in 13% cases, with a progressive increase within first 12 months, mainly explained by weariness or treatment side effects, and 27% patients forgot APT more than once a week at one year. More than 50% of APT oversights occurred within first month. Seven percent of patients admitted both self willed discontinuation and APT oversight.

Conclusion:
One third of patients admitted to be bad compliant to APT at one year follow up (including self-willed discontinuation and oversight), knowing that non-compliance is probably underestimated by a questionnaire. We observed two profiles of bad compliance: self-willed discontinuation, which progressively increased over the first year, and oversight, occur

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CT CORONARY ARTERY CALCIUM SCREENING, TRADITIONAL CAD PREDICTORS, AND EDUCATION: SYNERGY TO ADVANCE PREVENTATIVE MEDICINE FOR FIREFIGHTERS AND POLICE OFFICERS

P. Seibert[1], R. Hilvers[2], J. Valerio[1], C. DeHaas[1], S. Writer[3]
[1]Research Institute, Saint Alphonsus Regional Medical Center, Boise, USA
[2]Emergency, Emergency Responders Health Center, Boise, USA
[3]Cardiology Medical Group, Saint Alphonsus Regional Medical Center, Boise, USA

Introduction:

It is estimated that cardiovascular mortality associated with on-duty activity occurs in approximately 12% of the general population in the USA. This health threat increases dramatically for firefighters (44%) and police officers (22%). Although important to consider, traditional predictors of coronary artery disease (CAD) such as those attributed to lifestyle and heredity only account for 25-50% of cardiac events in the general population. CAD prediction increases in complexity in high risk groups.

Methods:

We designed a study testing the viability of CT coronary artery calcium screening (CACS) in conjunction with traditional CAD predictors and a comprehensive health education program as a tool to identify CAD risk and to promote lifestyle changes. Participants included male firefighters and police officers (inclusion criteria: over age 34, and all ages diagnosed with diabetes). Participants completed a baseline questionnaire, CACS, and comprehensive annual physical immediately after enrollment. Follow-up questionnaires occurred at 6-months and annually for five-years. Annual physicals included detailed health information and person-specific health education utilizing the Hilvers Metabolic Syndrome Reports. Five years post enrollment, a second CACS will be obtained.

Results:

We analyzed results from 98 firefighters (mean age 44.59) and 65 police officers (mean age 44.81) to track comprehensive health status and found a pattern of promising positive health changes. Comparison of findings specific to the firefighter and police officer groups indicated more similarities than differences; yet differences were revealed such as higher initial mean triglycerides, blood glucose, alcohol consumption, and sleep complaints for police officers.

Discussion:

Our findings emphasize the importance of a broad spectrum approach including CACS to assess CAD risk and to facilitate patient empowerment preventative medicine.

No conflict of interest

ESTIMATION OF FATAL CARDIOVASCULAR EVENT RISK ACCORDING TO THE RACE GROUPS: A HISPANIC POPULATION STUDY

E. Silva[1], J.J. Villasmil[1], A. Gonzalez[1], E. Clavell[1], G. Calmon[1], G. Bermudez[1], M. Villamizar[2]
[1]Research, Institute of Cardiovascular Diseases OF luz, Maracaibo, Venezuela
[2]Research, Institute of Cardiovascular Diseases of Luz, Maracaibo, Venezuela

Objective: To estimate the risk of fatal cardiovascular event (FCVE) in different race populations of Venezuela. **Methods**: This epidemiological study included 727 adults, 234 men and 493 women, who were categorized by race-group: whites, blacks and Amerindians. The risk of FCVE was defined according to the SCORE estimation in population at high cardiovascular disease risk, and the studied subjects was classified as low, moderated, high and very high risk. It was calculated the risk level estimation in all population and by race-group. The Chi^2 test was used to estimate the association between FCVE risk level and race-groups. **Results:** The FCVE risk frequencies were: 28.3%, 43.9%, 18.8% and 8.9% in low, moderated, high and very high risk groups, respectively. For the race-groups, the prevalence of risk levels were the following: in whites: 9.7%, 14.1%, 47.3% and 28.8%; in blacks s: 7.3%, 17.8%, 42.9% and 32.0%; in Amerindians: 22.8%, 23.3%, 29.6% and 24.3%, for low, moderated, high and very high risk groups, respectively. The Chi^2 analysis showed a statistically significant association between the race-groups and risk level ($p<0.0001$): whites showed the highest risk FCVE levels [50.2% and 44.2% for high and very high risk, respectively], followed by blacks [31.2% and 33.7% for high and very high risk, respectively]; the Amerindians showed the lowest values [18.6% and 22.1% for high and very high risk, respectively]. **Conclusions:** There are differents FCVE risk according to the race in this study. The FCVE risk is higher in the withes and black than in Amerindians.

No conflict of interest

ENDOCRINE ASSOCIATIONS WITH HEALTH-RELATED QUALITY OF LIFE IN CORONARY ARTERY DISEASE PATIENTS

M. Staniute[1], J. Brozaitiene[1], N. Mickuviene[1], R. Bunevicius[1]
[1]Behavioral Medicine Institute, Lithuanian University of Health Sciences, Palanga, Lithuania

Background. Thyroid hormone and cortisol metabolisms are associated with morbidity and clinical outcomes in patients with coronary artery disease (CAD). The aim of this study was to evaluate the effects of endocrine function on health-related quality of life (HRQoL) in CAD patients.

Methods. One hundred twenty two consecutive CAD patients (93 men and 29 women; mean age 56 years) attending a rehabilitation program were evaluated for HRQoL using the 36-item Short Form Medical Outcome Questionnaire, for serum concentrations of free tri-iodothyronine (T_3), free thyroxine (T_4), thyroid stimulating hormone, morning cortisol, afternoon cortisol and change in cortisol concentration; as well as for demographic factors, for CAD clinical characteristics, and for symptoms of depression and anxiety using the Hospital Anxiety and Depression Scale.

Results. Multivariate linear regression analyses adjusted for age, gender, body mass index, NYHA class, symptoms of depression and symptoms of anxiety, revealed that higher free T_3 concentrations were associated with fewer role limitations due to emotional problems (β=.358, p<.001) and with better perception of mental health (β=.169, p=.039). Higher free T_4 concentrations were associated with better physical functioning (β=.233, p=.014), with better social functioning (β=.214, p=.021), with greater energy/vitality (β=.187, p=.031) and with less pain (β=.264, p=.009). Higher morning cortisol concentrations and higher slope of cortisol were associated with more pain (β=-.226, p=.027; β=-.226, p=.022, respectively).

Conclusions. Suppressed thyroid hormone secretion is associated with worse physical and mental components of the HRQoL, and increased cortisol secretion with worse pain components of the HRQoL in CAD patients.

No conflict of interest

RELATIONSHIP OF HEALTH-RELATED QUALITY OF LIFE WITH FATIGUE AND EXERCISE CAPACITY IN PATIENTS WITH CORONARY ARTERY DISEASE

M. Staniute[1], A. Bunevicius[1], J. Brozaitiene[1], R. Bunevicius[1]
[1]Behavioral Medicine Institute, Lithuanian University of Health Sciences, Palanga, Lithuania

Objective. The study objective was to evaluate the relationship of health-related quality of life (HRQoL) with fatigue and exercise capacity in coronary artery disease (CAD) patients.

Methods. A total of 1072 consecutive CAD patients on admission to cardiac rehabilitation program were evaluated for HRQoL (36-item Short Form Medical Outcome Questionnaire; SF-36), body mass index, clinical characteristics (NYHA class, angina pectoris class, coronary interventions, treatment with betablockers, hypertension and diabetes), symptoms of depression and anxiety (Hospital Anxiety and Depression Scale), fatigue (Multidimensional Fatigue Inventory-20; MFI-20), and exercise capacity (bicycle ergometer test).

Results. In univariate regression analyses lower scores on all SF-36 domains were associated with greater scores on all MFI-20 subscales. Exercise capacity was associated with all SF-36 domains, except for social functioning and mental health domains. In multivariate regression analyses, after adjusting for age, gender, body mass index, NYHA class, angina pectoris class, coronary interventions, treatment with betablockers, hypertension, diabetes, and symptoms of depression and anxiety, greater limitation due to physical and due to emotional problems, poor social functioning, decreased energy/vitality, worse general health perception and reduced mental component summary were independently associated with higher MFI-20 general fatigue score; worse physical functioning, greater pain and reduced physical component summary, with physical fatigue; poor mental health, with mental fatigue.

Conclusion. In CAD patients undergoing rehabilitation, poor HRQoL is associated with greater fatigue and decreased exercise capacity independently from mental distress and CAD severity

No conflict of interest

SAGITTAL ABDOMINAL DIAMETER (SAD) IN IDENTIFICATION OBESE PATIENTS AT HIGHER CARDIOVASCULAR RISK

E. Stokic[1], A. Kupusinac[2], B. Srdic[3], D. Tomic-Naglic[1], E. Isenovic[4]
[1]Department of Endocrinology, Clinical Center of Vojvodina, Novi Sad, Serbia
[2]University of Novi Sad, Faculty of Technical Sciences, Novi Sad, Serbia
[3]Department of Anatomy, Medical faculty, Novi Sad, Serbia
[4]Laboratory for Molecular Genetics and Radiobiology, University of Belgrade, Belgrade, Serbia

Obesity is associated with a cascade of adipokine-mediated metabolic, inflammatory and haemostasic disturbances accelerating the process of atherosclerosis. Computerized tomography and magnetic resonance are the most reliable methods for abdominal fat assessment, but there is a need for a simple and non-invasive method to assess visceral fat. SAD - the distance from the small of the back to the upper abdomen - has been considered as more closely related to visceral fat and cardiovascular risk than the other anthropometric measures. In spite of many evidences that SAD is very good in capturing the cardiovascular risk, its application in clinical practice is limited due to a lack of specific cut-offs.

Our study included 1334 obese patients, 43.49±0.43 years. Following parameters were analyzed: age, BMI, SAD, fat mass, blood pressure, total-, LDL-, HDL-cholesterol, triglycerides, glucose and 10-year Framingham Risk Score. In order to investigate relationship between SAD and cardiovascular risk factors, we used methodology based on rough set theory applied to table–organized data with producing decision rules in the If –Then form and arti?cial neural network (ANN). SAD values ≥24.3cm correspond with increased cardiovascular risk in overweight and obese individuals presented by rough set method. ANN pointed out values of SAD ≥ 25,5 cm for men and SAD ≥ 23,4 cm for women, with the impact of age for these values.

The clinical application of SAD could be a useful method in identification persons with increased cardiovascular risk in an easy–to-measure and non-invasive way.

No conflict of interest

FLING WITH GIANT CORONARY AEURYSMS CAUSED BY KAWASAKI DISEASE

Y. Termachi[1], K. Suda[2], S. Ogawa[3], H. Kamiyama[4], K. Hamaoka[5]
[1]Pediatrics and Child Health, Kurume University, Kurume, Japan
[2]Pediarics and Child Health, Kurume University, Kurume, Japan
[3]Pediarics, Nippon Medical School, Tokyo, Japan
[4]Pediarics and Child Health, Nihon University, Tokyo, Japan
[5]Pediatric Cardiology and Nephrology, Kyoto Prefectural University of Medicine, Kyoto, Japan

BACKGROUND: To describe our multi-institutional experience of air travels that might have increased risk of thrombosis in patients with giant coronary artery aneurysms (gCAA) >= 8mm caused by Kawasaki disease (KD).

METHODS: We collected patient's data including sex, maximum size of gCAA, site of gCAA, age at air travel, number of air travel, flight time, medication at flight, pre-flight INR in case with warfarin administration, cardiac event, and age at final visit.

RESULTS: In total, 16 patients (13 male) with gCAA had 53 air travels without clinical cardiac event. GCAA was 14.7 ± 7.0 (8-33) mm in diameter and was at left coronary artery in 9, at both left and right coronary arteries in 5, and at right coronary artery in 2. Number of air travel was median of 1 (1-22) for each patient. Flight time ranged from 1.5 to 13 hours and was <3 hours in 48 (91%). Patients took warfarin at 35 air travels with 1.6 ± 0.7 (0.9-3.6) of INR, single or double anti-platelet drugs without warfarin at 16, and no thromboprophylaxis at 2. Purpose of the flight was mainly regular hospital visit (n=46), but was surgical (n=6) and catheter (n=1) intervention for coronary ischemia. All patients survived until 16.3 ± 7.9 (6.1-30.5) years old as the latest follow-up.

CONCLUSIONS: Though there is a theoretical risk of cardiac event in patients with gCAA during or after air travel, they can travel safely using air flight up to 3 hours.

No conflict of interest

THE METABOLIC SYNDROME PREDICTS ATHEROSCLEROSIS IN PROFESSIONAL FIREFIGHTERS WHILE STANDARD LIPIDS AND BMI DO NOT

R. Superko[1], B. Garrett[1], L. Pendyala[2], K. Momary[3], S. Frohwein[4]
[1]Research, Cholesterol Genetics and Heart Disease Institute, Portola Valley, USA
[2]Cardiology, University of Tennessee, Nashville, USA
[3]Pharmacology, Mercer University, Atlanta, USA
[4]Cardiology, Saint Josephs Medical Center, Atlanta, USA

Introduction:

Professional Firefighters have a 2-3 fold increased coronary heart disease (CHD) event risk. The metabolic syndrome (MetaSyn) is defined by elevated blood pressure, excess body fat, thrombogenic potential, insulin resistance, and dylipidemia, and linked to increased CHD risk.

Methods:

287 asymptomatic firefighters (mean age 47±5 yrs) were recruited and underwent risk factor screening along with coronary artery calcium (CAC) score determined on a 64-slice computed tomography system and quantitative measurement of carotid intimal thickening (CIMT). Subjects were characterized as having no CAC (-CAC) or with CAC (+CAC), and increased CIMT (> 800 microns, +IMT) or CIMT ≤ 800 microns (-IMT).

Results:

43.2% of asymptomatic professional firefighters had evidence of either +CAC or thickened CIMT. Standard lipoprotein measurements and measures of body fat were not associated with CAC or CIMT. Blood pressure, impaired glucose tolerance, and prothrombogenic characteristics were associated with subclinical atherosclerosis (Table).

	-CAC &-IMT	+CACorIMT	p
N	163	124	
SBP (mm Hg)	123±10	129±13	**0.0001**
DBP (mm Hg)	77.5±7.2	81.5±8.4	**0.0001**
FBG (mg/dl)	88.3±14.9	94.0±20.9	**0.01**
Plasminogen Activity (%)	98.7±16.5	105.0±17.4	**0.002**
Fibrinogen (mg/dl)	326±53	344±67	**0.01**
PAI1 (ng/ml)	17.1±10.6	20.2±15.8	**0.06**
BMI	29.7±4.4	30.0±4.9	0.59
Waist (in)	38.5±4.8	39.0±5.0	0.42
LDLC (mg/dl)	133+34	128±37	0.21
HDLC (mg/dl)	47.5±11.7	48.8±15.2	0.42

Conclusion: In a physically active group of firefighters blood pressure, impaired glucose tolerance, and pro-thrombotic characteristics of the MetaSyn were associated with subclinical atherosclerosis while standard lipids and measures of body fat were not. Reliance on measures of body fat and standard lipid measurements to predict CHD risk may be misleading in this population.

No conflict of interest

PSYCHOLOGICAL INTERVENTIONS FOR PATIENTS WITH CORONARY HEART DISEASE AND THEIR PARTNERS: A SYSTEMATIC REVIEW

D. Thompson[1], J. Reid[1], C. Ski[1]
[1]Cardiovascular Research Centre, Australian Catholic University, Melbourne, Australia

Objectives: Despite evidence that patients with coronary heart disease (CHD) and their partners report significant psychological distress, and suggestions that involving partners in interventions alleviates such distress, no systematic reviews have examined this. The objective of this study was to systematically review evidence on the effectiveness of psychological interventions for patients with CHD and their partners.

Methods: CENTRAL, Medline, EMBASE, CINAHL and PsycINFO databases were searched through October 2012. Randomized controlled trials evaluating psychological interventions for patients with CHD and their partners were included. Selection of studies, study appraisal, data extraction and analysis were undertaken using standard methods.

Results: Seven studies comprising 673 participants were included, two of which indicated that psychological interventions result in modest improvements in patients' depressive symptoms, anxiety, knowledge of disease and treatment, and satisfaction with care, and in partners' anxiety, knowledge and satisfaction. In partners, there was a non-significant trend for improvements in depressive symptoms. One study showed a beneficial effect on blood pressure. There was no evidence of a significant effect on mortality, morbidity or cardiovascular risk factors for patients or social support for patients and partner.

Conclusions: The small number of studies included in the review had generally poor methodology, as shown by the risk of bias, and were performed over 10 years ago. As only two of the seven studies resulted in modest improvements in outcomes, no firm conclusions can be drawn as to the effectiveness of such interventions in this population.

No conflict of interest

INFLUENCE OF ATRIAL-ARTERIAL MISMATCH ON PHYSICAL FITNESS IN ELDERLY MEN WITHOUT STRUCTURE HEART DISEASE

W. Tsai[1], J. Shih[2], J. Chen[1], P. Liu[1], L. Tsai[1]
[1]Internal Medicine, National Cheng Kung University Hospital, Tainan, Taiwan
[2]Internal Medicine, Chi-Mei Hospital, Tainan, Taiwan

Background: Both atrial and arterial functions are important in exercise performance. However, the effect of atrial-arterial (AA) coupling on physical fitness were not well studied.
Methods: We recruited 269 community-based, apparently healthy elderly men who were 65 years and older (mean age 74 ± 6 years) without structural heart disease. Average peak systolic strain of left atrium (LAS) during atrial filling was used as index for left atrial function. The ratio of peak early filling velocity (E) of mitral inflow to average early diastolic annulus velocity (e') of the annulus (E/e') was used as index for left ventricular filling. Arterial function was assessed by using self-developed dual-channel photoplethysmography. Peripheral arterial function was measured by compliance index (CI). Physical fitness was assessed by time for 15-foot walking and time for 8-foot up-and-go.
Results: Time for 15-foot walking was significant correlated with age ($r = 0.287$, $p < 0.001$), E/e' ($r = 0.208$, $p < 0.001$), biplane left ventricular ejection fraction (EF) ($r = -0.155$, $p = 0.016$), and LAS ($r = -0.230$, $p < 0.001$) Time for 8-foot up-and-go was significant correlated with age ($r = 0.265$, $p < 0.001$), E/e' ($r = 0.224$, $p < 0.001$), and LAS ($r = -0.268$, $p < 0.001$). Multivariate regression analysis showed age (B = 0.278), E/e' (B = 0.229), LAS (B = -0.207), and EF (B = -0.159) were independent factors for 15-foot walking test. Age (B = 0.227), E/e' (B = 0.238),and LAS (B = -0.199) were independent factors for 8-foot up-and-go test. By using CI divided by LAS as an index (CI/LAS) for AA coupling, the correlation was significantly increased for both 15-foot walking test (B = 0.338) and 8-foot up-and-go test (B = 0.426) than LAS along.
Conclusion: Mismatch of left atrial function and peripheral arterial function (represented by high CI/LAS) decreased physical fitness significantly in elderly men.

No conflict of interest

THE RELATION BETWEEN HEALTH-RISK BEHAVIOURS AND METABOLIC RISK MARKERS AMONG PATIENTS AFTER ACUTE CORONARY SYNDROME

J. Zycinska[1], J. Syska-Suminska[2], M. Jurczyk[2], A. Kuciej[2]
[1]Faculty in Katowice, University of Social Sciences and Humanities, Katowice, Poland
[2]Second Faculty of Medicine, Medical University of Warsaw, Warsaw, Poland

The aim of the study was to examine the relation between health-risk behaviours and metabolic risk markers (waist circumference, total cholesterol, LDL, HDL, triglycerides and plasma glucose) as well as depression among patients hospitalized due to the first acute coronary syndrome (ACS).

The study comprised 109 patients below the age of 66. The health-risk behaviours were measured using the *Godin Leisure-Time Exercise Questionnaire*, *Fagerström Test for Nicotine Dependence* and the scale for the diet evaluation designed on the basis of the *Diabetes Self-Care Activities Questionnaire*, while depression was assessed using the *Beck Depression Inventory*.

The two-step clustering method was used to classify patients into three homogenous groups (diet did not differentiate clusters). The analyses revealed statistically significant differences in levels of LDL, total cholesterol, depression (see Table 1) and waist circumference (only women).

Table 1: The comparison of metabolic risk markers and depression between clusters.

Metabolic risk markers and depression		Health-risk behaviours			Test χ^2/F
		Low[1] *N*=36	Moderate[2] *N*=38	High[3] *N*=35	
		%	%	$\chi^2_{(4)}/p$	
LDL (mg/dL)	<115	71.9	37.1	54.3	8.12/<.05
	≥115	28.1	62.9	45.7	
		M	*M*	*M*	$F_{(2,106)}/p$
Total cholesterol (mg/dL)		179.15	212.22	194.77	5.73/<.01
Depression		6.56	10.97	10.57	3.28/<.05

[1]Non-smoking patients with high-intensity exercise; [2]Patients with low nicotine dependence and moderate-intensity exercise; additionally with the highest social drinking; [3]Patients with high nicotine dependence and low-intensity exercise.

Not only did regular physical activity and refraining from smoking have an influence on optimal measures of metabolic risk markers, but also protected from depression after ACS which leads to better prognosis.

No conflict of interest

GLYCATEDHEMOGLOBIN AS A MARKER OF SUBCLINICAL ATHEROSCLEROSIS AND CARDIAC REMODELINGAMONG NON-DIABETIC ADULTS FROM THE GENERAL POPULATION

S.E.B.,W.L.,B.v.S. "R. Haring[1], S.B.F.,M.N.,H.W. Izke[2]
[1]Institute of Clinical Chemistry and Laboratory Medicine
[2]Institute for Community Medicine
[3]Department of Neurology,
[4]Department of Cardiology, University Medicine Greifswald, Greifswald, Germany

Background:
High glycated hemoglobin(HbA1c), a long term marker of glucose metabolism, is associated with increasedrisk of cardiovascular disease (CVD) and mortality in patients with diabetes,as well as in the general population. But little is known about potential mechanisms underlying the reportedassociations.

Methods:
Weused data of 1,862 non-diabetic participants from the population-based cohort Study of Health in Pomerania (SHIP) to investigate cross-sectional andlongitudinal associations of HbA1cwith subclinical atherosclerosis (common carotid artery intima-media thickness [CCA-IMT]), cardiac structure (left ventricular mass [LVM]), and cardiac function (fractional shortening), adjusted forconfounding factors.

Results:
Cross-sectional analysesrevealed a positive association between HbA1c and mean CCA-IMT with a 0.03 mm (95% confidence interval: 0.01 – 0.04) increase in CCA-IMT per 1% increase in HbA1c, and a similar positive trend across HbA1cquartiles (overall p-value < 0.001). We also observed a graded associationbetween HbA1c and high CCA-IMT (>75th percentile) with an oddsratio of 1.47 (95% CI: 1.18 – 1.84) per 1% increase in HbA1c. Longitudinalanalyses showed no consistent associations of baseline HbA1c with mean follow-upCCA-IMT. There were no consistentassociations of HbA1c with LVMi or fractional shortening in cross-sectional andlongitudinal analyses, respectively.

Conclusions:
The positive associationbetween HbA1c and CCA-IMT among non-diabetic adults in the general population may be a cruciallink between high-normal HbA1c levels and an increased risk of CVD andmortality. Future studies need to further explore longitudinal associations andelucidate underlying pathophysiological mechanisms.

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OPPORTUNISTIC SCREENING AS A TOOL FOR IDENTIFICATION OF EARLY DIABETES MELLITUS: ARE WE TARGETING THE RIGHT PEOPLE?

K. Leshabari[1], M. Mavura[2], M. Matemu[2], J. Gardner[3]
[1]Internal medicine, Walter Hospital, Dar es Salaam, Tanzania
[2]Diabetes clinic, Mwananyamala Municipal Hospital, Dar es Salaam, Tanzania
[3]Research & Publications Unit, Tanzania Diabetes Association, Dar es Salaam, Tanzania

Objective: To estimate the extent of unknown diabetics among residents of a typical cosmopolitan area in sub-Saharan Africa by using opportunistic screening technique.

Methods: A high risk cohort among residents that included relatives and friends of patients living with diabetes mellitus, at-risky staff of the municipal hospital, staff of the municipal director's office as well as relatives of other patients who seek care for CVDs at the municipal hospital during the national diabetes week were invited at random to participate in the study. For *opportunistic screening*, fasting blood glucose (FBG) as well as post-prandial glycaemic measurements (using capillary blood measurements) were taken together with other cardio-metabolic risk variables and analysed using SAS statistical software version 9.2. An alpha level of 5% was considered significant for disproving the null hypothesis. All screened positive respondents underwent further tests for confirmatory purposes.

Results: Out of 189 participants who were involved in screening exercise, about 3% were found to have blood glucose values in the diabetes range. About one in three (32.86%) of respondents reported to had positive family history of diabetes. There was a strong and positive correlation between family history of diabetes and hypertension (γ= 0.6, P<0.0001) However, a non-significant correlation between screened positive test and reported family history of diabetes was found (γ=0.05799, p-value = 0.4977) Age was found to be significantly influencing diabetes outcome (log OR= 0.0326, p-value= 0.0404) Diabetes screening status showed a significant correlation with hypertensive screening status (γ=0.29971, P=0.0004)

Conclusion: Using the conversional diagnostic tests, the positive yield for diabetes screening was relatively low in this study population. Glycaemic profile in this study population revealed to have a mixture distribution. Diabetes mellitus was found to be a significant predictor of hypertensive disease

Recommendations: Opportunistic screening needs to be well defined in different population groups so as to be of clinical and epidemiological value for usage in sub-Saharan African population. Genetic studies should be considered as part and parcel when designing interventions on glycaemic measurements among Africans.

No conflict of interest

IMPACT OF DIABETES MELLITUS ON THE HIGH-DOSE STATINS PRESCRIPTION AFTER ACUTE CORONARY SYNDROMES.

A. López-Cuenca[1], M.J. Sánchez-Galián[1], P.J. Flores-Blanco[1], M. Sánchez-Martínez[1], M. Navarro-Peñalver[1], I. De las Heras Gómez[1], A. García-Narbón[1], F. Marín[1], M. Valdés[1], S. Manzano-Fernández[1]
[1]Cardiology, Hospital Universitario Virgen de la Arrixaca, Murcia, Spain

Background and purpose: Current clinical practice guidelines recommend the use of high-dose statins (HDS) after an acute coronary syndrome (ACS). Furthermore, the use of HDS has been recently linked to a higher risk for diabetes mellitus (DM). The aim of this study was to evaluate the influence of DM in the HDS prescription in patients with ACS.

Method and results: From January 2012 to January 2013, 473 consecutive ACS patients (age 68 ± 13 years, 26% female) were included. HDS prescription was defined as the use of atorvastatin 80 mg, rosuvastatin 20 mg or pitavastatin 4 mg. A total of 222 (47%) patients had DM and 241 (51%) were discharged on HDS: 45% atorvastatin 80 mg, 51% rosuvastatin 20 mg and 4% pitavastatin 4mg. Compare to non-DM patients, patients with DM received less frequently HDS (54% vs. 40%, p = 0.003). After multivariate adjustment, DM was associated with a lower use of HDS (OR: 0.52, 95% CI 0.35 to 0.78, p = 0.002). In addition, advanced age, renal insufficiency, atrial fibrillation and conservative management were also associated with a lower rate of HDS use. By contrast, patients who were on HDS before hospital admission were more likely to received HDS at discharge.

Conclusion: Patients with concomitant DM and ACS represent a high-risk population, however they often do not receive HDS. The relationship between HDS use and an increased risk of DM may be involved in these findings. However, current clinical guidelines stronlgy recommend HDS prescription in these patients.

No conflict of interest

INFANCY-ONSET DIETARY COUNSELING IMPROVES INSULIN SENSITIVITY IN HEALTHY ADOLESCENTS. THE SPECIAL TURKU CORONARY RISK FACTOR INTERVENTION PROJECT (STRIP).

O. Oranta[1], K. Pahkala[1], S. Ruottinen[1], H. Niinikoski[2], H. Lagström[3], J.S.A. Viikari[4], A. Jula[5], B.M. Loo[5], T. Rönnemaa[4], O.T. Raitakari[1]

[1]Research Center of Applied and Preventive Cardiovascular Medicine, University of Turku, Turku, Finland

[2]Department of Paediatrics, University of Turku, Turku, Finland

[3]Child and Youth Research, Turku Institute for Child and Youth Research, Turku, Finland

[4]Department of Medicine, University of Turku, Turku, Finland

[5]Health and Welfare, Institute of Health and Welfare, Turku, Finland

OBJECTIVE - We reported previously that dietary counseling started in infancy improves insulin sensitivity in 9-year-old healthy children. The aim of this study was to evaluate the effect of life-long dietary counseling on insulin sensitivity in healthy adolescents between ages 15 to 20 years. In addition, we examined fiber intake and polyunsaturated + monounsaturated/saturated fatty acid ([PUFA+MUFA]/SFA) ratio in the intervention and control adolescents, and the association of these dietary factors with homeostasis model of insulin resistance (HOMA-IR).

RESEARCH DESIGN AND METHODS - The study comprised adolescents participating in the randomized, controlled STRIP study, which aim is to guide the study participants towards a diet beneficial for cardiovascular health. HOMA-IR was assessed annually between ages 15 and 20 years (n=518; intervention n=245, control n=273), along with diet, BMI, pubertal status, serum cotinine concentrations and physical activity. Dietary counseling was given biannually during the follow-up.

RESULTS - HOMA-IR was lower (on average 7.5%) in the intervention group than in the control group between ages 15 to 20 y (P=0.0051). The intervention effect was similar in girls and boys. The (PUFA+MUFA)/SFA ratio was higher (P<0.0001) and the fiber (g/MJ) intake was higher (P=0.0058) in the intervention group compared to the control group. There was no association between (PUFA+MUFA)/SFA ratio and HOMA-IR, while fiber intake (g/MJ) associated with HOMA-IR in girls (P<0.0001).

CONCLUSIONS - Dietary counseling initiated in infancy and maintained until age of 20 years was associated with improved insulin sensitivity in adolescents.

No conflict of interest

LIGATION OF A FISTULA BETWEEN LEFT MAIN CORONARY ARTERY AND BOTH OF THE PULMONARY ARTERY AND RIGHT VENTRICLE

I. algin[1]
[1]*kalp ve damar cerrahisi, Ozel Korfez hastahanesi, balikesir, Turkey*

The coronary artery fistula frequency among all coronary angiography patients is 0.1-0.2 %. Among them, the fistulisation of the coronary artery with the pulmonary artery and the right ventricle has been shown for 10-25 %. But the involvement of both the pulmonary artery and the right ventricle is a very seldom seen clinical antity (1, 2).

Patients may complain about chest pain, syncope or signs of heart failure, while most of them can be asymptomatic. The main factors of the symptoms to become apparent are; the radius of the coronary artery and the pulmonary artery, the pulmonary artery pressure and other accompanied comorbid diseases (DM, hypertension, coronary artery disease).

Our case report is about the ligation of such a fistula of a patient just complaining sometimes about chest pain, by a off-pump technique.

Keywords: coronary artery fistula, off pump, ligation

No conflict of interest

COMPARISON BETWEEN LOGISTIC EUROSCORE AND EUROSCORE II: THE ABILITY TO FORESEE IN-HOSPITAL MORTALITY IN ELDERLY PATIENTS UNDERGOING AORTIC VALVE REPLACEMENT

S. Mariani[1], F. Formica[1], P. Amigoni[1], A. Liakopoulo[2], S. Mariani[1], L. Colagrande[3], O. Ferro[3], G. Paolini[3]
[1]Surgical Science and Interdisciplinary Medicine, University of Milano-Bicocca San gerardo Hospital Monza, Monza (MB), Italy
[2]Cardio-Thorac- Vascular Surgery, University of Milano-Bicocca San gerardo Hospital Monza, Monza (MB), Italy
[3]Cardio-Thorac- Vascular Surgery, San Gerardo Hospital, Monza (MB), Italy

Background: Risk scores are used to identify patients with aortic valve disease suitable for non-surgical therapies. This study compares the EuroSCORE II to the Logistic-EuroSCORE and their ability to identify high mortality risk patients.

Methods: 187 patients, 75+ years, who underwent isolated aortic valve replacement (AVR; n=98) or combined AVR and coronary surgery (AVR+CABG; n=89) were included in our retrospective study. The discriminatory powers of the scores were assessed by the use of the receiver operating characteristic curves (ROC) and the area under the resulting curve (AUC). The optimal cut-off values based on ROC were determined. Model calibration was examined by the Hosmer-Lemeshow test.

Results: In every subgroup, EuroSCORE II underestimated mortality risk, whereas Logistic-EuroSCORE overestimated it (Figure 1). The model calibration was satisfactory with both scores (Table 1). The AUC for EuroSCORE II was higher than AUC for Logistic-EuroSCORE in every group with a significant difference in the overall population (Table 1). The cut-off values for EuroSCORE II (Table 2) described best high morbidity and mortality patients in the overall population and in the AVR+CABG group. No differences were noticed in other groups.

Conclusions: EuroSCORE II improves the Logistic-EuroSCORE in aged patients undergoing AVR, especially when CABG is associated. A cut-off value of 5.75 might be considered so to identify high-risk patients.

Figure 1

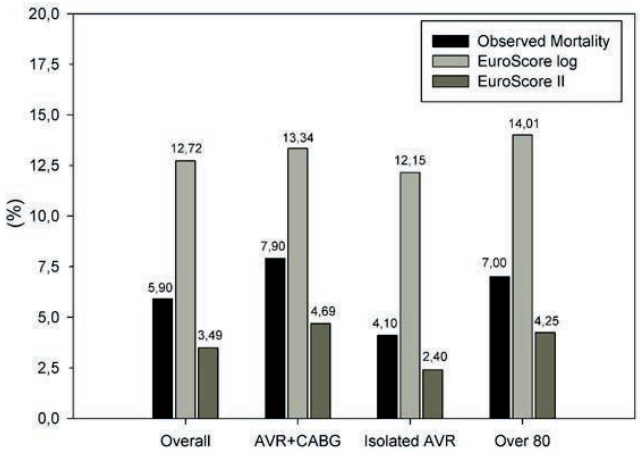


Table 1: Mortality prediction statistic

Variables	Overall (n = 187)	AVR + CABG (n = 89)	Isolated AVR (n = 98)	Over 80 (n = 71)
Logistic-EuroSCORE				
C-statistic (95% CI)	0.685 (0.613 - 0.751)	0.697 (0.59 - 0.79)	0.629 (0.526 – 0.724)	0.676 (0.554 – 0.782)
Hosmer-Lemeshow *p*-value	0.785	0.826	0.404	0.428
EuroSCORE II				
C-statistic (95% CI)	0.779 (0.713 - 0.836)	0.732 (0.627 – 0.82)	0.815 (0.724 – 0.886)	0.788 (0.675 – 0.876)
Hosmer-Lemeshow *p*-value	0.304	0.476	0.593	0.214
DeLong test *p*-value	0.047	0.579	0.111	0.293

AVR. Aortic Valve replacement; CABG. Coronary Artery Bypass Graft; CI. Confidence Interval

Table 2:Cut-off values in predicting hospital mortality

Variables	Overall (n = 187)	AVR + CABG (n = 89)	Isolated AVR (n = 98)	Over 80 (n = 71)
Logistic-EuroSCORE: cut-off	18.25	18.25	30.00	21.75
Sensitivity (95% CI)	54.55 (23.4 – 83.3)	57.14 (18.4 – 90.1)	50.00 (6.8 – 93.2)	60 (14.7 – 94.7)
Specificity (95% CI)	85.23 (79.1 – 90.1)	85.37 (75.8 – 92.2)	96.81 (91.0 – 99.3)	93.94 (85.2 – 95.3)
EuroSCORE II: cut-off	5.75	5.75	2.34	5.75
Sensitivity (95% CI)	54.55 (23.4 – 83.3)	57.14 (18.4 – 90.1)	75 (19.4 – 99.4)	60 (14.7 – 94.7)
Specificity (95% CI)	90.34 (85.0 – 94.3)	84.15 (74.4 – 91.3)	75.53 (65.6 – 83.5)	87.80 (77.5 – 94.6)

AVR. Aortic Valve replacement; CABG. Coronary Artery Bypass Graft; CI. Confidence Interval

No conflict of interest

SURGICAL ASPECTS

LONG-TERM SURVIVAL AFTER AORTO-BIFEMORAL BYPASS: INFLUENCE OF CORONARY ARTERY DISEASE

F. Garcia[1], J. Marchena[2], E. Sotgiu[3]
[1]Vascular Surgery, Hospital Provincial de Castellon- Universidad CEU, Castellon, Spain
[2]General Surgery, Hospital Dr. Negrin. Las Palmas de Gran Canaria, Las Palmas de Gran Canaria, Spain
[3]Vascular Surgery, Hospital Dr. Negrin. Las Palmas de Gran Canaria, Las Palmas de Gran Canaria, Spain

Background: Chronic infrarenal aortic occlusion is relatively infrequent. Aortobifemoral bypass have been traditional treatment. The objetive of this study was to evaluate the prognostic factors related to long-term survival and patency rates of chronic infrarenal aortic occlusion after aortobifemoral bypass.

Methods: We consecutively performed 278 aortobifemoral for aortoiliac occlusive disease. Among these, sixty-seven (24%) patients, 62 men (92.5%), with ischemia owing to aortic occlusion. Log-Rank test was used to determine predictors of long-term survival and graft patency in an univariate analysis. With a model of proportional-hazards Cox regression the independent prognostic factors of long-term survival were determined.

Results: The post-operative mortality was 8.9%. The estimated cumulative long-term survival for aortic occlusion patients was 56% and 38% at 10 and 20 years respectively. The estimated cumulative primary patency was 79% at 10 years and 40% at 20 years. The 20-years survival limb rate was 86%. There was no statistical difference in long-term survival and graft patency between TASCIC-D and IRAO. Previous coronary disease (p=0.008) and post-operative complications (p= 0.017) significantly decreased the survival of patients. Both variables retained significance on multivariable analysis. The presence of chronic renal failure significantly decreased the patency of aortobifemoral bypass (p= 0.013).

Conclusion: The aortobifemoral bypass for chronic infrarenal aortic occlusion has excellent primary patency rate with reasonable morbi-mortality. The presence of concomitant coronary disease and post-operative complications are prognostic factors of long-term survival.

Key words: Abdominal aorta. Coronary artery disease.

No conflict of interest

SURGICAL MANAGEMENT OF ABERRANT RIGHT CORONARY ARTERY

H. Khan[1], S. Chaubey[1], J. Desai[1], O. Wendler[1]
[1]Cardiothoracic, King's College London, London, United Kingdom

Objective:
Anomalous origin of right coronary arteries (RCA) can result in myocardial ischaemia and sudden death. Treatment using conventional coronary artery bypass grafting (CABG) is hampered by early graft failure due to concurrent flow through the native RCA.

Methods:
A retrospective review of all patients with aberrant RCA's who underwent surgery at our institution since 2004 was undertaken. We report about the surgical techniques used, initial outcome and mid-term follow-up.

Results:
A total of 8 patients (4 males, median age 55.5±7.9years) were identified over the last 8 years. The RCA originated from the left coronary sinus (n=7) or the left anterior descending coronary artery (LAD) (n=1). Where the RCA ostium was found in the left coronary sinus (n=6), the RCA was transferred into the right coronary sinus (n=4), or, if the RCA had a transmural course (n=2) directly unroofed. In 1 patient a vein graft was used to anastomose the proximal RCA to the right side. The patient who presented with the RCA origin directly from the LAD underwent 3-vessel-CABG.

Mean bypass time was 90±61min with an ischemic time of 57±27min. Four patients experienced post-op atrial fibrillation and median hospital-stay was 5 days (range 4 to 10). At median follow-up of 2.5years all patients are alive and free of their previous symptoms.

Conclusions: In patients with aberrant RCA's transfer of the RCA using an unroofing technique of the RCA or direct transfer carries low mortality and morbidity and results in excellent mid-term outcome.

No conflict of interest

MID-TERM RESULTS OF DIFFERENT SURGICAL TECHNIQUES TO REPLACE THE ASCENDING AORTA ASSOCIATED WITH BICUSPID AORTIC VALVE DISEASE

P. Nardi[1], A. Pellegrino[1], M. Russo[1], G. Saitto[1], B. Del Forno[1], F. Bertoldo[1], A. Scafuri[1], S. Grego[1], L. Chiariello[1]

[1]Cardiac Surgery Division, University of Rome "Tor Vergata", Rome, Italy

Aim of the study. To evaluate the effectiveness of three different surgical strategies to treat the dilation of the ascending aorta associated with bicuspid aortic valve (BAV). *Methods.* One-hundred and fifty consecutive patients affected by ascending aorta dilation (diameter >45 mm) and BAV underwent in a 5-year period to Bentall operation(n=45), separate aortic valve replacement (AVR) and(+) ascending aorta replacement (AAR)(n=77), and AAR only with or without(+/-) BAV repair in presence of normal or near-to-normal valve function(n=27). *Results.* As compared with AVR+AAR and AAR+/-BAV repair, patients undergone Bentall were younger and affected by more aggressive BAV aortopathy, in terms of aortic root dilation (48±5vs.42±5 and 43±3 mm), aortic regurgitation and reduced left ventricular function ($p<0.05$, for all comparisons). Operative times were longer in Bentall operation vs. AVR+AAR and AAR+/-BAV repair ($p\leq0.01$, for all comparisons). Operative mortality was 2.1%, 1.3%, absent, respectively(p=NS). Five-year survival (94%±4%vs.92%±3.4%vs.100%) and freedom from cardiac death (100%vs.99%±1.3%vs.100%) were not significantly different. No any patient required reoperation on the ascending aorta or experienced aortic complications. Following AVR+AAR and AAR+/-BAV repair, root dimensions not only did not increase, conversely were found significantly lower as compared with preoperative ($p<0.05$, for both comparisons). Aortic regurgitation grade after AAR+/-BAV repair did not increase (0.5±0.8/4+) in comparison with the preoperative (0.8±0.9/4+). *Conclusions.* Bentall operation still represents the gold standard for the treatment of more aggressive BAV aortopathy. In presence of mildly or normal root and normal BAV function at the time of operation, less invasive surgical procedures, BAV sparing or repair appear to confer satisfactory mid-term results.

No conflict of interest

ASSESSMENT OF MYOCARDIAL PROTECTION IN COURSE OF COMPLEX CORONARY ARTERY RECONSTRUCTION

G. Popoff[1], E. Ramoni[1], S. Scardi[2], E. Gliozheni[3]
[1]Cardiovascular Surgery, Maria Beatrice Hospital GVM care & research, Florence, Italy
[2]Intensive Care Unit, Maria Beatrice Hospital GVM care & research, Florence, Italy
[3]Hemodynamic Unit, Maria Beatrice Hospital GVM care & research, Florence, Italy

INTRODUCTION. As a consequence of increased use of PCI, the lesions of coronary arteries treated surgically have became more severe.

In case of complex or diffuse coronary disease we offer a coronary reconstruction (CR) technique which includes an extensive endarterectomy followed by internal thoracic artery (ITA) patch endothelial autograft.

Aim of the study was to assess myocardial damage after CR.

Data were prospectively collected.

PATIENTS AND METHODS. Between 09/2012 and 12/2012, 28 patients underwent extensive LAD CR with ITA-patch (group A). During the same period, 23 consecutive patients underwent our standard CABG-approach with extensive use of ITA "Y" graft (group B).

Myocardial protection was achieved through single dose antegrade cold cristalloid cardioplegia in both groups.

14 patients (50%) of group A underwent coronarographic control.

RESULTS.

Aortic cross-clamping (ACC) time was 85±14 in goup A and 48±13 minutes in group B ($p<0.0001$).

Intraoperative length of arteriotomy for LAD reconstruction was 86.4±23.6 mm; total length of the plaques excised from LAD and its branches was 141.7 mm; maximum thickness of the plaques from LAD was 5.9 ± 1 mm.

None patient died, required percutaneous coronary intervention or reoperation.

Bleeding from chest drain-tubes, as well as duration of mechanical ventilation and length of ICU stay, were similar in both groups.

Mean postoperative CK-MB was 50.7±53.7 ng/dL in group A and 31.44±22.54 ng/dL in group B (p=n.s.). No correlation was detected between postoperative CK-MB and length of LAD arteriotomy, length of the plaque excised from LAD, total length amount of the plaques excised from LAD and its branches, and aortic cross-clamping time.

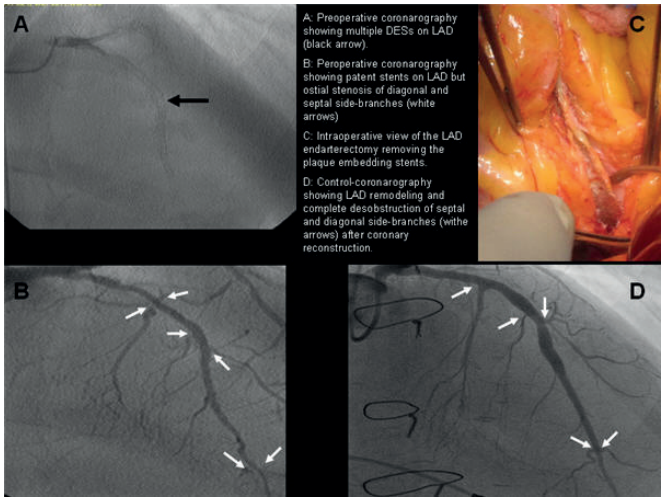
CONCLUSIONS. Despite complex CR involves longer ACC time, it can be safely performed with comparable outcome than standard CABG-approach.

No conflict of interest

"JAILING-STENT" SYNDROME: SUCCESSFUL TREATMENT OF ANGINA IN A PATIENT WITH MULTIPLE PATENT DES, THROUGH STENTECTOMY AND SURGICAL CORONARY RECONSTRUCTION.

G. Popoff[1], E. Ramoni[1], C. Agostini[2], A. Buonamano[3]
[1]Cardiovascular Surgery, Maria Beatrice Hospital GVM care & research, Florence, Italy
[2]Cardiology, Maria Beatrice Hospital GVM care & research, Florence, Italy
[3]Intensive Care Unit, Maria Beatrice Hospital GVM care & research, Florence, Italy

Introduction:The implant of multiple stents for complex CAD has become a routine procedure. Nevertheless, it is not unusual to find patients suffering from symptomatic recurrences after PTCA, deriving from both chronic and acute stenotic or occlusive phenomena which often require complex treatment. The presented case differs, however, on account of the absence of angiographic stent obstructions.
Material-and-Methods: Among a series of patients operated on for such an observed CAD, we selected this case. A 68-year-old male underwent multiple PTCA-stenting procedures with DES on RCA and LAD. Because of drug-resistant angina with demonstration of inducible ischemia, he underwent control coronography showing stent patency and the absence of stenosis on unstented major vessels tracts (Figure1). After "heart-team" discussion, he underwent surgical LAD stentectomy with side-branches desobtruction (Figure1), LAD reconstruction with endothelial autograft of 15 cm-right internal thoracic artery (ITA) patch plus CABG with left-ITA on LAD-patch.Postoperative course was uneventful. At periodic follow-ups, the patient was constantly asymptomatic. Twelve-month control-coronarography showed good result of operation with favorable remodeling of reconstructed LAD (Figure1).
Conclusion: Never before had an attempt been made to describe a "jailing-stent" syndrome. That is to say, a pathology not caused by stent restenosis, but by collateral arteries obstruction by plaque compression or in-stent hyperplasia. We believe that the case presented, characterized by drug-resistant angina surgically dealt by the removal of angiographically pervious stents, could be paradigmatic of such a particular CAD-syndrome.



No conflict of interest

SPINAL CORD INJURY AFTER ENDOVASCULAR TREATMENT FOR THORACO-ABDOMINAL AORTIC ANEURYSM: A SINGLE CENTER EXPERIENCE

S. Romagnoli[1], C. Pratesi[1], A. Fargion[1], A. Guidotti[1], P. Ruggiano[2], F. Ciappi[1], S. Bevilacqua[1], F. Pinelli[1], A.R. De Gaudio[2]

[1]Heart and Vessels, Azienda Ospedaliero-Universitaria Careggi. University of Florence, Florence, Italy
[2]Health Sciences Section of Anaesthesiology Intensive Care and Pain University of Florence, Azienda Ospedaliero-Universitaria Careggi. University of Florence, Florence, Italy

Background: the evaluation of the risk for spinal cord injury (SCI) in patients undergoing thoraco-abdominal aortic aneurysm (TAAA) endovascular repair (TEVAR), is one of the main issues for the physicians performing this type of procedures since guidelines and recommendations are still lacking. As a consequence, each center performing TEVAR adopt different strategies in order to prevent or to treat SCI. **Main results**: 23 patients affected by TAAA were treated with TEVAR from 2011 to 2013. During the first two years, all the patients (18/18) received, preoperatively, a cerebro-spinal fluid (CSF) drainage in order to prevent ischemic neurologic injuries – group 1. Differently, during the last year, the CSF catheter was placed only in patients with extremely high risk for SCI – group 2 (1/5; 20%). Table 1 summarizes the surgical characteristics of the procedures. The incidence of SCI was 27.7% in the group 1 and 20% in the group 2 (p=0.52). One patient (5.55%; group-1) had a complication by CSF drainage: intra-cranial hemorrhage. **Conclusions:** according to our initial experience, a conservative approach to the SCI seems to be safe. A careful risk stratification is mandatory during the preoperative planning.

Table 1.

	Length of covered aorta cm (SD)	Number of stent grafts	Intercostal and lumbar arteries covered	Left subclavian and/or hypogastric arteries coverage	Temporary SCI; n (%)	Permanent SCI; n (%)
Group 1 (n= 18)	29.7 (7.9)	2.4 (1.2)	7.3 (3)	0	4 (16.6)	1 (5.55)
Group 2 (n=5)	31.3 (6.9)	2.5 (1.3)	7.8 (3)	1	1 (20)	0

No conflict of interest

ASSESSMENT OF THE HEMODYNAMIC PARAMETERS BETWEEN THE RIGID LARYNGOSCOPY AND THE LIGHTED STYLET IN PATIENTS WITH CORONARY DISEASE

V.C.,S.M.,M.P.,M.L. "M. Salgado Filho[1,2]*, sso"*[3]
[1]*Cardiovascular Anesthesia, National Institute of Cardiology*
[2]*Anesthesia, Federal University of Rio de Janeiro, Rio de Janeiro*
[3]*UNIPAC, Juiz de Fora, Brazil*

"Background and objectives: During the airway management is possible to observe an important cardiovascular changes, mainly in patients with heart disease. In this study, we compare the hemodynamic parameters of rigid laryngoscopy and lighted stylet in patients with coronary disease.
Methods: This randomized clinical trial included 40 patients undergoing Coronary Artery Bypass Grafting assigned into two groups: lighted stylet and rigid laryngoscope. Besides time of tracheal intubation in each group, heart rate, mean arterial pressure, changes in ST segment, and central venous pressure were evaluated during patient preparation, 1 minute and 5 minutes after anesthetic induction, and 1 minute after tracheal intubation.
Results: Both groups were homogenous regarding demographic data. Time of tracheal intubation in the rigid laryngoscope group (24 ± 5 sec) was lower than that of the lighted stylet group (28 ± 7 sec), but without significance. Heart rate showed a reduction in both groups during anesthetic induction ($p < 0.05$), but 1 minute after tracheal intubation the heart rate increased to levels close to baseline levels in both groups ($p > 0.05$). In the
rigid laryngoscope group mean arterial pressure increased after tracheal intubation to levels close to those observed during patient preparation ($p > 0.05$), while in the lighted stylet group mean arterial pressure remained below baseline levels ($p < 0.05$). Central venous pressure increased on both groups at all times ($p < 0.05$).
Conclusions: We conclude that both techniques are safe for tracheal intubation in patients with coronary disease. However, lighted stylet has fewer repercussions on mean arterial pressure.

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PERIPARTUM SPONTANEOUS CORONARY ARTERY DISSECTION: OUTCOMES WITH CONSERVATIVE, PERCUTANEOUS, AND SURGICAL INTERVENTIONS.

G.A. Delgado[1], *A.G. Truesdell*[1], *J.D. Abbott*[1]
[1]*Cardiology, Brown University, Providence, USA*

Peripartum spontaneous coronary artery dissection (PSCAD) is a serious condition affecting young women without major atherosclerotic risk factors and in the absence of underlying significant coronary artery disease. Based on the affected population, the pathophysiology of PSCAD differs from other forms of coronary dissection and it is thought to be related to hormonal factors typical of the peripartum period. However, PSCAD is rare and its etiologic mechanisms, natural course, and ideal management strategy remain unknown. This is further compounded by the lack of consensus guidelines and a dearth of PSCAD-related literature. We present the largest series published to date describing the presentation, evolution, and outcomes of a series of six consecutive cases of PSCAD who received a combination of conservative, percutaneous, and surgical treatment at our institution over a 4 year period with longitudinal follow-up.

Table 1. Patient characteristics

Case	Age (yrs)	Event timing	Risk factors	Presentation	SCAD location	Peak TnI (ng/ml)	LVEF (%)	Initial Rx	Definitive Rx	Outcome	Follow-up period
1	34	13 days * postpartum	HTN, HLP	CP, STD	LCX	<0.15	55 †	Conservative medical	Conservative medical	Doing well, no further events	4 years
2	31	9 days * postpartum	HTN	CP, CHF, STE	LAD	400	25 †	Conservative medical	PCI, CABG	Recurrent ISR requiring CABG and repeat PCI	2.5 years
3	33	2 weeks ** postpartum	HLP, smoking	CP, CHF, STE	LM, LAD, LCX	50	30 †	Conservative medical	CABG	Symptomatic LM pseudo-aneurysm requiring PCI	2 years
4	34	6 days * postpartum	HTN	VF OHCA, STE, CHF #	LAD	177	30 †	PCI	PCI	Recurrent ISR requiring repeat PCI and brachytherapy	10 months
5	40	1 week ** postpartum	Smoking	CP, CHF, STE	LM, LAD	326	20 ‡	Conservative medical	CABG	Persistent severe LV dysfunction, ICD placement	9 months
6	40	16 weeks ** postpartum	HTN	CP, STE	LAD	234	35 ‡	Conservative medical	Conservative medical	LV clot requiring anticoagulation	4 months

CV: cardiovascular, TnI: troponin I, LVEF: left ventricular ejection fraction, HTN: hypertension, HLP: hyperlipidemia, CP: chest pain, STD: ST-segment depressions, STE: ST-segment elevations, LCX: left circumflex coronary artery, LAD: left anterior descending coronary artery, LM: left main coronary artery, CABG: coronary artery bypass graft surgery, ISR: in-stent restenosis, PCI: percutaneous coronary intervention, LV: left ventricular, ICD: implantable cardioverter-defibrillator, VF: ventricular fibrillation, OHCA: out-of-hospital cardiac arrest, *: vaginal delivery, **: C-section, †: as estimated by contrast ventriculography, ‡: as estimated by immediate echocardiogram, #: subsequent event on hospital day 4.

Table 2. Studies analyzing the incidence & outcomes of spontaneous coronary artery dissection.

Study (year)	Population (n)	Cases (n)	Women (n [%])	Peripartum (n [%])	Initial Rx (n [%])			In-hospital deaths (n [%])	Mean follow-up (months)	1-year event-free survival rate (%)	Ref.
					Medical	*PCI*	*CABG*				
DeMaio *et al.* (1989)	N/A	11	6 (54)	1 (20)	N/A	N/A	N/A	2 (7)	41	96	[22]
Pasalodos *et al.* (1994)	2241	5	1 (20)	0	3 (60)	0	2 (40)	0	18	100	[10]
Jorgensen *et al.* (1994)	9852	10	8 (10)	1 (10)	6 (60)	0	4 (40)	0	21	90	[11]
Zampieri *et al.* (1996)	2225	5	3 (60)	1 (20)	5 (100)	0	0	0	27	80	[12]
Hering *et al.* (1998)	3803	42	6 (14)	1 (2)	3 (7)	31 (74)	8 (19)	1 (2)	13	76	[13]
Celik *et al.* (2001)	3750	9	2 (22)	0	1 (11)	1 (11)	7 (78)	0	12	89	[14]
Maeder et al. (2005)	5054	5	5 (100)	0	3 (60)	1 (20)	1 (20)	0	13	100	[60]
Fontanelli *et al.* (2008–2009)	N/A	42	33 (79)	0	23 (54)	18 (44)	1 (2)	0	18	N/A	[85–87]
Vanzetto *et al.* (2009)	11,605	23	17 (74)	0	10 (44)	8 (34)	5 (22)	1 (4)	16	77	[3]
Mortensen *et al.* (2009)	32,869	22	17 (77)	2 (9)	7 (32)	13 (59)	2 (9)	0	35	100	[4]
Appleby *et al.* (2010)	N/A	5	5 (100)	5 (100)	1 (20)	3 (60)	1 (20)	0	N/A	100†	[18]
Motreff *et al.* (2010)	1780	12	12 (100)	2 (17)	2 (17)	9 (75)	2 (17)‡	1 (8)	51	N/A	[19]
Romero-Rodriguez *et al.* (2010)	9502	18	14 (78)	0	12 (67)	6 (33)	0	0	46	94	[83]
Kansara *et al.* (2011)	N/A	13	11 (85)	0	8 (61)	3 (23)	2(15)	0	48	50§	[15]
Ito *et al.* (2011)	N/A	23	23 (100)	7 (30)	13 (56)	4 (17)	6 (26)	0	N/A	N/A	[6]
Present study (2012)	N/A	5	5 (100)	5 (100)	1 (20)	2 (40)	3 (60)¶	0	25	60	

†*One patient required heart transplantation at 29 months after the index event.*
‡*One patient underwent PCI and subsequent CABG.*
§*Approximately 50% of these patients developed recurrent dissection within 1 month in a coronary artery different than index.*
¶*One patient initially treated with PCI required subsequent CABG.*
CABG: Coronary artery bypass graft surgery; N/A: Not applicable or not available; PCI: Percutaneous coronary intervention; Rx: Treatment

No conflict of interest

ACUTE ISCHEMIA, ACUTE CORONARY SYNDROMES AND MYOCARDIAL INFARCTION

ON-PUMP BEATING-HEART CORONARY ARTERY BYPASS GRAFT MIGHT REDUCE MYOCARDIAL INJURY EARLY AFTER ACUTE MYOCARDIAL INFARCTION

T. Takano[1], Y. Ohtsu[1], T. Seto[1], T. Terasaki[1], H. Tanaka[2], J. Amano[1]
[1]Cardiovascular Surgery, Shinshu University, Matsumoto, Japan
[2]Surgery, Okaya City Hospital, Matsumoto, Japan

On-pump beating-heart coronary artery bypass graft (OPBH) unloads left ventricle and avoids cardioplegic arrest during surgery for AMI and would reduce injury to non-infarcted myocardium. We evaluated myocardial injury of OPHB comparing conventional CABG with cardiac arrest (OPCA) within 24 hours after the onset of AMI.

We performed 31 solitary CABG for AMI from March of 2007 to April of 2013 in our institution. Of 31 cases, skin incision was started within 24 hours after the symptom of AMI started in 23 patients, and OPHB was done in 11 cases whereas OPCA in 12 cases.

Patients' basic characteristics, operative procedure, in-hospital mortality, morbidity, duration of IABP support, intubation period, ICU and hospital stay after the surgery, changes in creatinine phosphokinase (CK) and myocardial subset of CK (CK-MB) were retrospectively evaluated.

Pre-operative characteristics were not significantly different in 2 groups. Time interval between the onset of AMI symptom and skin incision was 14.7±8.0 and 15.4 ±6.7 hours in OPCA and OPBH group, respectively.

No significant difference was observed in the mortality and morbidity between 2 groups.

CK and CK-MB increased in 9 of 12 patients of OPCA and decreased in 9 of 11 patients of OPHB group after the surgery (p=0.01). CK and CK-MB significantly increased after the surgery (852±936 v.s. 1647±1532 IU and 88±113 v.s. 139±159 IU) in OPCA group although they did not significantly increase in OPBH group (2064±2203 v.s. 1830±1390 IU and 210±194 v.s. 165±117 IU).

OPBH might reduce myocardial injury during CABG early after AMI and would improve outcomes.

No conflict of interest

ACUTE ISCHEMIA, ACUTE CORONARY SYNDROMES AND MYOCARDIAL INFARCTION

MYOCARDIAL INFARCTION IN THE YOUNG - OUR RESULTS AND EXPERIENCE

I. Riecansky[1], J. Pacak[1], J. Pec[1], J. Melichercik[2]
[1]Cardiology, National Institute of Cardiovascular Diseases, Bratislava, Slovakia
[2]Innere Medizin und Kardiologie, Mediclin Herzzentrum, Lahr/Baden, Germany

Aims: Coronary artery disease in young adults is important task of contemporary cardiology. Presented our results experience were obtained by our long term investigation of myocardial infarction /MI/ in young patients under 40 years.

Methods:Two sets of patients were examined - 78 patients /74 men, 4 women/ hospitalised in pretrombolytic era in prospective 8 years follow up /1984-1992/ and 39 patients /35 men, 4 women/ admitted during period 2000-2010 analysed retrospective.

Results: MI in young age belongs roughly to two different groups with considerable overlap in pathogenetic mechanisms: 1.angiographycally normal coronary arteries or unilocular nonsignificant atherosclerotic stenosis /less 50%/ in 25-30% with thrombotic occlusion of one infarct related artery probably with substantial vasospastic component. Patients were younger /average 31.7 +/-3.7 years/, dominant risk factors smoking, hyperlipidemia,excesive physical and emotional stress. Disease course and prognosis are favourable. 2.premature accelerated atherosclerosis with significant /more 50%/ in 70-75% offen multivessel affection. Patients were significantly older /average 35.8+/-2.6. years;<0.001/, bad risk factors profile, worse clinical course and poore long-term prognosis.

Conclusions:Study of MI in young adults indicates: great role of risk factors, mainly smoking, hyperlipidemia, family history and type A behaviour, hostility with participation of low education level and social inequality /unemployment/. Noticeable are hypercoagulable states and trauma. Dominacy of men /90-95%/. Prognosis depends on age, extend of coronary atherosclerosis and residual cardiac function. Disease picture has not been changed during last 30 years. Agressive control over risk factors is unavoidable.Current requirement is to evalute impact of modern treatment strategy on long-term survival.

No conflict of interest

ACUTE ISCHEMIA, ACUTE CORONARY SYNDROMES AND MYOCARDIAL INFARCTION

CARE AND PROGNOSIS OF PATIENTS WITH ACUTE MYOCARDIAL INFARCTION – DATA FROM A COUNTRYSIDE VOLUNTARY REGISTRY

A. Jánosi[1], P. Ofner[1]
[1]Cardiology, "Gottsegen" National Institute of Cardiology, Budapest, Hungary

We have limited 'real world' data on care and prognosis of pts with acute myocardial infarction (MI). Purpose: Thirty-seven cardiology centres (16 PCI-capable hospitals) participated in a web-based voluntary myocardial infarction registry (MIR) to provide data on hospital care and prognosis of pts with MI. Methods: Between 01.01.2010 and 31.12.2011, 8582 pts were registered with MI, among them 4846 with ST elevation myocardial infarction (STEMI) and 3736 with non-ST elevation myocardial infarction (NSTEMI). Data on hospital care and on short- and long-term prognosis of pts were prospectively collected. We analysed the 30-day and 1-year mortality and the most important prognostic factors using logistic regression analysis. For survival analysis, the Cox proportional model was used. Results: The 8582 AMI pts evaluated by us were 28.6% of total cases treated in all hospitals in our country. In our database, the rate of male pts was higher in both groups (STEMI 62%, NSTEMI 59%). Pts treated with NSTEMI were older by almost 5 years compared to STEMI pts (mean age of 68.3 vs. 63.9 years). Women were older in both groups: in STEMI by an average of 7 years (68.3 vs. 61.1), while in the NSTEMI group by 5 years (71.1 vs. 66.3). Almost all (91.2%) STEMI pts were treated in PCI-capable centres, and 82% of them received primary percutaneous coronary intervention (PPCI). The survival of pts was as follows:

In-hospital mortality (%) 30-day mortality (%) 1-year mortality (%)

STEMI 3,7 9,5 16,5*

NSTEMI 4 9,8 21,7*

*Significant difference. Chi-square 37,6627 p<0.001

Independent prognostic factors of STEMI group 30-day mortality were (odds ratio [95%confidence intervals]): age (1.07 per year, P<0.001; [1.04-1.08]); diabetes mellitus (1.73, P=0.001; [1.22-2.46]); Killip class on admission (2.06, P<0.001; [1.58-2.67]); and PPCI (0.50, P<0.001; [0.34-0.73]). Gender, smoking habits, hypertension, and previous myocardial infarction provided limited prognostic information. Prognostic factors of STEMI 1-year mortality were: age (1.07 per year P<0.001; [1.05-1.10]); diabetes mellitus (1.90, P=0.01; [1.11-3.27]); previous stroke (2.22, P=0.019; [1.13-4.33]); and PPCI (0.43, P=0.004; [0.23-0.77]). Using the Cox proportional model, age (1.03, p<0.001), diabetes mellitus (1.24, P=0.003), stroke (1.48, p<0.001), Killip class (1.92, p<0.001) and PPCI (0.78, P<0.001) were significant variables. Conclusions:

1. STEMI and NSTEMI pts had similar short-term prognoses; however, 1-year mortality was found to be significantly higher in the NSTEMI group.

2. Using logistic regression analysis and Cox proportional model, age, previous stroke, diabetes and the Killip class were significant prognostic factors. The PPCI reduced the risk of death in the short- and long-term as well.

No conflict of interest

ACUTE ISCHEMIA, ACUTE CORONARY SYNDROMES AND MYOCARDIAL INFARCTION

ACUTE MYOCARDIAL INFARCTION AND MULTIVESSEL DISEASE: DIFFERENT PERCUTANEOUS REVASCULARIZATION STRATEGIES IN REAL WORLD

A. Manari[1], E. Varani[2], P. Guastaroba[3], M. Menozzi[1], M. Valgimigli[4], P. Magnavacchi[5], L. Vignali[6], A. Marzocchi[7], G. Casella[8]
[1]Interventional Cardiology, Azienda Ospedaliera IRCCS S.Maria Nuova, Reggio Emilia, Italy
[2]Cardiology, Maria delle Croci Hospital, Ravenna, Italy
[3]Statistic, Regional Health Agency, Bologna, Italy
[4]Cardiology, S. Anna Hospital University of Ferrara, Ferrara, Italy
[5]Cardiology, Baggiovara Hospital, Modena, Italy
[6]Cardiology, Maggiore Hospital, Parma, Italy
[7]Cardiology, S. Orsola-Malpighi Hospital, Bologna, Italy
[8]Cardiology, Maggiore Hospital, Bologna, Italy

Objectives. The purposes of this study were to examine the differences in cardiac outcomes for ST-segment elevation myocardial infarction (STEMI) patients and multivessel disease (MVD) undergoing culprit vessel primary percutaneous coronary intervention (PCI) or multivessel PCI, either during primary PCI or as a staged procedure.
> Background. A significant percentage of STEMI patients without hemodynamic compromise have MVD. However, the best revascularization strategy for non-culprit vessel lesions is still unknown.
> Methods and results. STEMI patients with MVD undergoing primary PCI and prospectively enrolled in the REAL Registry between July 2002 and December 2010, were considered. A total of 2061 patients were analyzed, treated with culprit-only primary PCI (706), multivessel PCI during the index procedure (367), or with a staged PCI within 60 days (988). Culprit-only primary PCI was associated with a higher risk of mortality as compared to a staged multivessel PCI [Hazard Ratio (HR): 2.81, 95% confidence interval (CI): 1.34-5.89, p=0.006 for 30-day mortality and HR: 1.96, 95% CI: 1.38-2.78, p=0.0002 for 2-year mortality, respectively). Acute multivessel PCI was associated with a higher short-term mortality risk as compared to a staged PCI (HR: 2.71, 95% CI: 1.07-6.84, p=0.03); such difference disappeared at 2-year follow-up (HR: 1.11, 95% CI: 0.65-1.90, p=0.69).
> Conclusions. Our findings support the current guidelines recommendation that culprit-only primary PCI should be performed in STEMI patients with MVD without hemodynamic compromise, followed by a staged non-culprit PCI within 60 days after the index procedure.

No conflict of interest

ACUTE ISCHEMIA, ACUTE CORONARY SYNDROMES AND MYOCARDIAL INFARCTION

COMORBIDITIES IN STEMI PATIENTS SUBMITTED TO PRIMARY PCI: TEMPORAL TRENDS AND IMPACT ON MORTALITY a 6-year single center experience

A. Mattesini[1], C. Lazzeri[1], M. Chiostri[1], P. Attana[1], C. Sorini Dini[1], G.F. Gensini[1], S. Valente[1]
[1]Heart and vessels, AOU Careggi, Florence, Italy

Background: Few data are available on the impact of comorbidities on outcomes in patients with ST-elevation myocardial infarction, submitted to primary percutaneous coronary intervention (PCI).

The aims of the present investigation, performed in 1268 consecutive STEMI patients all submitted to primary PCI admitted to our Intensive Cardiac Care Unit from 1st January 2004 to 31 th December 2010, are as follows:a) to assess the temporal trends in the number of comorbidities; b) to evaluated whether the number of comorbidities is able to affect mortality both during ICCU stay and at 1-year post-discharge; c) the temporal trends of mortality both at short and long terms

Results: Across the study period, the percentage of patients with two or more comorbidities significantly increased ($p<0.001$). Comorbidities were not associated with in-ICCU death while the presence of two or more comorbidities was associated with a significant lower follow up survival rate.

Conclusions: The main findings of our investigation are as follows: a) across the 6-year study period, the number of comorbidities progressive increased and was associated with advancing age and a more compromised hemodynamic status (as indicated by Killip class and LVEF); b) the progressive increase in the number of comorbidities was associated with a higher 1-year post discharge mortality but no difference was observed in in-ICCU mortality; c) throughout the overall study period it was observed a progressive decline in in-ICCU mortality, more pronounced in patients < 75 years and in one-year post-discharge mortality which was less evident in patients aged > 75 years.

No conflict of interest

ACUTE ISCHEMIA, ACUTE CORONARY SYNDROMES AND MYOCARDIAL INFARCTION

EFFECT OF FLAXSEED SUPPLEMENTATION AND EXERCISE TRAINING ON LIPID PROFILE, OXIDATIVE STRESS AND INFLAMMATION IN RATS WITH MYOCARDIAL ISCHEMIA

M. Deif[1], M. Shalaby[2]
[1]Physiology, Alexandria University, Alexandria, Egypt
[2]Biochemistry, King Saud University, Riyadh, Saudi Arabia

This study was carried out to evaluate the protective role of flaxseed and exercise on cardiac markers, lipids profile and inflammatory markers in isoproterenol (ISO)- induced myocardial ischemia (MI) in rats.

The research was conducted on 40 male albino rats, divided into 4 groups each of ten rats; group I served as control, group II was treated with ISO subcutaneously (85mg/kg) for 2 consecutive days for induction of MI, groups III and IV received flaxseed oil orally by gavage tube in a dose of 0.4 g/day for six weeks then MI was induced by ISO as described in group II. Additionally, group IV was trained with exercise preconditioning in the form of mere swimming

Alterations of lipid profile, cardiac and inflammatory markers [pentraxin- 3(PTX-3), interleukin-1β (IL-1 β), and tumor necrosis factor- α (TNF- α)] were observed in MI group. Flaxseed supplementation decreased cholesterol and LDL levels with more

obvious decrease in the group received exercise training combined with flaxseed supplementation Moreover, this combined group showed significant increase of HDL and

paraoxonase-1 (PON-1). On the other hand cardiac troponin, IL-1β and TNF- α levels were significantly decreased in the combined group as compared to myocardial ischemic group. This study concluded that the combination of flaxseed supplementations and exercise training is one of the promising cytoprotective elements for improving defense mechanisms in the physiological systems against oxidative stress and inflammation caused by MI.

No conflict of interest

ATHEROSCLEROSIS AND BASIC RESEARCH

Document not received

ATHEROSCLEROSIS AND BASIC RESEARCH

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ATHEROSCLEROSIS AND BASIC RESEARCH

Beyond cholesterol and beyond peroxidation; misfolding of ApoB, amyloidogenesis and atherogenesis

F. Ursini[1]
[1]*Department of Molecular Medicine, University of Padova, Padova, Italy*

Following the identification of high plasma level of LDL as a major risk factor for CVD, no evidence was obtained about the toxicity of this particle on arterial wall cells. This primed studies addressed to identify the modifications that could transform LDL into species competent for activating, in the sub-endothelial space, the "reaction to injury" response, generally seen as the first hallmark of atherogenesis. Searching for minimally oxidized LDL already 20 years ago we identified a species of negatively charged LDL (LDL-). This particle has been confirmed by several groups to be present in plasma associated to CVD and compatible, in vitro, with inflammation related events. The peculiar structural feature of LDL- is the misfolding of apoB leading to an aggregation that fulfills the criteria of amyloidigenesis. Indeed, in a specific loop of apoB an a to b structure transition takes place that drives the conformational shift of native LDL. Aggregates are detected by atomic force spectroscopy, identical to the fatty droplets observed in the sub-endothelial space. The misfolding of apoB is prevented by estradiol bound to a specific site in the protein, in agreement with epidemiological data and biophysical notion of the stabilization of the structure by a ligand. The misfolding of apoB can be induced by perturbation of the water lipid boundary. This can be produced by the activity of a phospholipase or mild lipid peroxidation. Notably, LDL- increases in the post-prandial phase when electrophiles are produced from lipids in the GI tract. The nutritional intake of lipids prone to peroxidation together nucleophiles in the same meal prevents the post-prandial increase of LDL-. The best nutritional source of nucleophiles in the GI tract preventing formation and the absorption of electrophiles is wine. Thus, protein biophysics nicely fits the folk Mediterranean wisdom suggesting to take wine only during meals.

No conflict of interest

ATHEROSCLEROSIS AND BASIC RESEARCH

Macrophage cholesterol homeostasis and atherosclerosis

T. Van Berkel[1], *J. Kuiper*[1], *M. Van Eck*[1]
[1]*Biopharmaceutics, Leiden University LACDR, Leiden, Netherlands*

MACROPHAGE CHOLESTEROL HOMEOSTASIS AND ATHEROSCLEROSIS

Th.J.C. Van Berkel, J. Kuiper, M. Van Eck.

LACDR - Biopharmaceutics, Leiden University, Einsteinweg 55, 2333 CC, Postbox 9502, 2300 RA, Leiden, Netherlands.

High plasma lipid levels form a prerequisite for the development of atherosclerosis. Once monocytes in the arterial wall are converted to macrophages, deposition of excessive amounts of cholesteryl esters, leading to foam cell formation can be considered as a key event in the progression of atherogenesis. Macrophage cholesterol homeostasis involves a delicate balance between lipid influx and lipid efflux. Macrophages are incapable of limiting the uptake of lipids via scavenger receptors and therefore largely depend on cholesterol efflux pathways to maintain cellular lipid homeostasis. Important mediators of macrophage cholesterol efflux are ABCA1, which mediates the efflux of cholesterol to lipid-poor apo A-I. Furthermore ABCG1 and SR-BI can efflux cholesterol to mature HDL. As a consequence of compensatory mechanisms, the single ABCA1, ABCG1 or SR-BI deficiency in macrophages only leads to moderate effects on cholesterol efflux and atherogenesis. Combined deletion of ABCA1 and ABCG1 leads to massive lipid accumulation and foam cell formation of tissue macrophages, while massive foam cell formation, atherosclerotic lesion development and inflammation is also observed by combined deletion of macrophage ABCA1 and SR-BI.. An enhancement of sytemic inflammation markers does accompany the extend of foam cell formation and the interaction between lipid accumulation and the inflammatory status might form an important factor for the pathological events during atherogenesis.

No conflict of interest

ATHEROSCLEROSIS AND BASIC RESEARCH

Novel LDL lowering strategies: beyond statins

P.K. Shah[1]
[1]*Cedars-Sinai Heart Institute, Los Angeles, USA*

LDL-C lowering with statins has been shown to reduce athero-thrombotic cardiovascular events in a broad spectrum of at risk patients in primary as well as secondary prevention settings. However 10-15% of patients are statin intolerant and in a significant minority of patients, statin are not sufficient to reduce LDL-C to acceptable levels and in homozygous FH, statins are relatively ineffective. Therefore there has been interest in developing non-statin LDL-C lowering medications. Currently there are 3 classes of medications that fall into this category. Lomitapide is an orally effective inhibitor of microsomal triglyceride transfer protein (MTP) that lowers LDL-C by nearly 50% in homozygous FH patients and was recently approved for this indication in the US. MTP inhibition blocks the formation of VLDL-C and LDL-C. Its major side effects include a)GI upset which can be reduced by dose reduction and low fat diet b) increase in hepatic fat accumulation. Another compound is Mipomersan which is an injectable antisence agains Apo B which reduces the synthesis of Apo B-which also reduces LDL-C by 20-30% in FH patients and has also been approved in the US for similar indications. Its major side effects include injection site reactions and hepatic enzyme elevation. Both Mipomersan and Lomitapide are expensive and insurance preauthorization is needed in the US. Although both drugs are officially approved for homozygous FH patients, off label use in statin intolerant patients or statin hypo-responders is likely. One of the more exciting advances in the field has been the development of inhibitors of PCSK9, a protease that degrades LDL receptors. These inhibitors are mostly monoclonal antibodies given by subcutaneous injection every 2-4 weeks. The PCSK9 inhibitors have shown large effects on LDL-C (50-70% LDL-C reduction even on a statin background) and preliminary safety data are reassuring. Several of these inhibitors are currently in phase 2-3 clinical trials.

No conflict of interest

ATHEROSCLEROSIS AND BASIC RESEARCH

Clinical use of flaxseed as a powerful nutritional intervention to treat cardiovascular disease

G.N. Pierce[1], D. Rodriguez[1], A. Edel[1], R. Guzman[1], M. Aliani[1]
[1]Canadian Centre for Agri-food Research in Health and Medicine, St Boniface Hospital, Winnipeg, Canada

THE CLINICAL USE OF FLAXSEED AS A POWERFUL NUTRITIONAL INTERVENTION TO TREAT CARDIOVASCULAR DISEASE

Grant N. Pierce, Delfin Rodriguez-Leyva, Andrea Edel, Randolph Guzman, and Michel Aliani

Canadian Centre for Agri-food Research in Health and Medicine (CCARM), St. Boniface Hospital, University of Manitoba, Winnipeg, Canada;

Flaxseed is enriched in the cardioprotective omega-3 fatty acid (alpha linolenic acid (ALA)), lignans and fiber. Peripheral arterial disease (PAD) is associated with hyperlipidemia and hypertension. The FlaxPAD Trial was initiated to determine if dietary supplementation with milled flaxseed in PAD patients could provide beneficial actions on a variety of cardiovascular disease parameters. The results of the trial will be reported here on the effects of milled flaxseed on blood pressure (BP) regulation and circulating cholesterol levels in patients with PAD. The FlaxPAD Trial involved a clinical population with PAD who were randomized into a ground flaxseed or whole wheat placebo group in which individuals were required to consume 30g of the appropriate intervention which was incorporated into different foods daily for a year. This Flax-PAD Trial was double-blinded and involved 110 patients. SBP was reduced by 10 mm Hg and DBP by 7 mm Hg in the flaxseed group relative to control following 6 months of intervention. SBP and DBP were correlated with the circulating ALA levels. DBP was correlated with both plasma enterolactone and total enterolignans. Both total and LDL cholesterol levels were reduced by flaxseed by 10-15%. We conclude that consuming ground flaxseed daily may offer a significant dietary strategy to lower both circulating cholesterol and BP.

No conflict of interest

ATHEROSCLEROSIS AND BASIC RESEARCH

Tissue engineering for vascular medicine

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ATHEROSCLEROSIS AND BASIC RESEARCH

Interplay of cytokines in the pathophysiology of heart failure

P.K. Singal[1]
[1]*St. Boniface Hospital Research Centre, Institute of Cardiovascular Sciences, Winnipeg, Canada*

Our understanding of the multiple in vivo functions of the proinflammatory cytokine, tumor necrosis factor (TFNα), is advancing at a rapid pace. In addition to its antitumor effects, overproduction of TNFα provokes tissue injury and organ failure. TNFα has also been shown to be cardiodepressent and responsible for various cardiovascular complications. Since trials with anti-TNFα were not a success, it appears that still much needs to be learned for a full comprehension of the role of TNFα in heart biology. Another cytokine, interleukin-10 (IL-10) has been shown to have anti-inflammatory properties. It is suggested to counterbalance many adverse effects of TNFα. IL-10 suppresses the production of TNFα and many other proinflammatory cytokines. We have recently reported that heart failure subsequent to myocardial infarction is associated with an increase in TNFα and a decrease in IL-10. TNFα–induced oxidative stress as well as apoptosis in isolated cardiomyocytes were shown to be mitigated by IL-10. Moreover, improvement in cardiac function after treatment with various drugs is also shown to be associated with an increase in IL-10 content. We have recently obtained evidence that IL-10 can also activate the innate signaling in cardiomyocytes. Such signaling may also involve an activation of TLR4, its co-receptor CD14 and a downstream protein MyD88 in an intricate manner to control apoptosis as well as synthesis of some of the primary cytokines. Based on these data, it is suggested that an optimal balance between IL-10 and TNFα may be a new therapeutic strategy for a healthier heart. (Supported by CIHR)

No conflict of interest

ATHEROSCLEROSIS AND BASIC RESEARCH

The contribution of circulating cells to atherosclerotic plaque calcification

G.P. Fadini[1], M. Albiero[2], L. Menegazzo[1], M. Rattazzi[1], A. Avogaro[1]
[1]Department of Medicine, University of Padova, Padova, Italy
[2]Laboratory of Experimental Diabetology, Venetian Institute of Molecular Medicine, Padova, Italy

Background. Several cell types contribute to atherosclerotic calcification. Myeloid calcifying cells (MCCs) are monocytes expressing osteocalcin (OC) and bone alkaline phosphatase (BAP), previously found to be associated to diabetes and cardiovascular disease.
Aim. Herein, we tested whether MCCs promote atherosclerotic calcification in vivo.
Methods and results. We show that the murine spleen contains OC^+BAP^+ cells with a phenotype similar to human MCCs, a high expression of adhesion molecules and CD11b, and capacity to calcify in vitro and in vivo. Injection of GFP^+ OC^+BAP^+ cells into 8- or 40-week $ApoE^{-/-}$ mice led to more extensive calcifications in atherosclerotic areas after 24 or 4 weeks, respectively, compared to control OC^-BAP^- cells. Despite OC^+BAP^+ cells had a selective transendothelial migration capacity, tracking of the GFP signal revealed that presence of injected cells within atherosclerotic areas was an extremely rare event and GFP mRNA was undetectable by qPCR of lesion extracts. By converse, injected OC^+BAP^+ cells persisted in the bloodstream and bone marrow up to 24 weeks, suggesting a systemic paracrine effect. Indeed, OC^+BAP^+ cell conditioned medium (CM) promoted calcification by cultured VSMC more than CM from OC^-BAP^- cells. An in-depth genomic and proteomic investigation of MCCs identified allograft inflammatory factor (AIF)-1 as a potential candidate of this paracrine activity. AIF-1 stimulated VSMC calcification in vitro. Monocyte-specific (CD11b-driven) AIF-1 overexpression in $ApoE^{-/-}$ mice increased calcium content in atherosclerotic areas.
Conclusion. We show that murine OC^+BAP^+ cells correspond to human MCCs and promote atherosclerotic calcification in $ApoE^{-/-}$ mice, through paracrine activity and modulation of resident cells by AIF-1 overexpression.

No conflict of interest

ATHEROSCLEROSIS AND BASIC RESEARCH

Goserline acetate protects from myocardial ischaemia/reperfusion injury and modulates apoptosis

N.R. Hadi[1], F.G. Al-Amran[2], K. Kareem[1]
[1]Pharmacology and Therapeutics, kufa college of medicine, kufa, Iraq
[2]Cardiovascular surgery, kufa college of medicine, kufa, Iraq

Objective

This study was undertaken to investigate the role of endogenous testosterone in regional myocardial ischemia reperfusion and in male rats.

Material and method

Twenty four Albino-Wistar rats were used in the study.The rats were randomized into 4 equal groups each of six. **Group 1** sham group, rat underwent the same anesthetic and surgical procedure as the control group except for surgical ligation of LAD, **Group 2** control group, rats underwent surgical ligation of LAD and subjected to regional ischemia for 25 min and reperfusion for 40 min, **Group 3** castrated, rats underwent surgical castration, left 3wks for recovery, then underwent surgical LAD ligation, and subjected to 25min of ischemia and 40min of reperfusion, **Group 4** treated, rats of this group take a S.C injection of goserline acetate 3wks before surgery, then subjected to surgical LAD ligation with 25min ischemia and 40min of reperfusion.

Results

Compared with sham group, levels of myocardial TNF-α & IL-1β, ICAM-1, plasma cTn i and ss DNA (marker for apoptosis) were significantly increased ($p<0.05$) in control group. Additionally, all control group animals histologically

showed significant myocardial injury ($P < 0.05$) compared with sham group. Both castration and Gozerlin treatment significantly counteract the increase in myocardium level of TNF-α, IL-1, ICAM-1, plasma cTn I and ss DNA ($P < 0.05$). Histological analysis revealed that both castration and Goserline administration markedly reduced ($P < 0.05$) the severity of cardiac injury.

Conclusion:

Surgical castration and Gozerlin may ameliorate regional myocardial I/R injury and apoptosis via interfering with inflammatory responses.

No conflict of interest

ATHEROSCLEROSIS AND BASIC RESEARCH

Intauterine growth restriction adversely impacts on the complement of cardiomyocytes at birth and life-long functional reserve

M. Black[1], M. Wlodek[2], K. Lim[3], O. Gezmish[1]
[1]Anatomy and Developmental Biology, Monash University, Clayton, Australia
[2]Physiology, The University of Melbourne, Parkville, Australia
[3]Neuropharmacology, Baker IDI Heart and Diabetes Institute, Prahran, Australia

There is strong epidemiological and experimental evidence to show that poor growth *in utero* can program for long-term cardiovascular disease, especially when the growth trajectory after birth does not reflect that *in utero*. This may relate to developmental changes to the structure of the heart and in the complement of cardiomyocytes at the time of birth. In general, cardiomyocytes undergo a process of maturation around the time of birth, whereby they stop dividing and become terminally differentiated in preparation for the hemodynamic transition at birth; after this time, subsequent growth of the heart is predominantly due to cardiomyocyte hypertrophy and/or extracellular matrix deposition. Using animal models of intrauterine growth restriction, (maternal protein restriction and bilateral uterine artery ligation) we have stereologically examined the total number of cardiomyocytes in the hearts of growth restricted offspring at birth. Importantly, we found a significant reduction in the number of cardiomyocytes at the time of birth. This is restored to normal when growth is normalised in the postnatal period, as cardiomyocytes continue to proliferate in the rodent heart in the first week after birth. Our findings suggest that babies who are growth restricted *in utero* will begin life with a reduced complement of cardiomyocytes and this will adversely impact on life-long functional reserve. In the case of the preterm infant, where their hearts (like rodents) are immature at birth, there may be a brief developmental window in the early neonatal period, whereby cardiomyocyte number can be restored to normal by improving body growth.

No conflict of interest

REGENERATIVE MEDICINE

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REGENERATIVE MEDICINE

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REGENERATIVE MEDICINE

Mode of action of stem cells in coronary artery disease

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REGENERATIVE MEDICINE

Bone marrow cells for the heart: emerging evidence and prospects

B. Dawn[1], V. Jeevanantham[1]
[1]Division of Cardiology, University of Kansas Medical Center, Kansas City, USA

On the basis of encouraging evidence from studies in animal models, numerous clinical trials of heart repair with adult bone marrow-derived cells (BMCs) have been completed over the past decade. These relatively smaller trials used diverse BMC types with highly variable cell numbers, injection routes, and timings of transplantation. Moreover, these trials included patients with acute myocardial infarction (MI), chronic ischemic heart disease (IHD), as well as ischemic cardiomyopathy. Although these differences in study design have sometimes resulted in discordant results, meta-analysis of pooled data indicates that BMC injection in patients with acute MI and chronic IHD results in significant improvements in cardiac parameters and patient outcomes without appreciable adverse effects. Nonetheless, a number of questions remain to be addressed in order to enhance the benefits of BMC therapy on cardiac structure, function, and clinical outcomes. The results from meta-analysis of cumulative data may offer important insights in this regard.

No conflict of interest

REGENERATIVE MEDICINE

Stem cell survival

M. Gyöngyösi[1], N. Pavo[1], J. Ankersmit[2], I.N.N.A. Sabdyusheva[2], M. Zimmermann[1], G. Maurer[1]
[1]Dept. Cardiology, Medical University of Vienna, Vienna, Austria
[2]Dept. Surgery, Medical University of Vienna, Vienna, Austria

A decade ago, stem or progenitor cells held the promise of tissue regeneration in human myocardium, with the expectation that these therapies could rescue ischemic myocyte damage, enhance vascular density and rebuild injured myocardium. The accumulated evidence in 2013 indicates, however, that these cells are unable to regenerate completely the human cardiac tissue. As the quest for a frontrunner continues, alternative cell types, such as resident cardiac cells, adipose-derived or phenotypic modified stem or progenitor cells have also been applied, aiming to increase the number and the retention and survival of the reparative cells in the myocardium. Beside further tremendous efforts to increase the efficacy of currently available methods, pre-clinical experiments using new techniques such as tissue engineering or exploiting paracrine effect hold promise to regenerate injured human cardiac tissue via improvement of angiogenesis. We have previously proved the biodistribution of the cells in the remote organs. In our current experiment we show the differences in gene expression profiles of the intramyocardially injected mesenchymal stem cells which retained in the myocardium or spleen.

No conflict of interest

REGENERATIVE MEDICINE

Myocardial regeneration by stem cells in cardiac surgery

Stem cells have been applied in numerous experimental and clinical studies to modify cardiac regeneration in postinfarction remodeling and in chronic ischemic heart disease. Several Phase I/II clinical trials showed safety and efficacy of autologous bone marrow stem cell transplantation in the context of coronary bypass surgery. Surgical stem cell implantation is performed into well exposed ischemic areas containing viable tissue allowing improvement of perfusion by induced angiogenesis. Applications have been employed in bypass surgery on pump or off pump as well as stand-alone therapy. Relevant animal models have to precede clinical testing to adress dose finding, toxicity testing, application technique and biodistribution. GMP-preparation of highly defined and purified stem cell preparations is mandatory for performance of clinical studies, which should be performed according to GCP-criteria. Validation of each cell product has to follow the drug development pathway with Phase I/II clinical trials and sequentially Phase IIb and Phase III trials to test safety and efficacy. This development is currently followed for stem cell products of cardiac or bone marrow source. Special attention to release criteria and cell quality has to be applied in cultured cell products. An attractive option for intraoperative stem cell harvesting and rapid production by point-of-care stem cell isolation procedures is currently under preclinical and clinical investigation. The own experience of develoment and setup of the first Phase III clinical multicentre trial in cardiac stem cell therapy is reported (PERFECT study; www.clinical-trials.com; identifier: NCT00950274).

No conflict of interest

REGENERATIVE MEDICINE

Treatment of peripheral arterial disease with stem cells

M. Brehm[1]
[1]*Department of Internal Medicine, Division of Cardiology and Angiology, Hannover, Germany*

Peripheral artery disease (PAD) becomes manifest as asymptomatic atherosclerosis of peripheral arteries, reduced walking distance (intermittent claudication) and as pain at rest or loss of tissue integrity in distal limbs (critical limb ischemia), resulting in major amputation in part of the lower extremity and subsequent death. The risk factors for progression of peripheral atherosclerosis include advanced age, on-going smoking, diabetes mellitus, dyslipidemia and arterial hypertension. Depending on the stage of circulatory disturbance, the basic medical treatment accordant to the guidelines is platelet aggregation inhibitor, ACE/ AT-1 inhibitor for blood pressure reduction and statins for increased LDL levels. In advanced peripheral artery disease revascularisation is mandatory, including endovascular or open surgical interventions, depending on the TASC II classification. In critical limb ischemia (CLI) appropriate revascularisation possibilities are often not usefull and the pharmacological potency with intravenous prostaglandins is limited. Thus, additional therapy options are necessary to reduce the number of major amputations and amputation free survival (AFS). In the past gene therapy of intramuscular injection of FGF plasmid has been extensively tested, the overall effect of the phase III trial was negative. A novel therapy is the intramuscular or intraarterial injection of regenerative autologous or allogenic cells e.g. bone marrow cells, peripheral mononuclear cells or mesenchymal stem cells. Current phase I / II trials applying stem cells in PAD are promising concerning the primary endpoints reduction of distal limb amputation rate and amputation free survival, but randomized placebo-controlled trials have to be awaited. Still, important questions like ideal application route, type of regenerative cells, point of time for application, proper method for harvesting regenerative cells are under debate. Not only in experimental studies but also in clinical settings new findings will be acquired. Furthermore, the point of time for treating the proceeding peripheral artery disease has to be discussed. Perhaps not only the no-option patients with advanced PAD has to be treated, maybe the patients with impending rest pain or threatened distal limb has to be treated earlier, to decrease or even cut the progression of the atherosclerotic progress in peripheral arteries.

No conflict of interest

REGENERATIVE MEDICINE

Does stem cell therapy for angiogenesis hold the promise to be more efficient than gene therapy?

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REGENERATIVE MEDICINE

Gene electro transfer of plasmid encoding VEGF to induce angiogenesis in a porcine ischemia model

R. Heller[1], R. Strange Jr.[2], L. Murray[3], C. Lundberg[1], N. Burcus[1], A. Bulysheva[1], B. Hargrave[1]
[1]Frank Reidy Research Center for Bioelectrics, Old Dominion University, Norfolk, USA
[2]Cardiovascular Surgery, Portsmouth Naval Facility, Portsmouth, USA
[3]Comparative Medicine, Sobran, Norfolk, USA

Nonviral gene therapy is an attractive method for treating cardiovascular disease; however, achieving appropriate gene expression levels is often problematic. To enhance expression, we have developed a delivery approach using *in vivo* electro transfer. Domestic farm pigs (weights 30 – 45 kg.) underwent a medial sternotomy under general endotracheal anesthesia. Plasmid (0.1 ml), either luciferase (gWizLUC) or vascular endothelial growth factor (pVEGF), was injected into the anterior wall of the left ventricle, followed by electro transfer at specific parameters synchronized with the QRS complex. Animals were maintained for up to seven weeks following delivery and at designated time points underwent injection site excision to determine expression levels or evaluated for level of perfusion in ischemic area. Several electro transfer conditions were tested and the levels of expression could be varied and/or maintained for 2-14 days depending on pulse conditions. Both luciferase and VEGF expression was enhanced when delivered with electro transfer. Additional experiments were performed following partial occlusion of the distal left anterior descending coronary artery. Delivery was performed around the ischemic area. The level of ischemia was quantitated before and after treatment. Within two weeks, treated animals had increased blood flow in the previously ischemic area. Arteriograms before treatment and at various time points following treatment indicated angiogenesis had occurred. Infarct size was reduced or absent in treated animals compared to controls. Based on these results, gene delivery to the heart can be successfully accomplished using *in vivo* electro transfer and evidence suggests the potential for a therapeutic effect.

No conflict of interest

NEW STRATEGIES INTERVENTIONAL CARDIOLOGY

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NEW STRATEGIES INTERVENTIONAL CARDIOLOGY

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NEW STRATEGIES INTERVENTIONAL CARDIOLOGY

Current device strategies for prevention of distal coronary embolization during percutaneous coronary intervention

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NEW STRATEGIES INTERVENTIONAL CARDIOLOGY

Biodegradable stent coatings

I.B.A. Menown[1]
[1]*Cardiology, Craigavon Cardiac Centre, Craigavon, United Kingdom*

Over the last decade, the practice of percutaneous coronary intervention (PCI), particularly in complex long anatomical subsets, has been revolutionised due to the highly efficacious reduction of in-stent restenosis (ISR) by drug eluting stents (DES). Central to success of DES has been the use of a polymer coating to control the release profile of an anti-proliferative drug.

However, the permanent polymers used in first generation Sirolimus and Paclitaxel eluting stents have been associated with small but important incidence of vascular hypersensitivity which may increase risk of very late stent thrombosis (VLST). Biodegradable polymer coatings for DES have thus been developed to control the release of drug over the short term but to biodegrade over the next several months. Long-term follow up data are emerging showing that such technology, compared with first generation DES, may improve clinical outcomes including VLST, particularly in more complex lesions.

A second safety concern is the need for prolonged dual antiplatelet therapy following both first generation DES and biodegradable polymer coated DES. Novel approaches to combine shorter duration dual antiplatelet therapy with drug elution include polymer free DES technology and drug eluting balloons +/- bare metal stent.

Latest clinical trial data for biodegradable polymer coated DES studies will be discussed along with ongoing trials with polymer free and drug eluting balloon strategies.

Conflict of interest

NEW STRATEGIES INTERVENTIONAL CARDIOLOGY

Direct coronary imaging to guide optimal PCI

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NEW STRATEGIES INTERVENTIONAL CARDIOLOGY

THE CLINICAL EVALUATION OF THE ENDEAVOR ZOTAROLIMUS-ELUTING CORONARY STENT IN JAPANESE PATIENTS: FINAL 5-YEAR FOLLOW-UP OF THE ENDEAVOR JAPAN STUDY

S. Saito[1], MD on behalf of the ENDEAVOR Japan Investigators
[1]Cardiology & Catheterization Laboratories, Shonan Kamakura General Hospital, Kamakura, Japan

Background: Angiographic and clinical outcomes associated with coronary stents eluting the new molecular entity zotarolimus have been well characterized in a variety of geographies and patient subsets. The Endeavor Japan study is the first prospective clinical trial to evaluate the safety and efficacy of the Endeavor zotarolimus-eluting stent (ZES) in the treatment of Japanese patients with single de novo lesions in native coronary arteries.

Methods and materials: This nonrandomized, prospective, multicenter, single-arm trial of 99 subjects with inclusion criteria (elective percutaneous revascularization of single native de novo coronary artery lesions with length ≥14 and ≤27 mm with reference vessel diameters between 2.25 and 3.5 mm) selected to enhance statistical comparability to the ENDEAVOR II randomized study as historical control. The primary end point was target vessel failure (TVF) at 9 months.

Results: At 9 months, the TVF rate was 5.2%, compared with 7.9% in the ZES arm of ENDEAVOR II (P=.412). Notable baseline differences between the Endeavor Japan and ENDEAVOR II populations were diabetes (38.4% vs. 18.2%; P<.001), and unstable angina (4.6% vs. 30.3%; P<.001). Despite cohort differences, acute, 9-month, and 5-year clinical outcomes were similar in the two groups, as were 8-month angiographic indices. Finally, out to 5 years, no stent thrombosis was observed in Japanese subjects.

Conclusions: These findings demonstrate that, in a Japanese population, the Endeavor ZES has similar safety and efficacy compared with other geographies, with sustained clinical benefit and safety to 5 years.

Conflict of interest

NEW STRATEGIES INTERVENTIONAL CARDIOLOGY

INTERVENTIONAL MICROVASCULAR OBSTRUCTION AFTER PERCUTANEOUS CORONARY INTERVENTION: EFFECT OF PREPROCEDURAL ASPIRIN RELOAD

V. Raparelli[1], G. Tanzilli[2], E. Mangieri[2], A. Placanica[3], M. Dominici[3], A. Arrivi[3], F. Barillà[2], P. Pignatelli[4], S. Basili[4], F. Violi[4]
[1]Internal medicine and Medical Specialties, Sapienza University of Rome, Rome, Italy
[2]Department of the Heart and Great Vessels "Attilio Reale", Sapienza University of Rome, Rome, Italy
[3]Department of Interventional Cardiology, Santa Maria University Hospital, Terni, Italy
[4]Internal Medicine and Medical Specialties, Sapienza University of Rome, Rome, Italy

Background: Incomplete aspirin (ASA) platelet inhibition and interventional microvascular obstruction (MVO) have been suggested as putative mechanisms of adverse clinical outcome in patients undergoing elective percutaneous coronary intervention (PCI). Thromboxane (TX) A_2 might be involved as a key mediator of platelet activation and as a potent coronary vasoconstrictor.
Aim and Methods: Pre-procedural Aspirin reload for Native coronary disease Treated by Angioplasty: Reperfusion indexes Evaluation and Improvement of clinical outcome (PANTAREI) study is an interventional, multicenter, randomized study planned to evaluate the effect of ASA reload (325 mg orally at-least 1 hour before elective PCI) on: (i) serum TxB_2 levels (stable metabolite of TxA_2) changes after 60 and 120 min; (ii) reperfusion indexes changes, evaluated by corrected TIMI Frame Count (cTFC) and myocardial blush grade (MBG); (iii) myocardial injury indexes (serum cardiac Troponin I) modifications at 6, 12 and 24 hours after PCI.
Results: Ninety-one patients (74 M, 66 ± 10 yrs.), already on chronic low-dose ASA therapy, scheduled for elective PCI were randomly assigned to receive preprocedural ASA reload (N=46) or no-reload (N=45). Compared to no-reload group, TxB_2 significantly decreased after 120' in reload group. Both groups showed a statistically significant reduction in cTFC and in patients percentage with MBG≤2 (Reload= 39%; No-Reload=69%). Reperfusion indexes were lower in reload group ($p<0.01$). Patients with MBG=3 after PCI showed a significantly lower TxB_2 levels.
Conclusions: ASA loading dose (325-mg) before elective PCI would provide a significant clinical benefit suggesting a possible physiopathological role of serum thromboxane complete inhibition in "interventional MVO" prevention.

No conflict of interest

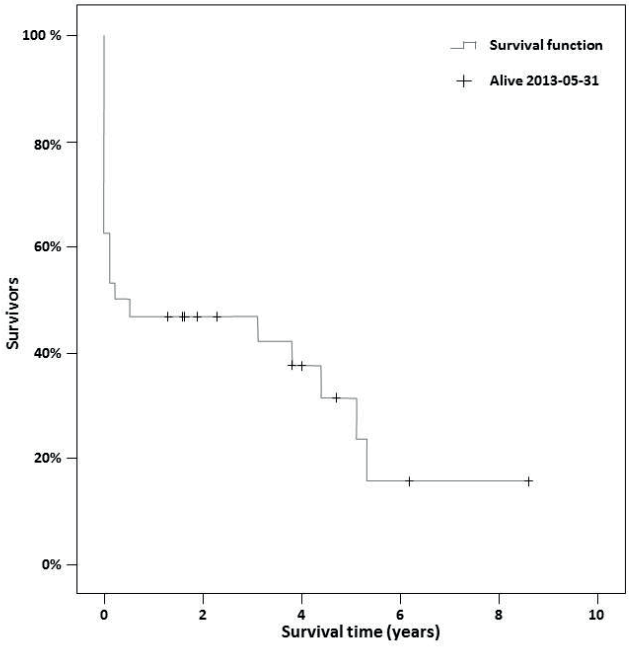
NEW STRATEGIES INTERVENTIONAL CARDIOLOGY

THE USE OF MECHANICAL CHEST COMPRESSIONS IN PROLONGED RESUSCITATION EFFORTS DURING SIMULTANEOUS PCI, A VALUABLE TOOL IN SAVING LIVES.

H. Wagner[1], B. Madsen-Hardig[2], M. Rundgren[3], J. Harnek[4], D. Zughaft[4], M. Gotberg[4], G.K. Olivecrona[4]
[1]Cardiology, Lund Univeristy, Lund, Sweden
[2]Pricncipal Scientist, Physio-Control Sweden/Jolife AB, Lund, Sweden
[3]Anaesthesiology and intensive care, Lund University, Lund, Sweden
[4]Cardiology, Lund University, Lund, Sweden

Background: Resuscitation in the catheterization laboratory (cath-lab) with mechanical chest compressions (MCC) and simultaneous percutaneous coronary intervention (PCI) is since 2010 a class IIa recommendation in AHA guidelines. Aim of current study was to compare the outcome in patients suffering cardiac arrest with prolonged MCC in the cath-lab in the last four years with the result from our 5-year experience study. **Material and methods:** Patients were admitted to the cath-lab with sustained circulation and sometime during the intervention suffering cardiac arrest and needed prolonged resuscitation efforts with MCC with the LUCAS™-device (Physio-Control Inc./Jolife AB) during simultaneous PCI or angiogram between April 2009 – April 2013. **Results:** 32 patients (23 STEMI, 4 Non-STEMI, 2 planned PCI, 1 angiogram, 1 stentocclusion, 1 IABP) were included. 21 patients were in cardiogenic shock, 24/30 were successfully treated with PCI. 25 interventions were performed during MCC. Treatment time with MCC (n=32) was median (range) minutes 34(5 – 90), discharged from cath-lab (n=15), 15(5 – 90), discharged from hospital (n=8) 10(5 – 45). This gives a survival rate of 25% for patients discharged from hospital. The survival time in a pooled analysis from both studies in patients discharged from the cath-lab shows a 6 month survival of 50%. (Figure 1).**Conclusion:** Our study confirms our previous study with an unchanged survival rate of 25% among patients treated with MCC during simultaneous PCI.

Figure 1.



Conflict of interest

NEW STRATEGIES INTERVENTIONAL CARDIOLOGY

HYBRID CORONARY REVASCULARIZATION (HCR) IN PATIENTS WITH MULTI-VESSEL CORONARY DISEASE (MVD): MID-TERM RESULTS.

A. Repossini[1], L. Di Bacco[1], M. Tespili[2], A. Saino[2], F. Rosati[1], I. Kotelnikof[1], L. Giroletti[1], C. Muneretto[1]
[1]Cardiac Surgery, University of Brescia, Brescia, Italy
[2]Cardiology unit, Ospedale Bolognini, Seriate, Italy

OBJECTIVE: Hybrid Coronary Revascularization, (Minimally Invasive Direct Coronary Artery Bypass (MIDCAB) combined with non-LAD PCI stenting), is considered a viable alternative to conventional CABG through sternotomy or to multi-vessel PCI stenting, to perform a functionally complete revascularization. We report our results and mid-term outcomes.

METHODS: Since January 2009 up to October 2012, 70 consecutive patients underwent hybrid revascularization after Heart Team evaluation. Demographic, pre-operative, intra-operative data and post-operative outcomes were obtained. Coronary risk was assessed by SYNTAX score, and patients were partitioned in tertiles according to the score categories (≤22 low risk, >22 and ≤33 intermediate risk, >33 high risk). Pre-operative risk assessment was upgraded to EuroSCORE II for all patients. Long-term outcomes, major adverse cardiac and cerebrovascular events (MACCE) rate and repeated target vessels revascularization (TVR) rate were evaluated by Kaplan-Meier curve and log-rank test.

RESULTS: Mean age was 66.3 ± 12.0 years, 83.8% males. Mean SYNTAX score was 28,22 ± 7 (in patients with Left Main (LM) 33,5 ± 4,5). Mean EuroSCORE II was 4,05 ± 1,83. PCI was performed in all patients (n=70), in 52 pts (75,2%) before and in 24,8% after surgery (interval 2,2 ± 1,3 months). In 12 patients (18,6%) LM was involved. No intra-operative or in-hospital deaths were reported. At follow-up one cardiac death for acute inferior myocardial infarction occurred.. At 25 ± 13 months follow-up the overall population freedom from MACCEs rate was 82,6% (CI: 79,5% to 85,7%) and the freedom from TVR rate was 86,1% (CI: 82,9% to 89,3%). MACCE and TVR rates were higher (p > 0,05) in patients with SYNTAX score >22.

CONCLUSIONS: Hybrid Coronary Revascularization is a viable option to achieve a minimally invasive functionally complete revascularization in patients at high risk for conventional revascularization. This strategy showed better results when performed on patients with a SYNTAX score ≤ 22.

No conflict of interest

PHARMACOTHERAPY

Biology of aging and heart therapy: what's new and what's missing?

B. Jugdutt[1]
[1]*Cardiology/Medicine, University of alberta, Edmonton, Canada*

The aging population and the burden of heart failure (HF) are increasing worldwide. Morbidity and mortality from myocardial infarction (MI) and hypertension (HTN), the two main causes of HF, and related costs are increasing in the elderly (age ≥ 65 years). While aging is a normal process, it is progressive and results in cardiovascular changes that impact disease expression and response to therapy. It is associated with increased risk for HTN, MI and HF. Emerging evidence suggests that several aging-related changes contribute to adverse cardiac remodeling and an accelerated march to HF. The remodeling involves changes in cardiovascular structure/function as well as cellular/subcellular, physiological/pathophysiological pathways and responses to stress/injury. For example, while optimal healing is essential for survival with a favourable outcome, defective post-MI healing with aging contributes to adverse remodeling and may explain poor outcomes. While better post-MI therapies have improved survival, therapy for optimizing post-MI healing is lacking. While early reperfusion therapy may reduce infarct size and accelerate healing, delayed reperfusion of large infarcts may result in reperfusion damage, impaired healing and adverse remodeling in the elderly. Progressive left ventricular remodeling and progression to HF are persistent problems in older patients. Changes with aging have important therapeutic implications. Therapy for the young may not be optimal for the old. Several recommended post-MI therapies can impact early and late phases of healing in positive or negative directions. Preclinical studies suggest that pathways during early and late phases can be targeted for optimizing post-infarct healing and the march to HF.

No conflict of interest

PHARMACOTHERAPY

The medical management of stable angina: an update

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PHARMACOTHERAPY

What is optimal therapy for stable angina/ischemic heart disease in the year 2013?

U. Thadani[1]
[1]*Medicine/Cardiovascular Section, University of Oklahoma and VA Medical Center, Oklahoma City, USA*

In the year 2013, optimal therapy for stable angina/ischemic heart disease comprises of abolition or near abolition of symptoms, improved quality of life
and reduction of the incidence of serious adverse cardiovascular outcomes (acute coronary syndrome, sudden cardiac death, stroke and heart failure). Lifestyle modifications (abstinence of smoking, regular exercise and lipid modifying treatment with statins, but not with niacin, or fibrates or HLD raising drugs, reduce the incidence of serious adverse cardiovascular outcomes. In addition, daily use of aspirin, and adequate control of blood pressure also reduce the incidence of adverse outcomes. Older and newer antianginal medications, as well as coronary artery revascularization (percutaneous or surgical) reduce the frequency of angina episodes, increase angina free exercise duration and improve quality of life, but have little impact on the incidence of serious adverse cardiovascular outcomes with a few exceptions (use of beta blockers and ACE inhibitors when left ventricular ejection fraction is reduced and coronary bypass surgery for left main CAD). Individualization of treatment strategy which takes into consideration patients' lifestyle and presence of any comorbidities is essential to achieve this goal.

Conflict of interest

PHARMACOTHERAPY

CV outcome trials for new type 2 diabetes drugs

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PHARMACOTHERAPY

Statin induced diabetes: incidence, mechanism and possible solutions

Y. Birnbaum[1], Y. Ye[2], S. Ling[2], M. Nanhwan[2], J.R. Perez-Polo[2], M. Bajaj[3]
[1]Medicine/ Cardiology, Baylor College of Medicine, Houston, USA
[2]Biochemistry and Molecular Biology, University of Texas Medical Branch, Galveston, USA
[3]Medicine/ Endocrinology, Baylor College of Medicine, Houston, USA

Background: High-dose statin therapy increases the incidence of insulin resistance and new onset diabetes. Studies in animal models have suggested that prolonged (>3d) statin therapy upregulates Phosphatase and Tensin Homologue on Chromosome 10 (PTEN) expression. PTEN levels are also elevated in the hear,t aorta and skeletal muscles of animals with diabetes, and the myocardium of diabetic patients. Increasing intracellular cAMP levels with subsequent activation of protein kinase A (PKA) decreases PTEN expression. We assessed whether prolonged treatment with high-dose statins induces diabetes and upregulates PTEN in the skeletal muscle of mice receiving Western Diet (WD) and whether cilostazol (CIL, a phosphodiesterase-3 inhibitor that increases cAMP levels) will attenuates the effects. **Methods:** Mice received normal diet or WD without (control) or with rosuvastatin (ROS, 10 mg/kg/d), CIL (10 mg/kg/d), or ROS+CIL for 30 days. Fasting serum glucose and insulin were measured as well as PTEN, Ser-473 P-Akt and total Akt levels in skeletal muscle. **Results:** WD alone caused significant increase in glucose and insulin. These levels were significantly higher in the ROS group. WD alone increased PTEN and decreased P-Akt levels. Levels of PTEN were significantly higher and P-Akt lower in the ROS than the control group. CIL normalized fasting glucose and insulin levels and attenuated the changes in PTEN and P-Akt concentrations in the ROS+CIL group. **Conclusions:** Long-term high-dose statins can induce diabetes by upregulating PTEN that attenuates Akt activation. CIL attenuates these changes. Further studies are needed to assess the ability of increasing cAMP levels by to prevent induction of diabetes by statins.

Conflict of interest

PHARMACOTHERAPY

Clinical relevance of the pharmacogenetics of warfarin in the Russian population

E. Panchenko[1], E. Kropacheva[1], A. Dobrovolsky[1], D. Trofimov[2]
[1]The laboratory of clinical promlems of atherothrombosis, Cardiology Research and Production Center, Moscow, Russia
[2]DNA-Technology Company, DNA-Technology Company, Moscow, Russia

Clinical Relevance of Warfarin Pharmacogenetics in Russian Population

E. Panchenko[1], E. Kropacheva[1], A. Dobrovolsky[1], D.Trofimov[2]

on behalf of WARFAGEN Study Investigators

Cardiology Research and Production Center[1], "DNA-Technology Company" [2] Moscow Russia

Warfarin (W) remains the most broadly used oral anticoagulant in prevention and treatment of thromboembolic complications. However, reaching of a stable effective W dose depends on multiple factors including genetic variability in drug response. **Aim of the study** was to evaluate the frequency of CYP2C9 and VKORC1 polymorphysms in Russian population and their impact on quickness and stability of target INR achievement and bleeding complications in the first 6 months of drug treatment. **Material and Methods:** Prospective and multicenter study involved 292 W naïve pts (avg. age 63,4±11,2 years with 51,8% M) randomized in pharmacogenetic (Gr1) and usual care (Gr2) groups with indications to VKA: AF- 69,6%, VTE-19,5%, artificial valves-8,5%, and LV thrombus-2,4%. Analysis of CYP2C9 and VKORC1 genotypic variations was performed with PCR. The loading and therapeutic W doses in Gr1 pts were calculated in accordance to genotyping by Gage algorithm. In Gr2 pts W loading dose was 5 mg. The INR was controlled every third day during first 2 weeks and then monthly in both groups of pts. The End Points: time to target INR achievement, TTR and bleedings (Bl) were followed up during 6 months. Results are presented as M±SD. **Results:** Gr1 and Gr2 were similar in indications for W therapy and frequency of main clinical factors. Mean TTR was 69±16,6 (95% CI 33-92,3).

Distribution of CYP2C9 genotypes in Russian pts needed W therapy					
*1/*1 *1/*2		*2/*2	*1/*3	*2/*3	*3/*3
66,2%	16,4%	1,8%	12,4%	3,1%	0,4%
Distribution of VKORC1 -1639 G>A genotypes in Russian pts needed W therapy					
GG		GA		AA	
41,3%		43,1%		15,6%	

Any of CYP2C9 and VKORC1 polymorphism combinations were found in 21,1% of pts. The combination of CYP2C9*3 or *2/*2 with VKORC1 AA was found in 12,8% of pts.

Results (efficacy)	Group1	Group2	p
Time to target INR(days)	12,5±4,56	20,8±8,36	0,047
Achievement of target INR up to 14 day (% of pts)	75,3	21,8	0,0001
TTR>60% during first month of therapy (% of pts)	64,0	38,2	0,04

There were total of 5 major bleedings with 4 occurred during first month.All of them were observed in Gr2 pts (p=0,06). The frequency of minor bleedings in Gr1 and Gr 2 was similar: 19,1% and 16,4%. During first month of W therapy the frequency of all bleeding and episodes of INR fluctuation >4,0 was significantly higher in Gr2 pts: 13,5% vs 42,7%, p=0,0046. **Conclusion:** In Russian population the combinations of CYP2C9*3 or *2/*2 with VKORC1 AA polymorphisms were observed in 12,8% pts. Genotyping reduced time to target INR; increased % of pts with TTR>60% during first month and decreased the frequency of all bleedings and episodes of INR fluctuation >4,0 during first month of W therapy.

Conflict of interest

PHARMACOTHERAPY

STATIN THERAPY IN WOMEN - FROM CONTROVERSY TO CONSENSUS? A SYSTEMATIC REVIEW AND META-ANALYSIS

J.A. Batty[1], *A.S. Hall*[2], *A.J. Balmforth*[2]
[1]*School of Medicine, University of Leeds, Leeds, United Kingdom*
[2]*Leeds Institute of Genetics Health and Therapeutics, University of Leeds, Leeds, United Kingdom*

Background
Despite substantial evidence demonstrating the efficacy of statins in the primary and secondary prevention of cardiovascular disease (CVD) in men, the risk-benefit profile for women remains poorly characterised.

Objectives
To systematically assess the gender-specific efficacy and adverse effect profile of statins in women.

Search Strategy
The Cochrane Central Register of Controlled Trials (CENTRAL; Issue 10, 2012), Medline (1946-2013), Embase (1947-2013), Web of Science (1980-2013) and ClinicalTrials.gov were queried for relevant studies. Reference lists of articles, including reviews and meta-analyses, were checked.

Selection Criteria
Randomised controlled trials of drugs of the statin class, with ≥100 adult participants, including women, followed up for ≥1 year.

Data Collection and Analysis
Studies were systematically selected for inclusion and appropriate data extracted. Primary outcome measures included incident CVD (fatal/non-fatal myocardial infarction and stroke) and all-cause mortality. Secondary outcomes included frequency of adverse events, serum total cholesterol (TC) and low-/high-density lipoprotein sub-fractions; (L/HDL-C). Odds ratios (ORs) and 95% confidence intervals (95%CIs) were calculated using the Mantel–Haenszel method.

Results
24 randomised controlled trials were comprehensively reviewed. 8 (n=26,013) recruited populations with a significant 10-year CVD risk profile; the remaining 16 (n=14,175) recruited patients with clinically-established CVD (e.g. previous myocardial infarction or stroke). Reductions in TC/LDL-C in statin-treated women translated into significantly reduced CVD endpoints in both primary (OR 0.88, 95%CI: 0.80-0.98) and secondary prevention (0.83, 0.78-0.88), but without reductions in all-cause mortality,

Conclusions
Statins are a safe and efficacious intervention for the prevention of cardiovascular events in women.

No conflict of interest

ATHEROSCLEROSIS UPDATE: PATHOPHYSIOLOGY AND CLINICAL IMPLICATIONS

Atherosclerosis and aging

M. Bennett[1], J. Wang[1], E. Yu[1], K. Gray[1], I. Gorenne[1]
[1]Division of Cardiovascular Medicine, University of Cambridge, Cambridge, United Kingdom

Atherosclerosis is classed as a disease of aging, such that increasing age is an independent risk factor for the development of atherosclerosis. Atherosclerosis is also associated with premature biological aging, as atherosclerotic plaques show evidence of cellular senescence characterised by reduced cell proliferation, irreversible growth arrest and apoptosis, elevated DNA damage, epigenetic modifications, and telomere shortening and dysfunction. Not only is cellular senescence associated with atherosclerosis, there is growing evidence that cellular senescence promotes atherosclerosis. Our recent work has provided evidence for cellular senescence in atherosclerosis, investigated the mechanisms underlying cellular senescence including reactive oxygen species, replication exhaustion and DNA damage, the functional consequences of vascular cell senescence, and the possibility that preventing accelerated cellular senescence is a therapeutic target in atherosclerosis.

No conflict of interest

ATHEROSCLEROSIS UPDATE: PATHOPHYSIOLOGY AND CLINICAL IMPLICATIONS

A novel haemodynamic model of plaque instability in mice that truly reflects the endstage of human atherosclerosis

K. Peter[1]
[1]*Baker IDI Heart & Diabetes Institute, Melbourne, Australia*

***Objective*:** The high morbidity/mortality of atherosclerosis is typically precipitated by plaque rupture and consequent thrombosis. However, research on underlying mechanisms and therapeutic approaches is limited by the lack of animal models that reproduce plaque instability observed in humans. Using flow measurements and computational fluid dynamics we developed and utilized a mouse model of plaque rupture that reflects the end stage of human atherosclerosis.

***Methods and Results*:** We applied a tandem stenosis to the carotid artery of ApoE-/- mice on high fat diet. At 7 weeks postoperatively, we observed intraplaque hemorrhage in ~50% of mice, as well as disruption of fibrous caps, intraluminal thrombosis, neovascularization and further characteristics typically seen in human unstable plaques. Administration of atorvastatin was associated with plaque stabilization and down regulation of MCP-1 and ubiquitin. Microarray profiling of mRNA and microRNA and in particular its combined analysis demonstrated major differences in the hierarchical clustering of genes and microRNAs between non-atherosclerotic arteries, stable and unstable plaques and allows the identification of distinct genes/ microRNAs, potentially representing novel therapeutic targets for plaque stabilization. The feasibility of the described animal model as a discovery tool was established in a pilot approach,identifying ADAMTS4 and miR-322 as potential pathogenic factors of plaque instability in mice and indeed ADAMTS4 as well as miR-322 have been localized in human plaques as well.

***Conclusions*:** Using combined analysis of mRNA and miRs several miRs could be identified which play a potential central pathophysiological role and are potential therapeutic targets. Conclusions: The newly described mouse model reflects human atherosclerotic plaque instability/rupture and represents a unique discovery tool towards the development and testing of therapeutic strategies aimed at preventing plaque rupture. In defining genes and microRNAs that can be linked to plaque instability this model allows a molecular dissection of the pathophysiology ultimately causing thrombosis and myocardial infarction..

No conflict of interest

ATHEROSCLEROSIS UPDATE: PATHOPHYSIOLOGY AND CLINICAL IMPLICATIONS

The role of oxidative stress in atherosclerosis

N.R. Madamanchi[1], A.E. Vendrov[1], M.S. Runge[1]
[1]McAllister Heart Institute Department of Medicine, University of North Carolina, Chapel Hill NC, USA

Background

Oxidative stress and vascular inflammation are implicated in higher incidence of cardiovascular disease (CVD), in conditions predisposing to accelerated atherosclerosis and with aging. Our investigations into NADPH oxidases relevant to CVD have focused on two subunits in vascular smooth muscle cells (VSMCs). NoxA1 is expressed preferentially in VSMCs in the vasculature. Nox4 is broadly expressed, which localizes to mitochondria causing mitochondrial oxidative stress.

Methods and Results

Animal studies were conducted using young (4 months) and aged (16 months) mice in ApoE$^{-/-}$ background. To assess the role of NoxA1, atherosclerosis was quantified in ApoE$^{-/-}$ and ApoE$^{-/-}$/NoxA1$^{-/-}$ mice on Western diet. NoxA1 deletion markedly diminished atherosclerosis (by 50%), confirming our earlier data that NoxA1$^{-/-}$ VSMCs were slower-growing whereas NoxA1-overexpressing VSMCs grew more rapidly than wild-type cells. Assessment of aging effects showed that aged ApoE$^{-/-}$/p47phox$^{-/-}$ mice (deficient in Nox1/2 activity) had increased atherosclerotic lesion area, aortic stiffness, and systolic dysfunction compared with their younger cohorts. Cellular and mitochondrial ROS levels were significantly higher in the aortic walls of aged ApoE$^{-/-}$ and ApoE$^{-/-}$/p47phox$^{-/-}$ and in VSMCs from aged wild-type and p47phox$^{-/-}$ mice. In VSMCs from aged mice, treatment with MitoTEMPO reversed these age-related changes as did suppression of Nox4 expression using shRNA. Increased mitochondrial ROS levels were correlated with enhanced mitochondrial Nox4 levels in aortic VSMCs from aged subjects and increase in Nox4 expression in carotid arteries with atherosclerotic lesion severity.

Conclusions

These data suggest that NoxA1 and Nox4 are two important VSMC NADPH oxidase subunits and, hence, may be potential targets for therapeutic intervention.

No conflict of interest

ATHEROSCLEROSIS UPDATE: PATHOPHYSIOLOGY AND CLINICAL IMPLICATIONS

Molecular imaging of human atherothrombotic disease

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ATHEROSCLEROSIS UPDATE: PATHOPHYSIOLOGY AND CLINICAL IMPLICATIONS

The influence of shear stress in the generation and destabilization of vulnerable plaques

J.J. Wentzel[1], F.J.H. Gijsen[1], P.W. Serruys[2], A.F.W. van der Steen[1]
[1]Biomedical Engineering, ErasmusMC, Rotterdam, Netherlands
[2]Interventional Cardiology, ErasmusMC, Rotterdam, Netherlands

Rupture of a vulnerable coronary atherosclerotic plaque is responsible for the majority of acute coronary events, which are the leading cause of morbidity and mortality in the western world.
Atherosclerotic plaques form at low shear stress regions, whereas moderate/physiologic and high shear stress regions are generally protected. Shear stress controlled compensatory outward remodeling plays an important role in preserving lumen dimensions during plaque progression, but when the expansive remodeling becomes excessive the low shear stress further promotes inflammation and lipid influx into the vessel wall, further destabilizing the plaque and potentially leading to an acute coronary syndrome.
Advanced plaques which start to encroach into the lumen experience high shear stress at their most stenotic region. At these locations often ulcerations are observed. Evidence is increasing for a role of high shear stress in plaque destabilization. The talk discusses the role of shear stress from early atherogenesis to early plaque formation, plaque progression to advanced high-risk stenotic or non-stenotic plaque and plaque destabilization. Current developments in technology to characterize local shear stress and plaque composition in-vivo may provide a rationale for innovative diagnostic and therapeutic strategies for coronary patients aiming to the prevention of clinical coronary syndromes.

No conflict of interest

ATHEROSCLEROSIS UPDATE: PATHOPHYSIOLOGY AND CLINICAL IMPLICATIONS

Inflammation and atherosclerosis

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ATHEROSCLEROSIS UPDATE: PATHOPHYSIOLOGY AND CLINICAL IMPLICATIONS

Novel therapeutic strategies for the treatment of atherosclerosis

R. Stouffer[1]
[1]*Cardiology, University of North Carolina, Chapel Hill, USA*

Atherosclerosis is multi-factorial disease that involves lipid-induced inflammation and complex interactions between various vascular cells, such as endothelial cells, smooth muscle cells, and macrophages. Lipid lowering therapy with statin medications remains the most widely used intervention to reduce the complications of atherosclerosis. The understanding of vascular biology has improved over time and many novel therapeutics are currently being developed. These include therapies to lower low-density lipoprotein cholesterol such as thyroid mimetics, antisense oligonucleotides targeted to human apolipoprotein B (apoB)-100 and monoclonal antibodies to proprotein convertase subtilisin/kexin type 9. Cholesteryl ester transfer protein (CETP)-inhibiting drugs effectively raise high-density lipoprotein cholesterol although clinical benefit has not been established. Torcetrapib was associated with increased mortality and cardiovascular events but dalcetrapib, evacetrapib and anacetrapib have not resulted in increased blood pressure or aldosterone levels. Clinical studies with dalcetripib have shown no benefit but studies utilizing the other drugs are oingoing. Novel anti-inflammatory approaches including chronic treatment with established anti-inflammatory agents (e.g. methotrexate) are also being studied.

No conflict of interest

TAVI AND VALVE INTERVENTIONS

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TAVI AND VALVE INTERVENTIONS

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TAVI AND VALVE INTERVENTIONS

TAVR: What have we learnt and where do we stand?

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TAVI AND VALVE INTERVENTIONS

TAVI in Japanese patients

S. Saito[1], O. On behalf of Kamakura Heart Team[1]
[1]Cardiology & Catheterization Laboratories, Shonan Kamakura General Hospital, Kamakura, Japan

Transcatheter aortic valve implantation (TAVI) is indicated as an alternative treatment modality to surgical aortic valve replacement for inoperable, high risk patients with severe aortic stenosis. Since the first percutaneous transcatheter aortic-valve implantation in humans in 2002, over 50,000 transcatheter aortic valves have been implanted worldwide. However, since this therapy is not yet approved for clinical use in Japan, little is known about its effectiveness and safety in Japanese people. According to Circ. J 2012; 76: 356-364, the mean BSA of surgical patients (?80 years old) undergoing a single aortic valve replacement was 1.44±0.16; which is relatively small compared to that of patients overseas. In this session we report the results of three TAVI cases performed in Japanese patients using the Corevalve system. All three patients were female and had symptomatic, severe aortic stenosis. Their overall condition put each at high-risk for conventional surgical AVR. Ethics committee approval was obtained to pursue private importation of the Corevalve system to treat their condition, and each patient provided oral and written informed consent prior to receiving the procedure. The ages of the patients were 86 yrs, 87yrs, and 83 yrs; and their BSA values were 1.43, 1.25, and 1.21; respectively. All three patients were successfully treated via the transfemoral approach.

Conflict of interest

TAVI AND VALVE INTERVENTIONS

Comprehensive percutaneous therapy in patients with severe aortic stenosis

R. Jaffe[1]
[1]*Cardiology, Carmel Medical Center, Haifa, Israel*

Coronary artery disease is common among patients with severe aortic stenosis (AS). Coronary bypass surgery and surgical valve replacement are the preferred therapies in patients with unprotected left main coronary (ULMCA) disease and severe AS, respectively. However, a sizable portion of AS patients have high surgical risk due to co-morbidities and are turned down by the surgeons. Trans-catheter aortic valve implantation (TAVI) is a less invasive treatment option for high-risk AS patients. A significant number of TAVI candidates also require coronary revascularization by percutaneous coronary intervention (PCI). Since AS patients have limited cardiovascular reserve, induction of myocardial ischemia during PCI poses unique procedural challenges. Comprehensive percutaneous therapy by combination of PCI and TAVI in complex patients with ULMCA disease and severe AS represents a new frontier for trans-catheter cardiac therapy. PCI to the ULMCA may be especially challenging in patients with severe AS since it involves induction of global myocardial ischemia during stent implantation. Conversely, presence of untreated ULMCA disease in AS patients undergoing TAVI may limit the ability of left ventricle to recover contractility following valve implantation. Additional challenges include potential interaction between the stent within the ostium of the left main coronary and the implanted valve as well as the potential need to access the coronaries in the future following valve implantation. There is limited data regarding the procedural safety of ULMCA PCI in patients with severe AS who are candidates for TAVI. Recent reports suggest that PCI may be performed safely in the presence of preserved left ventricular function.

No conflict of interest

TAVI AND VALVE INTERVENTIONS

TAVR for failed bioprosthetic surgical valves

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ACS MANAGEMENT UPDATE

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ACS MANAGEMENT UPDATE

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ACS MANAGEMENT UPDATE

What guidelines say about anti-thrombotics in ACS

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ACS MANAGEMENT UPDATE

How can we select suitable patients for potentially harmful antithrombotic intervention?

S. Goto[1]
[1]*Department of Medicine (Cardiology), Tokai University School of Medicine, Isehara, Japan*

Majority of acute coronary events, including myocardial infarction, unstable angina, and sudden cardiac death, is known to be induced by thrombotic occlusion of major coronary arterial branches. Antithrombotic therapy using antiplatelet and anticoagulant agents are effective in preventing such acute coronary events. On the other hand, risk of serious bleeding complication increases with the use of antithrombotic therapy. Evidence based approach was effective when the risk of thrombotic events was high in general. In 1980s, approximately 10% of patients experienced cardiovascular death within their 1 month hospitalization period. Once randomized clinical trial showed to reduce the risk of thrombotic in 25%, that results has strong impact in the medical practice. The 25% relative reduction shown by aspirin in case of acute myocardial infarction mean in-hospital mortality to be reduced from 10% within one month to 7.5%. Though the risk of bleeding events increased, aspirin become standard of care in patients with acute myocardial infarction. In 1990s, aspirin has already become standard of care. Clopidogrel in addition of aspirin was tested in acute coronary syndrome patients. Addition of clopidogrel could not demonstrate the mortality benefit with in one year follow up period. However, the incidence of CV death/MI/Stroke was significantly lower in clopigrel/aspirin group as compared to aspirin alone group. Clopidogrel in addition to aspirin become standard of care in patients with acute coronary syndrome in spite we recognized the increased risk of bleeding events in patients treated with aspirin/clopidogrel. In 21th Century, several additional studies have been conducted. However, the interpretation of these new trial become difficult. Both prasugrel and ticagrelor were tested in ACS patients treated by standard of care (meaning aspirin and clopidogrel). Both prasugrel and ticagrelor reduced the risk of CV death/stroke/MI. Unlike aspirin trial conducted in 1980s, those new therapy did not demonstrate homogeneous mortality benefit in whole population. Moreover, prasugrel increase the risk of fatal bleeding. We have to recognize that the new antithrombotic agents give benefit to some of the patients, but harmful for others. The same is true for the anticoagulant. Both rivaroxaban and apixaban reduced the risk of CV events, but apixan trial was stopped early due excess of bleeding. Rivaroxaban trial was completed, but we have to recognize some get benefit (reduced CV events), but some get harm (increased bleeding). From now on, we have to consider “How can we select suitable patients for potentially harmful antithrombotic intervention?””

Conflict of interest

ACS MANAGEMENT UPDATE

The use of tenecteplase as a pharmaco-invasive approach in STEMI: data from STREAM

C. Fresco[1]
[1]*on behalf of the STREAM Steering Committee, Azienda Ospedaliero Universitaria di Udine, Udine, Italy*

The benefit of reperfusion therapy is time dependent. Pre-hospital fibrinolysis is the fastest reperfusion therapy available, and, when coupled with timely coronary angiography, provides a clinical outcome similar to that with primary percutaneous coronary intervention (PCI) early after acute ST-segment elevation myocardial infarction (STEMI).

In the STREAM Trial a pharmaco-invasive approach with weight and age adjusted tenecteplase, clopidogrel, and enoxaparin followed by coronary angiography performed 6 to 24 hours later when clinical signs of reperfusion were present, or immediately in case of failure, resulted in effective reperfusion in patients with early STEMI who could not undergo primary PCI within 1 hour after the first medical contact. The primary end point (a composite of death, shock, congestive heart failure, or reinfarction up to 30 days) occurred in 116 of 939 patients (12.4%) in the fibrinolysis group and in 135 of 943 patients (14.3%) in the primary PCI group (relative risk in the fibrinolysis group, 0.86; 95% confidence interval, 0.68 to 1.09; P = 0.21).
In addition, the safety profile of tenecteplase was greatly improved by halving the dose in patients older than 75 years. Furthermore, the pharmacoinvasive approach allowed physicians to safely postpone to a more convenient time coronary angiography in two thirds of the patients.

The STREAM Trial results represent a unique opportunity to redefine the role of prehospital fibrinolysis in the modern treatment of acute ST-segment elevation myocardial infarction.

Conflict of interest

ACS MANAGEMENT UPDATE

Variability in response to the new anti-platelet drugs prasugrel and ticagrelor: is it a real problem with clinical significance?

E. Lev[1]
[1]*Cardiology, Rabin Medical Center, Petach Tikva, Israel*

With the increased use of the new anti-platelet medications – prasugrel and ticagrelor – in patients with acute coronary syndromes, new therapeutic issues and dilemmas have risen. Among these dilemmas are the management of bleeding complications or specific side effects attributed to the new drugs. Both bleeding complications and side effects pose a therapeutic challenge and raise important questions. How should the bleeding episode be managed (according to severity)? How should side effects be managed? Should the drug be discontinued? For how long? Should the patient be switched to an alternative anti-platelet drug, and if so how should the switching be carried out? These issues as well as others will be discussed taking into consideration, the frequency and presentation of bleeding complications and side effects, pharmcodynamic properties of the drugs (time to recovery of platelet function after drug discontinuation etc.) and pharmcodynamic studies of switching between anti-platelet drugs.

No conflict of interest

ACS MANAGEMENT UPDATE

STEMI systems of care

M. Tubaro[1]
[1]*Cardiovascular Department, San Filippo Neri Hospital - Roma, Rome, Italy*

STEMI systems of care are the cornerstone of the modern treatment of STEMI patients: they are based on networks among medical and cardiological institutions of different technogical levels, connected by an effective emergency medical service. They have a key-role in providing an equitable access to the most effective care to the vast majority of the STEMI patients.

Primary aim of the STEMI networks is to deliver reperfusion treatment to the greatest number of patients in the shortest time. There are two transfer models: the hub-and-spoke transfer system and the STEMI receiving centre organization. The purpose is to decrease the door-to-balloon interval, through a comprehensive strategy that includes the registration and transmission of pre-hospital ECG, activation of the cath-lab directly from the field, the presence of an attending cardiologist on site, a direct transportation of the patients from the field to the cath lab, bypassing both the Emergency Department and the ICCU. Administration of fibrinolytic therapy in the pre-hospital phase is mandatory in case of long transportation times, when the primary PCI can not be delivered within a proper time interval; anyway, the patient should be immediately transferred to a primary PCI-capable centre for rescue PCI or routine coronary angiography. The presence of a physician in the ambulance can be of some advantage, but is not mandatory, provided that paramedics and nurses have been properly trained and possible connected with a cardiological centre by telemedicine tools. The pre-hospital administration of antiplatelet agents (aspirin, P2Y12 receptor blockers, Gp IIb/IIIa inhibitors) as well as of anticoagulants is still a matter of debate.

No conflict of interest

ACS MANAGEMENT UPDATE

Changes in management and mortality of STEMI 2000-2010: The Israel nationwide ACSIS registry and database

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ISCHEMIA AND REPERFUSION

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ISCHEMIA AND REPERFUSION

A novel mitochondria-associated cell death pathway activated by myocardial ischemia/reperfusion

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ISCHEMIA AND REPERFUSION

MicroRNA and cardioprotection

R.C. Kukreja[1]
[1]*Pauley Heart Center Division of Cardiology, Virginia Commonwealth University, Richmond, USA*

MicroRNAs (miRNAs) have emerged as a novel class of endogenous, small, non-coding RNAs that negatively regulate gene expression via degradation or translational inhibition of their target mRNAs. In the heart, miRNAs have been involved in several clinical scenarios including ischemia/reperfusion and preconditioning suggesting that regulation of their function could be used as a novel cardioprotective strategy. In particular, miRNA-1, miRNA-21, miRNA-24, miRNA-29, miRNA-92a, miRNA-126, miRNA-133, miRNA-320, miRNA-199a, miRNA-208 and miRNA-195 have been shown to be regulated after myocardial infarction. Following ischemic preconditioning (IPC), we observed significant increase in miRNA-1, miRNA-21and miRNA-24 in the heart. Treatment with the miRNAs derived from the hearts subjected to IPC protected the hearts against ischemia/reperfusion injury, as shown by a reduction of infarct size as compared with saline or non-IPC miRNA-treated control. This protective effect was abolished by treatment with the miRNA-21 inhibitor. In addition, one of the powerful pharmacological preconditioning agent, sildenafil (Viagra) also resulted in upregulation of miRNA-21 in the heart. Pretreatment of hearts with adenoviral vector encoding miR-21eraser prior to sildenafil preconditioning abolished the infarct limiting effect of sildenafil. These results suggest that miRNA-21 is one of important mediator of cardioprotection induced by IPC and sildenafil.

No conflict of interest

ISCHEMIA AND REPERFUSION

Aldose reductase & RAGE: Novel therapeutic adjuncts for cardioprotection

R. Ramasamy[1]
[1]*Medicine-Diabetes Research Program, New York University Langone Medical Center, New York, USA*

Cardiovascular diseases are major cause of morbidity and mortality in the western world. Studies by us and others have implicated increased flux via aldose reductase (AR) and receptor for advanced glycation end products (RAGE) as key players in mediating host of cardiovascular diseases. Preclinical data indicate that increased flux via AR and RAGE interactions with its ligands perpetuates increased injury after myocardial infarction, accelerates atherosclerotic lesion formation, and promotes restenosis via multiple biochemical and signaling mechanisms. Importantly, emerging studies indicate that flux via AR generates key ligand precursors for RAGE and that AR mediates in jury, in part, via RAGE dependent signaling mechanisms. Taken together, these considerations place AR and RAGE in the center of biochemical and molecular stresses that characterize the cardiovascular diseases. Stopping AR and RAGE dependent signaling may hold the key to interrupting cycles of cellular perturbation and tissue damage in cardiovascular diseases. Presentation will provide a compelling rationale for targeting AR and RAGE as novel therapeutic adjuncts for protection of ischemic myocardium.

No conflict of interest

ISCHEMIA AND REPERFUSION

Mitochondrial division/mitophagy Inhibitor (Mdivi-1) protects right ventricle from severe heart failure

S. Tyagi[1]
[1]*Physiology & Biophysics, University of Louisville, Louisville, USA*

Chronic heart failure is common form of cardiovascular disease and is a leading cause of morbidity and mortality worldwide. Sustained pressure-volume overload induces pathological cardiac abnormalities, linked to mitochondrial dysfunction during right ventricular failure (RVF). In this study we tested the hypothesis that whether the mitochondrial division inhibitor (Mdivi-1) mitigates oxidative stress and in turn reverses the RV dilatation and dysfunction that occurs with chronic RV pressure-volume overloaded. We subjected pulmonary artery constriction (PAC) for 4 weeks in three (3) strains of mice (C57, FVB, and C3H), each with increasing resistance to oxidative stress. After surgery each strain was treated with Mdivi-1 (50mg/kg/day) or the DMSO vehicle. After PAC, mice developed increased cardiac mass, lower wall thickness, more oxidative stress and mitochondrial dysfunction. The Mdivi-1 treatment reversed RV dilatation and fibrosis, lowered oxidative stress and improved chamber function. Treatment also abolished the PAC-induced increase in LC3-A/B and p62 levels that was associated with PAC-induced increases in blood flow velocity (BFV). We conclude that Mdivi-1 treatment results in protection of RVF by mitigating mitophagy during pulmonary arterial hypertension. We suggest that inhibition of mitochondrial fission during RV dysfunction results in amelioration of RVF and this is accomplished by inhibiting abnormal autophagy/mitophagy and fibrosis during pulmonary arterial hypertension (PAH).

No conflict of interest

ISCHEMIA AND REPERFUSION

Molecular regulators of cell death pathways

L. Kirshenbaum[1], A. Biala[1], Y. Wang[1], R. Dhingra[1], H. Gang[1]
[1]Physiology, Institute of Cardiovascular Sciences, Winnipeg, Canada

Alternative gene splicing provides a versatile mechanism by which cells generate proteins with different or even antagonistic properties. Previously we determined the hypoxia-inducible protein Bnip3 is integral component of the mitochondrial death pathway that can signal apoptosis and autophagy but the precise mechanisms that differentially regulates these divergent processes remains cryptic. Herein, we provide novel evidence that inclusion or skipping of exon3 of Bnip3 mRNA by alternative splicing generates proteins with distinct and opposing actions on autophagy and cell survival. Metabolic stress imposed by hypoxia or nutrient deprivation resulted in the synthesis of two Bnip3 mRNA isoforms in post-natal ventricular myocytes in vitro and in vivo. Notably, one Bnip3 mRNA comprised of exons 1 through exon 6 encoded a protein of 26kDa, while a second mRNA generated by the fusion of exon2 and exon4 encoded a truncated Bnip3 protein of 8.2kDa. Sequence analysis revealed the truncated isoform encodes a conserved C-terminus domain that exclusively targets Bnip3 to the endoplasmic reticulum and not mitochondrion. While the 26kDa Bnip3 induced mitochondrial perturbations and autophagy, the spliced variant suppressed Bnip3- induced mitochondrial defects and autophagy. Furthermore, genetic knock-down or mutations within the C-terminus of the spliced variant defective for ER targeting sensitized cardiac myocytes to mitochondrial ROS production and death. To our knowledge our data provide the first direct evidence for a novel survival mechanism whereby the metabolic status of the cell programs autophagy or apoptosis by preferentially targeting Bnip3 isoforms to mitochondria or ER during metabolic stress.

No conflict of interest

NEW DIAGNOSTIC AND IMAGING TECHNIQUES

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NEW DIAGNOSTIC AND IMAGING TECHNIQUES

Target heart rate is not a valid endpoint for diagnostic exercise treadmill testing

F.J.T. Wackers[1]
[1]*Cardiology/Diagnostic Radiology, Yale University School of Medicine, New Haven Conn, USA*

Target heart rate is not a valid endpoint for diagnostic exercise treadmill testing

Background. Exercise testing should be symptom-limited. Nevertheless, 40 % of clinical laboratories applying for ICANL accreditation use 85% of maximal age-predicted heart rate (MPHR) as the primary exercise endpoint. We hypothesized that this approach importantly may underestimate exercise capacity and inducible ischemia.

Methods. Two patient cohorts were studied. 1.A prospective registry of patients referred for exercise testing. 2. A retrospective cohort of patients with positive exercise ECG.

Results. Of 306 registry patients, 211 (69%) continued exercising after reaching 85% MPHR to maximal HR of 101 ± 7% of MPHR. Forty-two patients (14%) stopped < 1 min after achieving 85% MPHR; 53 (17%) did not achieve 85% MPHR. More women (75%) than men (64%) achieved > 85% MPHR (p= 0.02). Of 300 patients with positive ECG, 232 patients (77%) exercised to > 85% MPHR. At 85% MPHR 144 patients (62%) had positive ECG (1.2 ± 0.7 mm ST-depression) compared to 232 patients (100%) at peak exercise (2.3 ± 0.9 mm ST-depression, p<0.001). Mean workload at 85% MPHR was 7.3±2.4 METs compared to 10.6±2.8 METs at peak exercise (p<0.001).

Conclusion. Achievement of 85% MPHR is not a valid diagnostic or functional exercise endpoint because it significantly underestimates exercise capacity and inducible ischemia.

No conflict of interest

NEW DIAGNOSTIC AND IMAGING TECHNIQUES

Speckle tracking echocardiography for the assessment of acute coronary syndromes

Z. Vered[1]
[1]*Department of Cardiology, Assaf Harofeh Medical Center, Zerifin, Israel*

Speckle tracking technique has recently been a major focus of research in the field of echocardiography. Since the first publications in 2004, the technique has developed into a real-time quantitative automatic software capable of measuring strain and strain rate, and more recently systolic and diastolic LV twist, rotation and torsion, as a measure of myocardial contraction and relaxation. We and others have shown that the technique is capable of differentiating between normal subjects and patients post myocardial infarction and correlates well with left ventricular ejection fraction. Recent research has focused on the accurate diagnosis of acute ischemia/reperfusion and also on myocardial viability. In studies with rats subjected to acute MI followed by reperfusion analysis of the LV in 3 layers of strain was shown to be advantageous in differentiating sub-endocardial as opposed to transmural global strain in these situations.

In a most recent study, in collaboration with senior research team at the Technion 10 pigs were subjected to balloon occlusion of the LAD for 90 minutes followed by reperfusion. Serial echocardiographic studies were performed before occlusion, immediately after and then at 24 hours, 30 and 60 days post reperfusion. Detailed histologigal analysis of the LV was performed. Time-to peak circumferential strain analysis after reperfusion could differentiate between stunned (areas of hypocontraction improving later) and infracted myocardium (areas with significant scar formation on pathology). Both circumferential and radial strain were able to detect acute ischemia during occlusion. Detailed results of this study will be shown.

3D/4D analysis of strain/strain rate and the implementation of these techniques into standard stress echocardiography will no doubt further enhance the possibility to better detect acute ischemia during these procedures.

No conflict of interest

NEW DIAGNOSTIC AND IMAGING TECHNIQUES

Coronary CTA: clinical update and unusual cases

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NEW DIAGNOSTIC AND IMAGING TECHNIQUES

Measurement of coronary artery calcification: does it contribute to cardiovascular risk assessment in high risk asymptomatic patients?

J. Shemesh[1]
[1]*The Grace Balas Cardiac Research Unit, Sheba medical center, Ramat Gan, Israel*

The contribution of coronary artery calcification (CAC) measurement to CV risk stratification has been consistently demonstrated. Compared to other humoral and clinical risk factors, CAC is the best predictor of CV events in asymptomatic but its relevance to high risk populations is not clear.

Current guidelines categorize diabetic patients into the highest CV risk and recommend intensive medical treatment. Elderly, smokers, and hypertensives are also at high CV and mortality risk. A substantial number of them are thus exposed to the side effects of the antihypertensive, anti hyperlipemic and antihyperglicemic medications. CAC measuring has been suggested to reclassify these populations. The current knowledge on the incremental prognostic vale of CAC score in these patiens can be summerized as follow:

- As much as one third of all diabetic patients do not have CAC and vave a very low risk to develop CV events similar to the non diabetics without CAC.
- Smokers may benefit from a low dose chest CT for the combined screening of early lung cancer detection and CV risk stratification using a single scan.
- Hypertensive patients at all stages as well as hypertensive-diabetics can be re-stratified by measuring CAC score.
- The absence of CAC in all these patients can identify a sub-group of patients that may be treated less intensively.

Despite the well documented prognostic value of CAC score in these high risk patients, further evidence are needed to prove that treatment intensity based on the CAC score, will improve their outcome above and beyond the current treatment categorization.

No conflict of interest

NEW DIAGNOSTIC AND IMAGING TECHNIQUES

Non-contrast cardiac MRI for the diagnosis of coronary artery disease

J. Zheng[1]
[1]*Mallinckrodt Instititue of Radiology, Washington University in Saint Louis, Saint Louis Missouri, USA*

The renal insufficiency, or renal failure, is a worldwide public health problem., More than 20 million population, aged 20 years or older in the United States have chronic kidney disease (CKD), one type of renal insufficiency. CKD is usually an irreversible and progressive disease and can lead to kidney failure. However, most patients with CKD actually die mainly from coronary artery disease, rather than progress to kidney failure. Therefore, early diagnosis of coronary artery disease in patients with CKD will help to stratify the risk factors for developing future cardiac events, or determine surgical risk and survival rate for renal transplant patients.

For the diagnosis of coronary artery disease, patients usually undergo contrast-enhanced x-ray or CT angiography with iodinated contrast agents. To detect myocardial ischemia and viability, cardiac MRI often involves first-pass perfusion imaging and contrast delayed enhancement with the administration of gadolinium-based contrast agents. However, patients with renal insufficiency are at risk of developing contrast induced nephrotoxicity with an iodinated contrast agent or at risk of nephrogenic systemic fibrosis with a gadolinium based MRI contrast agent. An alternative method is to apply non-contrast MRI techniques for patients with renal insufficiency or liver problem. Unfortunately, non-contrast MRI methods still face significant challenges for routine clinical practice. In this presentation, technical aspect of each of non-contrast MRI methods for imaging coronary artery anatomy, myocardial perfusion, and myocardial viability will be critically reviewed. Studies from us and others will be included to show the promise of these methods for the diagnosis of coronary artery disease without sticking any needle.

No conflict of interest

NEW DIAGNOSTIC AND IMAGING TECHNIQUES

Cardiovascular and non-cardiovascular outcomes in asymptomatic type 2 diabetics 5 years after coronary CT angiography

D.A. Halon[1], T. Gaspar[1], M. Azencot[1], R. Rubinshtein[1], B.S. Lewis[1]
[1]Interventional Cardiology, Lady Davis Carmel Medical Center, Haifa, Israel

Background: Cardiac CT angiography stratifies cardiovascular outcomes in various patient populations.

Aims: To examine the relationship of cardiac and non-cardiac outcomes at medium term (5 yr) follow-up to baseline CT coronary arterial findings in an asymptomatic population with type 2 diabetes mellitus.

Methods: Prospective population based CT angiographic study in 719 asymptomatic type 2 diabetics (63.5±5.3 yrs, 48.1% men) who were followed for major cardiac and non-cardiac events over 4-6 years. Kaplan-Meir survival and event-free survival were estimated in relation to extent of coronary atheroma.

Findings: Diabetes was diagnosed 10.1±7.6 yrs prior to study entry, hemoglobin A1C was 7.5±1.5%, 13.9% were current smokers, 65.9% were taking aspirin, 70.9% statins and 23.5% were insulin treated. At baseline the calculated 10 yr risk (UKPDS) for a coronary heart disease event was 18.1±11.1%. Triple vessel coronary artery atheroma (vs 0-2 vessel atheroma) predicted total mortality (7.5% vs 1.6%), total mortality or myocardial infarction (MI) (11.6% vs 2.4%), cardiovascular (CV) death or MI (6.5% vs 1.1%) all $p<0.001$, and non-CV death (carcinoma)(5.1% vs 1.6%, $p=0.01$) but not incidence of newly diagnosed malignancy (9.5% vs 7.5%, $p=0.33$). Baseline serum levels of the inflammatory marker, C-reactive protein, correlated with non-CV deaths but not with CV death or MI.

Conclusions: Extent of coronary atheroma on cardiac CT angiography predicted: 1. Five year adverse cardiac events in an asymptomatic type 2 diabetic population and 2. Mortality from non-cardiovascular causes. Relationship of these findings to pro-inflammatory mechanisms should be further elucidated.

No conflict of interest

NEW DIAGNOSTIC AND IMAGING TECHNIQUES

PREVALENCE AND SEVERITY OF ASYMPTOMATIC CORONARY AND CAROTID ARTERY DISEASE IN PATIENTS WITH LOWER LIMBS ARTERIAL DISEASE

F. Marsico[1], D. Ruggiero[1], A. Parente[1], E. Pirozzi[1], F. Musella[1], F. Lo Iudice[1], G. Savarese[1], T. Losco[1], G. Giugliano[1], G. Rengo[1], S. Dellegrottaglie[1], D. Leosco[1], G. Esposito[1], B. Trimarco[1], P. Perrone Filardi[1]
[1]Advanced Biomedical Sciences, University of Naples Federico II, Naples, Italy

Objectives: Lower limbs arterial disease (LLAD) portends high risk of cardiovascular events. Yet, the prevalence of significant occult coronary artery (CAD) and cerebrovascular (CVD) disease in patients without CAD and CVD has not been widely investigated. The purpose of this study was to evaluate the prevalence and severity of CAD and CVD in patients with LLAD of the lower extremities.
Methods: From January 2008 through December 2011 we studied 200 consecutive patients admitted for symptomatic LLAD, with normal global and regional systolic function, no symptoms of angina or dyspnea. During hospital admission all patients underwent carotid Doppler study and invasive angiography.
Results: Significant CAD was observed in 110 of 200 (55%) patients. Fifty-eight (53%) patients with significant CAD showed either left main (n=7), 3 vessels (n=35) or proximal left anterior descending (n=16) CAD, corresponding to 29% of total cohort. CVD was detected in 86(43%) patients (69% with concomitant CAD), including 30(35%) with severe and 15(17%) with significant disease. In thirty-two (37%) patients with CVD either left main (n=4), 3 vessels (n=18) or proximal left anterior descending (n=10) CAD was observed. The percent of patients with left main, 3 vessel or proximal left anterior descending stenosis among those with CVD was significantly higher (37%; p=0.03) compared to those without CVD.
Conclusions: Severe asymptomatic CAD and CVD are quite prevalent in LLAD, and 29% of patients fulfill indications for coronary revascularization. Cost-effective strategies to detect occult CAD or CVD in LLAD patients need to be investigated in large multicenter studies.

No conflict of interest

BLOOD PRESSURE AND HYPERTENSION

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Treatment of hypertension with CAD: AHA guidelines

C. Rosendorff[1,2]
[1]*Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, USA*
[2]*James J. Peters VA Medical Center, Bronx, NY, USA*

Successive reports of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNP) have lowered the blood pressure targets for therapy. The latest, JNC 7, recommended in 2003 a goal of < 140/90 mm Hg, and <130/80 for patients with diabetes and chronic kidney disease. An American Heart Association Scientific Statement (2007) added to this; patients with coronary artery disease, coronary artery disease equivalents, or who are at high risk for developing coronary artery disease, should also have as a B.P. goal <130/80 mm Hg. The problem with a "lower is better" strategy is that a low diastolic B.P., if below the lower limit of coronary autoregulation, will impair myocardial perfusion. This may result in critical myocardial ischemia, especially in conditions of high myocardial oxygen demand, such as exercise and left ventricular hypertrophy, or when there is reduced myocardial oxygen supply as in established occlusive coronary artery disease. Another area of controversy is the choice of anti-hypertensive agents for the various manifestations of coronary artery disease, and, in particular, the evidence for the lack of efficacy of beta-blockers in the primary prevention of CAD.
These issues are addressed in the revision of the AHA Guidelines, now co-sponsored by the ACC and ASH, and due to be released this year. These will be presented and discussed.

No conflict of interest

BLOOD PRESSURE AND HYPERTENSION

What should be the optimal levels of blood pressure: does the J-curve phenomenon really exist?

M. Banach[1]
[1]*Department of Hypertension, Medical University of Lodz, Lodz, Poland*

The blood pressure (BP) J-curve debate started in 1979, and we still cannot definitively answer all the questions. However, available studies of antihypertensive treatment provide strong evidence for J-shaped relationships between both diastolic and systolic BP and main outcomes in the general population of hypertensive patients, as well as in high-risk populations, including subjects with coronary artery disease, diabetes mellitus, left ventricular hypertrophy, and elderly patients. However, further studies are still necessary in order to clarify this issue. This is connected to the fact that most available studies were observational, and randomized trials did not have or lost their statistical power and were inconclusive. Perhaps only the Systolic Blood Pressure Intervention Trial (SPRINT) and Optimal Blood Pressure and Cholesterol Targets for Preventing Recurrent Stroke in Hypertensives (ESH-CHL-SHOT) will be able to finally answer all the questions. According to the current state of knowledge, it seems reasonable to suggest lowering BP to values within the 130-139/80-85 mmHg range, possibly close to the lower values in this range (what has been also confirmed in the current ESH/ESC 2013 guidelines), in all hypertensive patients and to be very careful with further BP level reductions, especially in high-risk hypertensive patients.

No conflict of interest

BLOOD PRESSURE AND HYPERTENSION

Hypertension 2013

C. Erol[1]
[1]*Cardiology, Ankara UniversityFaculty of Medicine, Ankara, Turkey*

HYPERTENSION 2013

Hypertension is the leading global risk for mortality in the world.It affects nearly 30% of the European population.Awareness is the most important issue for Hypertension.Both the doctors and the patients must be aware of the importance of this risk factor.There should be an international and national policy for the prevention and the treatment of this risk factor,because this is a treatable factor.

In order to guide this global risk factor many societies and institutions launch guidelines in determined intervals.This year CHEP(Canadian Hypertension Education Program) and ESH/ESC Guidelines for the management of arterial hypertension have been launched.

The similarities and the differences in these guidelines,and the changes from previous ones,and the most important points that they focused on
will be discussed.

No conflict of interest

BLOOD PRESSURE AND HYPERTENSION

USE OF AMBULATORY BLOOD PRESSURE MONITOR (ABPM) FOR GUIDING CARDIAC PATIENT MANAGEMENT

Y. Charuzi[1], R.W. Gao[2], J. Mirocha[3]
[1]Cardiology, Cedars Sinai Medical Center, Los Angeles, USA
[2]Biology, University of Southern California, Los Angeles, USA
[3]Statistics, Cedars Sinai Medical Center, Los Angeles, USA

Twenty-four-hours ambulatory blood pressure monitoring has been a useful tool to assess variability in blood pressure beyond office checks or self-measurement. We decided to investigate the impact of ambulatory blood pressure monitoring on patient management. Our retrospective study included 250 studies on 164 patients over the span of over 15 years. The study sample was 60% male and 40% female and ranged from 18 to 89 years of age. The common indication for applying the ABPM test was uncertainty of blood pressure fluctuations.

In patients who had more than one test, the shortest span between tests was 7 months. Tests were classified as normal (exhibiting satisfactory distribution of blood pressure with minimal deviation), as abnormal high (over 50% of readings over 140 mmHg, as abnormal low (with any readings below 80), or partially abnormal (mixed with under 50% of abnormal readings either high or low). The results showed that 49% of tests were satisfactory, 30% were abnormally high, 3% were abnormally low, and 18% were partially abnormal. The clinical assessment depended upon test results. In 50% of the tests, the patient was reassured and advised to continue current treatment; in 13%, a change in medication timing was advised; in 9%, an increase in medication dosage was indicated; in 3%, a decrease in medication was recommended; in 21%, a new medication was added, and in 4%, a behavioural change was advised. In conclusion, twenty-four-hours ambulatory blood pressure monitoring was a very valuable tool in assessing uncertainties of blood pressure control.

No conflict of interest

BLOOD PRESSURE AND HYPERTENSION

Hypertension and acute myocardial infarction: an overview

R. Pedrinelli[1]
[1]*Dipartimento Cardio Toracico, Università di Pisa, Pisa, Italy*

1. History of hypertension is a frequent finding in patients with acute myocardial infarction (AMI) and its recurring association with female gender, diabetes, older age, less frequent smoking and more frequent vascular comorbidities composes a risk profile quite distinctive from the normotensive ischemic counterpart.

2. Antecedent hypertension associates with higher rates of death and morbid events both during the early and long-term course of acute myocardial infarction (AMI) particularly if complicated by left ventricular dysfunction and/or congestive heart failure. Renin-angiotensin-aldosterone system blockade, through either converting enzyme inhibition, angiotensin II receptor blockade or aldosterone antagonism, exerts particular benefits in that high risk hypertensive subgroup.

3. In contrast to the negative implications carried by antecedent hypertension, higher systolic pressure at the onset of chest pain associates with lower mortality within one year from coronary occlusion while increased blood pressure recorded after hemodynamic stabilization from the acute ischemic event bears inconsistent relationships with recurring coronary events in the long-term follow-up.

4. Whether antihypertensive treatment in post-AMI hypertensive patients prevents ischemic relapses is uncertain. As a matter of fact, excessive diastolic pressure drops may jeopardize coronary perfusion and predispose to new acute coronary events although the precise cause-effect mechanisms underlying this phenomenon need further evaluation.

No conflict of interest

BLOOD PRESSURE AND HYPERTENSION

THERAPEUTIC POTENTIAL OF NITRIC OXIDE DONORS IN THE PREVENTION AND TREATMENT OF ANGIOGENESIS-INHIBITOR-INDUCED HYPERTENSION.

P. Kruzliak[1], M. Novak[1], O.L.G.A. Pechanova[2], G. Kovacova[3]
[1]International Clinical Research Center Department of Cardiovascular Diseases, St Anne University Hospital in Brno, Brno, Czech Republic
[2]Institute of Normal and Pathological Physiology, Slovak Academy of Sciences, Bratislava, Slovakia
[3]5th. Department of Internal Medicine, University Hospital and Comenius University, Bratislava, Slovakia

Angiogenesis is critical to tumor growth as well as to metastases. This process is tightly regulated by pro- and anti-angiogenic growth factors and their receptors. Some of these factors are highly specific for the endothelium-e.g., vascular endothelial growth factor (VEGF). A variety of drugs that target VEGF or its receptors have been developed for the treatment of different tumor types and a number of new agents is expected to be introduced within the coming years. However, clinical experience has revealed that inhibition of VEGF induces several side effects including hypertension and renal and cardiac toxicity. Angiogenesis-inhibitor-induced hypertension represents “crux medicorum” as it is often pharmacoresistant to antihypertensive therapy. We consider two most important pathomechanisms in the development of hypertension induced by angiogenesis inhibitors. The first represents direct inhibition of NO production leading to reduced vasodilatation and the second consists in increased proliferation of vascular medial cells mediated by NO deficiency and is resulting in fixation of hypertension. Based on the results of experimental and clinical studies as well as on our clinical experience, we assume that NO donors could be successfully used not only for the treatment of developed angiogenesis-inhibitor-induced hypertension but also for preventive effects. We thoroughly documented three clinical cases of cancer patients with resistant hypertension who on receiving NO donor treatment achieved target blood pressure level and a good clinical status.

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No conflict of interest

BLOOD PRESSURE AND HYPERTENSION

DEFENSIVE COPING INDUCES SILENT ISCHEMIA EVENTS AND STRUCTURAL WALL ABNORMALITIES:THE SYMPATHETIC ACTIVITY AND AMBULATORY BLOOD PRESSURE IN AFRICANS STUDY.

L. Malan[1], M. Hamer[2], M.P. Schlaich[3], G.W. Lambert[3], M. Reimann[4], T. Ziemssen[4], J.C.N. De Geus[5], Y.K. Seedat[6], N.T. Malan[1]
[1]Hypertension in Africa Research Team (HART), North-West University, Potchefstroom, South Africa
[2]Department of Epidemiology and Public Health, University College of London, London, United Kingdom
[3]Neurovascular Hypertension & Kidney Disease and Human Neurotransmitters laboratories, Baker IDI Heart and Diabetes Institute, Melbourne, Australia
[4]Department of Neurology, Dresden University of Technology, Dresden, Germany
[5]Department of Biological Psychology, Vrije Universiteit, Amsterdam, Netherlands
[6]Renal Hypertension Unit Nelson Mandela School of Medicine, University of Kwa-Zulu Natal, Durban, South Africa

Background Defensive active coping (AC) responses (being-in-control) have been associated with vascular hyper-responsiveness in urban Africans. However, the association between AC responses, silent ischemia, and ECG derived left ventricular hypertrophy (LVH) responses are unknown.

Objectives and methods Associations between BP, silent ischemia and ECG Cornell product LVH were assessed in 161 African and Caucasian males with AC responses identified by the Coping Strategy Indicator. BP, ECG and silent ischemia data were obtained from 24h ambulatory monitoring. Beat-to-beat BP was continuously recorded during stress testing and fasting resting blood samples obtained for biochemical analyses.

Results Enhanced ß-adrenergic central cardiac responses were evident in AC Caucasians as opposed to a predomination of α-adrenergic vascular responses in AC Africans. AC African men displayed higher 24h BP and prevalence of silent ischemia events compared to the Caucasian men. Regression analyses revealed that ***α-adrenergic responses*** were associated with silent ischemic events, adjusted R^2 0.21 (ß: 1.07 (95% CI 0.29 to 1.85). ***Ischemic events*** but not blood pressure predicted LVH in AC Africans (adjusted R^2 0.12 (ß: 0.35 (95% CI 0.11 to 0.59). ROC analyses indicated a defensive coping pathway cut point predicting silent ischemia of 16 in Africans as opposed to 32 in Caucasians with sensitivity/specificity 100%/96%.

Conclusions A defensive coping pathway revealed disturbed vascular function with apparent dissociation between behavioral and physiological ß-adrenergic AC responses in Africans. AC vascular responsiveness facilitated silent ischemia events and structural LVH changes which potentially explain an increased risk for coronary artery disease and incident ischemic stroke in black Africans.

Conflict of interest

LIPIDS, LIPOPROTEINS AND ATHEROSCLEROSIS

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LIPIDS, LIPOPROTEINS AND ATHEROSCLEROSIS

MECHANISMS OF ENDOTHELIAL PROTECTION MEDIATED BY N-3 PUFAS CARRIED IN CHYLOMICRON REMNANTS

S. Latham[1], R. Purcell[1], K. Botham[1], C.P.D. Wheeler-Jones[1]
[1]Comparative Biomedical Sciences, Royal Veterinary College, London, United Kingdom

Emerging evidence links chylomicron remnants (CR) to endothelial dysfunction and inflammation but the molecular basis of their effects on vascular cells remains elusive. Here, we have used CR-like particles (CRLPs), our established CR model, containing triglycerides (TG) extracted from four dietary oils: fish, DHASCO (algal), corn and palm and compared their direct effects on human aortic endothelial cells (HAEC) ***in vitro***. Microarray analysis was used to characterize the HAEC transcriptional responses to CRLPs and this revealed differential gene expression profiles dependent upon CRLP fatty acid (FA) composition and was validated by qPCR. n-6 FA(corn) or saturated FA (palm) CRLPs induced expression of E-selectin to a greater extent than n-3 PUFA CRLPs (fish and DHASCO) whereas n-3-PUFA-containing CRLPs strongly increased heme-oxygenase-1 (HO-1) expression with markedly less induction evident in cells exposed to corn or palm CRLPs. Incorporation of probucol (antioxidant) into CRLPs abolished CRLP-induced ROS production in ECs and showed that the effects on HO-1 induction were dependent upon the oxidation state of the particles. Experiments using selective pharmacological inhibitors and specific siRNAs indicated that Nrf-2, PPARδ and $p38^{MAPK}$ co-operatively regulate CRLP-induced HO-1 induction. Induction of VCAM-1 expression in response to TNF-α was reduced by pre-exposure to CRLPs, with DHA-rich (DHASCO) CRLPs exerting the greatest inhibitory effect. Together, our data provide evidence that CRLPs elicit cytoprotective actions on human ECs through Nrf-2-, PPARδ- and $p38^{MAPK}$-dependent mechanisms, show these effects are TG composition- and oxidation-state dependent, and support the hypothesis that n-3 PUFA carried in TG-rich lipoproteins have anti-inflammatory actions.

No conflict of interest

LIPIDS, LIPOPROTEINS AND ATHEROSCLEROSIS

DEREGULATED APOPTOSIS PATHWAYS AND RESISTANCE TO APOPTOTIC DEATH CHARACTERISE CD4+CD28NULL T CELLS FROM PATIENTS WITH CORONARY ATHEROSCLEROSIS

I.E. Dumitriu[1], E. Kovalcsik[1], R. Antunes[1], J.C. Kaski[1]
[1]Cardiovascular Sciences, St George's University of London, London, United Kingdom

Aim: $CD4^{+}CD28^{null}$ T cells mediate plaque instability and recurrence of acute coronary events through inflammatory cytokines and lysis of vascular cells. Acute coronary syndrome (ACS) patients have higher numbers of $CD4^{+}CD28^{null}$ T cells compared to stable angina (SA) and healthy individuals. Why $CD4^{+}CD28^{null}$ T cells accumulate in ACS is unknown. We recently showed that costimulatory receptors OX40 and 4-1BB regulate the inflammatory and cytotoxic effects of $CD4^{+}CD28^{null}$ T cells in ACS. These receptors also regulate T cell apoptosis. Our aim was to investigate apoptosis pathways in $CD4^{+}CD28^{null}$ T cells to uncover mechanisms underlying their accumulation in ACS.

Methods: Levels of Fas, FasL, anti-apoptotic (Bcl-2, Bcl-xL) and pro-apoptotic (Bax, Bim) proteins and apoptosis sensitivity of $CD4^{+}CD28^{null}$ T cells in ACS and SA patients was measured using flow-cytometry.

Results: We found that in ACS, $CD4^{+}CD28^{null}$ T cells Fas levels are significantly reduced compared to conventional $CD4^{+}CD28^{+}$ T cells. The pro-apoptotic proteins Bim and Bax were also significantly decreased in $CD4^{+}CD28^{null}$ T cells. Interestingly, Bim and Bax were significantly lower on $CD4^{+}CD28^{null}$ T cells from ACS rather than SA patients. Additionally, $CD4^{+}CD28^{null}$ T cells from ACS patients were resistant to Fas-triggered and ceramide-induced apoptosis.

Conclusion: $CD4^{+}CD28^{null}$ T cells from ACS patients have defects in molecules that regulate apoptosis and are resistant to apoptotic cell death. Importantly, the defects in pro-apoptotic molecules Bim and Bax were more pronounced in ACS than SA patients. Targeting these defects could restore apoptosis sensitivity of $CD4^{+}CD28^{null}$ T cells and prevent their accumulation and harmful effects in ACS.

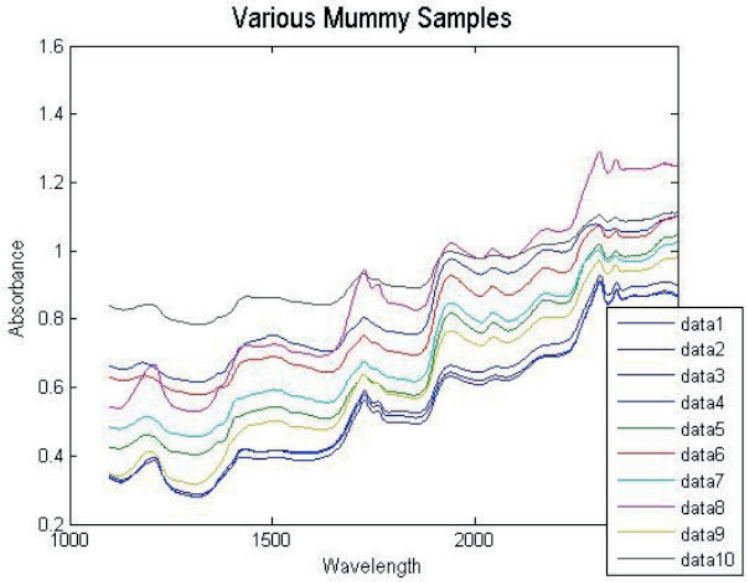
No conflict of interest

LIPIDS, LIPOPROTEINS AND ATHEROSCLEROSIS

HIGH PREVALENCE OF ATHEROSCLEROSIS IN ARTERIES OF ANCIENT MUMMIES DETERMINED BY NEAR INFRARED SPECTROSCOPY

M. Madjid[1], *K. Stutler*[2], *N. Fuenffinger*[2], *R. Lodder*[3]
[1]*Atherosclerosis Research, Texas Heart Institute, Houston, USA*
[2]*Dept. Biocehmistry, University of Kentucky, Lexington, USA*
[3]*Spheric, Spherix, Lexington, USA*

Previous studies using CT scan have demonstrated presence of calcification in vascular tissues of a fraction of ancient mummies. Calcified lesions generally present a later stage of atherosclerosis.
Methods: We used near infrared spectroscopy to determine the presence of molecular signature for cholesterol in ex vivo arterial samples from 5 ancient mummies. These vascular samples belonged to 35 to 55 year old men and women. Cause of death included pneumonia in 3 samples and unknown in one case. Three belonged to 2000 BC and one was from 350-1000 AD.
Results: We identified cholesterol deposition in arteries of all samples determined by increased signal in the 1700-2200 nanometer absorbance wavelengths, which is specific to atherosclerotic lesions. Figure illustrates the typical variability observed in the near-infrared region in blood vessels from mummies. Micro-CT study of these samples did not identify any calcification.



Conclusion: Near-infrared spectroscopy can detect deposition of cholesterol in arterial tissues of middle-aged mummies dying of non-cardiac causes. Unlike previous studies, our study demonstrates a higher prevalence of atherosclerotic lesions in ancient humans in absence of calcification.

No conflict of interest

LIPIDS, LIPOPROTEINS AND ATHEROSCLEROSIS

A COMBINATION OF SNPS IS ASSOCIATED WITH THE POSTPRANDIAL CHYLOMICRON TRIACYLGLYCEROL RESPONSE IN HEALTHY MALE ADULTS

C. Desmarchelier[1], J.C. Martin[1], R. Planells[1], M. Gastaldi[1], M. Nowicki[1], A. Goncalves[1], R. Valéro[1], D. Lairon[1], P. Borel[1]
[1]"Nutrition Obésité et Risque Thrombotique", UMR 1062 INSERM/1260 INRA/ Université d'Aix-Marseille, Marseille cedex 05, France

The postprandial chylomicron (CM) triacylglycerol (TG) response to dietary fat, which is positively associated with atherosclerosis and cardiovascular disease risk, displays a high inter-individual variability. This is assumed to be due, at least partly, to polymorphisms in genes involved in lipid metabolism. Existing studies have so far focused on single SNPs, resulting in a low explained variability. This study aimed to identify a combination of SNPs that could predict an elevated postprandial CM TG response.

Thirty-four healthy male volunteers were subjected to four standardized fat tolerance test meals and genotyped using whole-genome microarrays. Plasma CM TG were measured at regular interval times after each meal. The association of SNPs, in or near candidate genes (126 genes representing 6099 SNPs), with the high (> mean response + 1 SD) ***vs*** normal postprandial CM TG response (0 to 8 h postprandial AUC averaged for the four test meals) was assessed by partial least squares discriminant analysis, a multivariate statistical approach.

Data obtained allowed us to generate a validated significant model (P=2.6.10^{-7}) that included 28 SNPs in 14 genes (*ABCA1*, *APOB*, *BET1*, *CILP2*, *COBLL1*, *GALNT2*, *IRS1*, *LDLR*, *LIPC*, *MAP3K1*, *MC4R*, *PARK2*, *SLC27A6*, *ZNF664*) and explained 81% of the variance. Univariate analysis revealed several significant (P<0.05) differences in CM TG responses between subjects who bore different genotypes in the abovementioned SNPs.

Our results enable us to propose a genetic score that could suggest whether a subject belongs to the high responder phenotype and hence might be at increased risk of atherosclerosis and cardiovascular diseases.

No conflict of interest

LIPIDS, LIPOPROTEINS AND ATHEROSCLEROSIS

SYSTEMIC ACTIVE AND TOTAL MYELOPEROXIDASE LEVELS IN CORONARY ARTERY DISEASE

O. Gach[1], D. Serteyn[1], J. Magne[1], T. Franck[1], C. Brogneaux[1], V. Legrand[1]
[1]Cardiology, Chu Sart Tilman, Liege, Belgium

Backgound: Measurement of total Myeloperoxidase (MPO) by ELISA is considered as a marker of neutrophil activation but is not the true indicator of the degree of its activity.
In a dynamic pathology such as atherosclerosis, it may be important to measure the real active part of MPO because it represents the true witness of the oxidant potential of the enzyme.

Aim: To identify the relation between coronary artery disease identified by coronaro-angiography on measured serum total and active MPO levels and evaluate the correlation between these MPO levels and the presence of clinically defined unstable condition.

Methods: Prospective analyse of serum samples of patients before (within 30 min) coronaro-angiography. Total and active MPO concentrations were assessed by sandwich Elisa and SIEFED® method's respectively.

Results: Two hundred and twenty patients were included in this study (age: 66.1±10.7 years, 67% of male). Among these, 62% presented significant coronary artery disease (stenosis more than 60% at least in one épicardial coronary artery). Twenty four patients (11%) presented unstable coronary syndrome.

Mean active and total MPO in the general population were 50.1±63.5 and 147.6±223.3 $ng.mL^{-1}$ respectively. In comparison, mean active MPO was 47.1±47.9 $ng.mL^{-1}$ in stable patients and 75.1±135.2 $ng.mL^{-1}$ in unstable patients (p=0.04). Mean total MPO was 146.3±224.7 $ng.mL^{-1}$ in stable patients and 158.2±215.8 $ng.mL^{-}1$ in the unstable's one (p=0.8). There was a significant correlation between active MPO levels and instability (r=0.14, p=0.04) not present for total MPO levels (r=0.016, p=0.8).

Conclusion: We observed a correlation between active MPO and clinical instability while there was no correlation with total MPO. Our preliminary results suggest that this marker could be a powerful indicator of instability which could possess an important prognostic impact. This hypothesis requires an evaluation in wider population and during a prolonged follow-up.

No conflict of interest

LIPIDS, LIPOPROTEINS AND ATHEROSCLEROSIS

INFLAMMATION MOLECULES, APOLIPROTEINS AND EXTRACELLULAR MATRIX PROTEOGLYCANS IN A CORONARY ATHEROGENESIS MODEL: WHAT COMES FIRST?

S. Rocchiccioli[1], M. Puntoni[1], F. Viglione[1], S. Sbrana[1], A. Cecchettini[2], O. Parodi[1], M.G. Trivella[1], G. Pelosi[1]
[1]Istituto di Fisiologia Clinica, CNR, Pisa, Italy
[2]Dipartimento di Morfologia umana e Biologia applicata, University of Pisa, Pisa, Italy

The different pathophysiological hypotheses on coronary atherosclerosis initiation involve the same actors though in differently timed events. Inflammatory cells and mediators play a key role in atherosclerosis onset by leading to foam cells deposition and overexpression of extracellular matrix proteoglycans (ECM-PGs) enhances sub-endothelial lipoprotein trapping.
We evaluated the contribution of these factors to atherosclerotic lesion growth in high cholesterol diet (HC) experimental model of coronary artery disease. Farm pigs were fed either standard (CTRL, n. 6) or HC diet for 2 (HF, n. 6) and 4 months (HHF, n.6). Elisa assay of ICAM-1 and flow cytometry of its monocyte receptor CD18a were performed; SLA-DR, CD14 and CD16 monocyte receptors and plasma LDL, HDL and oxidized LDL were assessed. Histomorphometric indexes (intimal thickness, intima to media thickness ratio and lesional area) of coronary arteries were measured. Mass spectrometry-based proteomics analysis of released proteins from artery segments was performed.
Results show that baseline ICAM-1 and SLA-DR+ monocytes significantly correlate with atherosclerosis extent. LDL and oxidized LDL, ICAM-1 and its CD18a receptor, CD14low/CD16 high and SLA-DR+ subtypes positively correlate with end-diet histomorphometric indexes, while HDL level is negatively associated. ECM-PGs (biglycan and dermatan) and apolipoproteins AI and E are overexpressed in atherosclerotic segments and correlate with their concentration in blood.
Preexisting inflammatory/immunity factors are shown to be predictive markers of disease, circulating lipoproteins constitute the environmental predisposing elements, while ECM-PGs, detectable in blood, seem the most specific lesion-related molecules and could be considered potential biomarkers of atherosclerosis progression.

No conflict of interest

LIPIDS, LIPOPROTEINS AND ATHEROSCLEROSIS

NUCLEAR FACTOR-KAPPA BETA - A NOVEL MARKER MODULATING INFLAMMATION AND INSULIN RESISTANCE IN ISCHAEMIC HEART DISEASE

A. Suri[1], R. Singh[1], S. Tyagi[2], J. Bhattacharjee[3]
[1]Biochemistry, Lady Hardinge Medical College, New Delhi, India
[2]Cardiology, GB Pant Hospital, New Delhi, India
[3]Principal, Vardhaman Mahavir Medical College and Safdarjung Hospital, New Delhi, India

INTRODUCTION: Atherosclerotic progression results from micro-inflammation mediated by pro-inflammatory cytokines. Insulin resistance also contributes to atherosclerosis and is now regarded as an independent risk factor in its pathogenesis. Recent studies have implicated the role of NF-κB in atherogenesis by regulating genes involved in the inflammatory response and insulin sensitivity.

MATERIAL AND METHOD: 50 cases of angiographically proven ischaemic heart disease and 50 age and sex matched patients with no evidence of ischaemic heart disease on angiography were selected from G.B Pant Hospital, New Delhi, India. Serum levels of IL-6 and NF-κB were estimated by sandwich ELISA and serum level of insulin was estimated by CLIA in study group. HOMA-IR (fasting blood glucose (mg/dl) multiplied by fasting insulin (μIU/l)/405) was used for estimating insulin resistance.

RESULTS: Serum levels of IL-6, NF-κB, Insulin and HOMA-IR were significantly raised in cases. Upon correlation analysis, we observed that IL-6 has statistically significant correlation (Pearson's coefficient, r=0.196 and p=0.05) with NF-κB. Upon multivariate regression analysis, IL-6 had the strongest association (β=0.261, p=0.007) with severity of atherosclerosis. Upon binomial logistic regression analysis, NF-κB emerged as the best predictor of ischaemic heart disease (OD=16.43) followed by IL-6.

CONCLUSION: Higher IL-6 levels in cases suggests the role of smothering inflammation in atherosclerosis. The positive correlation between IL-6 and NF-κB confirms the role of NF-κB in IL-6 mediated signalling pathways. Our study throws light on the critical role of NF-κB in pathways of inflammation and insulin sensitivity (raised HOMA-IR) thereby promoting atherosclerosis.

No conflict of interest

LIPIDS, LIPOPROTEINS AND ATHEROSCLEROSIS

EFFICACY OF STATINS IN THE REDUCTION OF CARDIOVASCULAR ENDPOINTS AMONG PATIENTS WITH CKD AND THOSE ON HEMODIALYSIS : A META ANALYSIS

A. Domalanta[1]
[1]*internal medicinesection of Cardiology, University of Santo Tomas, Metro manila, Philippines*

The aim is to investigate efficacy of statin among patients with Chronic Kidney Disease as well those on hemodialysis in the reduction of coronary endpoints.

Five randomized, double-blind trials (18,507 patients) which evaluated if there exists a significant reduction of cardiovascular events or endpoints among patients with Chronic Kidney Disease. All the studies had the placebo group and a group subjected with statins. The primary outcomes in the five studies were occurrences of cardiovascular events, cardiac deaths, stroke, non fatal myocardial infarction, cerebrovascular events and all cause mortality. Heterogeneity of the trials was assesses using the Cochran Q Chi-square test, hence data were overviewed with random effects model. Efficacy of statins in reducing incidences of cardiovascular events was also further assessed only among patients with Chronic Kidney Disease who were undergoing maintenance hemodialysis

Compared with placebo, statins showed lower incidence of major cardiovascular, non fatal myocardial infarction and other coronary events.In terms of all-cause mortality. 4D (RR:0.956) ALERT (RR:0.789) TNT (RR:0.693) AURORA (RR:0.967) SHARP (RR:0.920).Three trials included in patients on hemodialysis.4D (2005), AURORA (2009) and SHARP (2011) reported less than 1 RR.Relative risk ratio of 0.954 suggests that patients subjected with statins are less likely to possess a cardiovascular disease, however this is not statistically significant at p-value = 0.254

Statins provide significant benefit among patients with CKD in the reduction of major cardiovascular events, non fatal myocardial infarction and cardiac deaths, but not significant for fatal or non fatal stroke, fatal or non fatal cerebrovascular events and all-cause mortality. Statins did not provide significant benefit in reduction of cardiovascular events among patients with Chronic kidney disease undergoing hemodialysis.

No conflict of interest

LIPIDS, LIPOPROTEINS AND ATHEROSCLEROSIS

META-ANALYSIS: THE EFFECT OF STATINS ON RENAL FUNCTION

Q. Geng[1], J.Y. Ren[1], S.F. Li[1], H. Chen[1]
[1]department of cardiology, Peking University People's Hospital, Beijing, China

Background:Statins can significantly improve the lipid profile and prevent cardiovascular events. But, beneficial effects of statins on renal function remain conflict.

Methods:Pubmed, the Cochrane Central Register of Controlled Trials, Web of knowledge and ClinicalTrials.gov website were searched to identify 39 randomized, controlled trials, involving 57,422 participants. The selected studies reported estimated glomerular filtration rate (eGFR), proteinuria and/or albuminuria during treatment with statins and control.

Results:Control group had significantly decreased eGFR as compared to statins group: the standardized mean difference (SMD) of eGFR in change-from-baseline was 0.05 (95% confidence interval [CI], 0.04 to 0.07; P<0.05) in patients with eGFR > 60 ml/min and 0.09 (95% CI, 0.01 to 0.17; P<0.05) in patients with eGFR 30 to 60 ml/min. In patients with urinary protein excretion of 30 to 300 mg/d, the reduction of proteinuria in statins group was greater than in control group (SMD, -1.12; 95% CI, -1.95 to -0.30; P<0.05). Similarly, in patients with urinary protein excretion more than 300 mg/d, the reduction of proteinuria in statins group was greater than in control group (SMD, -0.75; 95% CI, -1.37 to -0.13; P<0.05). However, there was no significant difference between statins and control group in patients with urinary protein excretion less than 30 mg/d. The change in eGFR did not reach statistical significance between atorvastatin and rosuvastatin groups.

Conclusions:Statin therapy seems to slow the rate of decline in eGFR in patients with stages 1-3 CKD and reduce pathologic proteinuria modestly.

No conflict of interest

ELECTROPHYSIOLOGY AND CARDIAC ARRHYTHMIAS

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ELECTROPHYSIOLOGY AND CARDIAC ARRHYTHMIAS

INCREASING SURVIVAL FROM VENTRICIULAR FIBRILLATION IN OUT-OF-HOSPITAL CARDIAC ARREST; EXPERIENCE WITH RAPID DEFIBRILLATION OVER 22 YEARS

R.D. White[1], D.G. Hankins[2], E.J. Atkinson[3]
[1]Anesthesiology/Internal Medicine/Emergency Medicine, Mayo Clinic, Rochester, USA
[2]Emergency Medicine, Mayo Clinic, Rochester, USA
[3]Biomedical Statistics and Informatics, Mayo Clinic, Rochester, USA

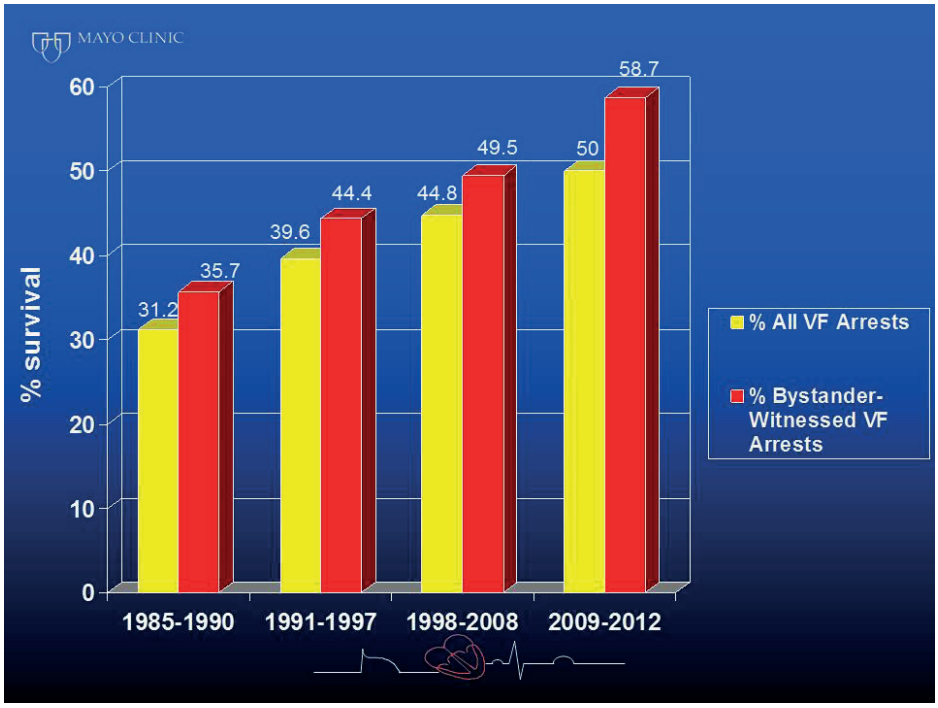
Aims: To observe outcomes from ventricular fibrillation (VF) out-of-hospital cardiac arrest (OHCA).

Methods: Calculation of survival rates for all patients in VF arrest from 1985-2012 in our location.

In the US average survival rate for VF arrest is 17% and in Europe it is 21%. In 1991 we initiated a community-wide rapid defibrillation program in which police officers were trained to use automated external defibrillators (AEDs). Police then responded along with paramedics. In 1998 fire-rescue personnel were added to the response. All three agencies were dispatched nearly simultaneously to assure rapid availability of defibrillation.

Results: Figure 1 depicts neurologically-intact survival of all patients in VF. The 1985-1990 period is the time before addition of police and fire-rescue. There was a significant linear increment in subsequent survival (p=0.005 for all VF arrests and p=0.006 for bystander-witnessed arrests, logistic regression). Therapeutic hypothermia (TH) was begun in 2006. Survival among patients receiving TH was 68% and 56% among those not receiving TH (p=0.275, chi-square test).

Conclusions: Coronary artery disease is the leading cause of sudden cardiac arrest. Our high survival is related to rapid defibrillation, regardless of which personnel arrive first. Population growth and expansion of coverage area are challenges to continuing high survival.



No conflict of interest

ELECTROPHYSIOLOGY AND CARDIAC ARRHYTHMIAS

PREDICTION MODEL FOR THE PRESENCE OR ABSENCE OF CARDIAC AUTONOMIC NEUROPATHY IN STAGE 4 CHRONIC KIDNEY DISEASE

M. Mylonopoulou[1], K. Katsaros[2], C. Papadopoulos[1], P. Mistylis[3], S. Antonopoulos[3]
[1]Dialysis Unit, Nephrolife Renal Dialysis Center, Athens, Greece
[2]Cardiology, Tzaneio General Hospital, Piraeus, Greece
[3]2nd Internal Medicine, Tzaneio General Hospital, Piraeus, Greece

INTRODUCTION AND AIMS: Cardiac autonomic neuropathy(CAN) is strongly associated with increased morbidity and mortality. Heart Rate Variability(HRV) is an established non-invasive evaluation method of CAN. Aim of our study was to extract the most important medical history, clinical and laboratory data and to correlate them with HRV parameters, in order to build a prediction model for the presence or absence of CAN in stage-4 chronic kidney disease(CKD) patients with or without type-2 diabetes mellitus(T2DM).

METHODS: 150 patients were enrolled: group A:50 stage4CKD patients with T2DM(M/F=12/13, mean age 67.9), group B:50 stage4CKD patients without T2DM(M/F=14/11, mean age 65.7), group C:50 T2DM patients without CKD(M/F=11/14, mean age 67.7). Medical history (6 parameters), clinical examination (7 parameters), laboratory testing (25 parameters) and 24-hoursECG-Holter monitoring were performed in all patients. We used multivariate factor analysis to extract the most significant variants among medical history, clinical and laboratory data, and the most significant HRV-parameters. A prediction model for the presence of CAN was reached using regression analysis of medical history, clinical and laboratory data over HRV-parameters.

RESULTS: The most statistically significant HRV parameter, representing sympathetic activity, was SDANN/5min. Regression analysis of all significant variants over SDANN/5min is demonstrated in Table1.

Table1.Regression analysis of variants over SDANN/5min

CKDstage4+T2DM	**CKDstage4**	**T2DM**
Age	Age	Age
Heart disease	BMI	Heart disease
Total cholesterol	Heart disease	Total cholesterol
HbA1c	Hct	HbA1c
High-sensitivityCRP	Total cholesterol	High-sensitivityCRP
NT-proBNP	WBC	NT-proBNP
	Albumin	

CONCLUSIONS: We can have a rough (though reliable) estimation of sympathetic activity, using this simple predictive model for the presence or absence of CAN in patients with stage 4CKD. Interestingly, CKD patients with T2DM display the same model with diabetics without CKD. Of course, those models do not intend to substitute Holter HRV studies in individual cases, but they offer a handy everyday-practice tool for the screening of CAN.

No conflict of interest

ELECTROPHYSIOLOGY AND CARDIAC ARRHYTHMIAS

PREDICTION OF ADVERSE ARRHYTHMIC CARDIAC EVENTS IN PATIENTS WITH A FIRST NON-COMPLICATED ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION. VALUE OF CARDIOVASCULAR MAGNETIC RESONANCE.

C. Bonanad[1], M. Izquierdo[1], F. Chaustre[1], C. Gómez[1], M.J. Forteza[1], P. López-Lereu[1], J.V. Monmeneu[1], F.J. Chorro[1], R. Ruiz[1], V. Bodi[1]

[1]Cardiology, Hospital Clinico Universitario de Valencia-INCLIVA, Valencia, Spain

Purpose. Outcome of ST-segment elevation myocardial infarction (STEMI) has dramatically improved since the routine use of reperfusion therapies. Over the last decade, cardiovascular magnetic resonance imaging (CMR) has emerged as the gold standard non-invasive imaging technique for an accurate evaluation of two key variables in the risk stratification of STEMI patients, namely ejection fraction (EF) and infarct size (IS). Prediction of adverse arrhythmic cardiac events (AACE) after STEMI is a challenge and reassessment in the current scenario is warranted.

Methods. Patients admitted for a first non-complicated STEMI to a university hospital were prospectively followed-up. Exclusion criteria were death, re-infarction, severe clinical instability during admission or any contraindications to CMR. The study group was made up of 450 patients with a first STEMI who underwent CMR 1 week after admission. Baseline clinical, ECG, biochemical and angiographic variables were recorded. CMR-derived EF and IS were quantified in a core lab. AACE included post-discharge sudden death, sustained ventricular tachycardia (VT) and/or ventricular fibrillation (VF) either spontaneous or recorded in implantable automatic defibrillator (IAD).

Results. During admission 436 patients (97%) were treated with reperfusion therapies. Of them, 188 were treated with primary angioplasty, 204 with thrombolysis (followed by routine angiography and angioplasty if needed) and 44 with delayed (>12h after chest pain onset) angioplasty. Within a 1-year median follow-up, 10 AACE (2.2%) were detected: 4 sudden deaths (0.9%), 4 spontaneous TV/FV (0.9%) and 2 TV/FV in AID (0.4%). In the whole study group AACE associated with more depressed EF (32±9 vs. 52±12%, p<0.001) and larger IS (45±16 vs. 21±15%, p<0.001). Both EF (area under the receiver operating characteristics curve, AUC=0.90) and IS (AUC=0.86) accurately predicted AACE (p<0.001 in both cases). On the basis of AUCs, EF <38% and IS >30% best predicted AACE. In a comprehensive multivariate analysis adjusted for clinical, ECG, biochemical, angiographic and CMR variables, the only independent predictor of AACE was EF (hazard ratio [95% confidence intervals]: 0.89 [0.84-0.94] per each 1% increase, p <0.001). In patients with depressed EF (<38%, n=69), 9 AACE (13%) took place; in this subset, IS (AUC=0.74, p=0.02) but not EF (AUC=0.43, p=0.6) predicted AACE. We created a combined score based on EF and IS. Overall, the AACE rate was (1/311, 0.3%) in patients with EF >38% and IS <30%, (0/70, 0%) in patients with EF >38% and IS >30% and (0/20, 0%) in patients with EF <38% and IS <30%. The vast majority of AACE (9/10, 90%) occurred in patients with simultaneous depressed EF and large IS (9/49, 18%).

Conclusions. In the era of generalized and timely reperfusion therapies, occurrence of AACE in patients with an in-hospital non-complicated first STEMI is extremely low. Depressed EF remains as the most powerful predictor. In this setting, assessment of CMR-derived IS allows for further optimization of AACE risk prediction and, probably, for IAD indication.

No conflict of interest

ELECTROPHYSIOLOGY AND CARDIAC ARRHYTHMIAS

ATRIAL FIBRILLATION:EVALUATION OF A LITTLE GROUP OF PATIENTS TREATED WITH DRONEDARONE

F. Orlando[1], D. Demarie[1], M. Imazio[1], S. Ferro[1], R. Belli[1]
[1]Cardiology, Ospedale Maria Vittoria, Torino, Italy

Background

Dronedarone is a potent blocker of multiple intracardiac ion channels with many electrophysiological properties in common with amiodarone.

Many clinical trials have shown that dronedarone, is effective in the prevention of AF relapses and the long-term maintenance of sinus rhythm.

Objiective

The aim of this report is evaluate the recurrence of atrial fibrillation in patients treated with dronedarone and its safety

Methods

From september 2010 to February 2013,78 patients with recurrence of atrial fibrillation were followed by our department. The mean age is 71,8.Forty two are male and 36 are females. All the patient were in class NHYA I-II with parossistic or persistent atrial fibrillation after satisfactory cardioversion. Patients with EF < 40% were excluded. The hepatic enzymatic control was performed after one., 3 and 6 months.The mean follow up is 19,2 months.

Results

In 38,4% atrial fibrillation recurs after 7,3 months of therapy

In one patient (1,2%) the drug was stopped because of increase of hepatic enzymes in another for renal failure and one died suddenly

Three patients (4,2%) had a lone atrial fibrillation, 75 (96%) had a structural heart disease: in 72 patients (96%) hypertension, in 43 (57,3%) previous myocardial infarction, and in 37 PTCA was performed. Six patients underwent to by pass (8%) and 3 (4.2%) had a valvular disease.

Conclusion

The vast majority of the patients had a structural heart disease. The drug was safety and well tolerated. The recurrence of atrial fibrillation is comparable with that of international literature..

No conflict of interest

ELECTROPHYSIOLOGY AND CARDIAC ARRHYTHMIAS

PREOPERATIVE HEMOGLOBIN A1C LEVEL AND INCIDENCE OF POST CORONARY ARTERY BYPASS GRAFTING SURGERY ATRIAL FIBRILLATION

T. Bhat[1], M. Shariff[1], M. Khan[1], J.M. Jr.[1], J. Nabagiez[1], J. Lafferty[1]
[1]Staten Island university hospital, Staten island, NY, USA

Objective: Diabetes mellitus are well recognized risk factors for the long term outcome after coronary bypass grafting.Recently studies have demonstrated association between preoperative hemoglobin A1c level and risk of postoperative AF. We aimed to investigate the association between preoperative hemoglobin A1C and incidence of AF after coronary bypass grafting surgery.

Methods: We conducted a retrospective review of our database. Our study included all patients who underwent CABG from January 2005 through September 2011.A total of 1356 were analyzed through group analysis with hemoglobin A1c level categorized in three tertiles; lower HbA1c < 5.6% Middle HbA1c 5.6-6.7 % and upper HbA1c ≥ 6.7%.

Results: AF occurred in 380 patients (28.0%) after surgery. The incidence of postoperative AF was 32.1% (51/159) in the lower tertile, 30.1% (209/695) in the middle tertile, and 23.9% (120/502) in the upper tertile (p for trend = 0.031). The unadjusted odds ratio (95% confidence interval) for the association between HbA1c and postoperative AF was 0.86 (0.79—0.93) per 1% increase and 0.41(0.45—0.98) for the upper versus the lower tertile. This association persisted after adjustment for the univariate predictors for the known risk factors 0.66 (0.78—0.92) per 1% increase 0.63 (0.43—0.95) for upper vs. lower tertile. The area under the receiver operator characteristic curve (95% confidence interval) for preoperative HbA1c as a predictor of postoperative AF was 0.639 (0.43—0.95) (p < 0.012), in addition to transfusions, congestive heart failure, and left main disease.

Conclusion: Higher preoperative hemoglobin A1c is independently related to decrease incidence of atrial fibrillation post CABG."

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ACUTE CORONARY SYNDROMES, MYOCARDIAL INFARCTION

EFFECT OF ISCHEMIC POSTCONDITIONING ON MICROVASCULAR OBSTRUCTION IN REPERFUSED MYOCARDIAL INFARCTION. RESULTS OF A RANDOMIZED STUDY IN PATIENTS AND EXPERIMENTAL MODEL.

C. Bonanad[1], J.M. Ruiz-Nodar[2], E. Feliu[2], G. Minana[1], J. Nunez[1], J. Sanchis[1], J.V. Monmeneu[1], M.P. López-Lereu[1], J. Martínez-Elvira[2], F.J. Chorro[1], V. Bodi[1]
[1]Cardiology, Hospital Clinico Universitario de Valencia-INCLIVA, Valencia, Spain
[2]Cardiology, Hospital General de Alicante, Valencia, Spain

Purpose. Ischemic postconditioning (PCON) appears as a potentially beneficial tool to complement primary angioplasty in ST-segment elevation myocardial infarction (STEMI). We evaluated the impact of PCON on microvascular obstruction (MVO) both in patients and in a highly controlled swine model.

Methods. In a multicenter study, 101 patients with a first STEMI were randomized to undergo primary angioplasty followed by PCON or primary angioplasty alone (non-PCON). MVO (lack of contrast uptake in the core of the hyperenhanced infarcted area) was quantified in late enhancement cardiac magnetic resonance imaging. In an anterior STEMI swine model based on a 90-min angioplasty balloon coronary occlusion and 3-day reperfusion, MVO was defined as a lack of thioflavin-S staining in the core of the infarcted area (with triphenyltetrazolium-chloride staining). The extent of MVO (% of left ventricular mass) was quantified in a core laboratory.

Results. In the clinical study, patients treated with (n=49) and without PCON (n=52) were well matched in terms of baseline characteristics and time to revascularization. MVO (> 1 segment in the 17 segments model) occurred in 12 (24%) PCON and in 18 (35%) non-PCON patients, p=0.3. PCON did not significantly reduce MVO (1.4±2.9% vs. 1.9±3.6% of LV mass, p=0.3). IS was similar in PCON and non-PCON patients (18±13 vs. 21±14% of LV mass, p=0.2). No significant differences were observed between PCON and non-PCON patients in LV volumes, ejection fraction or the extent of hemorrhage. In the swine model, MVO occurred in 4/6 (67%) PCON and in 4/6 (67%) non-PCON pigs, p=1. The extent of MVO (7.8±5.5% vs. 5.6±5.4% of LV mass, p=0.5) and IS (22±14 vs. 24±10% of LV mass, p=0.8) were not reduced in PCON compared with non-PCON pigs.

Conclusions. Ischemic postconditioning does not reduce microvascular obstruction in STEMI.

No conflict of interest

ACUTE CORONARY SYNDROMES, MYOCARDIAL INFARCTION

TEMPORAL TRENDS FOR MANAGEMENT AND OUTCOMES IN PATIENTS PRESENTING WITH THE FIRST ACUTE MYOCARDIAL INFARCTION: INSIGHTS FROM A 20- YEAR REGISTRY

E. Ahmed[1], J. Al Suwaidi[1], A. El-Menyar[2], H. AlBinAli[1], R. Singh[3], A.A. Gehani[1]
[1]cardiology, Hamad general hospital, Doha, Qatar
[2]clinical medicine & research, Hamad general hospital & Weill Cornell medical school, Doha, Qatar
[3]cardiology research, Hamad general hospital, Doha, Qatar

Introduction: Trends in the management and in-hospital outcomes of the first acute myocardial infarction (AMI) in Middle East are not well studied.

Aims: To define the temporal trend in the first AMI management and outcome and to determine the impact of health service used for the acute management during the last two decades in Qatar.

Methods: All patients hospitalized with first AMI between January 1991 and December 2010 were included. The collected data for each decade was analyzed according to age, gender, cardiovascular risk factors, in-hospital treatment and outcomes.

Results: A total of 10,915 patients were admitted with AMI; 6,406 (59%) were STEMI and 4,509 (41%) were NSTEMI. The overall mean age was 53±11.8 years and 88% of the patients were male. Comparing the two decades, the rates for hospitalization of AMI increased from 34% to 66%, for NSTEMI increased from 32% to 46% and the average length of hospital stays decreased from 6.4±3 to4.6±3.The use of antiplatelet agents increased from 84 % to 95%, β-blockers increased from 38% to 56 % and Angiotensin converting enzyme (ACE) inhibitors/ angiotensin receptor blockers (ARBs) increased from12 % to 36 % (all p for trend <0.001). The rates of PCI increased from 2.5%to14.6% and thrombolytic therapy decreased from 71% to 65% (all p for trend <0.001). The rate of in-hospital mortality decreased by 39% and short term outcomes were significantly declined. However, age-adjusted mortality rate was higher in female than in male patients in all age groups. The absolute mortality risk reduction rates were comparable in both genders. Higher utilization of ACE inhibitors/ ARBs, β-blockers and PCI were the main contributors to the improved in-hospital mortality and morbidity.

Conclusions: Over the study period, there was a significant increase in the hospitalization rate in patients presenting with AMI. Adherence to guidelines and evidence-based therapies has the potential to substantially reduce in-hospital mortality and outcomes.

No conflict of interest

ACUTE CORONARY SYNDROMES, MYOCARDIAL INFARCTION

ANGIOGRAPHIC AND CLINICAL CHARACTERISTICS OF TYPE 1 VERSUS TYPE 2 PERIOPERATIVE MYOCARDIAL INFARCTION

I. Hanson[1], J. Kahn[2], S. Dixon[1], J. Goldstein[1]
[1]Cardiovascular Medicine, Beaumont Hospital, Royal Oak, USA
[2]Cardiovascular Medicine, Detroit Medical Center, Detroit, USA

Objectives

The aim of this study was to analyze clinical and angiographic differences between the two etiologic subtypes of perioperative myocardial infarction (PMI).

Background

PMI is believed to occur by either reduced coronary blood flow attributable to acute plaque rupture and thrombosis (Type 1); or 2) Primary increase in oxygen demand in the setting of stable but stenotic lesions (Type 2). Incidence and mortality rates of PMI are substantial but angiographic and clinical features are not well characterized.

Methods

Consecutive patients with PMI were classified as “Type 1” or “Type 2” based on angiographic characteristics of culprit lesions. Clinical and angiographic characteristics of each subtype were compared using statistical analyses.

Results

Of the 54 patients analyzed, 32 (59%) cases had Type 1 PMI, whereas 22 others (41%) had Type 2 PMI. Compared to Type 2 patients, those with Type 1 PMI more often had ECG ST elevation (53% v. 23%, p=0.026), greater peak troponin (15.3 ng/dl v. 5.3 ng/dl, p=0.035), higher preoperative mean blood pressure (103 mmHg v. 93 mmHg, p=0.009), greater decrease in mean intraoperative blood pressure (-36 mmHg v. -26 mmHg, p=0.015). Type I patients trended toward greater in-hospital mortality (16% v. 5%, p=0.38) and length of hospitalization (13.5 days v. 9.0 days, p=0.13).

Conclusions

These results demonstrate that PMI not only results from “demand ischemia,” but that in nearly 60% of cases the cause is acute plaque rupture. Patients with PMI attributable to plaque rupture suffer more intraoperative hypotension, greater transmural ischemia, larger infarct size and trended toward worse outcome.

No conflict of interest

ACUTE CORONARY SYNDROMES, MYOCARDIAL INFARCTION

GRACE SCORE AND CARDIAC MAGNETIC RESONANCE FOR PREDICTING CARDIAC EVENTS AFTER HOSPITAL DISCHARGE IN ST-SEGMENT ELEVATION ACUTE MYOCARDIAL INFARCTION.

C. Bonanad[1], A. Eixerés[1], J.T. Ortiz[2], C. Gómez[1], F. Chaustre[1], S. García-Blas[1], F.J. Chorro[1], X. Bosch[2]
[1]Cardiology, Hospital Clinico Universitario de Valencia-INCLIVA, Valencia, Spain
[2]Cardiology, Hospital Clinic de Barcelona, Valencia, Spain

Purpose: Grace Score permits an early stratification of the risk of events in patients with ST-segment elevation acute myocardial infarction (STEMI). Cardiac magnetic resonance (CMR) is the reference imaging technique to quantify the infarction extent. The prognostic implications of a combined analysis of Grace Score and CMR to predict patients' outcome after STEMI has not been analyzed yet.

Methods: We prospectively included 461 patients admitted for a first STEMI. Grace Score was determined upon admission. CMR was carried out in the first week post-STEMI and a quantitative (% of ventricular mass) and semi-quantitative analysis (number of segments with late gadolinium enhancement (LGE) in >50% of wall thickness) of the infarction extent were performed. Events during follow-up (death, myocardial infarction, re-admission for heart failure) were registered. The additional prognostic value of CMR-derived infarction extent beyond Grace Score was determined in the study group and validated in an external cohort made up of 257 STEMI patients.

Results: CMR was performed in 388 patients; 73 were excluded due to early events during hospitalization or contraindication to CMR. During a median follow-up of 644 days, 52 patients (13%) had a first post-discharge event (17 deaths, 25 infarctions and 26 re-hospitalizations for heart failure). In the multivariate analysis, the independent predictors of cardiac events were a high risk in Grace Score (3.4 [1.4 to 8.3], p=0.007) and the infarction extent (1.3 [1.2-1.4] per each additional segment with LGE, p <0.001). The event rate in patients with low (≤ 125), intermediate (126-154) and high (≥ 155) risk in Grace Score was 6/106 (6%), 20/156 (13%) and 26/126 (21%) respectively (p <0.01). The event rate was 8% (23/296) in patients without and 31% (29/92) in those with infarction extent >5 segments. Grace score showed a weak association with the infarction extent (area under the curve to predict extensive infarcts 0.58 [0.52 to 0.63]). Infarction extent >5 segments allowed to discriminate the event rate in patients with low (1% vs. 23%, p = 0.001), intermediate (10% vs. 23%, p = 0.05) and high risk (11% vs. 46%, p <0.001) in Grace Score. In the external validation cohort, 31 events (12%) were registered. Infarction extent >5 segments displayed a tendency (p=ns) towards a higher event rate in patients with low (4% vs. 9%) and intermediate (8% vs. 12%, p = 0.04) risk in Grace Score. In parallel with the study group, striking differences in terms of events were detected in patients with high risk in Grace Score depending on the infarction extent (16% vs. 43%, p <0.001).

Conclusions: Our results illustrate that, especially in patients at the highest risk, the simple and early prognostic stratification obtained from Grace Score can be optimized by determining the infarction extent with CMR.

No conflict of interest

ACUTE CORONARY SYNDROMES, MYOCARDIAL INFARCTION

INTERACTION OF EXERCISE AND SIMVASTATIN ON MYOCARDIAL ISCHEMIA-REPERFUSION (I-R) INJURY.

J. Starnes[1], M.P. Meany[2], M. Meissner[2], M. Cannon[2]
[1]Kinesiology, University of North Carolina at Greensboro, Greensboro, USA
[2]Kinesiology, University of Texas at Austin, Austin, USA

Statins and exercise are widely co-prescribed, yet their interactions affecting cardiovascular health are not completely understood. Here we investigate the interaction of simvastatin and exercise on myocardial tolerance to I-R. Adult rats were separated into four groups of 22-24 each for four wks: sedentary (S), sedentary and fed 10 mg simvastatin/kg/day (SD), exercised on a treadmill (70% VO_2max, 60 min/day, 5 days/wk) (R), and exercise plus simvastatin (RD). Isolated working hearts were perfused without or with the non-specific inhibitor of nitric oxide synthase L-NAME (100 μM) and subjected to 30 min global ischemia and 30 min reperfusion. Without L-NAME, I-R recovery of pre-ischemic cardiac external work was 17.6±6.6% in S. Recovery was higher ($P<0.05$) in SD (37.7±7.7%) and R (40.1±7.7%) and tended to be highest in RD (49.7±7.1%). Lactate dehydrogenase release during reperfusion (necrosis marker) was dramatically decreased in SD, R and RD by approximately similar amounts compared to S. L-NAME abrogated protection in SD, but did not attenuate protection in R or RD. Compared to S, prostaglandin production was increased in SD and content of heat shock protein72 was increased in R and RD; however, no increases occurred for expression of endothelial nitric oxide synthase or antioxidant enzymes. Coenzyme Q was decreased in SD and RD compared to S and R without any change in mitochondria electron transport chain content or oxygen consumption. The results indicate that nitric oxide is a critical mediator of statin-induced protection, but not exercise-induced protection. Combining the treatments provides broader protection than either alone.

No conflict of interest

ACUTE CORONARY SYNDROMES, MYOCARDIAL INFARCTION

IN-HOSPITAL ACQUIRED ANEMIA IN ACUTE CORONARY SYNDROME. PREDICTORS, IN-HOSPITAL PROGNOSIS AND ONE-YEAR MORTALITY.

O. Merono[1], L. Recasens[1], M. Cladellas[1], C. Garcia-Garcia[1], N. Ribas[1], V. Bazan[1], J.A. Morales[1], A. Sainz[1], J. Comin[1], J. Bruguera[1]
[1]Cardiology, Hospital Del Mar, Barcelona, Spain

Introduction and objectives: Anemia at hospital admission predicts a poor outcome in patients presenting with acute coronary syndrome. It remains unclear whether in-hospital hemoglobin levels decrease (nosocomial anemia) not related to bleeding also implies a poor prognosis. We aimed to identify predictors of nosocomial anemia and its prognostic significance.

Methods: We prospectively included 221 acute coronary syndrome patients admitted in our institution during the years 2009-2010, with normal hemoglobin levels at admission. Nosocomial anemia was defined as a decrease in hemoglobin levels to <13g/dL in men and <12g/dL in women in the absence of apparent bleeding. Clinical variables and hematological inflammatory parameters were assessed in order to identify predictors for the development of nosocomial anemia. We compared the clinical outcome after a 1-year follow-up period of patients without anemia as opposed to those who developed nosocomial anemia.

Results: Nosocomial anemia was registered in 25% of study patients. A >3.1mg/dL value of C-reactive protein was highly predictive of developing nosocomial anemia (odds ratio=5.9; 95% confidence interval, 2.6-13.4; *P*<.001). The incidence of mortality and cardio-vascular morbidity was higher in the patients who developed nosocomial anemia (34.5% vs 9%; *P*<.001). Nosocomial anemia was a strong predictor of cardio-vascular morbidity and mortality in the long-term follow-up (hazard ratio=2.47; 95% confidence interval, 1.23-4.96; *P*=.01).

Conclusions: Nosocomial anemia predicts a poorer outcome in patients with acute coronary syndrome. Increased C-reactive protein levels, indicating inflammatory state, are predictive of developing in-hospital anemia unrelated to apparent bleeding.

No conflict of interest

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GLOBAL LONGITUDINAL STRAIN VALUE FOR PREDICTING LEFT VENTRICULAR REMODELING AFTER PRIMARY PERCUTANEOUS REPERFUSION THERAPY IN ACUTE MYOCARDIAL INFARCTION.

B. Mari-Lopez[1], J. Lacalzada-Almeida[1], J. Gonzalez[1], A. de la Rosa[1], M. Garcia[1], F. Bosa-Ojeda[1], M. Vargas[1], M. Izquierdo[1], A. Duque[1], I. Laynez-Cerdena[1]
[1]Cardiology, Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain

Background and objectives: After an acute myocardial infarction with ST-segment elevation (STEMI) treated with percutaneous coronary intervention (PCI), the left ventricle (LV) can either recover its function or undergo negative remodeling (R-), with different well-known prognostic implications. In order to identify viable myocardium, different cardiac image techniques have been used, including transthoracic echocardiography with speckle tracking imaging (TTE-STI), that allows assessment of ventricular deformity (strain and strain rate).

Material and methods: 83 patients (56.1± 11.4 years) admitted to our hospital with the diagnosis of STEMI at any LV localization and subjected to primary PCI (reperfusion time 5.1±2.9 hours). TTE-STI was performed two-three days after primary PCI. Strain global longitudinal (SGL) and other usual TTE parameters were analyzed. Left ventricular ejection fraction (LVEF) and ventricular volume were calculated using the modified Simpson's rule. Six months later, a further TTE-STI was performed. LV R- criteria were: LVEF increase ≤ 5% and end-diastolic volume increase ≥ 15%.

Results: Patients were classified into two groups according to these criteria: LV R- patients (n=35, 42%) and no LV R- patients (n=48, 58%). Bivariable demographic analysis only showed higher incidence of diabetes mellitus (41% vs 19%; p< 0.001) and higher TnI index (1.2 ± 2.1 ug/L vs 0.4 ±0.3 ug/L;p=0.005) in LV R- patients with respect to no LV R- patients. TTE-STI analysis revealed that LV R- patients had significativ lower basal LVEF (42.1 ± 4.0% vs 52.7 ± 6.6%) and left ventricular segmental movement index (1.90 ± 0.39 vs 2.6 ± 0.39) than no LV R- patients. SGL was -12.5 ± 5.6% in no LV R- patients and -6.5 ± 3.4 in LV R- patients. The analysis of ROC curves revealed that at the cut level of -11%, SGL identify LV R- with a sensibility of 70% and a specificity of 80% (AUC=0.82: IC 95% 0.75-0.91; p<0.002).

Conclusion: SGL assessment in the first days after primary PCI is useful in the prediction of LV R- independently of the of the myocardial infarction localization.

No conflict of interest

DIAGNOSIS AND IMAGING

ASSESSING THE AVAILABLE TECHNIQUES FOR TESTING MYOCARDIAL VIABILITY: WHAT DOES THE FUTURE HOLD?

B. Shapiro[1], P. Mergo[1], C. Austin[1], B. Kantor[2], T. Gerber[2]
[1]Cardiovascular Diseases, Mayo Clinic, Jacksonville Florida, USA
[2]Cardiovascular Diseases, Mayo Clinic, Rochester MN, USA

Left ventricular systolic dysfunction in the setting of severe coronary artery disease poses a major diagnostic and therapeutic dilemma. While this clinical scenario is common and generally associated with poor outcomes, some but not all patients may benefit from coronary revascularization. For example, patients with severe, transmural myocardial infarctions may derive little or no functional benefit from revascularization, as the underlying myocardium is irreversibly scarred. These patients may be exposed to high procedural risks with low likelihood of deriving perceivable benefit. Conversely, hibernating myocardium reflects a substrate whereby nonfunctioning myocytes are chronically ischemic but may be viable. Existing data are somewhat inconclusive with regard to the benefits of performing viability testing in patients with ischemic cardiomyopathy. While this testing may predict regional and global functional myocardial recovery, the ability of viability studies to predict survival and prognosis remains unproven in prospective studies to date. Yet, viability testing may still be a valuable tool to guide therapeutic options in selected patients. A variety of noninvasive viability tests are currently available and newer technologies such as positron emission tomography (PET) and cardiac magnetic resonance (CMR) imaging are likely to advance the scientific field in years to come.

No conflict of interest

DIAGNOSIS AND IMAGING

CAROTID PLAQUE QUANTIFICATION BY TWO-DIMENSIONAL ULTRASOUND AS A NOVEL IMAGING BIOMARKER TO HELP RULE OUT ANGIOGRAPHICALLY SIGNIFICANT CORONARY ARTERY DISEASE

A.M. Johri[1], M.N. Haqqi[1], P. Behl[1], P. Malik[1], H.C. Falkson[1], M.F. Matangi[1]
[1]Medicine, Queen's University, Kingston, Canada

Background: Carotid plaque assessment may re-stratify patients at risk of coronary artery disease (CAD). Quantification of the amount of carotid plaque remains a challenge. Since 3D quantification software is not widely available, we sought to determine whether a simple 2D ultrasound assessment of plaque height could rule out angiographically significant CAD in low to intermediate risk patients.

Method: Same day coronary angiography and carotid ultrasound (GE Healthcare) were performed on 320 consecutive outpatients. Mean carotid intimal medial thickening (CIMT) was measured in the distal far wall using automated edge detection. Plaque was defined by the presence of a protuberant lesion beyond the intima by ≥1mm with consideration of the Glagov phenomena. Maximal plaque height in either the bulb or the internal or external carotid arteries was measured by 2D ultrasound calipers. The highest value from either the right or left carotid arteries was obtained. Significant CAD was defined as luminal narrowing >50% in any major vessel by angiography. All measurements were conducted in a blinded manner. Chi-square and independent T tests were used for categorical and continuous variables respectively. Receiver operating characteristic (ROC) curves, negative likelihood ratios (LRN), and sensitivities of CIMT and plaque were determined.

Results: Maximal plaque height improved the LRN of having CAD relative to CIMT at the optimal threshold determined by Youden's index of ROC curves. The sensitivity and LRN of plaque height for CAD was significantly better than CIMT. The optimal CIMT value of 0.82mm from the ROC curve had a LRN of 0.64, whereas the optimal maximal plaque height value of 1.35mm had a significantly better LRN of 0.12 ($p< 0.05$).

Conclusion: Maximal carotid plaque height less than 1.35 mm ruled out the presence of significant angiographic CAD. Carotid plaque assessment by 2D maximal dimension may serve as a rapid and simple imaging biomarker to rule out significant CAD.

Figure 1: ROC curve comparing plaque height to CIMT for predicting angiographically significant CAD (p=0.0066).

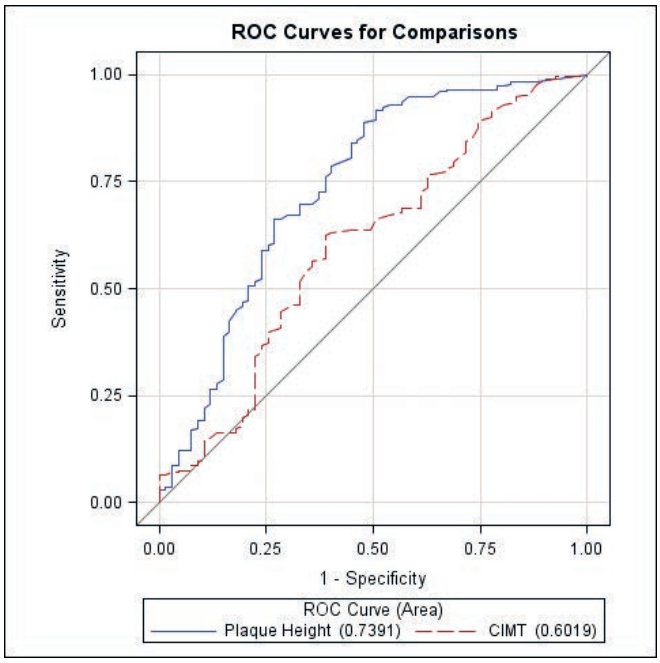

Table 1: Summary of sensitivity, specificity, and likelihood ratios for CIMT and plaque height using 2D ultrasound for coronary artery disease.

	CIMT < 0.82 mm	2D Plaque Height < 1.35 mm
Total Patients	304	298
Sensitivity (%)	60.9	94.8
Specificity (%)	60.9	41.8
+LR	1.56	1.63
-LR	0.64	0.12

No conflict of interest

DIAGNOSIS AND IMAGING

NONINVASIVE IDENTIFICATION OF LEFT MAIN CORONARY RESTENOSIS

M. Zabunova[1], I. Mintale[1], I. Narbute[1], S. Jegere[1], I. Zakke[1], A. Erglis[1]
[1]Latvian Centre of Cardiology, Pauls Stradins Clinical University Hospital, Riga, Latvia

The aim: Noninvasive identification of patients with left main (LM) coronary artery restenosis using exercise test.

Methods: The observational study was implemented from 2002 till 2011. The patients (n=513) with LM stenotic lesion (more than 50% of the artery lumen diameter) and performed percutaneous coronary intervention (PCI) of LM were included and consequently observed in defined follow-up visits by performing exercise test every three months after LM PCI. All patients underwent control coronary angiography. Two study patients' groups were extracted – with and without LM restenosis.

Results: There was no significant difference between both groups in evaluation of demographic parameters and risk factors. Restenosis was detected by clinical evaluation according to classical criteria (ST-segment deviation, ST/pulse index) and by control coronary angiography. The additional predictable parameter had been revealed on exercise testing (diagnostics in early follow-up period after PCI) – double (rate-pressure) product (DP). The results show the significance of DP targeted monitoring at exercise testing follow-up – in patients with LM restenosis it was less than 200 and without LM restenosis – more than 220 ($p < 0.001$).

Conclusions: 1) Powerful predictable capability of exercise test to identify high-risk patients; 2) Exercise testing – early identification of left main coronary restenosis; 3) Exercise testing follow-up – the control and prediction of stable period for high-risk patients.

No conflict of interest

DIAGNOSIS AND IMAGING

THE ROLE OF DOBUTAMINE STRESS ECHOCARDIOGRAPHY IN DETECTING CORONARY ARTERYDISEASE COMPARED WITH CORONARY ANGIOGRAPHY

M.B.,Z.K.,N.M., N. Naser[1]
[1]*Cardiology, Eurofarm Centar, Sarajevo*
[2]*Cardiology, University Clinical Center Tuzla, Tuzla*
[3]*Institute for Pharmacology and toxicology, Faculty of Medicine,Sarajevo*
[4]*Heart Center Sarajevo*
[5]*Clinic for heart disease, University Clinical Center Sarajevo, Sarajevo*
[6]*Cardiology, BiH Heart Center, Tuzla, Bosnia-Herzegovina*

b>Background: Ischemic heart disease (IHD) causes more deaths, disability and economic loss indeveloped and developing countries than any other disease. Our country belongs to the group ofcountries in transition, and it has seen a continuous growth in mortality andmorbidity rates caused by cardiovascular diseases.

Objectives: The aim of this study is to examine the occurrence of segmental wallmotion abnormalities during pharmacological stress and measurement of coronaryflow reserve (CFR) in order to establish the diagnostic value of Dobutaminestress echocardiography in detecting and assessing the degree of myocardialischemia and coronary stenosis in patients with suspected coronary artery disease,and to justify its wider application as a non-invasive diagnostic method.

Methods: The research study covered 86 adult subjects of both genders, referred todobutamine Stress echocardiography test and assessment of coronary flow reserveas part of their cardiological evaluation.

Results: The study results obtained indicate a high degree of sensitivity (97%),specificity (83%) and accuracy (95%) of the dobutamine stress echocardiographyas a non-invasive diagnostic method compared to invasive diagnostics i.e.coronary angiography. Measurement of coronary flow reserve representsa strong diagnostic and prognostic tool in evaluation patients with suspectedCAD.

Conclusions: The safety and cost-effectiveness of the dobutamine stressechocardiography as a diagnostic procedure has been proved. In moderncardiology, the DSE occupies a significant place in the evaluation of patientswith known or suspected coronary artery disease, which has contributed to itsaccessibility and availability in a great number of centers.

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DIAGNOSIS AND IMAGING

A MACHINE LEARNING APPROACH FOR THE IDENTIFICATION OF RISK FACTORS FOR CARDIOVASCULAR DISEASE

J.R. Coelho[1], I.M. Gaspar[2], A.M. Silva[3], A.T. Freitas[1]
[1]Computational Biology, INESC-ID/IST Technical University of Lisbon, Lisbon, Portugal
[2]Medical Genetics Service and Cardiogenetics Cardiology Department,
Hospital Egas Moniz and Hospital Santa Cruz Centro Hospitalar de Lisboa Ocidental, Lisbon, Portugal
[3]Head of Internal Medicine Services I and II,
Hospital Egas Moniz Centro Hospitalar de Lisboa Ocidental, Lisbon, Portugal

Cardiovascular diseases (CVD) are one of the major causes of morbidity and mortality. They are known to be complex, polygenic and multifactorial. Premature CVD (PCVD) usually appears in males and females until 55 and 65 years old, respectively.

In this study, we have analyzed patients (PT) with classical risk factors (CRF) and family history of CVD (FHCVD). The main objectives were the clinical and laboratorial characterization of patients with PCVD and the identification of major cardiovascular risk factors.

A machine-learning method called decision trees (DTs) was used to predict the incidence of PCVD in individuals with FHCVD. For PT, several clinical variables, namely CRF, FHCVD, biochemical and ultrasound phenotype were collected. This methodology uses a statistical measure to infer rules that characterize the disease. Using this group of PT we were able to identify which clinical variables are statistically more likely to be found in an individual with PCVD. Based on the DTs that were obtained, we identified PT at risk among a group of new PT, i.e., the ones more likely to suffer from PCVD, and work on its prevention and treatment. Using this methodology, we were able to identify that the dysfunctional HDL may be the cause of the 1st event PCVD, being the best feature to identify PT at risk. The presence of FHCVD, increases the risk of PCVD that can be anticipated by one or more CRF. The use of this machine-learning algorithm was instrumental on the identification of risk factors for the occurrence of PDCV.

No conflict of interest

LACTATE CLEARANCE IN CARDIOGENIC SHOCK FOLLOWING ST ELEVATION MYOCARDIAL INFARCTION: A PILOT STUDY

Attanà, "." [1], C. Lazzeri[1], M. Chiostri[1], C. Picariello[1], G.F. Gensini[1], S. Valente"[1]
[1]Intensive Cardiac Coronary Unit, Heart and Vessel Department, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy, Florence, Italy

Background: Recent studies documented that serial lactate measurements over time may be clinically more reliable than lactate absolute value for risk stratifi cation. The aim of the present investigation was to assess the role of lactate clearance in predicting early death in cardiogenic shock (CS) following ST-elevation myocardial infarction (STEMI) submitted to primary percutaneous coronary intervention (PCI). Methods: 51 consecutive patients with CS following STEMI were prospectively enrolled. Lactate was measured in Intensive Cardiac Care Unit (ICCU) on admission and on the twelfth hour. Logistic regression analysis was performed to identify the independent predictors for in-ICCU mortality. Receiver operating characteristic (ROC) curve was constructed in order to identify cut-off for admission lactate and for 12-h lactate clearance in relation to in-ICCU mortality. Follow-up survival rate were investigated by Kaplan – Meier curves. Results: At 12 h from admission, lactate clearance was higher in survivors (P ? 0.013). A higher in-ICCU mortality was observed in patients with 12 hours lactate clearance ? 10% (P ? 0.002). At follow up, patients with 12-h lactate clearance ? 10% showed a signifi cantly lower survival rate. Conclusions : In patients with CS following STEMI, 12-h lactate clearance ? 10% identifi es a subset of patients at higher risk for death at short and long term.

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CORONARY ANGIOGRAPHY AFTER FIBRINOLYTIC THERAPY – IS IT USEFUL AFTER 24 HOURS?

A. Baptista[1], C. Ferreira[1], P. Magalhães[1], S. Leão[1], P. Mateus[1], I. Moreira[1]
[1]Cardiology, Centro Hospitalar Trás-os-Montes e Alto Douro, Vila Real, Portugal

Introduction: Primary percutaneous coronary intervention (PCI) is the treatment of choice in ST-segment myocardial infarction (STEMI). In regions with difficult access to PCI, fibrinolytic therapy (TNK) may be considered first line treatment. After TNK, early on coronary angiography (CC) has shown additional benefit and is recommended between 3 and 24 hours after TNK. The 3 hour limit was defined by the three main trials in STEMI, but the 24 hour limit wasn't clearly demonstrated.
Aim: evaluate the impact on adverse events (AE) of CC more than 24 hours after TNK.
Methods: retrospective analysis of STEMI with TNK as the chosen strategy for reperfusion, during a 20 months period. Death, re-infarction and heart failure were the pre-specified AE.
Results: 80 patients were admitted after TNK. On average, patients presented with 1.4hours after symptom onset and the average ***door-to-needle*** time was 49 minutes [standard deviation of 33.9]. 13.8% of the cases were excluded for failed TNK. The 69 patients were divided into two groups according to the delay until CC. In the early intervention group (TNK-CC 3-24hours) the average TNK-CC time was 13.4 hours and in the late intervention group (TNK-CC >24hours) was 49.5. The TNK-CC time above 24 hours didn't lead to left ventricle systolic dysfunction or to increasing AE after an average follow-up of 18 months.
Conclusions: CC is recomended between 3 to 24 hours after successful TNK. However, our results suggests that in practice there may be no increase in AE if TNK-CC time is longer than 24 hours.

No conflict of interest

CLINICAL PROFILES AND OUTCOMES OF ACUTE CORONARY SYNDROME IN SMOKERS WHO ARE NOT DIABETIC VERSUS DIABETICS WHO DO NOT SMOKE

A.A. Gehani[1], A. El-Menyar[2], A. Shabana[1], H. AlBinAli[3], R. Singh[4], J. Al Suwaidi[3]
[1]cardiology, Hamad general hospital & Weill Cornell medical school, Doha, Qatar
[2]clinical medicine & research, Hamad general hospital & Weill Cornell medical school, Doha, Qatar
[3]cardiology, Hamad general hospital, Doha, Qatar
[4]cardiology research, Hamad general hospital, Doha, Qatar

Background: Smoking and Diabetes are recognized major risk factors for coronary artery disease (CAD) and acute coronary syndrome (ACS); however the difference of the etiological mechanisms may be of clinical significance

Aims: To study the impact of these two etiological mechanisms on the clinical profile and outcome in two mutually exclusive groups.

Methods: All patients hospitalized with ACS in 20 years (1991-2011) were included and categorized based on to whether they were smokers but not diabetic (Smokers) or diabetics but no Smokers (Diabetics). The collected data for each group were analyzed and compared.

Results : Out of 9192 patients admitted with ACS in 20 years, 3910 (42.5%) were smokers but not diabetic (Smokers), while 5282 (57.5%) were diabetics but no Smokers (Diabetics). In comparison to Diabetics, Smokers were younger (48.1 ± 10 vs 59±11, p< 0.001), had more ST-elevation myocardial infarction (54.3% vs 32.2%, p< 0.001), larger infarcts (peak CKMB 319 ±909 vs 58 ±652, p< 0.001). Smokers also had lower in-hospital mortality (2.9% vs 8.6%, p<0.001), despite the fact that Diabetics were more likely to be on ACE-Inhibitors, Beta-blockers and Anti-platelets agents (p<0.001 for all).. Diabetics, on the other hand, had more hypertension (62.2% vs 20.9%, p<0.001), chronic renal failure (6.9% vs 0.05%, p<0.001), more stroke (0.6% vs 0.1%, p<0.001) and frequently presented with atypical symptoms in comparison to Smokers. During admission, Smokers, received more thrombolysis (40% vs 18.3%, p< 0.001) and had greater rate of percutaneous coronary interventions (p=0.008). Using multivariate analysis; old age, female gender, prior MI, STEMI at presentation, were independent predictors for in-hospital mortality in both groups.

Conclusion: Although there are several studies comparing ACS in mixed groups of Diabetic and Smokers, this is the first study to analyze and compare patients with ACS who are either Smokers only or Diabetics. The two groups had significantly different clinical profiles and outcome results.

No conflict of interest

ISCHEMIC STROKE COMPLICATING ACUTE MYOCARDIAL INFARCTION: INCIDENCE, CLINICAL CHARACTERISTICS, AND IN-HOSPITAL OUTCOME

M. Yamamoto[1], K. Hukushima[1], N. Ikeda[1], S. Ito[1], H. Hara[1], S. Takeuchi[2], Y. Hiroi[1]
[1]Cardiology, National Center for Global Health and Medicine, Tokyo, Japan
[2]Neurology, National Center for Global Health and Medicine, Tokyo, Japan

Background
Although numerous clinical trials have reported the incidence of stroke following myocardial infarction (MI), these are among MI populations. A reduced left ventricular ejection fraction is associated with an increased risk of stroke after MI. The purpose of this study was to examine the incidence, clinical characteristics, and in-hospital outcome of ischemic stroke complicating acute MI.

Methods
This study included consecutive patients who were diagnosed as ischemic stroke by neurologist. Medical record review was used to ascertain baseline characteristics and death. Diagnosis of acute MI was based on Universal Definition of Myocardial Infarction published by European Society of Cardiology.

Results
A total of 523 patients with ischemic stroke were hospitalized between August 2010 and April 2013. The rate of stroke complicating acute MI was 2.7% (14 patients). The mean age of these 14 patients was 78 years, 64% were women, 64% had a history of hypertension, 29% had dyslipidemia, 21% had diabetes, and 64% had paroxysmal or chronic atrial fibrillation. 1 patient presented with chest discomfort, whereas the other 13 patients did not have chest symptom due to impairment of consciousness. Cardioembolism in classification of subtype of ischemic stroke accounted for 64%, and 2 patients died during hospitalization.

Conclusions
Among ischemic stroke population, acute MI was occasionally observed concomitant disease. Cardioembolic stroke particularly needs cardiovascular examinations to be aware of complicating acute MI.

No conflict of interest

NOVEL FUNCTIONAL APOB MUTATIONS OUTSIDE LDL-BINDING REGION CAUSING FAMILIAL HYPERCHOLESTEROLAEMIA

A.C. Alves[1], A. Etxebarria[2], A.K. Soutar[3], C. Martin[2], M. Bourbon[1]
[1]Departamento de Promoção da Saúde e Prevenção de Doenças não Transmissíveis, Instituto Nacional de Saúde Dr. Ricardo Jorge, Lisboa, Portugal
[2]Unidad de Biofísica (Centro Mixto CSIC-UPV/EHU) and Departamento de Bioquímica, Universidad del País Vasco, Bilbao, Spain
[3]Lipoprotein Group MRC Clinical Sciences Centre, Hammersmith Hospital, London, United Kingdom

APOB mutations are a rare cause of FH and until now only a few mutations have been reported to cause FH, being the APOB3527 the most common.

This study pretended to identify and characterize the genetic cause of severe hypercholesterolaemia in individuals with clinical diagnosis of FH, without mutations in *LDLR*, *PCSK9* or in fragments of exon 26 and 29 of *APOB* routinely screened.

The whole sequencing of *APOB* was performed by pyrosequencing for 65 index patients with clinical diagnosis of FH. LDL from 3 patients and relatives was isolated and marked with FITC to perform functional studies by flow cytometry with control lymphocytes and HepG2 cells. Proliferation assays were performed with U937 cells and patient's LDL.

A total of 10 alterations in the *APOB* (exons 19, 22,24, 26 and 29) were identified. *In vitro* analysis of p.Arg1164Thr and p.Gln4494del, showed a 40% decrease in binding and internalization of patient's LDL in lymphocytes and HepG2 cells, very similar to APO3527. The U937 cell proliferation assay showed reduced growth for both cases. Variant p.Asp1113His did not affect function in the 3 assays.

With the advances of NGS techniques it is now possible a new approach for studying the known genes and as well for discover new genes, causing FH. APOB should be analysed with a new perspective since many patients can have a non reported alteration in this gene. Probably the unknown causes of FH are related more to the old genes and novel disease mechanisms, than to novel genes.

No conflict of interest

EFFECT OF CHEMICAL OR OXIDATIVE MODIFICATION OF CHYLOMICRON REMNANTS ON MICROPARTICLE PRODUCTION FROM HUMAN MONOCYTES

K. Botham[1], A. Pollard[1], K. Jacks[1], C. Thomas[1], M. Avella[1], C. Lawson[1]
[1]Comparative Biomedical Sciences, Royal Veterinary College, London, United Kingdom

Background: Atherosclerosis is characterised by accumulation of lipid in the neointima, monocyte recruitment, and secretion of pro-inflammatory mediators. We have shown that chylomicron remnants (CMR), lipoproteins that transport dietary lipids in the blood, are taken up by monocytes and that oxidation of the particles enhances this effects. Microparticles (MP) are circulating vesicles <1μm in diameter, shed by monocytes and other cells during activation and apoptosis, which may have pro-inflammatory properties. They are increased in CVD patients, but the effects of CMR on their production are not known.

Aim To investigate the effects of CMR on MP production and chemokine secretion by monocytes, and how they are influenced by CMR oxidation or acetylation.

Methods and Results Model chylomicron remnant-like particles (CRLPs) were chemically modified by acetylation, or their oxidative state was varied by oxidation with $CuSO_4$ or by incorporation of the antioxidant probucol. MP production was determined by flow cytometry. After incubation of primary human monocytes with CRLPs (24h), MP production was increased, and this effect was enhanced by increasing oxidative state or acetylation of the particles. In contrast, secretion of the chemokine MCP-1 was reduced with increasing CRLP oxidative state or with acetylation.

Conclusion These results are the first demonstration that CMR promote MP secretion by primary human monocytes, and furthermore, that chemical/oxidative modification of the particles influences these effects, which are accompanied by decreased secretion of the pro-inflammatory chemokine, MCP-1. Further studies are required to establish the function of MP and the mechanisms by which their production is regulated.

No conflict of interest

INTRAPLAQUE HAEMORRHAGES IN CARDIAC ALLOGRAFT VASCULOPATHY

C. Castellani[1], A. Angelini[1], O. de Boer[2], C. van der Loos[2], M. Fedrigo[3], A. Frigo[3], L. Meijer-Jorna[2], X. Li[2], H. Ploegmakers[2], F. Tona[3], G. Feltrin[3], G. Gerosa[3], M. Valente[3], G. Thiene[3], A. van der Wal[2]
[1]Cardiac Thoracic and Vascular Sciences, University of Padua, Padova, Italy
[2]Pathology, Academic Medical Center / University of Amsterdam, Amsterdam, Netherlands
[3]Cardiac Thoracic and Vascular Sciences, University of Padua, Padua, Italy

Background:plaque hemorrhage, inflammation and microvessel density are key determinants of plaque vulnerability in native coronary atherosclerosis.

This study investigates the role of intraplaque haemorrhage(IPH) and its relation with inflammation and microvessels in cardiac allograft vasculopathy(CAV) in patients transplanted for dilated cardiomyopathy(DCM) and ischemic cardiomyopathy (ICM).

Methods: 70 coronary plaques were obtained from 12 patients transplanted for DCM (4 pts) and IHD (8 pts) and died because of CAV. For each patient we collected both the native heart and the allograft, respectively at the time of transplantation and autopsy. Immunohistochemistry and semi-quantitative analyses were applied to assess intra-lesion inflammation, microvessels and intraplaque hemorrhage.

Results: IPH was observed both in CAV lesions (60%) and in native atherosclerotic plaques (ATS,37.4%). Fresh and old IPH were presents in 12/21(57.14%) CAV lesions. Microvessels were detected in 26/35 (74.29%) of CAV lesions (p=n.s. versus ATS microvessels) with perivascular leakage as sign of endothelial damage in 18/26 (69.23%).

IPH was strongly associate with microvessels (p=0.0005). Fibrocellular plaques in CAV were associated with IPH presence in 11/29 (37.93%, p=0.0277).

Conclusions:IPH, associated with microvessel damage and inflammation, is an important feature of CAV. Fresh and old intra-lesion haemorrhages suggests ongoing remodelling processes possibly stimulating the lesion progression and vulnerability

No conflict of interest

CHOLESTERYL ESTER TRANSFER PROTEIN (CETP) TRANSGENIC MICE PRESENT INCREASED SURVIVAL RATE AND REDUCED TLR4 RECEPTOR IN THE LIVER

T.M. Venancio[1], R.M. Machado[1], E.C.R. Quintao[1], F.G. Soriano[2], P.M. Cazita[1]
[1]Dept. of Clinical Medicine, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil
[2]Emergency Care Research Unit, Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil

Aim: Cholesteryl ester transfer protein (CETP) plays a reverse cholesterol transport system role and is an anti-inflammatory candidate agent for belonging to the family of two anti-inflammatory proteins, LBP (lipopolysaccharide binding protein) and BPI (bactericidal permeability increasing protein). The aim of this study was to evaluate ***in vivo*** the influence of CETP on the innate immune response. For this purpose we utilized mice C57BL6/J that expressed human CETP (huCETP) as compared to wild type mice (WT = do not express CETP) submitted to polymicrobial sepsis by cecal ligation and puncture (CLP). We measured the mice mortality rate, hepatic protein expression of acyloxyacyl hydrolase (AOAH) and Toll-like receptor 4 (TLR4).

Methods and results: The ethics committee of the University of São Paulo Medical School approved this experimental protocol number 029/12. C57BL6/J male mice (N= 6 -15/group), age 8-12 weeks, huCETP and WT, were submitted to polymicrobial sepsis by CLP. The animal mortality rate was observed every 8 hours for 5 days. Mortality rates were 6.7% in huCETP mice and 40% in WT (***Log rank Test*** p=0.0267). CETP mice have decreased TLR4 (p=0.042) and AOAH (p=0.032) liver protein expression when compared to WT mice by immunoblotting.

Conclusion: This study demonstrated that CETP protects mice against inflammation by reducing TLR4 and AOAH in the liver suggesting that CETP is involved in the first step of inflammatory response. Studies with drugs that inhibit CETP activity should take into account that such anti-inflammatory elicited properties may bear undesirable effects.

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No conflict of interest

LEUKOCYTE TLR5 DEFICIENCY INHIBITS ATHEROSCLEROSIS BY REDUCED MACROPHAGE RECRUITMENT AND DEFECTIVE T CELL RESPONSIVENESS

S.C.A. De Jager[1], G.H. van Puijvelde[1], A.A. Anas[2], M. Bot[1], M. Asbach[1], A. Schoneveld[3], K.L.L. Habets[1], A.C. Foks[1], G. Pasterkamp[3], T. van der Poll[2], J. Kuiper[1]

[1]Biopharmaceutics, Leiden Academic Center for Drug Research/Leiden University, Leiden, Netherlands

[2]Center of Infection and Immunity Amsterdam (CINIMA), Academic Medical Center, Amsterdam, Netherlands

[3]Experimental Cardiology Laboratory, University Medical Center Utrecht, Utrecht, Netherlands

Background: Toll-like-receptors (TLRs) provide a critical link between innate and adaptive immune responses. It has been shown that TLR5 ligand Flagellin can enhance the suppressive capacity of regulatory T-cells (Treg), but can also functions as an adjuvant. The immune response in atherosclerosis is characterized by an imbalance of pro- and anti-atherogenic T-cells. We aimed to establish if the TLR5/Flagellin axis is involved in the immune response of atherosclerosis. **Methods**: We first assessed the effect of Flagellin exposure on macrophage maturation and T-cell polarization. Next, we created $TLR5^{-/-}$/$LDLr^{-/-}$ chimeras to study the TLR5/Flagellin axis in atherosclerosis. **Results**: Flagellin exposure to primary macrophages did not result in clear polarization differences, but we did observe a less migratory phenotype (decreased MCP-1, CCR2 expression) in $TLR5^{-/-}$ macrophages. Interestingly, expression of the T-cell polarizing cytokine IL-6 was induced by Flagellin exposure, a phenomenon not observed in $TLR5^{-/-}$ macrophages. Next, we assessed potential T cell polarizing properties of Flagellin. Flagellin can induce expansion of regulatory T-cells, however this induction is completely overruled when Flagellin is used as an adjuvant. Hematopoietic absence of TLR5 significantly attenuates atherosclerotic lesion formation by 25%. This was accompanied by a decrease in macrophage area and necrotic core size, while collagen content was similar between groups. Interestingly, plasma levels of IL-6 were significantly lower in $TLR5^{-/-}$ chimeras. Concomitantly, $TLR5^{-/-}$ chimeras displayed defective T-cell responsiveness, as seen by impaired proliferation and decreased splenic T cell content. **Conclusions:** Hematopoietic TLR5 deficiency inhibits atherosclerotic lesion formation by attenuated macrophage accumulation and defective T cell responsiveness.

No conflict of interest

HOMOCYSTEINE LEVEL AS AN INDEPENDENT RISK FACTOR FOR CORONARY ARTERY DISEASE

B. Sreckovic[1], V. Dimitrijevic-Sreckovic[2], J. Perunicic[3], I. Soldatovic[4]
[1]Cardiology, Clinical Center Bezanijska Kosa, Belgrade, Serbia
[2]Dpt. for nutrition and prevention of metabolic disorders, Clinic for endocrinology diabetes and metabolic diseases Medical Faculty University of Belgrade, Belgrade, Serbia
[3]Cardiology, Clinic for Cardiovascular Diseases Medical Faculty University of Belgrade, Belgrade, Serbia
[4]Medical Statistics and Informatics, Institute for Medical Statistics and Informatics Clinical Center of Serbia Faculty of Medicine University of Belgrade, Belgrade, Serbia

Background:Elevated level of homocysteine is an independent atherogenic factor. Its correlations with hyperlipoproteinemia (HLP), hypertension, hyperuricemia, abdominal obesity and microalbuminuria have been established. Atherogenesis includes several etiopathogenetic factors which are more often expressed in type 2 diabetes mellitus (DM2).

Aims: Determine serum homocysteine level in target groups and possible correlation with other atherogenic factors: abdominal obesity, hyperinsulinemia, hypertension, HLP, plasminogen activation inhibitor-1 (PAI-1) and C-reactive protein (CRP). Examine the influence of DM2 for the occurrence of cardiovascular disease (CD), the mutual relations of other atherogenic factors.

Material and methods: Patients were classified into four groups: 1. no DM2, no CD; 2. no DM2, myocardial infarction; 3. DM2, no CD; 4. DM2, CD. Serum homocysteine was measured by immunoassay method. Insulin resistance (IR) was determined by HOMA IR. Plasminogen activation inhibitor-1 (PAI-1) and C-reactive protein (CRP) markers of thrombosis and inflammation were determined.

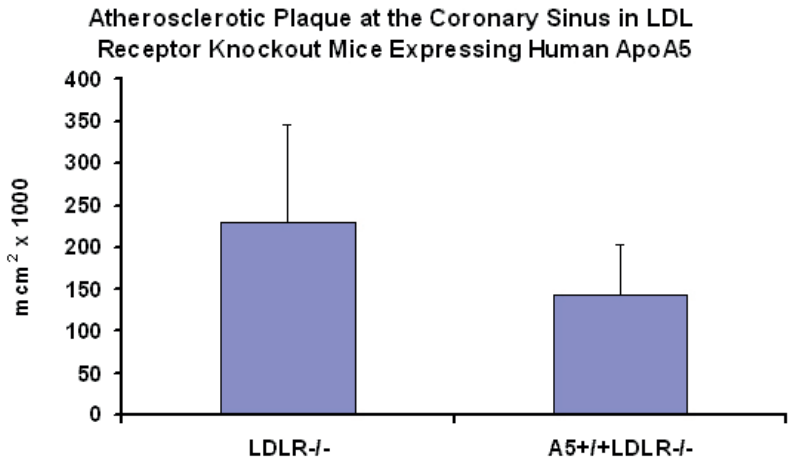
Results: Homocysteine limit values show no difference between non-diabetics with myocardial infarction and DM2 with CD. Patients without DM2 and myocardial infarction are male smokers having HLP and highest Lp(a) values. Patients with DM2 and CD are characterized by visceral obesity, metabolic syndrome (MS), HLP type IV and IR. Visceral fat tissue associated with inflammation (CRP) and thrombotic (PAI-1) factors, and also an increased LDL/HDL ratio, were most expressed in the DM2 and CD group. Individuals with DM2 have 2.5 times higher chances to become CD patients. **Conclusions**: Positive correlations of homocysteine with systolic pressure, triglycerides and negative correlations with HDL-cholesterol confirm relations of homocysteine and atherosclerotic complications.

No conflict of interest

APOLIPOPROTEIN A5 ATTENUATES ATHEROSCLEROTIC LESION IN LDL RECEPTOR DEFECIENT MICE FED HIGH FAT DIET

A. Ray[1,2], A. Shaish[1], Y. Kamari[1], I. Grosskopf[1,2]
[1]The Bert W. Strassburger Lipid Center, Sheba medical center, Ramat Gan, Israel
[2]Department of Medicine, Tel Aviv-Sourasky Medical Center, Tel Aviv, Israel

The role of triglyceride in development of the atherosclerotic plaque was debated over the past 4 decades. Although triglyceride plasma level was shown to correlate with the degree of atherosclerosis, and several studies found elevated triglycerides to be an independent risk factor for CAD, it appeared that atherogenicity has to do with the fate of triglyceride-rich lipoproteins (TRL) rather than the level of the triglyceride itself. Indeed, cholesteryl-ester within TRL and not triglyceride appears to be the culprit. Small dense cholestery ester-enriched TRL enter the subintimal space and are exceedingly atherogenic (5-fold more so than LDL on particle basis). Apolipoprotein A5 was shown to affect TRL metabolism by enhancing both intra-vascular lipolysis and removal of TRL from the circulation. LDL receptor knockout mice retain cholestery ester-enriched TRL in the circulation when fed high fat diet, and develop advanced atherosclerosis. Expression of human Apolipoprotein A5 in $LDLR^{-/-}$ mice was associated with decreased plasma cholesterol and triglyceride levels and significantly attenuated the atherosclerotic plaque. This may target apolipoprotein A5 gene for manipulations aimed at combating atherosclerosis.



No conflict of interest

TREATMENT WITH PURE TOCOTRIENOLS REDUCE AORTIC TISSUE ADHESION MOLECULE EXPRESSION IN EXPERIMENTALLY INDUCED SEVERELY ATHEROSCLEROTIC RABBITS

F. Hassim[1], N. Zulkafli[1], T. Rahman[1], N.K. Kornain[1], H. Nawawi[1]
[1]Centre for Pathology Diagnostic and Research Laboratories (CPDRL), Universiti Teknologi MARA, Sungai Buloh, Malaysia

Background: Suppression of cell adhesion molecule expression and macrophage accumulation by endothelium is believed to play an important role in the prevention of atherosclerosis.There have been several studies identifying cardioprotective properties of tocopherol-tocotrienol mixed fraction (TTMF) but they have yielded discrepant results, possibly owing to the attenuation of pure tocotrienols (TCT) activities by alpha tocopherol in TTMF. **Objective:** To determine the effects of pure delta (90%) and gamma (10%) TCT on tissue markers of endothelial activation in hypercholesterolaemic-fed,severe atherosclerotic rabbit model. **Methods:** Fifteen New Zealand white rabbits were divided equally into three intervention arms: TCT 4 mg/kg/D (TCT-4), 15 mg/kg/D (TCT-15) and placebo.Intervention was done following 2 months 1% high cholesterol diet (HCD). Entire lengths of aorta were obtained at the end of the study and representative sections were taken and submitted for expression of E-selectin, ICAM-1 and VCAM-1 by immunohistochemistry. **Results:** The aorta of all groups showed extensive atheromatous plaque formation.There were reductions in E-selectin and ICAM-1 expression in TCT-4 and TCT-15 intervention groups compared to placebo [mean±SEM: (27 ± 1 vs. 60±8 **%** $p<0.05$), (30± 7 vs. 60±8 %; $p<0.05$) and (37.9 ± 3.95 vs. 41.3 ±8.1 **%** $p<0.001$), (20.9± 4.3 vs. 41.3 ±8.1 %; $p<0.001$) respectively]. VCAM-1 was only reduced in the TCT-15 group (mean±SEM: 20.48 ± 3.3 vs. 35.55±2.5 **%** $p<0.01$). **Conclusion:** This study suggests TCT's potential role in reducing endothelial activation markers in severe atherosclerosis, making its use as an adjunct therapy to standard treatment regimes for atherosclerosis a strong possibility.

Acknowledgement: Fundamental Research Grant Scheme, Malaysian Ministry of Higher Education; American River Nutrition Inc, USA.

Author Keywords: pure tocotrienols, delta tocotrienol, gamma tocotrienol, endothelial dysfunction, atherosclerosis, tissue expression

No conflict of interest

THE ROLE OF AN EXPERIMENTAL MODEL OF ATHEROSCLEROSIS: APOE-KNOCKOUT MICE IN DEVELOPING NEW DRUGS AGAINST ATHEROGENESIS

J. Jawien[1]
[1]*Chair of Pharmacology, Jagiellonian University School of Medicine, Krakow, Poland*

"Although atherosclerosis was previously thought to be mainly a degenerative disease, it is now well ascertained that its pathogenesis is inflammatory. Since 1992 the mouse has become an excellent model for experimental atherosclerosis research. In 1992 the first line of gene targeted animal models, namely apolipoprotein E-knockout mice was developed. Of the genetically engineered models, the apoE-deficient model is the only one that develops extensive atherosclerotic lesions on a chow diet. It is also the model in which the lesions have been characterized most thoroughly. The lesions develop into fibrous plaques; however, there is no evidence that plaque rupture occurs in this model. The LDL receptor - deficient model has elevated LDL levels, but no lesions, or only very small lesions, form on the chow diet, however, robust lesions do form on the western-type diet. The creation of apoE-knockout mice has changed the face of atherosclerosis research. The apoE-deficient mouse model of atherosclerosis can then be used to: 1) identify atherosclerosis susceptibility modifying genes, by the candidate-gene and gene-mapping methods; 2) identify the role of various cell types in atherogenesis; 3) identify environmental factors affecting atherogenesis; and 4) assess therapies that might block atherogenesis or lesion progression. ApoE-deficient mice have also been used to look for environmental and drug effects on atherosclerosis and to test novel therapies. Gene-targeted mouse models has changed the face of atherosclerotic research and helped in creation of the new theory of atherosclerosis - as an inflammatory disease. Nowadays, apoE-knockout mice model is therefore used in developing new drugs against atherosclerosis."

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MDA-MODIFIED LOW-DENSITY LIPOPROTEINS ARE ALSO CHOLESTEROL-RICH

V. Lankin[1], *A.K. Tikhaze*[1]
[1]*Ministry of Heath, Russian Cardiology Research Complex, Moscow, Russia*

We have found that low-density lipoproteins (LDL) from human blood plasma, which was oxidized by animal C-15 lipoxygenase to form hydroperoxy-derivatives ingested by human cultivated macrophages with the same effectiveness as non-oxidized (native) LDL, but malonyldialdehyde-modified LDL (MDA-LDL) is captured by cultivated macrophages very actively. Based on differences in catabolism of LDL with various levels of primary and secondary products of free radical peroxidation, it was offered to discriminate oxidized LDL itself (lipohydroperoxide-rich LDL) and LDL that was chemically modified by secondary free radical peroxidation products of aldehyde nature (such as MDA). In this respect, aldehyde-modified (including MDA-modified), but not oxidized (lipohydroperoxide-containing) LDL are atherogenic. In epidemiological surveys we examined the level of oxidized LDL (mainly MDA-modified LDL) in the two groups of patients in Russia (Moscow) and Estonia (Tallinn) by immunochemical method ("Oxidized LDL ELISA" test kit Mercodia, Sweden). Significant positive correlation between the levels of MDA-LDL and LDL-cholesterol was indicated in blood of patients from russian ($n=1433$; $r=0.56$; $p<0.05$) and estonian ($n=782$; $r=0.61$; $p<0.05$) populations. In russian population MDA-LDL/HDL-cholesterol ratio was higher in the groups with highest risk of atherosclerosis development or manifest coronary artery disease.

Conclusions. Cholesterol-rich low density lipoproteins are also more oxidized. Estimation of MDA-LDL/HDL ratio may be used as an independent biochemical marker for atherosclerosis.

No conflict of interest

HIGH FAT MEALS CONTAINING N-3 PUFAS GENERATE TRIGLYCERIDE-RICH LIPOPROTEINS WITH PROTECTIVE ACTIONS ON AORTIC ENDOTHELIAL CELLS

R. Purcell[1], S. Latham[1], K. Botham[1], W. Hall[2], C.P.D. Wheeler-Jones[1]
[1]Comparative Biomedical Sciences, Royal Veterinary College, London, United Kingdom
[2]Diabetes & Nutritional Sciences Division, Kings College London, London, United Kingdom

Chronic supplementation with the n-3 polyunsaturated fatty acids (PUFA) eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) has beneficial effects on the cardiovascular system, but how these FAs influence vascular function when carried in triglyceride (TG)-rich lipoproteins (TRLs) in the postprandial phase is not defined. Here, we used a randomised, double-blind, crossover study to analyse the effects of high fat meals containing fish (EPA and DHA) and algal (DHA only; DHASCO™) sources of n-3 PUFAs on metabolic parameters and endothelial function in 16 healthy men (35-70 y), and evaluated the ***ex vivo*** actions of TRLs isolated from postprandial plasma (6 hours) on human primary aortic endothelial cells (HAECs). Ingestion of either fish or algal n-3 PUFA reduced arterial stiffness whereas measurements of plasma 8-isoprostane F2α concentration (a marker of oxidative stress) revealed differential effects of fish (increased) ***versus*** algal (reduced) n-3 PUFA consumption compared to the control meal (MUFA). Postprandial TRLs isolated after fish ingestion increased expression (4h) of heme-oxygenase-1 mRNA in HAECs compared to control meal and DHASCO meal TRLs, while thioredoxin reductase mRNA expression was enhanced following exposure to TRLs isolated after both fish and algal oil meals. The effects of postprandial TRLs on HAECs paralleled those of artificial chylomicron remnant-like particles prepared using TG extracted from fish and DHASCO™ oils. The results indicate that n-3 PUFA derived from different sources have varied effects on oxidative stress parameters ***in vivo*** and suggest direct beneficial actions of n-3 PUFAs carried in TRLs on endothelial anti-oxidant defence in the postprandial phase.

No conflict of interest

EFFECT OF GARLIC POWDER ON THE LIPID PROFILE AND ATHEROSCLEROSIS DEVELOPMENT IN THE MALE RATS FED WITH A HIGH-GHEE DIET

Y. moradi[1], F. fathi[1], S. hosseini zijoud[2], H. moradi sardareh[2], H. ghasemi[2]
[1]genetics and molecular medicine, kurdistan university of medical sciences, sanandaj, Iran
[2]nutrition and biochemistry, hamadan university of medical sciences, hamadan, Iran

Objective: Garlic is known to have a protective effect against hyperlipidemia and ghee, known as clarified butter or anhydrous milk fat, contains 47.8% saturated fat as a risk factor for hyperlipidemia.

Materials and Methods: We examined the effects of garlic administration on body weight, lipid profiles and plaque formation in the male rats fed with a high ghee diet. Twenty-four male Wistar rats were randomly assigned to one of three groups (n = 8). The control group consumed an ordinary diet, Group 2 received the 31% ghee pellets (high ghee diet) and group 3 received the 8% garlic+31% ghee pellets. After 9 months, serum levels of triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) and atherosclerotic index (AI) were examined. Changes in body weight and daily food intake and also plaque formation were assayed in this survey.

Results*:* The high ghee diet induced significant increases ($P<0.05$) in serum concentrations of TC, TG and HDL-C, and a decrease in LDL-C concentration (group 2). While garlic increased TG ($P<0.05$) and HDL-C levels and declined TC and LDL-C in treated rats (group 3). Meanwhile, ghee and garlic showed a favorable effect in reducing AI ($P<0.05$). No histopathological changes were observed in the Aorta of the rats.

Conclusion*:* Evidence obtained from this study indicates that ghee and garlic have potential in the prevention and control of hyperlipidemia complications and are beneficial when taken as a dietary supplement.

No conflict of interest

EFFECTS OF CHITOSAN ON PLASMA LIPIDS AND LIPOPROTEINS: A 4-MONTH PROSPECTIVE PILOT STUDY

R.V. Giglio[1], M. Rizzo[1], D. Nikolic[1], G. Pecoraro[1], G. Butera[1], A.M. Patti[1], C. Campanella[2], M. Cocchi[3], N. Katsiki[4], G. Montalto[1]

[1]Biomedical Department of Internal Medicine and Medical Specialties, University of Palermo, Palermo, Italy

[2]Department of Experimental Biomedicine and Clinical Neuroscience Section of Human Anatomy, University of Palermo, Palermo, Italy

[3]Paolo Sotgiu Institute for Quantitative and Evolutionary Psychiatry and Cardiology, L.U.de.S. University, Lugano, Switzerland

[4]Second Propedeutic Department of Internal Medicine Medical School, Aristotle University of Thessaloniki Hippokration Hospital, Thessaloniki, Greece

Objective: Chitosan is able to favourably modulate plasma lipids, but available data are not conclusive. Further, no study has so far investigated the effects of chitosan on plasma lipoproteins. Therefore, aim of the present study was to evaluate the effect of chitosan on plasma lipids and lipoproteins in patients with hypertriglyceridemia, not taking other lipid-lowering agents. **Research Design and Methods**: We studied 28 subjects with hypertrygliceridemia (e.g. plasma triglyceride levels greater than 150 mg/dL), 13 women and 15 men, with a mean age of 63±12 years, who were consecutively referred to our Unit of Cardiovascular Prevention for a clinical evaluation. All patients received a chitosan derived from fungal mycelium (Xantonet, Bromatech, Italy) at a fixed dose of 125 mg/day (e.g., two pills daily) on top of their current medications for a period of 4 months. Non-denaturing, linear polyacrylamide gel electrophoresis was used to separate and measure LDL subclasses. **Results**: After 4 months of therapy total-cholesterol reduced by 8%, LDL-cholesterol by 2%, triglycerides by 19%, with a concomitant 14% increase in HDL-cholesterol. We also found a beneficial effects of chitosan on LDL subclasses, with a significant increase in LDL-2 particles (from 37±8 to 47±8%, p=0.0001) and a decrease (although not significant) in atherogenic small, dense LDL. **Conclusions**: In a pilot study, we found a beneficial effect of chitosan on plasma lipids and lipoproteins after 4 months of therapy. Whether these findings may affect cardiovascular risk remains to be established in future studies.

No conflict of interest

BENEFICIAL EFFECTS OF LIRAGLUTIDE ON ATHEROGENIC SMALL, DENSE LOW-DENSITY LIPOPROTEINS IN PATIENTS WITH TYPE-2 DIABETES: A 2-MONTH PROSPECTIVE PILOT STUDY

D. Nikolic[1], M. Rizzo[1], R.V. Giglio[1], V. Di Bartolo[1], A. Ferlita[1], A. Zabbara[1], A. Tamburello[1], V. Giannone[1], G. Montalto[1], A.A. Rizvi[2]

[1]Biomedical Department of Internal Medicine and Medical Specialties, University of Palermo, Palermo, Italy

[2]Division of Endocrinology Diabetes and Metabolism, University of South Carolina School of Medicine, Columbia South Carolina, USA

Background: Elevated levels of small, dense low-density lipoproteins (LDL) significantly influence cardiovascular (CV) risk. Since liraglutide can favourably modulate plasma lipids, we hypothesized that this agent may also modulate small, dense LDL. **Methods**: Ten patients with type-2 diabetes (age: 52±8 years) were enrolled in a 2-month prospective pilot study to evaluate the effect of combined therapy with liraglutide (0.6mg/daily for the first 2 weeks, followed by a dose of 1.2mg/daily) and metformin (1500 mg/daily) on plasma lipoprotein subclasses. LDL size and subclasses were assessed by gel electrophoresis. Patients were newly diagnosed or previously treated subjects on stable does of oral hypoglycemic agents. All samples were fasting. Statistical analysis was performed using non-parametric Wilcoxon paired test. **Results**: At baseline patients had a body-mass-index (BMI) of 29±5, with average fasting glucose 8.7±1.4 mmol/L and HbA1c 8.4±0.6%. After 2 months of therapy fasting glucose and HbA1c decreased (to 7.6±0.9 and 7.5±0.8, respectively, $p<0.05$ for both), as well as BMI (28±3, $p<0.05$). Regarding plasma lipids, HDL-cholesterol significantly increased after therapy (39±7 vs. 36±6, $p<0.05$), while total-cholesterol, triglycerides and LDL-cholesterol slighty lowered (164±38 vs. 168±51, 161±73 vs. 173±98 and 93±41 vs. 97±35 mg/dl, respectively), although the differences did not approach the statistical significance. Large LDL-1 increased from 35±18 to 42±13%, while smaller LDL-3 and LDL-4 decreased from 21±11 to 9±6% and from 6±5 to 1±2%, respectively (all $p<0.05$). **Conclusion**: Liraglutide significantly reduced small, dense LDL. It remains to be tested by future studies whether these findings may have an impact on the cardiovascular outcome.

No conflict of interest

BENEFICIAL EFFECTS OF LIRAGLUTIDE ON CAROTID INTIMA-MEDIA THICKNESS IN PATIENTS WITH TYPE-2 DIABETES: A 8-MONTH PROSPECTIVE STUDY

A.M. Patti[1], M. Rizzo[1], V. Di Bartolo[1], A. Tamburello[1], A. Zabbara[1], A. Ferlita[1], G. Butera[1], V. Giannone[1], A. Rizvi[2], G. Montalto[1]

[1]Biomedical Department of Internal Medicine and Medical Specialties, University of Palermo, Palermo, Italy

[2]Division of Endocrinology Diabetes and Metabolism, University of South Carolina School of Medicine, Columbia South Carolina, USA

BACKGROUND AND AIMS: There is currently hightened interest in the extra-glycemic effects of incretin-based therapies. Although liraglutide, ***a GLP-1 analogue***, has been shown to have pleiotropic benefits, its effect on carotid intima-media thickness (CIMT), a recognized marker of subclinical atherosclerosis, is still largely unknown.

METHODS: We evaluated the effect of liraglutide on CIMT, as assessed by B-mode real-time ultrasound, in a prospective study of 64 patients with type-2 diabetes (age: 63±8 years), when added to metformin at a fixed dose of 1500 mg/daily. Subjects were newly diagnosed or previously treated with oral hypoglycemic agents. The dose of liraglutide was 0.6mg/daily for the first 2 weeks, followed by a dose of 1.2mg/daily. Laboratory and clinical parameters, including CIMT, were evaluated at baseline and after 4 months and 8 months of therapy. Statistical analysis was performed by ANOVA and the Spearman correlation method.

RESULTS: From baseline to 4 months and to 8 months of treatment, CIMT decreased significantly from 1.19±0.47 to 1.05±0.36 to 0.95±0.21 (p=0.0010), along with non-significant reductions in body weight (from 81±17 to 78±16 to 78±16 Kg, p=0.44) and waist circumference (from 105±14 to 102±13 to 102±13 cm, p=0.36). By contrast, there was a significant decrease in fasting glucose (from 8.9±3.8 to 7.1±1.6 to 6.8±1.9 mmol/L, p<0.0001) and hemoglobin A1c (from 8.4±0.8 to 6.7±0.9 to 6.5±0.8 %, p<0.0001). Upon correlational analysis, the changes in CIMT were not associated with changes in any other parameter.

CONCLUSION: Liraglutide significantly reduced CIMT and this was achieved independently of its effects on glucose metabolism.

No conflict of interest

ASSOCIATION BETWEEN GLYCATED HEMOGLOBIN (HBA1C) AND SYNTAX SCORE IN NON-DIABETIC PATIENTS UNDERGOING CORONARY ARTERY BYPASS GRAFTING (CABG)

T. Bhat[1], D. Chauhan[2], N. Shah[3], M. Shariff[4], F. Tamburrino[1], J. McGinn Jr[4]
[1]Division of cardiology, Staten Island university hospital, Staten island, USA
[2]Division of surgery, University of Medicine and Dentistry New Jersey (UMDNJ). Newark, New jersy, USA
[3]Department of Medicine, Staten Island university hospital, Staten island, USA
[4]Department of Cardiothroacic surgery, Staten Island university hospital, Staten island, USA

Aim: SYNTAX score is now increasingly used as an index to guide further revascularization measures in patients with coronary artery disease. This study is aimed at finding association of glycated hemoglobin (HbA1c) and coronary artery disease severity and lesion complexity as assessed by SYNTAX score in non-diabetic patients who ultimately underwent coronary artery bypass grafting (CABG).

Methods: Total 591 non-diabetic patients were selected who underwent CABG after coronary angiography in a community based hospital during the time period of January 2007 to March 2010. Each patient's SYNTAX score was calculated after coronary angiography. They were divided into four groups using quartiles of HbA1c. Logistic regression analysis was performed to evaluate association of HbA1c to SYNTAX score and areas of lesions in individual coronary arteries.

Results: There was no statistically significant association between HbA1c quartiles and SYNTAX score (p=0.54). There was no statistically significant association between HbA1c and total number of diseased vessels (p=0.72) or total number of grafts used (p=0.40) during CABG. We also found no statistically significant association between HbA1c levels and lesions at different anatomical sites (Left main (p=0.47), Proximal left anterior descending (LAD) (p=0.92), Mid LAD (p=0.89), left circumflex artery (p=0.52), right coronary/posterior descending artery (p=0.44).

Conclusion: There is no statistically significant association between HbA1c in non-diabetic patients and location of coronary artery disease, number of diseased vessels or SYNTAX score.

No conflict of interest

TRANSPLANTATION OF ADIPOSE TISSUE-DERIVED MULTI-LINEAGE PROGENITOR CELLS REDUCES SERUM CHOLESTEROL IN HYPERLIPIDEMIC WATANABE RABBITS.

M. Soeda[1], H. Okura[1], M. Morita[1], M. Moriyama[1], H. Moriyama[2], Y. Shizuya[3], T. Hayakawa[2], A. Ichinose[4], A. Matsuyama[1]
[1]Platform for realization of regenative medicine, Foundation for biomedical research and innovation, Kobe, Japan
[2]phamaceutical research and technology insutitute, Kinki university, Higashi-Osaka, Japan
[3]Department of internal medicine, Osaka University Graduate School of Medicine, Suita, Japan
[4]Department of Plastic Surgery, Kobe University Hospital, Kobe, Japan

Background: Familial hypercholesterolemia (FH) is an autosomal co-dominant disease characterized by high concentrations of pro-atherogenic lipoproteins and premature atherosclerosis. We examined the response to *in situ* stem cell therapy using adipose tissue-derived multi-lineage progenitor stem cells (hADMPC) in the LDL-receptor deficient Watanabe heritable hyperlipidemic (WHHL) rabbit, an animal model for homozygous FH.

Methods: WHHL rabbits received either normal control rabbit-derived, GFP-rabbit-derived or WHHL rabbit-derived ADMPC (normal-ADMPC, GFP-ADMPC and diseased-ADMPC, respectively) via the portal vein. This was followed by 12-week immunosuppressive therapy to avoid allogenic rejection. *In situ* survival and differentiation of the ADMPC into hepatocytes was examined by flow cytometry and immunohistochemical analysis, respectively. Lipid profile was examined before-, and 4-, 8- and 12 weeks after transplantation. LDL clearance was examined at the end of the study by ^{125}I-LDL turnover.

Results: *In situ* survival of GFP-ADMPC was confirmed after transplantation. The cells integrated into the hepatic parenchyma and co-expressed GFP and hepatocyte markers such as albumin, indicating that the cells were reprogrammed into hepatocytes-like cells *in situ*. Transplantation of normal-ADMPC but not diseased-ADMPC resulted in a significant reduction of serum total- and LDL- cholesterol after transplantation. ^{125}I-LDL turnover study showed significant improvement in the rate of LDL clearance in the WHHL rabbits with transplanted normal-ADMPC but not in those transplanted with diseased-ADMPC.

Conclusion: Transplantation of ADMPC but not diseased ones corrected the metabolic defects in WHHL rabbits, suggesting that ADMPC transplantation is a potentially useful therapy for FH.

No conflict of interest

NEWLY IDENTIFIED NON-ATHEROGENIC AND ATHEROGENIC LIPOPROTEIN PROFILE IN INDIVIDUALS WITH DYSLIPOPROTEINEMIA IDENTIFIED BY LIPOPRINT SYSTEM

S. Oravec[1], J. Bulas[1], L. Gaspar[1], I. Vacula[1], A. Dukat[1]
[1]2nd Department of Internal Medicine, Comenius University School of Medicine, Bratislava, Slovakia

A new method of electrophoretic lipoprotein separation on polyacrylamide gel (PAG) with the use of Lipoprint LDL System quantifies a non-atherogenic and atherogenic plasma lipoproteins including small dense LDL, the strong atherogenic lipoprotein subpopulations. With respect to the predominance of a non-atherogenic or an atherogenic lipoproteins in the whole lipoprotein profile in plasma, this method distinguishes a non-atherogenic lipoprotein profile phenotype A from an atherogenic lipoprotein profile phenotype B.
The contribution of this method is to confirm the existence of a non-atherogenic type of hyper-betalipoproteinemia and the existence of normolipidemia with atherogenic lipoprotein profile, along with the common and well known atherogenic hyperlipoproteinemia and a non-atherogenic normolipidemia. According to our preliminary analysis of normolipidemic population, the atherogenic lipoprotein profile was determined in more than 6 % of normolipidemic young healthy individuals. These persons represent a risk population. The facilities for identifying these normolipidemic individuals are limited for the time being. On the other hand a non-atherogenic hyper-betalipoproteinemia can be identified, which represents approx 20% of examined individuals with hypercholesterolemia and is not combined with a premature development of atherosclerotic arterial vascular impairment.

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No conflict of interest

IMMUNE MODULATORY ROLE OF LEPTIN IN ATHEROSCLEROSIS

K. Rajendran[1], M. Ragunathan[1], G. Manohar[1]
[1]Department of Genetics, University of Madras, Chennai, India

Leptin, adipocytic peptide hormone is a product of ***ob*** gene, originally considered as an anti-obesity hormone, but it is also crucial hormone for a number of diverse patho-physiological processes, including inflammation, immune modulator function and ultimately leads to atherosclerosis. It is fairly understood that how leptin's immune modulatory function contributes atherogenic metabolic abnormalities in coronary arteries and increasing pro-inflammatory actions. In recent years, several studies on obesity and inflammation have focused predominantly on expression of leptin and IL-6, C-reactive protein (CRP). We examined whether expression of leptin change could contribute to the increase in the concentration of pro-inflammatory markers found with atherosclerosis. The study population consisted of hundred atherosclerosis subjects in and around Chennai based and diagnosed at Department of Cardiology, Stanley Medical College, Chennai. Their serum levels of serum leptin, IL-6 and CRP were measured using ELISA method and compared with one hundred non-CVD controls. Values of leptin, IL-6 and CRP were elevated in CVD subjects and a significant positive relationship was also observed between leptin and BMI, IL-6 or CRP concentrations. An increased level of leptin along with IL-6 and CRP is indicative of the role of these factors involved in inflammatory cascade during Atherosclerosis. Details of which will be discussed later.

No conflict of interest

NEOVASCULARIZATION OF CORONARY TUNICA INTIMA (DIT) FROM ADVENTITIAL VASA VASORUM IS THE CAUSE OF CORONARY ATHEROSCLEROSIS. FACTS AND THE HYPOTHESIS.

V. Subbotin[1]
[1]*Vladimir M Subbotin, Vladimir M Subbotin, Madison, USA*

BACKGROUND:

Coronary atherosclerosis (CA) prevention remains unsatisfactory among high-risk patients. CA also occurs in people lacking accepted risk factors.

ANALYSIS:

It must be clearly stated that the normal human coronary *tunica intima* is not a single-layer endothelium covering a thin acellular compartment, as commonly claimed, but invariably forms a multi-layer cellular compartment, or diffuse intimal thickening (DIT).

If LDL-C invades the DIT from the coronary lumen, as suggested, initial depositions must be most proximal to lumen. Conversely, lipids are initially deposited in the deeper DIT, with no trace at surface. The contradiction is explained by facts that normal DIT is always avascular, receiving nutrients by diffusion, whereas in CA the deeper DIT is always neovascularized by permeable vasculature from adventitial *vasa vasorum*. The proteoglycan biglycan, confined to the deeper DIT in both normal and diseased coronaries, has high binding capacity for LDL-C. However, in normal avascular DIT biglycan-LDL-C interactions are prevented by diffusion distance. In CA, biglycan in the deeper DIT extracts lipoproteins directly from neovasculature. These facts explain all observations: initial lipid depositions occur in the deeper DIT; CA develops quicker at high LDL-C levels; CA can occur at lowered LDL-C levels. This mechanism is not unique to CA: the normally avascular cornea accumulates lipoproteins only after neovascularization, resulting in lipid keratopathy.

HYPOTHESIS:

Neovascularization of the avascular coronary DIT from the adventitial *vasa vasorum* is the cause of CA. CA is not related to inflammation and can occur in individuals with normal levels of LDL, consistent with established facts.

No conflict of interest

DIFFUSE INTIMAL THICKENING OF CORONARY ARTERY, PRECEDING ATHEROSCLEROSIS, DOES NOT CONSTITUTE INITIATION OF THE DISEASE. THEORETICAL CONSIDERATIONS AND PRACTICAL IMPLICATIONS.

V. Subbotin[1]
[1]*Vladimir M Subbotin, Vladimir M Subbotin, Madison, USA*

BACKGROUND:

Coronary atherosclerosis (CA) is always initiated inside diffuse intimal thickening (DIT) of this artery. DIT of coronary a long time has been known as atherosclerosis-prone region. Recent studies suggested that DIT, occurring after birth, is an early stage of CA, causing modern epidemic of coronary artery disease.

ANALYSIS:

In human development, arterial ***tunica intima*** (A*TI*) initially occurs as one-layer endothelium attached to basal membrane. Early in post-natal life, A*TI* evolved into two normal variants of stable cellular arrangements: one-cell layer endothelium, characteristic of small arteries, and multi-cell layered DIT, the feature of coronary and certain main/big elastic arteries. In non-diseased arteries both arrangements continue self-renewal and morphologic stability throughout life. The important fact is that epicardial arterial DIT occurs in all humans without exception and in all vertebrates, with a body mass similar to humans or larger. A morphogenesis, which obligatory occurs in the same anatomical conduit in all humans and a broad variety of vertebrates, is a norm by definition, and constitute biologic trait or phenotype. The popular notion that all human newborns are already affected by CA contradicts both biologic knowledge and common sense.

CONCLUSION:

While we do not know yet what regulations maintain normal DIT phenotype and what causes their imbalance in coronary artery disease, perception of DIT as an initiation of CA is misleading. Apart of logic inconsistency, such perception constitutes a pitfall for the study of CA, because this view discourages from searching for real causes of CA, which could be corrected or prevented.

No conflict of interest

PLASMA OMEGA-3 FATTY ACID DISTRIBUTION AND ATHEROSCLEROSIS IMPLICATIONS IN A UNITED STATES POPULATION

H.R. Superko[1], N.J. Clarke[2], M. Caulfield[2], M.M. Redor-Goldman[2], S. Goldman[2], J. Sninsky[3]
[1]Medicine, Celera, Alameda, USA
[2]Research, Nichols Laboratory, San Juan Capistrano, USA
[3]Research, Celera, Alameda, USA

Background: Omega-3 fatty acids play a role in atherosclerosis risk and prevention. Population distributions of blood levels are required to determine risk ranges. We undertook to determine the population distribution of omega-3 fatty acids in a free living US population obtained through a large National laboratory. In the JELIS trial an EPA/AA ratio >0.75 was associated with significantly lower CV events and has been suggested as a clinical goal. In the Physicians Health Study EPA+DHA % of total fatty acids <3.45% was associated with increased risk and in the Heart and Soul prospective study an EPA+DHA% > 3.6% was associated with reduced all-cause mortality.

Methods: Blood samples were obtained from 1,102 subjects. Plasma fatty acid concentration in plasma phospholipids (PL) was determined utilizing a liquid chromatography mass spectrophometric (LCMSMS) method. PL were extracted and hydolyzed before analysis of the FA by LCMSMS. Values are reported as individual PL or the sum of EPA + DHA, expressed as a weight percent of total FA present ('omega-3 index').

	Total	Female	Male	p F vs M
N	1,102	600	502	
Age yrs	56.6±15.7	56.2±15.6	57.0±15.8	0.82
Omega-3 Index	4.42±2.71	4.36±2.54	4.50±2.66	0.19
EPA%	1.03±1.11	0.96±1.03	1.13±1.18	0.99
DHA%	3.39±1.68	3.40±1.68	3.37±1.67	0.40
AA	0.72±0.69	0.69±0.60	0.77±0.78	0.98
EPA/AA	1.91±2.51	1.86±2.50	2.09±2.73	0.93

Conslusion: Blood levels of omega-3 fatty acids have a wide SD reflecting large intra-population variability. However, no gender differences were observed. Based on risk levels established in clinical trials, 32% had an omega-3 index < 3.5% and 44% had a EPA/AA < 0.75, reflecting increased CHD risk.

Conflict of interest

MECHANISM OF HYPERCHOLESTEROLEMIA IN PRAGUE HEREDITARY HYPERCHOLESTEROLEMIC (PHHC) RAT

M. Vlachova[1], R. Poledne[1], M. Jirsa[1], J. Kovar[1]
[1]Centre of Experimental Medicine, Institute for Clinical and Experimental Medicine, Prague 4, Czech Republic

PHHC rat develops hypercholesterolemia after cholesterol feeding (without the cholic acid). The hypercholesterolemia is due to accumulation of VLDL, IDL and LDL. However, its pathogenesis has not been explained yet.

Objectives: To explain pathogenesis of hypercholesterolemia and identify genes involved in its development in PHHC rat.

Methods: 1. Nascent VLDL of PHHC and control Wistar rats were characterised after tyloxapol administration. 2. The rate of disappearance of ^{125}I-labelled VLDL from PHHC and Wistar rats was determined in Wistar rats *in vivo*. 3. Hepatic transcriptome analysis was carried out in male PHHC and control Wistar rats fed chow or 1% cholesterol diet for 3 weeks. The results for selected genes were validated by qPCR.

Results: PHHC rats fed dietary cholesterol produce VLDL carrying twice as much cholesterol as VLDL of controls. Cholesterol-rich VLDL of PHHC rats are *in vivo* catabolised more slowly than VLDL of Wistar rats. No differences were found in the hepatic gene expression of both strains in response to dietary cholesterol. However, several genes were differently expressed between both strains independently of the diet (*Aldh1a7*, *Yc2*, *Apof*, *Ugt2b*, *Cdh17*, *Ltc4s*, etc.). *Apof* as the only gene of lipoprotein metabolism was sequenced and 17bp insertion found in PHHC rats.

Conclusions: PHHC rats produce cholesterol-rich VLDL that are catabolised more slowly. New candidate genes for hypercholesterolemia were identified in our experimental model. Their exact role in pathogenesis of hypercholesterolemia remains to be determined.

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No conflict of interest

EFFECTS OF EZETIMIBE + VS USUAL DOSES OF STATINS:DATA FROM EVERYDAY PRACTISE

K. Vukelic[1], M. Bunc[2]
[1]Diabestes, Health Centre Grosuplje, Grosuplje, Slovenia
[2]Cardiology, University Clinical hospital Ljubljana, Ljubljana, Slovenia

AIM/INTRODUCTION:

In patients at high cardiovascular risk efficacy of statin therapy to achieve recommended LDL-C goals is often limited. In the IN-CROSS randomized clinical trial, combination of ezetimibe+simvastatin (EZE+simva) was more effective in reaching lipid goals compared with uptitration of statin monotherapy. We sought to test efficacy and safety of EZE+simva compared with statin uptitration in a »real world« setting of high-risk patients.

METHODS:

In this program 100 patients with uncontrolled hypercholesterolaemia (LDL –C >2 mmol/L) taking a stable dose of statin and high cardiovascular risk with proven coronary disease, were randomised to two groups in a 1:2 ratio. Here, we report on the first 30 patients completing the program. At baseline, 10 patients were prescribed higher doses of their statin, while 20 were switched to EZE+SIMVA (10/40 mg). At 3 month follow-up, we checked serum lipid levels, and transaminases. End points: Achieving LDL-C <2 mmol/L, safety, and tolerability.

RESULTS:

Patients (66.6±9.35 years-old; 83% males) were mostly (86%) diabetics; 60% were in secondary prevention after myocardial infarction, and 40% had been revascularized for stableCAD. Antilipemic therapy was safe and well tolerated in both groups. There were no meaningful differences in laboratory values between the two groups, nor transaminase elevations. Seventy% of EZE+SIMVA patients achieved recommended LDL-C level, versus 60% in the uptitration group. Detailed statistical analysis is underway.

CONCLUSION:

Effective control of LDL-C levels is an important goal in secondary prevention of in high-risk patients. EZE+SIMVA therapy is a safe approach in »real world patients«.

No conflict of interest

LASER-RANIBIZUMAB TREATMENT FOR RETINOPATHY OF PREMATURITY IN THRESHOLD-PRETHRESHOLD DISEASE. THREE YEARS OF EXPERIENCE.

L.P. Orozco-Gomez[1], L. HERNANDEZ-SALAZAR[1], S. Moguel-Ancheita[1], M.A. Ramirez-Moreno[2], M.V. Morales-Cruz[2]
[1]Ophthalmology, Centro Medico Nacional "20 de Noviembre" ISSSTE, Mexico City, Mexico
[2]Neonatology, Centro Medico Nacional "20 de Noviembre" ISSSTE, Mexico City, Mexico

Retinopathy of prematurity (ROP) is the abnormal proliferation of retinal blood vessels in some preterm infants; the pathophysiology is not completely clear, however, it has been associated with hyperoxia/ hypoxia and other factors like vascular endothelial growth factor (VEGF).

The approved treatment for threshold-prethreshold stage of ROP according to the study ETROP is the diode laser application in the areas of the avascular retina to avoid the secretion of VEGF and, therefore, changes to more advanced stages of retinopathy. However, there is no control on VEGF secreted prior the laser treatment and it may influence treatment failure. Among the alternatives to block VEGF it has been suggested to use antiangiogenic molecules as intravitreal Ranibizumab which acts directly on all VEGF-A isoforms.

We designed a prospective, experimental, longitudinal study, including newborns of either <32 weeks of gestation or with a birth weight <1500 g, with threshold-prethreshold retinopathy.

We included 34 eyes of 17 patients. Age at birth was 29.9 ±2.6 weeks. Birth weight was 1,120 ± 253g. All patients received Ranibizumab and laser in the same session under sedation and we demonstrated regression of ROP in all cases from the first week after treatment without systemic side effects attributable to Ranibizumab.

No conflict of interest

THE EFFECT OF MAGIC SHEOSTM ON SUBJECTIVE AND HEMODYNAMIC PARAMETERS IN DIABETIC AND/OR PVD PATIENTS

E. Klainman[1], M. Stanetzki[2], Z. Klein[2], A. Yarmolovsky[3], G. Fink[3]
[1]Cardiology & Pulmonology, Gefen and pulmonology, Givatayim, Israel
[2]Cardiology, Gefen, Givatayim, Israel
[3]Pulmonology, Kaplan MC, Rehovot, Israel

Background: The "Magic Shoes"TM provides a physiological massage along with acupressure and reflexology functions, which might act mentally and physiologically.
Aim of study: To assess the effect of the "Magic Shoes", while using them for a month, 15-30 minutes each day, by subjective and objective parameters in diabetic and/or PVD pts.

Material and Methods: 30 pts were studied. 14 with DM only; 3 with PVD and 13 with both – DM and PVD. 24 males, mean age of 68+/-11y. PVD was confirmed by ankle-brachial index (ABI) of <0.9, with foot symptoms. All pts underwent fool examination twice, at baseline visit and after a month. It included: BP, HR and ECG; Two questionnaires relating to foot symptoms and sleep disorders; Hemodynamic evaluation by ICG for measuring total peripheral resistance (TPR), SV, among others. 6 parameters were scored, 1 point for each: BP, ABI, SV, TPR and the two subjective questionnaires – a total of 6 or -6 possible points for improvement or worsening of these parameters. Two weeks after baseline visit, pts were assessed by the questionnaires alone, while checking adverse events related to the treatment.

Results: There were significant release in foot pain,tingling and pain wakes at night ($p<0.05$). In the 6 point scoring assessment there were improvements in 17 pts (+3.3 mean scoring), worsening in 6 pts (-1.5 mean scoring), and no changes (0 scores) in 7 pts. The total ICG scoring of TPR and SV was+13, for ABI+10, and for BP+5. No adverse events were reported.

Conclusions: Significant improvements were observed in the subjective parameters as well as in the objective ones while using the "Magic Shoes". Such findings might indicate this tool as helpful in pts with DM or PVD, mentally and physiologically. Further data with larger sample of pts might strengthen the current results.

No conflict of interest

RELATIONSHIP BETWEEN POST-TREATMENT PLATELET REACTIVITY AND ISCHEMIC AND BLEEDING EVENTS AT 1-YEAR FOLLOW-UP IN PATIENTS RECEIVING PRASUGREL

M. Laine[1], S. armero[1], F. paganelli[1], L. bonello[1]
[1]Cardiology, Hôpital Nord, Marseille, France

Post-treatment platelet reactivity (PR) is associated with ischemic and bleeding events in patients receiving P2Y12 receptor antagonists.

OBJECTIVES:

We aimed to study the relationship between post-treatment PR after a 60-mg loading dose (LD) of prasugrel and 1-year thrombotic and bleeding events.

METHOD:

Patients were prospectively included in this multicenter study if they had a successful percutaneous coronary intervention (PCI) for acute coronary syndrome (ACS) and received prasugrel. The platelet reactivity index (PRI) was measured using the Vasodilator-Stimulated Phosphoprotein index (VASP) after a prasugrel LD. Endpoints included the rate of thrombotic events and bleeding events at 1 year.

RESULTS:

Among the 301 patients enrolled, 9 (3%) were lost to follow-up at 1 year. The rates of thrombotic and bleeding events at 1 year were of 7.5% and 6.8%, respectively. Receiver-operating curve (ROC) analysis demonstrated an optimal cut-off value of 53.5% of PRI to predict thrombotic events at 1 year. Using this cut-off value we observed that patients exhibiting high on-treatment platelet reactivity (HTPR) had a higher rate of thrombotic events (22.4% vs. 2.9%; $P < 0.001$). In parallel the optimal cut-off value of PRI to predict bleeding was 16%. Patients with a PRI $\leq$ 16% had a higher rate of bleeding events compared with those with a PRI > 16% (15.6% vs. 3.3%; $P < 0.001$). In multivariate analysis, the PRI predicted both thrombotic and bleeding events (OR: 1.44, 95% confidence interval [CI]: 1.2-1.72; $P < 0.001$ and OR: 0.75, 95% CI: 0.59-0.96; $P = 0.024$ [respectively, per 10% increase]).

CONCLUSION:

Platelet reactivity measurement after a prasugrel LD predicts both ischemic and bleeding events at 1 year follow-up for ACS patients undergoing PCI.

No conflict of interest

BIOLOGICAL EFFICACY OF A 600 MG LOADING DOSE OF CLOPIDOGREL IN ST-ELEVATION MYOCARDIAL INFARCTION

M. Laine[1], L.B. bonello[1], S. armero[1], F. paganelli[1]
[1]Cardiology, Hôpital Nord, Marseille, France

Optimal platelet reactivity (PR) inhibition is critical to prevent thrombotic events in primary percutaneous coronary intervention (PCI). We aimed to determine the relationship between high on-treatment platelet reactivity (HTPR) and ST-elevation myocardial infarction (STEMI) following a 600 mg loading dose (LD) of clopidogrel. We performed a prospective monocentre study enrolling patients on clopidogrel undergoing PCI. The VASP index was used to assess PR inhibition after clopidogrel LD. HTPR was defined according to the consensus as a VASP index ≥50%. The present study included 833 patients undergoing PCI. Most patients had PCI for an acute coronary syndrome (58.7%). The mean VASP index was 50 ± 23% with a large inter-individual variability (range: 1-94%). Patients with a VASP index ≥50% were significantly older (p= 0.03), with a higher body mass index (BMI) (p<0.001), more often diabetic (p=0.03), taking omeprazole (p=0.03), admitted for an acute coronary syndrome (ACS) and with a high fibrinogen level compared to good responders (VASP <50%). In multivariate analysis BMI, omeprazole use, ACS and high fibrinogen level (p<0.001) remained significantly associated with HTPR. Of importance, in this analysis STEMI was independently associated with HTPR when compared with the other forms of ACS (NSTEMI and unstable angina) with an odd ratio of 2.14 (95% CI: 1.3 -3.5; p=0.003). In conclusion, STEMI is associated with high on-treatment platelet reactivity following 600 mg of clopidogrel. The present results suggest that 600 mg of clopidogrel may not be able to achieve an optimal PR inhibition in STEMI patients undergoing PCI and more potent drugs may be preferred.

No conflict of interest

CLINICAL IMPACT OF GENETICALLY DETERMINED PLATELET REACTIVITY

M. Laine[1], L.B. Bonello[1], A.S. Arméro[1], F. Paganelli[1]
[1]Cardiology, Hôpital Nord, Marseille, France

Dual antiplatelet therapy associating aspirin and clopidogrel dramatically reduced the rate of major adverse cardiac events in the aftermath of percutaneous coronary intervention. Clopidogrel is a pro-drug requiring a two-step hepatic biotransformation thanks to the cytochrome P450 enzyme system (CYP450). Genetic polymorphism of CYP450 (e.g. CYP2C19*2) responsible for an altered clopidogrel metabolism is a major cause of high on treatment platelet reactivity (HTPR) and further of thrombotic events in stented patients. Studies demonstrated that HTPR could be overcome in poor metabolizers thanks to increased loading doses or maintenance doses of clopidogrel or even the use of more potent antiplatelet agents such as prasugrel. Other genetic polymorphisms have also been related to HTPR: ABCB1, ATP2B2, TIAM2. Large-scale randomized trials with clinical endpoints remains necessary in order to determine the appropriate antiplatelet therapy in patients presenting with loss of function alleles.

No conflict of interest

AMPUTATION RATE AND MORTALITY IN ELDERLY PATIENTS WITH CRITICAL LIMB ISCHEMIA NOT SUITABLE FOR REVASCULARIZATION

R. Martini[1], A. GM[1], D. A[1], C. R[1], Z. P[1], S. O[1], N. F.[1]
[1]"UOC Angiologia, Azienda Ospedale Università di Padova, padova, Italy"

"In spite of recent progress in revascularization and anesthesiology procedures, in vascular centers today there are still patients with Critical Limb Ischemia (CLI) considered not suitable for revascularization. Most of these patients are elderly, with high co-morbidity factors, poor run off arterial limb vessels, and often with a salvageable limb. They are absent or neglected in the literature, and untreated. We report details of 24- month amputations and mortality rates in 90 patients with CLI considered unsuitable for revascularization. Patients with endstage general conditions or needing immediate primary amputation were excluded. All patients received multidisciplinary assessment. The median age was 78.4 years; 28 patients (31.1%) had rest pain only, and 62 (68.8%) had ischemic skin foot-leg wounds or gangrene < 2 cm. Sixteen patients (37.7%) were assessed as unsuitable for revascularization because of poor functional status, and 76 (64.4%) because of inadequate outflow limb vessels. Drugs to manage pain were administered to all patients (100%), prostanoid infusions were given to 80 (88%), anti-platelet drugs to 87 (96%), low molecular weight heparin or oral anticoagulants to 13 (14%), spinal cord stimulation to 3 (3%), hyperbaric oxygen treatment to 16 (17%) and wound treatment to 62 (68.8%). Toe or other foot-sparing amputations had a rate of 13%. After 24 months, the major amputation rate was 9.3% and the mortality rate 23.2%. In conclusion our study shows that, in spite of progress in revascularization procedures, there are still patients with CLI considered unsuitable for revascularization and who could benefit from non-surgical treatment if a tailored approach is used"

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LACK OF ASPIRIN RESISTANCE IN PATIENTS WITH CORONARY ARTERY DISEASE

L. Muszbek[1], N. Homoródi[2], E.G. Kovács[1], E. Katona[1], Z. Bereczky[1], L. Balogh[2], A.G. Shemirani[3], H. Péterfy[4], R.G. Kiss[5], I. Édes[6]

[1]Clinical Research Center Medical and Health Science Center, Univesity of Debrecen, Debrecen, Hungary

[2]Institute of Cardiology Medical and Health Science Center, Univesity of Debrecen, Debrecen, Hungary

[3]Vascular Biology Thrombosis and Haemostasis Research Group of the Hugarian Academy of Sciences, Univesity of Debrecen, Debrecen, Hungary

[4]Research Laboratory, Diagnosticum Co., Budapest, Hungary

[5]Department of Cardiology, State Health Center, Budapest, Hungary

[6]Institute of Cardiology Medical and Health Science Center, University of Debrecen, Debrecen, Hungary

Due to its antiplatelet effect, aspirin is widely used in the prevention of atherothrombotic events. By acetylating Ser529 residue in platelet cyclooxygenase-1 (COX-1) it prevents the binding of arachidonic acid (AA) to the catalytic site and inhibits the production of thromboxane (TX) A_2. As aspirin prevents acute vascular events only in part of the patients, the controversial term aspirin resistance was introduced. We define aspirin resistance as the lack of sufficient acetylation of platelet COX-1 at Ser529 by aspirin, while insufficient protection against acute vascular events is considered as ineffectiveness. Most recently we developed a novel method that directly detects acetylated and non-acetylated COX-1 (acCOX-1, nacCOX-1) by specific monoclonal antibodies (Kovács et al. Thromb Res 2013;131:320-4). Determination of AA-induced TXB_2 production in platelet rich plasma was used as an indirect measure of COX-1 inhibition. Using these new methods we have demonstrated the lack of aspirin resistance in healthy volunteers. 159 patients with coronary artery disease, being on long-term aspirin monotherapy, were enrolled in the present study. If non-compliance was controlled, in none of them was aspirin resistance observed. COX-2 mRNA expression in platelets, as detected by RT-PCR, did not diminish the effect of aspirin. Results of AA-induced aggregation and ATP-release were in complete accordance with those obtained by the above methods, and only three patients failed to show definite aspirin effect by VerifyNow Aspirin assay. Platelet aggregation induced by ADP, epinephrine, collagen and PFA-100 assay (collagen/epinephrine cartridge) revealed the effect of aspirin only in part of the patients.

No conflict of interest

THE INFLUENCE OF PRE-ANESTHETIC MEDICATION WITH CLONIDINE ON GLYCEMIC RESPONSE IN CORONARY ARTERY BYPASS GRAFT SURGERY WITH CARDIOPULMONARY BY-PASS.

K.L.,P.L.,I.P. M. Salgado Filho[1,2]
[1]*"Anesthesia, Federal University of Rio de Janeiro, Rio de Janeiro*
[2]*Cardiovascular Anesthesia, National Institute of Cardiology, Rio de janeiro*
[3]*Cardiovascular Anesthesia, National Institute of Cardiology, Rio de Janeiro*
[4]*Enfermagem, Universidade Está*
cio de Sá
, Juiz de Fora, Brazil"

"Background: Clonidine is usualy used as pre-anesthetic medication (PM) in CABG. The objective of this study was to use clonidine as PM on patients undergoing CABG with CPB, and assessment the glycemia during the surgery and 24 hours after the surgery.
Methods: We performed a randomized clinical trial with 46 patients divided into two groups, the Clonidine Group (CG) and the Placebo Group (PG), who underwent CABG with CPB. We administered midazolam, and treatment with the placebo or clonidine (2.0 mcg/Kg) as PM. The anesthesiologist was blind. Glycemia was evaluated before anesthetic induction, during CPB and in 24 hours after surgery.
Results: Demographic data were homogeneous for both groups. The CG patients had higher sedation levels on the Ramsay scale than the PG patients (P=0.02). The CG and PG had hyperglycemia at CPB1, CPB2 and CPB3 when compared with the post-induction moment.
The CG had higher levels of glycemia than the PG at moment CPB3 ($p < 0.05$). In the intraoperative period, 16 (76,1%) of the CG patients needed insulin, while 5 (22,7%) in the PG needed insulin (p= 0.0007). In the postoperative, 12 (57,1%) of the CG patients and 5 (23,8%) of PG used insulin (p =0.03), and 6 (28,5%) of the CG patients and 1 (4,5%) of the PG had hypoglycemia (p = 0.04).
Conclusions: CG had higher levels of sedation, a greater need for the use of intravenous insulin in the intraoperative and postoperative and higher incidences of hypoglycemia in the postoperative period.

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EFFECTS OF EZETIMIBE ADDED TO ON-GOING PRAVASTATIN ON SERUM LIPOPROTEIN, CHOLESTEROL ABSORPTION AND GLUCOSE METABOLISM IN HYPERCHOLESTEROLEMIC JAPANESE PATIENTS

J. Sasaki[1], *Y.I. Ikeda*[2]
[1]*Postgraduate School, International University of Health and Welfare, Fukuoka, Japan*
[2]*Internal Medicine, Tagawa Municipal Hospital, Fukuoka, Japan*

Objective: A randomized trial was implemented to evaluate effects of ezetimibe (EZE) add-on to pravastatin (PRA) on the levels of serum lipoprotein, cholesterol absorption and glucose metabolism in Japanese. **Methods**: Study subjects were those who had LDL cholesterol of 120 mg/dL or greater with low-dose PRA (5,10mg/day) treatment, and were randomly allocated to either EZE (10mg/day) add-on or double-dose PRA treatment, and follow-up measurements were done after 3 months. The cholesterol absorption levels were measured by serum sitosterol (SIT), campesterol(CAM).

Results: 96 and 95 patients were allocated to EZE and PRA, respectively. LDL cholesterol and apo B decreased by 15.6% and 13.9% in the EZE group, and by 5.9% and 4.4% in the PRA group, respectively. SIT and CAM decreased by 48.0% and 36.3% in the EZE group, respectively, and increased by 17.0% and 14.1% in the PRA group, respectively. There were no significant changes in fasting glucose and HbA1c in both groups.Serum insulin and HOMA-IR increased significantly in both groups. Both treatments were well tolerated. **Conclusions**: These findings suggest that EZE added on low-dose PRA is more efficient for lipid management compared with the doubling dose of PRA. EZE inhibits cholesterol absorption and increases cholesterol synthesis. These two regimens did not show a different effect on glucose metabolism.

No conflict of interest

ROLE OF RIVAROXABAN IN THE TREATMENT OF VENOUS THROMBOEMBOLIC DISEASE ASSOCIATED WITH CANCER

M. Sharifi[1], T. Emami[2], F. Schwartz[3], C. Bay[4], T. Rouse[2]
[1]Endovascular Interventions, Arizona Cardiovascular Consultants& A.T. Still University, Mesa, USA
[2]Endovascular Interventions, Arizona Cardiovascular Consultants, Mesa, USA
[3]School of Osteopathic Medicine, A.T. Still University, Mesa, USA
[4]Biostatistics, A.T. Still University, Mesa, USA

Background: Deep venous thrombosis (DVT) in the setting of cancer is associated with a high mortality and morbidity rate. Warfarin resistance and failure are frequently seen in such patients which render warfarin as a suboptimal anticoagulant. Low molecular weight heparins are the recommended anticoagulants however their parenteral and usually twice daily administration make them inconvenient for many patients. The role of rivaroxaban in this setting has not been investigated.

Methods: 36 patients with extensive DVT in the setting of cancer underwent percutaneous endovenous intervention (PEVI). DVT was in the upper extremities or internal jugular vein in 6 patients, left and right lower extremity or iliac vein in 19 and 5 patients respectively and bilateral in 6 patients. 14 patients (39%) were on warfarin at the time of DVT with therapeutic INR in 10 of these patients (71%). PEVI was performed within 26±4 hours of admission. Heparin was given to the patients and stopped after completion of PEVI. Two hours after PEVI, rivaroxaban was initiated at 20 mg daily and continued indefinitely. The mean follow up was 9±2 months. The patients were evaluated for mortality, recurrent venous thromboembolic disease (VTE) and bleeding during the follow- up period.

Results: There was no bleeding or recurrent VTE in any patient. All patients tolerated the anticoagulation regimen. The mean duration of hospitalization was 34±6 hours. There were 3 deaths due to cancer at follow-up.

Conclusions: In patients with cancer and extensive DVT, administration of rivaroxaban following PEVI is safe and effective leading to a considerable reduction the duration of hospitalization and no early or late bleeding or recurrent VTE. It further obviates the inconveniences associated with long term parenteral anticoagulation.

No conflict of interest

EFFECT OF MELATONIN ON CARDIAC INJURY AFTER PRIMARY PERCUTANEOUS CORONARY INTERVENTION: A RANDOMIZED CONTROLLED TRIAL.

A. Talasaz[1], P. Ghaeli[2], S.S. Vejdani[3]
[1]Department of Clinical Pharmacy Faculty of Pharmacy Tehran University of Medical Sciences, Tehran Heart Center Tehran University of Medical Sciences, tehran, Iran
[2]Department of Clinical Pharmacy Faculty of Pharmacy Tehran University of Medical Sciences, Roozbeh Hospital Tehran University of Medical Sciences, tehran, Iran
[3]Department of Clinical Pharmacy Faculty of Pharmacy Tehran University of Medical Sciences, Department of Clinical Pharmacy Faculty of Pharmacy Tehran University of Medical Sciences, tehran, Iran

BACKGROUND:

Several studies have reported that the antioxidant properties of melatonin can provide cardiac protection through scavenging of free radicals. This study sought to investigate the efficacy of melatonin on cardiac biomarkers, myocardial-specific protein troponin-T and creatine phosphokinase-MB (CPK-MB), in patients with ST-segment elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (p- PCI).

METHODS:

In this randomized clinical trial, A total of 40 patients with STEMI planned to undergo p-PCI were randomly assigned to two groups of A- receiving melatonin plus standard treatment [n=20] and B-control group, receiving only standard therapy [n=20]. The following parameters: troponin-T and CPK-MB were assessed at the following time points: preoperatively (baseline) and at 6 hours after procedure.

RESULTS:

Melatonin could significantly reduce the level of CPK-MB (118.2 ± 21.09 IU/L in the treated group versus 198.24 ± 20.94 IU/L in the control group; p value = 0.01). But there was no difference in the mean cardiac troponin-T level between two groups (2491 ± 664 µg/L vs. 2801 ± 620 µg/L; p value = 0.73).

CONCLUSION:

Our results revealed that melatonin can be considered as a safe adjunctive medication to the standard regimen after p-PCI for the aim of decreasing cardiovascular events. But this was a pilot study with a small number of patients and further studies are needed to confirm the beneficial effect of melatonin in patients with STEMI.

No conflict of interest

PACEMAKER IMPLANTATION AS TRIGGER OF TAKOTSUBO SYNDROME

P.T.,C.G.,A.C.,J. "P. Awamleh[1], C.C. nez[2], bal"[2]
[1]Cardiology, Hospital Universitario de Getafe
[2]Cardiology, Hospital de Fuenlabrada, Madrid, Spain

"A 67 years old female patient received a VDD pacemaker because of complete AV block. She was admitted in our hospital for pacemaker implantation and it wasn´t necessary the use of catecholamines. A VDD pacemaker was implanted one day after admission, with no complications during the procedure. Sixteen hours after the implantion she started with oppresive chest pain that made the patient wakes up. Blood pressure was 190/90 mmHg, 78 bpm; ECG showed sinus rhythm with ventricular stimulated beats. The echocardiogram perfomed at this time was very typical of Tako-Tsubo syndrom. Ejection fraction was mildly depressed because of the presence of apical dyskinesia. (figure 1, panels A, B). Cardiac biomarkers were lighty elevated: maximun I-troponin 4.33 ng/ml, with maximun CK 290 U/i. A coronary angiography was perfomed and we found that coronary arteries were normal.

After treatment with intravenous nitrates, betablockers, aspirin and ACE inhibitors, patient became asymptomatic.

She was discharged a few days after, and revised 4 months later. She was asymptomatic, under treatment with aspirin, estatines, betablockers and ACE inhibitors. Blood pressure was normal, blood analysis was normal too. Pacemaker was revised, normally functioning. A new echocardiogram was perfomed, and we found that there was not apical disquinesia. Contractiliy was completely recoved. (figure 2, panels C, D)

This is the first reported case of Tako Tsubo syndrome after not complicated cardiac pacemaker implantation.

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INDUCED HEART RATE TURBULENCE USING SINGLE VENTRICULAR PREMATURE COMPLEX STIMULATION IN PATIENT WITH CORONARY ARTERY DISEASE

I. Firdaus[1], I.D.A.R. Mappangara[2], M. Munawar[3], S. Dharma[3], D. Juzar[3]
[1]Cardiology and Vascular Medicine, National Cardiovascular Center Harapan Kita Hospital, Jakarta, Indonesia
[2]Cardiology and Vascular Medicine, Wahidin Sudirohusodo Hospital, Makasar, Indonesia
[3]Cardiology and Vascular Medicine University of Indonesia, Harapan Kita Hospital National Cardiovascular Center, Jakarta, Indonesia

ABSTRACT

Background. Sudden cardiac death is common in patients with coronary artery disease (CAD). As autonomic imbalance plays an important role in the development of malignant ventricular arrhythmia, it is very important to characterize autonomic activity in patients with CAD. Recently, heart rate turbulence (HRT), a strong predictor of mortality, has been used as an accurate parameter of autonomic activity.

Objective. To characterize HRT in patients CAD and factors influencing its value.

Methods. This observational study used single ventricular premature complex stimulatin in patients with CAD who underwent percutaneous coronary intervention since March to June 2007 in National Cardiovascular Center Harapan Kita, Jakarta.

Results. From 29 patients enrolled, male patients were dominant (25 patients) with age range from 39 to 74 years old with mean of age 58.8 ± 9.6 years. HRT parameter showed broad spectrum of value, TO value was -1.19 ± 3.75% and TS value was 8.75 ± 8.1 ms/RRI. Abnormal HRT value was found in 14 CAD patients (48%). There were no independent factors associated with HRT value found from univariate analysis.

Conclusion. Almost half of CAD patients enrolled in this study had abnormal HRT value. There were no independent factors associated with HRT value.

Keywords: heart rate turbulence, turbulence onset, turbulence slope.

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DABIGATRAN REDUCE CANCELLATIONS AND DELAYS IN PATIENTS UNDERGOING ELECTIVE CARDIOVERSION FOR ATRIAL FIBRILLATION

A. Ramirez Moreno[1], J.C. Salas Serantes[2], C. Pera Rojas[3], R. Bravo Marqués[4], J.R. Siles Rubio[1], L. Fernández López[4], T. Gil Jiménez[4], L. Iñigo García[4], P. Chinchurreta Capote[4], J. Muñoz Bellido[4], F.J. Martínez García[4]
[1]CARDIOLOGY, HOSPITEN ESTEPONA, Málaga, Spain
[2]INTENSIVE CARE, HOSPITEN ESTEPONA, Málaga, Spain
[3]ANESTHESIOLOGY, HOSPITEN ESTEPONA, Málaga, Spain
[4]CARDIOLOGY, Hospital Costa del Sol. Marbella, Málaga, Spain

BACKGROUND: Procedural delays due to inadequate anticoagulation for patients undergoing elective cardioversion for atrial fibrillation are common. Guidelines require acenocumarol treatment resulting in a therapeutic INR (greater than 2) for at least 3 weeks pre cardioversion. We studied the impact of using Dabigatran with its predictable antithrombotic profile in this population. Procedural delays, waiting times, efficacy and complications were assessed.

METHODS: Patients who were diagnosed with atrial fibrillation for whom elective cardioversion was planned were anticoagulated to reduce the risk of periprocedural stroke. During the 12 month study period it was recommended that patients who were eligible and not on anticoagulation therapy previously use Dabigatran. The number of procedure cancellations for inadequate anticoagulation, wait times, procedural efficacy and complications were compared between this group and a historical control group (previous years elective cardioversions (2011)) who were using acenocumarol.

RESULTS: Cardioversion cancellations for inadequate anticoagulation occurred in 4.8% of patients taking Dabigatran. Whereas for patients taking Acenocumarol, 30% of procedures were cancelled and required rebooking ($p<0.01$). This resulted in an increase in mean days waiting from 16.1+/- 9 days for Dabigatran treated patients to 28.1+/- 27 days for Acenocumarol treated patients ($p<0.01$). There were no significant differences in cardioversion efficacy (97 vs 90 %, $p=0.09$) or complications between the groups.

CONCLUSION: Use of the anticoagulant Dabigatran as compared to Acenocumarol prior to elective cardioversion for atrial fibrillation resulted in more efficient care with fewer procedural cancellations and re-booking's, and shorter wait times without an increase in complications or effect on cardioversion efficacy.

No conflict of interest

THE ROLE OF ELECTROCARDIOGRAM FOR LEFT MAIN CORONARY ARTERY OCCLUSION DETECTION IN PATIENTS WITH ACUTE CORONARY SYNDROME

F. Sciarra[1], E. Perugini[1], G. Casella[1], S. Zagnoni[1], L. Riva[1], G. Di Pasquale[1]
[1]Cardiology, Maggiore Hospital, Bologna, Italy

Aim. To identify peculiar electrocardiogram (ECG) aspects associated with subocclusion or acute occlusion of the left main coronary artery (LMCA) in order to performe an emergency reperfusion strategy.

Methods. We retrospectively analyzed 24 ECG from patients (mean age 76 yrs; males 67%) admitted at Maggiore Hospital Bologna Italy CCU between January 2007 and January 2013 for acute coronary syndrome (ACS) associated with angiographic sub-occlusion (15 patients) or acute occlusion (9 patients) of the LMCA. Percutaneous coronary intervention was performed in 23 patients (96%). 12 patients were treated with intra-aortic balloon pump (IABP). Intra-hospital death occurred in 8 patients, 5 of them with angiographic evidence of acute LMCA occlusion.

Results. In 18 cases ECG showed ST-segment elevation in lead aVR ≥ 1 mm. Intraventricular conduction delay was documented in 16 cases (mean QRS-complex duration 130 msec) with a right bundle branch block ECG pattern in 3 patients and left bundle branch block ECG pattern in 4 patients. A widespread ST-segment depression with negative T waves and ST-segment elevation in the antero-lateral leads was respectively found in 7 (29%) and 5 (21%) patients.

Conclusion. In patients with ACS ST-segment elevation in aVR lead is predictive of LMCA involvement. In patients subgroup with acute occlusion of the LMCA, a right bundle branch block associated with left axial deviation and ST-segment elevation in the lateral leads is the most represented ECG pattern with a remarkable prognostic value.

No conflict of interest

PSYCHOSOCIAL DISTRESS IN IMPLANTABLE CARDIOVERTER DEFIBRILLATOR PATIENTS; A CROSS-SECTIONAL STUDY WITH A GENDER PERSPECTIVE

I. Thylén[1], D. Moser[2]
[1]Dept of Cardiology, County Council of Östergotland, Linköping, Sweden
[2]College of Nursing, University of Kentucky, Lexington, USA

Aim: Most patients cope well with an implantable cardioverter defibrillator (ICD), but psychosocial distress and ICD-related concerns have been reported in about 20% during the first year(s). Previous studies have not distinguished between genders, and the course of psychosocial distress over time is unknown. In this cross-sectional study we examined quality-of-life, prevalence of anxiety and depression, and ICD-related concerns from a gender perspective in ICD-patients.

Methods and Results: All Swedish ICD-recipients were invited to participate and 3067 patients (55% response; 80% male, mean age 66 years) completed standardized measures of quality-of-life, general anxiety and depression, and ICD-related concerns on one occasion. Time since implantation ranged from 1-23 years (mean 4.7 years). The majority (64%) had received their ICD for secondary prevention. A total of 36% of the men and 30% of the women had experienced defibrillating shocks ($p<0.01$). In connection with the latest shock, the pain as well as the anxiety experience was considered as moderate by the men (4.4 and 4.3, respectively) and as average by the women (5.1 and 5.4, respectively), when rated on a 10-point visual analogue scale ($p<0.01$, respectively, for gender comparison). Women reported worse quality-of-life (mean index 0.790 vs. 0.825), higher prevalence of anxiety (21% vs. 15%) and ICD-related concerns (31% vs. 25%) then did men ($p<0.001$, respectively), while there where no differences in depression (9%).

Conclusions: Most ICD-recipients described themselves having a good quality-of-life, without any emotional distress or ICD-related concerns, but among the minority with distress morbidity, women fare worse than men.

No conflict of interest

3D-ECHOCARDIOGRAPHY ALLOWS EASIER LOCATION OF MITRAL VALVE PROLAPSE FOR NON-EXPERT OPERATORS

G. Alunni[1], F. Conrotto[1], M. Giorgi[1], E. Picardi[1], E. Cerrato[1], A. Milan[1], S. Marra[1]
[1]Cardiology 2, Città della salute e della scienza di Torino- Molinette, Turin, Italy

BACKGROUND
A pre-operative assessment of mitral valve (MV) anatomy is essential in patients with organic MV prolapse. Although 2-dimensional (2D) transthoracic (TTE) and transesophageal (TEE) echocardiography provide precise information regarding MV anatomy; 3-dimensional (3D) TTE could increase the understanding of more complex abnormalities of MV apparatus and individual scallop identi?cation.
OBJECTIVES
The aim of this study is to compare the accuracy of 2D-TTE, 2D-TEE, 3D TTE versus surgical inspection in the recognition and localization of MV prolapse.
METHODS
Thirty patients with severe mitral regurgitation due to MV prolapse were prospectively evaluated. 27 patients underwent to a complete 2D-TTE, 3D TTE and 2D TEE before surgery and were enrolled in the study. Echocardiographic data were compared with surgical inspection. 2D-TTE, 3D TTE further evaluation was performed post-processing by non-expert operators and compared with surgical inspection.
RESULTS
The three-dimensional technique was feasible in 27/30 patients, with a mean execution times of 8 + / - 4 min.
The 3D echocardiography showed higher accuracy than the 2D method (89% vs. 77%) in identification of the posterior leaflet prolapse and in complex lesions (96% vs 81%) (where two or more scallops were interested or where there were broken chordal), with a similar accuracy in identification of the anterior leaflet prolapse (89% vs. 92%)
Moreover, 3D echocardiography showed higher diagnostic accuracy in the location of MV prolapse even when the analysis was performed by unskilled operators (77% vs 44% for posterior leaflet, 85% vs 70 % for anterior leaflets and 85% vs 77% for complex lesions.
Conclusions
3D trans thoracic echocardiography is feasible and useful in location of MV prolapse (single or complex) even if executed by an unskilled operator.

No conflict of interest

AORTIC PULSE WAVE VELOCITY AND CAROTID INTIMA THICKNESS IN DIFFUSE CORONARY ECTASIA: IS THERE A RELATIONSHIP ?

E.M.R.E. Yalcinkaya[1], C.E.M. Barcin[1], H. Kabul[1], U. Yuksel[1], Y. Gokoglan[1]
[1]Cardiology, Gulhane Military Medical Academy, Ankara, Turkey

Objectives: It has been show that carotid intima-media thickness (CIMT) and aortic pulse wave velocity (PWV) constitute important independent risk factors for cardiovascular disease. We hypothesized that CIMT, aortic PWV are increased in patients with diffuse coronary artery ectasia.

Study design: Diffuse coronary artery ectasia (CAE) has been defined as a diffuse dilatation (at least 50% greater than the diameter of the normal portion) in at least one coronary artery and localized or diffuse disease in other coronary artery. Study group consisted of 54 consecutive patients (43 males, 11 females; mean age 65.7±13.1 years) with diffuse CAE whereas 58 patients (47 males, 11 females; mean age 64.3±10.9 years) without CAE comprised the control group. CIMT, aortic PWV, serum uric acid levels and NLR were measured in two groups of patients who underwent coronary angiography.

Results: Study and control groups were similar in terms of age, sex, body mass index, and the frequencies of hypertension, hyperlipidemia, diabetes mellitus, and smoking (p>0.05). The mean CIMK and aortic PWV were higher in the study group compared to the control group (0.81±0.16 mm and 0.74±0.13 mm, p=0.021; and 11±2.4 m/sec and 9±2.7 m/sec, p<0.001). A significant but a weak relationship was found between CIMK and the presence of diffuse CAE (r=0.219; p=0.021).Compared to CIMT, a more powerful positive correlation was found between aortic PWV and the presence of diffuse CAE (r=0.361; p<0.001) Logistic regression analysis showed that the relationship between diffuse CAE and aortic PWV (OR 1.339; 95% CI 1.135-1.579; p=0.001) was independent of other factors. An aortic PWV ≥ 9.2 m/sec measured on admission had a 78% sensitivity and 62% specificity in predicting diffuse CAE at ROC analysis.

Conclusion: According to the results of the present study, both CIMT and PWV were increased in patients with diffuse CAE. Of note, only the PWV was found to have an independent relationship with the presence of CAE. It may be speculated that, the involvement of media compared to intima is more likely in patients with CAE. This pathophysiology may explain why PWV, compared to CIMT, has more powerful relationship with CAE.

No conflict of interest

CORONARY RISK STRATIFICATION IN OLD PATIENTS UNDERGOING KIDNEY TRANSPLANTATION

C. Bösmüller[1], G. Mayer[2], S. Eschertzhuber[3], A. Pomaroli[3], G. Pölzl[4], M. Frick[4], R. Öllinger[1], S. Schneeberger[1], J. Pratschke[1]
[1]Transplant Surgery, University Hospital, Innsbruck, Austria
[2]Nephrology, University Hospital, Innsbruck, Austria
[3]Anaesthesiology, University Hospital, Innsbruck, Austria
[4]Cardiology, University Hospital, Innsbruck, Austria

Purpose: Minimization of the cardiac risk by a preoperative coronary risk stratification in old patients transplanted within the Eurotransplant Senior Program (ESP).

Methods: Definition of 3 groups basing on coronary risk factors: Group 1 = low risk: 1-2 risk factors as age >50, hypertension, hyperlipidemia, obesity, smoking, familiar history of coronary artery disease (CAD). Group 2 = medium risk: >2 of these factors or mild peripheral artery disease (PAD) /congestive heart disease (CHD) /left ventricular hypertrophy. Group 3 = high risk: symptomatic CAD, proven signs of CAD, diabetes mellitus, severe PAD/CHD, cerebrovascular accident. Evaluation methods are adapted to the risk groups: Group 1:ECG, Echocardiography, exercise stress test. Group 2:stress-echocardiography / calcium score, in case of symptomatic CAD (or calcium score > 100): coronary CT, in case of suspected >50% stenosis (or calcium score>700):coronary angiography (CAG). Group 3: CAG or CT; revascularization in case of significant stenosis or acute angina pectoris; yearly reevaluations during the waiting time for transplantation. (Historical note: myocardial szintigraphy was performed prior to the establishment of coronary CT).

Results: in our center we experienced no letal cardiac event in the first 20 postoperative months in the > 70 years old patients (n= 19). (1 / 5 years patient survival 95 / 67%, graft survival 100 / 82%). All totally 4 patients who died for cardiac failure had a pretransplant CAG-proven CAD.

Conclusion: An exact preoperative coronary risk stratification contributes to acceptable results in > 70 years transplant recipients.

No conflict of interest

SEVERE BICUSPID AORTIC VALVE STENOSIS, SINGLE RIGHT CORONARY ARTERY AND MAIN STEM-EQUIVALENT ATHEROSCLEROSIS: A PATHOLOGICAL TRIAD PRESENTING WITH EFFORT-INDUCED SYNCOPE

T.J. Cahill[1], H. McConkey[1], R. De Silva[2], A. Kardos[1]
[1]Department of Cardiology, Milton Keynes Hospital, Milton Keynes, United Kingdom
[2]Department of Cardiothoracic Surgery, John Radcliffe Hospital, Oxford, United Kingdom

The presence of a single coronary artery is rare, identified in 0.02-0.07% in published series. The functional significance of a single right coronary artery (RCA) is variable, but has been reported to underlie effort-induced ischemia and sudden death, due to either retro-aortic compression or myocardial hypoperfusion. We report a patient with a triad of single RCA, atherosclerosis and severe bicuspid aortic valve (BAV) stenosis.

A previously fit and well 59 year-old man was admitted following syncope during a game of football. Admission ECG and blood tests were normal, but echocardiography revealed a heavily calcified BAV with a peak transvalvular gradient of 72 mmHg and valve area of 0.69 cm^2, consistent with severe aortic stenosis. Left ventricular size and function was normal. Subsequent coronary angiography demonstrated a single RCA arising from the right sinus of Valsalva, giving rise to the PDA and PLV before providing the OM and LAD branches. There was at least moderate atherosclerotic plaque prior to the origin of the OM branch, equivalent to left main stem disease. The patient underwent curative aortic valve replacement with a mechanical prosthesis and coronary artery bypass grafting (LIMA to LAD, SVG to circumflex).

To our knowledge, this is the first report of a patient with severe BAV, single RCA and atherosclerosis in the main stem-equivalent. We hypothesise that these three abnormalities are pathologically synergistic, leading to hypoperfusion of the myocardium on exertion, resulting in the clinical presentation with effort-induced syncope.

No conflict of interest

THE USE OF CONSCIOUS SEDATION IN TRANSOESOPHAGEAL ECHOCARDIOGRAM (TOE) PROCEDURES

P. Chew[1], A. Abdool[1], M. Ashe[1], M. Burgess[1]
[1]Cardiology Department, Aintree University Hospital, Liverpool, United Kingdom

Background: Mortality from Transoesophageal Echocardiogram (TOE) has been quoted as 0.02%. The use of conscious sedation, midazolam has been related to these events. The National Patient Safety Agency of NHS in England had received nearly 500 midazolam patient safety incidents between 2004-2008.

Aims: To examine the use of midazolam for conscious sedation in the TOE lab and to determine the incidence of complications in relation to sedation. Further analysis performed to determine the compliance rate of TOE proforma being completed.

Methods: Retrospective analysis of 58 patients who underwent TOE between 5th Jan – 12th May 2011 at Aintree University Hospital,Liverpool,UK were performed via electronic records. Clinical data were reviewed and the usage of TOE proforma sheet which records observations pre and post-TOE were recorded. Data analysed with simple mathematical calculations.

Results: Midazolam doses used varied between 1-10mg, with a mode of 4mg. Flumazenil was used in 1 case (2%) for reversal of sedation but no mortality was found. At least 50% of the sample population had either cardiac pathology or ≥ 2 co-morbidities. TOE proformas' were only used in 40% of the total population.

Conclusion: Careful uptitration of midazolam doses are important in TOE, especially in the elderly population with multiple co-morbidities. Adherence to TOE proforma for documentation of the procedure is sub-optimal. Other trusts are encouraged to evaluate their use of midazolam and to audit their use of the TOE proforma in order to reduce incidence of complications from sedation, and therein help to maintain optimal standards of patient care.

No conflict of interest

HYPERTENSION POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (PRES)

M. Darouichi[1]
[1]*Radiology, Hospital, La Chaux-de-Fonds, Switzerland*

Posterior Reversible Encephalopathy Syndrome (PRES) is a rare entity whose diagnosis is clinical and radiological. It results from acute hypertension and endothelial damage in the brain. The pathogenesis remains unclear.

Case report

Ten days after abdominal surgery, a 76 years-old woman presented with cortical blindness, epilepsy, left-sided motor hemisyndrome and severe arterial hypertension. CT showed bilateral cortical and subcortical hypodensities in the parieto-occipital region. MRI confirmed PRES with bilateral parietal and occipital hyperintensities on T2 and FLAIR imaging. No hemorrhagic lesions were detected. Antihypertensive treatment was administered immediately with a good evolution.

Discussion

The first description of the PRES was made by Hinchley in 1996, is an acute or subacute reversible neurological syndrome, associated with hypertension. Predisposing factors are pregnancy toxemia with underlying arterial hypertension, and drugs.

Physiopathology of PRES is unknown, two theories are suggested:1.Loss of autoregulation of cerebral blood flow leading to ischemia and cytotoxic cerebral edema.2.Arteriolar vasodilatation, endothelial dysfunction, hyperperfusion, and disrupting the blood-brain barrier secondary to high blood pressure, and temporary failure of autoregulatory capabilities of the cerebral vessels.

Symptoms include headaches, altered mental status, visual disturbances, epilepsy and severe hypertension with high blood pressure.

Diagnosis is confirmed by MRI with symmetrical bilateral edema in the posterior cerebral hemispheres. Brain stem or the cerebellum can be involved.

Decreased hypertension is an emergency within few hours and prognosis is fairly benign.

CONCLUSION

Hypertension and other worsening predisposing factors of PRES should be treated promptly. Rapidly favorable but delaying treatment may result cerebral hemorrhage, neurological disability and death.

No conflict of interest

CARDIAC NORADRENERGIC DENERVATION IN MULTIPLE SYMMETRIC LIPOMATOSIS – A PATHOPHYSIOLOGICAL INSIGHT

V.R. Fonseca[1], A. Militão[1], P. Mireille[1], R.M.M. Victorino[1]
[1]Clínica Universitária Medicina II, Hospital de Santa Maria, Lisboa, Portugal

Introduction: Multiple symmetric lipomatosis (MSL) is a rare disease of unknown etiology characterized by multiple subcutaneous lipomas with a symmetrical distribution. One interesting aspect about MSL is a high incidence of sudden cardiac death despite low incidence of metabolic syndrome and coronary arterial disease. Autonomic nervous system dysfunction may probably explain this feature of MSL as some studies showed.

Case Report: A 74-years old man was admitted with first episode of atrial fibrillation and symptoms of orthostatic intolerance. He had a morphotype suggestive of MLS. A 123I-metaiodobenzylguanidine (MIBG) myocardial scintigraphy was conducted for evaluation of cardiac autonomic nervous integrity, since atrial fibrillation precluded the classical Ewing approach. The heart-to-mediastinum ratio was 1.68 (normal > 2.2) and washout ratio was 6.94% (normal 10 ± 9%). Myocardial perfusion scintigraphy precluded ischemia as the cause for cardiac autonomic neuropathy.

Conclusion: This represents the first reported case of MSL autonomic neuropathy detected by 123I-MIBG scintigraphy and suggests this approach could have a role in MSL stratification by risk of sudden cardiac death and in exploring MSL disease mechanisms. In light of this report, we could propose that MLS is the final feature of a mitochondrial defect with autonomic neuropathy caused by beta-adrenergic receptors down-regulation.

No conflict of interest

ACUTE INFERIOR MYOCARDIAL INFARCTION CAUSED BY AORTIC DISSECTION, LOCALIZED IN THE RIGHT SINUS OF VALSALVA.

K. Furuhashi[1], F. Tabata[1], Y. Tsutsumi[2], M. Ishiyama[1], S. Taguchi[1]
[1]Cardiology, Mito Medical Center, Higashi-ibaraki-gun Ibaraki-m, Japan
[2]Emergency medicine, Mito Medical Center, Higashi-ibaraki-gun Ibaraki-m, Japan

Introduction

Aortic dissection is a life-threatening acute condition and may shows symptoms like an acute coronary syndrome. And it is well-known that stanford type A aortic dissection would be causing acute inferior myocardial infarction.We report the case of acute inferior myocardial infarction, complicated with aortic dissection localized in the right sinus of valsalva.

Case Report

A 70-year-old woman with no prior history presented to our emergency department with continuous chest pain from the day before arrival. Electrocardiography (ECG) showed a ST-segment elevation in leads II, III and aVF with idioventricular rhythm, suggesting an acute inferior myocardial infarction. Routine computed tomography (CT) was done for differential diagnosis, but it revealed no obvious findings of aortic dissection. Coronary angiography (CAG) was done.

Engaging the catheter to the right coronary artery was very difficult. CAG showed a double-contour around the right coronary and the right sinus of valsalva. We concerned about coronary and aortic dissection. Retrospectively reviewing CT again, it showed that was stanford type A aortic dissection localized in the right sinus of valsalva. The patient was transported to the aorta center to repair of aortic dissection.

Discussion

Localized dissection in the sinus of valsalva is rare case of the aortic dissection. We review and evaluate the image diagnostic methods in the routine CT to verify that type of the dissection. To reconstruct 3D-CT, the left anterior oblique (LAO) view-slice and other view of the sinus of valsalva will contribute to diagnose.

No conflict of interest

EFFECTIVENESS OF RADIAL APPROACH FOR CORONARY ANGIOGRAPHY IN OCTOGENARIAN PATIENTS WITH SEVERE AORTIC STENOSIS

I. Gomez Blazquez[1], S. Fernandez Barbeira[1], A.A. de Miguel Castro[1], G. Bastos Fernandez[1], V.A. Jimenez Diaz[1], A. Ortiz Saez[1], J.A. Baz Alonso[1], A. Iñiguez Romo[1]
[1]Interventional Cardiology, Hospital Meixoeiro, Vigo, Spain

Purpose: Octogenarians undergoing transcatheter valve implantation or surgical valve replacement for severe aortic stenosis are increasing worldwide. They have an increased risk for periprocedural complications associated to preoperative coronary angiography (CA). Although transradial approach (TRA) constitutes an alternative to reduce vascular complications, tortuosity of vessels and aortic root dilation in elderly patients with aortic stenosis might lead to TRA failure. Our aim was to evaluate the effectiveness of TRA for CA in octogenarians with severe aortic stenosis. Methods: From January 2006 to May 2013, 717 octogenarians with severe aortic stenosis underwent CA by TRA as initial route of access at our center. Procedural failure was defined as the need to change to another vascular route to complete the CA. Results: Mean age of patients was 83.7±3.0 years and 58.2% were females. The initial approach was right TRA in 637 (88.8%) patients and left TRA in 80 (11.2%) patients. Subclavian tortuosity (14.8% vs 8.8%,p=0.145) and radial tortuosity (16.6% vs 12.5%,p=0.343) were more frequent in right TRA compared with left TRA. Of total, 35 patients(4.9%) had severe spasm of radial artery. Aortic root dilation with diameter>50 mm was present in 49 patients (6.8%) and severe aortic regurgitation in 53 patients (7.4%). Vascular complication (hematoma>5 cm or radial perforation) occurred in 7 patients (1%). Procedural failure rate was 6.7% and crossover to femoral artery was required in 26 cases (3.6%). Logistic regression analysis identified as predictors of TRA failure: subclavian tortuosity (OR 4.37 [95%CI 2.28-8.37]), severe spasm of radial artery (OR 3.05 [95%CI 1.21-7.70]) and severe aortic regurgitation (OR 3.27 [95%CI 1.10-10.58]). Conclusions: In our series of octogenarian patients with severe aortic stenosis, TRA approach for CA was associated with a low rate of procedural failure, being subclavian tortuosity, severe spasm of radial artery and severe aortic regurgitation the main predictors of failure.

No conflict of interest

EFFICACY AND SAFETY OF RIGHT VERSUS LEFT TRANSRADIAL APPROACH FOR INVASIVE CORONARY PROCEDURES IN OCTOGENARIAN PATIENTS

I. Gomez Blazquez[1], S. Fernandez Barbeira[1], V.A. Jimenez Diaz[1], G. Bastos Fernandez[1], A.A. de Miguel Castro[1], A. Ortiz Saez[1], J.A. Baz Alonso[1], A. Iñiguez Romo[1]
[1]Interventional Cardiology, Hospital Meixoeiro, Vigo, Spain

Purpose: Although right subclavian tortuosity is one of the predictors of transradial approach (TRA) failure in octogenarian patients undergoing invasive coronary procedure, there is no conclusive data concerning benefits of using left (LRA) or right radial access (RRA) in this group of patients. Our aim was to evaluate the efficacy and safety of LRA compared with RRA in octogenarians undergoing invasive coronary procedure. Methods: We analyzed 3,153 consecutive invasive coronary procedures in octogenarians that were performed by TRA as initial route of access at our center, between 2006 and 2012. Procedural failure was defined as the need to crossover to another vascular route to complete the procedure. Hematoma >5 cm or radial artery perforation were considered as vascular complications. Results: Of total procedures 1,914 (60.7%) were diagnostic coronary angiographies and 1,239 (39.3%) were percutaneous coronary interventions. The initial approach was RRA in 2,905 patients (92.1%) and LRA in 248 patients (7.9%), with similar demographic characteristics in both groups. Subclavian tortuosity was more frequent in the right side (16.5% vs 8.6%; p=0.02), but procedural failure rate was similar in RRA and LRA groups (RRA 6.8% vs LRA 6.7%; p = 0.97). Mean procedural time (RRA 30±22 vs LRA 31±19 minutes; p = 0.47), mean fluoroscopy time (RRA 11±9 vs LRA 12±8 minutes; p = 0.28) and dose area product (RRA 93±91 vs LRA 91±84 Gy.cm^2; p = 0.81) were similar in both groups. Vascular complication rate was 2.1% and 2.2% with RRA and LRA, respectively (p=0.80). Conclusions: In our series of octogenarian patients, both RRA and LRA approach for invasive coronary procedures had low rates of failure and vascular complications. LRA was a valid alternative but its usage was not associated with a reduction in procedural failure rate.

No conflict of interest

PROGNOSTIC VALUE OF ECHOCARDIOGRAPHIC-DERIVED CALCIUM INDEX IN CORONARY ARTERY DISEASE DIAGNOSED BY 64-MULTIDETECTOR COMPUTED TOMOGRAPHY

B. Marí López[1], J. Lacalzada Almeida[1], J. Gonzalez[1], A. de la Rosa[1], M. Izquierdo[1], A. Duque[1], A. Barragan Acea[1], L. Laynez Cerdena[1]
[1]Cardiology, Hospital Universitario de Canarias, Santa Cruz De Tenerife, Spain

Recent studies have shown the ability of echocardiographic calcium index (ECI) of mitral annulus calcification (MAC) and aortic valve and wall calcification (AVC), to predict coronary artery calcium score (CACS) and the presence of obstructive coronary artery disease (CAD) assessed by multidetector computed tomography (MDCT) as well as the presence of obstructive CAD by invasive coronary angiography. However, none of these studies have shown whether ECI may determine prognosis. The aim of this study was to determine whether ECI assessed by TTE predicts future cardiovascular events. A prospective cohort study of 82 consecutive outpatients with low- moderate cardiovascular risk profile and chest pain referred for noninvasive coronary angiography by MDCT. ECI was blindly assessed by TTE and correlated with subsequent cardiovascular events during a follow up period of 36 months. Mean age 66 ± 13 years (46 males). No patients died during follow-up and there were 23 coronary ischemic events, 4 myocardial infarct (MI) and 19 angina Canadian Cardiovascular Society (CCS) class III or IV. In the event group, mean ECI was 7.7 ± 3.2, compared to 2.9 ± 1.9 in those without events ($P < 0.001$). AUC of ECI as a predictor of coronary ischemic events, MI and angina CCS class III or IV, post-MDCT was 0.92 (95% CI: 0.852–0.987); $P < 0.001$. ECI ≥ 7 had a sensitivity of 77.3% (95% CI: 54.6–92.2), a specificity of 90% (95% CI: 79.5–96.2), positive predictive value of 73.9% and negative predictive value of 91.5%. Kaplan–Meier survival analysis showed a significant difference between patients with ECI ≥7 and those with lower values regarding a subsequent ischemic event, (logrank,$\chi 2$: $P < 0.001$). ECI ≥ 7 seems to be a strong predictor of coronary ischemic events over a period of 36 months after measurement. ECI may be used to establish CAD prognosis.

No conflict of interest

LEFT ATRIAL MECHANICAL FUNCTION MEASURED BY TRANSTORACIC ECHOCARDIOGRAPHY PREDICTS POST-OPERATIVE ATRIAL FIBRILLATION

J. Gonzalez[1], J. Lacalzada-Almeida[1], B. Mari-Lopez[1], A. de la Rosa[1], J.L. Iribarren[2], J.J. Jimenez[2], M. Izquierdo[1], A. Barragan-Acea[1], A. Duque[1], I. Laynez-Cerdena[1]
[1]Cardiology, Hospital Universitario de Canarias, SANTA CRUZ DE TENERIFE, Spain
[2]Intensive Care, Hospital Universitario de Canarias, SANTA CRUZ DE TENERIFE, Spain

Background: Postoperative atrial fibrillation (POAF) is a frequent complication of cardiac surgery (CS), occurring in up to 40-50% of patients in the immediate postoperative period.

Objectives: The aim of this study was to examine whether left atrial (LA) mechanical function, measured by transthoracic echocardiography is a predictor of postoperative atrial fibrillation (POAF).

Methods: A total of 147 subjects (mean age 67±13 years) in sinus rhythm, underwent preoperative transthoracic echocardiograms and immediate postoperative echocardiograms. Left atrial (LA) mechanical function was measured with M mode and 2D variables, distance between mitral valve and upper left atrial side in four chambers view. Mitral inflow velocity, pulmonary venous flow velocity with Pulsed wave doppler and mitral annulus velocity was assessed with tissue doppler imaging (TDI).

Results: POAF occurred in 37 (25%) patients. On bivariable analysis, older patients had more POAF (69±16 vs 65±12, P<0,01; years old). Interestingly, preoperative echocardiographic variables associated with POAF included: greater distance between mitral valve and upper left atrial side (4.9±0.7 mm vs 4.3±0.9 mm; P<0.01), early diastolic E-wave velocity (90±33 cm/s vs 75±33 cm/s; P=0.01) and pulmonary venous flow reversal velocity (29±8.3 cm/s vs 26±5.3 cm/s; P=0.02); and low late diastolic mitral annulus velocity measured by TDI (7.5±1.7 cm/s vs 8.6±2.1 cm/s; P=0.02). Postoperative echocardiographic variables associated with POAF were late diastolic A-wave duration (153±60 ms vs 124±44 ms P=0.01). On univariate logistic regression analysis, the variables associated with POAF included preoperative LA volumes, postoperative late diastolic A-wave duration (ms) and pre-postoperative E/A transmitral variation (porcentual E/A transmitral variation ((E/A postoperative – E/A preoperative value)/ (E/A postoperative value) x 100), with 80% correct classified cases.

Conclusion: LA volume, mitral A-wave duration and pre-postoperative E/A transmitral variation are independent predictors of POAF. Preoperative and postoperative LA dysfunction assessed by Doppler-echocardiography correlates with greater risk of developing POAF. This might help us to identify patients with high risk of POAF in clinical practice.

No conflict of interest

METABOLIC SYNDROME IN OBESE PATIENTS WITH BINGE EATING DISORDER: FACTOR STRUCTURE

C. Grilo[1], T. Udo[1], S. McKee[1]
[1]Psychiatry, Yale University School of Medicine, New Haven, USA

Objective: Metabolic syndrome is strongly linked with cardiovascular disease, but there has been debate over which metabolic measures constitute metabolic syndrome. Obese individuals with binge eating disorders (BED) are one of the high risk patient groups for developing metabolic syndrome due to their excess weight and maladaptive eating patterns, yet, the clustering patterns of metabolic measures have not been examined in this patient group.

Methods: 347 adults (72% women; 62% white) were recruited for treatment studies for obese patients with BED. We used the VARCLUS procedure in the Statistical Analysis System (SAS) to investigate the clustering pattern of metabolic risk measures. VARCLUS extracts non-overlapping factors and is useful for comparisons across patient groups.

Results: VARCLUS yielded four factors: obesity (body-mass-index [BMI] and waist circumference), lipids (HDL and triglycerides), blood pressure (systolic and diastolic blood pressure), and glucose regulation (fasting serum glucose and Hb1Ac). Low R^2 ratios indicated variables fit strongly to assigned components which were well formed. The four factors accounted for 84% of the total variance, and each factor contributed similarly. Inter-correlations between the four factors were low. Subgroup analyses by sex and by race (white vs. black) yielded the same four factor structure.

Conclusion: The factor structure of metabolic syndrome in obese individuals with BED is generally consistent with previous studies with normative population samples and did not vary by sex or race. VARCLUS suggested that four factors make equivalent contributions to the metabolic syndrome which differs from non-PCA factor analytic findings in previous studies.

No conflict of interest

CARDIAC CT: VALUE FOR MONEY IN CORONARY DISEASE DIAGNOSIS

S. Guerrini[1], F.G. Mazzei[2], E. Casorelli[3], E. Foderà[1], A. Cirigliano[1], N. Cioffi Squitieri[1], J. Attene[3], F. Bui[3], M.A. Mazzei[1], L. Volterrani[1]

[1]Medical Surgical and Neuro Sciences Section of Radiological Sciences, University of Siena, Siena, Italy

[2]Medical Surgical and Neuro Sciences Section of Radiological Sciences, Azienda Ospedaliera Universitaria Senese, Siena, Italy

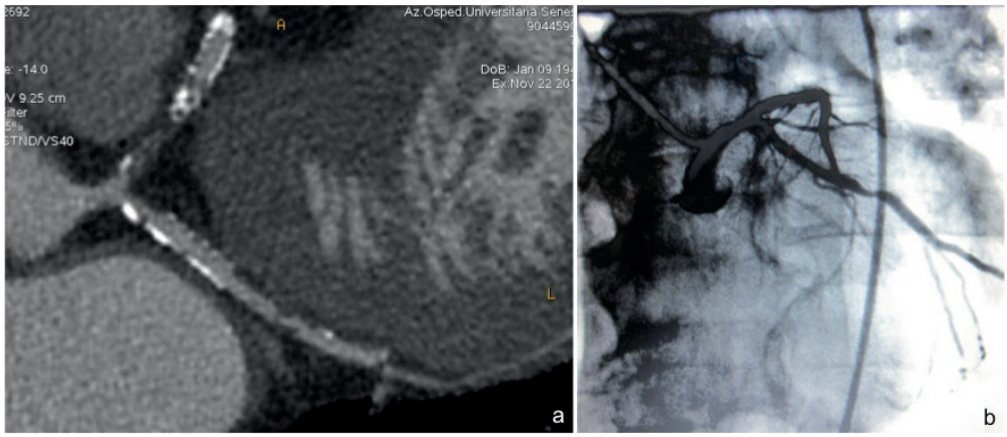
[3]UO Cardiologia/Utic, Ospedale Riuniti Val di Chiana - Ausl 7, Nottola, Italy

Aim: to assess the cost-effectiveness of diagnostic cardiac CT (CCT), in terms of benefits to the patients suitable for coronary angiography (CA).

Material and methods: Between January 2011 and April 2013, 123 patients (71 male and 52 female, mean age 58 years, range 25-91), from our cardiologic department underwent CCT. The inclusion criteria was: presence of aspecific chest pain, known or suspected coronary artery disease (CAD), and an uncertain or negative exercise stress test (EST). All patients were elegible for CCT examination. The cost expressed as Euros (€) in 2011-2013, the price was 2,027.88 for CA and 230.00 for CCT.

Results: All patients were divided into low risk (pre-test probability 20%), intermediate risk (69%) and high risk (11%) for CAD. Sixty-eight patients (55%) showed an uncertain EST, 44 (35%) a negative EST and 13 (10%) a positive EST. Among 123 patients 20 underwent elective CA after the results of CCT. Two patients had an acute coronary syndrome after CCT and were promptly managed during CA on the basis of CCT imaging (Fig. 1).

Conclusions: The economic evaluation results demonstrate that using CCT immediately after the exercise stress testing is a cost-effective diagnostic strategy to avoid ineffective invasive procedures, especially in patients with a low or intermediate risk and in an undedicated hospital.



No conflict of interest

CLINICAL AND ANGIOGRAPHIC PROFILE OF CORONARY ARTERY DISEASE IN PATIENTS WITH RECOVERY POSITIVE COMPARED TO CONVENTIONAL POSITIVE TREADMILL STRESS TEST

S. haque[1], W. dabdoob[1], U. bedradeen[1], G. maouf[1], W. khalid[1], H. alzaem[1], A. gehani[1]
[1]cardiology, hamad medical corporationheart hospital, Doha, Qatar

BACKGROUND: To study the clincial and angiographic profile of coronary artery disease (CAD) in patients with Recovery positive (RP) vs. Conventional positive (CP) treadmill stress test (TMT).

METHODS: This prospective study of 300 patients was conducted from 2005 to 2012 at Heart Hospital Doha Qatar. Coronary angiogpahy was performed within 6 months for 150 patients who had a positive TMT in the recovery period compared to 150 patients who had TMT positive after stage 2 and before the recovery phase.

RESULTS: Mean age was 52.5±7.4 years and similar in the two groups. Diabetes was more in RP than CP group (50% vs 24.7% respectively, p<0.0001 while Hypertension was similar (73.3% vs 69.0% respectively). Mean Ejection Fraction was also similar (56.3±5.9 vs 58.9±6.6 respectively). ST changes were seen very commonly in inferolateral leads in RP group 59.3% as compared to only 0.7% in CP group p<0.0001. In RP group 82(54.7%) of the patients had normal or insignificant CAD vs 51(34.9%) in CP group, p<0.0001. Left anterior descending (LAD) disease was higher in RP group (45.3%) than CP group (39.7%) p<0.329. Left circumflex (LCx) and Right Coronary (RCA) diesase was similar in both groups. Three vessel disease was seen more commonly 27(18%) in RP group vs 17(11.64%) in CP group, p<0.103.

CONCLUSION: Recovery phase positive TMT is associated with ST changes more commonly in inferolateral leads.Nearly half of Recovery positive TMT had either normal or insignificant CAD on angiogram but when positive they had higher proportion with three vessel disease involving the LAD.

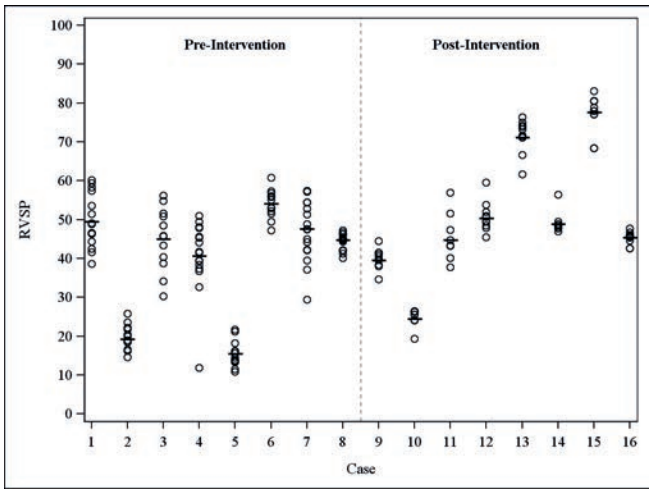
No conflict of interest

THE INTER OBSERVER VARIABILITY OF RIGHT VENTRICULAR SYSTOLIC PRESSURE MEASUREMENTS BY ECHOCARDIOGRAPHY CAN BE REDUCED BY GUIDELINE BASED TEACHING INTERVENTION.

A. Enzevaei[1], J. Hung[1], A. Day[1], C. Londry[1], A. Sanfilippo[1], C. DArsigny[1], H.C. Falkson[1], A. Johri[1]
[1]Medicine, Queen's University, Kingston, Canada

Background: Decisions to treat Pulmonary Hypertension (PH) and evaluation of response to therapy are known to be affected by Inter-observer variability (IOV) in the interpretation of RV systolic pressure (RVSP). This study's objective was to determine whether a teaching intervention could reduce IOV in RVSP interpretation. **Methods**: 8 cases with echo views of the right heart, the inferior vena cava (IVC), and Doppler profile of TR were shown to fifteen interpreters of varying experience. The cases were of varying technical quality and a wide range of RVSP. Participants anonymously provided assessments of RV size and function, TR, RAP and an estimate of RVSP (mmHg). Following baseline assessment of IOV, a 6 week teaching intervention including a review of the ASE Guidelines for the Assessment of the Right Heart and expert-led case-based discussions was implemented. A post-intervention test was performed with 8 new cases with similar range in quality and RVSP. The Shrout-Fleiss intra-class correlation (ICC) was used to compare IOV before and after the intervention. **Results**: Figure 1; the IOV in RVSP at baseline, pre-intervention (left) and post-intervention IOV (right). Compared with IOV pre-intervention ($p<0.05$), there was significant improvement post-intervention. The ICC and limits of agreement improved from 0.85 and 12 mmHg at baseline to 0.95 and 7 mmHg post-intervention. Several factors contributing to IOV were identified; incorrect averaging of TR gradients, inconsistency of RAP determination based on IVC findings, and inconsistent adjustment of RVSP based on functional and morphologic features of PH. **Conclusions**: Significant IOV existed among interpreter's RVSP assessment at baseline. In some cases, IOV was large enough to impact diagnosis and clinical decision making. This study suggests the feasibility of reducing IOV in the assessment of PH through a teaching intervention. Further study is required to determine whether this reduction in IOV is sustained.

Figure 1 (Left) Pre-intervention IOV for the first 8 cases **Figure 1 (Right)** Post-intervention IOV for the second 8 cases. Circles represent individual participant RVSP estimates for each case centered on the case mean (dash).



No conflict of interest

NON-INVASIVE CORONARY ARTERY DISEASE ASSESSMENT USING NOVEL IMAGING AND PLASMA BIOMARKERS

A. Johri[1], D.D. Anselm[1], M.Y. Tse[1], D.W.J. Armstrong[1], N.M. Ventura[1], A. Day[1], M.F. Hetu[1]
[1]Medicine, Queen's University, Kingston, Canada

BACKGROUND: Due to the up-surging prevalence of coronary artery disease (CAD), a need has arisen to develop methods for CAD diagnosis that are more cost-effective and non-invasive than the current clinical methods such as coronary angiography which have significant procedural risks and associated costs. Preliminary data suggests that Atrial Naturietic Peptide (ANP) can serve a plasma biomarker for CAD. Also, recently published findings indicated that Carotid Plaque can function as an imaging biomarker, with a high negative predictive value (NPV) for angiographic CAD. This study investigated whether concurrently measuring atrial ANP could further enhance the NPV of plaque to rule out significant CAD.

METHODS: 100 consecutive outpatients undergoing angiography were prospectively recruited for carotid ultrasound (iU33, Philips Healthcare) and plasma collection for ANP radioimmunoassay on the same day. Mean carotid intima-media thickness (CIMT) and maximal plaque height in the carotid bulb, internal or external carotid artery were measured by 2D ultrasound. Patients were divided into three groups based on the severity of their coronary or carotid disease as determined by carotid ultrasound. The non-parametric Kruskal-Wallis test compared average ANP ranking between the groups and Kendall's Tau-b measured concordance between the ordinal group and ANP values.

RESULTS: 92 patients had complete data for analysis. Of these, three patients had neither significant CAD nor carotid disease (Group 1); 45 patients had mild to moderate CAD or carotid disease (Group 2); and 44 patients had severe CAD (Group 3). Median plasma ANP was lower in patients without CAD or carotid disease (17 pg/mL) compared to those with mild to moderate CAD (77 pg/mL); and compared to those with severe CAD (87 pg/mL) ($p = 0.017$). Adding ANP to mean distal CIMT or to maximal plaque height did not improve the ROC area under the curve for predicting significant CAD.

CONCLUSION: The addition of ANP analysis did not significantly improve the NPV of carotid plaque measurement for ruling out angiographic CAD. Plasma ANP levels are significantly lower in patients without CAD or carotid disease compared to those with atherosclerosis. Used alone, plasma ANP levels correlated with the extent of CAD.

No conflict of interest

COMPUTED TOMOGRAPHY AND SCINTIGRAPHY VS. CARDIAC CATHETERIZATION FOR CORONARY DISEASE SCREENING PRIOR TO NONCARDIAC SURGERY

K. Kaneko[1], T. Takanashi[2], E. Hashizume[3], K. Owashi[4], H. Kaneko[5], Y. Ide[6]
[1]Department of Cardiology, Kitamurayama Public Hospital, Higashine, Japan
[2]Department of Radiology, Nihonkai General Hospital, Sakata, Japan
[3]Department of General Surgery, Nihonkai General Hospital, Sakata, Japan
[4]Department of Orthopedic Surgery, Nihonkai General Hospital, Sakata, Japan
[5]Department of Urology, Nihonkai General Hospital, Sakata, Japan
[6]Department of Obstetrics and Gynecology, Nihonkai General Hospital, Sakata, Japan

Objective: The goal of this study was to investigate the utility of multidetector-row computed tomography (MDCT) and adenosine triphosphate stress cardiac single photon emission computed tomography (ATP-SPECT) in evaluating coronary artery disease (CAD) in patients scheduled for non-cardiac surgery.
Methods: We routinely performed preoperative echocardiography and exercise stress electrocardiography to screen patients scheduled for non-cardiac surgery. Of 848 consecutive preoperative patients (Group A), 49 patients with screening examination abnormalities had MDCT and ATP-SPECT. Of 809 consecutive preoperative patients studied at an earlier time (Group B), 58 patients with screening examination abnormalities had cardiac catheterization in addition.
Results: The number of patients in Groups A vs. B having additional screening examinations was comparable, with no significant difference in perioperative cardiac events. Based on results of the additional tests in the two Groups, percutaneous coronary intervention (PCI) or coronary bypass grafting (CABG) for CAD was carried out in 2 Group A (1 PCI and 1 CABG) and 7 Group B (5 PCI and 2 CABG) patients, again with no significant differences between the groups. However, total medical expenses in patients having additional cardiac examinations were significantly reduced in Group A vs. Group B (140,030±34,800 vs. 187,170±26,120 yen, respectively, p=0.0002).
Conclusion: Non-invasive examination prior to noncardiac surgery using MDCT and ATP-SPECT in patients suspected of having CAD appears to be a useful screening procedure. Compared with invasive cardiac catheterization, CT testing has comparable diagnostic utility without an increase in perioperative cardiac events, and in addition has an improved cost-benefit profile.

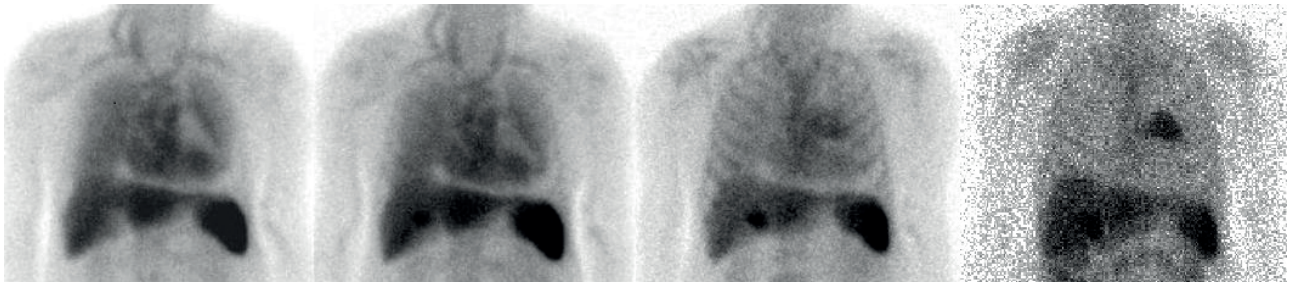
No conflict of interest

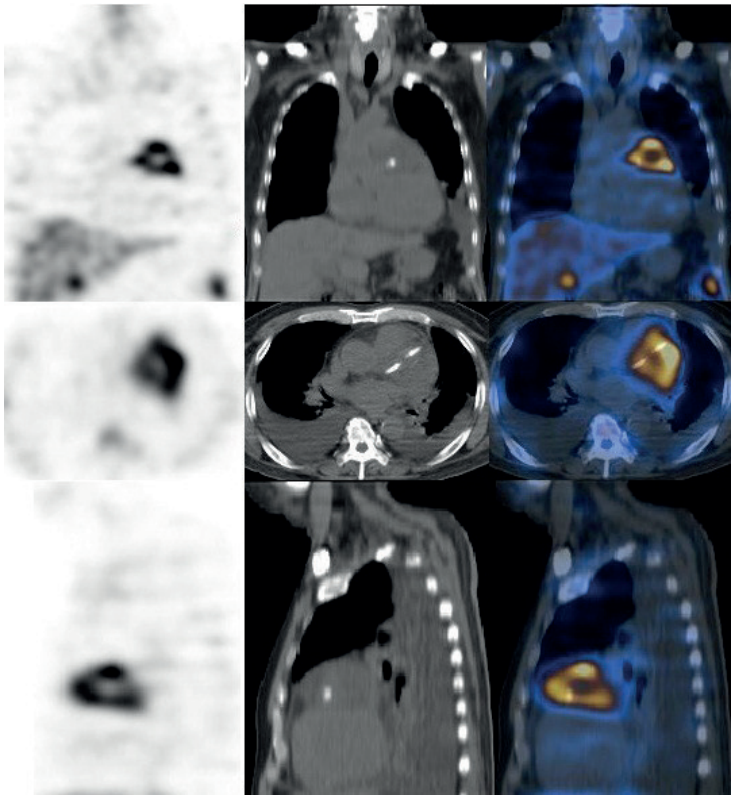
CORONARY ABSCESS FOLLOWING PCI AND INSERTION OF DRUG ELUTING STENT IDENTIFIED BY TC-99M HMPAO WHITE BLOOD CELL SCAN WITH SPECT/CT

K. Loke[1], H.C. Loh[1], C.E.D. Ng[1]
[1]Nuclear Medicine and PET, Singapore General Hospital, Singapore, Singapore

A middle aged Chinese Male was admitted with fever 4 days after insertion of a drug eluting stent (DES) to a completely occluded left anterior descending (LAD) artery. Blood cultures grew methicillin resistant Staphylococcus Aureus (MRSA). He remained bacteraemic for 13 days despite appropriate antibiotics. Cardiac MRI, 2D echo and CT scans did not identify the source of sepsis.

Nuclear ^{99m}Tc hexamethylpropyleneamine oxime labelled autologous white blood cell scan with SPECT/CT was performed the day after first negative blood cultures showing left paramediastinal tracer accumulation over 24 hours (top row image). SPECT/CT (bottom row image) correlation revealed a defect in LAD stent with radiotracer collection above it.





Cardiac catheterisation showed a pseudoaneurysm. Surgical debridement, removal of fractured stent, CABG with pseudoaneurysm ligation was performed. Pus from the stent similarly grew MRSA

Coronary artery stent fractures, aneurysms and infections, whilst rare following insertion of DES, carry high morbidity and mortality. Early diagnosis is crucial for appropriate intervention. Nuclear tagged WBC scintigraphy is a sensitive and non-invasive scan for the initial evaluation of acute bacterial infections; guiding further investigation and management and is not affected by antibiotic or steroid therapy.

No conflict of interest

PROMINENT CORONARY THEBESIAN SYSTEM: POSSIBLE CAUSE OF CHEST PAIN AND ABNORMAL ELECTROCARDIOGRAM RESULTS

Y. Mizuguchi[1], A. Takahashi[1], T. Yamada[1], N. Taniguchi[1], S. Nakajima[1], T. Hata[1]
[1]Cardiovascular Section, Sakurakai Takahashi Hospital, Kobe, Japan

Background: The presence of an abundant coronary Thebesian system (multiple coronary artery–left ventricular communications [CALVCs]) is very rare. The clinical significance of CALVCs has not yet been fully investigated.
Methods: We retrospectively analyzed 1823 consecutive patients who underwent diagnostic coronary angiography (CAG) in our hospital during the period from October 2010 to September 2012. The data were assessed for the presence of CALVCs and the coexistence of organic stenosis, and the clinical characteristics were investigated.
Results: CALVCs were identified in 20 patients (1%), 7 men and 13 women, aged 80 ± 8 years (mean ± standard deviation). In 19 patients, the ventricular communications were supplied from a diagonal branch of the left anterior descending coronary artery. Eighteen patients presented with chest pain and 11 of them underwent emergency CAG. The electrocardiogram (ECG) showed atrial fibrillation in 5 patients and a nonspecific abnormal ST-T change in 13 patients. Most patients had left ventricular hypertrophy detected by echocardiography. The CAG results showed that 2 patients with acute coronary syndrome had occlusion of the right coronary artery, and that 4 patients had significant coronary stenosis. The remaining 14 patients showed normal coronary findings and 6 of them underwent stress MPS; significant ischemic findings were detected in 3 of them.

Conclusions: CALVCs are an unexpectedly abundant possible cause of chest pain, abnormal ECG results, and arrhythmia, which are attributable to myocardial ischemia induced by the coronary artery steal phenomenon.

No conflict of interest

MULTIDETECTOR COMPUTED TOMOGRAPHIC CORONARY ANGIOGRAPHY AS AN ALTERNATIVE TO CONVENTIONAL CORONARY ANGIOGRAPHY IN NON-CORONARY SURGICAL PATIENTS

P. Nardi[1], M. Sperandio[2], A. Romagnoli[2], G. Saitto[1], M. Russo[1], A. Pellegrino[1], G. Simonetti[2], L. Chiariello[1]
[1]Cardiac Surgery Division, University of Rome "Tor Vergata", Rome, Italy
[2]Diagnostic Imaging and Interventional Radiology, University of Rome "Tor Vergata", Rome, Italy

Aim of the study. To evaluate Multidetector 64-slice Spiral Computed Tomography (MSCT) as an alternative to traditional coronary angiography (CA) to detect concomitant coronary artery disease (CAD) in patients initially admitted for non-coronary surgical procedures.

Methods. We have analyzed data of 380 consecutive patients operated from 2006 to 2008 (Group 1) initially admitted for aortic or mitral valve disease, ascending aorta aneurysm±aortic valve disease, or other combined diseases. Patients were submitted either to MSCT (n=112) or CA (n=268). CAD was definitively excluded in 85% of patients initially subjected to MSCT. Inclusion criteria to perform MSCT were progressively established: no previous myocardial infarction or documented CAD, normal left ventricular function, sinus rhythm, less than 2-3 premature ventricular or atrial contractions /min. By means of these selection criteria we have prospectively performed MSCT in 80 non-coronary surgical patients operated (2009-2012 period) (Group 2).

Results. In Group 1, as compared to those who underwent CA, patients who underwent MSCT were younger(64 vs. 70 years, p<0.0001), had less hypertension(p=0.0001), chest pain(p<0.05), peripheral vascular disease(p<0.05). Incidence of diabetes, smoking habit, family history of CAD were similar. Number of patients requiring CABG for concomitant significant CAD was higher in patients who underwent CA (57/268, 21.3%, vs. 9/112, 8%)(p=0.001). In Group 2, six patients(7.5%) required CA because of need to perform CABG(n=1), exclude false positive(n=2), detect coronary tree(n=3).

Conclusions. By systematical use of selection criteria, less invasive 64-slice MSCT can be an effective alternative to CA to rule out CAD in most surgical patients (>90%) initially referred for non-coronary cardiac diseases.

No conflict of interest

THE ROLE OF ECHOCARDIOGRAPHY IN DIAGNOSIS AND FOLLOW UP OF PATIENTS WITH TAKOTSUBOCARDIOMYOPATHY OR ACUTE BALLOONING SYNDROME

M.B.,Z.K.,I.T.,S.S. N. Naser[1]
[1]*Cardiology, Eurofarm Centar, Sarajevo*
[2]*Cardiology, University Clinical Center Tuzla*
[3]*Cardiology, BiH Heart Center Tuzla, Tuzla*
[4]*Clinic for heart disease, University Clinical Center Sarajevo, Sarajevo, Bosnia-Herzegovina*

b>Background: Takotsubo Cardiomyopathy characterized by transient apical and mid-ventricular LV dysfunction in theabsence of significant coronary artery disease. Echocardiography reveals during the acute phase a ballooning resembling the octopus trap configuration- the apex and lateral ventricular segments are hypokinetic while the base ishyperkinetic - along with reduced ejection fraction.

Aims: The objective of this study is to determine the role of echocardiography in detecting andestablishing the diagnosis of Takotsubo cardiomyopathy in patients with suspectacute coronary syndrome and during the follow upperiod.

Methods: The study covered 12adult patients. The majority are women. We evaluated clinical characteristics,LV systolic function, biomarkers, and prognosis in all patients.

Results: Among all the patients referred for echocardiographic evaluation for left ventricle motion abnormalities with suspect acute coronary syndrome, theecho exam revealed 12 patients with acute apical ballooning which involving the left ventricularapex and med-ventricle. The triggering factorswere physical stress in 4 patients (33%) and emotional stress in 8 patients(67%). The initial symptom was chest pain (n=8, 67%) rather than dyspnea(n=4, 33%). An initial electrocardiogram (EKG) presented ST-elevation (n=10,83%) and T-wave inversion (n=2, 17%), other data are shown that mong the allpatients 8 of them (66%) had normal EF by the 1st follow up (47 ±51 days), and the rest 4 patients (34%) had normal EF by 68 ± 96 days.

Conclusion: Widespread uses of echocardiography hascontributed tomore frequentrecognition of Takotsubo cardiomyopathy and highlight the role of this noninvasive method.

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EFFECTS OF LEFT ATRIAL DEFORMATION ON FUNCTIONAL FITNESS IN ELDERLY MEN

J.Y. Shih[1], W.C. Tsai[2], Y.S. Huang[2], C.C. Chen[1], J.Y. Chen[2], L.M. Tsai[2]
[1]Internal Medicine, Chi Mei Medical Center, Tainan City, Taiwan
[2]Internal Medicine, National Cheng Kung University Hospital, Tainan City, Taiwan

Background

Left atrial (LA) function is an important contributor to cardiac function in a variety of disease states and especially with exercise. The purpose of this study was to assess the relationship between LA deformation and functional fitness in elderly men.

Methods

We recruited 335 community-based, apparently healthy elderly men who were 65 years and older without structural heart disease. Echocardiogram was obtained from all of subjects. LA deformation was evaluated by speckle tracking echocardiography from apical 4 and 2 chamber views. Peak positive longitudinal strain (LASp) during atrial filling, peak strain rate in the reservoir phase of LA (LASRr), peak strain rate in the conduit phase (LASRc), and peak strain rate in the atrial contractile phase (LASRa) were identified from LA strain and strain rate curves. The ratio of peak early filling velocity (E) of mitral inflow to average early diastolic annulus velocity (e') of the annulus (E/e') was used as index for left ventricular filling. The status of functional fitness was assessed with 8-foot up-and-go test.

Results

Sixty-six subjects (20%) were excluded due to poor image for LA deformation analysis. The remaining subjects (mean age 74 ± 6 years) formed the basis of this study. LASp ($r = -0.269$, $p < 0.001$) and LASRr ($r = -0.242$, $p < 0.001$) were negatively correlated and LASRc ($r = 0.278$, $p < 0.001$) was positively correlated with time to complete the 8-foot up-and-go test but not LASRa. LASp ($r = -0.265$, $p < 0.001$) and LASRr ($r = -0.336$, $p < 0.001$) were negatively correlated and LASRc ($r = 0.295$, $p < 0.001$) and LASRa ($r = 0.214$, $p < 0.001$) were positively correlated with E/e'. E/e' was significantly correlated with time to complete the 8-foot up-and-go test ($r = 0.224$, $p < 0.001$). By multivariate analysis controlling for age, LA volume index, E/e', and left ventricular ejection fraction, LASp ($\beta = -0.202$, $P = 0.003$), LASRr ($\beta = -0.158$, $P = 0.026$), and LASRc ($\beta = 0.145$, $P = 0.035$) were independently correlated with the time to complete the 8-foot up-and-go test.

Conclusion

LASp, LASRr, LASRc, but not LASRa were independently correlated with functional fitness. LA function represented by deformation has major role in determination of exercise capacity in the elderly men.

Conflict of interest

THE ASSOCIATION OF CORONARY ARTERY CALCIUM SCORE WITH LV MASS INDEX AND SEPTAL E/E' IN SUBJECTS WITH NORMAL LVEF.

W.Y. Shin[1], U. Jeon[1], S.H. Park[1], S.W. LEE[1], S.J. Lee[1], D.K. Jin[1], S.W. Rha[2], B.G. Choi[2], C.U. Choi[2], D.J. Oh[2]
[1]Cardiology, Soonchunhyang University Cheonan Hospital, Cheonan, Korea
[2]Cardiovascular center, Korea University Kuro Hospital, Seoul, Korea

Objectives; The objective of this study is to determine if the association of coronary artery calcium score (CACS) with left ventricular mass index (LVMI) and septal E/E' ratio (E/E') relfecting global diastolic function exists in non-flow limiting asymptomatic coronary artery disease or stable angina pectoris with normal LV ejection fraction.

Background; There is little study for an independent association between CACS and LVMI and LV diastolic function. Also, It has not been established that LV diastolic dysfunction is associated with stable or non-flow-limiting asymptomatic coronary artery disease.

Methods; We investigated studied consecutive 1230 subjects, that CACS, LVMI and E/E' were measured. LVMI and septal E/E' ratio were compared between the CACS=0 group and CACS>0 group and according to severity of CACS (no, mild, moderate, and severe calcification).

Results; In multivariate regression analysis adjusted by age, gender, diabetes, hypertension, smoking, and estimate glomerular filtration rate, high-density lipoprotein cholesterol, LVMI, and E/E' were independent predictors of CACS>0. According to the composite of LVMI 90 g/m^2 and E/E' 15, three groups were categorized as follows; 'echo scoring system'=0,1,2. Each CACS of the 3 groups was 155.99±386.50, 287.51±745.52, and 489.00±913.49, respectively ($p<0.001$) and in the post hoc analysis, there was statistic significance between three groups. In the multivariate linear regression analysis, 'echo scoring system' was independent predictors of CACS.

Conclusions; In our study, HDL-cholesterol, LVMI and E/E' were associated with presence and severity of CACS. The combination with LVMI and E/E' can be more accurate predictor of CASC than separate LVMI or E/E'.

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HEART RATE RECOVERY IMPROVES THE DIAGNOSTIC ACCURACY OF TREADMILL EXERCISE TEST

L. Valera[1], *D.R. Reyes*[1]
[1]*Section of Cardiology, University of Santo Tomas, Manila, Philippines*

OBJECTIVES: To determine the predictive value of heart rate recovery in the diagnosis of significant coronary artery disease.

DESIGN: Retrospective Study

SETTING: University of Sto. Tomas Hospital España, Manila, Philippines

PATIENTS AND METHODS: Records of 78 patients who had positive Bruce protocol treadmill exercise test and underwent coronary angiography were reviewed. Heart rate recovery at first minute and second minute postexercise were recorded. Association of heart rate recovery with the presence of significant CAD was analyzed using Chi square test. Sensitivity, specificity, NPV, PPV were also determined.

RESULTS: Of the 78 patients, there were 48 (62%) males. Mean age was 54±7. Both heart rate recovery at first minute (HRR1) (p value 0.0.28) and heart rate recovery at second minute (HRR2) (p value 0.018) were significantly associated with the presence of significant CAD. For HRR1, the following were derived: NPV 65%, PPV 67%, sensitivity 36% and specificity 87%. For HRR2, the following were derived, NPV 100%, PPV 47%, sensitivity 100% and specificity 18%.

CONCLUSIONS. Abnormal HRR1 and HRR2 were associated with the presence of significant CAD. HRR in combination with positive treadmill exercise test can be used to predict presence of significant CAD. HRR2 was better than HRR1 in predicting significant CAD. Both were poor predictors of the absence of significant CAD.

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CHARACTERIZATION OF SKIN MICROCIRCULATION IN FLOW MEDIATED DILATION USING OPTICAL SENSOR WITH PRESSURIZATION MECHANISM

Y. Yamakoshi[1], K. Kotani[2], N. Taniguchi[2], N. Sunaguchi[1]
[1]Faculty of Science and Technology, Gunma University, Kiryu, Japan
[2]Department of Clinical Laboratory Medicine, Jichi Medical University, Shimotsuke, Japan

Microcirculation in capillaries may play a key role in whether individuals develop a wide variety of diseases and health conditions, including insulin resistance, metabolic syndrome and cardiovascular disease. We propose a novel method of measuring blood amount, outflow and reflow characteristics of dermis microcirculation.[1] An optical sensor (wavelength 571 nm) is pressed to the skin surface using a pressure higher than systolic arterial pressure. Hemoglobin concentration by change of the blood flow amount is estimated by the Beer-Lambert law. In conventional methods, a time-dependent signal component is measured to extract light absorption by blood. However, a problem of these methods is that the measurement is restricted to an artery. In our method, signal from blood is extracted by pressure applied to the skin. Hence, it is applicable for measuring the characteristics of microcirculation. This method is applied to the measurement of microcirculation caused by reactive hyperemia of flow mediated dilation (FMD). The target of the FMD measurement is the arterial extension; however, the blood amount in microcirculation are greatly affected by FMD and are observed as reactive hyperemia. Among three parameters which are evaluated using the proposed method, the one relating to the amplitude of arteriole's pulsation shows a close correlation with conventional plethysmography, while the other two parameters, which characterize the blood amount, outflow and reflow in microcirculation, show varying time responses. The proposed method may help better understand the mechanisms and diseases which are affected by microcirculation.

[1] Y. Yamakoshi et al., Biol. Eng. Comput. (2013) 51:497.

No conflict of interest

IMPACT OF LEFT VENTRICULAR STRAIN ON LEFT VENTRICULAR DYSFUNCTION PREDICTION AFTER ACUTE MYOCARDIAL INFARCTION

D. Zaliaduonyte-Peksiene[1], J.J. Vaskelyte[1], S. Simonyte[2], O. Gustiene[1], E. Tamuleviciute-Prasciene[1], V. Tamakauskas[1], V. Kviesiulaitis[1], E. Jankauskiene[1], V. Mizariene[1], R. Zaliunas[1]
[1]Cardiology, Lithuanian University of Health Sciences, Kaunas, Lithuania
[2]Institute of Cardiology, Lithuanian University of Health Sciences, Kaunas, Lithuania

Purpose. Left ventricular (LV) systolic function is an important prognostic factor after acute myocardial infarction (AMI). Despite modern medical and interventional AMI treatment, LV ejection fraction (LVEF) impairment is a common consequence of AMI. We sought to investigate the differences of LV circumferential, radial and longitudinal strain in patients with depressed LVEF and preserved LVEF and assess the impact of strain on LV dysfunction prediction after AMI.

Methods. 155 patients (mean age 59.2 ± 9.1) with a first AMI were included into the study. Within 24-72 hours of the onset of AMI symptoms and at 4-month period, 2-dimensional echocardiography with speckle-tracking imaging for evaluation of LV strain was performed. LV systolic function was considered depressed if LVEF was less than 45 % at 4-month follow-up.

Results. Incidence of LV dysfunction was 19.9%. Patients with depressed LVEF at follow-up, had lower initial global circumferential, radial and longitudinal strain if compared to patients with preserved LVEF (as follows, -12.1 % ± 3.8 vs. -15.3 % ± 4.3, p<0.001, 20.4 % ± 7.9 vs. 30.1 % ± 10.5, p<0.001 and -13.4 % ± 5.8 vs. -16.1 % ± 5.3, p<0.01, respectively). After adjustment for age, gender and localization of AMI, circumferential, radial and longitudinal strain were associated with a significantly higher risk of LVEF impairment (circumferential strain: OR = 8.83, 95% CI 2.40-32.48, p=0.001, radial strain: OR = 6.27, 95% CI 2.020-19.48, p=0.001, longitudinal strain OR = 4.49, 95 % CI 2.40-32.47, p=0.013).

Conclusions. LV circumferential, radial and longitudinal strain measured in the acute phase of AMI can predict LV dysfunction at 4-month period where circumferential strain has a superior role.

No conflict of interest

CORRELAZIONE TRA LA GEOMETRIA DEL VENTRICOLO SINISTRO E LE DIMENSIONI DELL´ATRIO DI SINISTRA NEI PAZIENTI OVER 70 YY

P.P.,P.S.,A.C.,C.A. V. Chimienti[1]
[1]*"Ambulatori di Cardiologia, Ospedale M O A Locatelli*
UOC di Cardiologia,A.O. Bolognini di Seriate, piario
[2]*UOC di Cardiologia H.Seriate- AO Bolognini di Seriate, Seraite*
[3]*UOC di Cardiologia H.Seriate-AO Bolognini di Seriate*
[4]*UOC di Cardiologia H.Seriate- AO Bolognini di Seriate*
[5]*UOC di Cardiologia Riabilitativa- AO Bolognini di Seriate, Seriate, Italy"*

"Introduzione:
Un ampio numero di studi ha dimostrato che la massa ventricolare sinistra è un forte predittore di morbilità e mortalità cardiaca e cerebrovascolare,indipendentemente dalla pressione arteriosa essenziale o da altri fattori di rischio.

Obbiettivi
Nella nostra ricerca abbiamo voluto studiare, la correlazione tra uno dei patterns geometrici dell´ipertensione arteriosa, la fibrillazione atriale e le dimensioni atrialii pazienti over 70
Abbiamo quindi effettutato la revisione dei repots di 400 pts giunti nell´ Ambulatorio di Cardiologia o nel Pronto Soccorso del nostro Opsedale

Dati estrapolati hanno evidenziato i seguenti risultati :
> il 45 % dei pazienti : 65 % maschi, 35 % femmine presentava **ipertrofia concentrica** con aumento severo delle dimensioni atriale ; la età media era 76 anni
>il 35 % dei pazienti : 60 % maschi, 40 % femmine presentava un **rimodellamento concentrico** con moderato aumento delle dimensioni atriale, la età media era 73 anni
>il 15 % dei pazienti : il 40 % maschi ed il 60 % femmine presentava una **geometria normale** con lieve aumento delle dimensioni atriali, età media 71 anni
> il 5 % dei pazienti : il 35 % maschi, 65 % femmine presentava un **ipertrofia eccentrica** e dimensioni atriale normale con età età media 70 anni

Conclusioni:
così come descritto nella letteratura, si evince dalla nostra coorte di pazienti che l´ingrandimento atriale più significativo è associato ad ipertrofia concentrica a seguire rimodellamento concentrico, con una relazione importante tra massa del ventricolo di sinistra e dimensione atriale."

Document not received

ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH EXAGGERATED BLOOD PRESSURE RESPONSE DURING TREADMILL STRESS TEST

A. Domalanta[1]

[1]*Department of Internal medicine Section of Cardiology, University of Santo Tomas, Metro manila, Philippines*

***BACKGROUND*:** Exaggerated blood pressure response to exercise has been associated with an increased risk for future hypertension and cardiovascular events. Impaired endothelial function in the setting of excessive elevations in exercise BP have been reported recently.

OBJECTIVE: This study aimed at the evaluation of the relationship of BP responses to exercise with endothelial vasodilator function as determined by Brachial artery flow-mediated vasodilation (FMD).

METHODOLOGY : A total of 42 patients who underwent treadmill stress test were qualified for the study (mean age = 41.7± 9.5 years old). FMD were correlated with the maximal SBP and DBP responses using Pearson's Correlations and linear regression.

RESULTS: In all patients, the maximal systolic BP have a positive linear relationship with BMI (pvalue 0.002). Eighteen out of the 42 subjects had exaggerated BP responses. The correlation of maximal SBP with the rate of percent change of FMD (pvalue 0.77) did not reach statistical significance. Variables that showed significant correlation with the maximal diastolic pressures are BMI (p value 0.074), %FMD (p value 0.029) and maximal heart rate (p value 0.002). Impact of the maximal diastolic BP to the patients' %FMD was investigated using simple linear regression with a p value of 0.029.

CONCLUSION: Exaggerated systolic BP response to exercise is not associated with impaired endothelial vasodilator function. However, endothelial dysfunction may play an important role in exaggerated diastolic BP response.

No conflict of interest

LOW VITAMIN D IN HYPERTENSIVE PATIENTS: NEW PREDICTOR FOR CORONARY ARTERY DISEASE IN A SUNNY COUNTRY

A. El-Menyar[1], A. Rahil[2], K. Dousa[2], W. Ibrahim[2], T. Ibrahim[2], R. Khalifa[2]
[1]clinical medicine & research, Hamad general hospital & Weill Cornell medical school, Doha, Qatar
[2]internal medicine, Hamad general hospital, Doha, Qatar

Background: Vitamin D deficiency is a well recognized medical problem worldwide. We aimed to evaluate the impact of low vitamin D in the presence of other cardiovascular risk factors in a sunny country from the Middle East.
Methods: Data were collected retrospectively from January 2008 and November 2009 at Hamad General hospital in the state of Qatar. Demographic and clinical profiles were analyzed in patients who had low vitamin D (< 30 ng/ml). Logistic regression analysis was performed for the predictors of coronary artery disease (CAD) in patients with low vitamin D.
Results: Among 547 patients, there were 498 patients (91%) who had low vitamin D level (< 30 ng/ml) with a mean age of 49 ± 12 years and 49 patients (9%) had normal vitamin D level (30 - 80 ng/ml) with mean age of 54 ± 13 years. Among low vit D group, 56% were females, 65% were obese, 38% had hypertension, 34% had dyslipidemia and 29% had diabetes mellitus. Multivariate logistic regression analysis showed that in the presence of low vitamin D, hypertension was the strong independent predictors of CAD (adjusted OR 8.0; 95% CI:1.67-39.82, P=0.01). **Conclusion**: Low vitamin D in the sunny regions becomes a nightmare. Hypertension in the presence of low vitamin D increases the risk of CAD by eight times regardless of gender. Therefore, screening and treatment of low vitamin D is important in hypertensive patients.

No conflict of interest

BLOOD PRESSURE CHANGES OVER 2 YEARS AFTER THE GREAT EAST JAPAN EARTHQUAKE AND ASSOCIATED CARDIOVASCULAR RISK FACTORS: THE WATARI STUDY

S. Konno[1], M. Munakata[1]
[1]Division of Hypertension, Tohoku Rosai Hospital, Sendai, Japan

Increases in blood pressure (BP) following earthquakes have been well documented. We have recently reported that BP among the public employees of Watari town, which was severely hit by the Great East Japan Earthquake on March 11, 2011, was significantly increased after the disaster compared with the general population. The aim of this study was to assess long-term changes in BP after the Earthquake and to clarify their contributing factors using the same cohort. Study population was 1232 individuals from the general population and 225 public employees of the town who received annual health check-ups both in 2011 (after the disaster) and 2012. Anthropometric measurements, sitting BP, and fasting blood samples were obtained. Information on insomnia, fatigue, and life disruption due to the disaster was collected using a questionnaire in 2011, and compared with the 1-year changes in clinical data from 2011 to 2012. The mean systolic BP among the public employees was significantly decreased in 2012 compared with the previous year (124.4±13.1 to 121.1±13.6 mmHg, $P<0.01$), while that of the general population was significantly increased (124.1±16.5 to 127.6±16.6 mmHg, $P<0.01$). The degrees of life disruption and damage to homes were found to be major contributing factors to the elevation of BP and body-mass index among the general population, whereas no association was found between these measures among the public employees. Our results suggest that the increase in cardiovascular risks after an earthquake may be prolonged more than a year, and that inadequate lifestyle and living conditions are possible contributing factors.

No conflict of interest

CONFIDENTIAL AND PROCEDURAL ISSUES FOR GENERATING GEOSPATIAL DATA IN A MULTI-SITE CLINICAL STUDY FOR HYPERTENSION

J. Lee[1], M. Malouhi[1], J. Sung[2], J. Perkins[1]
[1]RTRN DCC, RTRN DCC @ Jackson State University, Jackson, USA
[2]Biostatistics & Epidemiology, Jackson State University, Jackson, USA

Background: Multi-site studies designed to resolve the disparity problem of hypertension have frequently embraced the use of GIS tools as a method to investigate spatial clustering and the role of determinants of disease and health outcomes. However, study sites were reluctant to release patient' home address due to institution's internal policy for protecting patient confidentiality and willing to conduct onsite geocoding instead. In order to create reliable and valid spatial data through onsite geocoding, standardization of procedure (i.e., geocoding software, geospatial source data, algorithm, and methods) across the sites is a prerequisite. This study is to 1) describe the current practice to resolve the confidential and procedural issues for GIS data preparation in a multi-site clinical study and 2) validate the geospatial data generated by the study specific GIS application.

Methods: A client side web-based GIS application was developed to achieve the goal of confidentiality and procedural standardization. The client side application did not send confidential data to server, implying nobody except users in each site could observe the data. Open sources of Java scripts were utilized for the application development to abstract SES variables and racial segregation from 2010 US Census data, and derive fast-food restaurant density, walkability, and accessibility to healthcare facilities.

Results: Geospatial data generated by the study specific GIS application demonstrated satisfactory internal consistency and construct validity. No site difference of the reliability and validity was found. Results showed that the GIS variables were valid in discriminating patients who have severe hypertension from those who do not. With minor revision, the application can be utilized for supporting the other cardiovascular-related studies and/or social epidemiology studies.

Conclusion: Although geocoding was conducted from multiple sites, client side web-based GIS application allowed to obtain valid and reliable GIS data through the standardized procedures as well as to resolve confidential issue by secure interface environment. Therefore, study specific GIS application may be appropriate for supporting a multi-site clinical study which is subject to confidential issue.

This study is supported by the National Institute on Minority Health and Health Disparities (NIMHD) under Award Number of U54MD008149.

No conflict of interest

INCREASED C-REACTIVE PROTEIN LEVELS PROMOTE HYPERTENSION AND MYOCARDIAL DISORDERS IN THE SPONTANEOUSLY HYPERTENSIVE RATS.

H. Malinska[1], O. Oliyarnyk[1], L. Kazdova[1], M. Pravenec[2]
[1]Center for Experimental Medicine, Institute for Clinical and Experimental Medicine, Prague 4, Czech Republic
[2]Institute of Physiology, Academy of Science, Prague, Czech Republic

C-reactive protein (CRP), a marker and mediator of inflammation, is now recognized as an important factor to the development of cardiovascular disease. To investigate whether elevated CRP can promote increased risk for hypertension and disorders in myocardium, we measured blood pressure (BP), ECG and oxidative stress parameters in myocardium in spontaneously hypertensive rats (SHR) with transgenic expression of human CRP gene under control of the liver-specific ApoE promoter (SHR-Tg).

Systolic BP (24 hour averages) measured by telemetry were 10-15 mmHg greater in SHR-Tg than in SHR controls ($p<0.05$). SHR-Tg exhibited increased premature ventricular complexes (3200±248 vs 1150±96, $p<0.01$), duration of ventricular tachyarrhythmias (340±25 vs 101±8 s/h $p<0.01$), cardiac hypertrophy (0.42±0,014 vs 0.377±0,04 g myocardial weight/100g b.w., $p<0.05$), and increased microalbuminuria (178±35 vs. 32±7 mg/g creatinine, $p<0.01$). Triacylglycerols accumulation in myocardium (0.425±0.014 vs 0.377±0.004 μM/g, $p<0.01$) was associated with declined reduced glutathione (GSH) level (15.5±1.5 vs 27.4±1.1 mM/g protein, $p<0.001$). A negative linear correlation between triacylglycerols and GSH concentrations was observed ($R=-0.471$, $p<0.05$). In addition, we found reduced myocardial antioxidant enzymes activities: superoxide dismutase (0.452±0.037 vs 0.564±0.038 U/ml), glutathione peroxidase (360±28 vs 525±23 μM GSH/min/mg protein) and increased concentration of lipoperoxidation measured as TBARS (2.318±0.149 vs 1.756±0.142 nM/mg protein, $p<0.05$), suggesting that oxidative stress may be mediated by the adverse effects of elevated CRP.

In conclusion, increased CRP might directly contribute to pathogenesis of hypertension, predisposition to arrhythmias and oxidative stress. SHR rats with transgenic expression of human CRP could provide a valuable model for investigating mechanisms whereby human CRP enhances the risk for cardiovascular diseases.
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Conflict of interest

CONTRIBUTION OF THE ATHEROGENIC LIPOPROTEIN PROFILE TO THE DEVELOPMENT OF ARTERIAL HYPERTENSION.

S. Oravec[1], A. Dukat[1], P. Gavornik[1], M. Caprnda[1], M. Kucera[1], P. Sabaka[1]
[1]2nd Department of Internal Medicine, Comenius University School of Medicine, Bratislava, Slovakia

Atherogenic lipoproteins play an important role in the pathogenesis of arterial hypertension. A new method of lipoprotein separation by electrophoresis on polyacrylamide gel (PAG) - Lipoprint LDL System - quantifies non atherogenic and atherogenic plasma lipoproteins - including small dense LDL, the potent atherogenic lipoprotein subpopulation and identifies a non-atherogenic lipoprotein phenotype A, or an atherogenic lipoprotein phenotype B in plasma of examined individuals.

Contribution of this method points to:

1) High percentage - 93% of atherogenic hypertriacylglycerolemia and
- 86% of atherogenic mixed hyperlipidemia in subjects with arterial hypertension

2) Low percentage - 52% of atherogenic hypercholesterolemia in subjects with arterial hypertension

3) Atherogenic normolipidemia - 7% in control group of healty subjects

4) The presence of small dense LDL in plasma is decisive for declaration of an atherogenic lipoprotein profile in hyperlipoproteinemia as well as
in normolipidemia.

Key words: atherogenic vs. non-atherogenic lipoprotein profile, atherogenic hyperlipoproteinemia, atherogenic normolipidemia

No conflict of interest

ANTIISCHEMIC THERAPY IN THE HYPERTENSIVE PATIENTS AFTER POST CORONARY ARTERY GRAFT SURGERY

I. Riecansky[1], J. Pacak[1], V. Fridrich[1]
[1]Department of Cardiology, National Institute of Cardiovascular Diseases, Bratislava, Slovakia

Aims:Antiischemic treatment of hypertensive symptomatic patients /pts/ with prior coronary artery graft surgery /CABG/ remains still open issue

Methods: Retrospective analysis of 120 hypertensive pts /103 men, 17 women, mean age 64+/-8.8years/ was performed. 90 pts /75%/ overcame acute myocardial infarction before CABG. All pts underwent new-second coronary angiography with mean interval from first CABG 70 +/- 40 months and mean number of bypasses was 2.7/pts /in 76 pts used internal mammary bypass/.

Results: From angina pectoris suffered 100 pts /83.3%/, from acute coronary syndroms 12 pts /10%/. NYHA I-II comprised 93 pts /77.5%/, NYHA III-IV 27 pts /22,5%/. Mean ejection fraction was 47.1.+/-12.9%. Despite therapy 51 hypertensive pts /42.5%/ had BP over 140/90 mm HG and 39 pts /32,5%/ LDL-CH level over 3.5.mmol/l, 50 pts /41.7%/ smoked, 49 pts /40.8%/ were obese, 39 pts /32.5%/ had diabetes melitus. Pharmacological therapy consisted of RAAS inhibitors in 100 pts /83.3%/, beta blockers in 98 pts /81.7%/, Ca antagonists in 50 pts /41.7%/,acetylsalicylic acid in 78% pts /65%/, thienopyridines 52 pts /43.4%/. Treatment after second coronary angiography: drugs only in 81 pts /67.5%/, surgery in 9 pts /7.5%/: reCABG 7 pts, HTx 2 pts, from these MACE 5 pts; PCI in 30 pts /25%/, from these MACE 4 pts.

Conclusions: 1/ PCI in comparison with CABG is our preferred strategy for repeated revascularization 2/ management of post CABG symptomatic hypertensive pts besides of progerss in revascularization approach and irrespective of antianginal therapy, mainly depends on improvement of unsatisfactory hypertension control and oher atherothrombotic risk factors: - hyperlipidemia by intensive lipid lowering therapy by statins /reducing also failure of grafts/, - diabetes, - obesity,- smoking has to be abandoned /progression of graft disease/. 3 /our data showed some gaps remainig between ESC, ACC/AHA recommendations and usual care on hypertensive pts with coronary artery disease.

No conflict of interest

INSOMNIA AND SYSTOLIC BLOOD PRESSURE IN PATIENTS BEFORE DIAGNOSTIC CATHETERIZATION

V. Romero[1], J. Villasmil[2], E. Silva[3], F. Madueño[4]
[1]Clinical Psychology, Institute of Cardiovascular Diseases of LUZ, Maracaibo, Venezuela
[2]Statistical, Institute of Cardiovascular Diseases of LUZ, Maracaibo, Venezuela
[3]Medical Doctor, Institute of Cardiovascular Diseases of LUZ, Maracaibo, Venezuela
[4]engineer, Institute of Cardiovascular Diseases of LUZ, Maracaibo, Venezuela

To determine the effects of insomnia (I) on the systolic blood pressure (SBP) in patients before diagnostic catheterization. The participants were 120 Patients, males (n= 57) and females (n= 63), age-mean = 57, 63 years and standard deviation=9, 8. The Blood Pressures were recorded one day before the diagnostic catheterization using oscillometric method (Dinamap). All responded to the Hamilton Anxiety Scale where there is a specific item that evaluate insomnia: Assess the difficulty falling asleep, disrupted sleep, unsatisfying sleep and fatigue on awakening and they were classified in 4 categories: Absent Insomnia (AI), Light Insomnia (LI), Moderate Insomnia (MI), Severe Insomnia (SI) and Disabling Insomnia (DI). The Univariate linear model was used to study the effects of I on the SBP, taking as the dependent variable the systolic blood pressure and Insomnia as factors.The presence of I was 90.9% (n=109), for LI 17,5% (n=21), for MI 25% (n=30), for SI 29,2% (n=35) and 19,2% (n=23) for DI. The mean and standard deviation for SBP was: 131,87 ± 24, 66 in all patients. ANOVA´ s results showed a significant effect for Insomnia factor (F=2,892 p=0.025) affect systolic blood pressure in patients before diagnostic catheterization. The results provide evidence for an association between Insomnia and systolic blood pressure in patients before diagnostic catheterization. It is possible that there is a relationship between the discomfort created by insomnia product of fear of catheterization and some indications of abnormal autonomic nervous function that elevate systolic blood pressure before diagnostic catheterization.

No conflict of interest

Renin-angiotensin system gene polymorphisms and essential hypertension in Lithuanian children

S. Simonyte[1], V. Dulskiene[1], J. Medzioniene[1], R. Kuciene[1], V. Lesauskaite[1]
[1]Institute of Cardiology, Lithuanian University of Health Sciences, Kaunas, Lithuania

PURPOSE: Clinical and experimental studies have demonstrated a major role of the renin-angiotensin system (RAS) in hypertension. Polymorphisms within angiotensinogen (*AGT* M235T) and angiotensin II type 1 receptor (*AGTR1* A1166C) genes have been extensively studied in association with hypertension, however, findings are conflicting. Therefore the objective of the present study was to assess the contribution of polymorphisms within these genes on hypertension in Lithuanian children.

METHODS: In the case-control study *AGT* and *AGTR1* genes polymorphism were investigated in 189 (mean age 13.32±1.16; blood pressure (BP) 141,66±9,71/71,68±7,79 mmHg) hypertensive patients and 520 (mean age 13.22±1.12; blood pressure (BP) 113,75±9,27/63,00±6,98 mmHg) normotensive subjects. Single nucleotide polymorphisms (SNPs) in these candidate genes to determine their association with hypertension were analyzed by real-time and conventional polymerase chain reaction (PCR) reaction.

RESULTS: *AGT* and *AGTR1* genotypes distributions in both groups were consistent with Hardy-Weinberg equilibrium. No significant difference was observed in the allele frequencies and genotype distributions of *AGTR1* gene polymorphisms between two groups, whereas *AGT* TT homozygotes were more frequent in controls (77.0% vs. 23%, p<0.05). This became significant in men only. *AGT* TT genotype was associated with 40% decrease in risk of having hypertension (odds ratio: 0.59; 95% CI, 0.37 to 0.94, p=0.02) in children.

CONCLUSIONS: *AGT* M235T TT genotype confers a significantly decreased risk for the development of essential hypertension in children population. The role of AGRT1 gene polymorphism needs further investigation.

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No conflict of interest

PREVALENCE OF ARTERIAL HYPERTENSION AMONG TEACHERS

V. Serebryakova[1], V.S. Kaveshnikov[1], I.A. Trubacheva[1]
[1]Department of Population-Based Cardiology Studies, FSBI "RI Cardiology" SB RAMS, Tomsk, Russia

Objective: Objective of the study was to investigate prevalence of arterial hypertension among teachers of secondary schools in Tomsk and Tomsk region. Materials and Methods: A cross-sectional epidemiological study of organized population of secondary school teachers was conducted in a framework of multicenter preventive study titled "Rosprofilaktika" coordinated by Federal State Institution "National Research Center for Preventive Medicine" of the Ministry of Healthcare of the Russian Federation (Moscow). Standardized office blood pressure (BP) measurements were performed in the right arm twice a day by using mercurial sphygmomanometer. Criterion for administration of antihypertensive therapy was BP ≥ 140/90 mmHg (GFCF, 2010). Sample was formed based on the lists of employees from 11 secondary schools contractual to outpatient facilities located in correspondent territorial districts. A random representative sample of 766 school teachers (mean age: 46.5±12.2 years; 57 men, 709 women) was formed. Results: The incidence of hypertension in the study population was 44.7% (44.0% of women and 52.6% of men; $p>0.05$). Newly diagnosed hypertension was found in 31.9% of cases (47.4% of women and 30.7% of men; $p<0.01$). Among teachers who were aware about their hypertension, only 36.8% (women: 74.3%; men: 26.7%; $p<0.05$) regularly took hypotensive drugs. Only 31.7% of teachers with hypertension regularly controlled arterial hypertension at home. Conclusions: Data revealed high prevalence of hypertension. The study showed low rates of adherence to antihypertensive therapy among teachers. Data of this first-time monitoring of hypertension risk factor prevalence may be used to improve hypertension prevention measures in teachers of Tomsk region.

No conflict of interest

THE EXPRESSION OF ACE, ACE2, AT1 AND AT2 RECEPTORS IN THE HEART OF FRUCTOSE FED OVARIECTOMISED RATS-EFFECT OF ESTRADIOL

M. Bundalo[1], S. Tepavcevic[2], S. Romic[2], G. Koricanac[2], M. Zivkovic[1], A. Stankovic[1]
[1]Laboratory for Radiobiology and Molecular Genetics, Vinca Institute of Nuclear Sciences, Belgrade, Serbia
[2]Laboratory for Molecular Biology and Endocrinology, Vinca Institute of Nuclear Sciences, Belgrade, Serbia

Background: Heart disease or diabetes could be promoted in people who consume sugar. High dietary intake of fructose also increases risk for heart disease. The effects of fructose diet on metabolism, lipid profile and blood pressure are dependent of sex. Renin-angiotensin system (RAS) impairs insulin sensitivity, whereas hyperinsulinemia and insulin resistance promotes the development of cardiovascular disorders. We examined the effects of fructose rich diet (FRD) and estradiol (E2) on the expression of ACE, ACE2, AT1R and AT2R in the rat heart.
Methods and Results: 21 day old female rats were divided in control group and FRD group. At two weeks before sacrifice, animals were ovariectomised and half of the FRD rats were subjected to E2 replacement. FRD increased ACE ($p<0.001$) and AT1R ($p<0.05$) protein expression, while AT2R expression was decreased ($p<0.05$). ACE2 protein expression was unaltered. mRNA expression for AT1R was unaltered, as assessed by qPCR. E2 treatment significantly decreased protein expression for ACE ($p<0.001$) and AT1R ($p<0.01$), while ACE2 ($p<0.01$) and AT2R ($p<0.01$) expression was increased. Effect of E2 treatment on AT1R gene expression was not statistically significant but showed trend toward lowering AT1R gene expression. We didn't detected AT2R gene expression.
Conclusion: FRD affects almost all components of the RAS in the rat heart.The increase of the ACE and AT1R protein expression and decrease of AT2R expression could be the the way that leads to the development of cardiovascular disorders. The E2 shows strong protective effect in FRD through reversion of the changes in RAS components expression.

No conflict of interest

PROTECTIVE EFFECTS OF SHEN-YUAN-DAN, A TRADITIONAL CHINESE MEDICINE, AGAINST MYOCARDIAL ISCHEMIA / REPERFUSION INJURY IN VIVO AND VITRO

F.Y. Chu[1], J.J. Shang[1], B. Wu[2], A.Y. Li[1], T. Tong[1], H.X. Liu[1]
[1]Cardiology, Beijing Hospital of Traditional Chinese Medicine, Beijing, China
[2]Cardiology, Daxing Hospital of Traditional Chinese Medicine, Beijing, China

Objective The myocardial ischemia/reperfusion injury is a major problem in myocardial ischemia/reperfusion injury and pharmacological postconditioning could alleviate the injury.. The purpose of this study was to investigate the effects and mechanisms of Shen-Yuan-Dan (SYD), which is a widely used traditional Chinese medicine prescription, pharmacological postconditioning on myocardial ischemia/reperfusion injury.

Methods The rat ischemia/reperfusion model was established by ligation of left anterior descending coronary artery for 30 min and reperfusion for 3 h and the I/R model in vitro was performed on cultured neonatal cardiomyocytes subjected to simulated hypoxia/reoxygenation. Myocardial injury markers and histopathology staining were examined in rat model. In vitro experiment, cell viability was detected by 3-(4, 5-dimethylthazol-2-yl)-2, 5-diphenyl tetrazolium bromide assays. Cellular apoptosis was determined by hoechst33342 staining. The protein expressions of Bcl-2 and Bax in different groups were determined by immunocytochemistry assay.

Results Both low dose of SYD reduced lactic dehydrogenase and creatine kinase-MB activity and malondialdehyde content, increasing superoxide dismutase activity and attenuating histopathology injury. Meanwhile, SYD promoted cell viability and inhibited the cardiomyocyte apoptosis. The expressions of Bcl-2 and Bax were restored to the normal level by SYD pharmacological postconditioning. These effects of SYD were reversed by LY294002, the inhibitor of the phosphatidylinositol 3-kinase/Akt pathway.

Conclusion Out data suggested that SYD pharmacological postconditioning showed cardioprection against myocardial ischemia/reperfusion injury via activating the phosphatidylinositol 3-kinase/Akt pathway.

No conflict of interest

MORPHOLOGIC ALTERATIONS IN KNOCKOUT LDL-/- MICE AORTA SUBJECT TO DIETARY RESTRICTION

E.S. Melo[1], F.R. Azevedo[1], L.H. Monteiro[1], M.C. Jurado[1], P.S. Gutierrez[1], B. Caramelli[1]
[1]Cardiology, Heart Institute- University of São Paulo, São Paulo, Brazil

Objectives

To investigate morphologic alterations in knockout LDL-/- mice Aorta subject to Dietary restriction and its relation with cardiovascular risk factors.

Methods

Six weeks old LDL -/- Knockout mice were divided into 4 groups receiving daily 5 grams of each diet: Atherogenic (AT) – rich in cholesterol, saturated fatty acids and low in fibers; DASH– rich in mono and poli fatty acids and low in sodium, Intermittent Fasting (IF) – Standard chow supplemented with micronutrients, every other day and Control (Cont) – standard chow, every day. By the end of 15 weeks, all animals were anesthetized and euthanized, and the thickness of atherosclerotic plaques in their aortas were analysed macroscopically (dissections of the heart, the ascending aorta and aortic arch) and microscopically by Hematoxylin and Eosin method.

Results

Dissections were performed using an optical microscope. The atherosclerotic lesion area of each group was express as media between 6 measures of 10mm thick, and with 80µm distance between the cuts.

The atherosclerotic plaque area in AT (fig.1) was significantly ($p<0,05$) greater than IF (fig.2). The same was observed between DASH (fig.3) and IF, with a greater atherosclerotic plaque area detected in DASH. There were no significant difference between IF and Cont (fig.4).

Conclusion

In this animal model, intermittent fasting seems to have a less atherogenic profile, translated by a smaller area of atherosclerotic lesion.

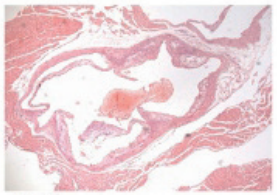
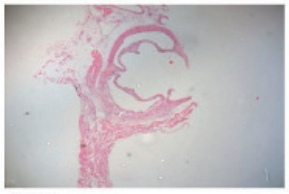


Fig.1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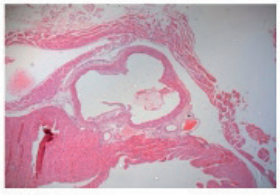
Fig.2

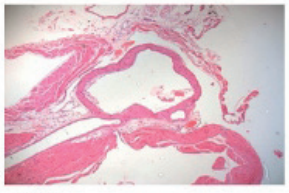
Fig.4

No conflict of interest

THYMOQUINONE REDUCES INTERCELLULAR ADHESION MOLECULE-1, VASCULAR CELL ADHESION MOLECULE-1, E-SELECTIN PROTEIN AND GENE EXPRESSIONS IN STIMULATED CORONARY ARTERY ENDOTHELIAL CELLS

F. Mohtar[1], M.H. Haron[2], T. Rahman[1], G.R.A. Froemming[3], H. Nawawi[1]
[1]Centre for Pathology Diagnostic and Research Laboratories, Universiti Teknologi MARA (UiTM), Sungai Buloh, Malaysia
[2]Faculty of Medicine, Universiti Teknologi MARA (UiTM), Sungai Buloh, Malaysia
[3]Institute for Medical Molecular Biotechnology, Universiti Teknologi MARA (UiTM), Sungai Buloh, Malaysia

Background: Atherosclerosis is recognized as a chronic inflammatory disorder where a pro-inflammatory state in endothelial cells and endothelial activation is characterised by increased expression of adhesion molecules such as intercellular adhesion molecule-1 (ICAM-1), vascular cell adhesion molecule-1 (VCAM-1), and endothelial-leukocyte adhesion molecule-1 (E-selectin). Thymoquinone (TQ), one of the bioactive compounds in ***Nigella sativa*** (black seed), has been postulated to have possible anti-atherosclerotic properties. However, its effects on expression of endothelial adhesion molecules are still poorly understood.
Objective: To determine the effects of TQ on ICAM-1, VCAM-1 and E-selectin protein and gene expressions in stimulated Human Coronary Artery Endothelial Cells (HCAECs).
Methods: HCAECs were stimulated with 1µg/ml for 24 hours lipopolysaccharide (LPS) with or without four different concentrations: 4.5, 9, 18 and 36µM of TQ. Positive and negative controls were performed in parallel. The gene and protein expressions were measured using QuantiGene 2.0 Multiplex Assay and commercial ELISA respectively.
Results: TQ significantly reduced ICAM-1, VCAM-1 and E-selectin gene and protein expressions: ICAM-1 [gene: at 36µM ($p<0.01$), protein: at 18µM and 36µM ($p<0.05$ and 0.001 respectively)], VCAM-1 [gene: at 9µM, 18µM and 36µM ($p<0.01$ and 0.001 respectively), protein: at 36µM ($p<0.05$)] and E-selectin [gene: at 18µM and 36µM ($p<0.01$ and 0.001 respectively), protein: at 9µM, 18µM and 36µM ($p< 0.001$)].
Conclusion: TQ reduces pro-inflammatory biomarkers of endothelial activation in a dose-dependent manner, suggesting its potential atheroprotective properties which could potentially be incorporated in standard treatment regimes to prevent atherosclerosis and its related complications.

No conflict of interest

-203A/C POLYMORPHISM AND REGULATION OF CHOLESTEROL 7ALPHA-HYDROXYLASE GENE (CYP7A1) EXPRESSION

M. Vlachova[1], R. Poledne[1], M. Jirsa[1], J. Kovar[1]
[1]Centre of Experimental Medicine, Institute for Clinical and Experimental Medicine, Prague 4, Czech Republic

Introduction: Cholesterol 7α-hydroxylase (CYP7A1), a key regulatory enzyme of bile acid biosynthesis, plays an important role in cholesterolemia regulation. The -203A/C polymorphism in CYP7A1 gene promoter affects the responsiveness of plasma cholesterol to dietary fat and/or cholesterol. However, the underlying mechanisms are not understood yet. Moreover, the -203A/C polymorphism is a part of a complex haplotype that includes also -469A/T polymorphism.

Aim: To determine the role of -203A/C and -469A/T polymorphisms in the regulation of *CYP7A1* expression in hepatocytes.

Methods: The fragments of *CYP7A1* promoter variants spanning -764 to +14 position carrying all possible combinations of variants in position -203 and -469 ([-203A; -469A], [-203A; -469T], [-203C; -469A], [-203C; -469T]) were prepared by targeted mutagenesis. Their activity was studied using dual luciferase assay (Dual-Luciferase Reporter Assay System, Promega) in HepG2 and HuH7 cells.

Results: In dual luciferase system, the expression of -203C variant was found to be severalfold higher than that of -203A variant in both HepG2 and Huh7 cells; the variants in position -469 did not affect the gene expression. There were no differences in the regulation of expression of *CYP7A1* variants by insulin, PPARα agonists and bile salts.

Conclusions: We found that the expression of -203C variant of *CYP7A*1 can be regulated to a larger extent than that of -203A variant which can explain the higher responsiveness of C allele to dietary fat and/or cholesterol. However, the exact underlying regulatory mechanisms remain to be clarified.

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No conflict of interest

HSPB7 IS REQUIRED FOR CARDIAC MYOFIBRILLOGENESIS.

Y. Yan[1], Y.L. Shih[2], P.C. Tsai[1], B.Y. Yang[1]
[1]Institute of Biomedical Sciences, Academia Sinica, Taipei city, Taiwan
[2]Institute of Biochemistry and Molecular Biology, National Yang-Ming University, Taipei city, Taiwan

HSPB7, also cardiaovascular small heat shock protein (cvHSP), is a member of small heat shock protein family. Though many sHSPs have been demonstrated containing molecular chaperone activity in vitro in cell-free conditions and the stress protection activity in animal disease models, the function of HSPB7 remains enigmatic. Recent genome-wide association studies (GWAS) have identified several SNPs in HSPB7 to be associated with idiopathic and sporadic dilated cardiomyopathy (DCM). In addition, we have found HSPB7 is a potential early biomarker after MI and can serve as an independent risk factor of acute coronary syndrome in patients with acute chest pain. HSPB7 is highly expressed in cardiomyocytes since the onset of heart formation, and localizes on myofibril with a dynamic pattern during heart development. Loss of HSPB7 in mouse results in embryonic lethality at E11.5 with sarcomere formation defects. In Hspb7 deficient heart, the disarray and fragmental sarcomere structures are observed by transmission electron microscopy. Furthermore, filamin C was identified as the interacting protein of HSPB7 in cardiomyocytes by protein pull-down and LC/MS/MS analysis. Abnormal location of several costamere complex proteins and Z disk proteins was detected in the homozygous mutant cardiomyocytes by confocal fluorescence microscopic analysis. Taken together, our findings highlight the novel role of sHSPs affecting the myofibrillogenesis of the cardiomyocytes and suggest the pathological role of HSPB7 in DCM.

No conflict of interest

BONE MARROW VERSUS ADIPOSE TISSUE DERIVED MESENCHYMAL STEM CELLS IN AN EXPERIMENTAL MODEL OF DIABETES AND HEART FAILURE

H.I. Ammar[1], H.E. El Said[1], M.B. Nashed[1], H.M. Gabr[2], R.I. Ammar[3], M.T. Hussien[4], M.A. Haidara[5]
[1]Department of physiology, Faculty of Medicine Cairo University, Cairo, Egypt
[2]Department of clinical pathology, Faculty of Medicine Cairo University, Cairo, Egypt
[3]Department of pediatric cardiology, Faculty of Medicine Cairo university, Cairo, Egypt
[4]Department of pathology, Faculty of Medicine Misr university for science and technology, Cairo, Egypt
[5]Department of physiology, College of Medicine King Khalid University, Abha, Saudi Arabia

Heart failure is a common association in diabetic patients. In this context, stem cell transplantation for cardiac repair is a promising solution. We aimed to evaluate a possible role and the relative efficacy of human bone marrow (BM-MSC) and adipose tissue (AT-MSC) mesenchymal stem cells in ameliorating cardiac function in an experimental model of diabetes and heart failure. Male Wistar rats (200-220gms) were treated withvehicle of saline(control group) ; with streptozotocin (65 mg/kg i.p) (D group) ; with streptozotocin (65 mg/kg ip)**,** followed after one month by Adriamycin (2.5mg/Kg ip) 3 times /week for 2 weeks (D - HF group); with BM-MSCs (1 ml of 2,000,000stem cells iv in rat tail vein) after induction and verification of diabetes and heart failure(BM- MSCs group); with AT-MSCs (1 ml of 2,000,000stem cells iv in rat tail vein) following induction of diabetes and heart failure as above(AT-MSCs group). Echocardiography showed that both BM-MSC and AT-MSC were equally effective in ameliorating the decline in cardiac function. In vitro study of cardiac contractility showed an equal significant improvement using BM-MSC or AT-MSC. Histopathological examination of cardiac and pancreatic tissue showed successful homing of BM-MSC and AT-MSC associated with preservation of vulnerable cardiomyocytes and regeneration of some pancreatic islets. A significant improvement of serum insulin which correlated with cardiac function was detected.

In conclusion, both BM-MSC and AT-MSC improved cardiac function in diabetic rats with heart failure. This improvement observed is in support of paracrine actions of transplanted cells.Comparison between BM-MSCs and AT-MSCs showed equal benefits.

No conflict of interest

ANGIOGENESIS AND CAPILLARY NETWORK DEVELOPMENT IN POROUS SILK FIBROIN FILM

L. Bai[1], K.H. Zhan[2], J.M. Xu[1], X.Q. Dai[1]
[1]School of Textile and clothing Engineering, Soochow University, Suzhou, China
[2]School of Mechanical and Electronic Engineering, Soochow University, Suzhou, China

Background. For design and development of biomaterials and their effective application, it is important to clarify the vascularization process in materials and its mechanisms. For this purpose by experimental observation and investigation of angiogenesis in Porous silk fibroin film (PSFF) implanted into rats, the angiogenesis process in materials and the relationship between tissue hypoxia and angiogenesis modes were studied.

Methods and principal findings. Based on the expression status of HIF-1α and VEGF in PSFFs, the angiogenesis environment in materials after implantation was evaluated, the angiogenesis modes and its mechanism were explained, and the process of capillary network formation was discussed. The results showed that the sprouting angiogenesis appeared frequently in the early period after implantation, the intussusceptions also were observed but rarely; and in later stage the capillaries come into being mainly by intussusceptions. According to the response effect of ECs to the VEGF concentration in microenvironment, the model of capillary network development in porous material was proposed (Fig.1).

Conclusions. Based on observed results it is deduced that the severe hypoxic state is the main reason of causing rapid vascularization by the sprouting way when the tissue cells invaded PSFFs. After the capillaries formed in materials, the degree of hypoxia would decline, which would cause the weak response of ECs and form new capillaries by intussusceptions.

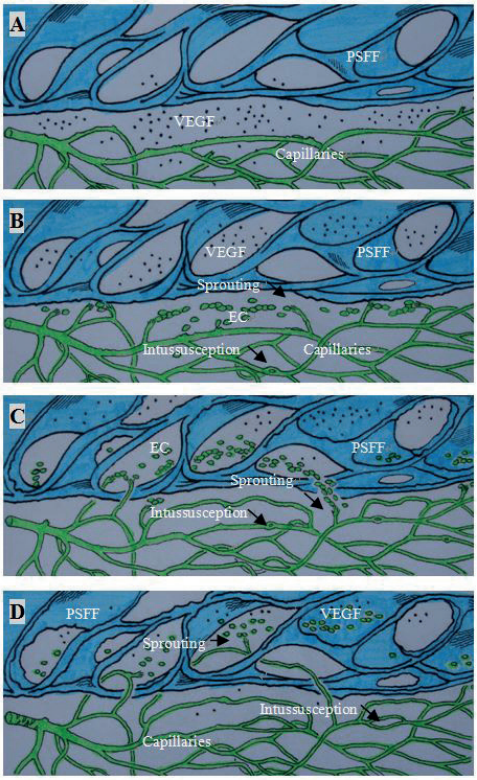

Fig.1 A model of capillary network development in porous materials

No conflict of interest

DELAYED RESOLUTION OF INFLAMMATION AND A DEFECT IN TGF-? SIGNALING CONSTITUTE A MECHANISM FOR IMPAIRED WOUND HEALING IN TYPE 2 DIABETES

M. bitar[1], W. al-ali[1], F. al-mulla[1]
[1]pharmacology, kuwait university, Safat, Kuwait

An indolent non healing wound (WH) and low-grade chronic inflammation are cardinal features of the diabetic state. Estrogen together with transforming growth factor-β1 (TGF-β1)/Smads and TNF-α/NF-κB in macrophages and fibroblasts appear to play a critical role in determining the rate and nature of WH. Herein, we hypothesized that delayed resolution of inflammation and a defect in TGF-β signaling constitute a mechanism for impaired wound healing in type 2 diabetes. Goto-Kakizaki (GK) rats were used as a genetic model of type 2 diabetes (T2D). Parameters related to the various stages of WH were assessed in a full-thickness excisional wound using histomorphometry, western blotting, real-time PCR and immunofluorescence microscopy. Retarded re-epithelialization, suppressed angiogenesis, delayed wound closure, reduced estrogen level and heightened state of oxidative stress were documented in T2D wounds. These abnormalities were associated with a defect in resolution of inflammation, impaired wound TGF-β1 signaling and enhanced TNF-α/NFκB activity. Human/rat dermal fibroblasts of T2D, compared to corresponding control values, displayed resistance to TGF-β-mediated responses including cell migration, myofibroblast formation, and p-Smad2 generation. A pegylated form of soluble TNF receptor-1 (PEG-sTNF-RI) or estrogen replacement therapy significantly improved re-epithelialization and wound contraction, enhanced TGFβ/Smad signaling, and polarized the differentiation of macrophages toward an M2 or 'alternatively' activated phenotype, while limiting secondary inflammatory-mediated injury. Our data suggest that delayed resolution of inflammation and a defect in TGFβ/Smad signaling-induced by estrogen deficiency contribute to the non-healing diabetic wounds. Intriguingly, most of these wound diabetic phenotypes were partially ameliorated using estrogen- and/or PEG-sTNF-RI-based therapy.

No conflict of interest

UTILISING ADENOVIRAL VECTORS FOR THERAPEUTIC TIMP 3 GENE TRANSFER INTO VASCULAR SMOOTH MUSCLE CELLS TO PREVENT RESTENOSIS FOLLOWING CORONARY BYPASS GRAFTING

S. Edwardson[1], K. White[1], A.H. Baker[1]
[1]Gene Therapy, Institute of Cardiovascular and Medical Sciences, Glasgow, United Kingdom

BACKGROUND: The use of adenovirus for gene therapy to treat post-bypass graft vein stenosis has many limitations. The vector's main cellular entry receptor (CAR) is not present on the smooth muscle cell surface. This has led to a necessity for high viral doses in order to obtain successful TIMP 3 gene expression. Increasing the affinity of the Ad5 vector for CD46 receptor (abundant on smooth muscle cell surface) can increase the vector's infectivity, using a reporter gene. This potentially facilitates reduction in necessary viral dose, thereby improving its safety.

We aimed to demonstrate that increasing the vector's CD46 affinity (to make T*35++) displays superior infection efficiency and TIMP3 expression in primary cell lines. We also aimed to demonstrate a further reduced cell number and average migration distance when T*35++ is used.

METHODS: Viral capsid structure was assessed via Silver stain. Western blot and immunofluorescence studies were performed to identify TIMP3 expression. 72 hours post-infection, cell number was counted manually. Average migration distance of the infected samples was assessed using a scratch assay.

RESULTS: T*35++ infected cell samples expressed more TIMP3 compared to Ad5 at each viral dose. Cell number was reduced in all infected samples, and was lowest in the T*35++. This was also reflected in the cells' average migration distance.

CONCLUSIONS: Increasing the CD46 affinity of Ad5 increases infection efficiency in primary smooth muscle cells, with superior functional outcome. This potentially allows for drastic reduction in necessary viral dose, thereby improving its safety for future clinical trials.

No conflict of interest

AGE-ASSOCIATED ACTIVATION OF UROKINASE SYSTEM AND MMPS IN ADIPOSE-DERIVED MESENCHYMAL STEM CELLS FROM PATIENTS WITH CORONARY ARTERY DISEASE (CAD)

A. Efimenko[1], N.A. Dzhoyashvili[1], N.I. Kalinina[1], R.S. Akchurin[2], Y.E.V. Parfyonova[3]
[1]Faculty of Medicine, Lomonosov Moscow State University, Moscow, Russia
[2]Cardiovascular surgery, Russian Cardiology Research and Production Complex, Moscow, Russia
[3]Laboratory of angiogenesis, Russian Cardiology Research and Production Complex, Moscow, Russia

Mesenchymal stem cells, including adipose-derived stem/stromal cells (ADSC) participate in tissue repair due to their differentiation capacities and abilities to stimulate the blood vessel and nerve growth. ADSC also produce metalloproteinases (MMPs) and urokinase mediating extracellular matrix (ECM) remodelling and proteolytic activation of growth factors. Aging is associated with impaired tissue repair. We analyzed how aging affects urokinase system and MMPs production by human ADSC.

ADSCs were isolated from subcutaneous fat tissue samples of 64 patients (age 43-77 years) with CAD. Cells were characterized as MSC according to their immunophenotype and differentiation capacity. Telomere length, urokinase (uPA), its receptor (uPAR), plasminogen activator inhibitor-1 (PAI-1), MMP2, MMP9 expression (real-time PCR) as well as uPAR surface expression (flow cytometry) were assessed in ADSC. Content of pro- and active forms of MMP2 and MMP9 (zymography) and PAI-1 (ELISA) was estimated in ADSC conditioned medium.

ADSC from aged patients had shorter telomeres (r=-0,6, p=0,006) and elevated uPAR and PAI-1 gene expression (r=0,46, p=0,001 and r=0,47, p=0,001) as well as uPAR surface expression (r=0,65, p=0,01). ADSC with shorter telomeres produced more PAI-1 to conditioned medium (r=-0,41, p=0,02). Content of pro-MMP2 and pro-MMP9 was higher in ADSC obtained from elder patients compared to younger patients (p<0,05) and we observed similar tendency for active forms of MMP2 and MMP9.

Aging is associated with up-regulation of urokinase system and MMPs in ADSC which can reflect cell response to age-related ECM remodelling and might be a compensatory mechanism for more efficient activation of fewer amounts of secreted growth factors.

No conflict of interest

IN SITU REPROGRAMMED SPERMINE TREATED-ADIPOSE TISSUE–DERIVED MULTI-LINEAGE PROGENITOR CELLS IMPROVE LEFT VENTRICULAR DYSFUNCTION IN A SWINE CHRONIC MYOCARDIAL INFARCTION MODEL.

H. Okura[1], M. Soeda[1], S. Miyagawa[2], Y. Sawa[2], A. Ichinose[3], A. Matsuyama[1]
[1]Platform for realization of regenative medicine, Foundation for biomedical research and innovation, Kobe, Japan
[2]Department of Surgery, Osaka University Graduate School of Medicine, Suita, Japan
[3]Department of Plastic Surgery, Kobe University Hospital, Kobe, Japan

Background: Spermine, known as one of polyamines, has been reported to make embryonic stem cells differentiate into cardiac lineage. In this study, we examined whether spermine could commit human adipose tissue–derived multi-lineage progenitor cells (hADMPCs) into cardiac lineage and whether the spermine treated-hADMPCs would differentiate into cardiomyocytes-like cells and improve left ventricular dysfunction in a swine chronic myocardial infarction model.

Methods and Results: After 24h-treatment with spermine, hADMPCs showed the augmentation of cardiac marker-expressions; nkx2.5, islet-1, alpha-cardiac actin and cardiac troponin I (11.2-, 27.5-, 43.6- and 19.1-fold to hADMPCs ***per se***, respectively). To examine the effect of spermine treated-hADMPCs on left ventricular dysfunction, swine chronic MI model were built up by first ballooning and reperfusion to first diagonal branch and second one to left ascending coronary artery (#6) 1 week-later. Four week-later second one, the swine (immunization with CyA 0.6mg i.m./kg/day) received transplantation of spermine treated-hADMPCs ($1x10^5$, $3x10^5$, $1x10^6$ and $3x10^6$ cells/kg) or lactic Ringer's solution via intracoronary (#6), and echocardiogram was examined at 0, 4, 8 and 12 weeks after transplantation. Follow-up showed rescue of function in the transplanted, and the most effective dose was $3x10^5$ cells/kg (EF; 33.4%, 47.0%, 51.5% and 52.9% at 0, 4, 8 and 12 week-after transplantation, respectively). Histologically, the spermine treated-hADMPCs were engrafted into the scarred myocardium and reprogrammed into human specific troponin I and alpha-cardiac actin positive cells ***in situ*** 12 week-after transplantation.

Conclusion: The transplantation of spermine treated-hADMPCs is a potentially effective therapeutic strategy for future cardiac tissue regeneration.

No conflict of interest

TRANSPLANTATION OF HUMAN ADIPOSE TISSUE-DERIVED MULTILINEAGE PROGENITOR CELLS BUT NOT ADIPOSE TISSUE-DERIVED STROMAL/STEM CELLS REDUCES SERUM CHOLESTEROL IN HYPERLIPIDEMIC WATANABE RABBITS.

H. Okura[1], M. Soeda[1], M. Morita[1], M. Moriyama[1], H. Moriyama[2], S. Yamashita[3], T. Hayakawa[2], A. Ichinose[4], A. Matsuyama[1]

[1]Platform for realization of regenative medicine, Foundation for biomedical research and innovation, Kobe, Japan

[2]phamaceutical research and technology insutitute, Kinki university, Higashi-Osaka, Japan

[3]Department of internal medicine, Osaka University Graduate School of Medicine, Suita, Japan

[4]Department of Plastic Surgery, Kobe University Hospital, Kobe, Japan

Familial hypercholesterolemia (FH) is an autosomal codominant disease characterized by high concentrations of proatherogenic lipoproteins and premature atherosclerosis secondary to low-density lipoprotein (LDL) receptor deficiency. We have supposed that human adipose tissuederived multilineage progenitor cells (hADMPCs, which were reported by Okura et al.) localized in the portal triad after transplantation via portal vein, subsequently integrated into the hepatic parenchyma and showed hepatocytic differentiation ***in vivo*** and lowered serum cholesterol in the WHHL rabbit, an animal model for homozygous FH. Here we showed that transplantation of hADMPCs but not human adipose tissue-derived stromal/stem cells (hADSCs, which were reported by Zuk et al.), could correct the metabolic defects of WHHL rabbit. Transplantation of hADMPCs via portal vein resulted in significant reductions in total cholesterol, and the reductions maintained for 12 weeks. On the other hand, the total cholesterol levels of hADSCs-transplanted group showed no significant difference to those of saline control group. To confirm transplantation of hADMPCs but not hADSCs reduces serum cholesterol in hyperlipidemic Watanabe rabbits, we examined LDL turnover studies using ^{125}I-labelled LDL. ^{125}I-LDL turnover study showed that the 24 hour clearance rate of LDL was significantly higher and LDL half-life was significantly shorter in the hADMPCs transplanted-WHHL rabbits than those of saline control group. There was no significant difference on the ^{125}I-LDL turnover study between hADSCs-transplanted group and saline control one. These results indicated that ransplantation of hADMPCs but not hADSCs could correct the metabolic defect of the WHHL rabbit and be a novel therapy for inherited liver diseases.

No conflict of interest

MICROVESSEL DENSITY IS HIGH IN CLEAR-CELL RENAL CELL CARCINOMAS OF UKRAINIAN PATIENTS EXPOSED TO CHRONIC PERSISTENT LOW-DOSE IONIZING RADIATION

A.R.-S.,L.M.-Q.,G.V. A. Romanenko[1]
[1]*Pathology, Institute of Urology AMS of Ukraine, Kiev, Ukraine*
[2]*Pathology, Valencia University Medical School, Valencia*
[3]*Pathology, University Hospital Ribera, Alzira, Spain*
[4]*University del Norte, Barranquilla, Colombia*
[5]*Urology, Institute of Urology AMS of Ukraine, Kiev, Ukraine*

"**Introduction:** During the 25-year period subsequent to the Chernobyl accident, the morbidity of malignant renal tumors in Ukraine has increased from 4.7 to 10.7 per 100,000 of the total population. This study aimed to examine the role of angiogenesis in clear-cell renal cell carcinomas (CCRCC) carcinogenesis associated with chronic persistent low-dose ionizing radiation (CPLDIR) exposure.**Materials and methods:** Paraphin-embedded specimens of 106 CCRCCs were studied. Control cases were 18 tumors from Spanish patients (group 1), 25 tumors from Ukrainian patients from so-called clean areas without radio-contamination (group 2), and 63 tumors from Ukrainian patients from radio-contaminated areas (group 3). For intratumoral microvessel density (MVD) determination, anti-CD31 antibody was used. A computerized image analysis program was used to quantitatively calculate the vascular density.**Results:** 73% of group 3 and 72% of group 2 CCRCCs displayed the highest MVD. A striking increase in MVD was seen in group 3 CCRCCs, in comparison with groups 1 and 2 ($p < 0.001$). The majority of hot spot vessels in group 3 were poorly differentiated. Moreover, MVD values for total vessels as well as for capillaries and tumor grade were strongly correlated. The ratio of the average total vessels and capillaries in the Ukrainian groups combined was 1.65:1 in comparison to the Spanish group.**Conclusions:** Our results provide evidence that CPLDIR exposure increases MVD (particularly capillary) in CCRCCs and is associated with a higher histological grade."

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ANGIOGENESIS IN BIOMATERIAL SCAFFOLDS WITH DIFFERENT BIODEGRADABILITY

K. zhan[1], L. Bai[2], L. Xie[3], X. Wang[3], B. Zuo[2]
[1]School of Mechanical and Electronic Engineering, Soochow University, Suzhou, China
[2]School of Textile and Clothing Engineering, Soochow University, Suzhou, China
[3]Department of Orthopaedics, The Second Affiliated Hospital of Soochow University, Suzhou, China

The angiogenesis in biomaterial scaffolds is an important part in tissue regeneration induced by the biomaterials. In order to explore the effects of the biodegradability of biomaterials on vascularization process, we performed animal experiments. A piece of porous silk fibroin film (SF) of easy biodegradation and a piece of porous polyvinyl alcohol film (PVA) of hard biodegradation were implanted into a same skin wound of adult rat, and the implanted biomaterials were sampled at several time points after implantation and were examined with CD34 immunohistochemistry. The results of the immunohistochemical staining showed that angiogenesis in the two biomaterials occurred at 3 days after implantation and a few days later the new blood vessels invaded throughout the thicknesses from the edges of the biomaterials. The statistical data of vascular density showed two peaks. The first peaks were all at 5 days which was in a vascularization phase from nothing to something, and the second peaks in the SF and PVA were, respectively, at 16 days and 41 days, which synchronized with the significant degradation of the biomaterials and were in a formation phase of the exuberant granulation tissues. Combining the evolution of the vascular diameter in the two biomaterials, we conclude that the poor biodegradability of PVA will lead the blood vessel network to be late to enter the remodeling phase and may lead to vascular redundancy, in contrast, the vascularization process of SF is faster, and therefore, SF is a better biomaterial conducive to fast angiogenesis and tissue regeneration.

No conflict of interest

PLASMA CIRCULATING ENDOTHELIN-1 IN ON-PUMP CORONARY SURGERY CARDIOPULMONARY BYPASS

S. Abdel-Sayed[1], J. Horisberger[1]
[1]Surgery, Cardiovascular research, Lausanne, Switzerland

Endotheline-1 (ET-1) is an endothelium-derived potent vasoconstrictor peptide of 21 amino acid residues. On-pump coronary surgery is realized with cardiopulmonary bypass (CPB) and initiates physiologic changes, which can induce ET-1 synthesis. The purpose of this study is to determine and compare the plasma ET-1values before and after CPB. Ten patients comprised 2 female and 8 male undergoing coronary artery bypass grafting are investigated, having CPB. EDTA-plasma samples are collected 10 minutes before the extracorporeal circulation (CPB), 1 hour and 24 hours postoperatively. ET-1 is extracted by acetone from 1 ml of plasma and subjected to a sensitive enzyme-linked immunosorbent assay. Plasma levels of ET-1 in the 10 subject before the CPB are 0.68 ± 0.11 fmol/ml (mean ± SD, n=10), ranging from 0.57 to 1 fmol/ml. At 1 hour CPB plasma ET-1 levels are 17 % and 39 % less in 1 male and 1 female patient respectively, as compared to Et-1 values before the operation. The same male and female patients showed 11 % and 33 % less ET-1 concentration respectively, after 24 hours from the operation. ET-1 concentration is significantly increased in only 1 male patient, by 20 % as compared to the base value. Pre- and postoperative plasma ET-1 concentrations are in the range of normal human subjects. The postoperative decrease of the ET-1 concentration in patients may be to its binding to ET receptors and thus reduce its circulating values. The increase of ET-1 level in one patient may be associated with endothelium injury.

No conflict of interest

ENDOTHELIAL DYSFUNCTION AND ABNORMAL GLUCOSE TOLERANCE IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

L. David[1], A.G. Grossu[2], A. Grosu[1]
[1]emergency cardiology, Institute of Cardiology, Chisinau, Moldova
[2]imaging, Institute of Cardiology, Chisinau, Moldova

A large proportion of acute myocardial infarction (AMI) patients (pts) without diabetes mellitus (DM) have abnormal glucose tolerance (AGT) and worse prognosis compared to those with normal glucose tolerance (NGT). Endothelial dysfunction (ED) is suggested to be a predictor of future events in AMI patients. Data on endothelial function in AMI pts with AGT are scarce.

Methods: In 80 AMI pts (age 55.7 ±2.5 years): 23 with known DM and 57 non-diabetics, stratified by an oral glucose tolerance test (day 10) into those with AGT (n=30) and NGT (n=27) we studied serum levels of hsCRP, von Willebrand Factor (vWF, by ELISA), fasting insulin, HOMA-IR and assessed endothelial function with flow-mediated dilatation of the brachial artery (FMD). Data were compared in pts with NGT, AGT and DM.

Results. There was no difference in demographical and clinical characteristics between groups. Insulin (29.6±3.6 vs 23.03±5.2 vs 8.1±1.0 μIU/ml, $p<0.01$), hsCRP (12.3±0.5 vs 10.9±0.4 vs 8.2±0.7 mg/l, $p<0.05$), vWF (180.2±0.8 vs 146.9±4.7 vs 119.5±6.8 %, $p<0.01$) levels were higher and FMD was significantly lower (5.8±0.7 vs 7.6±0.6 vs 12.4±0.56 %, $p<0.001$) in DM and AGT pts compared to NGT pts. FMD correlated negatively with hs-CRP ($r = -0.57$, $p=0.001$), vWF($r = -0.53$, $p<0.0001$), HOMA-IR ($r = -0.45$, $p<0.001$) and 2h post load glucose level ($r = -0.63$, $p=0.0001$).

CONCLUSION: AMI patients with AGT have more impaired endothelial function than those with NGT and comparable to that seen in DM. Endothelial dysfunction correlated with inflammation, vWF plasma levels, insulin resistance and 2h post load glucose level.

No conflict of interest

VASCULAR ORGAN CULTURE UNDER FLOW CONDITIONS

M. Funovics[1], G. Edelhauser[1], R. Borny[1], D. Berzaczy[1], J. Lammer[1]
[1]Cardiovascular and Interventional Radiology, Medical University of Vienna, Vienna, Austria

Objective. For the understanding of biological processes in the vessel wall after interventional procedures (neointimal hyperplasia, SMC migration, gene expression profiling, drug testing) an ex-vivo tissue culture model of human vascular segments accessible to interventional procedures and sufficient cultivation time to study their effects was constructed and characterised.

Methods. 17 saphenous vein segments of approximately 3 cm each were harvested from 12 patients undergoing bypass surgery of the leg. The vessel segments were placed in a customized glass chamber connected to a regulated roller pump, afterload valve, and reservoir. The chamber has a 7F port to allow for angioplasty or stent deployment directly in the vessel segment. Customized culture medium was pumped at a set flow rate and transmural pressure. The chamber was kept in a sterile environment in an incubator with daily medium changes. Vessel segments were cultured for 5 or 10 days.The samples were histologically examined with uncultivated and non perfused segments of the original vessel serving as controls. Morphology and integrity were investigated after haematoxylin-eosin, periodic acid-schiff, and elastica van gieson staining and immunohistochemistry for CD31 and 1A4.

Results. One sample was lost to infection, the 16 remaining samples were cultivated without detectable infection for the planned time period. Temperature, medium pH, and transmural pressure remained constant during the cultivation. Compared to the controls, medial thickness remained within 10% of the original values, no changes in elastin content, intimal morphology, or receptor distribution and density were detectable.

Conclusion. An ex-vivo tissue culture model was created and characterized that can maintain basic biomorphology and receptor status of human venous segments in vitro over 10 days. This model potentially allows for long-term investigation of human vessel segments including studying the effects of interventional procedures in a convenient, cost effective, controlled environment.

No conflict of interest

PROGNOSTIC VALUE OF HIGH MOBILITY GROUP BOX 1 IN YOUNG PATIENTS WITH CHEST PAIN

S. haghjooy javanmard[1], N. dana[1], M. Sadeghi[2], G. Maryam[2]
[1]Physiology Research Center, Isfahan University of Medical Sciences, Isfahan, Iran
[2]Cardiac Rehabilitation Research Center Isfahan Cardiovascular Research Institute, Isfahan University of Medical Sciences, Isfahan, Iran

BACKGROUND: Atherosclerosis is accepted as an inflammatory disease. Evidence suggests that inflammation evoked by injury plays a pathogenic role in all stages of atherosclerosis. This study aimed to investigate whether high mobility group box 1 (HMGB1) a proinflammatory cytokine /nuclear protein which is derived from both injured endothelium and activated macrophages/monocytes, could contribute to the progression of atherosclerosis and other cardiovascular diseases.

METHODS: 80 patients who referred to the hospital due to angina pectoris, had the diagnosis of unstable angina and were candidates of angiography were recruited in this study in Chamran hospital. At first, a questionnaire was filled for each patient including demographic factors and their medical history. Then a blood sample was taken to assess level of HMGB1. Data was analyzed using SPSS version 18.

RESULTS: The mean plasma level of HMGB1 in the case group was 27.16±2.9ng/ml while it was =19.6±1.9 ng/ml in control groups (p=0.03). The Odds Ratio for coronary artery plaque associated with high (>50th percentile) levels of HMGB1 was 2.5(95% CI, 1.02 to 6.17, p = 0.03).

CONCLUSION: Increased plasma HMGB1 concentration may be associated with an increased risk of coronary atherosclerosis.

Keywords: High mobility group box 1, Coronary artery diseases, Inflammation, biomarkers

No conflict of interest

EFFECTS OF TELMISARTAN ON ARTERIAL VASODILATION VIA PROTEASE-ACTIVATED RECEPTOR-2 ACTIVATION IN SHRSP.Z-LEPRFA/IZMDMCR RATS WITH METABOLIC SYNDROME

S. Kagota[1], K. Maruyama[1], H. Wakuda[1], J.J. McGuire[2], N. Yoshikawa[1], K. Nakamura[1], K. Shinozuka[1]
[1]Department of Phamracology School of Pharmaceutical Sciences, Mukogawa Women's University, Nishinomiya, Japan
[2]Cardiovascular Research Group Division of BioMedical Sciences, Memorial University, St. John's, Canada

We previously reported that chronic oxidative-nitrosative stress impairs coronary vasodilation in SHRSP.Z-*Lepr*^{fa}/IzmDmcr rats (SHRSP.ZF) with metabolic syndrome (MetS). Protease-activated receptor-2 (PAR-2) activation causes vascular inflammation and vasodilation, but its role in MetS remains uncertain. We examined alterations in vasodilation via PAR-2 activation and the effect of telmisartan on vasodilation by this mechanism in SHRSP.ZF.

Relaxation induced by 2-furoyl-LIGRLO-amide (2fly), the PAR-2 activating peptide, was unchanged in isolated first-order mesenteric arteries (MA) and slightly impaired in superior MA of 18-week-old SHRSP.ZF, compared to that observed in control Wistar–Kyoto rats (WKY). However, acetylcholine and sodium nitroprusside–induced relaxation decreased in both MA. Treatment with an NO synthase inhibitor partially inhibited 2fly-induced relaxation in both MA of the SHRSP.ZF, but the inhibition was greater than that observed in WKY. sGC mRNA levels decreased in both MA of the SHRSP.ZF, while PAR-2 mRNA levels remained unchanged in the first-order MA and decreased in the superior MA. Telmisartan treatment (10 mg·kg^{-1}·day^{-1}, p.o., for 8 weeks) increased acetylcholine- and 2fly-induced relaxations in both MA and decreased serum TBARS levels (an index of oxidative stress) in the SHRSP.ZF.

In SHRSP.ZF with MetS, vasodilation via PAR-2 activation is preserved in small MA in contrast to that in large MA, even under conditions involving the deterioration of NO-dependent pathway. NO and non-NO relaxing factor(s) contribute to PAR-2-mediated relaxation in resistant arteries, and the balance between these factors may be altered for preserving vasodilation in MetS. Telmisartan prevented the development of the vasodilator alterations in MetS.

No conflict of interest

ENDOTHELIAL CELL BIOMARKERS DISCRIMINATE OBESE PATIENTS WITH AND WITHOUT GLUCOSE INTOLERANCE

K. Korybalska[1], A. Kanikowska[2], J. Grzelczak[1], E. Swora-Cwynar[2], M. Grzymislawski[2], J. Witowski[1]
[1]Pathophysiology Department, University of Medical Science, Poznan, Poland
[2]Department of Internal Medicine Metabolic Disease and Dietetics, University of Medical Science, Poznan, Poland

Both obesity and glucose intolerance are associated with increased risk of endothelial cell dysfunction and coronary artery disease. As obesity and glucose intolerance often occur together, the present study aimed to determine whether the expression of biomarkers linked to endothelial cell status varies between individuals with similar obesity, blood pressure, fasting glucose, and serum cholesterol, but differing in the presence of glucose intolerance and/or hiperinsulinemia. Serum concentrations of selected parameters were measured with immunoassays. Proliferation of endothelial cells (EA.hy926 line) treated with patients' serum (20% v/v) was measured with the MTT test. The results were expressed as means ± SEM.

Parameter	Obesity with glucose intolerance and/or hyperinsulinemia (n=24)	Obesity (n=23)	p
Age (years)	38±9	39±14	0,7458
Gender (men %)	33	39	0,6793
BMI (kg/m^2)	40±1	39±1	0,2251
WHR	0,93±0,01	0,91±0,02	0,5058
Systolic BP (mm Hg)	130±3	128±2	0,4789
Diastolic BP (mm Hg)	83±2	80±2	0,3055
Fasting glucose (mg/dl)	103±4	97±2	0,3519
Cholesterol (mg/dl)	199±6	190±9	0,4192
CRP (mg/l)	6,9±1	3,0±0,7	0,0048
VEGF (pg/ml)	168±23	74±8	0,0004
MCP-1 (pg/ml)	95±10	96±11	0,7175
IL-6 (pg/ml)	20±11	21±19	0,1013
sICAM-1 (pg/ml)	116±4	116±5	0,9861
PAI-1(pg/ml)	358±73	197±65	0,0015
Adiponectin (µg/ml)	1,7±0,2	1,9±0,2	0,3546
Resistin (ng/ml)	17±2	20±2	0,2419
Leptin (ng/ml)	53±4	44±7	0,1229
Proliferation index (%)	206±21	175±22	0,1634

Compared to simple obesity, obese patients with impaired glucose tolerance display increased levels of CRP, VEGF, and PAI-1, which points to ongoing inflammation, neoangiogenesis, and increased pro-coagulant activity. These parameters may serve as potential biomarkers of developing endothelial cell dysfunction in obese individuals.

No conflict of interest

COMPARISON OF LINAGLIPTIN, SITAGLIPTIN AND LIRAGLUTIDE EFFECTS ON SURVIVAL AND VASCULAR COMPLICATIONS IN EXPERIMENTAL SEPSIS

M. Mader[1], M. Hausding[1], S. Schumacher[1], M. Oelze[1], S. Steven[1], S. Daub[1], E. Schulz[1], T. Münzel[1], T. Klein[2], A. Daiber[1]
[1]2nd Medical Clinic Department of Cardiology, Medical Center of the Johannes Gutenberg University, Mainz, Germany
[2]CardioMetabolic Diseases Research, Boehringer Ingelheim, Biberach, Germany

Background: Gliptins (dipeptidyl peptidase [DPP]-4 inhibitors) are a new class of drug for the treatment of hyperglycemia and recent studies revealed anti-inflammatory effects of DPP-4 inhibitors in experimental atherosclerosis and septic animals. The aim of the present study was to compare the effect of linagliptin with an alternative DPP-4 inhibitor, sitagliptin, and the direct glucagon-like peptide (GLP)-1 analogue liraglutide on survival and vascular complications in different experimental models of septic shock.

Methods: Mice or rats were treated with linagliptin, sitagliptin or liraglutide for 4-7 days. On Day 3 or 6 of treatment, mice or rats were injected with lipopolysaccharide (LPS, 10, 17.5 or 20 mg/kg i.p.) to induce septic shock. DPP-$4^{-/-}$ mice served as an additional control group. Survival was monitored over time and vascular function, nitrosyl-iron hemoglobin in whole blood or oxidative stress were measured 24 h after LPS treatment. The Gehan-Breslow-Wilcoxon-Test was used for statistical analysis of Kaplan-Meier curves.

Results: Linagliptin and liraglutide therapy or DPP-4 deficiency improved the survival of septic mice. Liraglutide improved vascular dysfunction in septic rats without improvement of inflammatory parameters such as nitrosyl-iron hemoglobin in whole blood or oxidative stress. Linagliptin and to a minor extend sitagliptin improved vascular dysfunction in septic rats with significant suppression of inflammatory parameters.

Conclusion: The therapy of diabetic patients with linagliptin and liraglutide is well established. The results reported here on the improvement in the survival of septic animals could provide additional evidence for the potential use of these drugs in patients with septic shock.

No conflict of interest

THE RAT MESENTERY ANGIOGENESIS ASSAY IN VIVO— A NON-TRAUMATIC, QUANTITATIVE ASSAY THAT UNIQUELY FEATURES AN INTACT NATIVELY VASCULARISED TEST TISSUE

K. Norrby[1]
[1]*Pathology, University of Gothenburg Institute of Medicine, Gothenburg, Sweden*

The assay is biologically appropriate and is exceptionally well suited to in vivo studies of angiogenesis. Angiogenesis induced in the membranous mesenteric parts by intraperitoneal injection of a pro-angiogenic factor can be modulated by systemic administration of modifying agents of choice.

The test tissue is extremely thin allowing the 2-D microscopic visualization of the entire microvascular network down to single cell level in situ. In adult rats, the test tissue lacks significant physiologic angiogenesis. The lack of trauma-induced inflammation and angiogenesis ensures high sensitivity and discriminatory ability of the assay. The assay allows assessments of objective, quantitative, unbiased variables pertaining to microvascular spatial extension, density, and network pattern formation, as well as capillary sprouting, thereby enabling robust statistical analyses of the dose-effect and molecular structure-activity relationships.

The assay reveals with high sensitivity the toxic effects of administered drugs and is highly suited to studies of the combined effects on angiogenesis of agents that are administered systemically in either a concurrent or sequential fashion.

The assay replicates the clinical picture, as the angiogenesis-modulating test drugs are administered systemically and the responses observed reflect the net effect of all the resulting metabolic, cellular, and molecular alterations.

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No conflict of interest

PROMOTING CARDIOPROTECTIVE NITRIC OXIDE USING CAVEOLIN-1 DERIVED PEPTIDES

A. Trane[1], *P.N. Bernatchez*[1]
[1]*James Hogg Research Centre, University of British Columbia, Vancouver, Canada*

Decreases in vascular nitric oxide (NO), a regulator of vascular homeostasis, is known as endothelial dysfunction, and has been associated with increased risk for cardiovascular diseases such as hypertension and atherosclerosis. In fact, most treatments for vascular diseases tend to increase vascular NO production. We believe this increase in NO production is one of the primary contributors to treatment benefits and should be considered a primary target for therapeutics. Currently, one of the few known negative regulators of endothelial nitric oxide synthase (eNOS), which produces vascular NO, is caveolin-1 (Cav-1), which is expressed in endothelial cell plasma membrane. Our lab has demonstrated that a sequence derived from the Cav-1 scaffolding domain (CSD) could be used to promote NO and reduce blood pressure *in vivo* in an eNOS dependent manner. Hence we are interested in isolating the relevant sequence in the CSD and use it as a basis for a pharmacophore to promote NO release.

To this end, we have identified an optimized motif from the CSD and demonstrated that a peptide from the sequence could be used to promote NO *in vitro* in an eNOS dependent manner. Interestingly, part of this effect was attributed to activation of eNOS via the phosphoinositide 3-kinase (PI3K)/Akt signaling pathway, and was significantly reduced in the presence of wortmannin, an irreversible PI3K inhibitor.

Hence, we have identified a motif that could promote NO production, which may serve as a basis for pharmacophore for development of novel therapeutic approaches for the treatment of endothelial dysfunction.

No conflict of interest

INTERVENTIONAL CARDIOLOGY

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A LARGER FIBROTIC PLAQUE VOLUME PRIOR TO BARE-METAL STENT IMPLANTATION PREDISPOSES TO MORE PRONOUNCED NEOINTIMA FORMATION.

S. Haine[1], K. Wouters[2], H. Miljoen[1], T. Vandendriessche[1], M. Claeys[1], J. Bosmans[1], C. Vrints[1]
[1]Cardiology, Antwerp University Hospital, Antwerp, Belgium
[2]Statistics, Antwerp University Hospital, Antwerp, Belgium

Purpose: To investigate whether lesion plaque composition is related to bare-metal in-stent restenosis.

Methods: IVUS with virtual histology was performed in 124 patients prior to the implantation of a single Vision stent in a de novo coronary artery lesion. Exclusion criteria were diabetes, STEMI, CK-MB levels > twice the upper limit of normal within the past month, ostial and bifurcation lesions.

Results: At 6 months, 80% of included patients presented for invasive follow-up. In-stent late luminal loss (LLL) was 0.88 [0.37-1.23] mm. Restenosis was also assessed on IVUS as maximal percentage area stenosis (42 [33-59] %) and percentage volume intima hyperplasia (neointima volume divided by stent volume: 27 [20-36] %). Multiple linear stepwise backward ridge regression, correcting for implanted stent length, diameter and plaque volume, showed that fibrous tissue volume prior to PCI (49 [30-77] mm^3) was significantly and independently (p=0.038) related to LLL. Moreover fibrous tissue percentage (56 [49-61] %) was also significantly related to LLL (p=0.011). Similarly, fibrous tissue volume pre-PCI proved independently related to maximal percentage area stenosis (p=0.041) and percentage volume intima hyperplasia (p=0.004). Neither absolute nor relative amount of fibro-fatty, calcified or necrotic core tissue appeared related to any of the restenosis parameters.

Conclusions: The lesion volume of fibrous tissue prior to PCI is positively related to late luminal loss, maximal percentage area stenosis and percentage volume intima hyperplasia at 6 months after bare-metal stent implantation. Plaques with more voluminous fibrotic tissue show more pronounced restenosis, even after correction for total plaque volume pre-PCI.

No conflict of interest

INTERVENTIONAL CARDIOLOGY

DUAL ANTIPLATELET THERAPY SHIFTING IN PATIENTS NON-RESPONDER TO PLATELET FUNCTION TEST CAN IMPROVE OUTCOME AFTER CORONARY STENT IMPLANTATION

V. Mecarocci[1], R. Calabretta[1], E. Cecchi[1], V. Spini[1], A. Cordisco[1], L. Innocenti[1], M. Chiostri[1], C. Giglioli[1]
[1]Department of Heart and Vessels, Azienda Ospedaliero-Universitaria Careggi, Florence, Italy

Background: Conflicting data exist on the effect of a tailored dual antiplatelet therapy (DAPT) after coronary stent implantation in patients non-responder to this treatment. Aim of our study was to evaluate if the strategy of shifting DAPT in the real practice could be more effective in reducing high on-treatment platelet reactivity and if it could improve outcome of patients with coronary artery disease treated with stent implantation.

Methods: We studied 242 patients undergone to coronary stent implantation either for acute coronary syndromes and stable coronary artery disease and monitored their response to DAPT by assessing platelet-function with the Born assay; aspirin dose was increased in patients with poor response to this drug and in non-responders to clopidogrel therapy was shifted to clopidogrel double dose, ticlopidine, prasugrel or ticagrelor. The primary end-point was the composite of death, myocardial infarction, intrastent thrombosis, stroke or urgent revascularization during a mean 9 months follow-up after stent implantation. Platelet function analyses were performed two days after PCI and repeated in the case of switching to another antiplatelet regimen.

Results: Non-responders to the initial DAPT (aspirin 100 mg/die and clopidogrel 75 mg/die) were 93/242 (38%) and non-responders to both antiplatelets were 24/242 (10%). Non-responders to the initial DAPT were switched to double dose of clopidogrel, ticlopidine, prasugrel or ticagrelor obtaining a significant reduction in the residual platelet reactivity to the Born test with ADP 10 microM (mean values 59%, 56%, 50% and 33%, respectively, vs. 76% in non-responders). No significant difference in the primary end-point occurred in non-responders treated with tailored DAPT as compared with responders.

Conclusions: These results suggest that shifting DAPT to a tailored treatment improves the response to antiplatelets, assessed with platelet function test, as well as the outcome of non-responder patients, suggesting that this strategy could be beneficial after coronary stent implantation.

No conflict of interest

INTERVENTIONAL CARDIOLOGY

A SINGLE CENTER ANALYSIS OF DEFINITE STENT THROMBOSIS OVER TWO DECADES IN 16,515 CONSECUTIVE PATIENTS

D. Trabattoni[1], F. Fabbiocchi[1], P. Montorsi[1], A. Lualdi[1], G. Teruzzi[1], C. Ferrari[1], G. Calligaris[1], P. Ravagnani[1], S. Galli[1], A.L. Bartorelli[1]
[1]Invasive Cardiology, Centro Cardiologico Monzino IRCCS, Milano, Italy

Background: Stent thrombosis (ST) is a dreaded complication of percutaneous coronary intervention. Aim of our study was to analyze the occurrence and timing of ST from 1992 to 2010 in a high-volume single center.

Methods: Consecutive pts (n= 16,515) undergoing PCI between 1992 and 2010 were clinically followed-up. The primary endpoint was the occurrence of ST, death and major adverse cardiac events (MACE) at any time after stenting. ST was classified according to ARC definition and to the timing of occurrence as early (within 30 days), late (between 31 days and 1 year) and very late (> 1 year).

Results: Definite ST occurred in 105 (0.63%) pts (86 men, mean age 62±11 years) treated with BMS (65/7855 pts, 0.8%) or DES (40/8609, 0.5%), p=0.003. Early ST occurred mainly in BMS (68% vs 32%, p=0.04), while late and very late ST accounted for 26% of BMS vs. 45% of DES ST (p=0.047). No difference in fatal ST was observed among the two groups (5/48 BMS vs 3/22 DES, p= 0.69). Regardless of ST timing, clinical presentation was acute MI in 61%, unstable angina in 28% and cardiac arrest in 11% of pts. Premature dual antiplatelet therapy (n=1) or aspirin withdrawal (n=6) determined 6.6% of all ST. Cumulative incidence of ST-related death was 10.5%.

Conclusion: ST albeit an infrequent event, remains the main safety concern after BMS and DES use, occurs in both stent groups and is frequently due to aspirin withdrawal.

No conflict of interest

INTERVENTIONAL CARDIOLOGY

DETERMINATS FACTORS OF FAILURE IN CHRONIC TOTAL OCCLUSIONS: A MULTIDETECTOR COMPUTED TOMOGRAPHY (MDCT) STUDY

V. Martin-Yuste[1], A. Barros[2], G. Pons[2], R. Letta[2], S. Brugaletta[1], M. Sabate[1]
[1]Cardiology, ITC H Clinic, Barcelona, Spain
[2]Cardiology, Hospital Santa Creu y San Pau, Barcelona, Spain

Percutaneous revascularization (PCI) of chronic total occlusions (CTO) is a technical challenge with a lower success rate. The use of a multidetector computed tomography (MDCT) can identify the unfavourable morphological characteristics of the occluded segment associated with PCI failure.

Methods: Prospective, single-centre study of 69 patients with 1 or > CTO and clinical indication for revascularization. Anatomical features, plaque composition, distribution and density of calcium in the CTO body were characterized by MDCT.

Results: patients characteristics: age 63.4 ± 9.6 years, 84% men, hypertension 78%, 77% dyslipidemia, 38% diabetes mellitus. 77 lesions were analyzed: length of occlusion 19.9 ± 14.3 mm, duration of occlusion 47 ± 62 months. Success rate of revascularization 62%. Leading cause of failure: inability to cross the lesion with any guide wire. The most powerful angiographic factor of failure: severe curve between the occlusion and the proximal vessel [OR = 3.8 (95%,1,2-12) p = 0.02]. MDCT revealed as the only predictor factor of failure an arch of calcium that affected more than 50% of the vessel circumference in the proximal (p=0.04) and middle (p=0.03) segment of the occlusion.

Conclusions: MDCT identifies the presence of a calcium arc of > 50% of the circumference of the vessel at the proximal border and the middle part of the body CTO multiplying by a negative factor > 3 the possibility of failure.

No conflict of interest

INTERVENTIONAL CARDIOLOGY

STENT COATED WITH ANTIBODY AGAINST VASCULAR ENDOTHELIAL-CADHERIN CAPTURES ENDOTHELIAL PROGENITOR CELLS, ACCELERATES RE-ENDOTHELIALIZATION, AND REDUCES NEOINTIMAL FORMATION

H.S. Kim[1]

[1]*Cardiovascular Center, Seoul National University Hospital, Seoul, Republic of Korea*

Objective—In contrast to CD34, vascular endothelial-cadherin (VE-cadherin) is exclusively expressed on the late endothelial progenitor cells (EPC) whereas not on the early or myeloid EPC. Thus, VE-cadherin could be an ideal target surface molecule to capture circulating late EPC. In the present study, we evaluated whether anti-VE– cadherin antibody-coated stents (VE-cad stents) might accelerate endothelial recovery and reduce neointimal formation through the ability of capturing EPC.

Methods and Results—The stainless steel stents were coated with rabbit polyclonal anti-human VE-cadherin antibodies and exposed to EPC for 30 minutes in vitro. The number of EPC that adhered to the surface of VE-cad stents was significantly higher than bare metal stents (BMS) in vitro, which was obliterated by pretreatment of VE-cad stent with soluble VE-cadherin proteins. We deployed VE-cad stents and BMS in the rabbit right and left iliac arteries, respectively. At 48 hours after stent deployment in vivo, CD-31–positive endothelial cells adhered to VE-cad stent significantly more than to BMS. At 3 days, scanning electron microscopy showed that over 90% surface of VE-cad stents was covered with endothelial cells, which was significantly different from BMS. At 42 days, neointimal area that was filled with smooth muscle cells positive for actin or calponin was significantly smaller in VE-cad stents than in BMS by histological analysis (0.950.22 versus 1.340.43 mm2, respectively, P0.02). Immuno-histochemical analysis revealed that infiltration of inflammatory cells was not significantly different between 2 stents.

Conclusion—VE-cad stents captured EPC successfully in vitro, accelerated endothelial recovery on stent, and eventually reduced neointimal formation in vivo.

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ACS AND ACUTE MYOCARDIAL INFARCTION

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MODULATION OF PROGRAMMED FORMS OF CELL DEATH BY INTRACORONARY LEVOSIMENDAN DURING REGIONAL MYOCARDIAL ISCHEMIA IN ANESTHETIZED PIGS.

E. Grossini[1], P.P. Caimmi[1], F. Platini[1], C. Molinari[1], F. Uberti[1], M. Cattaneo[1], G. Valente[1], D. Mary[1], L. Tessitore[1], G. Vacca[1]
[1]Translational Medicine, "A. Avogadro" University of Eastern Piedmont, Novara, Italy

PURPOSE: Powerful mediators of programmed cell death, such as apoptosis and autophagy, can contribute to myocyte cell loss during pathological cardiac conditions. Levosimendan has been shown to exert beneficial hemodynamic effects in presence of global myocardial ischemia and heart failure through vasodilatation and increase of cardiac contractility. Recently, the intracoronary administration of a bolus levosimendan was found to exert favourable cardiac anti-stunning effects without lowering arterial pressure, which limits the use of levosimendan mainly in coronary artery disease. Here we tested whether the intracoronary administration of levosimendan can beneficially modulate programmed cell death in acute regional myocardial ischemia. METHODS: Acute regional myocardial ischemia was induced in 20 anaesthetized pigs and intracoronary levosimendan 15 min bolus administration was started 4 h afterwards. The effects of levosimendan on coronary blood flow and cardiac function were evaluated and myocardial biopsies were examined for criteria of autophagy and apoptosis. RESULTS: The administration of levosimendan caused a significant increase of coronary blood flow ($p < 0.05$) in absence of changes in cardiac function. Moreover, levosimendan prevented the down-regulation of the anti-apoptotic gene, Bcl-2, and the up-regulation of the apoptotic markers Bax and cytochrome c, which resulted in a reduced expression of TUNEL fragmented nuclei ($p < 0.05$). Furthermore, levosimendan maintained Beclin 1 at 4 h and potentiated LC3 II expression, these results being consistent with autophagy activation. CONCLUSIONS: Such effects of intracoronary levosimendan bolus administration during regional myocardial ischemia indicate the occurrence of cardio-protection by modulation of programmed form of cell death

No conflict of interest

ACS AND ACUTE MYOCARDIAL INFARCTION

THE DISSOCIATION OF PENTAMERIC TO MONOMERIC C-REACTIVE PROTEIN (CRP) ON MICROPARTICLES DRIVES INFLAMMATION IN PATIENTS WITH MYOCARDIAL INFARCTION

J. Habersberger[1], A. Scheichl[1], F. Strang[1], S.U. Eisenhardt[1], N.M. Htun[1], K. Peter[1]
[1]Atherothrombosis & Vascular Biology, Baker IDI Heart & Diabetes Institute, Melbourne, Australia

Rationale: Elevated serum C-reactive protein following myocardial infarction (MI) is associated with poor outcomes. Although animal studies have indicated a direct pathogenic role of CRP, the mechanism underlying this remains elusive. Dissociation of pentameric CRP (pCRP) into pro-inflammatory monomers (mCRP) may directly link CRP to inflammation. We investigated whether cellular microparticles found in the blood of patients following myocardial infarction can convert pCRP to mCRP and transport mCRP in the circulation causing endothelial cell activation and thereby potentially disseminate inflammation.

Methods and Results: Microparticles were obtained from cell cultures and whole blood samples collected from patients following acute MI and from control groups. Samples were analysed by native Western blotting and flow cytometry. Microparticles were loaded with mCRP *in vitro* and incubated with endothelial cells prior to staining with monoclonal antibodies to asses mCRP transfer. HUVEC activation was assessed in flow cytometry measuring VCAM-1 expression. *In vitro* experiments demonstrated that microparticles were capable of converting pCRP to mCRP. Significantly more mCRP was detected on microparticles from patients following MI compared to control groups by Western blotting and flow cytometry. Following a STEMI the mean mCRP fluorescence (MFI) detected was 525 ± 72 (n=13; standard error of the mean, SEM). Samples from patients with unstable angina recorded MFI of 282 ± 65 (SEM) (n=13; $p<0.5$, compared to STEMI group). In samples from patients with stable coronary artery disease (n=7) and healthy coronary arteries (n=7) MFL was 133 ± 43 (SEM) ($p<0.05$) and 93 ± 49 (SEM) ($p<0.001$), respectively. Microparticles containing mCRP were able to bind to the surface of endothelial cells causing subsequent endothelial cell activation.

Conclusion: Circulating microparticles can convert pCRP to mCRP in patients following MI and subsequently bind mCRP on their surface; demonstrating for the first time mCRP generation *in vivo* and it's detection in circulating blood. Microparticles can bind to cell membranes and transfer mCRP to the surface of endothelial cells suggesting a possible transport role for microparticles in the circulation. Subsequent endothelial cell activation caused by mCRP containing microparticles supports the hypothesis that mCRP has an active biological role in vascular disease and can disseminate inflammation and also potentially amplify inflammation at the site of myocardial ischemia and necrosis. This suggests a role of the pCRP - mCRP dissociation axis as a major mechanism driving inflammation in MI and also identifies a potential therapeutic approach using mCRP inhiting agents in patients with MI.

No conflict of interest

ACS AND ACUTE MYOCARDIAL INFARCTION

PROPOFOL POST-CONDITIONING CONFERS ISCHEMIC CARDIOPROTECTION BY ACTIVATING HO-1/STAT3 SIGNALING: ROLE OF PEROXYNITRITE

H. Ziqing[1], X.W. Mao[2], H. Li[2], G.T. Wong[2], C.W. Cheung[2], M.G. Irwin[2], Z. Xia[2]
[1]Department of Anesthesiology, 3rd Affiliated Hospital of Sun Yat-sen University, Changzhou, China
[2]Department of Anesthesiology, The University of Hong Kong, Hong Kong, China

Aims: Propofol, an anaesthetic agent with antioxidant and peroxynitrite scavenging capacity, when given during early reperfusion (i.e. post-conditioning) can attenuate myocardial reperfusion injury. However the mechanism by which propofol mediated post-conditioning cardioprotection is unclear. Both heme oxygenase-1 (HO-1) and STAT3 are key proteins in post-conditioning cardioprotection. We hypothesized that propofol confers post-conditioning cardioprotection by scavenging peroxynitrite and involves the activation of the HO-1/STAT3 pathway.

Methods: Adult Sprague Dawley rats were subjected to myocardial ischemia/reperfusion (I/R) ***in vivo*** achieved by 30 min coronary artery occlusion and 90 min reperfusion. Rats in various groups (n=7 per group) were respectively treated either with sham operation, ischemia reperfusion with or without propofol (2mg/kg), peroxynitrite generator SIN-1(1.5 mg/kg), peroxynitrite scavenger FeTPPS (10 mg/kg), or ischemic post-conditioning during I/R. Cardiac injury, oxidative stress and HO-1/STAT3 protein expression were assessed. In a separate study, isolated primarily cultured adult rat cardiomyocytes were subjected to hypoxia/re-oxygenation in the absence or presence of peroxynitrite generator or scavenger. HO-1 and STAT3 siRNA were applied in H9C2 cells to confirm the role of HO-1/STAT3 signaling.

Results: Propofol post-conditioning (PPC) showed similar cardioprotection to ischemic post-conditioning in reducing post-ischemic myocardial infarction and cellular injury compared to control group. Scavenging peroxynitrite by FeTPPS further reduced cardiac injury, while up-regulation of peroxynitrite production by SIN-1 abolished PPC cardioprotection evidenced as augmented myocadial infarct size and CK-MB release. HO-1 and phosphorylated STAT3 protein expression was increased in PPC group compared to control group which was accompanied with decreased peroxynitrite production and increased antioxidant capacity. PPC also attenuated post-hypoxic lactate dehydrogenase ***in vitro***. However, HO-1/STAT3 gene knockdown abolished the protective effect of PPC.

Conclusion: PPC has cardioprotective effects as efficient as ischemic post-conditioning and it does so by reducing peroxynitrite production and subsequently activating HO-1/STAT3 signaling.

No conflict of interest

ACS AND ACUTE MYOCARDIAL INFARCTION

THE CC VARIANT (RS 1333049) OF 9P21 INFLUENCES THE DEVELOPMENT OF ACUTE CORONARY DISEASE, BUT NOT THE STABLE ANGINA

M. Mendonca[1], S. Gomes[1], B. Silva[1], A. Pereira[1], R. Rodrigues[1], A. Sousa[1], A. Freitas[1], S. Freitas[1], D. Pereira[1], R. Palma dos Reis[2]
[1]Unit Research, Funchal Central Hospital, Funchal, Portugal
[2]Unit Research, New University of Lisbon, Lisbon, Portugal

Several independent studies have demonstrated an association between some polymorphisms in 9p21 locus and the coronary risk disease. However, it remains unknown whether these genes influence the coronary morphology (atherogenic process, affecting dominantly the vessel wall) or tendency to thrombogenesis expressed by the occurrence of acute vascular accidents.
Objective: Evaluate whether the SNP rs1333049 of 9p21 locus influences the development of the acute coronary syndrome (ACS) or more complex coronary lesions.

Methods: Two case-control studies were performed. The first one included 1655 individuals: 728 consecutive coronary patients with ACS diagnosis and 923 controls without coronary events. The second study consisted of a total of 1018 individuals: 202 patients with stable angina submitted to coronariography, and 816 controls without coronary disease. In both studies, cases and controls were matched by gender and age. Subsequently, the coronary morphology was assessed in terms of Leaman score, evaluating the extension and severity of coronary lesions. The CC variant was analyzed (blind method), using specific primers. Hardy-Weinberg equilibrium was calculated and a bivariate analysis (tables 3x2) was performed to determine the coronary risk disease according to genotypes. The OR and 95% CI were calculated.
Results: The CC variant is significantly related with ACS risk (OR=1.28; P=0.019), but not with stable angina (OR=1.11, P=0.55). Through Leaman Score evaluation, the severity and extension of coronary lesions were found to be similar for the three genotypes.

Conclusions: The present study supports the fact that the CC variant of 9p21 locus is a risk factor for the onset of ACS. Carriers of this genotype should be approached with particular attention in terms of primary prevention. Nevertheless, this study showed that the coronary morphology was not affected by this variant, suggesting that the 9p21 locus may be an initiator mechanism of the disease with an effect more thrombogenic than atherogenic.

No conflict of interest

ACS AND ACUTE MYOCARDIAL INFARCTION

COMPARISON OF TWO DIFFERENT RISK SCORES WITH THE AIM OF EARLY HOSPITAL DISCHARGE IN PATIENTS WITH ST-ELEVATION MYOCARDIAL INFARCTION

O. Merono[1], L. Recasens[1], A. Fernandez[1], D. Bueno[1], V. Bazan[1], C. Garcia-Garcia[1], N. Ribas[1], J.A. Morales[1], S. Mojal[1], J. Bruguera[1]
[1]Cardiology, Hospital Del Mar, Barcelona, Spain

INTRODUCTION: A Zwolle Risk Score (ZRS) value of ≤ 3 identifies STEMI patients treated with primary angioplasty in whom early discharge is presumably safe. The ZRS evaluates age, Killip class, infarct localization, ischemia time, multivessel disease and TIMI flow post-angioplasty. The Grace Score at discharge (GSD) evaluates the 6-month mortality risk after STEMI, and has not been used to assess the safety of early-discharge strategy. We aimed to assess the utility of both scores in identifying low-risk patients in whom an early-discharge strategy could be applied.

METHODS: During 2009-2012 193 STEMI patients treated with primary angioplasty were included. We analysed demographic and clinical variables, ZRS, GSD and follow up outcome. Patients were considered as low risk when ZRS scoring of ≤ 3 and GSD of <3%.

RESULTS: The mean age was 63.1(± 15 years) and 29.0% were female. Nine(5%) patients died during hospitalization, and 3(2%) and 3(2%) more died within the first and between the first and sixth month after discharge, respectively. A total of 142(74%) and 122(63%) patients had low risk according to the ZRS and GSD scores, respectively. One patient with SRZ<3 died during hospitalization and another during follow up. No patient with GSD<3% died. One presented malignant ventricular arrhythmia the fourth day after STEMI. This patient scored ZRS<3 and GSD>3%.

CONCLUSIONS: In our population, the SRZ is generally a satisfactory indicator of patient outcome however 3 patients with SRZ<3 died and/or presented late malignant arrhythmia. None of the patients with GSD<3% died or presented serious arrhythmic late complications.

No conflict of interest

ACS AND ACUTE MYOCARDIAL INFARCTION

EMERGENCY CABG SURGERY IN PATIENTS WITH CORONARY ARTERY DISEASE WITH/OR WITHOUT ACUTE MYOCARDIAL INFARCTION USING THE MINIMIZED EXTRACORPOREAL CIRCULATION MECC

M. Rufa[1], J. Schubel[1], A. Bauer[2], C. Ulrich[2], H. Hausmann[1]
[1]Cardiac surgery, MediClin Herzzentrum Coswig, Coswig Anhalt, Germany
[2]Cardiac Perfusion, MediClin Herzzentrum Coswig, Coswig Anhalt, Germany

OBJECTIVE

The purpose of the study was to compare the outcome of emergency CABG operations using MECC or CCPB, with a minimal variety of the surgical procedures. At the moment the main application of MECC is reserved for elective operations, like CABG or replacement of the aortic valve. We've investigated all emergency CABG operations between 01/07 and 02/13, which were performed by only one surgeon, in order to exclude the differences in surgical technique.

METHODS

Between 01/07 and 02/13 we've investigated retrospectively 176 CABG's (104 MECC vs. 72 CCPB). The followed criteria were in-hospital mortality, major events after surgery, postoperative hospitalization, peri-operative transfusion rate. The mean logistic euro-score was comparable, MECC 16,75% vs. CCPB 19,17% and the number of bypasses per patient was similar in both groups, MECC (2,95) vs. CCPB(2,84).

RESULTS

There was no significant difference in the postoperative hospitalization or in major postoperative complications. The in-hospital mortality was higher in the CCPB group 7% vs. the MECC group 3,8%. The peri-operative transfusion rate was less by using the MECC 20% compared with the use of CCPB 48%.

CONCLUSIONS

In our hands the use of the MECC by urgent CABG procedures is sure and shows no disadvantages compared with CCPB. Emergency operations with MECC system showed better results concerning the blood transfusion rate and the time spent in ICU.

No conflict of interest

ACS AND ACUTE MYOCARDIAL INFARCTION

MANAGEMENT OF PATIENTS WITH ACUTE CORONARY SYNDROME IN 52 ITALIAN INTENSIVE CARE UNITS: THE MANTRA REGISTRY

L. riva[1], M. pallotti[1], M. scherillo[2], A. maggioni[3], G. di pasquale[1]
[1]cardiology, maggiore hospital, bologna, Italy
[2]cardiology, azienda ospedaliera rummo, benevento, Italy
[3]centro studi anmco, centro studi anmco, firenze, Italy

Aim. To evaluate guidelines' adherence in the management of patients affected by acute coronary syndrome (ACS) with or without ST-elevation (STEMI or NSTEMI) in 52 Italian intensive cardiac care units representative of the Italian network.

Methods. The analysis was based on data of the MANTRA registry, a multicentre, observational, nationwide study, which enrolled 6394 consecutive patients with ACS (respectively 2858 STEMI and 3536 NSTEMI) between April 2009 and December 2010.

Results. 80% patients with STEMI receive early reperfusion (63.7% PCI, 16.1% fibrinolysis). Time for reperfusion therapy is longer in patients transferred to HUB centers (Door-to-balloon median time in case of transfer to HUB center 130 minutes, in case of direct access 81 minutes, p<0.0001). Coronary angiography is performed in the majority of NSTEMI patients (78%) during hospitalization. Pharmacological therapies are summarized in the Table. In-hospital mortality is 4.2% in the STEMI group and 2.5% in the NSTEMI patients.

	STEMI (N=2858)				**NSTEMI** (N=3536)		
	Fibrinolysis (n=460)	PCI (n=1821)	No reperfusion (n=577)	p	PCI (n=1225)	No PCI (n=2311)	p
UFH, %	93.0	76.4	73.0	<0.0001	71.2	67.2	0.014
Fondaparinux, %	3.7	7.3	14.6	<0.0001	16.2	20.6	0.002
Aspirin, %	96.5	95.9	90.5	<0.0001	96.5	92.4	<0.0001
Clopidogrel, %	94.6	96.4	77.5	<0.0001	95.2	81.6	<0.0001
Aspirin+Clopidogrel, %	91.7	93.2	74.2	<0.0001	92.3	78.4	<0.0001
GP IIb-IIIa inhibitors, %	12.2	66.4	20.5	<0.0001	42.6	11.6	<0.0001
ACE-inhibitors/ARBs, %	62.0	62.2	62.9	0.94	67.3	66.0	0.44
Beta-blockers, %	59.4	64.6	58.1	0.006	71.1	64.1	<0.0001
Calcium channel blockers, %	1.3	2.9	6.2	<0.0001	11.5	12.7	0.30
Diuretics, %	18.7	20.5	38.1	<0.0001	23.3	34.8	<0.0001
Nitrates, %	62.4	39.7	60.0	<0.0001	56.0	66.3	<0.0001
Statins, %	87.8	77.3	68.5	<0.0001	81.2	77.9	0.02
n-3 PUFA, %	14.4	19.1	12.1	0.0001	16.7	10.6	<0.0001

Conclusions. In the context of the ACS Italian network patients are generally treated according to current guidelines. In the subgroup of STEMI reperfusion therapy is early performed in the majority of cases.
In patients with not reperfused STEMI and with NSTEMI treated conservatively there is an underuse of recommended therapies with a higher in-hospital mortality.

No conflict of interest

ACS AND ACUTE MYOCARDIAL INFARCTION

EXTRACORPOREAL SHOCKWAVE MYOCARDIAL REVASCULARIZATION: A PROMISING THERAPY FOR REFRACTORY ANGINA.

G. Alunni[1], I. Meynet[1], M. D'Amico[1], P. Garrone[1], L.U.C.A. Checco[1], S. Marra[1]
[1]Cardiology 2, Città della Salute e della Scienza di Torino- Molinette, Turin, Italy

Purpose. The incidence of refractory angina due to end stage CAD not suitable to CABG or PCI is increasing. Extracorporeal shockwave myocardial revascularization (ESMR) is a new treatment that can reduce symptoms of myocardial ischemia. The current study was designed to assess the effect of ESMR on myocardial perfusion and symptoms.
Methods. 25 consecutive patients with refractory angina despite optimal medical therapy, not amenable to further PCI or CABG were included. All patients underwent clinical interview, echocardiography and SPECT at baseline and 6 months after the treatment.
Results. ESMR significantly improved myocardial perfusion after 6 months with a 39% relative reduction of summed stress score (SSS, $p<0.001$) and a 45% relative reduction of summed rest score (SRS, $p<0.001$). CCS class improved from a mean of 2.8 to 1.3 ($p<0.001$). Nitroglycerin consumption and hospitalization rate significantly reduced ($p <0.001$). Echocardiographic left ventricular ejection fraction significantly improved, from a mean of 56% to 60% ($p=0.005$). No patient had any complication or discomfort.
Conclusion: ESMR improves myocardial perfusion and function and reduces symptoms and need for hospitalization in patients with refractory angina, and is thus a valid option for the treatment of patients with CAD and no further possible revascularization.

No conflict of interest

PROGNOSIS, PROGRESSION AND PRACTICE PATTERNS

LONG-TERM PROGNOSIS OF PREMATURE, FAMILIAL CORONARY ARTERY DISEASE: 10-YEAR ANALYSIS OF THE BRITISH HEART FOUNDATION FAMILY HEART STUDY (BHF-FHS)

J.A. Batty[1], A.S. Hall[2], P.S. Braund[3], C.P. Nelson[3], N.J. Samani[3], A.J. Balmforth[2]
[1]School of Medicine, University of Leeds, Leeds, United Kingdom
[2]Leeds Institute of Genetics Health and Therapeutics, University of Leeds, Leeds, United Kingdom
[3]Department of Cardiovascular Sciences, University of Leicester, Leeds, United Kingdom

Background
15% of all coronary artery disease (CAD) is early-onset; thought to be associated with recurrent thromboembolic events, refractory to secondary prevention and thus prognostically-unfavourable. Few data exist regarding the long-term prognosis of familial CAD, or implications for the siblings of prematurely-affected individuals.

Methods
10-year analysis of the prospectively-maintained British Heart Foundation Family Heart Study (BHF-FHS) cohort (n=5472 CAD-affected, prematurely
affected at <66 years of age; n=2521 unaffected siblings) was performed. The primary outcome was 10-year relative mortality, compared to age- and sex-matched members of the UK general population. Secondary outcomes included use of a Cox proportional hazards approach to identify risk factors for 10-year cause-specific mortality.

Results
Absolute 10-year mortality was greater in CAD affected vs. unaffected subjects (18.5 vs. 5.8 deaths per 1000 patient-years follow-up, respectively). CAD-affected participants were more likely to have a cardiovascular/cardiac specific cause of death (hazard ratio, HR 1.51 and 2.48; p<0.001) as opposed to CAD unaffected participants. 10-year observed survival rates for both groups closely approximate those which would be expected in matched members of the UK population. However, relative survival was greater than expected in CAD-affected participants (SR=1.04; 95% CI: 1.03-1.05; p<0.001), and worse than expected in CAD-unaffected participants (SR=0.98; 95% CI: 0.97-0.99; p<0.001). Significant predictors of 10-year mortality included male gender, age, diabetes, smoking, and baseline pharmacotherapeutic regimen.

Conclusions
Prematurely CAD-affected participants were at below population risk for all-cause 10-year mortality, and CAD-unaffected siblings were at above population risk. Efficacious preventative pharmacotherapeutic regimens in CAD-affected individuals may explain this finding.

No conflict of interest

PROGNOSIS, PROGRESSION AND PRACTICE PATTERNS

HAPTOGLOBIN GENOTYPE AS A PROGNOSTIC FACTOR FOR OPERATION-RELATED MORBIDITY IN CORONARY ARTERY BYPASS GRAFTING (CABG) PATIENTS

Y. Barac[1], U. Milman[2], I. Lavi[3], V. Rubchevsky[1], D. Aravot[1], C. Shapira[4]
[1]The Cardiothoracic Department, Rabin Medical Center, Petach-Tikva, Israel
[2]Clinical Research Unit, Clalit Health, Tel-Aviv, Israel
[3]Biostatistics and Consultation Unit, Carmel Medical Center, Haifa, Israel
[4]Hospital Management, Carmel Medical Center, Haifa, Israel

Background:

The haptoglobin (Hp) gene has two classes of alleles, encoding Hp 1 and Hp 2, where the latter has been shown to be an inferior antioxidant, when compared to the former. The Hp 2-2 genotype renders diabetic individuals at a 500% increased risk of developing cardiovascular disease, when compared to Hp 2-1 and Hp 1-1. The Hp 2 allele has also been linked to both increased myocardial infarct (MI) size and increased susceptibility to repeated percutaneous coronary intervention (PCI) and stenting among diabetics.

Methods:

Coronary heart disease outcomes of 3054 diabetic patients, drawn from 47 primary care practices, were prospectively followed for seven years. All treatment decisions regarding routine care remained at the discretion of the primary care physician.

Results:

Surgical intervention was required in 144 patients, with a genotypic breakdown of 15 Hp 1-1 (5.55%), 47 Hp 1-2 (4%), and 81 Hp 2-2 (5.66%). Although, no statistically significant differences were found between patient groups regarding the lengths of bypass surgery or aortic cross clamp, the number of arterial grafts used and mortality rates, a significant difference was found in the duration of hospitalization periods among Hp 2-bearing patients, when compared to Hp 1 carriers.

Conclusion:

The Hp 2 allele may have prognostic potential with respect to extended postoperative hospitalizations, reflecting complex post-operative recovery, and possible post-CABG surgery complications. Taken together with earlier reports correlating the Hp 2 allele with increased susceptibility to repeated PCI and stenting, closer follow-up should be considered for this specific population of diabetes patients.

No conflict of interest

PROGNOSIS, PROGRESSION AND PRACTICE PATTERNS

IMPACT OF A RANDOMIZED TRIAL OF A CARDIAC EMERGENCY DEPARTMENT NURSING INTERVENTION ON REVISITS, CONTINUITY OF CARE, SELF-CARE AND ANXIETY

N.F.-S.,A.V.,J.M. S. Cossette[1]
[1]"Montreal Heart Institute Research Center / University of Montreal
[2]Centre hospitalier de l'Université
de Montré
al-Montreal Heart Institute-McGill University
[3]Emergency department, Montreal Heart Institute Research Center / University of Montreal
[4]Emergency Department, Ste-Marys Hospital
[5]Coordinating Center, Montreal Heart Institute Research Center / University of Montreal, Montreal, QC, Canada"

"Cardiac patients' repeat visits to emergency departments (EDs) contribute to delay in care and suboptimal use of cardiac services. We carried out a randomized trial of a nursing intervention at ED discharge aiming to reduce ED revisits after 30 days by supporting the transition from hospital to home. Secondary outcomes included perceived continuity of care, self-care abilities, and anxiety. Eligible patients were 1) discharged home from the ED of a specialized cardiac hospital, 2) prescribed ≥ 6 different medications and 3) had at least one ED visit in the previous year. The sample of 265 patients (133 control; 132 experimental) was randomized before discharge. The experimental treatment included 3 individual nurse-patient meetings, based on the evaluation of seven spheres of patient-centered clinical issues followed by interventions relevant for each sphere. The primary results showed no significant group difference in cardiac ED revisits (experimental group 18%. control group 20%; p =.81 log-rank test). The ANCOVA analyses showed that the experimental group improved significantly in the continuity of care total score (p =.003), self-care abilities (p=.023) and anxiety (p =.037). Although the transitional nursing program had no impact on ED revisits, it appears to have improved patient's abilities to manage their health problems and to reduce anxiety. Future research should focus on exploring the specific needs of ED users at risk for cardiac ED utilization besides those already known in the literature, in order to better target future interventions, aiming to decrease cardiac ED use if and when suitable."

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PROGNOSIS, PROGRESSION AND PRACTICE PATTERNS

HEALTH INSURANCE AND THE GRAND OLD DUKE OF YORK: STATIN ADHERENCE WHEN PATIENT DRUG COST-SHARING GOES UP AND DOWN AGAIN

J. Hsu[1], *M. Price*[1]
[1]*Mongan Institute for Health Policy, MGH/Harvard Medical School, Boston, USA*

Objective: Insurance benefit designs often include fluctuating patient cost-sharing, e.g., coverage gaps or deductibles, which theoretically incentivize patients to use care more judiciously. We examined statin drug adherence as patients experienced cost-sharing increases then decreases.

Methods: We exploited a Medicare natural experiment: subjects had constant drug coverage in 2006; standard Part D coverage gap in 2007 (loss of coverage after drug spending exceeded a limit, i.e., gap entry); and, resumption of coverage as benefits reset in 2008. Among 12,325 subjects with continuous plan enrollment, we examined monthly drug adherence using linear fixed-effects regression models and measures of drug supply based on the proportion of days covered (PDC). To account for endogeneity of gap entry, we adjusted for expected drug use, i.e., modeled use in the absence of cost-sharing changes; nearly all (93%) of subjects expected to enter the coverage gap did so.

Results: Subjects spent less on statins ($17.06), and had fewer days supply (4.5days/30days) in months after losing coverage. Overall, 14.6% became non-adherent with gap entry, i.e., PDC decreases to <0.8; and 4.2% stopped picking up their drugs entirely. The adjusted odds ratio of adherence after gap entry was 0.78, 95%CI:0.71-0.85. With the reset of drug benefits in 2008, there was no significant change in drug supply, nor net increase in patients adherent to therapy.

Conclusions: With complex benefit designs in which drug cost-sharing goes up and down again, many patients become and remain non-adherent. These designs could interfere with therapy and represent futile efforts to improve efficiency.

No conflict of interest

PROGNOSIS, PROGRESSION AND PRACTICE PATTERNS

FIVE YEARS OUTCOMES OF SURGICAL OR PERCUTANEOUS MYOCARDIAL REVASCULARIZATION IN DIABETIC PATIENTS

G.A. Contini[1], F. Nicolini[1], D. Fortuna[2], D. Pacini[3], D. Gabbieri[4], L. Vignali[5], C. Zussa[6], F. Pigini[7], P. Guastaroba[2], R. De Palma[2], R. Grilli[2], T. Gherli[8]

[1]Unità Operativa di Cardiochirurgia Dipartimento Cardio-nefro-polmonare, Azienda Ospedaliero Universitaria, Parma, Italy

[2]Governo Clinico, Agenzia Sanitaria e Sociale Regionale della Regione Emilia-Romagna, Bologna, Italy

[3]Dipartimento Cardio-Toraco-Vascolare, Azienda Ospedaliero-Universitaria S.Orsola-Malpighi, Bologna, Italy

[4]Hesperia Hospital, Azienda Ospedaliero-Universitaria S.Orsola-Malpighi, Modena, Italy

[5]Unità Operativa di Cardiologia Dipartimento Cardio-nefro-polmonare, Azienda Ospedaliero-Universitaria, Parma, Italy

[6]Department of Cardiac Surgery, Villa Maria Cecilia Hospital, Cotignola - RA, Italy

[7]Department of Cardiac Surgery, Villa Torri Hospital, Bologna, Italy

[8]Unità Operativa di Cardiochirurgia Dipartimento Cardio-nefro-polmonare, Azienda Ospedaliero-Universitaria, Parma, Italy

Background

The study compares five years clinical outcomes of CABG vs PCI in a real world population of diabetic patients with multivessel coronary disease since it is not clear whether to prefer surgical or percutaneous revascularization.

Methods

Between July 2002 and December 2008, 2,885 multivessel coronary diabetic patients underwent revascularization (1,466 CABG and 1,419 PCI) at hospitals in Emilia-Romagna Region, Italy and were followed for 1827±617 days by record linkage of two clinical registries with the regional administrative database of hospital admissions and the mortality registry. Five-year incidences of MACCE (mortality, acute myocardial infarction [AMI], stroke, and repeat revascularization [TVR]) were assessed with Kaplan-Meier estimates, Cox proportional hazards regression and cumulative incidence functions of death and TVR, to evaluate the competing risk of AMI on death and TVR. The same analyses were applied to the propensity score matched subgroup of patients undergoing CABG or PCI with DES and with complete revascularization.

Results

PCI had higher mortality for all causes (HR: 1.8 CI 95% 1.4-2.2 p<0.0001), AMI (HR: 3.3 CI 95% 2.4-4.6 p<0.0001) and TVR (HR: 4.5 CI 95% 3.4-6.1 p<0.0001). No significant differences emerged for stroke (HR: 0.8 CI 95% 0.5-1.2 p=0.26).

The higher incidence of AMI caused higher mortality in PCI group. Results did not change comparing CABG with PCI patients receiving complete revascularization or DES only.

Conclusions

Diabetics show a higher incidence of MACCE with PCI than with CABG: thus diabetes and its degree of control should be considered when choosing the type of revascularization.

No conflict of interest

NEW DIRECTIONS IN CARDIAC, CAROTID AND PERIPHERAL INTERVENTIONS

Which asymptomatic carotid lesions need treatment, irrespective of stent or CEA?

B. Gewertz[1], A. Shah[1]
[1]Surgery, Cedars-Sinai Medical Center, Los Angeles, USA

Recent randomized trials have furthered our understanding of the natural history of asymptomatic carotid stenosis. In one large multi-national study, patients experienced a reduction in stroke risk over 10 years (reduction for men 17.1% to 10.8% and for women 14.7% to 6.5%). However, the benefit of surgery was markedly narrowed in all patients when the end point was defined as any stroke or perioperative death; the risk of such undesirable outcomes at 10 years in non-operated patients was 17.9% while the risk in operated patients was 13.4%. (HALLIDAY A et al,. ***Lancet*** 2010;376:1074-1084.)

There is increasing evidence that plaques prone to embolization have a different character then those apt to remain clinically silent. As such, our attention should be focused on defining the likelihood of later embolization of asymptomatic lesions based on the composition of bifurcation plaques and other morphologic criteria. Methods could include ultrasound, MRI, embolic detection and other noninvasive techniques.

In most cases, patients over 75 years of age with lesions of less than 80% should receive medical management. Intervention should be reserved for younger patients with complex plaques as documented by CT angiograms. Decision making can be further improved with embolic detection protocols and ancillary tests such as MRI to detect clinically silent infarcts and morphologic features of unstable plaques.

No conflict of interest

NEW DIRECTIONS IN CARDIAC, CAROTID AND PERIPHERAL INTERVENTIONS

Optimal stenting in symptomatic carotid lesions

Document not received

NEW DIRECTIONS IN CARDIAC, CAROTID AND PERIPHERAL INTERVENTIONS

Endovascular treatment of obesity

Document not received

NEW DIRECTIONS IN CARDIAC, CAROTID AND PERIPHERAL INTERVENTIONS

ANGIOPLASTY AND PROVISIONAL STENTING OF COMMON FEMORAL ARTERY LESIONS

A.R.,S.s.,U.b.,E.N. R.F. Bonvini[1]
[1]*University Hospitals of Gneva, Geneva, Switzerland*
[2]*Herzzentrum Bad Krozingen, Bad Krozingen, Germany*

"***Introduction:*** Isolated atherosclerotic common femoral artery (CFA) disease is a rare cause of symptomatic peripheral arterial disease. While surgical endarterectomy is considered the therapy of choice, little is known about outcomes of percutaneous treatment.

Methods: Using a prospectively maintained single center database, we retrospectively analyzed outcomes of consecutive patients undergoing isolated percutaneous revascularization of CFA disease between 1996 and 2007. In all cases, the intended strategy was balloon angioplasty with provisional stenting in case of poor angioplasty results. Out of 516 consecutive procedures involving the CFA, 419 were excluded because of non-atherosclerotic disease (N=156) or because of additional vascular segments treatment during the same procedure (N=263). Procedural success (i.e.,< 30% residual stenosis), in-hospital vascular complications (major: requiring surgical or percutaneous treatment; minor: treated conservatively), as well as 12-month restenosis and target lesion revascularization (TLR) rates were assessed for the remaining 97 interventions.

Results: CFA bifurcation lesions were present in 40 cases (41.2%) and required treatment of the deep femoral artery in 25 cases (25.8%). Chronic total CFA occlusions accounted for 11 cases (11.3%). Balloon angioplasty was performed in 96 cases (98.9%) and provisional stenting was necessary in 37 cases (38.1%). The procedure was successful in 89 cases (91.8%). Thirty-day minor and major vascular complications occurred in 3 (3.1%) and 4 (4.1%) of the cases, respectively. At 12-months, restenosis >50% and TLR were observed in 19.5% and 14.1% of the cases, respectively.

Conclusions: This series confirms that isolated CFA lesions may be safely and efficaciously treated with angioplasty and provisional stenting.

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NEW DIRECTIONS IN CARDIAC, CAROTID AND PERIPHERAL INTERVENTIONS

SAFETY, EFFICACY AND ONE-YEAR RESULTS OF USE OF DIRECTIONAL ATHERECTOMY AND PACLITAXEL COATED BALLOON FOR COMMON FEMORAL ARTERY LESIONS

A. Cioppa[1], L. Salemme[1], V. Ambrosini[2], E. Stabile[2], G. Popusoi[2], A. Pucciarelli[2], L. Cota[2], T. Tesorio[2], G. Sorropago[2], E. Laurenzano[2], G. Biamino[2], P. Rubino[2]
[1]Division of Invasive Cardiology, a59sd8, Mercogliano, Italy
[2]Division of Invasive Cardiology, Montevergine Clinic, Mercogliano, Italy

BACKGROUND: Atherosclerotic common femoral artery (CFA) lesions are a known cause of symptomatic peripheral arterial disease. Although surgical endarterectomy is considered the therapy of choice for this condition recently some large single center series have shown encouraging results for endovascular techniques. The purpose of this study was to evaluate the technical feasability, safety, acute and 1-year efficacy of the endovascular treatment of atherosclerotic CFA obstructions with combined use of Directioal Aterectomy (DA) and Paclitaxel Coated Balloon (DCB).
METHODS AND RESULTS During the 2011 30 consecutive patients were treated for severely symptomatic CFA obstructions using DA with Turbo Hawk (Covidien) followed by DCB (In-Pact Medtronic) prolonged (3') dilatation. Provisional stenting was allowed for subotpimal result after prolonged balloon dilatations, flow limiting dissection, abroupt vessel.
Results: Procedural success meaning the ability to perform DA and DCB dilatation was reached in all cases (100%), whereas stenting was needed for suboptimal angioplasty in 3 (10%) cases. Procedure failure defined as a final angiographic result with a >50% residual stenosi was never observed. In-hospital major and minor complications occurred in 0 (0%) and 1 (0,3%) procedures, respectively. One-year follow-up was performed for 29 patients (96%). Restenosis >50% by duplex scanning and target lesion revascularization were observed in 3 of 29 (10%) and 2 of 29 (8%) procedures, respectively. Secondary patency rate was 93%.
CONCLUSIONS This study suggests that the combined use of DA and DCB is a safe, and effective, alternative to the surgery, treatment for the CFA lesions and provides encouraging results in this setting.

Keywords: Peripheralvesseldisease.Common-FemoralArtery.Atherectomy.Drug-Coated-Balloon.

No conflict of interest

NEW DIRECTIONS IN CARDIAC, CAROTID AND PERIPHERAL INTERVENTIONS

TRANSAPICAL TRANSCATHETER AORTIC VALVE IMPLANTATION WITHOUT PRIOR BALLOON AORTIC VALVULOPLASTY – FEASIBLE AND SAFE

L. Conradi[1], M. Seiffert[2], J. Schirmer[1], P. Diemert[2], D. Koschyk[2], H. Treede[1], S. Blankenberg[2], H. Reichenspurner[1]
[1]Cardiovascular Surgery, University Heart Center Hamburg, Hamburg, Germany
[2]Cardiology, University Heart Center Hamburg, Hamburg, Germany

Objective: Currently, pre-implant balloon aortic valvuloplasty (BAV) is considered a prerequisite for successful transapical transcatheter aortic valve implantation (TA-AVI) using balloon-expandable devices. However, cerebral embolization has been shown to originate in part from BAV procedures. Omitting BAV may reduce neurologic events after TAVI and facilitate the procedure while yielding non-inferior hemodynamic and clinical outcomes.

Methods: A total of 50 consecutive patients received TA-AVI without pre-implant BAV (TA-AVI^{-BAV}) using Edwards Sapien XT devices (54% male, age 77.7±8.4 years, log EuroSCORE I 20.5±14.0%). Data were prospectively entered into a dedicated database, retrospectively analyzed and compared to a consecutive series of conventional TA-AVI using the same device (control group, n=50).

Results: Device success rate was 92% (46/50) and 90% (45/50) in TA-AVI^{-BAV} and control groups (p=1.0). Procedure time was similar TA-AVI^{-BAV} and control groups (88.2±30.8 vs. 91.1±24.5 min, p=0.60), while significantly less contrast was used (137.6±67.8 vs. 182.9±78.1 ml, p<0.001) in the TA-AVI^{-BAV} group. Postprocedural peak and mean transvalvular gradients were 16.0±6.6 and 7.9±3.3 mmHg in the TA-AVI^{-BAV} group and 18.7±8.5 and 9.3±4.7 mmHg in the control group (p=0.08 and p=0.09). Paravalvular leakage ≥ grade 2 was present in 2% and 8% in TA-AVI^{-BAV} and control groups (p=0.36). Rates of 30-day mortality and periprocedural stroke were 6% and 10% (p=0.72) and 2% and 6% (p=0.62) respectively.

Conclusions: TA-AVI^{-BAV} is feasible and safe and has become our default technique for TA-AVI with balloon-expandable devices. It resulted in less contrast agent used and facilitated the procedure without compromising valve performance. Effects of TA-AVI^{-BAV} on the incidence of cerebrovascular events or hemodynamic valve performance need to be verified in larger patient numbers before general recommendations can be made.

No conflict of interest

NEW DIRECTIONS IN CARDIAC, CAROTID AND PERIPHERAL INTERVENTIONS

THE ITALIAN OBSERVANT STUDY: COMPARATIVE EVALUATION OF TRANSCHATETER AORTIC VALVE IMPLANTATION VS SURGICAL AORTIC VALVE REPLACEMENT IN SSAS PATIENTS

P. D'Errigo[1], F. Seccareccia[1], M. Barbanti[2], C. Tamburino[2], S. Rosato[1], F. Onorati[3], R.D. Covello[4], C. Grossi[5], M. Ranucci[6], F. Santini[7], G. Santoro[8], G. Badoni[1]
[1]CNESPS, Istituto Superiore di Sanità, Rome, Italy
[2]Division of Cardiology, Ferrarotto Hospital University of Catania, Catania, Italy
[3]Division of Cardiac Surgery, University of Verona Medical School, Verona, Italy
[4], IRCCS San Raffaele, Milano, Italy
[5]Division of Cardiac Surgery, S Croce e Carle Hospital, Cuneo, Italy
[6]Department of Cardiothoracic and Vascular Anesthesia, IRCCS Policlinico San Donato, Milano, Italy
[7]Division of Cardiac Surgery, S Martino Hospital University of Genoa, Genova, Italy
[8]Division of Cardiology, Careggi Hospital, Firenze, Italy

Aims: OBSERVANT aims to describe patients with severe and symptomatic aortic stenosis (SSAS) undergoing TAVI or SAVR procedures and compare procedural and post-procedural outcomes in a TAVI/SAVR propensity-matched population.

Methods and Results: OBSERVANT is a national observational prospective multicenter cohort study, enrolling SSAS patients undergoing SAVR or TAVI. Propensity score method was applied to analyze procedural and post-procedural outcomes. Pairs of patients with the same probability score were matched (caliper matching).

The enrolled population comprises 5864 SAVR and 1935 TAVI patients. Patients undergoing TAVI are older and sicker than patients undergoing SAVR (mean log-EuroSCORE 14.3±12.5% vs 6.7±7.4%, respectively; p=0.000). The matched population comprises 886 patients for each procedure.

The analysis of risk factors standardized differences (SD) confirmed the success of the propensity procedure in selecting two comparable subgroups (SD<10% for each factor). Thirty-day mortality was 4.2% for SAVR and 4.6% for TAVI (p=0.637). A longer hospital stay (11.8±10.8 SAVR and 9.4±10.5 TAVI; p=0.004) were reported across the surgical group whereas a higher incidence of major vascular damage (6.6% vs 0.2%; p=0.000) pacemaker implantation (15.8% vs 3.5%; p=0.000) and residual aortic regurgitation (50.7% vs 10.5%; p=0.000) were reported in the TAVI group.

Conclusions: Patients undergoing transcatheter and surgical treatment of severe AS are still different. In the analyzed propensity-matched population similar 30-day mortality rates were found but SAVR shows to be associated with a longer hospital stay and TAVI with an increased rate of vascular damage, permanent AV block and residual aortic valve regurgitation.

No conflict of interest

VENTRICULAR FUNCTION AND HEART FAILURE

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VENTRICULAR FUNCTION AND HEART FAILURE

Pharmacologic reversal of cardiac remodeling due to myocardial infarction

N.S. Dhalla[1]
[1]*Physiology, Institute of Cardiovascular Sciences University of Manitoba, Winnipeg, Canada*

Although several pharmacological interventions are currently used for the treatment of heart failure due to myocardial infarction (MI), all these drugs appear to delay the progression of heart failure without affecting the mortality. Earlier we have shown that pretreatment of infarcted rats with angiotensin II receptor (ATR) or β-adrenoceptor (β-AR) blockers markedly attenuated cardiac dysfunction, cardiac remodeling and subcellular defects primarily due to reduction in infarct size. On the other hand, treatment of 3 wks infarcted animals with AT_1R or β_1-AR antagonists attenuated cardiac and subcellular abnormalities partially without affecting the infarct size. Furthermore, treatment of 12 wks infarcted animals with AT_1R or β_1-AR antagonists, partially reversed the MI-induced cardiac remodeling, alterations in cardiac function and sarcoplasmic reticular (SR) Ca^{2+}-pump activity without affecting the infarct size, depressed SR Ca^{2+}-release or myofibrillar Ca^{2+}-stimulated ATPase activities. These observations provide evidence that the effectiveness of different drugs used for the treatment of heart failure due to MI is dependent upon the time of their administration following the ischemic episode. Furthermore, the actions of pharmacologic agents in preventing the progression of subcellular defects determine their beneficial effects on cardiac performance in the failing heart. (Supported by a grant from the Canadian Institutes of Health Research)

No conflict of interest

VENTRICULAR FUNCTION AND HEART FAILURE

Bendavia, a first-in-class mitochondrial protectant, for the treatment of heart failure

H. Sabbah[1]
[1]*Medicine, Henry Ford Health System, Detroit, USA*

Background: Mitochondria (MITO) in heart failure (HF) manifest structural and functional abnormalities evidenced by hyperplasia, reduced size and diminished respiration that lead to a defect in ATP synthesis. Bendavia (MTP-131), a novel, first in class MITO-targeting peptide, improves the efficiency of MITO electron transfer chain by improving ATP synthesis in multiple organs including kidney and skeletal muscle. We examined the effects of monotherapy with Bendavia on LV systolic function and MITO function in dogs with advanced HF.
Methods: Dogs with coronary microembolization-induced HF were randomized to 3 months therapy with subcutaneous injections of Bendavia (0.5 mg/kg once daily, n=7) or saline (Control, n=7). LV end-diastolic (EDV) and end-systolic (ESV) volumes, EF, heart rate (HR), mean aortic pressure (AP), LV end-diastolic pressure (EDP) and peak LV +dP/dt were measured before (PRE) and after 3 months of therapy (POST). Treatment effect, Δ, within each group was calculated as the difference between PRE and POST. MITO ATP synthesis, ATP/ADP ratio, state-3 respiration, permeability trabnsition pore (mPTP) opening, and membrane potential (ΔΨm) were measured in isolated LV cardiomyocytes obtained at of therapy.
Results: Bendavia had no effect on HR or mAP. Compared to Control, Bendavia decreased EDV, ESV and EDP, increased EF and peak LV +dP/dt and increased ATP synthesis and ratio of ATP/ADP. Bendavia increased ΔΨm, improved state-3 repiration and reduced opening of the mPTP.
Conclusions: In HF dogs, long-term monotherapy with Bendavia improves LV systolic function without increasing HR or decreasing mAP. Bendavia normalized mitochondria function and increased ATP synthesis; a likely mediator of improved LV function.

Conflict of interest

VENTRICULAR FUNCTION AND HEART FAILURE

Sepsis and the cardiovascular system: going to the heart of the matter

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VENTRICULAR FUNCTION AND HEART FAILURE

Stress cardiomyopathy: new clinical and pathogenetic insights

J.D. Horowitz[1], T.H. Nguyen[1], C.J. Neil[1], K. Singh[1], C. Chong[1], J. Licari[1], B. Raman[1]
[1]Cardiology Department, The Queen Elizabeth Hospital and University of Adelaide, Adelaide, Australia

Stress Cardiomyopathy (Tako-Tsubo Cardiomyopathy, TTC) has been increasingly recognised over the past 10 years, especially in ageing women. At present TTC appears to account for 8 – 10% of "STEMI" cases in women aged >50 years and a substantial proportion of women presenting without S-T segment elevation. Apart from gender, the main risk factor is exposure to high concentrations of catecholamines, via emotional stress, physical illness (especially including stroke) or medical administration. Similarly, TTC may occur more frequently in patients receiving those antidepressants which inhibit reuptake of noradrenaline. Diagnosis, once essentially of exclusion, is expedited by the findings of marked BNP/NT-proBNP release, typical regional wall motion abnormalities on echocardiography, and myocardial oedema throughout the left ventricle on MRI.

While TTC may have a benign clinical course, tachyarrhythmias and shock (usually without pulmonary oedema) are common early complications. IABP insertion may be necessary in cases of shock. Recovery from TTC is slower than initially thought : while LVEF is usually normal within 2 weeks, dyspnoea and lassitude persist, together, with evidence of ongoing myocardial inflammation, for at least 3 months. Recurrence rates are approximately 3% per annum.

The development of specific treatment measures (other than avoidance/withdrawal of catecholamine exposure) requires greater understanding of precisely how catecholamine exposure induces an intense inflammatory reaction with the myocardium. In rodent models, aberrant responses to β_2-adrenoceptor stimulation have been implicated, but precise mechanisms of oxidative stress remain to be elucidated. Given that approximately 50% of TTC patients remain symptomatic 2 years after index episodes, such therapeutic endeavours are justified.

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VENTRICULAR FUNCTION AND HEART FAILURE

Tako-tsubo cardiomyopathy: perspective from Tako-tsubo Italian Network

G. Parodi[1], R. Citro[2], B. Bellandi[1], M. Marrani[1], E. Bossone[2], D. Antoniucci[1]
[1]Cardiology, Division, Florence, Italy
[2]Cardiology, Division, Salerno, Italy

BACKGROUND. In the medical literature several cases of Tako-tsubo cardiomyopathy (TTC) with coronary artery disease (CAD) have been reported, and in clinical practice some typical TTC cases show relevant stenoses of the coronary arteries. **OBJECTIVE.** This study sought to evaluate the prevalence, characteristics and outcome of patients with TTC and CAD. **METHODS:** In 26 centers, 450 patients admitted with the diagnosis of TTC underwent coronary angiography within 48 hours of hospital admission and were prospectively included in the Tako-tsubo Italian Network (TIN) Registry. **RESULTS:** Overall, 43 (9.6%) patients had at least 1 relevant (≥ 50%) coronary stenosis not supplying the dysfunctional myocardium, while 407 (90.4%) had irrelevant stenosis or angiographically normal coronary arteries. TTC patients with relevant CAD were more likely to have advanced age, diabetes, familial history of CAD, and acute functional mitral regurgitation as compared with those without. At 6-month follow-up, the incidence of death, TTC recurrence and rehospitalization rates in patients with and without relevant CAD were similar. At multivariable Cox analysis, independent predictor of death was Charlson comorbidity index, while the presence of CAD did not significantly influence mid-term outcome. **CONCLUSIONS.** The presence of CAD is a rather common finding in a substantial proportion of patients with TTC. Thus, when the stenotic artery does not supply the dysfunctional myocardium or when the extent of dysfunctional myocardium is wider than the territory of distribution supplied by a single stenotic coronary artery, the presence of angiographically relevant CAD should not be considered an exclusion criteria for TTC.

No conflict of interest

VENTRICULAR FUNCTION AND HEART FAILURE

Tako-tsubo cardiomyopathy, what is it? Polish viewpoint

A. Rynkiewicz[1]
[1]*Department of Cardiology, Medicak University of Gdansk, Gdansk, Poland*

Takotsubo cardiomyopathy (TC), also known as “stress cardiomyopathy,” transient left ventricular (LV) “apical balloonin syndrome,” or “broken heart syndrome,” is a clinical condition mimicking an acute myocardial infarction. TC is a disease concept first presented by Dote et al in 1990. The name is derived from the image on left ventriculography at the end-systolic stage, with excessive contraction of the base of heart that compensates for the extensive lack of contraction occurring mainly at the left ventricular apex. Takotsubo refers to a vase-like contraption used to fish for octopus.

It was not until a report by Desmet and colleagues3 in 2003 that this disease began to be known to develop in persons other than the Japanese. The following were indicated as pathogenic mechanisms: (1) stunned myocardium due to multivessel spasm, (2) intramyocardial microvascular contraction, (3) myocarditis, (4) myocardium injury due to catecholamine (pheochromocytoma), (5) orthosympathetic myocardial injury (subarachnoid hemorrhage), and (6) high level of b-adrenergic receptor concentration due to the apical myocardium. In prospective studies from Western countries, between 2% and 3% of the patients undergoing coronary angiography because of suspected ACS eventually are diagnosed as having TTC.

Several questions about TC remain unanswered, including why it is induced by stress, what differentiates the stress that induces this disease from other types of stress that do not induce it, why women are more likely to develop this disease, why the apical part of the heart is affected, and how it is different from the subtype in which the base and middle parts are affected.

No conflict of interest

VENTRICULAR FUNCTION AND HEART FAILURE

DOXORUBICIN CARDIOTOXICITY IN MICE IS BLUNTED BY LATE INA INHIBITION WITH RANOLAZINE, WITH IMPROVEMENT IN HEART FUNCTION, FIBROSIS AND APOPTOSIS.

N. Maurea[1], C. Coppola[1], G. Piscopo[1], C. Cipresso[1], D. Rea[2], C. Maurea[1], E. Esposito[3], C. Arra[2], C.G. Tocchetti[1], M. De Laurentiis[3]
[1]Cardiology, Istituto Nazionale Tumori di Napoli, Naples, Italy
[2]Animal Facility, Istituto Nazionale Tumori di Napoli, Naples, Italy
[3]Breast Oncology Division, Istituto Nazionale Tumori di Napoli, Naples, Italy

Purpose. Doxorubicin (DOX) produces a cardiomyopathy through multiple mechanisms as Ca2+ overload. DOX increases demand for oxygen, setting the stage for metabolic ischemia that activates late INa, target of ranolazine (RAN). We aim at assessing whether RAN prevents DOX cardiotoxicity. **Methods.** We measured left ventricular (LV) fractional shortening (FS) and radial strain (RS) in C57BL6 mice, pretreated with RAN per os for 3 days. RAN was then administered for 7 days, alone and together with DOX. We evaluated mRNA expression, interstitial fibrosis and apoptotic pathway on excised hearts.

Results. After 7 days with DOX, FS decreased to 50±2%, p=.002 vs 60±1% (sham). RAN alone didn't change FS (59±2%). In mice treated with RAN+DOX, the reduction in FS was milder: 57±1%, p=.01 vs DOX alone. DOX-cardiotoxicity was accompanied by elevations in ANP, BNP, CTGF and MMP2 mRNAs, while co-treatment with RAN lowered these genes compared to DOX. The alterations in extracellular matrix remodeling were confirmed by an increase of interstitial collagen with DOX, which was normal in hearts co-treated with RAN. The levels of PARP and pro-Caspase 3 were decreased with DOX, with an increase in cleaved caspase 3, but not with RAN+DOX. RS was decreased after 2 days of DOX: 34±4%, p=.0003 vs sham (64±4%), but RAN+DOX-treated mice showed a higher value: 49±3%, p=.01 vs DOX alone.

Conclusions. In mice, DOX produces LV dysfunction which can be predicted by early radial strain abnormalities. RAN is able to blunt such cardiotoxicity at the functional, histological and molecular levels.

No conflict of interest

CARDIAC SURGERY: CURRENT ISSUES

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CARDIAC SURGERY: CURRENT ISSUES

Surgical options for CABG using synthetic, biodegradable vascular grafts

B. Walpoth[1], D. Mugnai[1], S. de Valence[2], W. Mrowczynski[1], J.C. Tille[3], X. Montet[4], R. Gurny[2], M. Moeller[2], A. Kalangos[1]
[1]Cardiovascular Surgery, University Hospital of Geneva, Geneva, Switzerland
[2]Pharmaceutics & Biopharmaceutics EPGL, University of Geneva, Geneva, Switzerland
[3]Pathology, University Hospital of Geneva, Geneva, Switzerland
[4]Radiology, University Hospital of Geneva, Geneva, Switzerland

Objectives: Shelf-ready, synthetic, small-calibre vascular prostheses are needed in CABG surgery. We assessed the long term results of synthetic, biodegradable small-calibre vascular grafts compared to stable ePTFE for aortic replacement in the rat.

Methods: 14 anaesthetised Sprague Dawley rats received an infrarenal aortic graft (8-biodegradable; 6-ePTFE) replacement (end-to-end; 2mm ID) and 6 sex/age-matched rats served as controls. Biodegradable grafts (polycaprolactone=PCL) were produced by random micro/nano-fibre (porosity 80%) electro-spinning. After a mean survival of 15.5±3.0 months, *in vivo* ultra-sonography and angiography were performed to assess patency (%), stenosis, aneurysm formation, and compliance (**%**/100mmHg). After explantation micro-CT, histology, immuno-histology, scanning electron microscopy (SEM) and morphometry were carried out for assessing (%): calcification, cellularity, intimal hyperplasia.

Results: Patency was 100% for PCL and 67% for ePTFE. No aneurysmal dilatation or stenoses were found in the PCL or ePTFE group. Compliance was significantly lower for ePTFE compared to PCL (5.7±0.7 vs. 8.2±1.0; $p<0.01$) but markedly reduced compared to native aortas of the controls (21.2±2.8). Despite better compliance calcification (% volume) was higher in PCL than ePTFE grafts (7.0±5.0 vs. 15.8±3.2;$p<0.03$) and absent in controls. Histologically, low cellular ingrowth was found in ePTFE whereas PCL showed significantly higher homogenous cellularity producing an autologous extra-cellular matrix, replacing the degrading (65% molecular weight reduction) PCL scaffold (10.8±4.0 vs. 32.1±9.2;$p<0.0001$). Morphometry showed 100% neoendothelialisation for both grafts. Intimal hyperplasia thickness, length and area were higher in ePTFE compared to PCL. SEM revealed a confluent endothelial coverage for PCL grafts.

Conclusion: Synthetic, biodegradable small-calibre nano-fibre polycaprolactone grafts show better patency, compliance, endothelialisation and less intimal hyperplasia compared to the clinically used ePTFE grafts after long-term implantation in the rat aorta. Thus, such novel in situ tissue engineered grafts could become a promising option for cardiovascular revascularisation procedures.

No conflict of interest

CARDIAC SURGERY: CURRENT ISSUES

Long-term survival after CABG and impact of concomitant procedures

S. Silberman[1], O. Merin[1], R. Tauber[1], A. Alshosha[1], D. Bitran[1]
[1]Cardiothoarcic Surgery, Shaare Zedek Medical Center, Jerusalem, Israel

Introduction: Coronary artery bypass (CABG) is the preferred procedure for complete revascularization in patients with multi-vessel coronary artery disease. We analyzed early outcomes and late survival in patients undergoing CABG at our center over a 20 year period.

Patients: Between 1993-2012, 4913 patients underwent CABG with or without concomitant procedures. A retrospective analysis was performed to determine early outcomes. Long-term survival was established from data from the Ministry of Interior.

Results: Isolated CABG was performed in 3950 (80%). Over time, patients undergoing surgery are older ($p=0.002$) and the incidence of concomitant procedures increased from 20% to 61% ($p<0.0001$). Predicted operative mortality increased ($p<0.0001$) however observed mortality remained the same ($p=0.5$). Long-term survival was reduced in patients requiring concomitant procedures ($p<0.0001$) and in patients with reduced LV function ($p<0.0001$). Survival after isolated CABG is 86% and 70% at 5 and 10 years respectively. Late survival was affected by age and co-morbid conditions. Reduced LV function and the presence of preoperative mitral regurgitation emerged as cardiac predictors for late mortality.

Conclusions: Patients undergoing CABG are older and have more extensive co-morbidity. Despite this, operative mortality has not increased. Long-term survival is affected by age, LV function and co-morbid conditions.

No conflict of interest

CARDIAC SURGERY: CURRENT ISSUES

Is there a difference between small, medium and high volume centers of cardiac surgery

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CARDIAC SURGERY: CURRENT ISSUES

Advantages and pitfalls of OPCAB surgery

J. Ennker[1]
[1]*Cardiothoracic Surgery, Mediclin Heart Institute Lahr/Baden Germany, Lahr, Germany*

Off-Pump Coronary Artery Surgery

Off-pump CABG has remained at 15 – 20 % in Europe and the USA. In particular, the vision that off-pump surgery would lead to inferior revascularization due to reduction of peripheral anastomoses. In addition to this, no study was able to demonstrate any documented clinical advantage of the off-pump technique versus the traditional technique using cardiopulmonary bypass.

Numerous clinical studies analyzed the clinical outcome of off-pump versus on-pump surgery in regard to death, non-fatal stroke and non-fatal myocardial infarction and also found a raise of transfusion, reoperation for perioperative bleeding, respiratory complications and acute kidney injury. These studies over all documented the excellence of conventional coronary artery bypass surgery regardless of performed on- or off-pump.

In particular, certain subgroups of patients benefited from the off-pump method as high-risk patients and diabetic patients. The incidence of perioperative stroke and neurological deficit was lower in patients operated off-pump. In this regard, an aortic no-touch technique using Y- or T-grafts resulted in the greatest benefits.

My personal experience started in September 1997. In 2005 our entire group switched to complete off-pump surgery, predominantly complete arterial, using Y-graft and the aortic no-touch technique. In 2012 the incidence of off-pump surgery was 96.5 %, 30-day mortality was 0.6 %. Complete arterial revascularization was used in 98 % of my personal patients. As studies as the ROBY- Trial did not show any significant benefit of the off-pump surgery, it should be pointed out that the results of the off-pump technique heavily depend on surgical experience, skills and team motivation.

No conflict of interest

CARDIAC SURGERY: CURRENT ISSUES

International humanitarian causes in the era of global health care and concerns

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CARDIAC SURGERY: CURRENT ISSUES

MULTIPLE ARTERIAL GRAFTS IMPROVE LATE SURVIVAL OF PATIENTS WITH MULTIVESSEL DISEASE UNDERGOING CABG

C. Leker Locker[1], H.V. Schaff[1], J.A. Dearani[1], L.D. Joyce[1], S.J. Park[1], H.M. Burkhart[1], R.M. Suri[1], K.L. Greason[1], J.M. Stulak[1], Z. Li[2], R.C. Daly[1]
[1]Cardiovascular Surgery, Mayo Clinic, Rochester, USA
[2]Biomedical Statistics and Informatics, Mayo Clinic, Rochester, USA

Background: The use of left internal mammary artery (LIMA) in multivessel coronary artery disease (MVCAD) improves survival following coronary artery bypass graft surgery (CABG); however, survival benefit of multiple arterial (MultArt) grafts is debated.
Methods and Results: We reviewed 8,622 Mayo Clinic patients who had isolated primary CABG for MVCAD from 1993 to 2009. Patients were stratified by number of arterial grafts: LIMA plus saphenous veins (LIMA/SV) group (n=7,435), and MultArt group (n=1,187). Propensity score analysis matched 1,153 patients. Operative mortality was 0.8% (n=10) in MultArt and 2.1% (n=154) in LIMA/SV (*P*=0.005); however, not statistically different (*P*=0.996) in multivariate analysis, or in propensity matched groups (*P*=0.818). Late survival was greater for MultArt versus LIMA/SV (5-, 10-, and 15-year survival (y/s) were 95%, 84%, and 71% vs 85%, 61%, and 36%, respectively [*P*<0.001] in unmatched groups, and 96%, 83% and 70%, vs 93%, 80% and 60%, respectively [*P*=0.0025] in matched groups). MultArt subgroups, with bilateral internal mammary artery (BIMA)/SV (n=589) and BIMA only (n=271), had improved 15-y/s (97%, 86%, 76%, and 94%, 82%, 75% at 5-, 10-, and 15-years, [*P*<0.001]), and BIMA/radial artery(RA) (n=147) and LIMA/RA (n=169), had greater 10-y/s (95%, 84% and 93%, 78% at 5- and 10-years, [*P*<0.001]) versus LIMA/SV. In multivariate analysis, MultArt grafts remained a strong independent predictor of survival (HR= 0.79, 95 % CI, 0.66-0.94, [*P*=0.007]).
Conclusions: In patients with MVCAD undergoing isolated CABG with LIMA to left anterior descending (LAD) artery, arterial grafting of the non-LAD vessels, conferred 15-year survival advantage compared with SV grafting.

No conflict of interest

CARDIAC SURGERY: CURRENT ISSUES

EARLY AND MIDTERM OUTCOMES OF ONE-STOP HYBRID CORONARY REVASCULARIZATION FOR THE TREATMENT OF MULTIVESSEL CORONARY ARTERY DISEASE

S. Hu[1], S. Shen[1], X. Xu[2], Z. Zheng[1], Z. Zhao[1]
[1]Department of Cardiovascular Surgery, National Center for Cardiovascular Disease China & Fuwai Hospital, Beijing, China
[2]Department of Cardiology, National Center for Cardiovascular Disease China & Fuwai Hospital, Beijing, China

Objective This study sought to discuss early and midterm clinical outcomes of one-stop hybrid coronary revascularization for the treatment of multivessel coronary artery disease (CAD).

Methods From June 2007 to December 2010, 147 patients (mean age 62.2 ± 9.8 years) with multivessel CAD underwent one-stop hybrid procedure at Fuwai hospital. Minimally invasive direct coronary artery bypass procedure was first performed for bypassing the left internal mammary artery (LIMA) to the left anterior descending artery (LAD). After closure of the thorax, angiography was immediately performed to confirm patency of LIMA-LAD graft and then percutaneous coronary intervention (PCI) was performed on non-LAD lesions simultaneously. The main in-hospital complications and the cumulative major adverse cardiac or cerebrovascular events (MACCE) were recorded.

Results Of the total 147 patients, 145 patients (98.6%) were successfully treated with one-stop hybrid procedure, and 2 patients (1.4%) were converted to conventional bypass surgery because of LIMA harvest failure and the obtuse marginal branch dissection during PCI, respectively. 141 patients underwent one-stop HCR with drug eluting stent implantation in non-LAD, and 4 patients with bare metal stent implantation. There were no in-hospital deaths, cerebrovascular accidents, myocardial infarctions, acute renal dysfunctions, or reoperation for bleeding. At a mean follow-up of 3.3 years, the actuarial survival was 97.2% (141/145), and the cumulative MACCE rate was 9.7% (14/145).

Conclusions One-stop hybrid coronary revascularization provided favorable early and midterm outcomes for selected patients with multivessel coronary artery disease. It might provide a feasible and reproductive alternative to conventional revascularization strategies.

No conflict *of interest*

CARDIAC SURGERY: CURRENT ISSUES

MULTICENTER EXPERIENCE WITH AN ADJUSTABLE ANNULOPLASTY DEVICE (ENCOR SQ) IN THE TREATMENT OF FUNCTIONAL MR

M. Czesla[1], J. Goette[1], V. Voth[1], N. Doll[1]
[1]Heart surgery, Sana Herzchirurgie GmbH, Stuttgart, Germany

Functional or ischemic MR continues to represent a major challenge for cardiac surgeons. Mitral valve repair is associated with a significant incidence of recurrent severe MR approaching 25-30% in patients suffering from ischemic MR.

The concept of ring adjustment after implantation of the device under beating heart conditions led to the development of the EnCorSQ Mitral Valve Repair System (Micardia). Late activation can be performed weeks or even months after surgery when recurrent mitral regurgitation occurs by accessing a subcutaneous lead. By elevating the temperature a few degrees using radiofrequency energy, the anterior posterior diameter of the device can be reduced without affecting the effective orifice area.

The goal of this study was to assess the efficacy and safety of this new device. A total of 31 patients in 5 European centers were included into this non-randomized, single arm clinical trial.

No severe adverse events or mortalities occurred. Intraoperative moderate downsizing was performed by reducing the diameter by one size with initially good results. Two patients developed recurrent severe MR three and six months after surgery and subsequently underwent successful late activation resulting in trace MR. The remaining patients included in the DYANA II study were found to have either no or mild MR.

The concept of late activation seems to be a good alternative in the treatment of this challenging patient population and will decrease the need for high risk re-do mitral valve surgery.

Conflict of interest

CARDIAC SURGERY: CURRENT ISSUES

TWENTY YEAR EVOLUTION OF OUTCOMES BY SOCIETY OF THORACIC SURGEONS RISK-ADJUSTED SCORES IN 712 OCTOGENARIANS UNDERGOING CORONARY ARTERY BYPASS GRAFTING

A. Zapolanski[1], C.K. Johnson[1], G. Ferrari[2], R.E. Shaw[1], R.L. Saporito[1], R.J. Saporito[1], M.E. Brizzio[1], J.B. Grau[1]
[1]Cardiac Surgery, The Valley Columbia Heart Center, Ridgewood, USA
[2]Perelman School of Medicine, The University of Pennsylvania, Glenolden, USA

Introduction: The current population of octogenarians in the US is 9.36 million. This study examines the trends in outcomes of very elderly patients undergoing Coronary Artery Bypass Grafting (CABG) over time using the Society of Thoracic Surgeons Risk-Adjusted Scores (STSRAS) as a basis for a legitimate comparison.

Methods: From 1994-2013, 6,666 patients underwent CABG. Of these patients, 712 were over the age of 80. These patients were broken up into 3 'eras' based on year of surgery: 1994-2000 (n=290, 40.73%), 2001-2005 (n=221, 31.04%), and 2006-2013 (n=201, 28.23%). The STSRAS was used to evaluate expected outcomes. Observed/Expected (O/E) Ratios were used to test if the actual results performed better than predicted.

Results: The outcomes and O/E ratios are displayed in Table 1. In three of the eight categories (Length of Stay >6 Days, Length of Stay >14 Days, and Renal Failure), there was a steady decline in O/E ratio over time. The O/E ratios for the 06-13 era were lower than those of the 94-00 era for all outcomes. The 06-13 era outperformed the 01-05 era in all categories except one (Permanent Stroke).

Conclusion: Our analysis demonstrates the very elderly patients perform better than expected when undergoing CABG. In our most recent era, there is a clear improvement of observed outcomes when compared to what was expected. This likely reflects the changes in both surgical approaches and critical care management. Careful judgment must be exercised when denying the benefit of CABG to this group of patients.

No conflict of interest

CARDIAC SURGERY: CURRENT ISSUES

CORONARY ARTERY BYPASS GRAFTING VS. PERCUTANEOUS CORONARY INTERVENTION IN A "REAL WORLD" SETTING: INSIGHTS FROM THE COOPERATION STUDY.

F. Nicolini[1], D. Fortuna[2], G.A. Contini[3], D. Pacini[4], D. Gabbieri[5], C. Zussa[6], F. Pigini[7], A. Agostinelli[3], R. De Palma[2], T. Gherli[1]
[1]Clinical and Experimental Medicine, University of Parma, Parma, Italy
[2]Agenzia Sanitaria e Sociale Regionale, Regione Emilia-Romagna, Bologna, Italy
[3]Cardio Nephro Pulmonary Department, Azienda Ospedaliero Universitaria, Parma, Italy
[4]Dipartimento Cardio Toraco Vascolare, Azienda Ospedaliero Universitaria S. Orsola Malpighi, Bologna, Italy
[5]Dipartimento Cardiologia medico chirurgica toraco vascolare, Hesperia Hospital, Modena, Italy
[6]Dipartimento di Cardiologia e Cardiochirurgia, Casa di Cura Villa Maria Cecilia, Cotignola, Italy
[7]Unità di Cardiochirurgia, Villa Torri Hospital, Bologna, Italy

Objectives

Most studies comparing coronary artery bypass grafting (CABG) and percutaneous coronary interventions (PCI) showed that fewer patients after CABG require repeat revascularizations, without any difference in survival. However, long-term real-world evidence on patients in whom both procedures are technically feasible is not yet available.The purpose of this study was to compare 5-year rates of death, myocardial infarction (MI), target vessel revascularization (TVR), and stroke in a large cohort of patients with LMCA or multivessel disease, treated with CABG or PCI (with or without DES) or PCI with DES only.

Methods

Two propensity score (PS) matched cohorts of patients who had revascularization procedures at the regional public and private centers of Emilia-Romagna region (Italy) over the period July 2002 - December 2008 were used to compare long-term outcomes of PCI (6,246 patients) and CABG (5,504 patients).

Results

PCI was associated with higher risk of death (HR=1.6 CI 95% 1.4-1.8), MI (HR=3.3 CI 95% 2.7-4.0) and TVR (HR=4.5 CI 95% 3.8-5.2) at five-years. No significant difference was shown for stroke (HR=1.1 CI 95% 0.9-1.4). CABG benefit was more evident on the risk of death in patients with two vessel disease plus LMCA and in those with three vessel disease, with LVEF<35%, congestive heart failure, and diabetes.

Conclusions

In the 'real-world' setting of this study, CABG was associated with significantly lower rates of death, MI and TVR, in patients with LMCA or multivessel disease so it remains the standard of care, particularly for patients with more extensive coronary disease and diabetes.

No conflict of interest

CARDIAC SURGERY

Document not received

CARDIAC SURGERY

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CARDIAC SURGERY

MIDTERM OUTCOMES OF ONE-STOP HYBRID CORONARY ARTERY REVASCULARIZATION FOR LEFT MAIN CORONARY ARTERY DISEASE

S. Hu[1], S. Song[1], S. Shen[1], X. Xu[2], Z. Zheng[1]
[1]Department of Cardiovascular Surgery, National Center for Cardiovascular Disease China & Fuwai Hospital, Beijing, China
[2]Department of Cardiology, National Center for Cardiovascular Disease China & Fuwai Hospital, Beijing, China

Background: The study sought to evaluate the feasibility, safety and midterm outcomes of one-stop hybrid coronary revascularization for left main coronary artery disease, compared with conventional off-pump coronary artery bypass grafting (OPCAB).

Methods: From June 2007 to December 2011, 38 consecutive patients (mean age 61.4±10.0 years) with left main coronary artery disease underwent one-stop hybrid coronary revascularization at Fuwai Hospital. Using propensity score methodology, these patients were matched with 38 patients who had undergone off-pump coronary artery bypass grafting via median sternotomy during the same period. We compared two groups' in-hospital clinical outcomes and freedom from major adverse cardiac or cerebrovascular events at a mean follow-up of 24.5 ± 11.8 months.

Results: All baseline clinical characteristics of the 2 groups were similar. All patients in the 2 groups underwent surgery uneventfully without conversion to on-pump coronary artery bypass grafting. The hybrid procedure required longer operative time and incurred higher in-hospital costs, but had shorter intubation time (10.6 ± 6.1 versus 13.9 ± 7.0 hours, $P < 0.05$), intensive care unit length of stay (30.5 ± 16.6 versus 54.3 ± 36.7 hours, $P < 0.05$) and postoperative in-hospital length of stay(8.3 ± 2.6 versus 9.6 ± 4.5 days, $P < 0.05$). Hybrid group had significantly less chest tube drainage (664 ± 315 versus 804 ± 283 ml, $P < 0.05$) and need for blood transfusion (15.8% versus 44.7%, $P < 0.05$). At a mean follow-up of 24.5 months, the freedom from major adverse cardiac or cerebrovascular events is in favor of hybrid group (94.7% versus 81.6%; $P < 0.05$).

Conclusions: The midterm follow-up outcomes indicated that one-stop hybrid coronary revascularization procedure is feasible and safe, and it might provide a promising alternative for selected patients with left main coronary artery disease.

No conflict of interest

CARDIAC SURGERY

ON-PUMP VS. OFF-PUMP CORONARY ARTERY BYPASS GRAFTING: MID-TERM RESULTS

P. Nardi[1], A. Pellegrino[1], R. Mani[1], G.A. Chiariello[1], C. Bassano[1], J. Zeitani[1], L. Chiariello[1]
[1]Cardiac Surgery Division, University of Rome "Tor Vergata", Rome, Italy

Aim of the Study. To evaluate mid-term results after ON-pump CABG vs. off-pump(OP)-CABG.

Methods. Data from 166 consecutive OP-CABG patients compared with those of 206 ON-pump CABG patients operated on the same time of OP-CABG operations were retrospectively analyzed.

Results. As compared to OP-CABG, in the ON-pump CABG co-mordid conditions, severe coronary disease and urgent or emergency surgery were more frequently observed ($p \leq 0.03$, for all comparisons). Mean number of grafts /patient was higher in ON-pump CABG (2.9±0.9vs.2.3±0.9, $p<0.0001$). Operative mortality was 3.8% in ON-pump CABG vs. 1.2% in OP-CABG (p=NS), postoperative major complications 12% vs. 10% (p=NS). Re-exploration for bleeding (9.7%vs.3.6%, $p=0.02$) and need for blood transfusion (62%vs.54%, $p=0.01$) were significantly higher in the ON-pump CABG. Clamp-less OP-CABG reduced the incidence of neurological complications (1.2%vs.3.3%, $p=0.06$). Operative costs /patient was 1.060,00 € for ON-pump and 2.980,00 € (including the use of PAS-port system) for OP-CABG.

At 4 years, survival (91%±13% in the ON-pump CABG vs. 84%±19% in the OP-CABG) freedom from MACE (82%±9%vs.76%±14%) and MACCE (80%±11%vs.72%±16%) were not significantly different, although better after ON-pump CABG. Freedom from cardiac death was slightly significant higher after ON-pump CABG (98%±4%vs.90%±10%, $p=0.05$). Follow-up CCS class was better in ON-pump CABG in comparison with OP-CABG (1.2±0.6vs.1.4±0.6, $p=0.02$).

Conclusions. Based on clinical practice, ON-pump CABG should be still considered the standard surgical treatment. Mid-term follow-up freedom from cardiac events appears to be better after ON-pump CABG. Clamp-less OP-CABG technique is effective to reduce perioperative rate of neurological complications. Off-pump surgery requires more expensive surgical technology.

No conflict of interest

CARDIAC SURGERY

EXTERNALLY MESH-SUPPORTED SAPHENOUS VEIN GRAFTS IN CORONARY ARTERY SURGERY: ONE YEAR CT ANGIOGRAPHIC RESULTS

O. Reuthebuch[1], D. Inderbitzin[1], R.W. Emery[2]
[1]Clinic for Cardiac Surgery, University Hospital Basel, Basel, Switzerland
[2]Cardiovascular Surgery, St Joseph`s Hospital, St Paul MN, USA

Long-term patency of saphenous vein grafts (SVG) in coronary surgery (CABG) is inferior to internal thoracic arteries due to endothelial damage and neointimal hyperplasia. An external Nitinol mesh (eSVS® mesh, Kips Bay Medical, Minneapolis, USA) prevents SVG endothelial damage by avoiding vessel shear wall stress. We present patency rates at one year post-operative (PO).

The mesh is a highly flexible, semi-compliant, kink-resistant tubular prosthesis of knitted Nitinol wire deployed on the outside of the vein. From 06/2010 to 06/2011 22 patients received a mesh in isolated CABG (n=18) or combined with aortic valve replacement (n=4). Three patients were excluded from post-hoc analysis due to non-device related in-hospital (n=2) or post-discharge death. All 19 surviving patients (mean age 70.4 ± 9.5 years, 3 female) completed an ECG triggered CT angiographic (CTA) assessment of all grafts 12 +/- 0.1 months PO. A total of 32 mesh supported and 8 unmeshed SVGs as well as all arterial grafts were evaluated.

All meshes were deployed safely and transit time flow-measurement patency was intraoperatively documented. With an average of 2.8 grafts per patient, all arterial and unmeshed venous grafts were patent on CTA. However, of 32 mesh supported anastomoses 5 were occluded (16%): one to the left and 4 to the right system. All patients were asymptomatic. Data from both systems are shown in the tables.

The eSVS® mesh had an overall 1 year patency rate of 84% on CTA. Predilection of meshed graft occlusion to the right coronary system may reveal a site dependency. Further long-term studies are warranted.

Table 1: Results associated with the left coronary system

Graft	Distal Anastomosis	No (n)	Mean Flow (ml/min)	Pulsatility Index	Patent	Occluded CT
LIMA	Single	15	40 ± 32.4	2.0 ± 0.6	15	0
	Jump	2	39	2.2	2	0
RIMA	Jump	4	44 ± 19.3	1.4 ± 0.4	4	0
Radial Artery	Single	1	19	1.2	1	0
Vein unmeshed	Jump	5	38 ± 19.8	2.4 ± 1.0	5	0
Vein meshed	Jump	10	73 ± 56.2	1.6 ± 0.4	9	1
Total		**37**			**36**	**1 (2.7%)**

Table 2: Results associated with the right coronary system

Graft	Distal Anastomosis	No (n)	Mean Flow (ml/min)	Pulsatility Index	Patent	Occluded
Vein unmeshed	Single	2	67 ± 20.5	1.25 ± 0.07	2	0
	Jump	1	58	2	1	0
Vein meshed	Single	10	41 ± 28.1	1.5 ± 0.8	6	4
	Jump	1	78	2	1	0
Total		**14**			**10**	**4 (28%)**

Conflict of interest

CARDIAC SURGERY

POSTOPERATIVE OUTCOME OF ISOLATED TRICUSPID VALVE OPERATION USING ARRESTED-HEART OR BEATING-HEART TECHNIQUE

B. Pfannmueller[1], P. Davierwala[1], M. Misfeld[1], M.A. Borger[1], J. Garbade[1], F.W. Mohr[1]
[1]Heart Surgery, Heart Center Leipzig, Leipzig, Germany

Objectives: Few studies have focused on the outcomes of tricuspid valve (TV) surgery in beating-heart technique vs. cross-clamping.

Methods: Retrospective analysis of 121 patients undergoing TV surgery with isolated tricuspid valve repair or replacement in beating-heart technique (n=65) or with arrested heart (n=56). Mean patient age was 59.3±15.9 years, 44.6% were male, and average logEuroSCORE was 11.6±11.2%. 47.9% of the operations were redos. Follow up was 98% complete with a mean duration of 30±36 months.

Results:
Overall thirty day mortality was 7.4%, 5-year survival was 71.0% for patients operated in beating-heart technique and 74.9% for patients operated with cross-clamp.
During follow up eight patients underwent TV reoperation resulting in a 5-year event-free rate of 86.7% for patients operated in beating-heart technique and 87.7% for patients operated with the arrested heart.

Conclusions: Postoperative results after TV surgery are good and comparable for patients operated in beating heart technique or with the arrested heart.

No conflict of interest

CARDIAC SURGERY

MORTALITY PREDICTION AFTER CORONARY SURGERY USING THE EUROSCORE II

B. Mihajlovic[1], N. Cemerlic-Adjic[2], L. Velicki[1], S. Nicin[1], B.B. Mihajlovic[2], M. Fabri[1]
[1]Cardiovascular surgery, Institute of cardiovascular diseases Vojvodina, NOVI SAD, Serbia
[2]Cardiology, Institute of cardiovascular diseases Vojvodina, NOVI SAD, Serbia

Backround: Over the last several years many authors have found that European Systems for Cardiac Operative Risk Evaluation (EuroSCORE) in both of its forms - additive and logistic, overestimated risk in cardiac surgery. It was mainly the considerable improvement in cardiac surgery and changed patients risk profile, that affected the precision of the model. The new EuroSCORE II has been recently introduced, as an update to a previous version. The aim of the study: to asses prognostic value, sensitivity and specificity of the EuroSCORE II.

Methods: The research included 704 consecutive patients who had undergone isolated coronary surgery in the period January 2012. - March 2013. The predicted mortality according to the EuroSCORE II and observed, 30 - day mortality, were compared. Patients were divided into 3 groups with regard to their estimated risk according to the initial EuroSCOR model: low risk 0 - 2%; medium risk 3 - 5% and high risk - over 5%.

Results: Table 1

Coronary surgery	No pts.	Predicted mortality	Observed mortality	p – value	AUROC	Cut – off	Sensitivity	Specificity
Total	704	1.6%	1.8%	0.602	0.807	1.98	76.9%	82.3%
Low risk	267	0.85%	0.4%	0.395	0.835	1.11	100.0%	83.5%
Medium risk	314	1.6%	1.6%	0.991	0.837	1.98	80.0%	84.8%
High risk	123	3.24%	5.7%	0.126	0.592	2.47	71.4%	58.6%

Conclusion: Our results demonstrate excellent accuracy of the EuroSCORE II in terms of calibration and discriminative power in the whole group of isolated coronary surgery patients, and also in low and medium risk groups. However in high risk group the EuroSCORE II does not provide satisfactory predictive and discriminative power.

No conflict of interest

CARDIAC SURGERY

IMPACT OF TRANSFUSIONS ON 10-YEAR MORTALITY IN 636 PROPENSITY-MATCHED PATIENTS WHOM UNDERWENT CABG WITH NO STS DEFINED 30-DAY COMPLICATIONS

C.K. Johnson[1], G. Ferrari[2], R.E. Shaw[1], R.J. Saporito[1], R.L. Saporito[1], M.E. Brizzio[1], A. Zapolanski[1], J.B. Grau[1]
[1]Cardiac Surgery, The Valley Columbia Heart Center, Ridgewood, USA
[2]Perelman School of Medicine, The University of Pennsylvania, Glenolden, USA

Objective

Blood transfusions have been associated with reduced long-term survival in coronary artery bypass grafting (CABG). However, past studies have not addressed the confounding effect that short-term complications have on long-term mortality. Here, we describe the effects of blood transfusion in a propensity-matched cohort of 636 patients whom underwent CABG with 0% 30-day complications by Society of Thoracic Surgeons (STS) criteria.

Methods

Between 2004 and 2011, 1,693 patients underwent first time isolated CABG. After excluding those who experienced post-operative complications 1,134 patients were used for analysis. From these, 407 had received intraoperative blood products. Two groups (transfused and non-transfused) of 318 patients were created by propensity-matching for their likelihood of transfusion based on 22 pre-operative variables. STS Risk Adjusted Score for mortality was not statistically significantly different between the two groups (Non transfused 1.8% and Transfused 1.6%)

Long-term mortality was assessed using the Social Security Death Index.

Results

After propensity matching, there were no significant differences between the transfused and non-transfused patients on baseline characteristics. There were significantly more deaths in the transfusion group at 10 years follow up (13.8% vs. 7.5%; p=0.007). Kaplan Meier curves also demonstrated a trend towards significance.

Conclusion

There are many factors that affect long-term mortality. However, in the absence of perioperative complications and very similar preoperative STS Risk Adjusted Scores, patients receiving blood transfusions after isolated CABG still suffer significantly higher rates of long-term mortality at 10 years follow up. Strict adherence to transfusion guidelines at the time of CABG is recommended.

No conflict of interest

ANOMALOUS RIGHT CORONARY ARTERY ORIGINATING FROM THE LEFT MAIN CORONARY ARTERY

I. algin[1], N. Akçar[2]
[1]kalp ve damar cerrahisi, Ozel Korfez hastahanesi, balikesir, Turkey
[2]cardiovascular suergery, Ozel OSM Ortadogu Hastahanesi, sanliurfa, Turkey

ABSTRACT

Rare congenital coronary artery anomalies often accompanied by coronary artery disease and aortic stenosis e.t.c with no such asymptomatic disease identified. Our case is a 71 year old patient.

Chest pain developed with limited exercise accompanied by co-morbid disease, after coronary angiography anomalous right coronary artery originating from the left main coronary artery was observed the patient was operated on electively. Saphenous vein grafts was used to bypass CxOm1 and RCA, LIMA was used to D1-LAD sequential bypass. Patient was discharged postoperatively 7 th day.

CASE REPORT

Our case is a 71 year old male patient.

Coronary angiogram was taken after chest pains developed with exercise. Anomalous RCA originating from LMCA close to the ostium along with detected stenosis of 90,70,90,80% repectively at CX branch,after RCA crux, D1 and LAD. The patient was operated on following preoperative routine of biochemical analysis, carotid Doppler, TTE, pulmonary function tests with a

4-6 intermediate risk EuroSCORE.

OPERATION NOTES

ITGA and with the patient in the supine position, following median sternotomy and preparation for LIMA and SVG (saphenous vein graft) uni caval cannulation to CPB. Mid hypothermia with Aortic root, antegrade cold blood infused cardioplegia given the heart is arrested, after which the distal bypasses were performed using the prepared saphenous vein graft first the RCA crux followed by the OM1.Next the D1 and LAD sequential bypasses were performed using the prepared LIMA. We next performed the proximal saphenous vein graft. The patient was warmed and removed from cardioplegia. The heart started with spontaneous sinus rhythm.

Patient was removed from CPB without problem or the need for inotropic support and following decannulation was closed according to the anatomic layers. After observing patient in ICU for one day patient was moved to ward on day 2 and discharged 7th postoperative day.

No conflict of interest

SUBXYPHOID PLEURAL DRAIN AS A DETERMINANT OF FUNCTIONAL CAPACITY AFTER OFF-PUMP CORONARY ARTERY BYPASS GRAFT: A RANDOMIZED CONTROLLED TRIAL

D. Alves[1], D.W. Bolzan[1], A. Cancio[1], R.S.L. Moreira[1], S. Faresin[1], A.C.C. Carvalho[1], W.J. Gomes[1], S. Guizilini[1]

[1]Cardiology, Federal University of São Paulo, São Paulo, Brazil

Background: Previous reports showed that changing the pleural drain insertion site to the subxyphoid region promoted better preservation of lung volumes and capacities after CABG with the LITA graft. The aim of this trial was to compare functional capacity, pulmonary shunt fraction, and clinical outcomes between patients undergoing pleurotomy with pleural drain inserted in the subxyphoid position and patients with a pleural drain placed in the intercostal position after off-pump CABG (OPCAB). **Methods**: Sixty-eight patients were randomized into two groups according to the pleural drain site: Group IC (n=33 interscostal pleural drain); Group SS (n=35 subxyphoid pleural drain). Functional capacity was assessed by the distance walked in the six-minute walking test (6MWT) which was performed preoperatively and on 5th postoperative day (POD), pulmonary function was assessed preoperatively and on POD1 and POD5, pulmonary shunt fraction was assessed preoperatively and on POD1, clinical outcomes were recorded throughout the study. **Results**: Functional capacity was significantly reduced in both groups after surgery, group SS showed better preservation of functional capacity (343,6±35,81 vs. 389,5±45,84; p=0.0001). Pulmonary shunt fraction was significantly higher in both groups postoperatively, however group SS showed a smaller pulmonary shunt fraction (0.26 ± 0.04 vs. 0.21 ± 0.04; p=0.0014). Group SS had better postoperative clinical results, with lower incidence of atelectasis and pleural effusion (p=0.03; p=0.02), lower pain scores (p<0.0001) and shorter intubation and hospitalization lengths (p=0.0003; p<0.0001). **Conclusion**: Subxyphoid pleural drain position determined better functional capacity and exercise tolerance with improved clinical outcomes when compared with intercostal pleural drainage.

No conflict of interest

SURGICAL MYOCARDIUM REVASCULARIZATION FOLLOWING PERCUTANEOUS CORONARY INTERVENTION IN THE DEPARTEMENT OF CARDIAC SURGERY UNIVERSITY OF DEBRECEN BETWEEN 2007-2012

P. Csizmadia[1], T. Debreceni[1], T. Szerafin[1]
[1]Cardiac Surgery, Medical University of Debrecen, Debrecen, Hungary

Background: Percutaneous coronary intervention (PCI) is the most common treatment for revascularization of ischaemic myocardium. Following successful PCI 15-30% of patients require repeated coronary intervention. **Objective:** This study examines the outcome, morbidity and mortality of cardiac surgery following percutaneous coronary intervention. **Patients and methods:** Between 1. January 2007. and 31. December 2012. 2596 patients underwent isolated coronary artery bypass grafting (CABG) in our departement. 592 patients had previous percutaneous coronary intervention or interventions: 146 women and 446 men with the mean age of 60,6 ± 9 at the time of surgery. **Results:** More often restenosis developed after initially successful PCI or progression of the coronary artery disease, less cases PCI failure and unsuccessful intervention were the indication for CABG. At the first procedure the patients who had 1 or 2 vessel disease, by the time of the surgery mostly 3 vessel disease were developed. Therefore the mean number of the distal anastomoses was higher. Mostly the operations were performed on-pump. In our investigation the in-hospital mortality was 1,4%. **Conclusion:** Based on our results an increasing number of patients PCI procedures have been performed before they are referred to CABG. The interval between PCI and surgical myocardium revascularization, moreover the high rate of patients with multivessel disease emphasise the importance of proper patient selection before PCI.

No conflict of interest

BENEFITS OF CARDIAC SURGERY IN ELDERLY –A POSTOPERATIVE QUALITY OF LIFE ASSESSMENT OVER 75 YEARS

L. Palotas[1], T. Debreceni[1], P. Csizmadia[1], T. Szerafin[1]
[1]Cardiac Surgery, Medical University of Debrecen, Debrecen, Hungary

Introduction: Assessment of postoperative quality of life in patients over 75 years after cardiac surgery after isolated coronary artery bypass grafting (CABG) **Patients and methods:** Quality of life of n=130 patients over 75 years at operation (77.4±2.1) (75-86), undergoing isolated CABG between 2007.01.01. and 2012.07.01. was reviewed. Preoperatively 98% presented in NYHA-class III/IV. Mean ejection fraction (EF) was 51.0%±9,3 (range 20-70). Quality of life assessment was performed via a modifyed Seattle Angina Qestionnaire. Follow-up was 75% complete for a total of 99.6 ±20.2 month. **Results:**Five year survival was 83% after CABG,. Better quality of life was remarkable after surgery($p < 0.00001$). Overall 89 patients (82%) were not or little disabled in their daily activity. 104 patients (96%) were considerably less symptomatic. 89% of patients reported to be very satisfied or satisfied with their current quality of life. **Conclusions:** A remarkable quality of life and important improvement in functional status after cardiac surgery in patients over 75 paired with a satisfactory medium-term survival emphasised the importancy and reason for the existence of surgical intervention. The suitability of this population for the surgical procedure demanding a multidisciplinar judgement in the referral practice. We should taking into account the higher age, the biological state and comorbidity of the patients having regards to riscs and benefits of planned surgical procedure.

No conflict of interest

MONOCYTE CHEMOTACTIC PROTEIN-1 AND E-SELECTIN INFLAMMATORY PATTERNS IN CABG SURGERY WITH THE MINIATURIZED EXTRACORPOREAL CIRCULATION: A RANDOMIZED CLINICAL TRIAL.

S. Mariani[1], F. Formica[1], F. Broccolo[2], R. Caruso[3], F. Sangalli[4], S. D'alessandro[5], F. Corti[5], G. Paolini[1]
[1]Surgical Science and Interdisciplinary Medicine, University of Milano-Bicocca San gerardo Hospital Monza, Monza (MB), Italy
[2]Clinical Medicine and Prevention, University of Milano-Bicocca, Monza (MB), Italy
[3]Cardio-Thorac- Vascular Surgery Perfusion Service, San Gerardo Hospital, Monza (MB), Italy
[4]Cardiothoracic and Vascular Anaesthesia Intensive Care Unit, San Gerardo Hospital, Monza (MB), Italy
[5]Cardio-Thorac- Vascular Surgery, San Gerardo Hospital, Monza (MB), Italy

Background: Inflammatory response and hemodilution are the main drawbacks of extracorporeal circulation. We hypothesize that the use of a miniaturized extracorporeal circulation might induces a lower systemic and cardiac inflammatory response and a lower endothelial activation compared to a standard system and the off-pump coronary surgery.

Methods: Sixty-one patients undergoing isolated coronary artery bypass graft were prospectively randomized to a miniaturized extracorporeal circulation (n=19), a standard extracorporeal circulation (n=20) or an off-pump surgery (n=22). Blood samples were collected from radial artery and coronary sinus to analyze blood lactate, hemodilution and markers for inflammation and endothelial activation such as tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), monocyte chemotactic protein-1(MCP-1) and E-selectin.

Results: No differences were observed in early clinical outcome. IL-6 levels increased in every group during and after cardiac surgery while TNF-a values increased only in the standard system group (p=0.05). E-selectin systemic values decreased during and after operation (p=0.001) in every group. MCP-1 systemic and cardiac levels raised only in the standard system group (p=0.014) after aortic clamp removal.

Conclusions: The miniaturized extracorporeal circulation is comparable to the standard extracorporeal circulation and the off-pump technique in the clinical outcome of low-risk patients and it might be extensively used with no additional intraoperative risk. The analysis of the inflammatory patterns of endothelial activation shows the miniaturized extracorporeal circulation as effective as the off-pump technique, suggesting further studies to clarify miniaturized extracorporeal circulation recommendation in high-risk patients.

No conflict of interest

PREVENTION OF POSTOPERATIVE AF AFTER OPCAB BY TEMPORARY RIGHT ATRIAL PACING WITH CONCOMITANT INTRAVENOUS LANDIOLOL

M. Fujii[1], M. Kambe[1], D. Nishina[1], R. Bessho[1], M. Ochi[1]
[1]Cardiovascular Surgery, Nippon Medical School, Tokyo, Japan

Background and Aims: Atrial fibrillation (AF) is the most common arrhythmia after coronary artery bypass surgery, even though off-pump procedure (OPCAB). Prophylactic β-blocker administration and atrial pacing have been reported to be effective for the prevention of AF after cardiac surgery. The purpose of this study was to evamine the efficacy of intravenous landiolol, an ultra-short acting β-blocker, with/without right atrial pacing (RAP) in the prevention of AF during ICU stay after OPCAB. Methods: We retrospectively compared 24 consecutive patients who have received intravenous landiolol infusion 2-10 μg/kg/minute (γ) to 28 consecutive patients who have received intravenous landiolol infusion 2-10 γ and temporary right atrial overdrive pacing for approximately 60 hours starting immediately after OPCAB. AAI pacing with a pacing rate of 10 beats/minute above the baseline heart rate was used. Patients had continuous ECG-monitoring. The primary end point was the first episode of AF. Results: The incidence of postoperative AF in the intravenous landiolol with/without RAP groups did not differ from each other (17.9 % vs.12.5% respectively, p=0.71). The dose of landilol in the patients with RAP significantly lowered compared to those without RAP (4.0 γ vs. 6.4 γ respectively, p=0.0002). Intravenous landilol infusion have never interrupted in the both groups because of hypotension or bradycardia. Conclusion: RAP did not have an additive effect on landiolol to prevent the incidence of postoperative AF. However, RAP was able to reduce the dose of landiolol and decrease the cost.

No conflict of interest

SUCCESSFUL SURGICAL REMOVAL OF AN ENTRAPPED INTRAVASCULAR ULTRASONOGRAPHY CATHETER IN THE LEFT CIRCUMFLEX CORONARY ARTERY

M. Hamamoto[1], K. Morifuji[1]
[1]Onomichi General Hospital, Hiroshima, Japan

Entrapment of an intravascular ultrasonography (IVUS) catheter is an infrequentbut serious complication associated with percutaneous coronary intervention(PCI). A 67-year-old man who presented with exertion-alchest pain had an angiographic finding of 99% stenosis of left circumflexcoronary artery. PCI with stent implantation was performed successfully with anassessment by IVUS showing adequate stent expansion and apposition. When theIVUS catheter was retracted, it became trapped at the stent strut. The stentwas deformed and the IVUS catheter became stuck there. Ventricular fibrillationsuddenly occurred with deterioration of the coronary flow. He was transferredto the operating room just after insertion of intra-aortic balloon pumping. TheIVUS catheter, the guidewire, and the deformed stent were all removed undercardiopulmonary bypass. Coronary artery bypass graft with a saphenous vein wasalso performed at the more distal segment from the entrapment site. Thepostoperative course was uneventful with no graft occlusion. Incases in which interventional retrieval is difficult, surgical removalincluding CABG is feasible under cardiopulmonary bypass.

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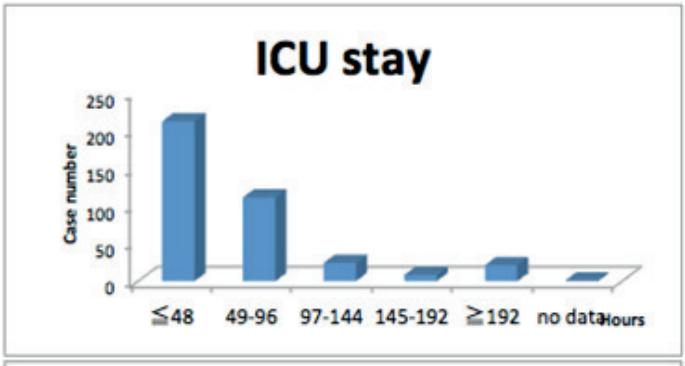
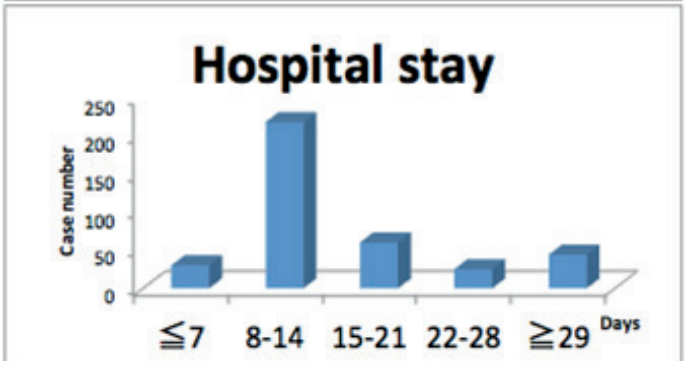
STERNUM-SPARING CORONARY ARTERY BYPASS SURGERY: SINGLE CENTER 10-YEAR EXPERIENCE

J.H. Huang[1], K.M. Chiu[1], J.S. Chen[1], S.H. Chu[1]
[1]Cardiovascular center, Far Eastern Memorial Hospital & Oriental Institute of Technology, New Taipei City, Taiwan

Background: Convential coronary artery bypass grafting (CABG) carries a substantial risk of morbidity. The most fearful complications include cerebrovascular accident and mediastinitis. Many patients also have psychological barries regarding the 'big wound' of sternotomy, thus delaying or neglecting the often necessary treatment. Sternum-sparing CABG is a ideal solution, providing with direct vision good revascularization and low morbidity.
Methods: Retrospective review of the medical charts were performed. The sternum-sparing CABG includes all the coronary bypass surgeries without a median sternotomy. The chest was most often entered through 5th intercostal space. The left internal mammary artery was harvested as the inflow artery via direct vision using specially-designed retractor, or under videoscope assistance using robotic system.
Results: In 2003~2012, we performed 2191 CABGs, of which 1892 cases being off-pump CABG (OPCAB, 86%). In the 1892 OPCAB group, 377 were sternum-sparing CABG cases (20%). Male predominant (M: F= 292:85). The mean number of anastomosis is 1.93. The ICU and hospital stay are shown in the figures.
Conclusion: Sternum-sparing CABG is a safe and reproducible technique combining the benefit of good revascularization and low morbidity. It provides great improvement in clinical outcomes regarding to wound infection rate, length of hospital stay, blood transfusion, and cosmesis.





No conflict of interest

ANOMALOUS ORIGIN OF THE LEFT CORONARY ARTERY: USEFULNESS OF MULTISLICE COMPUTED TOMOGRAPHY AND SURGICAL TECHNIQUE

Y. Ishii[1], K. Nakajima[1], K. Tanaka[1], M. Seki[1], S. Shimoyama[1], T. Kobayashi[1], A. Murakami[2], T. Miyamoto[2]
[1]Cardiology, Gunma Children's Medical Center, Gunma, Japan
[2]Cardiovascular Surgery, Gunma Children's Medical Center, Gunma, Japan

Background

Anomalous origin of a left coronary artery is a rare congenital heart anomaly that may cause congestive heart failure, myocardial ischemia and sudden death. Precise diagnosis and optimal surgical intervention are necessary. We present our experience with the diagnosis and surgical treatment of this rare coronary anomaly.

Method

Between April 2010 and March 2013, 5 consecutive patients were diagnosed with congenital anomalous origin of a left coronary artery.

Three patients had anomalous origin of the left coronary artery from the pulmonary artery (Bland-White-Garland syndrome) and 2 patients had anomalous left coronary artery arising from the wrong coronary sinus. The 2 younger patinets presented with cardiac dysfunction and 2 patients presented with exertional syncope and acute myocardial infarction. Another patient was diagnosed by catheterization for assessment of pulmonary hypertension. Contrastenhanced, 128-slice multidetector computed tomography was performed in 4 patients.

Results

All patients underwent surgical repair at a mean of 72.8±60.9 months. Three patients had coronary artery implantation with the spiral method, 1 patient unroofing procedure and 1 patient pericardial patch enlargement of the left coronary artery. Follow-up was 4 months to 3.2 years and there was no mortality. The postoperative coronary angiograms revealed the excellent patency without stenosis.

Conclusion

Multidetector computed tomography imaging is reliable for the diagnosis of these coronary anomalies. They are surgically correctable, though individual coronary anatomy may cause the surgical approach to vary. The postoperative outcome is excellent. Because of the risk of sudden death and cardiac dysfunction, aggressive surgical management and close follow-up are necessary.

No conflict of interest

CARDIAC ECHINOCOCCUS CASE REPORT

M.D. Hovaguimian H.[1]
[1]*Cardiac Surgery Intensive Care Unit, Nork Marash Medical Center, Yerevan, Armenia*

In May, 2011, a 24-year old man was admitted to our hospital for evaluation of palpitations and dyspnea over the past 2 weeks. Results of routine examination and laboratory studies were within normal limits. The ECG indicated sinus rhythm with isolated PVCs. Two-dimensional echocardiography showed a round, cyst like structure in the intraventricular septum with diameter of 5.8 x 4.6cm that bulged toward the LV outflow tract without obstruction. LVEF was measured as 50%. Cardiac CT confirmed the diagnosis and showed concomitant hepatic infestation (Figure 1). Excision of the cardiac cyst was planned by using cardiopulmonary bypass. The cyst was first aspirated and completely sterilized by injecting hypertonic saline solution. Cytology was consistent with the diagnosis of hydatid cyst. After sterilization cyst was enucleated and cavity was suture closed. A plasty was done on an intraventricular septum with autopericardial patch (Figure 2). After surgery ECG showed RBBB. Albendazol therapy was continued. Indirect hemagglutination test was positive and was repeated every 6 months after discharge. Six months later the patient underwent surgery for removal of hepatic cyst. Chemotherapy was stopped despite the positive test. The patient was free of any symptoms during 24 months.

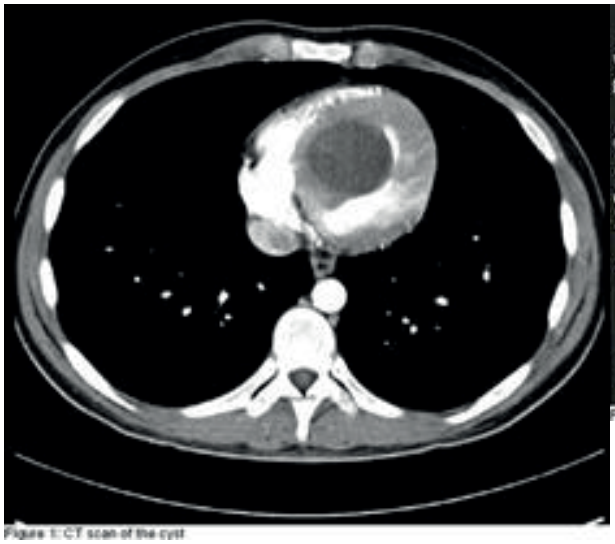


Figure 1: CT scan of the cyst

Figure 2: Echocardiographic imaging of the cyst

No conflict of interest

A PERIODIZED MODEL FOR EXERCISE IMPROVES THE INTRA-HOSPITAL EVOLUTION OF PATIENTS AFTER MYOCARDIAL REVASCULARIZATION: A PILOT RANDOMIZED CONTROLLED TRIAL

R. Macedo[1,5], J. Faria Neto[1], C. Ortiz Costantini[2], M. Olandoski[1], K. Carvalho[3], A. Macedo[4], A. Muller[5], C. Roberto Costantini[2], V. Amaral[1], L. Guarita Souza[1]

[1]Post Graduation in the Health Sciences, Pontifical Catholic University of Paraná, Curitiba, Brazil

[2]Hemodynamics, Costantini Cardiac Hospital, Curitiba, Brazil

[3]Post Graduation Department, Little Prince Institute, Curitiba, Brazil

[4]Rehabilitation, Costantini Cardiac Hospital, Curitiba, Brazil

[5]Physical Therapy, Costantini Cardiac Hospital, Curitiba, Brazil

Objective: To compare models of the postoperative hospital treatment phase after myocardial revascularization. **Design:** A pilot randomized controlled trial. **Setting:** Hospital patients in a hospital setting. **Subjects:** Thirty-two patients with indications for myocardial revascularization were included between January 2008 and December 2009, with a left ventricular ejection fraction (LVEF) ≥50%, 1-second forced expiratory volume (FEV1) ≥60 and forced vital capacity (FVC) ≥ 60% of predicted value. **Interventions:** Patients were randomly placed into two groups: one performed prescribed exercises according to the model proposed by the American College of Sports Medicine (ACSM) and the other according to a periodized model. **Main measures:** Partial pressure of O2 (*P*o2) and arterial O2 saturation (*S*ao2), percentage of predicted FVC and total distance on the six-minute walking test (6MWT). **Results:** Twenty-seven patients were re-evaluated upon release from the hospital . In the preoperative period the variables *P*o2, *S*ao2, % FVC and 6MWT were similar. In the postoperative period, a reduction was observed for all parameters in both groups. Upon comparison of the groups, a difference was observed in *P*o2 (ACSM = 68.0 ± 4.3 vs. PP = 75.9 ± 4.8 mmHg; $P < 0.001$), Sao2 (ACSM = 93.5 ± 1.4 vs. PP = 94.8 ± 1.2%; $P = 0.018$) and 6MWT (ACSM = 339.3 ± 41.7 vs. PP = 393.8 ± 25.7 m; $P < 0.001$). There was no difference in % FVC. **Conclusion:**Patients after myocardial revascularization following a periodized model of exercise presented a better intra-hospital evolution when compared to those using the ACSM model.

No conflict of interest

THE RISK FACTORS CONTRIBUTING TO HOSPITAL INFECTIONS AFTER CORONARY SURGERY

B. Mihajlovic[1], N. Cemerlic-Adjic[2], K. Pavlovic[2], B.B. Mihajlovic[2], S. Nicin[1], L.J. Markovic Denic[3], M. Fabri[1]
[1]Cardiovascular surgery, Institute of cardiovascular diseases Vojvodina, NOVI SAD, Serbia
[2]Cardiology, Institute of cardiovascular diseases Vojvodina, NOVI SAD, Serbia
[3]Epidemiology, Institute of epidemiology Medical faculty Belgrade, Belgrade, Serbia

Background: Hospital infections after coronary surgery are associated with higher morbidity and are one of the leading cause of postoperative mortality. The increased hospital length of stay, large use of antimicrobial drugs, and the need for isolation significantly contribute to higher costs, as well. The aim of the study: to identify the independent risk factors for hospital infections following coronary surgery.

Methods: This prospective study included 664 consecutive patients who had undergone isolated coronary surgery from January 2012. to December 2012. at our Clinic. In order to detect the possible risk factors, the 58 variables (20 patients-related factors, 16 cardiac-related factors, 16 operation-related factors, and 6 intensive care unit stay-related factors), were analyzed. In all cases the diagnosis of infection was clinically and/or microbiologicaly confirmed.For statistical analysis univariate and multivariate binary logistic regression were used.

Results**:** Hospital infection occured in 2.8% (19/664).Surgical site infection, pneumonia, bloodstream infection, and enterocolitis were registered in 9, 5, 4, and 1 patient respectively. Postoperative mortality for the whole group was 2.1%. In group of patients without hospital infecion PM was 1.4% (9/636) vs. 26.3% (5/19) in group of patients with hospital infection ($p < 0.0005$). Multivariate logistic regression showed the only independent risk factors significantly contributing to development of hospital infection was ejection fraction ($p = 0.001$; Odds ratio 0.939 (0.903 - 0.975)).

Conclusions: In order to prevent hospital infections after isolated coronary surgery special attention has to be paid to the patients with low ejection fraction.

No conflict of interest

DIRECT SUPERIOR MESENTERIC ARTERY FENESTRATION FOR TYPE B DISSECTION WITH VISCERAL ISCHEMIA

Y. Saitoh[1], H. Ohmori[2], Y. Satoh[2], Y. Hari[3], H. Harada[1], T. Nakahara[1], T. Soeda[1]
[1]Cardiovascular Surgery, Matsue Red Cross Hospital, Matsue, Japan
[2]Surgery, Matsue Red Cross Hospital, Matsue, Japan
[3]Digestive and General Surgery, Shimane University Faculty of Medicine, Izumo, Japan

Objective: Visceral ischemia is a life-threatening complication of acute type B aortic dissection. However, the optimal operative approach is still being disputed. In these situations, there have been few reports on direct mesenteric artery (SMA) fenestration to maintain the visceral blood supply against malperfusion due to the acute aortic dissection.
Methods: A 68-year-old man was admitted with acute type B aortic dissection, which was dissected from the distal aortic arch to the terminal aorta, with both SMA and right renal artery dissections. Immediately, anti-hypertensive medical treatment was started. At 11 days after the onset, CT scan showed a superior mesenteric artery obstruction. We fenestrated and connected the true lumen with the false lumen of the superior mesenteric artery, and performed a thrombectomy for both lumens. Immediately, a bowel resection was performed and transverse-colostomy was created.
Results: Postoperative magnetic resonance imaging revealed a patent SMA, and another visceral branch. The transverse-colostomy was closed at 3 months after the operation. He was discharged after recovery.

Conclusions: The direct SMA fenestration and thrombectomy performed in this case maintained the visceral blood supply against malperfusion due to acute aortic dissection. This procedure is easier than surgical abdominal aorta fenestration, aortic graft replacement or SMA bypass grafting, because this procedure is performed entirely by exposure of the abdominal aortic branch, without any manipulation of the aorta. This is a very useful option if the patient is in poor general condition with multi organ failure due to type B aortic dissection complicated by severe visceral ischemia.

No conflict of interest

RUPTURED GIANT GRAFT ANEURYSM IN SAPHENOUS VEIN AFTER AORTOCORONARY BYPASS GRAFTING

T. Satsu[1], T. Saga[2], M. Onoe[3]
[1]Department of Cardiovascular Surgery, Kinki University school of Medicine, Osaka-sayama, Japan
[2]Department of Cardiovascular Surgery, Kinki University school of Medicine, Osaka-sayama, Japan
[3]Department of Cardiovascular Surgery, Kishiwada City Hospital, Kishiwada City, Japan

Aneurisms of saphenous vein grafts are rare but potentially fatal complications after coronary artery bypass grafting. We describe a giant saphenous vein graft aneurysm that compressed right atrium, resulting in right heart failure.
Computed tomography demonstrated a giant saphenous vein graft aneurysm with a maximal diameter of about 40?60 mm that compressed the right atrium of a 72-year-old woman 20 years after undergoing coronary artery bypass grafting on the right coronary, left anterior descending and left circumflex arteries. Angiography of the bypass grafts revealed contrast medium leakage in the mid portion of this graft aneurysm to right coronary artery. Aneurysmectomy was performed without re-grafting.
Postoperative myocardial scintigraphy demonstrated the absence of significant myocardial ischemia.
The ischemic effect of non-revascularization should be pre-operatively considered due to difficulties with re-grafting.

No conflict of interest

POSTOPERATIVE DIAPHRAGMATIC HERNIA AFTER RIGHT GASTROEPIPLOIC ARTERY CORONARY ARTERY BYPASS SURGERY

Y. Shimamura[1], K. Maisawa[1], N. Okamoto[2], K. Yamafuji[2]
[1]Cardiovascular Surgery, Saitama City Hospital, Saitama, Japan
[2]Surgery, Saitama City Hospital, Saitama, Japan

Diaphragmatic hernia following coronary artery bypass surgery with the right gastroepiploic artery is a rare but potentially fatal complication. A review of the literature was performed using MEDLINE, and the clinical manifestations, diagnosis, and treatment were investigated retrospectively. Diaphragmatic hernia was reported in 12 patients (11 men, mean age 58 years), occurring from 1 week to 9 years after coronary artery bypass surgery. The right gastroepiploic artery was routed posteriorly (retrohepatically) or anteriorly (antehepatically), and either route resulted in diaphragmatic hernia through the right gastroepiploic artery orifice. All reported posterior route hernias extended into the pleural cavity, and 4 of the 5 anterior route hernias extended into the pericardial cavity. Herniated viscera involved the stomach, small bowel, liver, or omentum, and stomach herniation was most common. Mechanical obstruction of the incarcerated bowel by the diaphragmatic incision caused various abdominal symptoms (e.g., pain, nausea, and vomiting). Intrathoracic hernia manifested with respiratory symptoms. Multi-slice computed tomography scanning with coronal and sagittal reformatted images provided excellent anatomical details of the hernia contents and resulting complications. Eleven patients were symptomatic with acute onset, all of whom were rescued with emergent surgery including direct closure of the diaphragm, patch plasty, and gastropexy. Careful operative management of the right gastroepiploic artery during initial coronary surgery and a high degree of suspicion of this complication contribute to early diagnosis, accurate treatment, and prevention of potentially fatal complications.

No conflict of interest

SILENT ISCHEMIC HEART DISEASE WITH ABDOMINAL AORTIC ANEURYSM

Y. Takahara[1], K. Mogi[1], M. Sakurai[1], K. Matsuura[1], N. Ogasawara[1], Y. Yakita[1]
[1]Cardiovascular Surgery, Funabashi Municipal medical Center, Funabashi, Japan

Purpose: Patients suffering from abdominal aortic aneurysm (AAA) are often associated with ischemic heart disease (IHD). We evaluated concomitant IHD by coronary angiogram, MDCT or myocardial scintigram preoperatively, and analyzed the outcome of patients with silent IHD, symptomatic IHD and without IHD comparatively.

Methods: From April 2007 to March 2013, 233 consecutive patients underwent scheduled operation for AAA in our hospital. Patients who were diagnosed with AAA of more than 5cm in diameter and IHD with an indication of coronary artery revascularization underwent simultaneous CABG and grafting, or endovascular abdominal aortic repair (EVAR) and staged PCI. Patients with AAA of less than 5cm in diameter underwent primary PCI or CABG, and staged grafting or EVAR.

Result: There were 52 patients with the silent IHD group, 58 patients with the symptomatic IHD group and 123 patients the without IHD group. There were one hospital death in the symptomatic group and one hospital death in the without IHD group. Freedoms from coronary events at 60 months after the operation were 93.9 +/- 3.4%, 66.4 +/- 13.5% and 93.4 +/- 4.7% in the silent group, the symptomatic group and the without IHD group. There was significant difference between the symptomatic group and the without IHD group ($p = 0.0375$). Survival rates and freedom from aortic event were not significant difference among the tree groups.

Conclusion: The rate of patients with silent IHD was 22.3%, preoperatively. There was no significant difference between the silent IHD group and the without IHD group concerning freedom from coronary event 5 years postoperatively.

No conflict of interest

FULL-METAL JACKET : A BAD STRATEGY

J. Jose Rubio Alvarez[1], J. Sierra Quiroga[1], L. Reija Lopez[1], A. Granda[1], J.M. Martinez Cereijo[1], C. Rubio Taboada[2]
[1]Cardiac Surgery, Universitary Hospital Santiago de Compostela, Santiago de Compostela, Spain
[2]Vascular Surgery, Universitary Hospital Elche, Elche, Spain

Multiple overlapping drug-eluting stents have increasingly been used to treat coronary disease, but the safety and efficacy of this approach remains unclear. An increasing number of patients are being referred for coronary artery bypass grafting after previous percutaneous coronary interventions.

We report a complete metal jacket case using 17 stents for a triple vessel coronary disease in a 74-year-old man with a history of diabetes, and hypertension. He was admitted with unstable angina on June 2011 and a coronary angiography revealed a severe and proximal lesions of left anterior descending artery, circunflex, right coronary artery and obtuse marginal. From first June 2011 and August 24, 17 stents were implanted. On January 2012 he was admitted with unstable angina and after a failed attempt at angioplasty, he was referred for urgent surgery but the patient died before it. The last coronary angiography showed a full-metal anatomy of the coronary tree.

In our opinion,this case may have significant teaching for clinical practice, suggesting that greater emphasis should be placed on selecting
the optimum initial revascularization strategy.

No conflict of interest

A SUCCESSFUL TREATMENT FOR A LESION OF CHRONIC TOTAL OCCLUSION USING A VIRTUAL 3 FR GUIDING CATHETER

R. Nakamura[1], K. Ota[1], N. Miyai[1], T. Sawanishi[1], N. Kinoshita[1], K. Matsumoto[1]
[1]Cardiovascular center, Kouseikai Takeda Hospital, Kyoto, Japan

A 56-year-old man was admitted due to effort related chest squeezing for 6 months. Coronary angiogram showed a total occlusion of the proximal right coronary artery (RCA) with collateral vessels from left anterior descending artery. PCI was performed via radial artery using 5-Fr sheathless guiding catheter. The 3F JL3.5 was inserted into left coronary artery via left radial artery for simultaneous contra lateral angiography. We considered the presence of microchannel because of the tapering shape of proximal occluded stump, and tried to pass through the lesion using Wizard 78 under Corsair. In spite of careful manipulation, the wire was advanced to subintimal space just beside the distal lumen. HT Progress 40T wire was advance along with the former wire. The latter wire was advanced to the distal of the RCA through the occluded lesion. A 1.2 mm diameter, 6 mm long Lifespear balloon easily passed the lesion and dilated from the distal through proximal lesion. The balloon was changed to a 2.0mm diameter, 15mm long Lacrosse balloon and inflated throughout the diseased lesion to 14atm. The IVUS imaging revealed diffuse plaque from the distal through proximal lesion. Three 2.5 mm × 28 mm XIENCE stents was inserted from distal to mid RCA, and a 3.0 mm × 15 mm XIENCE stent was inserted to proximal RCA. The final angiographic result showed well expanded stent. CTO treatment could be possible even slender device by getting hold of the characteristics of the device and evaluating an objective assesment of lesion characteristics.

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SUCCESSFUL PERCUTANEOUS CORONARY INTERVENTION OF AN ANOMALOUS RIGHT CORONARY ARTERY WITH HIGH ANTERIOR TAKEOFF USING A DIO THROMBUS ASPIRATION CATHETER

T. Komatsu[1], A. Kudoh[1], N. Tsukada[1], T. Kuroyanagi[1], A. Fujikake[1], T. Yufu[1], S. Komatsu[1], F. Ozaki[1], I. Yaguchi[1], Y. Sakai[1]
[1]Department of Cardiology, Dokkyo Medical University Koshigaya Hospital, Koshigaya, Japan

A 70-year-old man was diagnosed angina pectoris and underwent coronary artery angiography via the right radial approach. Selective cannulation of the RCA could not be achieved with Judkin's right catheter. Nonselective injection into the ascending aorta revealed the aberrant high anterior takeoff of the RCA from the aorta and revealed stenosis at the RCA. We inserted a 4Fr multipurpose angiographic catheter into a DIO thrombus aspiration catheter to deliver it to the ascending aorta. DIO was functionally-stabilized to find the RCA ostium by manipulating the angiographic catheter. When the angiographic catheter successfully engaged the RCA ostium, we glided the DIO forward and pulled out the angiographic catheter to perform angiography. RCA injection clearly revealed 90% stenosis with calcification. After that, we performed PCI of the RCA.
Selecting an appropriate guiding catheter is the most important determinant of procedural PCI success. Especially, an anomalous RCA with high anterior takeoff is rather complicated. We present a case of successful stent implantation in an anomalous right coronary artery with high anterior takeoff using DIO. This method is useful when selection of the guiding catheter is rather complicated such as in the case of congenital coronary anomalies.

No conflict of interest

LAD CTO VIA SEPTAL BRANCH WITH ONE CATHETER

N. Miyai[1], K. Oota[1], K. Isoda[1], R. Nakamura[1], T. Sawanishi[1], N. Kinoshita[1], K. Matsumoto[1]
[1]Cardiology, Kouseikai Takeda Hospital, Kyoto, Japan

The case is a 56-year-old Japanese male with no symptom. His coronary risk factor was diabetes melittus, hyperlipidemia, and hypertension.

He underwent a treadmill exercise stress test on Bruce protocol as a periodic medical examination. Treadmill exercise stress test demonstrated 1 mm ST depression in II, III, aVF, V4, V5 and V6 leads on electrocardiogram. He was suspicious of ischemic coronary artery disease and admitted to hospital. Coronary angiography revealed moderate stenosis of mid-portion of the right coronary artery and total occlusion of mid-portion of the left ascending coronary artery (LAD). Angiogram showed the disatal of the LAD was filled by rentrop grade 3 collaterals. A proximal septal branch just before the CTO was connected to the distal septal branch. The diagnostic image showed the form of the blockage of the central stump is an abrupt type.

Target lesion was total occlusion of mid-portion of LAD. The coronary system was cannulated using the 8 Fr VL3.5 guiding catheter with a side hole by right femoral artery approach. Firstly, an antegrade approach was conducted. The proximal edge of the CTO was just before the first diagnol branch where it was confirmed by intravascular ultrasound. Initial wire system was the XTR with the corsair catheter. The wire did not reach the distal true lumen. If the false lumen was expanding, we considered apprehensive about the disappear of the second diagnol branch. At this point, wiring by the antegrade approach was abandoned and treatment was shifted to that from the retrograde approach. The filder FC wire with the corsair catheter was used for the septal-septal channel selection. The wire was advanced into the septal branch, passed the connection, and preceded to the distal septal branch retrogradely. However, the corsair catheter was not advanced into the connection because of the sharp angle. So, the retrograde wire was not advanced into the distal cap of the CTO lesion, and we could not change the retrograde wire. We tried to change the antegrade wire from the XTR to the gaia first wire. The gaia first wire with the corsair catheter was advanced into the second diagnol branch by kissing wire technique. The ultimate bros 3g with crusade catheter was advanced into the distal site of LAD. We performed IVUS study and deployed a 2.5x30mm Resolute integrity stent at the mid-portion of LAD. After deploying stent, we tried to perform IVUS. IVUS showed the deformation of the proximal of the stent. So, we expanded the stent with a 3.0mm non-compliant balloon and the final angiogram showed TIMI 3 grade flow.

No conflict of interest

THREE CASES OF SUB-ACUTE STENT THROMBOSIS AFTER THREE DIFFERENT TYPES OF DRUG-ELUTING STENTS IMPLANT TO ANGINA PECTORIS.

S. Ito[1], H. Suesada[1], N. Katayama[1], T. Amemiya[1], M. Hashimoto[1]
[1]Cardiology, Nishitokyo central general hospital, tokyo, Japan

In the era of the drug-eluting stent, sub-acute stent thrombosis(SAT) has been a very serious issue in the percutaneous coronary intervention (PCI). First case of angina pectoris(AP): a biolimusA9-eluting stent (BES) was implanted for the mid-stenotic left anterior descending artery (LAD) and a BES was deployed for the mid-stenotic lesion in the left circumflex artery (LCX). Second case of AP: a zotatolimus-eluting stent (ZES) was implanted for the proximal-stenotic LAD. After PCI, anemia, hives and liver dysfunction occurred as the side effects due to clopidogrel. We changed anti-platelet medicine, clopidogrel, to cilostazol. After that, the side effects disappeared. Within 30 days after PCI, they complained of a chest pain and we diagnosed it as an acute myocardial infarction (AMI). Emergent CAG revealed total thrombotic occlusion in-stent sites: in BESs of LAD and LCX, and ZES of LAD. They underwent intracoronary aspiration thrombectomy and additional stents were implanted the thrombotic lesions. Third case of AP, sirolimus-eluting stent (SES) was implanted for the distal-stensotic LCX. 17 days after PCI, he was admitted to our hospital because of AMI. Emergent CAG revealed a thrombotic occlusive lesion in the stent site of LCX. Intravascular ultrasound findings of stent thrombosis before PCI are related to an incomplete stent apposition and positive vessel remodeling. Then we deployed a bare-metal stent in the thrombotic occlusion stent after balloon angioplasty. In these cases, we suggest that giving the clopidgrel and keeping the complete stent apposition are necessary to prevent SAT.

No conflict of interest

A CASE WITH NEWLY ONSET EFFORT ANGINA AFTER EVT WHO WAS TREATED WITH PCI BY IMPLANTATION OF DRUG ELUTING STENTS

K. Saito[1], K. Jujo[1], K. Arai[1], I. Ishida[1], A. Kim[1], Y. Suzuki[1]
[1]Department of Cardiology, Nishiarai Heart Center Hospital, Tokyo, Japan

A case was 83 years old woman who complained of intermittent claudication in the left leg. Angiogram revealed chronic total occlusion in the external iliac artery (EIA) and multiple 90% stenoses in the left anterior descending artery (LAD) and the first major septal branch (SB). As intermittent claudication was refractory against medical treatment, percutaneous endovascular treatment was performed. Finally, a SMART Control vascular stent was implanted and successful result was achieved. Immediately after successful revascularization of the left EIA with EVT, however, the patient had been suffered from angina pain on slight effort. Because it was obvious that improvement in exercise capacity after EVT caused effort angina pectoris, percutaneous coronary intervention (PCI) treatment for the stenotic lesions in the coronary arteries was operated. Three drug eluting stents were implanted at two lesions in the LAD and at one lesion in the dominant first SB. After the PCI procedure, anginal symptom has disappeared completely. Follow-up angiogram was performed 8 months after PCI, all the lesions in the left EIA and the coronary arteries where stents were implanted kept good patency.

No conflict of interest

MANAGEMENT OF DIASTOLIC HEART FAILURE IN THE POST OP HEART

A.A. Alsaddique[1], C.F. Royse[2], M.A. Fouda[1], A.G. Royse[3]
[1]Dept of Cardiac Sciences, King Fahad Cardiac Center King Saud University, Riyadh, Saudi Arabia
[2]Dept of Pharmacology, University of Melbourne, Melbourne, Australia
[3]Cardiac Surgery, University of Melbourne, Melbourne, Australia

MANAGEMENT OF DIASTOLIC HEART FAILURE IN THE POST OPERATIVE HEART

It has been established that diastolic heart failure is just as common as the systolic failure. Notwithstanding, in assessing risk cardiac surgeons in general look at the ejection fraction which reflects the systolic function of the left ventricle. There is mounting evidence that diastolic dysfunction can lead to acute diastolic heart failure. Because of the nearly identical clinical features it is important to make the distinction between diastolic or systolic heart failure. We are half way in a joint prospective study to look into DHF in the post op heart.
In this meeting we would like to shed light on the management of this interesting condition because it is diametrically different from management of systolic cardiac failure in spite of the similar presentations.

The points that stand out in the management of diastolic heart failure

1- Careful use of diuretics in diastolic heart failure
2- Ionotropes are to avoided in pure diastoic heart failure
3- One can anticipate this kind of failure and can with proper planning prevent it
4- Vasodilators have a greater role
5- Better outcome than systolic failure in the post op setting

No conflict of interest

CLINICAL IMPLICATION OF RIGHT VENTRICULAR STROKE WORK INDEX IN PATIENTS WITH ADVANCED HEART FAILURE

E. Özenc[1], N. Arat[1], O. Yildiz[2], O. Demirozu[1], C. Cavlan[1], N. Yazicioglu[2]
[1]Cardiology, Medical School of Istanbul Bilim University, Istanbul, Turkey
[2]Cardiology, Sisli Florence Nightingale Hospital, Istanbul, Turkey

OBJECTIVE: We aimed to investigate the relation of right ventricular stroke work index (RV SWI), an invasive hemodynamic parameter of right ventricle (RV) with prognosis and cardiac events in patients with advanced heart failure (HF).
METHODS: The 132 patients admitted to heart failure clinic between April 2011 to November 2012 with diagnosis of advanced HF, (M/F=104/28, age 24-81 years) were retrospectively reviewed. The files of patients were searched retrospectively and patients called by phone for ascertain of prognosis. All patients' medical history, demographic characteristics, cardiovascular risk factors, comorbid illnesses, NYHA functional class, echocardiographic evaluations and basal right heart catheterizations performed were detected. The relation of RV SWI values with ventricular assist device insertion, heart transplantation, cardiac resyncronisation therapy, rehospitalisation due to decompansation composite end-points and with mortality were evaluated.
RESULTS: During 20 months follow-up, total mortality was observed in 18(13.6%) patients. 34 of 132 patients needed to rehospitalization due to cardiac decompansation (CD). In the patients with CD, RV SWI 6.1 ± 2.5 gr/m2/beat and 8.5 ± 3.4 gr/m2/beat in the group without CD. The relation between RV SWI and mortality did not reach statistical significance (p=0.773). In patients who died, mean RV SWI value was 7.5±3.4 g/m2/beat, those who survived had RV SWI mean value 8.0±3.4 gr/m2/beat. The left ventricular EF (p<0.001) and RV systolic diameter (p<0.001) had statistically significant relation with mortality. In patients who survived without cardiac events RV SWI value was significantly different from those who survived with cardiac events (p=0.003).
CONCLUSION: RV SWI is a predictor of event free survival among patients with advanced stage HF. Our study did not support RV SWI as single parameter of predictor of mortality. Risk models should consist of invasive, non-invasive and clinical parameters for prediction of all-cause mortality in advanced stage HF.

No conflict of interest

THE PERCEPTIONS OF PATIENT, CARERS AND HEALTHCARE PROFESSIONALS REGARDING THE TRANSITION TO PALLIATIVE CARE IN ADVANCED HEART FAILURE

A. Gadoud[1], U. Macleod[1], M.J. Johnson[1]
[1]Hull York Medical School, University of Hull, Hull, United Kingdom

Background: Palliative care is recognised as important for patients with advanced heart failure but has not been widely introduced. The view of patients, carers and healthcare professionals where palliative care has been implemented has not been researched.

Aim: To explore how barriers to palliative care were overcome, what difficulties remain and the effect of palliative care.

Methods: Semi-structured interviews with patients recognised as having a palliative approach to care, their nominated carers and healthcare professionals. Framework analysis was used to identify themes.

Findings: 19 patient interviews (9 joint with spouse) and 3 separate carer and 18 healthcare professional interviews. The main themes were initiating communication about palliative care and poor prognosis, managing uncertainty and patient factors such as symptoms and coping.

Healthcare professionals were reluctant to initiate conversations and decisions about a change in a focus of care especially if uncertainty if the patient was irreversibly deteriorating. Patients welcomed these discussions and some had initiated them. Once the decision had been made and communicated, all three groups were in agreement with this approach to care and found it beneficial, even if the patient went on to have periods of stability or improvement. Patients were concerned about symptoms and showed various mechanisms for coping with their illness.

Conclusions: Clinicians' fears about initiation of difficult conversations were unfounded in this group**.** The approach to care was felt to be beneficial even in those who stabilised or improved. Uncertainty should not prevent exploration of patients' wishes about the focus of their care.

No conflict of interest

PLASMA ADIPONECTIN LOWERING AFTER LEFT VENTRICULAR ASSIST DEVICE IMPLANTATION IS ASSOCIATED WITH 1-MONTH SURVIVAL IN PATIENTS WITH ADVANCED HEART FAILURE.

A. D'Amico[1], R. Caruso[2], M. Cabiati[1], T. Prescimone[1], A. Verde[2], S. Del Ry[1], M.G. Trivella[1], D. Giannessi[1], C. Caselli[1]
[1]CNR, Institute of Clinical Physiology Pisa, Pisa, Italy
[2]CNR, Institute of Clinical Physiology Pisa, Milano, Italy

Purpose. In advanced heart failure (HF), high circulating levels of adiponectin, an adipokine known to mediate metabolic and anti-inflammatory effects in the heart, are associated to a negative outcome. We aim at investigating the effect of hemodynamic correction, through implantation of left ventricular assist devices (LVAD), on circulating adiponectin in order to evaluate adiponectin as a possible prognostic biomarker useful in clinical setting.

Methods. Total adiponectin was measured by a dedicated ELISA in blood samples obtained from 26 end-stage HF patients (NYHA class III/IV; LVEF%<25) before (day 0) and at 4 h, 1, 3, 7, 14, and 30 days after LVAD implant; 20 patients survived up to 1 month after LVAD (S) and 7 died of multi-organ failure between days 7 and 1 month (NS).

Results. At pre-implant, no difference was observed in plasma adiponectin between NS and S groups. At 4 h, S showed a significantly greater decreasing than NS [36% (23%-50%) vs. 24% (1%-28%), S vs. NS, median (25°-75° percentiles), $p<0.05$]. In S, plasma adiponectin was significantly lower until 7 days after LVAD implant than at pre-implant (day 0: 19.9 (7.6-29.5); 4 h: 11.6 (4.7-17.9); day 1: 8.8(5.7-16.3); day 3: 8.0 (6.3-16.2); day 7: 12.2 (6.7-18.1); $p<0.001$ day 0 vs. 4 h and day 1, $p<0.05$ day 0 vs. day 3 and 7), while no time-course modulation was observed in NS.

Conclusion. In patients with advanced HF, mechanical unloading of the failing myocardium by LVAD implant led to a decreasing of adiponectin plasma levels mainly in S patients. This decreasing soon after LVAD implant could be involved in patients survival, suggesting that early monitoring of adiponectin may be a valuable tool for outcome prediction in LVAD recipients.

No conflict of interest

ANALYSIS OF THE CORRELATION AMONG BNP h-CRP and LVEF IN PATIENTS WITH AMI

J.Y.-X.J. Yan-xia[1], D. Wen-jie[1], L. Zhen-fang[1], W. Juan[1]
[1]The Affiliated Hospital of Medical College Qingdao University, QingDao, China

"Abstract：Objective To investigate the correlation and clinical value among BNP ，hs-CRP and LVEF in patients with acute myocardial infarction（AMI）. Methods 50 patients with AMI who prepared for elective percutaneous coronary intervention（PCI）were retrospected and analyzed，measure the level of BNP and hs-CRP with ELISA and automatic biochemical analyzer at first visit and hospital the next day separately，echocardiograph was done in survivors after 1 week，30 patients hospital the same period were compared as a control group.Results （1）The level of BNP and hs-CRP with AMI is higher than that of control group significantly （493.59±40.12 vs 112.10±29.00，$P < 0.01$；36.39±7.33 vs 12.2±5.7，$P < 0.01$ ），it was a positive correlation between them （$r = 0.621$，$P < 0.01$），however，left ventricular ejection fraction （LVEF） after 1 week of 43 survivors is lower than that of control group significantly （43.3±7.3 vs 67.2±6.6，$P < 0.01$），and it was a negative correlation among LVEF after 1 week and the level of BNP and hs-CRP separately （$r = -0.565$，$P < 0.01$；$r = -0.533$，$P < 0.01$）.（2） The level of BNP and hs-CRP of dead patients is higher than that of survivors separately （1177.87±133.94 vs 382.19±116.32 ，$P < 0.01$；85.57±29.67 vs 28.39±18.76 ，$P < 0.01$）.Conclusion Plasma BNP，hs-CRP levels were correlated with prognosis significantly，they can be used for risk stratification and prognosis of AMI."

Document not received

NONSIGNIFICANT DIFFERENCE IN SEGMENTAL LEFT VENTRICULAR DYSFUNCION BETWEEN TRIPLE 50% AND A SINGLE 75% STENOSIS OF THE SAME CORONARY ARTERY

R. Kakihara[1], *C. Naruse*[1], *Y. Moutai*[1]
[1]*Department of Cardiology, Private Kakihara Clinic, Toyohashi, Japan*

[Purpose] We have stressed the importance of a single 50% coronary artery stenosis (CAS) on segmental left ventricular wall (SLVW) dysfunctions. This study analyzed the influences of multiple 50% CASs of the same coronary artery (CA) on SLVW functions.

[Method] 112 patients (pts) with a single and multiple 50% CAS (69pts ×1, 52pts ×2, 34pts ×3) and 44 pts with 44 CAs of a single 75% CAS were employed. SLVW functions were estimated by echocardiographical strain rate (SR). Systolic function was evaluated by Z variable: Z = 4.91+ 1.02×(100-ms SR value)+1.23×(200-ms SR value)–0.46×(minimum SR value)+4.83× (mean SR value). Diastolic function was evaluated by E/E variable: E/E = peak E/E time %/sec^2 (E time: time from aortic valve closure to peak E).

[Results] The Z values were : 50%×1 = - 0.02±1.60, 50%×2 = 0.78±1.26, 50%×3 = 1.55±0.47 and 75%×1 = 1.81±0.62. There were significant differences in SLVW Z values between 50%×1, 50%×2 and 75%×1 ($p<0.0001$). No significant difference was observed between 50%×3 and 75%×1 ($p = 0.07$). The E/E values were : 50%×1 = 10.39±6.33, 50%×2 = 8.94±4.63, 50%×3 = 7.39±5.62 and 75%×1 = 7.09±3.64. There were significant differences in SLVW E/E values between 50%×1, 50%×2 and 75%×1 ($p<0.0001$). No significant difference was observed between 50%×3 and 75%×1 ($p = 0.99$).

[Conclusion] The results of this study indicate triple nonsignificant 50% CASs influences systolic and diastolic dysfunction of SLVW the same as a single significant 75% CAS.

No conflict of interest

ENDOTHELIN-1 LEVELS IN CHRONIC CONGESTIVE HEART FAILURE

M. ohmae[1]
[1]*internal medicine, kochi general rehabilitation hospital, kochi, Japan*

Abstract

Background: Endothelin-1 levels in patients with chronic congestive heart failure were evaluated with respect to the severity of cardiac dysfunction. The relationship between 3 neurohormones, brain natriuretic peptide (BNP), human atrial natriuretic peptide (HANP), and endothelin-1,was evaluated.

Methods: Forty patients (17 men and 23 women, aged 64-98 years) with chronic congestive heart failure were studied. Echocardiography was performed in each patient, and the left ventricular ejection fraction(EF) was calculated. Titers of HANP, BNP and endothelin-1 in the serum were measured. Exclusion criteria included acute myocardial infarction,unstable angina,and renal dysfunction (serum creatinine >1.6mg/dl). it is well known that endothelin-1 levels are increased in renal dysfunction. In this study, patients with renal dysfunction were excluded. **Results**: Endothelin-1 levels were correlated with HANP ($r = 0.675$, $p < 0.0001$) and BNP ($r = 0.616$, $p< 0.0001$)levels. Endothelin-1 levels were not correlated with the left ventricular ejection fraction or end-diastolic volume.BNP levels were correlated with the left ventricular ejection fraction ($r=0.315$, $p = 0.057$).

Conclusion: The findings indicate that endothelin-1 interacts with HANP and BNP in patients with chronic congestive heart failure. Endothelin-1 is suggested to play an important role in chronic congestive heart failure with preserved ejection fraction.This study indicates that it takes some time for endothelin-1 to stimulate HANP, and that HANP counters the actions of the former.

No conflict of interest

EXTRACORPOREAL LIFE SUPPORT: EXPERIENCE FROM A SINGLE CARDIAC SURGERY UNIT.

G. Olivo[1], S. Romagnoli[1], F. Pinelli[1], F. Ciappi[1], S. Bevilacqua[1]
[1]Cuore e vasi, Cardioanestesia, florence, Italy

Introduction: Extracorporeal life support (ECLS) is a system for mechanical cardio-circulatory (and pulmonary) assistance in patients with cardiogenic shock of different origins. The use of such a device, has gained wider application in clinical practice. The present study is aimed at presenting the experience, in ECLS implantation, of a cardiac surgery unit of a teaching University hospital.

Method: Data was collected **f**rom January 2012 to January 2013. 10 patients underwent mechanical assistance for cardiogenic shock.

Results: The mean age was 66.70 (8.30 SD) years, the mean log. EuroSCORE was 40.68 (28.35 SD)%. ECLS was implanted for weaning failure from CPB in 9/11 patients (80%). In 1 patient (10%) the ECLS was placed in the Cath. Lab. for refractory cardiac arrest occurring during a PCI, and 1 patient (10%) received the ECLS in the Emergency Department for an out-of-hospital cardiac arrest. Hospital survival rate was 3/10 (30%), ECLS-related complication rate was 3/10 (30%), and re-sternotomy was necessary in 3/10 (30%) patients. Median time of ECLS was 6.5 days (3-9; 25th-75th interquartile), range 1-23 days. Two of the three survived patients belonged from the CBP weaning failure group and the last one received the ECLS in the Cath Lab after a PCI. **Discussion:** Our early experience, although in a very limited number of patients, with this type of mechanical support suggests that: 1) ECLS is a feasible technique to support patients with cardiogenic shock originating from different causes; 2) complications related to the ECLS implantation after CS are not rare and mainly related to bleeding; 3) since our experience has just begun, Extracorporeal Life Support Organization (ELSO) demonstrated to be of a great help in managing these patients [1]. The mortality and complication rates in our small cohort of patients is similar to those reported from other, more experienced, centres; 4) the primary disease may influence the outcome; 5) peripheral cannulation seems to be as safe as central cannulation when an appropriate management of “Harlequin Syndrome” or leg ischaemia is performed; 6) bleeding complications with ECLS or post-cardiotomy requiring re-sternotomy can occur.

References:

1. ELSO guidelines; http://www.elso.med.umich.edu/WordForms/ELSO%20Pt%20Specific%20Guidelines.pdf; accessed January 2013.

Conflict of interest

EPICARDIAL ADIPOSE TISSUE AND INSULIN RESISTANCE IN PATIENTS WITH CORONARY ARTERY DISEASE WITH OR WITHOUT LEFT VENTRICULAR DYSFUNCTION.

A. Pratesi[1], N. Bartoli[1], A. Foschini[1], A. Marella[1], I. Bracali[1], F. Orso[1], M. Di Bari[1], N. Marchionni[1], S. Baldasseroni[1], F. Tarantini[1]

[1]Medicina Clinica e sperimentale, SOD Medicina e Cardiologia geriatrica, Firenze, Italy

Introduction. Epicardial adipose tissue (EAT) is a visceral fat that fulfills two main functions, lipid-storage and secretion of adipokines, but also with pro-inflammatory and proatherogenic properties. It has been suggested that EAT may affect the pathogenesis of atherosclerosis and the clinical course of coronary artery disease (CAD) and alter myocyte contractility. In patients with obesity, diabetes and metabolic syndrome, EAT is enlarged.

Hypothesis. Little is known about the role of EAT in left ventricular dysfunction. Aim of this study was to evaluate the ability of insulin resistance to predict EAT thickness in patients with significant CAD and systolic dysfunction.

Methods. We enrolled 114 subjects diagnosed with CAD by angiography. The majority underwent revascularization after an acute coronary syndrome. Patients were considered affected by significant left ventricular dysfunction when EF was ≤40%. Three indexes of insulin resistance, the HOMA IR index, the insulin sensitivity QUICKI index, and the novel adiponectin/resistin index (ADIPO-IR_{AR}) were calculated and correlated to EAT thickness. Epicardial fat was measured by echocardiography according to Iacobellis criteria.

Results. Subjects with diabetes and with a history of hypercholesterolemia had thicker EAT compared to controls. Potassium levels and all three indexes of insulin resistance were the best independent predictors of EAT both in the whole study population (Table.1) and in the subset of patients with left ventricular dysfunction (Table.2). In the latter group the novel ADIPO-IR_{AR} index displayed the strongest predictivity.

Conclusion. Insulin resistance is an independent predictor of EAT thickness in patients affected by CAD, also in the presence of significant left ventricular dysfunction.

	Model 1 R^2=0.25,	Model 2 R^2=0.29	Model 3 R^2=0.28
	Beta; p value	Beta; p value	Beta; p value
Age	0.06; p=0.682	0.16; p=0.164	0.03; p=0.843
Gender	-0.02; p=0.866	0.04; p=0.736	0.03; p=0.840
Waist circumference	0.06; p=0.652	0.01; p=0.952	0.05; p=0.787
Type 2 diabetes	0.09; p=0.466	0.03; p=0.805	0.18; p=0.169
Hypercholesterolemia	0.08; p=0.514	0.04; p=0.751	0.09; p=0.436
Potassium	**0.42; p<0.001**	**0.40; p<0.001**	**0.35; p=0.005**
6-WT	-0.15; p=0.211	-0.08; p=0.566	**-0.24; p=0.047**
Septal thickness	0.12; p=0.311	0.10; p=0.374	0.12; p=0.313
Tdec	0.16; p=0.177	0.13; p=0.226	0.14; p=0.244
HOMA index	**0.26; p=0.021**		
QUICKI index		**-0.34; p=0.002**	
ADIPO IR_{AR} index			**0.28;p=0.016**

	Model 1 R^2=0.32	Model 2 R^2=0.38	Model 3 R^2=0.35
	Beta; p value	Beta; p value	Beta; p value
Age	-0.21;p=0.680	-0.18; p=0.738	0.29; p=0.241
Gender	-0.25; p=0.342	-0.27; p=0.291	-0.34; p=0.188
Waist circumference	-0.23; p=0.323	-0.14; p=0.597	-0.28; p=0.184
Type 2 diabetes	0.18; p=0.508	0.20; p=0.439	0.03; p=0.911
Hypercholesterolemia	-0.18; p=0.505	-0.23; p=0.429	0.05; p=0.834
Potassium	0.08; p=0.848	0.07; p=870	**0.61; p=0.016**
6-WT	-0.28; p=0.353	-0.27 p=0.295	-0.04; p=0.966
Septal thickness	-0.36; p=0.123	-0.20; p=0.374	-0.03; p=0.913
Tdec	**0.47; p=0.061**	**0.51; p=0.038**	0.24; p=0.294
HOMA index	0.47; p=0.060		
QUICKI index		**-0.54; p=0.028**	
ADIPO IR_{AR} index			**0.69; p=0.008**

Table.1 Multivariable analysis (whole study population) Table. 2 Multivariable analysis (EF ≤ 40 % population)

No conflict of interest

EARLY POST-ACUTE CORONARY SYNDROME REFERRAL TO CORONARY ARTERY BYPASS GRAFTING: ACUTE CORONARY SYNDROME ISRAELI SURVEY (2000-2010)

Y. Barac[1], R. Lempfner[2], I. Goldberg[2], D. Aravot[1]
[1]The Cardiothoracic Department, Rabin Medical Center, Petach-Tikva, Israel
[2]The Leviev Heart Center, Sheba Medical Center, Tel Aviv, Israel

Background: Primary angioplasty is the treatment of choice in patients with acute myocardial infarction (MI). However, early surgical revascularization may be warranted in complex multi-vessel coronary disease. During the past decade, both percutaneous coronary interventions (PCI) and coronary artery bypass grafting (CABG) have evolved tremendously.

Methods: We evaluated trends in early coronary revascularization strategies and associated outcomes in acute coronary syndrome (ACS) patients, as reported in six Acute Coronary Syndrome Israeli Surveys (ACSIS) conducted between 2000-2010.

Results: Of the 11,536 patients included in the study, 566 (4.9%) were referred to CABG during their stay at the ICU. Patients undergoing early CABG displayed higher risk characteristics when compared to patients referred for PCI during the index hospitalization, including a higher admission Killip class, anterior location of MI, moderate or severe left ventricular dysfunction and use of mechanical ventilation ($p<0.05$ for all). Over the past decade, the use of PCI has significantly increased, while an opposite trend was observed for early CABG procedures. Patients undergoing PCI during 2006-2010 had an improved survival compared to previous years (8.5% vs. 11.9%; $p<0.001$), whereas mortality of patients undergoing early CABG did not significantly change between these periods (14.3% vs. 10.1%; $p=0.15$).

Conclusions: Over the past decade, there has been a decline in referral to early CABG in ACS patients, which does not correlate with significant improvement in survival rates, possibly due to the high risk clinical characteristics of these patients.

No conflict of interest

NURSE ASSISTED PROGRAMME FOLLOWING CORONARY ARTERY BYPASS GRAFTING ACHIEVES BETTER CONTROL OF ARTERIAL HYPERTENSION AND HYPERLIPOPROTEINIMA THAN CONVENTIONAL TREATEMNT.

S. Boric[1], M. Brajkovic[1]
[1]Cardiology, Dedinje Cardiovascular Institute, Belgrade, Serbia

Objectives: To assess short-term safety and efficacy of nurse assisted programme following coronary artery bypass grafting (CABG) in patients with arterial hypertension and hypelipoproteinema.
Methods: Two nurses underwent thorough 15 days training in life stylemodifying techniques for arterial hypertension and hyperlipoproteimia. Prior to discharge after CABG they counseled patients for 45 minutes about goals and methods of life-style modifications, including physical exercise and dietary restrictions (sodium and unsatured fatty acids). They also performed telephonic counseling after discharge if patients needed further advice and explanation. All patients received standard medical therapy.
Results: Study group consisted of 95 patients (72 men, mean age 58±10 years) with CABG who participated in nurse assisted programme, whereas control group consisted of 30 age, sex and clinically matched patients who did not participate in the programme. Arterial pressure, total cholesterol, HDL, LDL and triglycerides were measured on admission, and after 1 and 6 months post CABG. There were no differences between the groups on admission and at 1 month in systolic and diastolic arterial pressure, as well as in total cholesterol, HDL; LDL and triglycerides. However, after 6 months patients who received counseling had lower systolic (134±9 vs 148±8 mmHg, p=0.04) and diastolic pressures (85±8 vs 89±8 mmHg, p=0.01), as well as lower total cholesterol (4.91±0.98 vs 5.34±1.1, p=0.04) and HDL (2.83±0.64 vs 3.11±0.70, p=0.04). There were no major cardiovascular events in both groups,except for one hemorrhagic stroke in control group.
Conclusions: Our data indicate that nurse assisted programme is both safe in effective in patients following CABG who have concomitant arterial hypertension and hyperlipoproteinema.No conflict of interest

MOTOR AND COGNITIVE IMPAIRMENT AFTER STROKE

L. Cengic[1], V. Vuletic[2], M. Karlic[3], M. Dikanovic[4], V. Demarin[5]
[1]Neurology, Regional Hospital, Vinkovci, Croatia
[2]University Department of Neurology, Dubrava University Hospital, Zagreb, Croatia
[3]Internal medicine, Regional Hospital, Vinkovci, Croatia
[4]Neurology, Regional hospital, Slavonski Brod, Croatia
[5]University Department of Neurology, University Hospital Center, Zagreb, Croatia

SUMMARY- Cognitive abilities have a great impact on rehabilitation program in stroke patients. Therefore fast and practical psychometric assesment as an indicator of individual rehabilitation program is of great importance. The aim of this study was to analyse and compare motor and cognitive impairment in stoke patients in acute, subacute and chronic phase of illness, in view of age, sex, education, stroke risk factors, lateralisation and type of stroke. The study included 50 stroke patients, 33 male and 17 females. 78% of the patients were diagnosed with ischemic stroke, and 22% of the patients with hemorrhagic stroke. Hypertension was the leading stroke risk factor in 82% the of patients. Cognitive impairment in acute, subacute and chronic phase of the illness was noticed in 12% of stroke patients with ischemia in the left brain hemisphere, with mMMSE average score 31, and SKT score 19, IQ under 90. Better motor recovery in acute and subacute phase of stroke was followed with better cognitive status. All cognitve impaired stroke patients were of little education, some had accomplished elementary education and others had not, all much bellow the dementia risk age of 75 years. The exclusion of the patients with severe stroke from the study had lead to an overastimation of the results. Finally, a coherent algorithm for the stroke patients somatic and cognitive stroke assesment poses itself as imperative as guideline for plastic, individualised, quality rehabilitation.

Key words: Stroke and cognition; Functional neurological scale and stroke; CT assesment and stroke

No conflict of interest

KNOWLEDGE TRANSLATION TO REDUCE HEART FAILURE (HF) READMISSION RATES

C. daley[1], K. Kelly[2], M. Cafiero[2], J.D. Filippone[3]
[1]heart failure, st peters hospital, albany, USA
[2]Nursing, The Sage Colleges, Troy, USA
[3]cardiology, St peters Healthcare, Albany, USA

Hypothesis:

1. Heart failure patients who receive education that is health literacy appropriate will have increased knowledge of disease self-management.

2. Heart failure patients who receive education that is health literacy appropriate will have decreased 30-day heart failure readmission rates.

Methods: Forty-five heart failure patients admitted to a single upstate New York hospital were screened for health literacy using the Newest Vital Sign (NVS) tool. When medically stable, health literacy appropriate patient education was provided by a heart failure nurse specialist. Additionally, pre and post testing of patients' knowledge of heart failure and their treatment were assessed using the Dutch Heart Failure Knowledge Scale and subsequent 30-day heart failure readmission rates were evaluated.

Results: Mean age was 77 years; Gender: 44% male, 56% female; Ethnicity: Caucasian 98%, African American 2%; Health literacy screening using the (NVS) assessment tool, suggests limited literacy in 80% of the study group; Despite limited literacy, knowledge of HF increased in 67% of HF patients post individualized HF education; In addition, the 30-day overall readmission rate was only 2%, compared with 15.8% (2009) at this same hospital.

No conflict of interest

THE EFFECT OF A CARDIAC REHABILITATION PROGRAM IN PATIENTS WITH CORONARY ARTERY DISEASE

S. Kim[1], E. Han[1], B. Kim[1], S. Kim[2], K. Kim[2], S. Joo[2]
[1]Rehabilitation Medicine, University of Jeju College of Medicine, jeju, Korea
[2]Internal Medicine, University of Jeju College of Medicine, jeju, Korea

Objectives

To investigate the effect of cardiac rehabilitation program in patients with coronary artery disease after applying critical pathway.

Methods

The subjects were patients (N=23) who received percutaneous coronary intervention and participated in cardiac rehabilitation program. All subjects underwent the exercise tolerance test (ETT) using a modified Bruce or Ramp protocol before and after cardiac rehabilitation program. The supervised exercise group (N=8) participated in 6-8 weeks of aerobic exercise training with telemetry ECG monitoring in hospital. The self-exercise group (N=15) was instructed to participate in self-exercise training with specialized exercise planner in a community.

We evaluated exercise capacity of both supervised exercise and self-exercise groups. The variables of the exercise capacity included maximum oxygen consumption (VO_2 max), 6 minute walk test (6MWT), metabolic equivalent (MET), resting and maximal heart rate (RHR, MHR) and resting and maximal systolic blood pressure (RsBP, MsBP), resting and maximal diastolic blood pressure (RdBP, MdBP), rate pressure product (RPP).

Results

In the supervised exercise group, VO_2 max, 6MWT, MET, RPP improved significantly after cardiac rehabilitation program. However, in the self-exercise group, only 6MWT was significantly increased. Compared with the self-exercise group, changes in VO2 max tended to increase in the supervised exercise group (p=0.076).

Conclusion

We found that cardiac rehabilitation program in hospital was helpful in improvement of cardiopulmonary exercise capacity. Therefore, we recommend the supervised cardiac rehabilitation to patients who received percutaneous coronary intervention.

No conflict of interest

NONINVASIVE FOLLOW-UP - A KEY POINT AFTER LEFT MAIN PERCUTANEOUS CORONARY INTERVENTION

M. Zabunova[1], I. Mintale[1], I. Narbute[1], S. Jegere[1], I. Zakke[1], A. Erglis[1]
[1]Latvian Centre of Cardiology, Pauls Stradins Clinical University Hospital, Riga, Latvia

The aim: To show the role of exercise test follow-up by reflecting the control of patients' compliance and medication adherence in order to optimize management process and monitoring of the outcomes after percutaneous coronary intervention (PCI).

Methods: The observational study (2009 – 2011) included the patients (n=405) with left main (LM) stenotic lesion (more than 50% of the artery lumen diameter) and performed LM PCI, which were followed by performing exercise test for every three months after invasive treatment. The patients groups with regular and irregular exercise test follow-up were analyzed. Phone follow-up survey performed in 364 patients, patients with exercise test follow-up – 136. Mean follow-up period – 19.38 ± 8.16 months. The information included clinical events and medication adherence.

Results: Myocardial infarction developed in 1.2% vs 3.8% of the patients with regularly and irregularly performed exercise test and stroke was documented in one patient with irregular control visits (12 months after LM PCI). Significant difference was observed in use of statins therapy – 97.6% vs 86.3% in both groups (p=0.01).

Conclusions: 1) Difference in use of medications shows the significance of regular follow-up, especially in high-risk patients compliance (LM group); 2) Regular follow-up is evaluated as significant as invasive treatment in management process of the outcomes; 3) Precisely preplanned, regularly performed of high quality follow-up can be like „a tool" to stabilize the positive benefit of invasive treatment and clinical outcomes control in the future.

No conflict of interest

SAFETY AND COST-EFFECTIVENESS OF ENOXAPARIN FOR BRIDGE THERAPY RELATED TO INVASIVE DENTAL PROCEDURES IN PATIENTS WITH MECHANICAL HEART VALVE

K. Won[1], H. Chang[2]
[1]Cardiology, Myongji Hospital, Goyang, Korea
[2]Cardiology, Yonsei Cardiovascular Center, Seoul, Korea

Background: Invasive dental procedures have the risk of excessive bleeding with regard to highly vascular supporting structures in patients with mechanical heart valves (MHV) receiving warfarin therapy. Bridge therapy with low molecular weight heparin (LMWH) may be an attractive option during invasive dental procedures, but the safety and cost-effectiveness compared with unfractionated heparin (UFH) is uncertain.
Methods: This study investigated the safety and cost-effectiveness of enoxaparin compared with unfractionated heparin (UFH) for bridge therapy in 165 consecutive patients (57±11 years, 35% men) with MHV during invasive dental procedures.
Results: This study included 75 patients treated with UFH-based bridge therapy (45%) and 90 patients treated with enoxaparin-based bridge therapy (55%). HAS-BLED Score was significantly higher in enoxaparin group than UFH group (1.5±1.2 vs. 1.1±1.0, $p < 0.018$). The bleeding risk of dental procedures and the incidence of clinical adverse outcomes were not significantly different between UFC group and enoxaparin group. However, medical costs were significantly higher in UFC group than in enoxaparin group ($p < 0.001$). After multivariable adjustment, old age (≥ 65 years) was associated with increased risk of total bleeding (OR, 2.51; 95% CI, 1.15–5.48; $p = 0.022$), and bridge therapy with enoxaparin ($\beta = -0.694$, $p < 0.001$) and major bleeding ($\beta = 0.296$, $p = 0.045$) were associated with the medical costs within 30 days after dental procedures.
Conclusions: Enoxaparin may be more efficient than UFH considering the safety and cost-effectiveness for bridgy therapy in invasive dental procedures of patients with MHV.

No conflict of interest

LONG-TERM OUTCOME OF EXTRACORPOREAL SHOCKWAVE MYOCARDIAL REVASCULARIZATION THERAPY FOR REFRACTORY ANGINA.

G. Alunni[1], F. Condotto[1], A. Deberardinis[2], M. Campana[2], E. Picardi[1], A. Fanelli[1], S. Marra[1]
[1]Cardiologa 2, Città della salute e della scienza di Torino - molinette, Turin, Italy
[2]Nuclear medicine, Città della salute e della scienza di Torino - molinette, Turin, Italy

Purpose. Extracorporeal shockwave myocardial revascularization (ESMR) is a new treatment for patients with refractory angina, not eligible for further percutaneous or surgical revascularization. The immediate effect of the therapy is a reduction in symptoms and an improvement of myocardial perfusion and function, confirmed by SPECT and echocardiography. We wanted to evaluate the clinical long-term effect of this therapy.
Methods. The first 20 patients who underwent ESMR therapy from November 2009 to January 2011 at our Institution were called for a 2-year follow-up visit (range 24 to 38 months).
Results. Mean CCS class, that improved from 2.8 at baseline to 1.3 at 6 months, remained stable at 1.3 at the end of follow-up ($p<0.001$). None of the treated patients experienced myocardial infarction or was hospitalized because of angina. The extra nytroglicerin consumption for angina was significantly reduced ($p <0.001$). 3 patients (15%) died: they were all more than 78 years old; one patient died for septic shock, the remaining 2 for sudden cardiac death at 5 and 22 months after the treatment; none of them complained of angina anymore after the treatment.
Conclusions. The clinical improvement of patients treated with ESMR for refractory angina lasts over time, suggesting a real and durable myocardial neo-vascularization effect of shock waves.

No conflict of interest

PREDICTIVE VALUE OF CORONARY COMPUTED TOMOGRAPHY ANGIOGRAPHY AND CORONARY CALCIUM SCORING IN DETECTING AND EVALUATING ACUTE CORONARY SYNDROME

A. Bunch[1]
[1]*Emergency Department, Memorial Hermann Healthcare System, Conroe, USA*

Cardiovascular disease is the leading cause of death and disability in the United States. Chest pain is often the first presenting symptom of coronary artery disease and the second most common presentation to the emergency department. Millions of patients present to the emergency department each year for evaluation of chest pain, which presents a major challenge to emergency department physicians. A substantial number of patients presenting to the emergency department with chest pain are non-cardiac in origin costing billions of dollars per year for a negative evaluation.

The gold standard for detecting coronary artery disease is the invasive coronary angiogram (ICA). The high negative predictive value of the CCTA to detect coronary artery disease (CAD) establishes an effective non-invasive alternative to ICA in well defined low to intermediate risk populations to predict future major cardiovascular events (MACE). There was a direct correlation with major cardiovascular events and higher calcium scores indicating coronary artery calcium scores are stronger predictors of the prognosis of CAD rather than detecting angiographic findings.

A systematic review of literature will be presented to determine if there is a predictive value of coronary computed tomography angiography (CCTA) as compared to coronary artery calcium scoring (CACS) as non-invasive diagnostic alternatives in detecting coronary artery disease, and evaluating acute coronary syndrome associated with major cardiovascular events within an acute care setting.

No conflict of interest

RESULTS OF SYSTEMATIC USE OF PRIMARY ANGIOPLASTY AS THE REPERFUSION TREATMENT FOR ACUTE MYOCARDIAL INFARCTION.

F. Cambronero[1], J. Nieto[2], J.A. Hurtado[3], J.R. Gimeno[3], J. Lacunza[3], J. García de Lara[3], R. Valdesuso[3], M. Valdes[3], E. Pinar-Bermúdez[3]
[1]Cardiology, Hospital Morales Meseguer, Murcia, Spain
[2]Cardiology, Hospital del Noroeste. Caravaca, Murcia, Spain
[3]Cardiology, Hospital Universitario Virgen de la Arrixaca, Murcia, Spain

Introduction: Primary angioplasty (PCIp) represents the best available strategy for treatment of ST-segment elevation myocardial infarction (STEMI). When used in experienced centers it gives a clear short term benefits compared to fibrinolysis.

Objective: Analyze the clinical profile, short and long term follow up in patients treated with PCIp in the area of a PCI capable hospital.

Methods: Retrospective study in a cohort of 530 consecutive patients in a hospital with a primary angioplasty program. Data of clinical characteristics, procedure until the end of hospitalization and follow up were collected. All deaths were considered cardiac unless stated otherwise.

Results: Between January 2006 and December 2010 530 PCIp were performed (age 64,3 ± 14,1, 76,6% males). The prevalence of classic risk factors was high (HTA 59,4%, DLP 39,6%, Diabetes Mellitus 36,4% and smoking 60%). The mean time from the symptoms onset to angioplasty was 4,3 hours. The anterior descendant artery (AD) was the most frequently affected (43,32%) followed by right coronary artery (41,8%). Only 4,7% percent of the cases were secondary to a thrombosis of stents previously implanted. Mean number of implanted stents was 1,39 and half of them were drug eluting stents. The procedure was a success in 96% of cases and severe complications were low (1,1%). Short and long term results are summarized in the attached table.

Eventos	**30 days**	**1 year**
Total mortality (%)		12
9		
Cardiovascular Mortality (%)	8	10
Myocardial infarction (%)	1	4
Restenosis (%)	0	2
Stroke (%)	2	3

Conclusión: PCIp as elective treatment for STEMI presents adequate clinical results in our region with a total mortality of 9% and 12% at 30 days and one year respectively. Only few complications were presented during the procedure.

No conflict of interest

IDENTIFICATION OF MICRORNAS AS POTENTIAL MODULATORS OF HEMOSTATIC SYSTEM IN UNSTABLE ANGINA PATIENTS

S.F. Li[1], J.Y. Ren[1], G.P. Han[1], Q. Geng[1], J.J. Li[1], H. Chen[1]
[1]Department of Internal Medicine, Peking University People's Hospital, Beijing, China

Background and Purpose:

The activation of hemostatic system plays a critical role in the incidence of acute coronary events. It was demonstrated that microRNAs (miRNAs) could regulate the expression of haemostatic proteins in some diseases. The aim of our study was to identify microRNAs as potential modulators of hemostatic system in unstable angina (UA) patients.

Methods:

To determine the differential expression of plasma miRNAs, we analyzed miRNA expression profile in plasma of patients with chest pain attributable to non-cardiac causes (Control group, n=9) and patients with typical unstable angina (UA group, n=9) using TaqMan MicroRNA Low Density Array. To identify miRNAs related with hemostatic system, we first searched main genes involved in coagulation and fibrilysis system in KEGG database, and then searched for potential miRNAs for the determined target genes using two different miRNA target prediction algorithms, TargetScan and miRanda. To confirm our findings obtained from the miRNA profiling, we selected 5 miRNAs of the plasma from another 25 UA patients and 15 controls for further validation by real-time PCR assays.

Results:

We found 36 circulating miRNAs were significantly up-regulated in UA group. MiRNA/target gene analysis suggested that 17 of 36 miRNAs were probably associated with hemostatic system. Consistent with the data of the profile, circulating levels of selected 5 miRNAs were obviously up-regulated in patients with unstable angina compared with controls.

Conclusions:

MiRNAs may involve in the regulation of hemostasis system imbalance in UA patients before acute coronary events happening.

No conflict of interest

COMPARISON OF THE CLINICAL AND ANGIOGRAPHIC PROFILE OF PATIENTS EARLY POSITIVE VERSUS CONVENTIONAL POSITIVE ST SEGMENT DEPRESSION DURING TREADMILL TEST

W. Dabdoob[1], S. Saifulhaq[2], B. Unis[2], W. Abdullatef[2], H. Alzaim[2], A.A. Gehani[1]
[1]Heart Hospital Cardiology Department, Hamad Medical Corporation/ Weill Cornell Medical College, Doha, Qatar
[2]Heart Hospital Cardiology Department, Hamad Medical Corporation, Doha, Qatar

Background: The clinical and angiographic profile in patients with early positive Exercise Test (EP-EST) may differ from those with conventional positive Exercise Stress Test (CP-EST) (After stage 2).

Methods: Among 2,400 patients with positive Exercise Test (ET), in 7 years (2005- 2012), 90 patients had EP-EST (≥2mm ST depression during stage 1-2) and Coronary angiography within 6 months. The Clinical and Angiographic profile were compared with matched 146 patients with CP-EST (≥2mm after stage 2).

Results: As compared to CP-EST, patients with EP-EST were more often diabetic and smokers (55.60%, 24.4% vs, 24.7%, 0.7% respectively), but lower prevalence of Dyslipidemia (30%vs 54.8%, P≥ 0.001). ST Changes were more often Infero-lateral and Anterior leads (77.8%, 17.8% vs 0.7%, 2.1%, P≥ 0.0001). EP-EST also had higher overall angiographic prevalence of Coronary Artery Disease (CAD) than CP-EST, (88.9% vs 65.1%, P ≥ 0.0001), particularly in the Left main (4.4% vs 0.0%, P ≥ 0.001) and the LAD (82.2% vs 39.7%, P ≥ 0.0001). The positive predictive value of EP-EST was 88.9%, with less False positive results (11.1% vs 34.9%, P≥ 0.0001). EP-EST had higher tendency to have Multi-vessel CAD (47.7% vs 11.64%, P ≥ 0.0001).), and more frequent intervention (PCI and CABG) as compared to CP-EST, (81% vs 49.3%, P ≥ 0.001).

Conclusion: As compared with CP-EST, coronary angiography in patients with early positive had higher probability of severe and multi-vessel CAD, including left main, and more need for Coronary interventions.

No conflict of interest

ACUTE MYOCARDIAL INFARCTION OUTCOMES IN FOUR AGE GROUPS DIABETIC PATIENTS

L. David[1], A. Grosu[1], A. Raducan[1]
[1]cardiac emergencies, Institute of cardiology, Chisinau, Moldova

Aim. To evaluate clinical characteristics and outcomes in four age groups (AG) of patients (pts) with diabetes mellitus (DM) and acute myocardial infarction (AMI).

Material and methods. In 114 consecutive AMI pts with DM, age 64,1±0,9 years, 56% men, stratified into 4 AG: I AG <50, II AG: 50 to 64, III AG: 65 to 75, IV AG over 75 years we compared risk factors, clinical characteristics, short and long-term (2,5 years) mortality.

Results. DM duration rose with age ($p<0,05$). Percentage of women was higher in AG III and AG IV ($p<0,01$). Diabetics under age 50 smoked more often ($p<0,05$), had higher cholesterol ($p<0,01$) and triglycerides ($p<0,05$) levels than other AGs. Incidence of hypertension ($p<0,05$), prior heart failure (HF) ($p<0,01$) increased with age, previous MI prevalence didn't differ. AG I developed more frequently Q-wave AMI ($p<0,05$), had hyperglycemia on admission ($p<0,01$) compared to other AG. Patients over age 65 developed more often Killip class>2, atrial fibrillation, in-hospital HF than younger subjects ($p<0,05$). In-hospital mortality was highest in AG III ($p<0,01$), followed by AG I, AG IV, AG II. Young diabetics had a higher in-hospital mortality than their non-diabetic counterparts ($p<0,05$). Post-AMI mortality (2,5 years) increased with age ($p<0,05$).

Conclusions. Diabetic AMI patients below age 50 were more often men, obese, smokers, hypertensive, had high cholesterol and triglycerides levels, hyperglycemia on admission, Q-wave AMI, and increased risk of in-hospital death. Diabetics aged over 65 were more often women, had much comorbidity, developed frequently HF, had high short and long-term mortality.

No conflict of interest

INFLAMMATION DOES NOT PREDICT EMBOLIZATION AFTER PERCUTANEOUS CORONARY INTERVENTION

O. Gach[1], L. Davin[1], J. Magne[1], V. Legrand[1]
[1]Cardiology, CHU Sart Tilman, liege, Belgium

Background: High sensitivity C-reactive protein predicts future cardiovascular events in patients with unstable as well as stable coronary syndromes. Few data are available about the incidence, the prognostic significance and the relation to inflammation of troponin elevation following percutaneous coronary intervention.

Methods: We prospectively analyzed 200 patients treated by percutaneous coronary intervention for stable or Braunwald IIA class unstable angina. The patients were followed during a mean period of 32 months. Major adverse cardiac events were defined as the occurrence of death, myocardial infarction or recurrent angina requiring repeat percutaneous coronary intervention or coronary artery bypass grafting.

Results: During the follow-up period, 58 major adverse cardiac events were observed. By multivariate analysis, independent predictors for the occurrence of adverse events were unstable angina and troponin I level after intervention ($p < 0.0001$ for both).

No correlation was found between baseline inflammation and significant troponin I elevation post intervention and by multivariate analysis, no biological variable was predictor of troponin I elevation occurred after intervention.

Conclusions: Baseline inflammation cannot predict onset of minor myonecrosis damage (expressed by troponin elevation) induced by percutaneous coronary intervention which predict long term outcome however.

No conflict of interest

CHANGES IN PROPERTIES OF RED BLOOD CELLS AFTER SINGLE EXERCISE BOUT IN ISCHEMIA HEART DISEASE

K. Gwozdzinski[1], A. Pieniazek[2], J. Czepas[3], J. Brzeszczynska[3], A. Jegier[4], L. Pawlicki[5], R. Irzmanski[5]
[1]Department of Molecular Biophysics, University of Lodz, Lodz, Poland
[2]Department of Thermobiology, University of Lodz, Lodz, Poland
[3]Department of Molecular Biophysics, University of Lodz, Lodz, Poland
[4]Department of Preventive Medicine, Medical University of Lodz, Lodz, Poland
[5]Department of Internal Medicine, Medical University of Lodz, Lodz, Poland

Physical activity is a major factor in cardiac rehabilitation of patients after myocardial infarction. The aim was to examine the properties of erythrocytes after physical exhaustion of men after myocardial infarction before and after cardiac rehabilitation.

Blood was taken and all parameters were measured before, immediately after and 1h after 6 min cycling test performed by male volunteers after myocardial infarction with balanced diet (non-smokers, non-drinkers): age (52.2 ± 6.4 years); height (172 ± 3 cm), weight (84.2 ± 12.9 kg), BMI (28.3 ± 4.2). Erythrocyte properties such as lipid membrane fluidity, internal viscosity and osmotic fragility were studied before and after four week rehabilitation. Lipid membrane fluidity was determined using three spin probes: 5-, 12- and 16-doxyl stearic acids (5-DS, 12-DS, 16-DS). A decrease in fluidity indicated by 5-DS and 12-DS just after exercise and 1 hour later was observed. Changes before and after cardiac rehabilitation were not found. Internal viscosity estimated using Tempamine and maleimide spin labels (MSL) was higher in the group before rehabilitation and did not change during physical exercise. Contrary, upon rehabilitation the decrease in this parameter 1 hour after exercise was found. Osmotic fragility of erythrocytes did not change during exercise before cardiac rehabilitation and after it was finished.

The results suggest that decrease in lipid membrane fluidity and in internal viscosity lead to changes of erythrocyte rheology and shape.

Acknowledgment: This study was supported by the grant 404 117 33 from the Polish Ministry of Science and Higher Education.

No conflict of interest

MULTI-VESSEL CORONARY ARTERY DISEASE TREATMENT IN ACUTE CORONARY SYNDROMES.

P. Jebavy[1]
[1]*Cardiology, Kardiologie na Bulovce s.r.o., Prague, Czech Republic*

Introduction: Primary coronary intervention (PCI) is the prefered method of treatment of acute coronary syndromes (ACS) in the Czech Republic long since.

Aim of the study: To analyze single private center's exerience of treating patients with ACS suffer multi-vessel coronary artery disease (MVD).

Patients studied: 5035 patients in time from 1998 to 2012 with ACS were analyzed. According to coronary angiografy (CAG) we determined 3991 patients as subjects to PCI treatment. Age: 64,3 (26-91) years, male prefered 72%. Culprit coronary artery was closed in: 62%, or tight stenosis in: 38% of the patients. MVD was present in 39% of the patients: Stenosis exceeded 60% of the diameter in one or two non-culprit wessel.

Strategy of treatment: Patients with MVD were determined to repeat CAG after 2 month. All culprit lesions suitable for PCI, with some rare exeptions, were treated interventionaly, regardles angina. Lesions unsuitable for PCI and/or repeated restenosis were treated surgically. Acute multi-vessel PCI had never been used, with rare exception.

Results: Technical success – 95,3%. Failure of PCI in 4,7% of the patients: guide wire - 79%, balloon didn´t pass - 21%, no difference in MVD. In-hospital mortality -3,85%. Mortality is cosiderably higher in MVD.

Conclusions: MVD were treated prefentially by way of PCI, but approach was individualized. In lack of the guidelines of treatment of MVD we have considered according to: 1) Patients preference, 2) Institution preference according to groving clinical experience, 3) Age of the patients, and later by 4) presence of diabetes. PCI treatment was much more frequent as a surgical approach.

No conflict of interest

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No conflict of interest

THE CLINICAL IMPLICATIONS OF INCREASED CYCLOPHILIN A LEVELS IN PATIENTS WITH ACUTE CORONARY SYNDROMES

Y. Jinchuan[1], Z. Xuan[1], C. Rui[1], W. Cuiping[1], Y. Wei[1]
[1]Department of Cardiology, Affiliated Hospital of Jiangsu University, zhenjiang, China

Background: Cyclophilin A is a secreted molecule that has a physiological and pathological role in cardiovascular diseases. However, limited information is available on the relationship between cyclophilin A level and acute coronary syndromes (ACS). This study aims to investigate whether cyclophilin A level is related to the stability of coronary atherosclerotic plaque in patients with ACS.

Methods: The present study included normal controls (n=50), patients with stable angina (SA) (n=60) and patients with ACS, including unstable angina (UA) (n=60) and acute myocardial infarction (AMI) (n=90). Serum soluble cyclophilin A, matrix metalloproteinase 9 (MMP-9), MMP-3 and C-reactive protein levels (CRP) were measured by enzyme-linked immunosorbent assay kit. All coronary stenosis were assessed by angiographic coronary stenosis morphology.

Results: Serum cyclophilin A level in ACS(UA and AMI) subjects were significantly higher than those in patients with SA and controls ($p< 0.05$). Serum cyclophilin A correlated positively with serum MMP-3 and MMP-9 and CRP in ACS patients($r_1=0.69$, $r_2=0.52$, $r_3=0.49$ $p< 0.0001$), but not in control. Furthermore, the increased cyclophilin A levels was associated with the number of complex coronary stenoses ($r_1=0.63$, $p< 0.0001$), but not smooth lesions or stenosis severity, in coronary artery disease patients. Logistic regression analysis also demonstrated that serum cyclophilin A level was an independent predictor factor for ACS(OR, 2.721, 95% CI 1.563-4.042, p=0.001).

Conclusion: Patients with ACS showed that increased levels of cyclophilin A may be a valuable marker for predicting the severity of ACS."

Document not received

CARDIAC REHABILITATION REDUCES GLUCOSE SWING DURING 75G ORAL GLUCOSE TOLERANCE TEST IN PATIENTS WITH ACUTE CORONARY SYNDROME

H. Kan[1], H. Adachi[1], R. Kawaguchi[1], H. Hoshizaki[1], S. Oshima[1]
[1]Cardiology, Gunma Prefectural Cardiovascular Center, Maebashi-shi, Japan

Background: Recently, glucose swing is reported to induce ischemic events. Although cardiac rehabilitation is necessary to reduce onset of ischemic heart disease, it isn't clear the effect of cardiac rehabilitation on glucose swing, yet.

Purpose: We aimed to investigate the effect cardiac rehabilitation on glucose swing.

Method: Consecutive 80 patients with ACS who underwent PCI and 75g Oral Glucose Tolerance Test(OGTT) from May 2011 to September 2012 were enrolled. Patients with DM were excluded. 75g OGTT was performed twice before hospital discharge and 6 to 9 months later to assess glucose metabolism. Change of glycemic profile was compared between patients who participated in the cardiac rehabilitation and those who didn't. Glucose swing was defined as follows: maximum glucose level – minimum glucose level during OGTT.

Results: Normal glucose tolerance, IGT and DM was observed in 23 patients(28.8%), 40 patients(50.0%) and 17 patients(21.3%), respectively. Of the 40 patients who could check follow up OGTT, 18 patients participated in the cardiac rehabilitation program and 22 patients didn't participate in it. Glucose swing was significantly attenuated in patients with cardiac rehabilitation as compared with patients without rehabilitation(-5.8±39.4mg/dl vs. 23.5±33.5mg/dl, p=0.015). No significant differences were observed in HOMA-R(-0.38±0.81 vs. -0.08±0.73, p=0.22) and insulinogenic index(-0.12±0.62 vs. -0.23±0.53, p=0.58) between two groups. Patients with cardiac rehabilitation showed significant decrease in HOMA-β compared with those without rehabilitation(-46.8±104.7 vs. 12.7±52.8, p=0.028).

Conclusions: Cardiac rehabilitation reduces glucose swing during 75g OGTT although it improves neither insulin resistance nor initial insulin secretion.

No conflict of interest

NONINVASIVE THERAPY FOR THE MANAGEMENT OF PATIENTS WITH ADVANCED CORONARY ARTERY DISEASE (CAD)

W. Kazmi[1], S.Z. Rasheed[2], A. Samad[2]
[1]Nephrology, Karachi Medical and Dental College, Karachi, Pakistan
[2]Cardiology, Karachi Institute of Heart Disease, Karachi, Pakistan

Objectives: To determine the efficacy of cardiac shock wave therapy (CSWT) in the management of patients with end-stage CAD.

Introduction: Patients with end-stage CAD have symptoms such as recurrent angina, and breathlessness despite having had a coronary artery bypass surgery or a percutaneous coronary intervention. These patients are refractory to optimal medical therapy, are not fit for a redo procedure, and are often termed as 'no option' patients.

Methods: We carried out a prospective cohort study to examine the effects of CSWT application in patients who had end-stage CAD and were no option patients. Characteristics such as angina class scores and functional status scores among cases (patients with end-stage CAD who received CSWT) and controls (patients with end-stage CAD who did not receive CSWT) were compared at baseline and at 6 months after CSWT therapy.

Results: There were 43 cases and 43 controls. The mean age of the cases was 58.7±9.5 years and 56.6±11.6 years in the controls. Clinical results showed a significant improvement in exercise time between the cases and the controls 6 months after treatment with CSWT (20.1±15.7 min in cases vs. 10.1±4.2 min in controls; P <0.0001), and symptomatic improvement in the CCS class scores (1.95±0.80 in cases and 2.63±0.69 in controls; P < 0.0001) and NYHA class scores (1.95±0.80 in cases vs. 2.48±0.59 in controls; P < 0.001).

Conclusion: The present study shows that CSWT application to the ischemic myocardium in patients with refractory angina pectoris improved angina class scores and functional class scores at 6 months after CSWT treatment compared with the baseline.

No conflict of interest

THE INFLUENCE OF ETHNICITY AND GENDER ON NAVIGATING AN ACUTE CORONARY SYNDROME EVENT

K.M. King-Shier[1], S. Singh[2], C. Mather[3], N. Khan[4], H. Quan[5]
[1]Nursing and Community Health Sciences, University of Calgary, Calgary, Canada
[2]Nursing, University of Calgary, Calgary, Canada
[3]Anthropology, University of Calgary, Calgary, Canada
[4]Medicine, University of British Columbia, Vancouver, Canada
[5]Community Health Sciences, University of Calgary, Calgary, Canada

Purpose. Ethnicity and gender may influence acute coronary syndrome (ACS) patients recognizing symptoms and making the decision to seek care. We aimed to examine these potential differences in Caucasian, Chinese and South Asian ACS patients.

Methods. In-depth interviews were conducted with 57 patients recently hospitalized for ACS. Twenty Caucasian (10 men/10 women), 18 Chinese (10 men/8 women), and 19 South Asian (10 men/9 women) ACS patients were purposively sampled from a cohort of patients participating in another study. Patients engaged in in-depth interviews, in the language of preference, to examine the process of identifying symptoms and seeking care. Analysis of transcribed interviews was undertaken using constant comparative methods.

Results. All participants followed a similar process from the time of symptom onset to seeking medical attention: having symptoms; waiting/denying; justifying; disclosing/discovering; acquiescing; and taking action. However, concerns regarding language barriers, being a burden to others, cost (despite Canada's healthcare system being publically funded), and transportation to seek urgent care varied, for example, based on participants' ethnicity. Women's general tendency to feel responsibility to their home and family negatively impacted the timeliness in their decisions to seek care. This was particularly so for South Asian women. Also, men tended to disclose their symptoms to receive help, whereas women often waited for their symptoms to be discovered by others who then obtained help.

Conclusions. Ethnic- and gender-based differences suggest that education regarding navigation of ACS and access to care, be specifically targeted to ethnic communities. Culturally appropriate knowledge translation will be imperative.

No conflict of interest

TROPONIN T IN ACUTE ISCHEMIC STROKE: RESULTS FROM THE HISTORY STUDY

M. Kral[1], D. Sanák[1], T. Veverka[1], M. Hutyra[2], D. Vindis[2], A. Bártková[1], T. Dornák[1], J. Zapletalová[3], R. Herzig[1], D. Skoloudík[1]
[1]Comprehensive Stroke Center, University Hospital Olomouc, Olomouc, Czech Republic
[2]Department of Internal Medicine I - Cardiology, University Hospital Olomouc, Olomouc, Czech Republic
[3]Department of Biophysics and Statistics, Palack? University, Olomouc, Czech Republic

Background: Multiple interactions are considered to occur between the various forms of cardiovascular and cerebrovascular diseases. The aim of the study was to assess the serum level profile of cardiac troponin T (cTnT) in acute ischemic stroke (AIS) patients to evaluate factors associated with increased serum level of cTnT.

Methods: AIS patients admitted within 12 h from stroke onset were enrolled in this prospective observational study. Neurological examination and brain CT or MRI at admission, standard laboratory tests, including cTnT and other cardiac markers, at admission and 4h later, and repeated electrocardiograms were performed in all patients. Correlations between cTnT and baseline parameters were tested and multivariate regression analysis was used to assess the predictors of cTnT elevation.

Results: In total, 107 consecutive AIS patients (65 males, mean age 67.2±14.2y) were enrolled. 39 (36.4%) patients presented with elevated cTnT above the upper limit. The cTnT levels correlated significantly with age (r=0.448) and the levels of NT-proBNP (r=0.528), cystatin C (r=0.457), CK-MB mass (r=0.253), urea (r=0.281), and albumine (r=-0.219). Multiple logistic regression analysis found creatinine >90 µmol/L (OR=3.45; 95% CI: 1.09-10.85), NT-proBNP (OR=1.09 per 100 µg/L increase; 95% CI: 1.03-1.16) and CK-MB mass (OR=1.45 per 1 µg/L increase; 95% CI: 1.04-2.04) to be associated with cTnT elevation in AIS patients.

Conclusion: Elevated cTnT can be relatively frequently detected in AIS patients. To reliably identify the patients with current acute myocardial impairment, more in-depth clinical investigation is needed.

Trial registration information: ClinicalTrials.gov NCT01541163. Supported by the IGA MH CR grant number NT/11046-6/2010.

No conflict of interest

TROPONIN T SERUM LEVEL IS NOT ASSOCIATED WITH THE LOCATION AND VOLUME OF ACUTE BRAIN INFARCTION: RESULTS FROM HISTORY STUDY

M. Kral[1], D. Sanák[1], T. Veverka[1], M. Hutyra[2], D. Vindis[2], A. Bártková[1], E. Cecháková[3], K. Langová[4], R. Herzig[1], D. Skoloudík[1]
[1]Comprehensive Stroke Center, University Hospital Olomouc, Olomouc, Czech Republic
[2]Department of Internal Medicine I - Cardiology, University Hospital Olomouc, Olomouc, Czech Republic
[3]Department of Radiology, University Hospital Olomouc, Olomouc, Czech Republic
[4]Department of Biophysics and Statistics, Palack? University Olomouc, Olomouc, Czech Republic

Objectives: To investigate possible correlation between location and volume of brain infarction and cardiac troponin T (cTnT) serum level in acute ischemic stroke (AIS).

Background: cTnT is frequently elevated in AIS patients. However, possible relationship, between cTnT level and brain infarction remains unclear.

Methods: 200 consecutive patients (65 males; median age 68, mean 67.7±14.2 years) admitted within 12 h since AIS onset were enrolled. Location and volume of acute brain infarction was assessed using magnetic resonance imaging at admission and after 24 h. Standard laboratory tests, including cTnT, and repeated electrocardiograms, were performed at admission and after 4 h. Correlations between cTnT level and location and volume of brain infarction and baseline parameters were tested with Spearman correlation coefficient. Univariate and multiple logistic regression analysis (LRA) were used to determine possible predictors of cTnT elevation.

Results: Elevated cTnT was present in 71 (36%) patients. No correlation was found between cTnT serum levels and neither location (P>0.05) nor volume of brain infarction (r=0.05, P=0.48). LRA identified creatinine (OR: 1.26 per 10 µmol/L increase; 95% CI: 1.043–1.524), NT-proBNP (OR: 1.05 per 100 µg/L increase; 95% CI: 1.018–1.093) and male gender (OR: 3.674; 95% CI: 1.025–13.164) as significant independent predictors of pathological elevation of cTnT.

Conclusions: Although the elevation of cTnT serum level is relatively frequent in AIS patients within first 12 h since stroke onset, it is not related to the location and volume of brain infarction.

Trial registration information: ClinicalTrials.gov NCT01541163. Supported by IGA MH CR grant NT/11046-6/2010.

No conflict of interest

COMPARATIVE ANALYSIS OF MYOCARDIAL INFARCTION AND MYOCARDIAL REINFARCTION RUPTURE FREQUENCY

L. Kulic[1], M. Kne?evic[2], G. Arsic-Komljenovic[1], M. ?ijan-Gobeljic[1], M. Jovanovic[3]
[1]Management department, Health College of Preffesional Carrer Studies "Milutin Milankovic", Belgrade, Serbia
[2]Institute of Pathology, University of Kragujevac Faculty of Medicine, Kragujevac, Serbia
[3]Medical department, Agency for Medicines and Medical Devices Agency of Serbia, Belgrade, Serbia

Mortality in acute myocardial infarction (AMI) is such that sudden death counts half the number of cases, usually caused by numerous and various complications of AMI, and in 20-25% of cases sudden death of the initial and the first mode of clinical manifestation of ischemic heart disease and acute myocardial infarction. The average length of life after acute myocardial infarction is between 5 and 10 years. Repeted infarction, re-infarction, occurs in about 20 to 50% of cases, with a more frequent mortality, especially sudden death, which amounts to 50% of cases. The aim of this study was to analyze the pathological analysis of heart in dead patients with ischemic coronary heart disease (ICHD) and to determine the incidence of heart rupture (HR) with respect to whether it is the first acute myocardial infarction (AMI) or re-infarction. From 152 autopsied with atherosclerotic coronary artery disease, 121 or 79.6% of the respondents had acute myocardial infarction, so about 80% of dead have acute myocardial infarction. 79 or 52% of patients had acute myocardial infarction with scar, respectively, about half of the dead had two heart attacks. Of 121 cases of AMI, heart rupture was found in 21 cases (13.8%). cardiac left ventricular aneurysm was registered in 21 cases (13.8%). Heart rupture in AMI was more frequent in cases with first AMI than in cases of re-AMI.

KEY WORDS: acute myocardial infarction, heart rupture, reinfarction, dissected

No conflict of interest

RED CELL DISTRIBUTION WIDTH AND CRUSADE SCALE AS PREDICTOR OF MAJOR BLEEDING IN NON-ST ELEVATION ACUTE CORONARY SYNDROME

A. López-Cuenca[1], A. García-Narbón[1], P.J. Flores-Blanco[1], M. Sánchez-Martínez[1], J.M. Andreu-Cayuelas[1], R. Rodríguez-Rubio[1], I. De las Heras Gómez[1], F. Marín[1], M. Valdés[1], S. Manzano-Fernández[1]

[1]Cardiology, Hospital Universitario Virgen de la Arrixaca, Murcia, Spain

Background: Red cell distribution width (RDW) has been associated with a worse prognosis in several cardiovascular diseases. However, its usefulness as predictor of bleeding complications is not clearly established. The aim of this study was to evaluate the complementary value of RDW and CRUSADE scale to predict major bleeding (MB) in patients with acute coronary syndrome without ST-elevation (NSTE-ACS).

Methods: We prospectively included 272 consecutive patients (68±12 years, 69% male). At inclusion, RDW was measured in a non-blind fashion. MB was defined according to BARC criteria.

Results: During a follow-up period of 782 days [510-1112], 30 (10.2%) patients had MB. Patients with higher levels of RDW showed an increased rate of MB (p=0.02). ROC analysis identified an RDW value of 13.8% as the best cut-off point (Sensitivity=73%, Specificity=52%, PPV=14% and NPV=94%). After multivariate Cox regression adjustment including CRUSADE scale, RDW value >13.8% was associated with higher risk of MB (HR 2.67 95% CI 1.17-6.10, p=0.02). Patients with RDW <13.8% and CRUSADE <40 (low-intermediate risk) had the lowest event rate, while patients with RDW >13.8% and CRUSADE >40 points (high and very high risk) had the highest rate of MB (log-rank p<0.001). Further analysis of reclassification (NRI and IDI) showed that RDW values ??added prognosis information to CRUSADE scale.

Conclusion: In NSTE-ACS patients, high RDW levels are associated with an increased risk of MB and provide additional information to the CRUSADE scale. Future studies should evaluate the usefulness of including RDW levels into the bleeding risk scales for these patients.

No conflict of interest

IMPACT OF SSRIS AS A TREATMENT FOR DEPRESSION AND ANXIETY IN THE SURVIVAL OF PATIENTS WHO SUFFERED TAKOTSUBO CARDIOMYOPATHY

A. Macedo Dias[1], E. Franco[1], K. Hebert[2], A. Mercedes[1], I. Gogichaishvili[2], D. Messina[1], H. Quevedo[3]
[1]Internal Medicine, Danbury Hospital, Danbury, USA
[2]Cardiology, University of Miami, Miami, USA
[3]Cardiology, Tulane University, New Orleans, USA

Past studies have correlated depression and anxiety with increased sympathetic activity and diminished reuptake of norepinephrine which may be responsible for prolonged cardiac sympathetic stimulation and place patients with depression at higher risk of developing Takotsubo cardiomyopathy (TTC) when exposed to a stressful event.
We conducted a retrospective descriptive study in patients with the discharge diagnosis of TTC from 2003-2012 at Danbury Hospital. A total of 78 patients were included in the study. We aim to measure on admission and at 6 months after the acute event: all-cause mortality, development of heart failure, TTC recurrence, and left ventricular ejection fraction (LVEF).
The mean age was 70.5 ± 14 years, 87% women. Depression and anxiety were present in 20.5% and 30.8% respectively and 77% had a stressful event that triggered TCC.
Fifteen patients were taking selective serotonin reuptake inhibitors (SSRI´s). Seven patients died from 2003-2012, five of them during their hospitalization and three of these were taking SSRIS. The use of SSRIs was associated with all-cause mortality during hospital admission (OR 7.6; 95% CI 1.1 - 50.3; $p < 0.05$). On admission, mean LVEF for patients taking SSRIs was 36.3% ± 11.4 and for patients not taking SSRIs was 36.7±11 (p=0.91).Repeated LVEF at 6-months revealed statistically significant recovery of the LVEF in each group but relatively lower LVEF in patients taking SSRI´s ($p < 0.05$). SSRI's patients had lower survival rates compared with patients not taking SSRI's (p= 0.04). Our results suggest that prior administration of SSRI's may increase the likelihood of in hospital death and affects survival.

No conflict of interest

CLINICAL FEATURES OF TAKOTSUBO CARDIOMYOPATHY - SINGLE CENTER EXPERIENCE

A. Macedo Dias[1], E. Franco[1], K. Hebert[2], A. Mercedes[1], I. Gogichaishvili[2], D. Messina[1], H. Quevedo[3]
[1]Internal Medicine, Danbury Hospital, Danbury, USA
[2]Cardiology, University of Miami, Miami, USA
[3]Cardiology, Tulane University, New Orleans, USA

Takotsubo cardiomyopathy (TTC) also known as transient apical ballooning syndrome or stress-induced cardiomyopathy is a unique reversible condition often affecting postmenopausal women after a stressful event characterized by sudden temporary systolic dysfunction of the apical and/or mid segments of the left ventricle. The underlying mechanisms have not been completely elucidated yet but several hypotheses include catecholamine cardio toxicity, microvascular dysfunction and coronary artery spasm. We conducted a retrospective descriptive study in patients with the discharge diagnosis of TTC from 2003-2012 at Danbury Hospital. A total of 78 included in the study. We aim to describe clinical characteristics at baseline, past surgical and medical history including psychiatric records as well as medication upon admission among patients who suffered TCC. The mean age was 70.5 ± 14 years, 87% (n = 68) were women, of which 11.7% (n = 8) aged ≤55 years. Depression was present in 20.5% of TCC patients (n=16) and anxiety in 30.8% (n=24). Twenty-one patients (27.3%) reported a preceding emotional stressful event and 31 patients (40.3%) had a preceding physical stressor. Fifty patients (64.1%) presented with chest pain. Twenty-eight patients (35.9%) had ST-segment elevation on admission. Five patients (6.3%) died during their hospital stay. TTC is becoming an increasingly recognized condition and clinicians should include it in the differential diagnosis of patients presenting with a suspected acute coronary syndrome. It is frequent in postmenopausal women frequently preceding physical or emotional stress and overall prognosis is good among patients who survived the initial acute phase of heart failure.

No conflict of interest

DIFFERENCES IN MANAGEMENT AND PROGNOSIS OF FIRST ACUTE CORONARY SYNDROME VERSUS REINFARCTION.

O. Merono[1], L. Recasens[1], D. Bueno[1], A. Fernandez[1], M. Cainzos[1], B. Andres Perez[1], C. Garcia-Garcia[1], N. Ribas[1], J.A. Morales[1], J. Bruguera[1]
[1]cardiology, Hospital Del Mar, Barcelona, Spain

INTRODUCTION: There are no recent studies describing whether there are differences in the management and prognosis of patients depending on if they have a first acute coronary syndrome (ACS) or a reinfarction. The aim of our study is to analyze if these differences exist.

METHODS: We consecutively admitted 696 ACS patients in our institution during 2009-2012. We collected clinical and income data, survival and in-hospital complications.

RESULTS: There were 549 patients with first ACS (Group 1) and 147 with reinfarction (Group 2). There were no differences in age or sex between groups. There was a higher proportion of hypertension, dyslipidemia and diabetes in group 2 ($p < 0.05$). At admission, 86.4% of Group 2 patients were receiving antiplatelet agents, 70.5% beta-blockers and 78.1% statins. The 38.1% of patients in group 1 had an ST elevation ACS compared with 18.3% in group 2 ($p < 0.01$). There were no differences between groups in Grace Score or in medical treatment administered. More coronary angiograms were performed on Group 1 (85.7% vs 70.7%;$p<0.01$) and more angioplasties done (68.6% vs 54.2%;$p<0.01$). No significant differences were found in cardiovascular complications rate and in mortality.

CONCLUSION: ACS with ST segment elevation was more frequent in patients with first ACS. More coronary angiograms and more angioplasties were performed on patients with first ACS and there were no differences in medical treatment. We didn't found differences in in-hospital outcomes. The vast majority of patients admitted for a reinfarction were receiving previous treatment for secondary prevention with antiplatelet drugs, beta blockers and statins.

No conflict of interest

COMBINED REVASCULARISATION IN ACUTE CORONARY SYNDROME

M. Rosic[1], M. Fabri[1], R. Jung[2], S. Kacar[1], B. Mihajlovic[3], S. Nicin[1]
[1]Cardiovascular surgery, Institute of cardiovascular diseases Vojvodina, NOVI SAD, Serbia
[2]Cardiology, Institute of cardiovascular diseases Vojvodina, NOVI SAD, Serbia
[3]Cardiovasular surgery, Institute of cardiovascular diseases Vojvodina, NOVI SAD, Serbia

Background: Myocardial revascularisation in acute coronary syndrome (ACS) is possible to achieve by combining two procedures: percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG). Both of these procedures can be performed during the index hospitalization, or with CABG being performed in the next hospitalization.

The aim of the study was to assess whether PCI and CABG performed during the same hospitalisation improve patient outcome with regards to mortality and morbidity.

Methods:A consecutive group of 139 patients, treated due to ACS, in the period from July 2011 to March 2013 was analyzed. In 31 patients (22.3%), PCI and CABG, were done during the same hospitalization due to clinical instability after PCI (Group I). Delayed CABG was done in 108 (77.7%) clinically stable patients (Group II). Estimated risk according to the EuroSCORE II was similar in both groups (p=0.685). The median ejection fraction in Group I and II was 45.0 (40.0- 55.0) vs. 55.0 (47.0-59.0) respectively (p=0.022). The postoperative mortality within 30 days (PM), intensive care unit (ICU) length of stay (LOS), hospital LOS and the number major adverse cardiac and cerebrovascular events (MACCE)_were analyzed.

Results: Table 1.

	Group I (31 pts)	Group II (108 pts)	p
Postoperative mortality	3.2%	2.8%	1.000
ICU LOS	0,97 (0,88 – 1,92)	0,98 (0,84 – 1,95)	0.911
Hospital LOS	8,0 (7,0 – 10,0)	8,0 (7,0 – 11,0)	8,0 (7,0 – 9,75)
MACCE	19.4%	7.4%	0.084

Conclusion: Postoperative mortality in patients with combinbed PCI and CABG during the same hospitalisation compared to those with delayed CABG is similar. There is no difference in ICU and hospital LOS, between the groups.However, patinets treated during the index hospitalization have a higher number of MACCE.

No conflict of interest

HELICOBACTER PYLORI INFECTION AND ACUTE MYOCARDIAL INFARCTION

D. Nakic[1], A. Vcev[2], A. Jovic[1], K. Backov[1], I. Leto[1]
[1]Internal medicine, General Hospital Zadar, Zadar
[2]Internal medicine, University Hospital Osijek, Osijek, Croatia

The aim of study was to determine whether H.pylori infection is an independent risk factor for acute myocardial infarction (AMI), is there link between H.pylori infection and severity of disease, find is there a link between H.pylori infection and well known risk factors for coronary disease. In this prospective, single center study, were enrolled 100 patients with AMI and control group was consisted 93 healthy individuals. The results of this study showed no difference between H.pylori seropositivity distribution in the investigate and control group (29 vs.26 %) and there was no significant difference on the severity of the disease. There was significant association in the patients with three and more risk factors, where the patients with lower blood pressure (124.4/77.4 vs.145.9/87.7 mmHg) and better controlled diabetes (HbA1c 6,1%vs.6.9%) had greater risk for AMI if they are H.pylori seropositive. The large multicentric trials would be needed to define a precise role of H.pylori infection on the development of AMI.

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TESTING THE ARABIC ILLNESS PERCEPTION QUESTIONNAIRE FOR HEART DISEASE IN A LEBANESE SAMPLE

S. Noureddine[1], E.S. Froelicher[2]
[1]Hariri School of Nursing, American University of Beirut, beyrouth, Lebanon
[2]School of Nursing, University of California San Francisco, San Francisco, USA

Purpose: To examine the cultural validity and psychometric properties of an Arabic version of the Illness Perception Questionnaire (IPQ) pertaining to cardiac illness. Knowing people's illness perceptions can be used in designing awareness campaigns for cardiovascular health promotion.

Methods: Secondary analysis of data collected from 401 healthy adults recruited while visiting relatives in 2 large hospitals in Beirut, Lebanon. Participants were interviewed using an Arabic version of the IPQ for heart disease. Forward and backward translation of the IPQ was made by professional translators and health professionals. Statistical tests included Cronbach's alpha coefficient calculation, confirmatory and exploratory factor analyses.

Results: Content validity of the IPQ was supported. Cronbach's alpha coefficients of the identity and causes scales were acceptable (.78 and.76, respectively); yet Cronbach's alpha of the timeline (.59), control (.45) and consequences (.57) scales were lower than expected. Confirmatory factor analysis of the timeline-consequences-control scales did not support the three-factor model of Leventhal's common sense model of illness representation. Exploratory factor analysis yielded 4 factors, explaining 42% of the variance. Exploratory factor analysis of the causes scale yielded two factors (internal and external causes), explaining 42% of the variance.

Conclusions: Cultural and language differences and the lack of personal experience of the participants with heart disease may account for the divergence of some of the results from the literature. Further psychometric testing of the IPQ in healthy Lebanese adults using cognitive interviewing is recommended. Replicating this study in Lebanese cardiac patients is also recommended.

No conflict of interest

MYOCARDIAL BRIDGING : AN UNCOMMON CAUSE OF CHEST PAIN

B. Perera[1], A. Dias[1], E. Franco[1], T. Daniele[2]
[1]Internal Medicine, Danbury Hospital, Danbury, USA
[2]Cardiology, Danbury Hospital, Danbury, USA

Myocardial bridging occurs when a segment of a major coronary artery, the “tunneled artery” runs intramurally through the myocardium. This is a common congenital anatomical variant previously thought to be benign, but recent studies show they may present with myocardial ischemia, myocardial infarction, arrhythmia and sudden death.

We report a 47-year-old man admitted to the ED with midsternal, squeezing and nonradiating chest pain. He has had similar episodes before but never sought medical treatment. He quit smoking 15 years ago. There was no personal or family history of coronary artery disease. Electrocardiogram showed ST elevations in V2 – V4. Echocardiogram showed normal ejection fraction with no regional wall motion abnormalities. Coronary angiography showed a long area of mid left anterior descending artery bridging with compression during systole. No other significant angiographic disease identified. He was discharged on aspirin and a beta blocking agent.

Myocardial bridges have been reported with an incidence of 1.5% to 16% angiographically.Mainly confined to the left anterior descending artery and the typical angiographic finding in myocardial bridging is systolic narrowing of the segment of the coronary vessel. Past reports have shown atherosclerosis seems to have a predilection to involve the proximal segment of the affected vessel and spare the tunneled segment. Several therapeutic approaches have been described: beta blockers, calcium antagonist, stenting of the tunneled segment, surgical myotomy, and CABG.

This case illustrates the importance of having a high index of suspicion for myocardial bridging specially in patients presenting with atypical chest pain with no significant cardiac risk factors.

No conflict of interest

APPROACH TO CORONARY HEART DISEASE PATIENTS AT A COUNTY HOSPITAL-ZABOK GENERAL HOSPITAL

K. Pesek[1], T. Pesek[1]
[1]Internal medicine, General Hospital Zabok, Zabok, Croatia

The aim of the study was to determine health care measures taken in coronary patients hospitalized at Zabok General Hospital in order to identify the problems and accomplishments acquired during the 7-year period of observation.

Nowadays, cardiovascular diseases are the leading cause of mortality and morbidity in the world and in this area. This fact was the main reason for monitoring patients treated at Department of Internal Medicine, Zabok General Hospital with the diagnosis of coronary heart disease. Data on all patients treated for coronary heart disease in 7 years time period were analyzed. Coronary disease was diagnosed on the basis of history data, clinical examination, laboratory tests for biochemical coronary markers and electrocardiogram. Depending on the diagnosis, patients were treated at Intensive Care Unit, Cardiology Department, or were referred for emergency percutaneous coronary intervention (PCI).

Patients were analyzed according to the diagnosis, age and sex, and results were graphically presented/ figures 1,2/. A relatively small number of STEMI patients were referred for PCI /figure 3/. The main reason was the fact that patients came to the hospital too late, i.e. the time elapsed from symptoms onset was too long. Another reason was rather poor organization of the invasive cardiologist teams that could perform the operation 24 hours a day. This type of the work organization was introduced 1.year in Zagorje County, with an increase in 2.year and at the Zagreb Ring level in 3.year.

The treatment and approach to coronary heart disease patients at our County Hospital is the same as at University Hospitals. It has been ensured by the application of guidelines on the approach and treatment of these patients, along with the organization of invasive approach and treatment through the Croatian Society of Cardiology. Additional education of the population at large is still necessary in order to minimize the treated for coronary heart disease as our final goal.

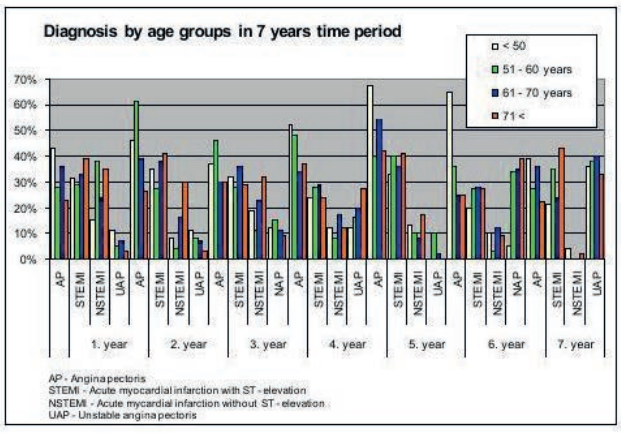


Figure 1.

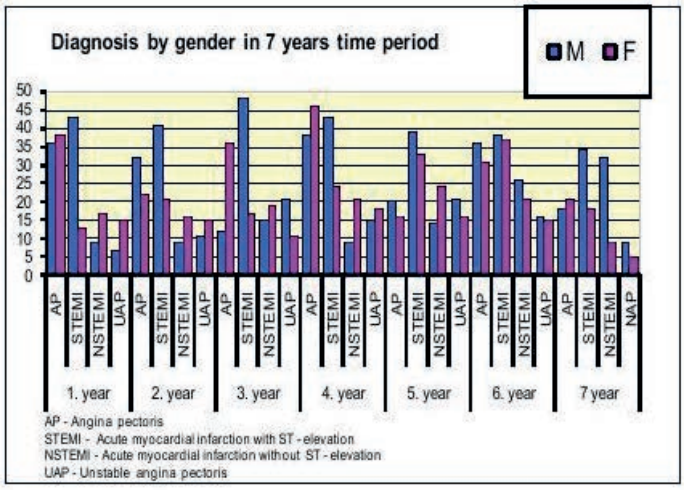
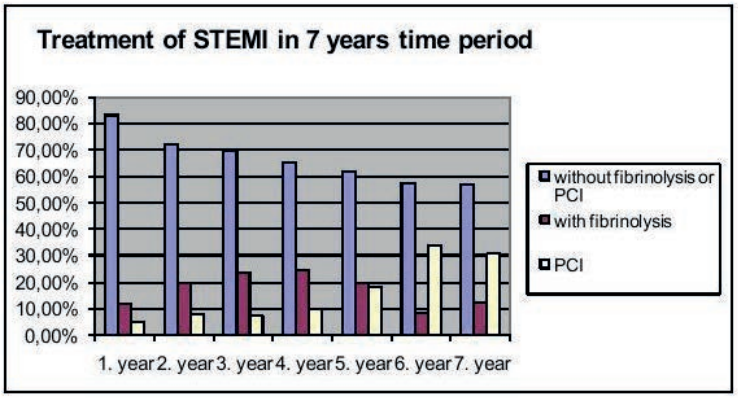


Figure 2.



PCI- percutaneous coronary intervention
STEMI- acute myocardial infarction with ST elevation

Figure 3.

No conflict of interest

ONSET DIFFERENCES BETWEEN PATIENTS WITH ST ELEVATION ACS AND PATIENTS WITHOUT ST ELEVATION ACS: THE MANTRA REGISTRY

L. riva[1], G. casella[1], L. oltrona-visconti[2], A. maggioni[3], G. di pasquale[1]
[1]cardiology, maggiore hospital, bologna, Italy
[2]cardiology, irccs foundation, pavia, Italy
[3]centro studi anmco, centro studi anmco, firenze, Italy

Aim. To evaluate differences in cardiovascular risk factors and previous cardiovascular events and analyze the clinical presentation of patients with ST elevation ACS (STEMI) and patients without ST elevation ACS (NSTEMI).

Methods. The analysis was based on data of the MANTRA registry, a multicentre, observational, nationwide study, which enrolled between April 2009 and December 2010 6394 consecutive patients with ACS (2858 STEMI and 3536 NSTEMI) in 52 ICCUs.

Results. The Table summarizes the main results.

	STEMI (N=2858)	**NSTEMI** (N=3536)	**p**
Age (yrs, mean ± SD)	65 ± 13	68 ± 12	**<0.0001**
Females (%)	26.8	31.9	**<0.0001**
Smoking status: smokers (%) previous smokers (%) not smokers (%)	 42.1 20.5 37.4	 29.7 26.7 43.6	**<0.0001**
Hypercholesterolemia (%)	42.3	49.0	**<0.0001**
Hypertension (%)	58.3	70.2	**<0.0001**
Diabetes (%)	21.6	30.8	**<0.0001**
CAD family history (%)	26.6	23.9	**0.02**
Stable angina (%)	6.5	15.2	**<0.0001**
Prior myocardial infarction (%)	11.5	24.3	**<0.0001**
Previous coronary revascularization (PCI/CABG) (%)	10.6	25.2	**<0.0001**
Heart failure (%)	1.5	5.0	**<0.0001**
Prior stroke/TIA (%)	5	6.6	**0.009**
Peripheral arterial disease (%)	6.5	13.4	**<0.0001**
HR (bpm, mean ± SD)	77 ± 19	80 ± 20	**<0.0001**
SBP (mmHg, mean ± SD)	135 ± 28	142 ± 27	**<0.0001**
DBP (mmHg, mean ± SD)	79 ± 16	81 ± 15	**<0.0001**
Killip class III-IV (%)	7	6.4	0.39

eGFR (ml/kg/min, mean ± SD)	82 ± 27	77 ± 29	**<0.0001**
Previous cardiovascular drug use			
Aspirin (%)	25.1	45.5	**<0.0001**
ACE-inhibitors/ARBs (%)	35.4	48.2	**<0.0001**
Beta-blockers (%)	17.4	28.5	**<0.0001**
Calcium channel blockers (%)	11.8	18.7	**<0.0001**
Diuretics (%)	11.7	21.1	**<0.0001**
Nitrates (%)	7.1	16.4	**<0.0001**
Statins (%)	16.3	29.9	**<0.0001**
n-3 PUFA (%)	2.5	5.0	**<0.0001**

Conclusions. Patients with STEMI are youger than patients with NSTEMI, more frequently smokers and without previous cardiovascular treatment at the time of the event. Patients with NSTEMI are more often affected by hypertension, diabetes and hypercholesterolemia and have previous cardiovascular events.

No conflict of interest

PHARMACOLOGICAL TREATMENT FOR ACUTE CORONARY SYNDROME IN THE ITALIAN NETWORK: THE MANTRA REGISTRY

L. riva[1], G. casella[1], S. zagnoni[1], M. scherillo[2], A. maggioni[3], G. di pasquale[1]
[1]cardiology, maggiore hospital, bologna, Italy
[2]cardiology, azienda ospedaliera rummo, benevento, Italy
[3]centro studi anmco, centro studi anmco, firenze, Italy

Aim. To analyze guidelines' adherence in prescription of recommended cardiovascular drugs during hospitalization and at discharge in patients affected by ST elevation acute coronary syndrome (STEMI) and non-ST elevation acute coronary syndrome (NSTEMI).

Methods. The analysis was based on data of the MANTRA registry, a multicentre, observational, nationwide study, which enrolled between April 2009 and December 2010 6394 consecutive patients with acute coronary syndrome (respectively 2858 STEMI and 3536 NSTEMI) in 52 Italian intensive cardiac care units representative of the Italian network.

Results. The Tables summarize in-hospital early pharmacological treatment (prescribed within 24 hours in case of STEMI and 48 hours in case of NSTEMI) in relation to reperfusion in STEMI or invasive/conservative strategy in NSTEMI. Discharge therapies are reported in accordance with discharge diagnosis.

In hospital	**STEMI** (N=2858)				**NSTEMI** (N=3536)		
Fibrinolysis	(n=460)	PCI (n=1821)	No reperfusion (n=577)	p	PCI (n=1225)	No PCI (n=2311)	p
UFH, %	93.0	76.4	73.0	<0.0001	71.2	67.2	0.014
Fondaparinux, %	3.7	7.3	14.6	<0.0001	16.2	20.6	0.002
Aspirin, %	96.5	95.9	90.5	<0.0001	96.5	92.4	<0.0001
Beta-blockers, %	59.4	64.6	58.1	0.006	71.1	64.1	<0.0001
Aspirin+Clopidogrel, %	91.7	93.2	74.2	<0.0001	95.2	81.6	<0.0001
Clopidogrel, %	94.6	96.4	77.5	<0.0001	95.2	81.6	<0.0001

At discharge	**STEMI** (N=2650)	**NSTEMI** (N=3006)	p
Aspirin, %	97.2	93.4	<0.0001
Clopidogrel, %	92.7	83.1	<0.0001
Aspirin+Clopidogrel, %	91.3	79.6	<0.0001
Beta-blockers, %	78.7	76.3	0.034
ACE-inhibitors/ARBs, %	78.9	75.2	0.001
Statins, %	91.5	88.4	<0.0001
n-3 PUFA, %	32.1	20.2	<0.0001

Conclusions. In the MANTRA registry an undertreatment of non-reperfused STEMI patients and conservatively treated NSTEMI patients is present, despite an increased cardiovascular risk. In addition in NSTEMI patients recommended discharge cardiovascular therapies are less prescribed than in patients affected by STEMI.

No conflict of interest

DIASTOLIC AUGMENTATION AND SYSTOLIC UNLOADING DURING EXTERNAL COUNTERPULSATION WITH DOUBLE OR SINGLE LUMEN CUFF SYSTEM

T. Shimizu[1], Y. Suematsu[2], S. Morizumi[2], M. Kawata[2], T. Ando[3], S. Kyo[4]
[1]Cardiovascular Surgery, Nagano Matsushiro General Hospital, Nagano, Japan
[2]Cardiovascular Surgery, Tsukuba Memorial Hospital, Tsukuba, Japan
[3]Clinical Engineering, Tsukuba Memorial Hospital, Tsukuba, Japan
[4]Therapeautic Strategy for Heart Failure, The University of Tokyo, Tokyo, Japan

OBJECTIVES: External counterpulsation (ECP) is a non-invasive treatment for coronary artery disease. However, leg pain and skin abrasion are complications of conventional ECP therapy with the single lumen cuff system (SLC). To reduce the impact of cuff inflation and improve compliance with ECP therapy, the double lumen cuff system (DLC) has been developed. The aim of the present study was to compare the counterpulsation effect between DLC and SLC during ECP therapy.
METHODS: Eight patients with angina and/or ischemic change in the radionuclide test underwent ECP alternately with DLC (Compact CP) and SLC (EECP) between 8 month and 2 years after coronary artery bypass. The noninvasive radial artery pressure wave forms obtained by pressure tonometry were compared using a waveform analysis software.
RESULTS: Percent diastolic augmentation (DLC 23±9% vs. SLC 18±7%, p=0.779) and diastolic/systolic pressure ratio (0.86±008 vs. 0.86±0.07, p=0.999) were comparable, however, Time to peak augmentation pressure was longer in DLC (181±40msec vs. 127±17msec, p=0.017). Percent systolic unloading calculated from mean pressure was better in DLC (5.6±2.1% vs. 3.2±2.0%, p=0.021), while %systolic unloading calculated from end-diastolic pressure was better in SLC (6.4±4.3% vs. 12.4±5.3%, p=0.049). The pain level of DLC was lower than that of SLC (1.5±0.8 vs. 2.4±1.1, p = 0.038).
CONCLUSIONS: Although some pressure wave characteristic differences are identified between DLC and SLC, ECP using DCL will provide comparable diastolic augmentation with the higher comfort level in patients with coronary artery disease. Further investigations are needed to confirm our results.

No conflict of interest

SYMPTOMATIC PATENT FORAMEN OVALE: A RARE CASE OF ST ELEVATION MYOCARDIAL INFARCTION

V. Stefan[1], S. Bodenseh[1], K. Chakraborty[1], B. Sanwald[1], J. Hemker[1], S. Kapper[1], H. von Korn[1]
[1]Cardiology, Krankenhaus Hetzelstift, Neustadt an der Weinstrasse, Germany

Introduction: Paradoxical embolism can lead to ischemic stroke, peripheral vascular occlusions and rarely to acute myocardial infarction.
Case report: We report the case of a 57 year-old male presenting with a STEMI of the anterior wall. A coronary angiography was immediately performed, revealing a thrombus in the first diagonal branch. The coronaries were otherwise free from atherosclerosis.
A Gp IIb/IIIa antagonist was administered intracoronary, followed by thrombectomy and bare metal stenting due to thrombus persistance. A final TIMI III flow was achieved. A combination of aspirin and prasugrel was started orally.
The TTE showed a preserved left ventricular ejection fraction and a hypermobile atrial septum. The suspicion of an atrial septum aneurysm (ASA) was confirmed by TEE, which furthermore revealed a patent foramen ovale (PFO). After excluding other sources of embolism (atrial fibrillation, endocarditis, thrombophilia) we set the diagnosis of paradoxical coronary embolism. A deep vein thrombosis could not be identified.
We performed an interventional closure of the PFO using a 30 mm Amplatzer occluder. The 6-month follow up TEE showed no residual shunts, the clinical course was uneventful.
Discussions: Coronary embolism is a rare case of STEMI. Besides atrial fibrillation, endocarditis and thrombophilia, paradoxical embolism is one of the seldom mechanisms. The association of PFO and ASA is thought to have an increased embolism risk, simulating “atrial fibrillation” pathophysiology.
Conclusion: paradoxical embolism should be suspected in cases of AMI and normal coronaries. TEE helps identify an unknown PFO. Interventional occlusion of the PFO is a simple and safe strategy in such cases.

No conflict of interest

A RARE CASE OF CEREBRAL ISCHEMIA: DRUG INDUCED TAKO-TSUBO CARDIOMYOPATHY WITH EVIDENCE OF THROMBUS IN THE LEFT VENTRICLE

V. Stefan[1], S. Bodenseh[1], K. Chakraborty[1], B. Sanwald[1], J. Hemker[1], S. Kapper[1], H. von Korn[1]
[1]Cardiology, Krankenhaus Hetzelstift, Neustadt an der Weinstrasse, Germany

Introduction: the Tako-Tsubo Cardiomyopathy is a rare syndrome displaying clinical, ECG and biochemical features of an acute coronary syndrome. It is mostly reversible within a short period of time.
Case presentation: a 58 year-old male presented to our clinic with fluctuating neurological symptoms (speech and visual impairment, dizziness), occuring repeatedly withing the last days. He admited having consumed cocaine several days before. The clinical examination revealed slight aphasia and ataxia. The brain-RMI showed multiple recent ischemic infarction areas of both hemispheres, suggestive of an embolic pattern. The standard investigations (ECG monitoring, carotid ultrasound) revealed no pathology.
The ECG showed a slight ST segment elevation arising from the S curve of the QRS complex in V3-V6 and negative T waves over the anterior and inferior wall. The patient denied having angina, the troponin was elevated. We immediately performed a TTE which revealed a typical Tako-Tsubo pattern with a reduced EF (40%). Furthermore a 1,5 cm thrombus was identified at the left ventricular apex. The coronary angiography showed normal coronaries, no ventriculography was performed. A cardiac MRI excluded myocarditis and confirmed Tako-Tsubo Cardiomyopathy.
After 3 months of therapy with warfarin, ACEI and betablockers, the TTE revealed a normal wall motion, intact EF and absence of apical thrombus.
Conclusions: the Tako-Tsubo Cardiomyopathy is a rare syndrome triggered by emotional stress and also drug abuse (cocaine). The wall motion abnormalities rarely persist over a longer period of time to allow apical thrombus formation. Furthermore is the clinical presentation with neurological deficits extremely seldom.

No conflict of interest

A MARATHON RUNNER FELL INTO SUDDEN CARDIAC ARREST BY ACS JUST BEFORE GOAL, EARLY CPR,DIAGNOSIS AND PCI WITH DOCTOR-HELI.

F. Tabata[1], F. Kyousuke[1], T. Syuuichi[1], T. Yusuke[2], T. Asuka[2]
[1]Cardiovascular Internal Medicine, Mito Medical Center, Ibaraki Machi, Japan
[2]Emergency, Mito Medical Center, Ibaraki Machi, Japan

Introduction:
Helicopter Emergency Medical System (HEMS) are widely operated all over the world. In Japan physicians are part of the HEMS called Doctor-Heli. HEMS main two advantages to traditional ground ambulance emergency medical system is speed of response and transport, and the advanced skills that crews typically bring to the patient. Especially our HEMS, Emergency department and Cardiovascukar Internal Medicine physicians are participated as crew. In systems that include physician potentially early precise diagnosis can be accomplished in particular conditions like Acute Coronary Syndromes (ACS). These skills allow the earlier administration of potentially life-saving measures.
Case Report:
61 year old man participated in a citizen marathon race. No risk factor for coronary artery disease (CAD). Ran 42.190km and just before the goal he fell into SCA. Bystander cardiopulmonary resuscitation (CPR) was done immediately.5minute CPR achieved return of spontaneous circulation (ROSC) and our HEMS was called. We arrived in 10minute at the rendezvous point. The patient complained no chest pain but just only both lower leg pain. But ECG showed ST elevation in V2.3 leads and negative T in V4.5 leads. It suggested like LAD reperfusion with sever stenosis so transported directory to our hospital and emergency CAG revealed LAD #7 99% stenosis. PCI was performed successfully. Following clinical course was good and discharged days 16th without any complications.
Discussion:
Reported Marathon associated SCA occurs in approximately 1 in 57,000 runners. Such life-threatening incidents might be occurred if patients were advanced age or with history of CAD. Even though this patient had no risk for CAD but fell into SCA due to ACS. In this case, bystander CPR was effective and HEMS early diagnosis, early hospital notification, rapidly preparation in hospital and succeeded PCI saved the patient.
Our HEMS contributes to prehospital emergency care and saving lives.

No conflict of interest

DOCTOR BOARDED HELICOPTER EMERGENCY SYSTEM DECREASES DOOR-TO-BALOON TIME IN ACUTE MYOCARDIAL INFARCTION PATIENTS

Y. Tsutsumi[1], K. Furuhashi[2], F. Tabata[2]
[1]emergency medicine, Mito medical center, Higashiibarakigun, Japan
[2]cardiology, Mito medical center, Higashiibarakigun, Japan

[Objective]Helicopter emergency medical systems (HEMS) are widely operated all over the world. In some countries, emergency ambulance personnel board these helicopters. It contributes not only early delivery from the site to the hospital but beginning the treatment such as infusion and basic resuscitation. Moreover in Japan and some European countries, emergency physicians board the helicopters. In such system, even early precise diagnosis can be accomplished in particular conditions including acute myocardial infarction (AMI). Therefore, it shortens the duration between hospital arrival and definitive care due to rapid preparation in hospital. We hypothesis that doctor boarded helicopter system (DH) significantly reduces the door-to-balloon time (i.e. from hospital arrival to ballooning) in acute myocardial infarction (AMI) due to completion of diagnosis at the site and rapid preparation for percutaneous cardiac intervention (PCI) in hospital.

[Methods]This is retrospective observational study. All AMI patients directly delivered from the site to our hospital in daytime (8:30 – 17:30) between January 2007 and September 2012 were included. Among them, the door-to-balloon time (DBT) and the door-to-angiography time (DAT) were compared between Doctor Heli delivered group (DHG) and grand ambulance car delivered group (GACG).

[Results]Total 32 patients were included and all patients were survived. Seven patients were DHG and the other 25 patients were GACG. All DHG were diagnosed as AMI at the site by doctor of the helicopter with mobile 12-lead electrocardiography. DHG had significantly shorter average DBT and DAT than GACG (45.3 min±12.0 vs 78.6±30.2 min p <0.01 and 19.1 min±5.3 vs 49.5±26.0 min p <0.01).
[Conclusion]Our results revealed DH is effective for shortening DBT and DAT. These were mainly due to early diagnosis and rapid PCI preparation in hospital.

No conflict of interest

THE CLINICAL TWINS, ACUTE CORONARY SYNDROME AND TAKOTSUBO SYNDROME: ARE THEY MUTUALLY EXCLUSIVE?

S. Y-Hassan[1], L. Henareh[1]
[1]Cardilogy, Karolinska Institute, Stockholm, Sweden

Background and Objectives: Post-ischemic myocardial stunning (PIMS) is "caused" mainly by acute coronary syndrome (ACS). In spite of being a major physical stressor, ACS is still regarded as an exclusion criterion for takotsubo syndrome (TS). The aim of the study is to find out an association between ACS, PIMS and TS.

Methods: A series of nineteen patients with ACS having an acute coronary culprit lesion on coronary angiography and signs of left ventricular wall motion abnormality (LVWMA), which extended beyond the supply region of the diseased coronary artery, were studied.

Results: Thirteen out of the nineteen patients (68%) were women. Ages ranged from 37 to 85 years old. Eleven of the patients had non ST-elevation myocardial infarction and eight had ST-elevation myocardial infarction. All patients had clinical signs consistent with PIMS. The distribution of the LVWMA went beyond the supply region of the diseased coronary artery in all patients. Interestingly, the stunned myocardium was remote from the diseased artery in some of the patients. The pattern of the LVWMA had also a peculiar ballooning appearance during systole in 18 of the patients. These features and the reversible nature of the LVWMA were also consistent with TS. In all patients, there was no evidence of any emotional or physical stress factor apart from the ACS event.

Conclusion: PIMS and TS are two (among others) different names for the same clinical condition. ACS and TS are not mutually exclusive. ACS, as any other physical stress factor, may trigger rather than exclude TS.

No conflict of interest

SAFETY AND EFFICACY OF FEMORO-POPLITEAL CHRONIC TOTAL OCCLUSIONS RECANALISATION USING THE OCELOT, OCT-GUIDED INTRALUMINAL CROSSING SYSTEM. SINGLE CENTER EXPERIENCE.

A. Cioppa[1], L. Salemme[1], E. Stabil[1], A. Pucciarelli[1], G. Popusoi[1], V. Ambrosini[1], L. Cota[1], T. Tesorio[1], G. Sorropago[1], V. Virga[1], E. Laurenzano[1], G. Biamino[1], P. Rubino[1]
[1]Division of Invasive Cardiology, Montevergine Clinic, Mercogliano, Italy

Background: Superficial femoral artery(SFA) total chronic occlusion (CTO) is a challenge procedure for the interventionists. This procedure is time consuming, with a large amount of X-Ray for the patient and clinicians and with poor procedural success and not so cost-effectiveness. The aim of this study was to evaluate the safety and effectiveness of a new system, based on Optical Coerence Tomography (OCT) and rotation to intraluminally pass with conventional guidewires through CTO of the SFA and popliteal artery.
METHODS&RESULTS The OCELOT System (Avinger, USA) uses a combination of OCT tecnology and rotational power for intraluminal crossing of long CTO. The system was evaluated in 30 severely symptomatic patients (Rutheford Class ≥4) patients (24 men; mean age 69 years (range 41-87) with femoropopliteal CTOs averaging 135 mm in length (range 70-310). Only acute trhombotic or severely calcified occlusion were excluded. After successful recanalization occluded segments were treated with balloon angioplasty, drug eluting balloon and provisional stents based on the operators choice. **Results:** Procedure success was 94% (28/30). The average activation time was 7.5 minutes (range 3,5 -18). In the remaining true lumen was achieved with support catheter in one case and Pioneer re-entry System (Medtronic) in the other. All the CTOs were successfully recanalized. No perforation or other procedural related complication occurred. Stent implantation was needed in 11 cases (39%) with mean stented segment length was 85 (range 30-150).
CONCLUSIONS This system, is a safe and effective device for the treatment of peripheral CTOs in terms of time and materials consuming and fluoro exposure.
Femoro-Popliteal-Artery.Crhonic-Total-Occlusion.Optical-Coherence-Tomography.Recanalization-procedure.

No conflict of interest

ENDOCARDITIS AFTER TRANSFEMORAL AORTIC VALVE IMPLANTATION IN A PATIENT WITH OSLER-WEBER-RENDU SYNDROME.

A. Castiglioni[1], A. Pozzoli[1], F. Maisano[1], O. Alfieri[1]
[1]Heart Surgery, San Raffaele Scientific Institute, Milano, Italy

Transcatheter aortic valve implantation (TAVI) was introduced in 2007 as an alternative treatment for patients with severe aortic stenosis, who are considered at too high risk for surgical replacement. Few cases of postoperative infection by TAVI device are reported in the literature. We report the case of a patient with Osler-Weber-Rendu (OWR) syndrome, in which the TAVI procedure was preferred at the outset to avoid the risk of bleeding. He was diagnosed with endocarditis on the TAVI device one year later; he then underwent an uneventful surgical aortic valve replacement. In these complex clinical cases it is difficult to determine a 'golden standard' treatment and the possibility of offering patients both the percutaneous treatment and the surgical replacement appears to be desirable. Correction of the valve disease improves the outcome, reducing the episodes of haemorrhage and the need for blood transfusions.

No conflict of interest

PERCUTANEOUS AORTIC VALVE IMPLANTATION IN PATIENTS WITH SEVERE AORTIC STENOSIS AND PORCELAIN AORTA: MEDIUM TERM FOLLOW UP.

I. Pascual[1], P. Avanzas[1], A.J. Muñoz-Garcia[2], D. Lopez-Otero[3], M.F. Jimenez-Navarro[2], B. Cid-Alvarez[3], R. Del Valle[1], J.H. Alonso-Briales[2], R. Ocaranza-Sanchez[3], F. Alfonso[4], J.M. Hernandez[2], R. Trillo-Nouche[3], C. Moris[1]
[1]Cardiology, Hospital Universitario Central de Asturias, Oviedo, Spain
[2]Cardiology, Hospital Universitario Virgen de la Victoria, Malaga, Spain
[3]Cardiology, Hospital Clinico Universitario, Santiago de Compostela, Spain
[4]Cardiology, Hospital Clinico San Carlos, Madrid, Spain

Introduction and objectives
Little is known about transcatether aortic valve implantation in patients with severe aortic stenosis and porcelain aorta. The primary end point was to evaluate 2 year total mortality rate after self-expanding CoreValve prosthesis implantation, in severe aortic stenosis patients with and without porcelain aorta.

Methods
Multicenter, observational and prospective study. An expandable CoreValve prosthesis was implanted in 449 patients with symptomatic severe calcified aortic stenosis at three centers. 36 (8%) met porcelain aorta criteria.

Results
Porcelain aorta group showed higher rates of extracardiac arteriopathy [11(30,6%) vs 49(11,9%), p=0,002], previous coronary revascularization [15(41,7%) vs 98(23,7%), p=0,017] and dyslipidemia [26(72,2%) vs 186(45%), p=0,02]. General anesthesia [15(41,7%) vs 111(16,9%), p=0,058], and axillary approach [9(25%) vs 34(8,2%), p=0,004] were more frequently used in the porcelain aorta group. Success rate (94,4% vs 97,3%, p=0,28) and complications rate [7(19,4%) vs 48(11,6%), p=0,20] were similar in both groups. There were no differences in the primary endpoint at 24 moths follow up [8 (22,2%) vs 66 (16%), p=0,33]. In multivariate analysis, the presence of complications during the procedure (HR 2,6; IC 95% 1,5-4,5; p=0,001) was the unique independent predictor of 2 year mortality.

Conclusions
Transcatheter implantation of the CoreValve self-expanding aortic valve prosthesis in patients with severe aortic stenosis and porcelain aorta, rejected for surgery, is feasible and safe.

No conflict of interest

CLINICAL FOCAL NEUROLOGICAL IMPAIRMENT AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION

P. Avanzas[1], R. Del Valle[1], I. Pascual[1], A. Suarez[1], B. Camacho[1], E. Suarez[1], M. Martin[1], C. Corros[1], M. Rodriguez[1], A. Garcia[1], J. De la Hera[1], J. Rubin[1], D. Calvo[1], D. Perez[1], F. Fernandez[2], C. Moris[1]
[1]Cardiology, Hospital Universitario Central de Asturias, Oviedo, Spain
[2]Anesthesia, Hospital Universitario Central de Asturias, Oviedo, Spain

Background and aims
Very limited information is available in relation to the problem of cerebral embolism in patients undergoing transcatheter aortic valve implantation (TAVI). The aim of this study was the prospective investigation of neurological impairment after transfemoral aortic valve implantation (TAVI).

Material and methods
The study included patients with severe symptomatic aortic stenosis. Other inclusion criteria were: aortic valve area <1 cm^2 (<0.6 cm^2/m^2); aortic valve annulus diameter in the range 20-27 mm; diameter of the ascending aorta at the level of the sinotubular junction ≤40 mm (small prosthesis) or ≤43 mm (large prosthesis), and femoral artery diameter >6 mm. The endpoint of the study was the presence of any clinical focal neurological impairment until discharge.

Results
The study included 100 patients with a mean age of 79.9±6.3 years, a mean aortic valve area of 0.67±0.2 cm^2 and a mean logistic EuroSCORE of 15%±13.6%. All patients underwent aortic valvuloplasty. After valve implantation, the maximum echocardiographic transaortic valve gradient decreased from 83±19 to 12.2 ±4 mm Hg. No patient presented with greater than grade-2 residual aortic regurgitation on angiography. The procedural success rate was 100%. No patient died during the procedure. Definitive pacemaker implantation was carried out for atrioventricular block in 25 patients (25%). Regarding neurological evaluation, the endpoint presented in two patients (2%) that developed cerebellar ataxias; one of them transient and another persistent.

Conclusions
Our early experience indicates that percutaneous aortic valve replacement is a safe therapeutic option for patients with severe aortic stenosis who are at a high surgical risk. The incidence of clinical neurological impairment due to the procedure is low.

No conflict of interest

COMPLICATED COURSE AFTER IMPLANTATION OF AN LAA CLOSURE DEVICE WITH EMBOLIZATION

V. Stefan[1], S. Bodenseh[1], K. Chakraborty[1], B. Sanwald[1], J. Hemker[1], H. von Korn[1]
[1]Cardiology, Krankenhaus Hetzelstift, Neustadt an der Weinstrasse, Germany

Introduction: the left atrial appendage (LAA) closure device is a modern therapeutic alternative to prevent cardiac embolism in patients with atrial fibrillation with high thromboembolic risk and contraindications for oral anticoagulation.
Case description: a 69 year-old patient with permanent atrial fibrillation, a high CHADSVASc Score (4) and a history of cerebral bleeding related to warfarin overdosage presents to our clinic for an elective LAA closure. Following standard preparations and transseptal puncture, a pigtail catheter was inserted into the LAA. After measuring the size, an Amplatzer Cardiac Plug (26x28 mm) was successfully implanted into the LAA. A tug test was performed and the sheath removed. Shortly afterwards the device embolized into the left atrium, then into the left ventricle.
A microsnare system was brought into the left ventricle, the device captured and slowly removed through the aorta to the femoral artery, where it was safely extracted. The patient suffered no procedural complications. We assume that a certain deviation of the planar axis of the device was responsible for an insufficient adherence to the LAA and for the embolization.
Conclusion: a safe retrieval of an embolized LAA closure device is possible without a surgical procedure.

No conflict of interest

CATHETER DIRECTED THROMBOLYSIS AND MECHANICAL THROMBECTOMY IN THE COMPLICATIONS OF DEEP VENOUS THROMBOSIS (PHLEGMASIA CERULEA DOLENS, PULMONARY EMBOLISM)

Z. Ruzsa[1], E. Zima[2], K. Tóth[3], Z. Vámosi[3], N. Kovács[3], Z. Jambrik[1], G.Y. Szabó[1], B. Merkely[1]
[1]Cardiac and Vascular Center, Semmelweis University, Budapest, Hungary
[2]Cardiac and Vacular Center, Semmelweis University, Budapest, Hungary
[3]Invasive Cardiology, Bács-Kiskun County Hospital, Kecskemét, Hungary

Introduction: Percutaneous thrombectomy and catheter directed thrombolysis (CDT) represent well established techniques for treatment of massive deep venous thrombosis (DVT) and submassive pulmonary embolism (SPE). The purpose of CDT is to dissolve thrombus and to restore the lumen without causing distal embolization as fast as possible. Phlegmasia cerulea dolens (PCD) is limb-treating and pulmonary embolism is a life-treating disease and both are frequent complications of a massive iliofemoral thrombosis.

Methods: We have analysed our patients clinical and interventional data treated in 2011 and 2012 with complicated DVT. We have examined retrospectively the efficacy and safety of CDT in the treatment of SPE and PCD. Diagnosis was made by clinical examination, duplex ultrasound and in the case of SPE with computer tomography. The access site for SPE was the femoral, and for PCD the femoral or the popliteal vein. Caval filters were implanted from jugular or from femoral veins. After the sheath advancement, occlusions were passed with a 0.035 guidewire and CDT was started with Alteplase for 24 hours. After 24 hours, control angiography was performed and the CDT was maintained when the thrombus burden was flow limiting. The CDT was stopped when the thrombus disappeared. When the CDT was not successfull, manual thrombectomy was performed. In the case May Turner syndrome, angioplasty was performed and self-expandable stents were implanted. Postoperatively, patients were treated with systemic anticoagulation, compression hose, and interval follow-up.

Results: 24 patients were treated with a mean age of 65±23 years. CDT was successful in all petients treated with SPE (n=14, 100%) and with PCD (n=10, 100%). The CDT time in SPE was 28 ± 7 hour, but in PCD was 32 ± 8 hor. Mechanical thrombectomy was performed in one patient (n=1, 7.1%) in PE and in six patients (n=8, 80%) in PCD. Nine patients (n=9, 100%) had resolution of PCD, but in one patient surgical embolectomy was necessary. Venous angioplasty and stenting was necessary in 4 patients. Additional caval filters were implanted in 6 cases in the whole population (n=6, 28.6%).

Conclusion: Percutaneous treatment of complicated DVT has excellent results with catheter directed thrombolysis, however additional mechanical thrombectomy and angioplasty is necessary in several patients.

No conflict of interest

MILD STENOSIS MAKES PROGNOSIS OF VASOSPASTIC ANGINA WORSE

H. Watanabe[1], F. Takatsu[1], A. Miura[1], K. Hirayama[1], N. Kano[1], M. Ito[1], S. Ishikawa[1], M. Koyasu[1], T. Uchikawa[1], K. Takemoto[1], M. Watarai[1]

[1]cardiology, Anjo Kosei Hospital, Anjo, Japan

>Objective. Several studies have demonstrated that significant coronarynarrowing make the prognosis of vasospastic angina (VAP) worse. However, the effectsof various factors on the prognosis of patients without significant arterialnarrowing have not yet been demonstrated. **Methods and Results.** We investigated 1,248 consecutive patients with VAP who had not coronarystenosis of 50%. The meanfollow-up was 11.7±6.8 years.Ninety-one patients (7.3%) developed unstable angina, acute myocardialinfarction, or effort angina with new coronary narrowings. Thirty patients(2.4%) died suddenly. Multivariate analysis showed that the presence ofcoronary stenosis, even if trivial, made the prognosis worse (p=0.027, odds-ratio [OR], 1.66; and 95% confidence interval [CI], 1.06-2.61). And, curiously,female patients had a better prognosis than males (p=0.007;, 0.35; and 95% CI,0.16-0.75). Other factors, such as hyperlipemia,diabetes and hypertension did not affect the prognosis.

Conclusions. In patients with VAP, the presenceof coronary narrowing, even if mild, was associated with worse

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CLINICAL MEANING OF FRAMINGHAM RISK SCORE, FLOW-MEDIATED DILATION, PULSE WAVE VELOCITY, AND BIO-MARKERS IN PATIENTS WITH STABLE ANGINA

K. Park[1], W. Park[1], S. Jo[1], H. Kim[1], S. Han[1]
[1]Cardiology, Hallym University Sacred Heart Hospital, Anyang Gyeonggi-do, Korea

Background: Although the age-adjusted Framingham risk score (AFRS), flow-mediated dilation (FMD), brachial-ankle pulse wave velocity (baPWV), high-sensitivity C-reactive protein (hsCRP), and fibrinogen predict future cardiovascular events (CVEs), a comparison of these risk assessments for patients with stable angina has not been done.

Methods and Results: Among 187 consecutive patients with stable angina, 104 (56%) patients had significant coronary artery disease on coronary angiography and 76 (41%) patients underwent percutaneous coronary intervention or coronary artery bypass graft surgery. All patients had a three-year clinical follow-up and were evaluated for CVEs, including myocardial infarction, de-novo coronary artery revascularization, in-stent restenosis, stroke, and cardiovascular death. During the study period, CVE occurred in 17 (9.1%) patients. ROC analysis was used to predict CVEs. For AFRS, hsCRP, and FMD, the area under the ROC curves were 0.778, 0.744, and 0.733, respectively (all $p<0.01$). However, the baPWV and fibrinogen showed marginal significance in predicting CVEs (0.647, $p=0.055$ and 0.639, $p=0.063$, respectively). A Cox proportional hazard analysis showed that AFRS was an independent predictor of CVE (HR 3.596, 95% CI 1.619-7.985, $p<0.01$) and FMD showed marginal significance (HR 0.878, 95% CI 0.770-1.002, $p=0.05$).

Conclusions: In patients with stable angina, AFRS was an independent predictor of CVEs, and FMD showed marginal significance. In addition, there was no addictive predictive value of FMD on the AFRS in predicting CVEs.

No conflict of interest

PREDICTORS OF REGRESSION OF CORONARY ARTERY ANEURYSMS AFTER KAWASAKI DISEASE

Y. Kudo[1], K. Suda[1], S. Kishimoto[1], Y. Teramachi[1], H. Yoshimoto[1], T. Matsuishi[1]
[1]Pediarics and Child Health, Kurume University, Kurume, Japan

Background: To determine predictor of regress of coronary artery aneurysms (CAA) caused by Kawasaki disease (KD).

Method: Subjects were 57 (41 males and 16 females) patients with KD treated with intravenous immunoglobulin (IVIG). Dilation with coronary artery diameter more than 1.5 times of population normal was registered as CAA. Forty one patients required additional treatment including IVIG (12) and steroid (25). Age at onset was 2.7 years old and fever lasted 13.5 days. All patients were placed on oral aspirin and underwent regular follow up with echocardiography and coronary angiography. We determined regression by coronary angiography when CAA disappeared with smooth vessel wall. Demographic and laboratory data were compared in regressed CAA and persistent CAA and the predictor of regression was determined using Cox proportional hazard analysis.

Results: In 57 patients, we found 96 CAA (53 in LCA and 43 in RCA). The size of CAA was 4.9 mm in LCA and 4.8 mm in RCA. Though 85% regressed in LCA, but only 63% regressed in RCA ($p<0.02$) at 0.7 (0.03-3.2) years after the onset. In regression of CAA, max CAA was significantly smaller (4.5 vs. 6.5 mm, $p<0.0002$ in LCA and 4.3 vs. 5.6 mm, $p<0.04$ in RCA) and min Alb was significantly higher (27 vs. 22 g/L, $p=0.05$ in LCA and 29 vs. 25 g/L, $p<0.05$ in RCA) than in persistent CAA. Cox proportional hazard analysis identified max CAA [Exp=0.774 (0.611-0.982), $p<0.03$] as the predictor of regression. CAA <5.5 mm significantly more regressed than CAA >= 5.5 mm (97% vs. 63%, $p<0.002$ in LCA and 75% vs. 27%, $p<0.01$ in RCA).

Conclusions: CAA after KD frequently regresses less than 1 year after the onset with significantly higher tendency in LCA. Obviously we must control inflammation as soon as possible to prevent development of CAA.

No conflict of interest

SYSTEMATIC LITERATURE REVIEW OF PROGNOSTIC VARIABLES ASSOCIATED WITH BEING IN THE LAST YEAR OF LIFE IN PATIENTS WITH HEART FAILURE

A. Gadoud[1], U. Macleod[1], M.J. Johnson[1]
[1]Hull York Medical School, University of Hull, Hull, United Kingdom

Background: Palliative care is recognised as important in advanced heart failure but is complex with no clear evidence for any specific model of care and has not been widely introduced. One barrier is the perceived difficulty in prognostication.

Aim: To determine prognostic variables associated with being in the last year of life in adult patients with heart failure (with left ventricular dysfunction and preserved function).

Methods: Systematic literature review. Cochrane Library, MEDLINE, Embase, CINAHL, BNI, AMED, Web of knowledge (including conference proceedings) and trial registers were searched.

Results: 189 full text articles were retrieved and 32 met the eligibility criteria. Even excluding poor quality studies there remains a plethora of proposed prognostic variables. However the studies were often in restricted populations such as trial patients or patients awaiting transplant and so not generalised to the population as a whole. Prognostic variables identified included demographic, clinical, laboratory, ECG and echocardiographic as well as models with multiple predictors. Descriptive analysis was undertaken as most variables were only identified once or were adjusted using different variables in the regression models making meta-analysis unfeasible.

Conclusions: The large number of variables confirms that prediction of the last year of life is not easy in this patient group. Change over time may be more helpful. However, for the assessment of supportive and palliative care needs, it is likely that use of prognostic markers will not provide a clinically useful prompt. An integrated approach with palliative care based on need rather than prognosis may be more useful.

No conflict of interest

ISCHEMIC STROKE DUE TO SERIOUS VIPER ENVENOMATION

C.M. chani[1]
[1]*Pôle d'anesthésie-réanimation, hôpital militaire mohamed V, Rabat, Morocco*

Ischemic stroke due to serious viper envenomation

(Author Pr M.Chani)

An ischzmicstrokeisa rare complication of viper envenomation, probably to multifactorial pathophysiological mechanism.
We report a case of a 55 years old patient who was bitten by a snake (species cerastes cerastes). The patient had been admitted to the ICU with multiple organs failure (Disturbance of consciousness, disseminated intravascular coagulation (DIC), rhabdomyolysis, anuria and elevated troponin). The persistence of impaired consciousness prompted the use of a brain scan which revealed a bifocal stroke ischemia. The recovery was successful a few weeks later by injecting Heparin by hemodialysis, despite the initial infusion of inappropriate antivenom (FavAfrique) due to late identification of reptile.

Snake's bites rarely develop to cerebral infarction: in series of 309 patients, only eight cerebrovascular complications (2.6%) have been reported, including seven of hemorrhagic and only one of ischemic type. The complex venom of the species C cerastes contains several procoagulant proteins that produce hypotension, tissue necrosis, kidney damage and coagulopathies type DIC. Preventive treatment of complications of envenomation by C. cerastes is based on specific antivenom (Favirept ®).

No conflict of interest

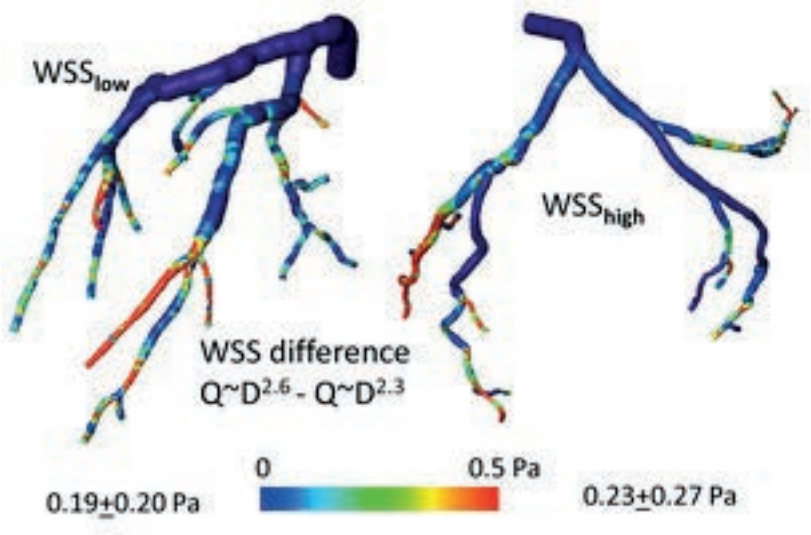
SENSITIVITY OF WALL SHEAR STRESS CALCULATION IN CORONARY ARTERIES TO CHANGES IN MODELING OF BRANCHING FLOW

E. Wellnhofer[1], J. Osman[2], R. Mevert[2], U. Kertzscher[2], K. Affeld[2], L. Goubergrits[2]
[1]Internal Medicine/Cardiology, German Heart Center Berlin, Berlin, Germany
[2]Biofluid Mechanics Laboratory, University Medicine Charité, Berlin, Germany

Background:
Side-branches have a crucial impact on calculation of wall shear stress (WSS) by numerical integration of the Navier-Stokes differential equations for incompressible fluids (CFD) due to splitting of flow (Q) at bifurcations. The ratio of Qbranch1 to Qbranch2.is related to branch diameter (D) by a power law with exponents (E) experimentally determined between 2.6 and 2.3. The impact of these variations of modelling the the splitting of flow at bifurcations on the sensitivity of WSS by CFD is analyzed.

Methods:
Vascular trees from 2 left coronary arteries stratified with respect to WSS (obstructive CADwith 16 end branches (WSShigh) and aneurysmatic CAD (WSSlow) with 15 outlets) were reconstructed from biplane angiograms. Flow simulations were performed by CFD based on patient specific data. Outlet conditions were assumed as $Q \sim D^{2.6}$ and $Q \sim D^{2.3}$ respectively. Percent area with WSS<0.4 Pa, mean WSS and correlation were assessed.

Results:
Mean WSS was 4.2±3.3 Pa and 4.2±3.5 Pa in WSShigh and 1.87±1.69 Pa and 1.83±1.77 Pa in WSSlow. Mean local differences are presented fig):



The difference is small (deep blue = ~0), is similar in aneurysmatic and obstructive CAD, but increases with decreasing vessel diameter. Percent area with WSS<0.4Pa was 1.15 % and 0.8 % in WSShigh and 7.56 % and 7.55 % in WSSlow. Squared correlation ranged between 0.9849 and 0.9867 and the regression slope was 1.059 with E=2.6 as y and E=2.3 as x.

Conclusion:
Calculation of wall shear stress in coronary arteries by numerical simulation is not sensitive to small changes in outlet boundary conditions.

No conflict of interest

COMPUTER APPLICATIONS

EFFECTIVENESS OF NEW TECHNOLOGIES OF INFORMATION AND COMMUNICATION IN STEMI: REDUCING TIME DELAYS – INCREASING CORONARY REPERFUSION

M. García-González[1], F. Bosa-Ojeda[1], M. Cordero[1], E. Gonzalez-Cabeza[1], M. Posca-Maina[2], F. Redondo Sevilla[2], M. Padilla-Perez[1], J. Gonzalez-Gonzalez[1], A. Jimenez-Sosa[1], M. Santana-Martín[3]
[1]Coronary Care Unit, Hospital Universitario de Canarias, La Laguna, Spain
[2]112 - SUC, Servicio Canario de la Salud, La Laguna, Spain
[3]112-SUC, Servicio Canario de la Salud, La Laguna, Spain

Objective: To analyze the impact of new information and communication technologies (ICTs) device Mbeat implementation in ambulances of Emergency Department of Canary Islands (SUC – 112) during the first year of operation of a network of care for STEMI.

Method: We studied a cohort of 177 consecutive patients with STEMI from December 2011 to March 2013. The study population was divided according to the access path into two groups: Group 1: patients that directly access to catheterization laboratory by SUC-112 after completion of ECG 'on the ground', transmitted electronically to the cardiologist on call; Group 2: patients who access by conventional means. The following times are defined and studied: T1: (delay attributable to the patient), T2: (diagnostic delay) T3: (delay attributable to the system) and T4: (total ischemia time).

Results: The mean age in group 1 was 60,4±11,5years) versus 62,4±14,6). The GRACE score in group 1 was 164±42 vs 175±60 (p <0,05). There were no significant differences between the groups with regard to electrocardiographic infarct location. In group 1 there were treated a significantly higher number of patients treated with primary PCI (95.4% vs 63.3%, P <.01). In addition, it was observed in group 1 significantly greater reduction in T1: 80 min vs 120 min (p <0.003); T3: 128 min vs 187 min (p <0.01); and T4: 210 min vs 330 min (p <0.001). There were no difference in T2: 5 min vs 9 min (p = 0.058).

Conclusions: The use of the new device MBeat in emergency health care of STEMI patients is highly effective to increase the level of primary coronary revascularization and minimize delays for implementing the same.

No conflict of interest

THE ACOUSTIC CAD-SCORE - A NOVEL NON-INVASIVE METHOD FOR DIAGNOSING CORONARY ARTERY DISEASE

S. Winther[1], S.E. Schmidt[2], H.E. Bøtker[3], E. Toft[2], J.J. Struijk[2], M. Bøttcher[4]
[1]Department of Cardiology, Aarhus University Hospital, Aarhus N, Denmark
[2]Department of Health Science and Technology, Aalborg University, Aalborg, Denmark
[3]Department of Cardiology, Aarhus University Hospital, Skejby, Denmark
[4]Department of Cardiology, Hospital Unit West, Herning, Denmark

Purpose

An acoustic CAD-Score is an easy, safe and low cost alternative to diagnose CAD. CAD-Score is obtained by computed analysis of diastolic heart sounds from the chest wall. The aim of this study was to investigate the added diagnostic value of combining CAD-Score with the coronary calcium score (CCS).

Method

We included 182 patients with symptoms of CAD referred to either invasive coronary angiography (CAG) (n=113) or cardiac CT (n=69). All patients were CT-scanned for CCS. When significant coronary stenosis was not ruled out in the cardiac CT group a CAG was performed. Significant CAD was defined as ≥50% stenosis in CAG measured by quantitative analysis. We excluded 61 patients from the study because of previous coronary stent treatment (n=25), short diastasis period (n=23), arrhythmias (n=3), recordings with excess noise (n=9) and lack of CCS (n=1).

Results

Study characteristics for patients with and without coronary stenosis and logistic regression analysis are listed in Table 1. There was a weak correlation between CAD-Score and CCS (Spearman's rho: 0.42).Diagnostic accuracy for detecting coronary stenosis evaluated by area under the receiver-operating curves was 76 (CI: 66-87) for CAD-Score, 80 (CI: 71-89) for CCS and 83 (CI: 73-90) for the combined CCS and CAD-Score. The results were not statistically significant.

Conclusion

This study indicated that the physiological origin of coronary microbruits is related to stenosis and not cononary calcium. The diagnostic accuracy for CAD-Score is comparable to the CCS and interestingly the study revealed a trend towards increased diagnostic accuracy when combining these tests.

Coronary stenosis	**Yes (n=28)**	**No (n=93)**	**p-value**	**Odds ratio for coronary stenosis**
Age, years	65 (±8)	60 (±10)	<0,01	1,030 (CI: 0,974-1,088, p=0,30)
Gender, male	68%	45%	<0,05	1,526 (CI: 0,549-4,245, p=0,42)
Diabetes	11%	7%	=0,51	1,173 (CI: 0,210-6,545, p=0,86)
Calcium score	666 (±852)	167 (±335)	<0,0001	1,001 (CI: 1,000-1,002, p=0,06)
CAD-Score	34 (±12)	22 (±12)	<0,0001	1,051 (CI: 1,008-1,095, p=0,02)

Table 1: Study characteristic *for patients with and without coronary stenosis* (±SD), p-value and *odds ratio for verified coronary stenosis*

Conflict of interest

LIPIDS AND ATHEROSCLEROSIS

STTHOMASHOSPITALCARDIOPLEGIC SOLUTION ADDED TO THE PROPOFOL IS AFFECT OF ISCHEMIA REPERFUSION INJURY ON ISOLATED PERFUSED NORMAL AND HYPERCHOLLESTEROLEMIC RABBIT HEARTS

I. algin[1]
[1]*kalp ve damar cerrahisi, Ozel Korfez hastahanesi, balikesir, Turkey*

Objective: Propofol is an anesthetic agent that is used in cardiovasculer surgery. It is known that propofol is cardioprotective at supratherapetic doses. The aim of the study was the effect of propofol addition to St.Thomas Hospital cardioplegic solution on ischemia-reperfusion injury in isolated perfused normal and hypercholesterolemic rabbit hearts.

Material- Method: Male New Zeland rabbits weighing between 2500 and 3500 g were used. Half of the rabbits were feeded by normal diet, half of them were feeded by hypercholesterolemic diet. Rabbits were fasted but allowed free access to water overnight before the onset of the experiments. The rabbits were anesthetized with 60 mg/kg of sodium pentobarbital injected by ear vein. The thorax was opened hearts were rapidly excised, immediately cooled in iced in Krebs Henseleit buffer and perfused by an aortic canula delivering warm oxygenated buffer at a constant flow. After the stabilization period at the 10th minute ischemi induced. At the beginning of the ischemic period 20 ml/ kg ST Thomas Cardioplegic solution was injected via aortic canula. At the 10th and at the 20th minute of the ischemic period 10 ml/ kg ST Thomas cardioplegic solution were injected. At the groups with propofol 100µ? propofol was added the ST Thomas Hospital cardioplegic solution. At the end of the ischemic period heart was perfused by oxygenated Krebs Henseleit buffer again and experiment ended. Data were expressed mean ± Standard derivation. Statistical analysiswas evaluated by Student's t test. The p value less than 0.05 was considered to be statistically significant.

Results: Propofol addition to St.Thomas Hospital cardioplegic solution onischemia-reperfusion injury in isolated perfused normal rabbit hearts were inhibited dp/dt_{max} level at 2., 4., 6., 8. and 10. minutes and hypercholesterolemic rabbit hearts were were inhibited dp/dt_{max} level at 6., 8. and 10. minutes statistically significant ($p<0.05$).

No conflict of interest

CHANGES OF MEAN PLATELET VOLUME AFTER EXTRACORPOREAL LDL-CHOLESTEROL ELIMINATION

M. Blaha[1], M. Kostal[1], V. Blaha[2], M. Lanska[3], P. Zak[3]
[1]4th Dpt. of Medicine Hematology,
University Hospital Hradec Králové and Medical Faculty Charles University in Hra, Hradec Králové, Czech Republic
[2]3rd Dpt of Medicine Geriatry and Metabolism,
University Hospital Hradec Králové and Medical Faculty Charles University in Hra, Hradec Králové, Czech Republic
[3]4th Dpt of Medicine Hematology,
University Hospital Hradec Králové and Medical Faculty Charles University in Hra, Hradec Králové, Czech Republic

Objective: Mean platelet volume (MPV) is arousing increasing interest as a new independent cardiovascular risk factor. Large platelets are likely to be more reactive. If MPV would drop after LDL-lowering therapy, decreased MPV could be one of the markers of successful therapy. Therefore, we investigated mean platelet volume after extracorporeal LDL-cholesterol elimination.
Methods: MPVas investigated in patients with severe familial hypercholesterolemia long-term treated (3-12 years) by LDL-apheresis (immunoapheresis) or cascade filtration. Plasma was obtained by centrifugation. Adsorbers Lipopak 400 were used for immunoapheresis and filters Evaflux 4A were used for cascade filtration. 95 pair samples were measured (before and after the procedures) in a group of 12 patients - each patient 8 times in 4 years.

Results: MPVefore the procedures was 10.891 fl, CI 10.25-11.53. MPV after the procedures decreased - 10.478 fl, CI 09.84-11.11. The difference is statistically significant (p = 0.036). MPV did not correlate with age, sex, platelet count, duration of therapy. At the same time, we used rheohemapheresis in the therapy of 40 patients with age-related macular degeneration. But mean platelet volume was not changed.

Conclusion: MPV is easily available and is often disregarded, and sometimes may suggest the need for a careful assessment in patients with familial hypercholesterolemia. MPV could be one of the markers of therapeutic efficacy in patients with familial hypercholesterolemia treated by extracorporeal LDL-cholesterol elimination that are simple and inexpensive.

Acknowledgements
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No conflict of interest

LIPOPROTEIN ASSOCIATED PHOSPHOLIPASE A2 (LP-PLA2) IS INCREASED AFTER TRANSCATHETER AORTIC VALVE IMPLANTATION (TAVI) IN PATIENTS OLDER THAN 80 YEARS

V. Bláha[1], J. Bis[2], J. Stásek[2], C. Andrys[3], J. Vojácek[2], L. Sobotka[1]
[1]IIIrd Dept.Internal Medicine - Metabolism and Gerontology,
University Hospital Hradec Králové and Medical Faculty Charles University in Hra, Hradec Králové, Czech Republic
[2]Ist Dept.Internal Medicine - cardioangiology,
University Hospital Hradec Králové and Medical Faculty Charles University in Hra, Hradec Králové, Czech Republic
[3]Dept. Immunology and Alergology,
University Hospital Hradec Králové and Medical Faculty Charles University in Hra, Hradec Králové, Czech Republic

Objective: Lp-PLA2 is extensively expressed within the necrotic core of advanced human atherosclerotic lesions, and may play a role in promoting plaque instability. We hypothesize that Lp-PLA2 will associate with advanced atherosclerosis in the elderly and will further increase after TAVI indicated due to the degenerative aortic valve stenosis.
Methods: 44 patients (19 men, 25 women) aged 82.3 ± 5.8 years with symptomatic severe aortic stenosis undergone TAVI (n=35; or transfemoral, n=27; or transapical, n=8) or balloon angioplasty (BA) (n=9). Plasma Lp-PLA2 mass was measured using an enzyme-linked immunosorbent assay (USCN Life Science, P.R.C.) before and 3 days after procedure.
Results: In-hospital combined safety endpoints comprised 1 death (3%) due to the cerebrovascular event after TAVI. During the 2 year follow-up period, there were 3 (9%) deaths in the TAVI group (1 cardiovascular, 1 cerebrovascular and 1 infectious event). Lp-PLA_2 mass was elevated in patients older than 80 years with symptomatic severe aortic stenosis (1290 ± 60 ng/mL before TAVI; 1435 ± 86 ng/mL before BA), and further increased after TAVI (1609 ± 85 ng/mL, P<0.01) or BA (1788 ± 105 ng/mL, P<0.01).
Conclusion: Elevated Lp-PLA2 may be a novel biomarker of vulnerability of rupture-prone atherosclerotic lesions with lipid necrotic core in selected patients aged ≥80 years with symptomatic severe degenerative aortic valve stenosis. While it further significantly increases after treatment with TAVI the selective inhibition of Lp-PLA2 should be considered as a strategy to treat advanced atherosclerosis.
Acknowledgements: Supported by projects IGAMH CR NT/12287-5, PRVOUK P37/12.

No conflict of interest

IMBALANCE OF VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) IN DIABETES MELLITUS TYPE 2

V. Bláha[1], J. Stásek[2], C. Andrys[3], J. Bis[2], J. Vojácek[2], L. Sobotka[1]
[1]3rd Dept. Internal Medicine - Metabolism and Gerontology,
University Hospital Hradec Králové and Medical Faculty Charles University in Hradec Králové,
Hradec Králové, Czech Republic
[2]1st Dept. Internal Medicine - Cardioangiology,
University Hospital Hradec Králové and Medical Faculty Charles University in Hradec Králové,
Hradec Králové, Czech Republic
[3]Dept. Immunology and Alergology,
University Hospital Hradec Králové and Medical Faculty Charles University in Hradec Králové,
Hradec Králové, Czech Republic

Objective: Expression of vascular endothelial growth factor (VEGF) contributes to formation of collateral vessels in coronary atherosclerosis, but there has been shown an insufficient collateral vascular formation in diabetic patients. Therefore, we investigated VEGF in the elderly patients with advanced atherosclerosis, and evaluated the impact of the endovascular therapy of symptomatic severe degenerative aortic valve stenosis.
Methods: Patients with advanced atherosclerosis and diabetes mellitus type 2 (T2DM) (n=18; age 79,2 ± 1,6 years) and non-diabetic subjects (n=25; age 84,4 ± 0,7 years) with symptomatic severe aortic stenosis undergone endovascular therapy by transcatheter aortic valve implantation (n=35) or balloon angioplasty (n=9). Plasma VEGF was measured using an enzyme-linked immunosorbent assay kit (Quantikine human VEGF, R&D Systems, USA) before and after procedure.
Results: Plasma VEGF significantly increased after endovascular procedure in both groups (with and without T2DM) (P< 0,05). However, the VEGF in T2DM patients was constantly significantly lower than in non diabetic patients (P< 0,05).

VEGF (pg/ml)	**Before procedure (mean ± SD)**	**24 hours (mean ± SD)**	**72 hours (mean ± SD)**	**1 month (mean ± SD)**
Non-diabetics (n=26) 325±22		440±30*	489±47*	386±38
T2DM (n=18)	295±76#	387±64*	323±69*#	283±47#

*[*P<0,05 during the time, #P<0,05 T2DM vs non diabetic patients]*

Conclusion: Increased plasma VEGF associates with advanced atherosclerosis in the elderly patients with symptomatic severe degenerative aortic valve stenosis. However down regulation of the VEGF can be involved in aggravation of ischemic state in diabetic patients.
Acknowledgements: The study was supported by projects IGA MH CR No.NT/12287-5, PRVOUK P37/12.

No conflict of interest

GINSENOSIDE RG2 INHIBITS LIPOPOLYSACCHARIDE-INDUCED ADHESION MOLECULE EXPRESSION IN HUMAN UMBILICAL VEIN ENDOTHELIAL CELL

Y. Cho[1], C. Kim[1], H. Ahn[1]
[1]Pharmacology, Chungbuk National University College of Medicine, Cheongju, Korea

Vascular cell adhesion molecule 1 (VCAM–1), intercellular adhesion molecule 1 (ICAM–1), P– and E–selectin play a pivotal role for initiation of atherosclerosis. Ginsenoside, a class of steroid glycosides, is abundant in ***Panax ginseng*** root*,* which has been used for prevention of illness in Korea. In this study, we investigated the mechanism(s) by which ginsenoside Rg2 may inhibit VCAM–1 and ICAM–1 expressions stimulated with lipopolysaccharide (LPS) in human umbilical vein endothelial cell (HUVEC). LPS increased VCAM–1 and ICAM–1 expression. Ginsenoside Rg2 prevented LPS–mediated increase of VCAM–1 and ICAM–1 expression. On the other hand, JSH, a nuclear factor kappa B (NF–κB) inhibitor, reduced both VCAM–1 and ICAM–1 expression stimulated with LPS. SB202190, inhibitor of p38 mitogen–activated protein kinase (p38 MAPK), and wortmannin, phosphatidylinositol 3–kinase (PI3–kinase) inhibitor, reduced LPS–mediated VCAM–1 but not ICAM–1 expression. PD98059, inhibitor of mitogen–activated protein kinase kinase/extracellular signal–regulated kinase (MEK/ERK) did not affect VCAM–1 and ICAM–1 expression stimulated with LPS. SP600125, inhibitor of c–Jun N–terminal kinase (JNK), reduced LPS–mediated ICAM–1 but not VCAM–1 expression. LPS reduced IkappaBα (IκBα) expression, in a time–dependent manner within 1 hr. Ginsenoside Rg2 prevented the decrease of IκBα expression stimulated with LPS. Moreover, ginsenoside Rg2 reduced LPS–mediated THP–1 monocyte adhesion to HUVEC, in a concentration–dependent manner. These data provide a novel mechanism where the ginsenoside Rg2 may provide direct vascular benefits with inhibition of leukocyte adhesion into vascular wall thereby providing protection against vascular inflammatory disease.

No conflict of interest

ATHEROGENIC DYSLIPIDEMIA PATTERN AMONG NEWLY DIAGNOSED,UNTREATED PATIENTS WITH TYPE 2 DIABETES MELLITUS.

L. Mistrikova[1], A. Dukat[2], S. Oravec[2], L. Fabryova[3], P. Sabaka[2], D. Balaz[2], L. Gaspar[2]
[1]Dept.of Cardiosurgery, East Slovakian Inst.of Cardiology, Kosice, Slovakia
[2]2nd.Dept.Internal Medicine, Comenius University, Bratislava, Slovakia
[3]Diabetol.unit, MetabolClinics, Bratislava, Slovakia

Introduction: Type 2 diabetes mellitus is considered to be the coronary disease (CAD) equivalent and is presented with atherogenic dyslipidemia. This is presented with the increased concentrations of triglycerides, LDL cholesterol and decreased concentrations of HDL cholesterol.

Aim: Newly diagnosed, type 2 diabetes mellitus patients, previously untreated with antidiabetic and hypolipidemic treatments, referred to the diabe-tologic centre were examined to obtain the basal pre-treatment lipid concentrations and lipid size particles.

Methods: 30 patients with newly diagnosed, manifested and untreated type 2 diabetes mellitus were examined. Followed group consisted of 11 men and 19 women age of 55.6±5.5 years, BMI 32.63±4.95, systolic BP 133.13±12.65 mmHg, diastolic BP 82.04±7.6 mmHg, C peptide 2.74±1.0, hsCRP 5.1±3.3.The results were compared to match controls (untreated, without any manifest disease, renal or malignant disease). Statistical analysis pairing was done after the age, sex, BMI (with accuracy to 3 points BMI), with paired t-test and normal distribution was confirmed with Kolmogorov-Smirnov test.

Results: Newly diagnosed type 2 diabetes mellitus pre-treatment patients have significantly increased VLDL ($p \leq 0.05$), large LDL ($p \leq 0.05$) and middle IDL ($p \leq 0.001$) concentrations, while LDL sizes remained unchanged yet. If early targeted hypolipidemic treatment could be administered, the decrease of the high residual cardiovascular risk among this group of patients can be acchieved.

Conclusions: Different pattern of atherogenic dyslipidemia is present among type 2 diabetes mellitus patients before prior treatment initializations.

Only later on during the course of the disease known typical pattern of atherogenic dyslipidemia develops.

No conflict of interest

SHORT-TERM EXERCISE AND SIZE OF LIPOPROTEIN PARTICLES AMONG HEALTHY SEDENTARY MALES.

A. Dukat[1], L. Mistrikova[2], S. Oravec[3], P. Sabaka[4], D. Balaz[5], L. Gaspar[5]
[1]2nd.Dept.Internal Medicine, Comenius University School of Medicine, Bratislava, Slovakia
[2]Dept of Cardiosurgery, East Slovakian Inst.of Cardiology, Kosice, Slovakia
[3]Comenius University, 2nd.Dept.Internal Medicine, Bratislava, Slovakia
[4]2nd.Dept.Internal Medicine, Comenius University, Bratislava, Slovakia
[5]Comenius University, 2nd.Dept.Internal Med, Bratislava, Slovakia

Introduction: Recent ESC guidelines for the primary and secondary prevention of the coronary artery disease (CAD) include regular physical activity.
Aim:Influence of short-term regular daily exercise training among young healthy sedentary males on lipoprotein subfractions in plasma was followed-up.

Subjects and methods: 19 healthy sedentery male volunteers (21-29 years old) with normal history,familiar history, physical and biochemical examina-tions, non-smokers, non-addicts with normal body mass index took part in 14 days controlled exercise programme. This consisted of quick walking and slow runing each of 15 minutes. Basal and post exercise analysis of lipoprotein subfractions concentrations (VLDL, IDL 1-3, LDL 1-7and HDL 1-10) were followed with Quantimetrix Lipoprint System Rando Beach, USA. For statistical analyses D´agostino-Pearson and Kolmogorov-Smirnov tests were used.

Results: Short-term exercise programme leads to the decrease leads to the decrease of plasmatic VLDL concentrations (26.60±6.988, 23.40±5.011,
P=0.016), as well as the large IDL particles (16.33±4.047, 14.40±3.738, P=0.005). Concentrations of the middle and small IDL remained unchanged.
Despite the unchanged total LDL concentration, significant decrease of LDL 2 (14.27±6.341, 10.93±4.234, P=0.001) was present. Small dense LDL 3-7 were present in 6 probands on basal examinations and disappeared completely after the exercise training (0.53±0.743, 0.00±0.000, P=0.031). Middle HDL particles decreased significantly (25.93±3.494, 22.93±2.963, P=0.001), but the total concentrations of HDL remained unchanged.

Conclusions: Effects of short-term exercise on serum lipids in sedentary young men to those with regular physical activity and is recommended in recent guidelines for primary prevention of CAD.

No conflict of interest

NON HIGH-DENSITY LIPOPROTEIN CHOLESTEROL IS A PRACTICAL PREDICTOR FOR LONG-TERM CARDIAC DEATH AFTER CORONARY ARTERY BYPASS GRAFTING

Y. Fukushima[1], H. Ohmura[1], H. Mokuno[1], T. Kasai[1], K. Miyauchi[1], A. Amano[2], H. Daida[1]
[1]Cardiovascular Medicine, Juntendo University, Tokyo, Japan
[2]Cardiovascular Surgery, Juntendo University, Tokyo, Japan

Background: Most universal guideline proposes non HDL-C as secondary target of lipid modification followed by LDL-C in primary and secondary prevention. However, there are few studies to investigate predictive value of non HDL-C for long-term prognosis in patients with coronary heart disease (CHD). We investigated whether non HDL-C can predict long-term cardiovascular events in CHD patients who underwent coronary artery bypass grafting (CABG).

Methods: We enrolled 1074 consecutive patients who underwent CABG at Juntendo University Hospital between 1984 and 1994, and obtained all mortality data through 2000. To investigate predictive value of non HDL-C, we divided patients into 2 groups by the median non HDL-C level and used Kaplan-Meier curves with log-rank test for statistical analyses. Cox proportional-hazard regression model was used to calculate the relative risk for cardiac death.

Results: The mean follow-up period was 10.6±3.5 years. The survival rate of cardiac death was significantly lower in the high non HDL-C group than that in the low non HDL-C group(p=0.006). Furthermore, in multivariate analysis adjusted for conventional coronary risk factors, metabolic syndrome, statin treatment, and use of artery bypass graft, the increased levels of non HDL-C remain to be independent predictor for cardiac death beyond other lipid parameters.

Conclusions: The increased levels of non HDL-C were significantly associated with an increased risk of cardiac death. Non HDL-C levels may be a practical predictor for long-term cardiac death in CHD patients who underwent CABG. We have to investigate an efficacy of non HDL-C lowering therapy for preventing cardiovascular events.

No conflict of interest

SCLO1B1 TRANSPORTER AND STATIN TREATMENT EFFICACY

J.A. Hubacek[1], D. Dlouha[2], V. Adamkova[3], M. Snejdrlova[4], M. Vrablik[4]
[1]DEM, Instutite for Clinical and Experimental Medicine, Prague, Czech Republic
[2]DEM, Institute for Clinical and Experimental Medicine, Prague, Czech Republic
[3]DPC, Institute for Clinical and Experimental Medicine, Prague, Czech Republic
[4]3rd Department of Internal Medicine 1st Faculty of Medicine, Charles University, Prague, Czech Republic

Introduction: Statins belong to drugs of first choice in patients with increased cardiovascular risk. There exists a significant inter-individual variability in statin treatment efficacy that is likely to have a strong genetic background. Gene for SCLO1B1 (codes for organic anion transporter, regulates the hepatic uptake of statins) belongs to the candidates with potential to influence the statin treatment efficacy.

Materials and methods: *SCLO1B1* rs4363657 (T>C) polymorphism was analysed on group of 310 (141 males) patients with dyslipidemia treated by statins (~90% on simvastin or atorvastatin, 10 or 20 mg per day) and 376 control males. Polymorphism was analysed using PCR-RFLP. Total-, LDL-, HDL- cholesterol and triglycerides were analysed before the treatment and after 8 - 12 weeks of treatment.

Results: After treatment, there was a significant decrease both in total (7.4±1.3?5.4±1.0 mmol/L, P<0.0001) and LDL-cholesterol (4.7±1.2?3.2±0.9 mmol/L, P<0.0005). Distribution of the individual genotypes in Czech patients (TT=62%, CT=32%, CC=6%) was similar (P=0.25) to the controls (TT=64%, CT=33%, CC=3%). Decrease of both total cholesterol (29% vs. 24%) and LDL cholesterol (34% vs. 30%) was non - significantly higher in the carriers of the CC genotype in comparison with the T allele carriers.

Conclusions: Results of the pilot study suggests that the rs4363657 variant within the gene for *SCLO1B1* transporter could be one of the genetic determinants of statin treatment efficacy. Because of the low frequency of the potentially advantageous genotype, it is necessary to analyse larger group of patients.

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No conflict of interest

ACUTE CARDIOVASCULAR TOXICITY OF STERILIZERS, PHMG AND PGH: SEVERE INFLAMMATION IN HUMAN CELLS AND HEART FAILURE IN ZEBRAFISH

J.Y. Kim[1], K.H. Cho[1]
[1]Biotechnology, Yeungnam university, gyeongsan, Korea

A putative toxicity of humidifier disinfectants in the blood circulation system was investigated in this study. In an in vivo test, zebrafish and embryos were exposed to sterilization solution containing either polyhexamethylene guanidine phosphate (PHMG) or oligo-[2-(2-ethoxy)-ethoxyethyl)-guanidinium-chloride (PGH, Akacid®). Both PHMG and PGH-treated macrophages showed increased oxLDL uptake, and HDF cells showed the most severe cellular aging. Disinfectants caused severe embryonic toxicity along with attenuated developmental speed. All zebrafish exposed to PHMG (final 0.3%) and PGH (final 10 mM) died within 75 min and displayed acute increases in serum TG level, hepatic inflammation, and fatty liver induction. Zebrafish killed by the disinfectants also showed severe accumulation of fibrous collagen in the bulbous artery of the heart with severe production of reactive oxygen species. These results suggest that household disinfectants could cause impairment of human circulation and reproduction. This work was supported by the Korea Foundation for the Advancement of Science & Creativity(KOFAC) grant funded by the Korean Government(MEST).

No conflict of interest

ACRYLAMIDE TREATMENT CAUSED MODIFICATION OF LIPOPROTEINS AND ACUTE SENESCENCE AND INFLAMMATION IN HUMAN CELLS AND ZEBRAFISH MODEL

S.M. Kim[1], K.H. Cho[1]
[1]School of Biotechnology, Yeungnam university, gyeongsan, Korea

We tested a putative toxicity of acrylamide, which is enriched in fast food and french fries, in lipoprotein metabolism and aging using human macrophage, dermal fibroblast (HDF) cell and zebrafish. Function and electromobility of HDL and LDL was modified by the acrylamide (final 50 mM) treatment with multimerization. In macrophage and human dermal fibroblast (HDF) cell, acrylamide was cytotoxic upto 1 mM (final conc.) and cause early senescence and atherogenesis. Under presence of acrylamide in cage water (final 150 ppm), the zebrafish died within 2 days with acute elevation of blood glucose and inflammation. Conclusively, acrylamide could affect lipoprotein and glucose metabolism in human serum to cause atherosclerosis and cellular senescence. Live zebrafish and its embryo showed impairment of glucose homeostasis were occurred to result acute inflammatory death.

No conflict of interest

EFFECTS OF GARLIC ON SERUM LIPID LEVEL AND A NUMBER OF EFFECTIVE HORMONES ON LIPID METABOLISM IN HYPERGLYCEMIC AND/OR HYPERLIPIDEMIC INDIVIDUALS

Y. moradi[1], F. fathi[1], S. hosseini zijoud[2], S. froughi[2], H. moradi sardareh[2], H. ghasemi[2]
[1]genetics and molecular medicine, kurdistan university of medical sciences, sanandaj, Iran
[2]nutrition and biochemistry, hamadan university of medical sciences, hamadan, Iran

Diabetes mellitus is one of the worldwide largest growing metabolic diseases. In this study the effects of consumption of raw garlic on serum lipid level, blood sugar and a number of effective hormones on lipid and sugar metabolism (thyroid hormones and insulin) in individuals either with high level of blood sugar or lipid were investigated. Eighty five volunteers having following clinical history enrolled in the study: Group 1: having blood sugar more than 126 mg/dl (30 volunteers); Group 2: having cholesterol higher than 245 mg/dl (30 volunteers); Group 3: having blood sugar over 126 mg/dl and cholesterol more than 245 mg/dl (25 volunteers). In group 1, there wasn't a significant differences between biochemical factors before and after garlic consumption, whereas, in the second group after 6 weeks of garlic consumption a decline in cholesterol ($P < 0.001$), FBS and TG ($P < 0.01$) was observed but HDL-C ($P < 0.001$) was increased. Six weeks after termination of garlic consumption, cholesterol ($P < 0.001$), FBS and TG ($P < 0.05$) were in- creased and HDL-C ($P < 0.01$) was decreased. In the third group, total cholesterol ($P < 0.001$), FBS ($P < 0.01$) and HbA1c decreased while HDL-C was in- creased. Other factors, including thyroid hormones (T3, T4), TSH and insulin showed no significant alteration. In conclusion our results shown that raw garlic consumption can reduce the FBS and Lipid in hy- perglycemic and/or hyperlipidemic individuals.

No conflict of interest

LDL-APHERESIS FOR THE TREATMENT OF PATIENTS WITH SEVERE AUTOSOMAL DOMINANT HYPERCHOLESTEROLAEMIA AND CORONARY DISEASE: THE AUSTRALIAN EXPERIENCE

R.C. OBrien[1], M. Page[2], E. Ekinci[1], G.F. Watts[2]
[1]Medicine Austin Health, University of Melbourne, Heidelberg, Australia
[2]Medicine Royal Perth Hospital, University of Western Australia, Perth, Australia

Introduction: Low density lipoprotein (LDL)-apheresis offers radical therapy for severe dyslipidaemias. We have employed this treatment at Austin Health, Melbourne and Royal Perth Hospital since 2003 and herewith present the first eight cases.

Methods: Retrospective review of hospital records and patient interviews: data extracted related to demographic, clinical and genetic status, laboratory and imaging findings, and LDL-apheresis procedures.

Results: Four patients had homozygous familial hypercholesterolaemia (FH), three had clinically heterozygous FH and one had heterozygous familial defective apoB-100. Patients had angiographically proven coronary disease. Age at commencement of LDL-apheresis was 44 ± 20 years (range 14-69). Six patients were female. LDL-apheresis was performed by cascade filtration, once every one to four weeks. 604 procedures were performed since 2003. Pre-treatment LDL-cholesterol was 9.5 ± 4.0 mmol/L (range 5.4-16.9) All patients continued on maximal cholesterol-lowering drug therapy if tolerated. Mean lowering of LDL-cholesterol with each procedure was 72.0 ± 7.4% (P<0.001); long-term time-averaged lowering was 41.3 ± 18.8% (P<0.001). Triglyceride, apolipoprotein B, lipoprotein(a) and HDL-cholesterol were also lowered. Serial ultrasonography of tendons and carotid arteries and coronary angiography were consistent with stabilisation/regression of lesions. All patients remained clinically stable. Problems included iron deficiency, adverse reactions to one batch of filtration columns and vascular access. The mean annual cost per patient was AUD $32,133 (23,081 Euro).

Conclusion: LDL-apheresis by cascade filtration is a safe, effective and well-tolerated treatment for severe hypercholesterolaemia and should be incorporated in clinical services for patients with autosomal dominant hypercholesterolaemia

No conflict of interest

OSTEOPROTEGERIN GENE POLYMORPHISM IS NOT ASSOCIATED WITH ANGIOGRAPHIC CORONARY ARTERY STENOSIS AND CALCIFICATION IN KOREAN

W. Park[1], K.H. Park[1], S.H. Jo[1], S.J. Han[1], H.S. Kim[1], S.A. Kim[1]
[1]Cardiology, Hallym University Sacred Heart Hospital, Anyang, Korea

Background: Serum level of osteoprotegerin (OPG) has been suggested to be associated with osteoporosis, early coronary artery disease and coronary calcification. However, there was little data regarding the relation of the coronary artery disease and calcification with OPG gene mutation.

Methods and Results: Four hundreds and thirty four patients referred for coronary angiography due to their chest pain were enrolled. All the patients have undergone coronary angiography and were investigated for their genetic mutations with regard to four genes: - A163G, G209A, T245G, T950C of OPG gene. Of the patients received coronary angiography, 51.8% (225/434) patients had a coronary artery stenosis defined as ≥50% diameter stenosis in at least one coronary artery. The allele frequency and polymorphisms in the 4 promoter region of OPG gene were not different between CAD and non-CAD patients (at least 1 mutant among 4 polymorphisms, 67.6% vs 65.6%, respectively, p=0.658) and were not associated with the coronary calcification.

Conclusions: OPG gene mutation was not related with coronary artery calcification or stenosis in Korean population.

No conflict of interest

SERUM AMYLOID A AS A BIOMARKER INDICATIVE OF CARDIOVASCULAR DISEASE

E. York[1], P. McKavanagh[2], P. Donnelly[2], N. Nadeem[1], P. Ball[2], L. Lusk[2], T. Trinick[3], I. Young[1], J. McEneny[1]
[1]Centre for Public Health, Queen's University Belfast, Belfast, United Kingdom
[2]Cardiovascular Research Department, Ulster Hospital, Dundonald, United Kingdom
[3]Clinical Biochemistry, Ulster Hospital, Dundonald, United Kingdom

Introduction: Atherosclerosis is characterised by the build-up of lipid-derived plaques in arterial blood vessels. High-sensitive C-reactive protein (hsCRP) is an independent cardiovascular-risk factor. Serum amyloid A (SAA) is a biomarker of chronic inflammation, transported in plasma associated with high-density-lipoproteins (HDL). This study compared the sensitivity of CRP to SAA as a candidate biomarker to screen for future cardiovascular morbidity and mortality.

Methods: Subjects referred to the rapid chest pain clinic with stable symptoms (n=500) had atherosclerotic burden assessed by cardiac computerised tomography (CCT) and conventional exercise stress test. Subjects randomised to CCT-arm (n=240) were classified as: 1) no-CVD; 2) mild-CVD, area stenosis <50%; 3) moderate/severe-CVD, area stenosis >50%. In the CCT-arm, HDL_2 and HDL_3 were isolated from serum by rapid-ultracentrifugation, serum-CRP was measured by immunoturbidity, serum-, HDL_2- and HDL_3-SAA were measured by an ELISA methodology. Concentrations were compared with CCT scores.

Results: CRP was not different across the groups; however, SAA significantly increased across the groups.

CCT-arm	No-CVD (n=106)	Mild-CVD (n=58)	Moderate/ Severe-CVD (n=76)	Trends Across the Groups
Serum-hsCRP (mg/L)	2.7±0.6[a]	2.1±0.27[a]	2.8±0.38[a]	0.132
Serum-SAA (µg/L)	17382±1511[a]	16675±1746[a]	22346±2214[b]	0.044
HDL_2-SAA (µg/mg protein)	3.7±0.27[a]	4.3±0.51[a]	5.9±0.55[b]	0.001
HDL_3-SAA (µg/mg protein)	0.33±0.04[a]	0.32±0.04[a]	0.46±0.05[b]	0.029

Results are mean±SEM. Results with different superscript letters indicate differences between groups.

Conclusion: This study has shown SAA to be more sensitive than CRP in identifying patients with stable chest-pain classified with different stages of CVD-burden. This pilot study suggests that SAA may be a valuable tool to identify patients at higher CVD-risk.

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No conflict of interest

ACUTE ALCOHOL CONSUMPTION AFFECTS LIPOPROTEIN LIPASE ACTIVITY IN VIVO.

K. Zemankova[1], J. Kovar[1]
[1]Laboratory for Atherosclerosis Research, Institute for Clinical and Experimental Medicine, Prague 4, Czech Republic

Introduction: Long-term moderate alcohol consumption has multiple effects on lipoprotein metabolism - it increases HDL-cholesterol and also lipoprotein lipase (LPL) activity. However, alcohol consumption also adversely affects the magnitude of postprandial lipemia and such an effect could be explained by an acute inhibition of LPL activity. Therefore, we tested whether alcohol consumption can acutely affect LPL activity.

Methods: Two examinations were carried out in 8 healthy male volunteers. The activity of LPL in vivo using intravenous fat tolerance test (IVFTT) was measured before, 2 and 4 hours after consumption of 32 g of ethanol (vodka). In control examination the water was given to subjects instead of alcohol. Moreover, the LPL activity and mass were measured in postheparin plasma at the end of each examination. The order of both examinations was randomized.

Results: The LPL activity measured using IVFTT was 25% and 24% lower 2 and 4 hours after alcohol administration, respectively, and was not affected in control experiment. Similarly, the LPL activity measured in postheparin plasma at the end of experiments was lower after alcohol consumption (4.6 ± 1.3 vs 6.0 ± 1.4 mmol/l/h, $p < 0.05$). The LPL mass was not significantly affected (356 ± 84 vs 403 ± 120 ng/ml).

Conclusions: The LPL activity is acutely suppressed by alcohol administration.

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No conflict of interest

Postprandial lipemia testing - does fat alone affects insulinemia during early postprandial phase?

K. Zemankova[1], L. Ourednikova[2], J. Kovar[1]
[1]Laboratory for Atherosclerosis Research, Institute for Clinical and Experimental Medicine, Prague 4, Czech Republic
[2]Faculty of Science, University of South Bohemia, Ceske Budejovice, Czech Republic

Introduction: The increased postprandial lipemia magnitude is associated with a higher risk of cardiovascular disease, however, the examination of postprandial lipemia is not usually carried out due to its length. Moreover, there is no standardized methodology of the test. Some authors use fat load alone, others prefer mixed meals containing carbohydrate. The postprandial response of insulinemia seems to be one of the most important factors regulating postprandial lipemia and it is not clear whether fat load alone can induce insulin response. Therefore we compared the response of insulinemia to a fat load and to a fat load together with carbohydrate.

Methods: Two examinations were carried out in six healthy male volunteers – they received an experimental breakfast containing 75 g of fat (cream) or 75 g of fat + 25 g of carbohydrate. The concentrations of insulin, glucose, triglyceride and nonesterified fatty acids (NEFA) in plasma were measured within 2 hours after breakfast. The order of both examinations was randomized.

Results: The addition of 25 g of carbohydrate to 75 g of fat induced a pronounced insulin response after 30 minutes (32 mIU/l increase). The fat load alone affected neither insulinemia nor glycemia. There were no significant differences in the changes of concentration of triglyceride and NEFA in early postprandial phase.

Conclusions: The addition of small amount of carbohydrate (25 g) to fat load induces physiological response of insulin and should be therefore preferred during postprandial lipemia testing.

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No conflict of interest

Addendum

PROGNOSIS, PROGRESSION AND PRACTICE PATTERNS

HYPERGLICEMIA IN ACUTE CORONARY SYNDROMES: A RISK-MARKER OR JUST A FUTILITY?

A. Castro[1], A. Pereira[1], N. Moreno[1], R. Santos[1], M.C. Queirós[1], P. Pinto[1]
[1]Cardiology, Centro Hospitalar Tamega e Sousa, Penafiel, Portugal

Introduction: Hyperglycemia is associated with in-hospital adverse outcomes in patients (pts) with acute coronary syndromes (ACS). Its association with long-term adverse outcomes is less established. Our purpose was to evaluate if admission glucose (AGL), first fasting glucose (FFG) and their variation predict adverse outcomes in ACS.

Methods: this is a retrospective study of 214 pts with ACS. In-hospital death and the occurrence of death and/or re-hospitalization for heart failure/ACS at 3, 6 and 12 months after discharge were evaluated. Pts were divided in groups according to the occurrence of those outcomes and compared regarding their demographic and clinical characteristics, type of treatment received and the occurrence of in-hospital adverse events.

Results: Of 214 pts enrolled **(**66.9 ± 13.1 years; 32% female), 7 (3.2%) died during hospitalization. These had higher FFG (p=0.003) and more often a positive variation between FFG and APG (p<0.001). In multivariate analysis FFG was independently associated with in-hospital death (p=0.046). At 3 months adverse outcomes were associated with higher APG in univariate (p=0.029) but not in multivariate analysis. No glycemic parameters were associated with adverse outcomes at 6 and 12 months.

Conclusion: In this study FFG measurement was a predictor of in-hospital death in ACS pts, which reinforces the idea that FFG values should be measured and used for risk stratification during hospitalization. However, the glycemic parameters analyzed didn´t predict adverse outcomes after discharge. Since hyperglycemia in ACS is a stress response it probably relates better with in-hospital morbidity and mortality than with long-term adverse outcomes.

No conflict of interest
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Endothelium, Vascular Biology

MULTIFACTORIAL RISK FACTOR INTERVENTION REDUCES CAROTID INTIMA-MEDIA THICKNESS IN PATIENTS WITH TYPE 2 DIABETES

N. Tripolt[1], S.H. Narath[2], M. Eder[1], T.R. Pieber[1], T. Wascher[3], H. Sourij[1]
[1]Endocrinology and Metabolism, Medical University of Graz, Graz, Austria
[2]Institute for Biomedicine and Health Sciences, Joanneum Research, Graz, Austria
[3]1st Medical Department, Hanusch Hospital, Vienna, Austria

Background and aims*:* Despite intensified multifactorial risk factor intervention patients with type 2 diabetes (T2DM) remain at elevated risk for cardiovascular morbidity and mortality. Common carotid artery intima-media thickness (CCA-IMT) is a well validated surrogate marker of preclinical atherosclerosis and future cardiovascular events. The aim of the study was to investigate the impact of a target oriented intensified treatment of cardiovascular risk factors in patients with T2DM without previous cardiovascular events on CCA-IMT.

Materials and methods*:* 97 patients with T2DM not reaching at least two out of three of the following treatment targets: HbA_{1c} <6.5% (58.5mmol/mol); LDL-cholesterol <3.1mmol/l or blood pressure <130/80mmHg were included in this single-center, prospective, open 2-years clinical trial. Subjects received a target oriented, intensified treatment of risk factors according to current diabetes guidelines. The primary outcome was the change of common carotid artery intima media thickness (CCA-IMT), measured by B-mode ultrasound.

Results*:* Blood glucose, lipids and blood pressure were significantly improved during the 3 months intensified treatment period, which was sustained over the 2 years of follow up. Mean CCA-IMT significantly decreased from baseline to 2 year (0.883±0.120 mm vs. 0.860±0.130 mm; p=0.021).

Conclusion*:* Intensification of risk factor intervention in type 2 diabetes leads to CCA-IMT regression over a period of 2 years. Future research is needed to investigate whether CCA-IMT could be used to identify treatment non-responder in order to tailor cardiovascular risk factor management in patients with type 2 diabetes.

No conflict of interest
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Heart Failure, Ventricular Function

EARLY EFFECTS OF IVABRADINE AND B-BLOCKER THERAPY VERSUS B-BLOCKER UPTITRATION ON LV SYSTOLIC FUNCTION AND AUGMENTATION INDEXES IN CAD PATIENTS

K. Amosova[1], I. Katsytadze[1], Y. Rudenko[1], E. Andreev[1], A. Bezrodniy[1], L. Cherednichenko[1]
[1]Internal Medicine #2, O.Bogomolets National Medical University, Kiev, Ukraine

Purpose: To compare the effect of Ivabradine (Iv) plus bisoprolol (Bs) and Bs uptitration on exercise tolerance, NTproBNP, LV systolic function and augmentation index (AI) in CAD patients with moderate lowering of EF.

Methods: In single-blind, parallel-group study 28 patients aged<60 years (55±2,5) in sinus rhythm >70 bpm with CAD (stable angina CCS class I-II), documented MI>3 months, mild hypertension and EF<45%, were randomized in 2 groups. In Group 1 (n=13) Bs was uptitrated to 5mg pd and Iv was added (5mg bid uptitrated to 7.5 mg bid, 12.7±0,51mg pd), in Group 2 (n=15) Bs was uptitrated to 10 mg od (9,3±0,37 mg). At baseline (M0) and 2 months (M2), symptom-limited treadmill test (TT, Bruce protocol), aortic blood pressure (ABP) and AI were assessed with pulse wave analysis (PWA, SphygmoCor), plasma NTproBNP - with ELISA.

Results: Resting HR, systolic brachial BP and EF were similar in both groups at M0 (78±3,5 vs 80,1±3,6bpm, 137±6,1 vs 135±5,8mmHg and 41,3±1,78 vs 40,7±1,69%), and at M2 (64,8±2,92 vs 65±2,93bpm, 122,5±5,5 vs 118±5,3mmHg and 44,5±2,00 vs 44,5±2,00%, p>0,05). Results of TT, PWA and NTproBNP in the Table.

Conclusions: In patients with CAD and moderate EF lowering equivalent HR control at rest with Iv plus Bs, compared to Bs uptitration, was associated with improvement of exercise tolerance in spite of increase of chronotropic reserve, as well as, plasma NTproBNP lowering and more pronounced AI reduction by 2 months.

Group	Time	Systolic ABP, mmHg	AI, %	HR at exercise peak, bpm	Chronotropic reserve, bpm	Metabolic equivalent, MET	NT proBNP, pg/ml
1	M0	128,1±5,8	18,6±0,84	130,3±5,21	56±2,24	5,73±0,22	186±11,2
1	M2	111,4±5,0#	12,1±0,56##**	146,3±5,85#*	74,1±2,96##*	6,2±0,27#*	164±9,4#
2	M0	130,2±5,9	19,5±0,88	134,4±5,42	59,8±2,39	5,4±0,22	173±10,4
2	M2	114,7±5,1#	16,7±0,75#	131,1±5,27	64±2,56	5,7±0,25	167±10, 1

- p<0,05, ## - p<0,01 compared to M0; * - p<0,05, ** - p<0,01, *** - p<0,001 compared to Group 2

No conflict of interest
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Acute Coronary Syndromes, Acute Myocardial Infarction

M-2 AS A NEW INHIBITOR OF POST-MYOCARDIAL INFARCTION CARDIOMYOPATHY DEVELOPMENT IN RATS

T. Krzeminski[1], K. Mitrega[1], J. Nozynski[1], M. Porc[1]
[1]Chair and Department of Pharmacology, Medical University of Silesia, Zabrze, Poland

The aim of the study was to establish the optimal period of oral treatment with M-2, the furnidipines' metabolite, for preventing or delaying the post-myocardial infarction (MI) cardiomyopathy development in Sprague-Dawley rats.

Based on our previous findings we established that morphological process of heart tissue after untreated MI correlates with hemodynamics (working-heart set-up), however it is slightly delayed. The experimental MI was induced by the permanent left anterior descending coronary artery occlusion and the survived rats were treated with M-2 (4 mg/kg daily) from 21st to 28th, 11th to 28th, 21st to 35th, 11th to 35th or from 6th to 35th day after the MI for morphological features routine estimation.

Our study showed that M-2 treatment during the longest period after MI induces the following effects: 1) 'revitalisation' of the vessels and infarct scars, 2) strong intensification of angiogenetic events, 3) prevent remodeling of the myocardial tissue.

The significant reduction of cardiomyopathy development in rats treated with M-2 from 21-28th day after MI in comparison to control (0.9% NaCl) and between control and vehicle (0.4% DMSO) ($P < 0.05$) was rather the consequence of DMSO administration. In rats treated with M-2 from 11-28th, 11-35th or 6-35th day after MI, the complete protection of cardiomyopathy development ($P < 0.05$) was the result of M-2 itself.

We conclude that good tolerance, long duration of action, low toxicity and relatively large therapeutic window, determine M-2 as a promising candidate to become a precursor for a new chemical class of cardio-protective drugs.

No conflict of interest
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Acute Coronary Syndromes, Acute Myocardial Infarction

BENEFICIAL EFFECTS OF LONG-TERM ORAL TREATMENT OF FURNIDIPINES' METABOLITE (M-2) AFTER MYOCARDIAL INFARCTION IN RATS

K. Mitrega[1], *T.F. Krzeminski*[1]
[1]*Chair and Department of Pharmacology, Medical University of Silesia, Zabrze, Poland*

Our previous studies have established that M-2, an active metabolite of furnidipine, had cardio-protective and antiarrhythmic effects and did not evoked cardio-depressive influence. The aim of this study was to investigate when to start and how long after the myocardial infarction (MI) M-2 should be administered to achieve cardio-protective effect on myocardium to prevent the cardiomyopathy development.

The MI was induced by the left anterior descending coronary artery permanent occlusion and the survived Sprague-Dawley rats were treated with M-2 administered orally (4 mg/kg daily) from 21st to 28th, 11th to 28th, 21st to 35th, 11th to 35th or from 6th to 35th day. The following parameters have been measured or calculated in the model of working heart (WH; 60 min): aortic systolic and diastolic pressure, heart rate (*HR*), coronary flow (*CF*), aortic flow, myocardial oxygen consumption (MVO_2), preload pressure, $\pm dP/dt$ and the oxymetric parameters.

M-2 exhibited the most beneficial effects given from the 6th to 35th day after MI, when a marked increase of *CF* without a significant increase of MVO_2 were observed. Moreover, M-2 did not evoked a depressive influence on pressures parameters hence did not altered HR.

We conclude, that the earliest and the longest oral administration of M-2 after MI reveals the most beneficial effects on hemodynamic parameters estimated in WH model mainly due to CF increase without a significant cardio-depressive effects. Unlike furnidipine, M-2 do not only possess calcium channel blocking activities, therefore is a potentially promising cardio-protective agent representing a new structural class of drugs.

No conflict of interest
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ACUTE ISCHEMIA, ACUTE CORONARY SYNDROMES AND MYOCARDIAL INFARCTION

EFFECT OF FLAXSEED SUPPLEMENTATION AND EXERCISE TRAINING ON LIPID PROFILE, OXIDATIVE STRESS AND INFLAMMATION IN RATS WITH MYOCARDIAL ISCHEMIA

H. Nounou[1,2], M. Deif[3], M. Shalaby[2]
[1]Medical Biochemistry Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt
[2]Biochemistry Department, College of Science, King Saud University, Riyadh, Saudi Arabia
[3]Medical Physiology Department, Faculty of Medicine, Alexandria University, Alexandria, Egypt

This study was carried out to evaluate the protective role of flaxseed and exercise on cardiac markers, lipids profile and inflammatory markers in isoproterenol (ISO)- induced myocardial ischemia (MI) in rats.
The research was conducted on 40 male albino rats, divided into 4 groups each of ten rats; group I served as control, group II was treated with ISO subcutaneously (85mg/kg) for 2 consecutive days for induction of MI, groups III and IV received flaxseed oil orally by gavage tube in a dose of 0.4 g/day for six weeks then MI was induced by ISO as described in group II. Additionally, group IV was trained with exercise preconditioning in the form of mere swimming
Alterations of lipid profile, cardiac and inflammatory markers [pentraxin- 3(PTX-3), interleukin-1β (IL-1 β), and tumor necrosis factor- α (TNF- α)] were observed in MI group. Flaxseed supplementation decreased cholesterol and LDL levels with more obvious decrease in the group received exercise training combined with flaxseed supplementation Moreover, this combined group showed significant increase of HDL and paraoxonase-1 (PON-1). On the other hand cardiac troponin, IL-1β and TNF- α levels were significantly decreased in the combined group as compared to myocardial ischemic group. This study concluded that the combination of flaxseed supplementations and exercise training is one of the promising cytoprotective elements for improving defense mechanisms in the physiological systems against oxidative stress and inflammation caused by MI

No conflict of interest
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Diagnostic Methods, Imaging Techniques

PREVALENCE OF ANOMALOUS ORIGINATION OF A CORONARY ARTERY FROM THE OPPOSITE SINUS IN AN ADULT POPULATION UNDERGOING MULTI DETECTOR-ROW COMPUTED TOMOGRAPHY

C. Graidis[1], D. Dimitriadis[1], V. Karasavvidis[1], M. Giannadaki[1], G. Dimitriadis[1], K. Gourgiotis[1], G. Spiromitros[1], G. Karakostas[1], D. Krikidis[1], I. Kirmbas[1]
[1]"Euromedica-Kyanous Stavros, Thessaloní
ki, Greece"

Background: Anomalous origination of a coronary artery from the opposite sinus (ACAOS) is estimated to be present in 0.2-2.0% of the population.

Purpose: The aim of this study was to evaluate the prevalence of ACAOS in consecutive symptomatic patients, who underwent cardiac 64-slice MDCT coronary

Methods: This retrospective study included 2572patients who underwent coronary 64-slice MDCT coronary angiography from January 2008 to March 2012.

Results: Of the 2572 patients, twenty (0.78%) were diagnosed with ACAOS, with a mean age of 54.8 ±9.5 years. In 9 patients (0.35%)the RCA arose from the opposite sinus of Valsalva with a separate ostium for RCA and LM. In four patients the anomalous RCA had a malignant inter-arterial course. In 6 patients (0.23%) an abnormal origin of LCX from the right sinus of Valsalva (RSV) was found. A single coronary artery was seen in 3patients (0.12%). It was originated from the RSV in one patient and from LSV in two patients. In two patients the anomalous vessel (RCA=1, LMCA=1) had a malignant course between the pulmonary artery (PA) and the aorta. In 2patients (0.08%) left coronary trunk originating from the RSV with separate ostium.

Conclusion: The results of this study support the use MDCT coronary angiography as a safe and effective noninvasive imaging modality for defining ACAOS in an appropriate clinical setting, providing detailed three-dimensional anatomic information that may be difficult to obtain with invasive angiography.

Diagnostic Methods, Imaging Techniques

INCIDENCE OF ANOMALOUS ORIGIN OF THE LEFT CIRCUMFLEX CORONARY ARTERY IN 12401 PATIENTS FROM NORTHERN GREECE, UNDERGOING CORONARY ANGIOGRAPHY

C. Graidis[1], D. Dimitriadis[1], V. Karasavvidis[1], M. Giannadaki[1], G. Dimitriadis[1], K. Gourgiotis[1], G. Spiromitros[1], D. Krikidis[1], I. Kirmbas[1], G. Karakostas[1]
[1]"Euromedica-Kyanous Stavros, Thessaloní ki, Greece"

Introduction: Anomalous origin of the left circumflex coronary artery from the right sinus of Valsalva or proximal right coronary artery is the most common congenital coronary anatomical abnormality with prevalence at coronary angiography of 0.18–0.67%, depending on populations studied.

Patients and Methods: We retrospectively analyzed the angiographic records of 12401 consecutive adult patients who had undergone coronary angiography at our institution between 1stJan 2003 and 30th December 2011

Results: Anomalous origin of the Cx from the right aortic sinus or the 1st portion of the RCA was observed in 43 patients (0.35%).Thirty three patients were men (76.7%) and 10 were women (mean age, 65.1±10.4years). In all cases, the initial course of the Cx was posterior to the aorta with RCA dominance in 37 patients (86%). Coronary artery disease was found in27/43 patients (62.8%). The disease in anomalous Circumflex arteries was comparable in the severity to the diseases of the rest coronary arterial tree, suggesting a generalized coronary atherosclerotic process. Anomalous origin of the Cx was found with an increased incidence in aortic valve disease (6/43, 13.9%).

Conclusion: From this study it is concluded that anomalous origin of the circumflex coronary artery from the proximal right coronary artery or right sinus of Valsalva is a relatively common anatomic variation and appears to be more common in men than in women. We believe that disease of the anomalous circumflex artery was part of a random coronary atherosclerotic process and not different from the diseases of non-anomalous vessels in any given patient.

Electrophysiology and Cardiac Arrhythmias

ARRHYTHMIA PREDICTION: A PHASE-SPACE RECONSTRUCTION BASED APPROACH

G. Cappiello[1], S. Das[1], G. Koulaouzidis[2], E.B. Mazomenos[1], K. Maharatna[1], P.E. Puddu[3]
[1]School of Electronics and Computer Science, University of Southampton, Southampton, United Kingdom
[2]Cardiology, Southampton University Hospital, Southampton, United Kingdom
[3]Department of Cardiovascular Sciences, Sapienza University of Rome, Rome, Italy

Background: Automatic recognition of arrhythmias from ECG recordings is important for clinical diagnosis and treatment as well as for understanding the mechanisms of arrhythmias.We look at the diagnostic validity of a new index in the differential diagnosis of normal sinus rhythm and ventricular arrhythmias based on phase space reconstruction (PSR).

Methods: Recorded used in this study are from the PTB Diagnostic ECG database and from the Creighton University Ventricular Tachyarrhythmia database. The simplest method to reconstruct the phase-space of a time-series X(t) is to use the method of delays. In this method we insert a delay "τ" in the original time-series X(t) which produces a delayed version of X(t): $Y(t) = X(t-\tau)$. Following the phase-space is reconstructed by plotting Y(t) against X(t). After the reconstruction of the phase-space diagram, using a window of ten ECG beats, a pixel-counting method was applied to obtain the mean (μ), the standard deviation (σ) values of the number of black pixels in each diagram and the coefficient of variation (*CV*) were calculated and plotted: $CV = \sigma/\mu$

Results: In 20 subjects with sinus rhythm, PSR showed a diagram with regular structure while *CV* is always bounded within a small numerical value ($0 < CV < 0.05$). On the other hand, in 11 subjects with ventricular tachycardia followed by ventricular fibrillation PSR produced a diagram completed irregular and the value of *CV* was >0.05. Furthermore, the onset of arrhythmia occurs from 5.14 min to 11.36 min after *CV* crossed the threshold value 0.05 in the worst and best case respectively.

Conclusion: According with our preliminary results *CV* has a potential to be applied as an effective clinical tool for prediction and diagnosis of arrhythmia.