I Guidelines of the Cardiogeriatrics Department of the Brazilian Cardiology Society

by

The Geriatrics Cardiology Department
of the Brazilian Cardiology Society (DECAGE/SBC)

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Degrees of Recommendations and Levels of Evidence used in this document	
Degrees of Recommendations	**Definition**
A) Definitely recommended	• Always acceptable and safe • Definitely useful • Proven efficacy and effectiveness
B) Acceptable	• Acceptable and safe, clinically useful, but not definitely confirmed by randomized study or meta-analysis
B1) Very good evidence B2) Reasonable evidence	• Considered a treatment of choice • Considered an optional or alternative treatment
Unacceptable	• Clinically useless, may be harmful

Level of Evidence	**Definition**
Level 1	Wide randomized studies and reviews
Level 2	At least one randomized study and meta-analysis
Level 3	Small sample studies
Level 4	Recommendations of expert groups in guidelines or other meetings

Foreword

In 2020, Brazil will be the sixth largest elderly population in the world. It is therefore necessary that the physician becomes ever more familiarized with the structural, functional and hemodynamic changes related to aging and with the information obtained from problem based medicine, so that he/she is able to assist the elderly better. However, the elders are frequently excluded from the large clinical studies, making it difficult to establish a standardized conduct for this age bracket.

Considering these impacting facts, the DECAGE/ SBC (Brazilian Department of Geriatric Cardiology, from the Brazilian Cardiology Society) directors assembled a group of expert physicians, with the purpose of establishing diagnostic, therapeutic and preventive rules for cardiovascular disorders of the elderly based, whenever possible, on evidence available in the literature.

Geriatric Cardiology was divided in six issues of general interest: Arrhythmias and Syncope, Congestive Heart Failure, Coronary artery disease, Arterial Hypertension, Valvopathies and Cardiovascular Prevention. The proposed subjects were previously distributed to the participants according to their area of interest, allowing them to send to the group coordinators and to the general coordinators a preliminary paper about their designated theme before the meeting. Therefore, the coordinators had the opportunity to analyze each preliminary paper in depth.

A general meeting with the participants took place from April 5 – 8, 2002, with two discussion phases: the first one among the members of each group and their coordinator; the second one, among all participants (plenary meeting). The final decisions are transcribed in the present guidelines, whose purpose is to serve as a treatment guide for the elderly. The doctor's actions may be adapted and individualized, according to the elderly patients' characteristics.

This work is the result of a harmonic joint project. We would like to thank the participants' and coordinators' intense effort, diligence and availability, for the excellent papers and extensive reviews of the themes dealt with. It is also noteworthy the support received from the scientific directors of SBC and the full support provided by the event management team.

We hope this document helps us all to deal with the elderly patient and stimulates future research about the best clinical-therapeutic conduct with individuals in this age group.

Claudia F. Gravina Taddei / Roberto Franken

Introduction

The elderly presents typical characteristics of disease manifestations, in response to therapy and side effects of medications. It is a group of higher risk for degenerative illnesses, in general, and cardiovascular diseases, in particular, in addition of presenting more co-morbidities.

The interview may be somehow difficult due to reduced sensitivity to pain and memory deficits, resulting in diagnostic and iatrogenic mistakes;

auditory deficits, making it difficult to understand questions asked by the physician, and reducing the information preciseness; omission of symptoms, for fear of the diagnostic and possible loss of freedom, and to avoid being a burden to the family; underestimation of their symptoms, considering them "according to the age"; overestimation of their symptoms due to depression and need of family support.

The physical exam may be confusing. The jugular stasis may be caused by the sinuous and atherosclerotic thoracic vessels, or by compression due to long aortic arch; lung stertors may be caused by atelectasis or chronic obstructive lung disease; hepatomegaly due to lowered diaphragm resulting from chronic obstructive lung disease, and edema due to venous failure, gravity action or extrinsic compression caused by a tumor.

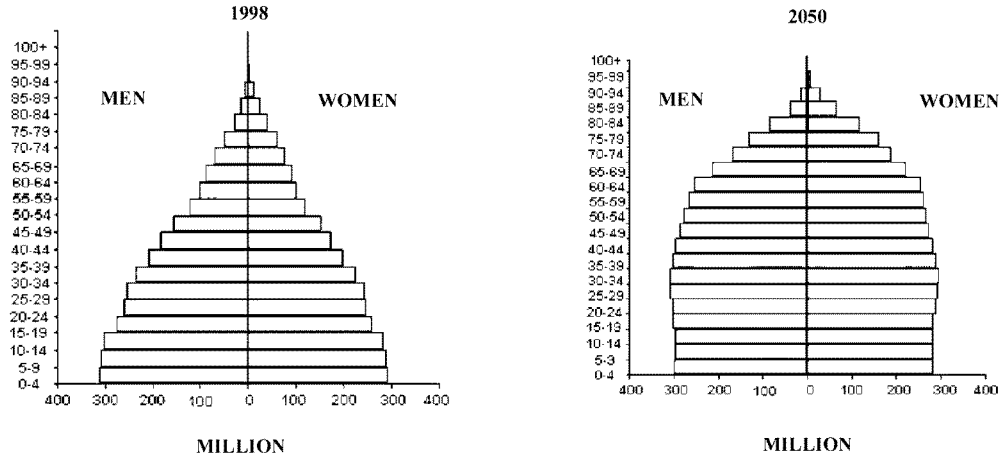
The treatment must be carried out carefully. The alterations that take place with aging lead to changes in drugs' pharmacokinetics and pharmacodynamics, with consequent changes in their distribution, metabolism and excretion, in addition to their resulting action and effect on the aging organism. These facts demand adequate medication doses. In addition, medication interactions caused by polypharmacy, which is usual in this age range, associated to the low toxic-therapeutic index of some cardiovascular drugs, demand attention from the professional when prescribing the indicated medications. The frequency of atypical reactions to drugs is higher than in the adult patient. Thus, the assistance to the elderly must be different and the doctor must be attentive to the peculiarities on how to approach and treat several cardiovascular diseases in this age range, as well as to the differences regarding younger adults.

Population Aging and Demographic Data

The elderly are the fastest growing population segment, especially the oldest individuals. According to data from the United Nations[1], in 1998, approximately 66 million people were 80 years or older. This age range represents 1.1% of the world population. From 1970 to 1998, while the world population increased 60%, the 80 years old or older population increased 147% (from 26.7 to 66 million). The projection to 2050 shows even more impressive numbers, estimating a population six times larger than the current one in this age range (370 million).

It is estimated that in 1998, approximately 89% of this population (59 million) was composed of octogenarians, 11% of nonagenarians (7 million) and 0.2% of centenarians (153,000). Projecting to 2050, the octogenarian population will grow approximately 5 to 6 times, the nonagenarian, almost 8 times, and the centenarian, 16 times, reaching 2.2 million people. When the gender ratio is analyzed, there is a predominance of women over 80 (190 women to 100 men). Among the octogenarians the feminization ratio is 181/100, among the nonagenarians it is 287/100 and among de centenarians is even higher (386/100).

Figure: Men Women Men Women
Million Million



Source: United Nations Population Division, *World Population Prospects: The 1998 Revision*, forthcoming

The Aging Heart

Aging produces progressive heart structural changes. The thickening of aortic and mitral valves may be observed. Calcification and fibrosis lead to increase of their thickness and rigidity, possibly interfering with closing. Although these phenomena may lead to aortic stenosis (the most affected of all valves), the functional commitment through these mechanisms is not frequent[2-4]. The blood vessels present a degeneration of extracellular matrix, especially of the elasticin fibers, producing a reduction of vascular wall

elasticity, making them more rigid[2,4,5]. There is increased pigmentation in the myocardium due to lipofuscin deposits in the sarcoplasm, in its paranuclear area. The number of myocytes decreases, leading to the enlargement of the remaining ones and more deposit of adipose cells[2,6]. Fat accumulation in the epicardium is observed, especially on the right ventricle. Bands of thickened pericardium are also observed. The functional meaning of such data is still speculative[7]. There is cellular loss and replacement with adipose and fibrotic tissue in the generating and conductance stimulus system. In the sinusal node, a substantial reduction of the number of pacemaker cells is observed: approximately 10% compared to the 20-year old healthy individual. There is fat deposit around the sinusal node, leading to a complete isolation of this structure. These mechanisms may produce sinusal dysfunction. The conductance system is no exception, undergoing deposit of fat tissue, cell loss, fibrosis and amyloid deposit. In addition, calcification of the left myocardial skeleton is evident, altering the integrity of conductance system[2,4,8-10].

At rest, the cardiac debt remains normal. With the lower heart rate, the increase of systolic volume is responsible for the sustained cardiac debt. With exercise, the inability to reach the maximum heart rate prevents the elderly to reach maximum oxygen consumption when compared to young individuals.

I – Cardiac Arrhythmias

Atrial and ventricular arrhythmias

With the increased life expectancy, the diagnosis of cardiac arrhythmia is ever more often in the clinical practice. Several authors showed that its incidence increases with aging[12-14]. Depending on the origin, frequency, complexity and presence of cardiopathy, the meaning of these events may be very variable.

The analysis of electrocardiograms of 674 patients, 80-years or older[15], Rajala et al., found some kind of extra-systole in 29% of the patients without cardiopathy, in 33% of bearers of ischemic cardiopathy and in 39% of congestive heart failure. In patients without cardiopathy, supraventricular

extra-systoles (VES) predominated. The presence of ventricular extra-systoles and atrial fibrillation, found in 3% of the patients without cardiopathy and in 24% of the patients with heart failure, was significantly correlated with cardiomegaly. In the 24h Holter of patients 80-years or older without cardiopathy there were no pauses longer than 2s. Supraventricular extra-systoles were observed in all patients, and 65% of them presented more than 20 VES/h. Episodes of ectopic atrial tachicardia were recorded in one patient and supraventricular tachicardia in two. Atrial fibrillation (AF) was observed in one patient and a short episode of atrial flutter in another one. Ventricular extra-systoles (VE) findings were quite frequent, where 96% of the patients presented at least one VE during the exam; one half with 10 VE/h or less; one third with 10 to 50 VE/h. Only two patients presented more than 100 VE/h. In most of the patients (81%) VE were monomorphic and only 8% presented pairings. In one patient there was an episode of non-sustained ventricular tachicardia, with 6 beatings. AV dissociation was observed in only one patient, who also presented polymorphic ventricular pairings and two short AF episodes.

Therefore, in this population group, the incidence of atrial and ventricular arrhythmias is very frequent; however, complex arrhythmias or disorders of conductance or of impulse generation were rare. Similar results were observed by the *Cardiovascular Health Study*[17].

Fleg et al.[18] evaluated the long-term prognosis (average follow-up of 10 years) of arrhythmias in a population free of cardiopathy, 60 years or older (from the *Baltimore Longitudinal Study of Aging*). Ninety eight patients were studied, of which 69 were men. The distribution of cardiac arrhythmias is presented on table I. Transient alterations of the ST segment were observed in 16 patients: five of them with an infra drop of the ST segment ≥ 1 mm with descending aspect and 11 patients with an infra drop of ascending aspects.

In the average 10-year follow-up, 14 patients developed coronary events (chest angina in seven patients, non-fatal myocardium infarct in three and sudden death in four). Maximum, mean and minimum heart rates did not vary significantly among the groups that presented coronary events and those who remained event-free. This behavior was also repeated in the groups with or without arrhythmias (Table II).

Regarding the alterations of the ST segment, the survival curves showed a significant survival reduction in the group with altered ST segment, either of ascending or descending features.

Table I – Prevalence of arrhythmias	
Arrhythmia	Prevalence (%)
Supraventricular	
≥ 30 VES/h	22
≥ 100 VES/h	26
SVPT	13
Ventricular	
≥ 10 VE/h	29
≥ 30VE/h	12
≥ 100 VE/h	17
Pairings or NSVT	15

VES – supraventricular extra-systole; VE – ventricular extra-systole; supraventricular paroxysmal tachicardia; NSVT - non-sustained ventricular tachicardia.

Atrial Fibrillation

Of all tachyarrhythmias, AF is the most prevalent, therefore deserving emphasis. Ryder et al.[19] estimated that AF chronically or intermittently affects 2.2 million people in the USA, with a total prevalence of 1.5 to 6.2%. The average age of these patients was 75 years. AF prevalence in people 40 years or older is 2.3% and 5.9% after 65 years of age. Approximately, 70% of AF patients are placed between 65 and 85 years of age. AF occurrences increase with age, almost doubling each decade. Thus, 0.5 to 0.9% of the patients between 50 and 59 years of age present a history of AF, whereas 6.7 to 13.2% presented it during the 9th decade. Men developed AF 1.5 more often than women. However, due to the greater longevity, it is estimated that 53% of AF are women.

In the Framingham study, Benjamin et al. [20] analyzed the risk factors for the development of atrial fibrillation, where independent risk factors were congestive heart failure, arterial hypertension, valve disease and myocardial infarct.

Myocardial infarct was the independent risk factor for men, whereas women showed a higher probability to develop AF with valve disease than men.

AF is a common post-surgical arrhythmia in non-cardiac (4.4%), as well as in cardiac surgeries (up to 33% in the post-operative myocardial revascularization). Hyperthyroidism, usually sub-clinical in the elderly, increased significantly the risk of AF development (odds ratio of 3.7). Abnormal echocardiographic findings, such as left atrial increase, proved to be an independent factor for AF development. Reduced shortening fraction of the left ventricle and increased thickness of the left ventricle wall were also independent risk factors[19].

Table II – Groups with and without arrhythmias

Arrhythmia	Rate of events (%)	
Supraventricular	With arrhythmias	Without arrhythmias
≥ 30 VES/h	18	13
≥ 100 VES/h	20	12
SVPT	15	14
Ventricular		
≥ 10 VE/h	14	14
≥ 30VE/h	17	14
≥ 100 VE/h	18	14
Pairings or NSVT	20	13

Same abbreviations as the previous table. There was no significant difference in the comparison.

When the incidence of ischemic stroke (iSTROKE) was adjusted to age, it doubled with the presence of coronary arterial disease, tripled with arterial hypertension and quadruplicated with congestive heart failure. The presence of fibrillation increased almost five times the risk for iSTROKE than in the control population[20]. The changes of fatal iSTROKE almost doubled in the presence of AF[21], as well as the hospitalization stay, which was longer[22].

In a prospective study in Rotterdam[23], the number of dementia cases was twice as frequent in AF patients. One of the speculated mechanisms was the occurrence of silent brain infarcts.

Finally, AF was predictive of mortality both in men and women (odds ratio of 1.5 and 1.9, respectively), after age adjustments, cardiopathy and other risk

factors[24-26]. These data indicate the severity and malignancy of this arrhythmia, so frequent and sometimes underestimated.

Disorders of impulse generation and conductance

The above mentioned changes in the sinusal node, and the reduced sensitivity to the adrenergic stimulation lead to the higher incidence of sinusal dysfunction. Heart rates lower than 43 bpm and sinusal halts longer than 2s were not found in normal elders older than 80 years[16].

Atrial ventricular and branch blockades also increase with age. The presence of type I 1st and 2nd degrees AV blockades is benign, which does not happen with type II 2nd degree and 3rd degree AV blockade, which usually mean advanced disease of the conductance system[15,27]. Right branch blockade was found in 3% of the normal individuals over 85, and in 8-10% of those with cardiopathy[15,27]. Left branch blockade (LBB) showed a strong correlation with age, with 1% of the 50 year-old individuals and in 17% of the 80 year-old individuals. No relationship between LBB, ischemic cardiopathy or mortality was found, being probably a marker of the progressive degenerative myocardial disease. Unspecific intraventricular conductance disorder (QRS complex > 120 ms in length) was observed in 2% of the individuals over 70 in the Framingham's study, being related to the presence of the systemic organic s disease[28,29].

Syncope

Aging induces a diminished heart sensitivity to beta-adrenergic agonists, reduced reactivity to chemo- and baroreceptors, and lower ability to regulate sodium[10,11]. There are several causes of syncope, including cardiac, neurological, cerebrovascular, metabolic, among others. Aging patients are particularly susceptible to the hypotensive effect of drugs, due to the diminished sensitivity of baroreceptors, reduced brain flow, kidney loss of sodium and lower fluid intake[30]. They are also more susceptible to stimulation of the carotid sinus (hypersensitive carotid sinus syndrome). Hypersensitivity of the carotid sinus can be detected in asymptomatic patients, and this finding must be carefully evaluated. Among the tachicardias, the ventricular is the one which causes syncope more often. However, in the elderly, the most frequent cause of faint-heart is the supraventricular paroxysmal tachicardia due to the difficulty of adaptations of the peripheral

resistance to abrupt changes of frequency, both at the beginning and the end of paroxysm. Neurological disturbances are less frequent causes of syncope, representing less than 10% of all causes[30].

Syncope is a frequent event in the elderly, presenting an incidence of 6% per year in an institutionalized population with average age of 87 years. The prevalence in 10 years was 23% and the rate of recurrence was 30%. In these patients, the cause was determined in 69%. In 21% of the cases a cardiac origin for the syncope was detected and in 48% of the cases the origin was not cardiac. In the remaining 31%, the syncope remained unexplained. Those who presented syncope were functionally more fragile and labile. However, mortality curves did not show significant differences. In this population, syncope was rather a manifestation of co-morbidity than a mortality predictive factor[31,32].

The risk factors for syncope, based on the population of the Framingham study were: previous history of stroke and transient ischemic stroke, use of cardiovascular medication and arterial hypertension. The mechanisms involved in stroke may be hypotension mediated by the central nervous system, lack of autonomic control or side effects of medications. Hypotension and bradichardia may result from cardiovascular medications, especially in the elderly, whose mechanisms of blood pressure auto-regulation and heart rate are depressed. Arterial hypertension was found in 60% of the patients; this ratio was even clearer in the older age range. Curiously, no electrocardiographic marker showed a significant predictive value. The authors raise the possibility of underestimation due to the low number of patients with this marker in the population studied[33].

Clinical manifestations of cardiac arrhythmias

The clinical manifestations of cardiac arrhythmias are variable, including palpitations, syncope, pre-syncope, precoridal pain or even sudden death. Of these, the most frequent is palpitation. A detailed clinical history is an important tool to characterize this symptom, which may occur with or without cardiac arrhythmia. The following must be sought: characteristics (not-sustained, sustained, fast or not, regular or not, and location where palpitation is noticed), how it begins and ends, frequency of the symptom, associated symptoms and triggering factors. It is important to notice that palpitations may occur in the absence of cardiac arrhythmia, many times generated by sudden changes of autonomic control, such as in anxiety states. On the other hand, it is possible to

observe clinically relevant arrhythmias in asymptomatic patients, even with non-sustained ventricular tachicardia.

Low cerebral flow-determined syncope or pre-syncope depends on the heart rate, ventricular function and peripheral adaptability. In normal hearts, only very elevated heart rates determine significant hypotension. In cardiopathies with depressed ventricular function, lower heart rates may cause loss of consciousness. The physical exam during tachicardia gives information about the heart rate, rhythm regularity, and the relationship between atrial and ventricular contraction. An irregular rhythm (i.e., AF) will generate irregular dupps of variable intensity. The presence of atrioventricular dissociation in ventricular tachicardia will produce cannon dupps. In this situation, the jugular venous pulse will show cannon waves. When the patient is examined outside the paroxysm, the information collected are related to the semiologycal findings that may lead to evidence of cardiopathy. It is noteworthy that the normal physical exam does not exclude the possibility of arrhythmia. The 12-derivation electrocardiogram during the tachicardia is very important, allowing a precise differential diagnostic of cardiopathies[34].

Treatment of arrhythmias

Treatment of arrhythmias will be presented briefly, using squares. The possibility of clinical occurrences are represented by small case alphabetical characters (a, b, c, d, e, f, g, h, ...), vertically placed in the square, and described on the side. Horizontally are the degress of recommendation (A, B1, B2, C). Inside the cells are the levels of evidence (1, 2, 3, 4).

"How and when to treat ventricular arrhythmias with medication"

Using the first square as an example, it is possible to notice that, in case of *ventricular extra-systole,* situation "*a*" considers ventricular extra-systole "asymptomatic in patients without cardiopathy". In this case, the degree of recommendation for the use of medication is C (unacceptable use), and the level of evidence is 3 (based on report or case series). In case of hypothesis "*b*" (ventricular extra-systole "asymptomatic in patient with cardiopathy"), individualized treatment has degree of recommendation B2 (reasonable evidence), level of evidence 4 (experts' consensus). In case of hypothesis "*c*" (ventricular extra-systole "symptomatic in a patient without cardiopathy") the indicated treatment is with beta-blockers: degree of recommendation B1 (very good evidence), level of

evidence 3 (based on report or case series). In case of hypothesis "*d*" (ventricular extra-systole "symptomatic in patient with cardiopathy"), the indication of treatment with other medications presents degree of recommendation B2 (reasonable evidence) , level of evidence 3 (based on report or case series). In case of hypothesis "*e*" (ventricular extra-systole "symptomatic in patient with cardiopathy), the proposed treatment is beta-blockers or amiodarone: level of recommendation B1 (very good evidence), level of evidence 4 (based on experts' consensus). In case of hypothesis "*f*" (ventricular extra-systole "symptomatic or asymptomatic in patient with cardiopathy), treatment with medication class I is unadvisable: degree of recommendation C (unacceptable), level of evidence 4 (based on experts' consensus).

The other squares follow the same type of presentation, targeting the immediate identification of arrhythmia treatment for the elderly'.

How and when to treat ventricular arrhythmias with medications?

A) Ventricular extra-systole

	A	B1	B2	C
a				3
b			4	
c		3		
d			3	
e		4		
f				4

a. Asymptomatic in patient without cardiopathy

b. Asymptomatic in patient with cardiopathy: individualized treatment

c. Symptomatic in patient without cardiopathy: beta-blockers

d. Symptomatic in patient without cardiopathy: other medications

e. Symptomatic in patient with cardiopathy: beta-blockers or amiodarone

f. Symptomatic or asymptomatic in patient with cardiopathy: medications class I

B) Sustained monomorphic ventricular tachicardia (SMVT): reversion of crisis

	A	B1	B2	C
A	4			
B	4			

a. With hemodynamic instability: electrical cardioversion (ECV)
b. Without hemodynamic instability: IV procainamide or amiodarone are the first choice medications. In case of refractoriness to the first selected drug or even as a first choice, ECV must be used.

C) Sustained monomorphic ventricular tachicardia: recurrence prophylaxis and sudden death prevention.

	A	B1	B2	C
a		2		
b			2	
c			4	
d		4		
e		2		
f			4	
g		3		
h			2	

a. SMVT with EF ≥ 35%: amiodarone with or without implantable cardioversor-defibrillator (ICD)
b. Similar to item "a": metropolol
c. SMVT with EF < 35%: amiodarone
d. Recurrent SMVT in patient with ICD: amiodarone, betablockers
e. Similar to item "d": sotalol
f. Similar to item "d": class I anti-arrhythmia, eventually
g. SMVT in a normal heart, depending on catecholamines or induced by effort: beta-blockers

h. Idiopathic SMVT: beta-blockers, verapamil, sotalol, amiodarone, class I anti-arrhythmia

D) Primary prophylaxis of sudden death: post-myocardial infarct

	A	B1	B2	C
a				1
b	1			
c			2	
d		4		

a. Class I anti-arrhythmia medications
b. Beta-blockers: all patients if there is no contra-indication – continuous use
c. Amiodarone: high risk patients
d. Amiodarone: symptomatic ventricular arrhythmia (patients using ECAI and beta-blockers).

E) Primary prophylaxis of sudden death: heart failure (HF)

	A	B1	B2	C
a				1
b	2			
c			2	
d		4		

a. Class I anti-arrhythmia medications
b. Beta-blockers (carvedilol, metoprolol or bisoprolol): patients in FC I, II, III or IV compensated, reduced EF, using ECAI + digitalis + diuretic.
c. Amiodarone: non-ischemic HR, FC III/IV.

d. Amiodarone: symptomatic ventricular arrhythmias (patients using ECAI and beta-blockers).

How and when to treat supraventricular arrhythmias with medication?

	A	B1	B2	C
a				4
b		4		
c				4
d		4		

a. Asymptomatic.
b. Symptomatic with LV dysfunction: individualized anti-arrhythmia
c. Symptomatic with LV dysfunction: class I anti-arrhythmia
d. Symptomatic with LV dysfunction: classes II and III anti-arrhythmia

Initial evaluation of a recovered cardiorespiratory arrest

	Procedure	Degree of recommendation
1. All patients	Conventional ECG	A
	Bi-dimensional Eco	A
	Holter	B1
2. Without cardiopathy	Cardiac catheterism	B2
	Electrophysiological study	B2
	Test of effort	B2
3. With cardiopathy	Cardiac catheterism	B1
	Electrophysiological study	B1
	Test of effort	B1

How and when to reverse an atrial fibrilation (AF) and to maintain the sinusal rhythm?

A) Crisis reversal

	A	B1	B2	C
a	4			
b			3	
c		2		
d		2		
e	3			
f		3		
g		4		
h				3
i			2	

a. Elevated HR and hemodynamic instability

b. < 48h: CV without previous anticoagulant

c. > 48h or undefined length of time, or less than 48h with mitral valvopathy, previous embolism or HF: CV with pre- (4 weeks) or post- (4 weeks) anticoagulant.

d. > 48h and early CV, trans-esophagic eco without thrombus: peri-CV heparinization and oral anticoagulant for 4 weeks

e. Similar to item "d" with thrombus: postpone CV and begin oral anticoagulant.

f. CV in AF with pre-ventricular excitation and stable hemodynamic status.

g. Similar to item "f": reversal with procainamide, amiodarone or propafenone.

h. Similar to item "f": reversal with verapamil, digitalis or beta-blocker.
i. Chemical CV: propafenone, procainamide, amiodarone or quinidine.

B) Maintenance of sinusal rhythm

	A	B1	B2	C
a				4
b			2	
c			2	
d		2		
e				2

a. Anti-arrhythmic after the first well-tolerated AF episode, without risk factors for relapse
b. Class I or class II anti-arrhythmic in cases of structural cardiopathy and without risk factors for relapse
c. Amiodarone in cases of structural cardiopathy and without risk factors for relapse
d. Amiodarone in cases of structural cardiopathy and with risk factors for relapse
e. Class I anti-arrhythmic in cases of cardiopathy.

Electrophysiological assessment of patients with unidentified palpitations

	A	B1	B2	C
a	3			
b			4	
c				4

a. Patients with recurrent sustained tachycardiac palpitations, paroxysmal, with hemodynamic or quality of life commitment, not identified by non-invasive assessment.
b. Patients with sustained tachycardiac palpitations without electrophysiological documentation
c. Patients with tachycardiac palpitations due to non-cardiac reasons

Electrophysiological study (EPS) of patients with unexplained syncope

	A	B1	B2	C
a				4
b			2	
c			2	
d		2		

a. Patients with structural cardiopathy and syncope remaining unexplained after non-invasive investigation
b. patients without structural cardiopathy, with recurrent syncope, after non-invasive investigation
c. Patients with structural cardiopathy, with one episode of syncope with body lesion with inconclusive non-invasive investigation.
d. Patients with syncope of undetermined reason in which the EPS will not contribute to the treatment.

Electrophysiological study for stratification of sudden death

	A	B1	B2	C
a		2		
b				4

a. Patients with previous AMI, with non-sustained ventricular tachycardia (NSVT) and left ventricle ejection fraction < 35%
b. Patients with life expectancy reduced by concomitant diseases.

Electrophysiological study of patients recovered from cardiorespiratory arrest (CRA)

	A	B1	B2	C
a	2			
b				4

a. Recovered CRA, documented, not related to the acute phase of myocardial infarct (> 48h), with undetermined causes and not associated with reversible factors, in patients with or without apparent structural cardiopathy.

b. CRA related to the acute phase of myocardial infarct (< 48h), and/or associated to reversible factors.

Indications for the electrophysiological study of patients with sinusal bradyarrhythmia

	A	B1	B2	C
a			4	
b				2

a. Symptomatic patients, with suspicion of disease of the conductance system, after non-conclusive invasive investigation

b. Asymptomatic patients.

Indications for the electrophysiological study of patients with atrioventricular blockade (AVB)

	A	B1	B2	C
a	2			
b		2		
c			3	

d				2

a. Patients with 2nd or 3rd degree AVB, with implanted pacemaker, normal functioning, in which the symptoms are persistent and another arrhythmia is suspected to be the cause

b. Asymptomatic 1st degree AVB, with intraventricular conductance disorder, in which there is suspicion of lesion in the His-Purkinje system.

c. Asymptomatic patients with 2nd degree AVB with disorders of intraventricular conductance.

d. Total AV blockade.

Indications for the electrophysiological study of patients with disorders of intraventricular conductance

	A	B1	B2	C
a	2			
b			4	

a. Patients with implanted pacemaker, normal functioning, who remain asymptomatic, where arrhythmia is suspected.

b. Patients who need medication with major action in His-Purkinje system.

Indications for the electrophysiological study of patients with sustained tachycardia with narrow QRS or pre-ventricular excitation

	A	B1	B2	C
a	2			
b			4	

a. Patients for whom non-pharmacological therapy is considered.

b. Patients who do not accept non-pharmacological therapy; patients with asymptomatic pre-ventricular excitation.

Indications for the electrophysiological study of patients with sustained tachycardia with wide QRS

	A	B1	B2	C
a	4			
b				4

a. Patients with wide QRS tachycardia in which the arrhythmia mechanism and/ or origin are ill-defined by non-invasive methods; patients with supraventricular tachycardia with erratic or pre-excitation intraventricular conductance, clearly defined by non-invasive methods, in which the non-pharmacological therapy was considered.

b. Patients with supraventricular tachycardia with erratic or pre-excitation intraventricular conductance, clearly defined by non-invasive methods, where non-pharmacological therapy is not considered.

II – Congestive Heart Failure

Aging-associated cardiovascular alterations

Regardless of related diseases, the aging process is associated to important cardiovascular alterations[1]. The arteries tend to become stiff with aging, decreasing elasticity and complacency of the aorta and major arteries[2]. In the average, layers of smooth muscle become thick, elasticin gets progressively fragmented, being replaced by collagen with firm crossed bonds, not distensionable and the calcification increases. The stiff arteries become less passively distensionable, and also present a lower ability to actively dilate, resulting in lower increase of blood flow in response to higher demands and physiological stress[3-6]. These physical alterations tend to significantly increase the mechanical overload in the elderly heart, which needs to propel blood through stiffer, not elastic and less distensionable arteries. The systolic arterial pressure increases and the diastolic pressure drops, once the stiff arteries lose the required elasticity to maintain the intravascular pressure during systole. The outcome is a pressure increase[3-9]. Increased impedance to left ventricular ejection results in slight myocardial hypertrophy and interstitial fibrosis[6-7].

In the intima, the size, shape and axial orientation of endothelial cells become less homogenous, so that the intraluminal blood flow becomes less laminar and lipid deposit may increase regardless of other factors[1]. The sub-endothelial layer thickens and the connective tissue, calcium content and lipids increase.

One of the most remarkable characteristics of the aging heart is the slower relaxation, partly due to the augmented left parietal rigidity, reduced filling velocity and consequently lengthening of the time of ventricular filling. The incomplete filling during the early diastole makes the aging heart highly dependent on the atrial contraction during the end of the diastole. Diastole shortening, which occurs during tachycardia, or loss of regular atrial contraction, such as in the atrial fibrillation, additionally endangers the ventricular filling and reduces the cardiac debt more in the elderly than in other age group. The diastolic dysfunction is an important cause of heart failure in the elderly.

The myocardial contractility is not significantly altered as a function of age, but by associated diseases, especially hypertension and coronary artery disease, common in the aging population. The cardiac debt tends to remain normal at rest. During exercise, however, a reduced capacity to reach maximum heart rate and maximum oxygen consumption is observed in the elderly, compared to younger individuals[8]. Moreover, it is possible that signaling pathways of the nuclear cell surface may be altered by aging and the mitochondria of cardiac cells are more susceptible to oxidative damage than other parts of the cell. These alterations may contribute to myocardial dysfunction, especially during periods of increased metabolic demand or cardiovascular stress.

At the cellular and sub-cellular levels, heart fibrosis, a decreased number of cardiomyocytes, compensatory increased size and capacity of remaining myocytes and lower cardiovascular response to beta-adrenergic stimuli, probably due to reduction of adrenergic receptors[9] and of baroreceptors sensitivity are observed. The decline of baroreceptor and $beta_1$-adrenergic responsiveness may result in absence of compensatory tachycardia and in exacerbated hypotension with the use of vasodilators and nitrates in elderly patients.

Cellular loss is associated with increased formation of connective tissue, collagen deposit and hard crossed bonds of its fibers, calcium and amyloid protein between the cells of the ventricular wall. These alterations make the cardiac muscle more rigid and more resistant to shape alterations, requiring more energy for the heart to distend[10].

Aging retards the inactivation of type L calcium channels, increasing the amount of calcium inflow in each cardiac cycle, which may be important to preserve the contractile function. On the other hand, the dissociation of ionized calcium from the myofilaments and its collection in the cytoplasm by the sarcoplasmic reticulum reduces with aging, contributing for the diastolic dysfunction in the elderly. Moreover, both the extent and density of calcium outflow current diminish with aging, contributing together with the delay of the inactivation of type L calcium channels, to the extension of the length of action potential.

The excitoconductive system undergoes cellular loss, which may endanger up to 50% to 75% of the node's pacemaker cells, resulting in drop of the intrinsic and maximum sinusal rate. The cells of the atrioventricular node are usually preserved, although atrioventricular conductance delay and extension of the PR interval may occur. The augmented fibrosis of the atrioventricular rings fibrotic skeleton and loss of specialized cells of the His' bundle and its branches may induce the occurrence of several blockades. The cardiac valves, especially aortic and mitral, thicken and base calcifications appear[11].

It must be emphasized that the diastolic dysfunction in the elderly usually precedes the systolic dysfunction, including the development of left ventricular hypertrophy. The percentage of diastolic heart failure in this population is high, corresponding to 40 to 50% of the cases in individuals over 75 years old.

Regulation of the arterial pressure also presents age-associated alterations, due to the lower arterial distension ability and smaller baroreceptor response[12]. Alterations of plasmatic concentrations of noradrenaline, renin, angiotensin II, aldosterone, vasopressin and natriuretic peptides contribute to the increase of arterial pressure with aging[1].

Prevalence

Heart failure is a frequent cause of morbidity and mortality in the adult population. Its prevalence increases progressively with age, with 1 to 2% between 50 and 59 years, and even 10% in individuals older than 75 years[13,14]. In the USA the prevalence of heart failure is estimated at around 4,500,00 patients, with 550,00 new cases diagnosed each year[15]. Currently, heart failure is the most frequent cause of hospitalization and release in the geriatric population of Western countries[16,17].

Despite the constant reduction of the incidence of coronary artery disease and cerebrovascular disease, both the incidence and prevalence of heart failure is growing. This trend is mainly due to the population aging and to the better survival of patients with cardiovascular disease, of which heart failure is the final common pathway.

In the geriatric population, more than 70% of the cases of heart failure present arterial hypertension or ischemic cardiopathy as the underlying etiology. Other relatively frequent causes are valvopathies, mainly stenosis and/or aortic and mitral failure, and the idiopathic dilated, hypertrophic or restrictive myocardiopathies[13,18,19].

Treatment

The best knowledge of the HF pathophysiology and of the cellular and molecular mechanisms that heighten its evolvement provided considerable advances in the syndrome therapy. The current treatment aims not only to relieve the symptoms, to improve the functional capacity and quality of life, but also to prevent the development and evolvement of the HF, to reduce the ventricular remodeling and to decrease mortality. Especial attention must be given to neuro-humoral alterations associated to systolic left ventricular dysfunction and to its appropriate control. On the other hand, especially in the elderly, the diastolic ventricular dysfunction, isolated or associated to the systolic, has been better recognized, diagnosed and valued. The HF therapeutic schedule is complex, including preventive procedures, non-pharmacological general measures, several medications, surgical procedures, use of heart pacemaker and electromechanical devices (panel I).

Panel I – Treatment schedule for heart failure
To determine the etiology and to remove the cause
To eliminate or correct precipitating factors
Identification of predominating pathophysiological mechanisms
Non-pharmacological measures and modification of life habits
Angiotensin converting enzyme inhibitors
Digitalis
Non-inotropic digitalis
Vasodilators
Beta-adrenergic blockers

Anti-arrhythmic
Anticoagulants
Pacemaker – implantable defibrillator
Supervised circulation
Surgical procedures
Heart transplant

Identification and treatment of reversible etiologies – The accurate diagnostic of HF etiology and its specific treatment are vital measures. Control of arterial hypertension, including isolated systolic hypertension, common in the elderly, must be strict and constant. When myocardial ischemia is an important factor for manifestation of left ventricular dysfunction, the anti-ischemic medication therapy, the percutaneous interventions and surgery of myocardial revascularization may result in great benefit, especially if the ventricular dysfunction is due to a transient myocardial ischemia (stunned or hibernating heart). Mitral stenosis may be treated by balloon valvuloplasty or surgically. When the mitral failure is important, even if secondary to ring dilation in major cardiomegalies, mitral plasty or valve prosthesis may contribute significantly for the improvement of clinical features. In the severe, symptomatic aortic stenosis, the surgical treatment is indicated, regardless of age. In general, in the elderly patient, especially the very old, the tendency is to act in a more conservative way than in younger patients. Nonetheless, intervention and surgical procedures may be considered and employed judiciously, after critical evaluation of general, physical and psychological status of the patient and associated co-morbidities. On the other hand, regardless of its correction, the correct etiologic diagnostic is important for treatment planning. **Degree of recommendation A, level of evidence, 4.**

To eliminate or correct precipitating or aggravating factors – Certain cardiac and associated extra-cardiac conditions may precipitate or aggravate HF (Panel II). Suppression or correction of these factors may contribute significantly to improve heart failure. **Degree of recommendation A, level of evidence, 4.**

Panel II – Cardiac and extra-cardiac conditions which precipitate or aggravate heart failure
Infectious endocarditis
Pulmonary embolism
Cardiac arrhythmias, tachyarrhythmias, bradyarrhythmias, frequent and complex ventricular extra-systole, atrioventricular advanced blockade, left branch blockade with very wide QRS.
Anemia
Infection
Thyrotoxicosis
Excessive administration of salt and fluids
Medications with negative inotropic activity (anti-arrhythmic, non-dihydropiridine calcium channel antagonists, triyclic anti-depressants, lithium)
Medications that depress cardiac function: alcohol, cocaine
Sodium and water retainer medications: non-humoral anti-inflammatory
Non-adherence to treatment

Non-pharmacological measures – Life style changes – Used together with the proper medication, the non-pharmacological measures make the treatment more efficient.

Diet – Nutricional aspects in the elderly show peculiarities inherent to the conditions of this age range, regarding their anatomic and functional structure, in addition to the socioeconomic conditions and co-morbidities. Evaluation of the elderly's nutricional status includes history of eating habits, physical exam, anthropometric measurements (weight, height, thickness of the tricipital and

subscapular skin fold and arm circumference) and biochemical analyses. The body mass index is useful for nutricional screening (Table I).

Nutricional intervention aims to maintain the ideal weight, with appropriate proteins, carbohydrates, fat supply and sodium restriction. Obesity increases heart work, especially during physical activity. Weight reduction is important for the symptomatic improvement, besides reducing the activity of the renin-angiotensin system and the sympathetic nervous system. Sodium chloride restriction depends on HF functional class. A diet with 4g of sodium chloride is a reasonable and realistic target for mild and moderate HF. This intake level allows salt in food preparation, avoiding the salt addition (salt shaker) and sodium-rich foods. A diet with 2g of sodium chloride must be restricted to more severe cases. Salt in food preparation should be restricted, salt addition should not be permitted, and sodium-rich foods should be avoided. Very intense sodium restriction may be harmful for the elderly, inducing malnutrition, because structural changes inherent to aging lead to loss of appetite, reduced capacity of mastication, deglutition and food absorption. Panel III shows the main sources of sodium.

Patients who present malnutrition (cardiac cachexia), must have nutricional support, with a high energy diet in small amounts. In case of oral feeding impossibility, enteral or parenteral nutrition is indicated.

Table I – Nutricional status as a function of body mass index (BMI)

Nutricional status	BMI
Malnutrition	< 22
Eutrophia	22-27
Obesity	> 27
BMI = weight (kg)/height (m^2)	

Panel III – Main sources of sodium

Salt addition: salt shaker
Industrialized and preserved foods: concentrated beef bouillon, beef jerk, cod fish, dry and smoked meat, packed soup
Seasonings in general: mustard, ketchup, soy sauce
Pickles, olives, asparagus, hearts of palm
Medications: anti-acids with sodium bicarbonate
Addictive: monosodium glutamate

Liquid intake can usually be free according to the patient's needs, and excess or lack must be avoided. In case of severe heart failure, with dilutional hyponatremia (Na < 130 mEq/l), liquid restriction is necessary. During periods of intense heat, diarrhea, vomit or fever, liquid intake may be increased, or the dose of diuretics reduced, in order to avoid dehydration.

Alcohol depresses myocardial contractility and may precipitate cardiac arrhythmias. In face of alcoholic cardiomyopathy, alcohol intake must be prohibited. In other cases, daily intake must not exceed 30g.

Vitamin and mineral supplements are advised, due to the loss of hydrosoluble vitamins associated to diuresis and reduced gastrointestinal absorption of liposoluble vitamins. Until now, there is no evidence that antioxidant therapy, Q10 co-enzyme, carnitine or growth hormone are beneficial to HF.

Aging patients with HF tolerate better small and more frequent pasty or semi-liquid meals. Larger meals are tiring to consume, may cause abdominal distension and increase oxygen consumption. In summary, any dietetic plan must take into consideration the current needs and replacement of possible deficits, respecting the patient´s habits as far as possible. **Degree of recommendation A, level of evidence 4.**

Physical activity – Long-term bed rest, as recommended in the past, is not necessary for most of HF patients, being indicated only temporarily to those with acute or chronic advanced HF. Prolonged immobilization must be avoided, because it increases the risk of venous thrombosis and pulmonary embolism, in addition to disconditioning skeletal muscles. It is important to consider the risks of such immobilization, especially in the elderly, due to possible complications, such as deterioration of functional capacity, loss of postural vasomotor reflexes, muscle atrophy, osteoporosis, urinary retention, intestinal obstipation and lung infections.

On the other hand, several small studies demonstrate the benefit and safety of programs of well-planned physical conditioning for HF patients, including the elderly, resulting in increased tolerance to the exercise. Prescription of physical activity must be individualized, according to the functional class and age, at levels that do not produce symptoms. A program of low intensity exercise (walking), once or twice a day, may be the best option to avoid the negative, physiological or psychological, consequences of inactivity. The distances traveled may be gradually

increased with intervals of several days or weeks, once they are tolerated. **Degree of recommendation B1, level of evidence 2.**

Pharmacological Treatment

The elderly tolerate less the standard doses and especially the maximum doses of medications recommended by large clinical trials. Moreover, they are more prone to medication side effects, due in part to the co-morbidities and polypharmacy.

Digitalis

The digitalis exert moderate myocardial positive inotropic effect in individuals of all ages. They present singular properties that distinguish them from other positive inotropic medications. They modulate the neuro-humoral activation, reduce the sympathetic activity and stimulate the vagal action, reducing heart rate. They increase the sensitivity of baroreceptors and cardiopulmonary reflexes. Moreover, for its probable anti-aldosterone action, they reduce collagen interstitial deposit.

The aging heart responds less to the inotropic effects of digitalis, without concomitant reduction of toxic effects; on the contrary, the elderly are more susceptible to digitalis intoxication[20-23]. Since digoxine is primarily excreted by the kidneys (approximately 85% in the unaltered form), the deterioration of renal function in the elderly may reduce the clearance of the medication up to 40% and proportionately increase its plasma half-life[24]. Reduction of distribution volume, due to reduction of body muscle mass, is associated to higher myocardial concentration to the same dose; the lower protein binding results in higher proportion of free drug[24].

The digitalis has a very low therapeutic/toxic index. Small increases in serum levels, above the therapeutic level, may produce side effects. In the elderly, such effects may happen even when serum concentrations are within the therapeutic range. The most frequent symptoms of digitalis saturation in the elderly are related to the digestive system (lack of appetite, nausea, and vomiting) and to the central nervous system (sedation, sleepiness, confusion, lethargy). More important, however, are the electrophysiological consequences, which may result in bradycardia, ventricular and supraventricular arrhythmias and different levels of sinoatrial and atrioventricular blockade[25,26].

Digitalis intoxication is more frequent in the geriatric population. The following factors may be involved: lower positive inotropic response, higher myocardial sensitivity to the medication, probably due to myocardial potassium and magnesium depletion, and renal (digoxine) or liver (digitoxine) failure27.

Multiple interactions may occur when digoxine is administered simultaneously with other cardioactive medications. Quinidine and verapamil reduce renal clearance of digoxine by approximately 50%. Amiodarone and spironolactone increase serum levels of cardiotonics, by reducing its renal tubule secretion. In all of these associations, the digoxine dose must be reduced 30 to 50%.

In the geriatric patient, the digoxine dose is lower than in young adults, and must be half in patients above 75-80 years. The daily dose of digoxine must not be over 0.25 mg and usually is around 0.125 mg. The determination of serum concentration of digoxine – which in the elderly must vary between 0.5 and 1.5 mg/ml – is useful to adjust the doses and in case intoxication is suspected.

The withdrawal studies, PROVED[28] and RADIANCE[29], evidenced the importance of digitalis in the symptomatic control and tolerance to exercise in patients with HF FC II and III, in the use of diuretics, or of diuretics and ACE inhibitors, respectively. The large clinical trial DIG[30] showed that digoxine did not influence total mortality compared to the placebo; however, mortality and hospitalizations due to heart failure were reduced.

Digoxine is a first-line medication for treatment of atrial fibrillation-associated HF. **Degree of recommendation A, level of evidence 2**. In patients with sinusal rhythm it is also useful to improve the symptoms and tolerance to exercise, as well as to reduce the hospitalizations due to HF. **Degree of recommendation B1, level of evidence 1**.

Non-digitalis inotropics

Several studies were performed with several non-digitalis positive inotropic medications, in patients with heart failure FC III/IV and ages between 50 and 74 years[31-34]. These agents may improve heart performance, by increasing myocardial contractility and producing peripheral and renal vascular dilation. However, despite these hemodynamic effects and relieving of the symptoms in the short-term, deleterious effects in the patients' evolution are observed in all studies, with significant increase of mortality in the long-term treatment[35]. The deleterious action is probably due to a combination of effects: increased myocardial oxygen

consumption, increased ventricular arrhythmias, exhaustion of cellular energy, alteration of ventricular relaxation, reduced density and sensitivity of heart beta-receptors, cell death and progression of myocardial disease[35]. Therefore, non-digitalis inotropics should not be used in chronic stable HF. **Degree of recommendation C, level of evidence 1**.

On the other hand, two classes of such agents – beta-adrenergic agonists (dobutamine) and phosphodiesterase inhibitors (milrinone) – which improve myocardial contractility by increasing the myocardial concentrations of cyclic adenosine monophosphate, if used intravenously, may be useful and necessary in some short-term conditions: acute HF, low debt syndrome, after acute myocardial infarct, after myocardial revascularization surgery and HF refractory to conventional treatment. **Degree of recommendation B2, level of evidence 3**.

Diuretics

Diuretics antagonize sodium retention in HF by inhibiting its reabsorption in specific sites of the renal tubules. Of the commonly used agents, furosemide, torasemide and bumetanide act at the Henle loop, whereas thiazides, chlortalidone and potassium sparing diuretics act on the distal tubules[36].

Even through different mechanisms, all diuretics increase urinary volume and sodium excretion[37]. Loop diuretics increase sodium excretion at a rate of 20 to 25% of filtered volume and depuration of free water. Thiazide diuretics increase sodium excretion in only 5 to 10% of the filtered volume, tend to progressively reduce the depuration of free water and lose their efficacy in patients with moderate renal dysfunction (creatinine depuration < 30 ml/min)[36-38]. As a consequence, loop diuretics have been preferred in heart failure.

Although the efficacy of diuretics in HF have been evaluated with the same strictness as ACE inhibitors, digitalis and beta-blockers, and even though there have been no comparative studies on mortality, the benefits of their use are universally accredited, especially in edematous states. Moreover, it is important to remember that several studies which showed favorable effects on the survival of heart failure patients using the above mentioned medications, involved the use of diuretics as standard therapy.

Diuretics play a crucial role on the clinical manipulation of HF. First, they can alleviate pulmonary and periphery edema in a few hours or days, whereas the

effects of digitalis and ACE inhibitors may require several days or weeks[39]. Diuretics are the only medications capable of adequately controlling fluid retention and sodium balance on HF. The adequate use of diuretics may allow a dose reduction after stabilization of the clinical features, as well as the full use of digitalis, ACE inhibitors and beta-blockers.

Diuretic therapy may begin with low doses, i.e., 20 to 40 mg/day of furosemide, with progressive dose increase until the desired effect is reached. When the goal is achieved, the treatment must be limited to the prevention or relapse of liquid retention, and the doses may be reduced or readjusted according to the need. Due to its sustained effect, hydrochlorotiazide may be valuable in heart failure associated to arterial hypertension. However, loop diuretics are preferred in most patients, especially with intense fluid retention or renal failure. Therapeutic response and adverse reactions, including electrolytic and metabolic, must be monitored more strictly in the geriatric population. Volume depletion must be prevented by adequate replacement of liquids and potassium by dietetic and drug supplements. The addition of potassium sparing diuretic is convenient in the absence of renal failure.

Resistance to treatment in the refractory heart failure may be by-passed with: 1) intravenous use of loop diuretics; 2) association of diuretics acting at different locations in the nephron; 3) use of drugs that increase the renal plasma flow, such as dopamine and dobutamine. Sodium retention drugs and renal prostaglandin synthesis inhibitors, such as non-hormonal anti-inflammatories must be avoided[40].

In heart failure of the elderly, the indication of diuretics is also universally accepted for edema reduction and other signs of hydric retention, improvement of symptoms of visceral congestion, improvement of exercise capacity and treatment of acute edema of the lung. **Degree of recommendation A, level of evidence 4**.

Adverse effects and precautions – Elderly are more prone to develop adverse reactions to diuretics. A major complication is the volume depletion, to which elderly are more vulnerable. Volume depletion increases the reduction of heart debt, inducing asthenia, fatigue, apathy, psychological alterations, hyperazotemia and orthostatic hypotension. When the reduction of plasma volume is too quick, and especially in patients who remain in bed or seated for a long time, orthostatic hypotension is more intense and may lead to dizziness, falls and even syncopes.

Potassium-depletion diuretics (thiazides and loop) may produce hypopotassemia[41], associated to the reduced dietetic potassium intake and reduced

gastrointestinal ion absorption. The reduction of muscle mass may reduce further the total potassium reserves of the body. On the other hand, potassium sparing diuretics (amiloride, triamterene and spironolactone) may produce hyperpotassemia, especially in elderly with renal failure and/or in association with ACE inhibitors. Extended spironolactone use, especially administered with digitalis, often induces gynecomastia or mammary pain. Elderly are also more predisposed to present hyponatremia, due to the reduction of glomerular filtration speed, an alteration of renal function inherent to the aging process. Hyponatremia and hypomagnesemia are also more common in the elderly. The visceral overload may lead to urinary retention in predisposed patients. Contra-indications for the use of diuretics are: hypovolemia, intense hypopotassemia, hypotension. **Degree of recommendation C, level of evidence 4**.

Spironolactone

Although ACE inhibitors reduce aldosterone plasma concentrations, this effect is transient and there are other sources of its stimulation[41,42].

Spironolactone is a specific aldosterone antagonist. Recently, the RALES study[43] (Randomized Aldactone Evaluation Study), which involved 1,663 patients with HF FC III/IV, 25% mean ejection fraction, of ischemic etiology or not, showed that the addition of spironolactone in a low dose (25 mg/day), was associated to a 27% reduction of total mortality (primary objective), of 36% of hospitalizations due to HF and of 22% in the combined risk of death or hospitalization by any cause (all $p < 0.0002$). Spironolactone was well-tolerated, except by the occurrence of gynecomastia or mammary pain in approximately 10% of the cases.

It is important to emphasize, for clinical applicability, that patients with serum potassium > 5 mmol/dL and/or creatinine > 2.5 mg/dL were excluded from the protocol. Regarding the participation of elderly patients in this study, the mean age was 65 ± 12 years and the analysis of subgroups showed persistence of benefits in patients aged > 67 years.

The use of spironolactone in low doses must be considered in patients with HF FC IV, with normal potassium serum levels and creatinine < 2.5 mg/dL. Potassium serum levels must be monitored in the first weeks of treatment or if the dose of the drug is increased. **Degree if recommendation A, level of evidence 2**.

Angiotensin-converting enzyme inhibitors

Angiotensin-converting enzyme (ACE) inhibitors act on the renin angiotensin system by inhibiting the enzyme responsible for the conversion of angiotensin I in angiotensin II. Moreover, by inhibiting kininase II, an enzyme identical to ACE, to prevent deterioration of kinins, especially bradikinin, and increase synthesis of prostaglandin (PGE_2 and PGI_2) and nitric oxide, mediated by this substance[44,45].

ACE inhibitors are mixed vasodilators, exerting a balanced action on arterial and venous beds. As a consequence, they reduce the post-charge and pre-charge, improving the cardiac debt[45]. By inhibiting angiotensin II constrictive action on renal glomerular efferent arteriole, reducing intraglomerular pressure, in the initial phase of treatment of severe HF, they can reduce renal function temporarily. However, in hypertensive and/or diabetic patients, the intraglomerular pressure attenuating effect is beneficial in the long-term, preventing the sclerosant action caused by the increased intraglomerular pressure. Besides the hemodynamic actions, the neuro-humoral actions of ACE inhibitors contribute significantly to the prevention and reduction of ventricular and vascular remodeling.

Clinical studies – Several randomized, double-blind and placebo controlled clinical studies demonstrated that ACE inhibitors produce beneficial clinical effects in chronic HF of all functional classes, of ischemic etiology or not. These benefits are translated as improvements of symptoms, physical capacity, functional class and life quality, and reduced hospitalizations due to worsening of HF. Moreover, reduced ventricular dimensions and improvement of left ventricle ejection fraction are observed during extended treatment[46,47].

The Cooperative North Scandinavian Enalapril Survival Study (CONSENSUS)[48], SOLVD Treatment Trial[49] and the Vasodilator Heart Failure Trial (V=HeFT II)[50], showed with no doubt that ACE inhibitors reduced the mortality and risks of syndrome progression in HF of functional classes II to IV and improved the prognostic of asymptomatic ventricular dysfunction.

Three studies – Survival and Ventricular Enlargement (SAVE) trial[51], Acute Infarction Ramipril Efficacy (AIRE)[52], Trandolapril Cardiac Evaluation study (TRACE)[53], in patients with left ventricular dysfunction (EF < 40%), symptomatic or not, after acute myocardial infarct, showed that the early and prolonged treatment with ACE inhibitors resulted in significant reductions of total mortality and risk of developing severe HF.

Although none of these studies have included a large number of elderly individuals, several of their findings indicate that ACE inhibitors are as effective in patients > 70 years, including octogenarians, as in younger patients[21,49,52]. However, the elderly presented more frequent side effects to these agents.

The most significant averse effect of ACE inhibitors in the HF treatment is the symptomatic arterial hypotension that may present itself as a first-dose phenomenon, as a consequence of the suspension of angiotensin II hemodynamic support and of the sympathetic tonus. This manifestation is not common and can be avoided with an initial low dose, increasing gradually, according to the tolerance. Those who present higher risk for the first-dose phenomenon are: elderly patients with severe HF, low systolic blood pressure (< 90 mmHg) and sodium plasma level < 135 mEq/L.

Another usual side effect is a dry, irritating cough that prevents the continued use of the drug in about 10 to 20% of the cases. It is a class-specific effect, that does not depend on the dose and the length of medication use.

Hyperpotassemia may develop during the treatment, especially in the elderly, diabetics and in case of renal failure. Concomitant potassium supplement or potassium sparing diuretics are not generally necessary and periodic electrolytes monitoration is required. Allergic reactions, including angioedema, happen very rarely.

In the beginning of ACE inhibitors therapy, discrete serum creatinine increase may be observed, especially if the patient presents some level of kidney failure. When it is mild, there is no further worsening and it may even delay its evolution.

In the clinical practice, association of severe HF, hypotension and kidney failure is relatively frequent due to the low cardiac debt and reduction of renal plasma flow, with serum creatinine higher than 2.5 mg/dL. In such cases, the risk of worsening renal failure may be balanced with more important potential benefits, especially for those more severe patients[48]. The best attitude is to adequately balance the hemodynamic and volemic state, with digitalis and diuretics, before starting on ACE inhibitors.

ACE inhibitors must be cautiously used and the patients should be monitored if serum creatinine levels is > 3mg/dL and serum potassium > 5.5 mEq/L; they are counter-indicated in bilateral stenosis of the renal artery and pregnancy.

All patients with systolic HF (FC II/IV), or major asymptomatic left ventricular dysfunction (EF ≤ 0.40), must receive ACE inhibitors, except if they

present intolerance to this class of medication or it is counter-indicated. **Degree of recommendation A, level of evidence I.**

Among the several agents clinically available, the use of those with proven significant survival benefits in randomized studies is recommended[54]. Therapy with ACE inhibitors, especially for the elderly, must begin with low doses, with gradual titration aiming the recommended target dose, as long as tolerated (table II). During the titration period, blood pressure, kidney function and serum potassium must be carefully monitored.

The ATLAS study[55] aimed to evaluate the effects of low doses (2.5 mg to 5 mg) compared to high doses (32.5 mg to 35 mg) of lisinopril on clinical events. Intermediate doses were not tested. Patients who received the higher doses presented non-significant reduction of mortality; nonetheless total hospitalizations and hospitalizations from HF were significantly reduced (12%, p = 0.021 and 22.6%, p = 0.002, respectively).

Angiotensin II receptor antagonists

Compared to ACE inhibitors, angiotensin II receptor antagonists (ARAs) presented some pharmacological differences that would support their use[56]. 1) The main harmful effects related to renin-angiotensin-aldosterone system are due to the action of angiotensin II on AT_1 receptors, which are efficiently blocked by ARAs. Its mechanism of action would be more effective, especially because angiotensin II may be generated by other pathways independent of ACE, such as quimase, CAGE and cathepsin. 2) AT_2 receptors are not blocked by ARAs and may respond to increased angiotensin II concentrations resulting from AT_1 blockade. Activation of AT_2 receptors may be cardioprotective, because among other effects, it increases bradikinin production, inducing vasodilation, and is probably anti-proliferative. 3) The incidence of side effects, such as cough and angioedema, is extremely low.

Few large studies tested ARAs effects on mortality by HF. Although an initial ELITE study[57] involving 722 patients had suggested greater benefit of losartan (50 mg/day) over captopril (50 mg, thrice/day) on mortality of aging patients with HF, the ELITE II study[58], which included more than 3,000 patients, showed a tendency (NS) for a better evolvement and less sudden deaths with captopril.

Tolerability was better with losartan, primarily due to the higher incidence of cough with captopril.

Table II – Angiotensin-converting enzyme inhibitors		
Medication	Initial dose	Target dose
Captopril	6.25 mg, 3x/day	50 mg, 3x/day
Enalapril	2.5 mg, 2x/day	10 mg, 2x/day
Lisinopril	2.5 – 5.0 mg/day	20 mg/day
Ramipril	2.5 mg/day	10 mg/day
Benazepril	2.5 mg/day	10 mg/day
Cilazapril	1 mg/day	5 mg/day
Fosinopril	5 mg/day	20 mg/day
Perindopril	2 mg/day	4 mg/day
Quinapril	10 mg/day	30 mg/day

The RESOLVD study[59] compared the effects of candersatan with those of enalapril and with the association of both in 768 HF patients FC II/IV for 43 weeks. The outcomes concerning tolerance to exercise, functional class and quality of life were similar in the three groups, whereas ejection fraction increase and neuro-hormones drop were observed in the association group. In the enalapril group a tendency (NS) to lower mortality was observed.

In the VAL-HeFT study[60], 5,010 HF patients classes II and III were medicated with ACE inhibitors, diuretics or valsartan (40 mg to 160 mg, twice a day). After two years of follow-up, total mortality was similar in both groups; however, there was a reduction of hospitalizations due to HF in the valsartan group.

Based on these studies, ACE inhibitors are still the agents of choice to block the renin-angiotensin system in HF. ARAs may be used in the elderly and in

patients who present side effects of adverse reactions to ACE inhibitors. **Degree of recommendation B1, level of evidence 2**.

Hydralazine and isosorbide dinitrate

The only favorable clinical experience with long-term vasodilator therapy for HF was with the association of hydralazine and isosorbide dinitrate (IDN). These two medications were initially combined due to their complementary, arterial and venous, vasodilator effects on the peripheral circulation, reducing the pre- and post-load[61,62], in addition to their favorable effects on myocardial and vascular remodeling and on HF progression[63-67].

Two large trials[50,68] evaluated the effects of combined IDN (up to 160 mg/day) and hydralazine (up to 300 mg/day) added to diuretic and digoxine therapy, in HF patients FC II/III. Beneficial effects on mortality, tolerance to exercise and ejection fraction were observed. It is worth mentioning that the doses of these medications usually tolerated are well below the ones used in these trials.

Combined IDN-hydralazine must be considered in patients who do not tolerate or present contra-indication to ACE inhibitors, although in this case ARAs are preferred. Nitrates may be used for angina treatment and relief of acute dyspnea.

Beta-blockers

The mechanisms by which beta-blockers cause beneficial effects on HF are complex and result from hemodynamic, electrophysiological and especially neuro-humoral actions. The hemodynamic effects during chronic administration differ from the acute ones in many aspects. The reduction of heart rate decreases myocardial oxygen consumption and may increase the length of coronary perfusion by prolonging diastole, with favorable effects on myocardial ischemia. Systolic blood pressure tends to drop in the beginning of the treatment, but it stabilizes or even increases later[69].

Chronic therapy of HF with beta-blockers progressively reduces the left ventricular volume[70-74] and the myocardial mass, increases the left ventricle ejection fraction[70-77] much more than that observed with any other medication. It improves the left ventricle geometry, which shows a less spherical shape and reduces mitral regurgitation[78]. Therefore, beta-blockers may reverse all alterations associated to ventricular remodeling[79]. This process is usually present after two

months of treatment and continues for up to 12 to 18 months[80]. These compounds increase the parasympathetic tonus and readjust baroreceptors' sensitivity[80], restore the variability of heart rate, reduce the dispersion of QT interval and prevent catecholamine-induced hypopotassemia, exerting anti-arrhythmia effects.

The neuro-humoral actions of beta-blockers on HF are multiple and include the inhibition of the sympathetic activity and of noradrenaline direct cardiotoxic effects; reduction of noradrenaline in the coronary sinus (carvedilol); inhibition of the renin-angiotensin-aldosterone system; reduction of endothelin synthesis (carvedilol); increase of atrial (ANP) and brain (BNP) natriuretic peptides; attenuation of the myocardial expression of tumor necrosis factor alpha and interleukin-1β[81,82]; improvement of beta-receptors regulation, expression and uncoupling, as well as of G-inhibiting protein; anti-oxidant action (carvedilol)[83,84]; anti-proliferative action (carvedilol)[85].

At the cellular level, beta-blockers prevent cyclic AMP elevation and the calcium myocardial overload, as well as activation of the calcium-dependent ATPase and, consequently, reduction of highly energetic phosphate induced by adrenergic stimulation. All of these mechanisms lead to myocites protection, to prevention and regression of ventricular remodeling, reducing the progression of left ventricular dysfunction.

Multiple clinical trials convincingly showed that addition of a beta-blocker to the conventional HF therapy with diuretics, ACE inhibitors and digitalis, chronically induces improvement of symptoms, functional class and left ventricular function, translated by the significant increase of ejection fraction[86-89]. The effects on maximum exercise capacity are inconsistent. Regardless of an initial clinical worsening in some cases, probably due to removal of adrenergic support, these studies showed a long-term clinical improvement on HF evolvement, reducing the worsening episodes of the syndrome and the need of hospitalizations in groups treated with beta-blockers. Subsequently, several randomized, double-blind and controlled studies also showed a significant mortality reduction with beta-blocker therapy. Four major studies must be emphasized.

Metoprolol CR/XL Randomized Intervention Trial in Heart Failure (MERIT HF)[90] included 3,991 HF patients FC predominantly II and III and some FC IV, with ejection fraction ≤ 0.40, of ischemic etiology or not. Patients were randomized in placebo or metoprolol, a selective β1 blocker, in increasing doses of up to 200 mg (average = 159 mg/day), added to the conventional triple therapy. After a mean follow-up of 12 months, the metoprolol group showed 34% reduction of total

mortality (primary outcome; p = 0.0062), of 40% mortality due to aggravation of HF (p = 0.0023) and of 41% on sudden death (p = 0.002).

The second Cardiac Insufficiency Bisoprolol Study (CIBIS II)[91] involved 2,647 patients with left ventricular ejection fraction ≤ 0.35 and moderate or severe HF (most of them, FC III), due to ischemic myocardiopathy or not. Placebo or bisoprolol, a selective β1 blocker, were randomly added to the conventional therapy. The mean follow-up was 1.3 years. Bisoprolol treatment was associated to 34% of all mortality causes (p < 0.0001), of 44% on sudden death (p = 0.0011) and of 32% on hospitalization risk due to HF aggravation (p < 0.0001). The study was interrupted earlier after the second interim analysis.

The US Heart Failure Study[92] included 1,094 patients with left ventricle ejection fraction ≤ 0.35 and HF FC II, randomly assigned to receive placebo or carvedilol, a β1, β2 and α1-adrenergic blocker, in progressive doses of 3.125 mg, twice a day, up to 25 mg, twice a day. After an average 6 month follow-up, total mortality was 7.8% in the placebo group and 3.2% in the carvedilol group (RRR = 65%; p < 0.001). Moreover, carvedilol treatment was associated to 27% on the risk of hospitalizations due to cardiovascular causes (p = 0.036) and 38% on the combined risk of hospitalizations or death (p < 0.001).

The Carvedilol Prospective Randomized Cumulative Survival Study – COPERNICUS[93] – was planned to evaluate carvedilol effects on HF patients FC IV, LVEF ≤ 0.25 and clinically euvolemic. After an average follow-up period of 10.4 months, carvedilol treatment was associated to 35% mortality reduction (p = 0.0014) and of 24% on combined risk of death or hospitalization (p < 0.001).

Although none of these studies have included a significant number of elderly individuals, the benefits were similar for patients younger than 65 years, as well as on HF of ischemic etiology or not.

Chronic HF patients, FC II/IV, EF ≤ 0.40, stable and with adequate maintenance diuretics doses, ACE inhibitors, with or without digitalis, must receive beta-blockers, except if unable to tolerate it, or when counter-indicated.

Degree of recommendation A, level of evidence 1.

Contra-indication to use beta-blockers include: bradycardia, especially symptomatic, advanced atrio-ventricular blockade (except if treated with a pacemaker), hypotension (SBP < 90 mmHg) and bronchospasm disease. Beta-

blocker should not be initiated in patients with uncompensated HF, especially if acute or in need of treatment with a beta-agent inotropic agonist.

Posology – Treatment of HF with beta-blocker must begin with very low doses: carvedilol, 3.125 mg, twice a day; continuous release metoprolol, 12.5 mg, once a day; bisoprolol, 1.25 mg, once a day[94,95]. The increases must be gradual, doubling the dose (if well tolerated) every two to four weeks. If side effects occur, the increases must be postponed until they disappear. Recommended target doses are: 25 mg, twice a day for carvedilol; 200 mg, once a day for CR metoprolol; and 10 mg for bisoprolol[94,95]. Although target doses used in large clinical trials should be reached, lower doses should be maintained if the higher doses are not tolerated.

Side effects – Most common side effects, especially in the beginning of the treatment or with beta-blocker dose increase, which require attention and appropriate manipulation are hypotension, bradycardia and atrio-ventricular blockade, fluid retention and HF aggravation. As a consequence, patients must be strictly monitored regarding blood pressure, heart rate, fluid retention (body weight) or worsening of HF, during the onset of dose titration. As excessive fluid depletion may potentialize the risk of hypotension and its retention increase the risk of HF aggravation, the doses of diuretics, as well as of ACE inhibitors and digoxine, must be optimized before and during treatment with beta-blockers[94,95]. In the large clinical trials, approximately 90% of patients tolerate the treatment in the short- and long-terms.

Two relevant aspects of beta-blocker treatment must be emphasized and informed to the patient: 1) the initial adverse effects are usually transient and generally do not impose suspension of the medication; 2) the beneficial clinical responses may take weeks and even 2 to 3 months to become evident[70]. Even if the symptoms do not improve in a short-term, the treatment must be chronically maintained to reduce the risk of important clinical events. In patients with ischemic cardiopathy, the beta-blocker should not be abruptly interrupted.

Anticoagulants

Patients with chronic HF are likely to present a higher risk of thromboembolism due to blood stasis in the hypokinetic dilated cardiac chambers and in the lower limbs[96], and due to the increased activity of pro-coagulant

factors[97]. However, in large studies, the risk of thromboembolism was relatively low (1 to 3% a year)[98].

There are no controlled clinical trials on the use of anticoagulants and other anti-thrombosis agents in HF patients. Although some authors recommend that anti-coagulation for patients with major cardiomegaly and very low LVEF, current recommendations for the chronic use of oral anti-coagulants in HF are: previous thromboembolism phenomena, atrial fibrillation and presence of intra-cavity thrombus, especially if sessile (or non-pedicular). **Degree of recommendation B1, level of evidence 4**.

The use of subcutaneous heparin is justified in uncompensated and bedridden HF patients.

III – Coronary artery disease

Coronary artery disease (CoF) currently represents the main cause of death in the elderly. Autopsy studies demonstrated a 70% prevalence of coronary arterial disease (CAD)[1]. These findings may be accidental, and the disease may remain silent for the person's whole life. Approximately only 20 to 30% of the elderly present CoF clinical manifestations[2]. In several elderly, the disease manifests earlier, but in others it remains silent until the 7th or 8th decade.

Despite being such a prevalent disease, there is some diagnostic difficulty, probably due to distinct CAD clinical manifestations in the elderly or not elederly[3]. The typical effort angina is generally the first CoF manifestation in the non-elderly, being easily recognizable. In the elderly, however, typical prechordal pain occurs in only half of coronarypathies[4]. It may be less severe, or absent, due to limited physical activity. It may also be present as "*angina equivalents*" and more frequently myocardial ischemia appears as *dyspnea* (due to a transient increase in the final left ventricle diastolic pressure, caused by ischemia overlapped with reduced ventricular complacency caused by the aging process); *acute pulmonary edema*; *cardiac arrhythmia* (palpitation, syncope); or *silent form*, as *silent ischemia, acute infarct or sudden death*[5]. Precordialgia in the elderly may also be atypical and come in distinct forms, such as shoulder or back pain (may be mistaken by degenerative disease), epigastric pain (may be mistaken by peptic ulcer), post-prandial or nocturnal pain (suggesting hiatus hernia or gastroesophagic reflux), making a

differential diagnosis necessary with esophagus reflux and spasm, peptic ulcer, cholecystolithiasis, neural-muscle-skeletal disorders and states of anxiety[6].

1) Chronic stable angina

Up to 65 years of age, the prevalence of symptomatic coronary arterial disease (CAD) is higher in men than in women, being equivalent in both sexes after the 8th decade. Chronic stable angina (CSA) is defined as that in which ischemia symptoms are present in unaltered form for at least two months[7,8]. CSA may be the first CAD manifestation or may appear after acute myocardial infarct (AMI) or unstable angina.

Diagnosis

The diagnosis is made by anamnesis, physical exam, and request for exams solicitation[9,10]. Underlying illnesses must be searched and treated, such as anemia, systemic arterial hypertension, diabetes and thyroid diseases[11].

Request for laboratory exams: fast glicemia and lipid profile (total cholesterol, HDL cholesterol, triglycerides and calculated LDL): **degree of recommendation A, level of evidence 1**; hemoglobin: **degree of recommendation A, level of evidence 4**; urea and creatinine: **degree of recommendation B1, level of evidence 4**.

Request for complementary exams:

1) Electrocardiogram: **degree of recommendation A**;

2) Ergometric test (ET): the high prevalence of severe coronarypathy increases the test sensitivity to 84% and decreases its specificity to 70%, thus increasing the incidence of false-negatives. On the other hand, the concomitant left ventricular hypertrophy (LVH), secondary to ASH and conductance disorders, also increases the prevalence of false-positive tests[12]. *Degrees of recommendation for performing ET*: **degree of recommendation A, level of evidence 2 –** patients with intermediate pre-test probability to CAD, including those with complete blockade of the right branch or depression of ST segment < 1 mm at rest, except for the ones listed below on degrees B and C; **degree of recommendation B1, level of evidence 4 –** patients suspected of having vasospastic angina; **degree of recommendation B2, level of evidence 2 –** patients with high pre-test probability for CAD, based on age, sex and symptoms; patients with low pre-test probability of CAD, based on age, gender and symptoms; patients taking digoxine, who presented depression of

ST segment < 1 mm on baseline ECG; **degree of recommendation B2, level of evidence 2** – patients with electrocardiographic criteria of left ventricular hypertrophy and depression of ST segment < 1 mm at baseline ECG; **degree of recommendation C, level of evidence 2** – patients with pre-excitation Wolf-Parkinson-White (WPW) syndrome, use of artificial pacemaker, depression of ST segment > 1 mm, complete blockade of the left branch (CBLB).

3) Rest trans-thoracic echodopplercardiography (RTE) – It is a very useful method for evaluation of left ventricle (LV) global and regional function. Abnormalities of wall movement such as: hypokinesia, akinesia, diskinesia, absence of systolic thickening are generally observed in previous AMI, transient ischemia, chronic ischemia (hibernating myocardium) and myocardial fibrosis of any nature. RTE is also useful to detect and quantify occasional presence of LVH and of cardiac valvopathies, whose distinct diagnosis is extremely important[8]. *Degrees of recommendation for performing RET*: **degree of recommendation A, level of evidence 4** – patients with systolic murmur suggestive of valvopathies (aortic stenosis, mitral valve prolapse with regurgitation) or of hypertrophic myocardiopathy; evaluation of ischemia extension when the exam can be obtained during the episode of prechordal pain; **degree of recommendation C, level of evidence 4** – patients with normal ECG, without past AMI and suggestive signs of CCF, valvopathies or hypertrophic myocardiopathy.

4) Stress trans-thoracic echocardiography (SE) – an expressive number of elderly referred for evaluation of thoracic pain are incapable of performing an adequate ET, making SE with dobutamine an alternative for CAD evaluation. This type of investigation is also useful for those with branch blockade of Hiss bundle, as well as for bearers of baseline ECG alterations, common findings in the myocardial revascularization post-operative period (MRS). The sensitivity and specificity of SE with dobutamine for CAD diagnostic in the elderly is 80% and 70%, respectively, and side effects are similar to those observed in the adult population[13].

5) Myocardial perfusion scintigraphy (MS) – usually performed together with the ergometric test. However, pharmacological techniques with dipiridamol or with adenosine are alternatives for those unable to exercise adequately[14]. The most frequently used radiomedications are thallium 201 and sestamib technetium (MIBI), with similar diagnostic accuracy. *Degrees of recommendation to perform SE and MS*: **degree of recommendation A, level of evidence 2** – patients with intermediate pre-test probability for CAD, who present WPW syndrome at ECG or depression of ST segment > 1 mm; patients with past myocardial revascularization;

degree of recommendation B2, level of evidence 2 – patients with low or high pre-test probability for CAD, with ECG showing WPW syndrome or depression of ST segment > 1 mm; patients with intermediate probability for CAD, using digoxine and ST depression < 1 mm at ECG; left ventricular hypertrophy, with depression of ST segment < 1 mm at ECG; as an initial exam in patients with normal rest ECG who are not using digoxine.

Obs: For patients unable to exercise or those with PM and LBCB, myocardium perfusion with adenosine or dipiridamol or SE with dobutamine should be used.

6) Cinecoronarygraphy – most accurate method for CAD diagnostic. Compared to the younger patients, the risk of this procedure in the elderly is slightly higher. *Levels of recommendation to perform cinecoronarygraphy*: **degree of recommendation A, level of evidence 2** – patients with possible or established angina who survived sudden death or present sustained VT; **degree of recommendation A, level of evidence 4** – patients with high pre-test probability of lesion on the left coronary stem or triarterial disease; **degree of recommendation B1, level of evidence 4** – patients who remain with inaccurate CAD diagnosis after performing a non-invasive test in which the benefits of a diagnostic confirmation exceed the risk and costs of the exam; patients unable to take a non-invasive test due to physical incapacity, illness or morbid obesity; patients with ergometric test positive for myocardial ischemia; **degree of recommendation B2, level of evidence 4** – patients with recurrent hospitalizations due to prechordal pain, for whom a definitive diagnostic is considered necessary; **degree of recommendation C, level of evidence 4** – patients bearing significant co-morbidities, for whom the risk of the exam exceeds its benefits and/or a low life expectancy.

Treatment

Treatment of CSA aims to improve the prognostic, preventing infarct and sudden death, and improving the quality of life by reducing symptoms[8]. A regression or stabilization of the atherosclerotic plaque, preventing its complications, especially thrombosis, and protecting the myocardial should be stimulated, by means of an increase of the coronary flow. It is necessary to act on the risk factors and to establish a clinical, surgical or interventionist treatment, according to the situation.

Clinical Treatment

Left ventricular function and presence of co-morbidities must be considered.

Aspirin and hypolipidemic drugs must be used, due to the evidence of reduction of death risk and of non-fatal AMI on studies of primary and secondary preventions[7].

Beta-blockers (BB) are also first line medication; they reduce the incidence of cardiac effects at post-AMI and mortality in ASH patients. However, BB are still underused by the elderly[11].

Nitrates do not reduce mortality for CAD bearers; however, they reduce the frequency and intensity of angina episodes and increase tolerance to effort. They can be used in association with BB and/or CCA[8].

Calcium channel antagonists and short-action dihydropiridines must be avoided, since they increase the incidence of cardiac events in CAD patients. The long-action ones and the non-dihydropiridines, verapamil and diltiazen, however, are efficient to relieve symptoms in CSA, without increasing the occurrence of adverse cardiac effects[15]. Verapamil and diltiazen must not be used in patients with significant left ventricular dysfunction.

Nitrates, BB and some long-action dihydropiridines may be used in left ventricular dysfunction. In case of asthma and peripheral arterial disease, CSA and nitrates must be preferred, although selective BB may also be used with caution.

Degrees of recommendation for the clinical treatment of CSA – **degree of recommendation A, level of evidence 1** – aspirin in the absence of contra-indications; hypolipidemic in individuals with suspected or documented CAD, with LDC cholesterol > 130 mg/dl and target value of LDL < 100 mg/dl; **degree of recommendation A, level of evidence 2** – BB as initial therapy without contra-indications, in previous AMI bearers; BB as initial therapy without contra-indications in individuals without history of AMI; CCA (except short-action dihydropiridines), or long-action nitrates, as initial therapy, when BB are counter-indicated; CCA (except short-action dihydropiridines) or long-action nitrates, combined with BB, when initial treatment with BB is not satisfactory; **degree of recommendation A, level of evidence 4** – CCA (except short-term dihydropiridines) and long-action nitrates as BB replacement, if the initial treatment produces unacceptable side effects; sublingual nitroglycerine for immediate disappearance of angina; **degree of recommendation B1, level of**

evidence 2 – thienepiridines (clopidogrel, tychlopidine), when ASA is absolutely counter-indicated; hypolipidemic medication in documented or suspected CAD patients and LDL cholesterol between 100 and 129 mg/dl and LDL target value < 100 mg/dl.

Treatment with percutaneous coronary intervention (PCI)

PCI is a widely used procedure for the treatment of CSA, initially using a catheter-balloon and, more recently, with stents. Compared to the isolated angioplasty, the use of stent reduces the incidence of complications in the elderly, although the specialized literature on the subject is still scarce[16].

Until now, there is no convincing evidence that the PCI is superior to the drug treatment, regarding AMI and death reduction in patients with CSA. However, an interventionist technique is significantly better regarding the reduction of symptoms, although re-interventions are necessary in order to maintain improvement.

Treatment with myocardium revascularization surgery (MRS)

A recent study (ARTS)[17] showed that both MRS and PCI offer the same protection regarding the incidence of AMI, death and stroke in coronariopaths with multivascular disease. Nonetheless, PCI is less costly, although more interventions were necessary to maintain the results.

Levels of recommendation for myocardium revascularization with PCI or surgery: **degree of recommendation A** – patients with clinical and/or anatomical suggestion of very high risk, in which the isolated clinical treatment is unfavorable, such as lesion in the left coronary stem, large ischemic areas (lesion of one or more vessels), LV dysfunction, congestive heart failure; patients who needed correction of associated anatomical defects, such as mitral regurgitation and LV aneurysms.

2) Infarct with no ST infra drop and unstable angina

Anatomopathological and angioscopic studies show that unstable angina (UA) and acute myocardium infarct (AMI) are different clinical presentations

resulting from a common pathophysiological mechanism, which is the rupture or fissure of the atherosclerotic plaque, with different levels of thrombosis and coronary obstruction[18]. Therefore, the expression "acute coronary syndromes" (ACS) has been used to describe several clinical conditions including UA, AMI with no Q wave (usually there is no increase of the ST segment – AMINEST) and AMI with Q wave (usually presenting an increase of the ST segment). The clinical manifestations and treatment of UA are similar to those of AMINEST[19,20].

The elderly present higher incidence and worse prognosis of ACS without ST infra than the younger patients[21].

Diagnosis

a) ***Symptoms and signs*** – Prechordial pain is the main clinical manifestation, usually occurring at rest, may be located on the epigastric, dorsal, mandibular and upper limb regions. Myocardial ischemia should also be suspected when the patient presents dyspnea, loss of consciousness, unexplainable indigestion, sudoresis, weakness and mental confusion. The physical exam is unspecific; however, the presence of the 3rd dupp at the admission has prognostic implication of hospital mortality in elderly patients[22].

b) ***Electrocardiogram*** – The frequent coexistence of abnormalities such as LVH may cause difficulty for the ECG interpretation in the elderly patient. However, this exam must be made immediately after the patient's arrival at the emergency room, because electrocardiographic alterations have diagnostic and prognostic implications. Drop of the ST segment or occurrence of LBCB indicate high incidence of cardiac events (death, myocardial infarct and recurrent angina) in the following 60 days[22].

c) ***Laboratory evaluation*** – The patients must be submitted to an appropriate laboratory evaluation to identify possible anemia, dislipidemia, diabetes mellitus and thyroid dysfunction. Besides these, serum levels of biological markers of myocardial necrosis should be taken in order to make the differentiation between UA and AMINEST possible. The two-fold raise of CK-MB characterizes AMI and therefore makes it possible to identify AMINEST. On the other hand, T and I cardiac troponins are elevated in all AMINEST patients and in a subgroup of UA patients who will have a worse prognosis and who will benefit from the early use

of PCI and with the parenteral use of inhibitors of the glucoprotein IIb/IIIa (GP IIb/IIIa) complex and heparin.

d) ***Transthoracic rest echodopplercardiography*** – TRE is a useful procedure to help the clinical decision for the UA patient, since it can identify the presence of transient parietal movement deficit during an ischemic episode, signs of early AMI, left ventricular dysfunction and associated diseases, such as mitral regurgitation.

Degrees of recommendation to perform the diagnostic investigation in UA-AMINEST: **degree of recommendation A, level of evidence 4** – ECG with 12 derivations; assays of biological markers of myocardial injury (CK-MB and troponins), **degree of recommendation B1, level of evidence 4** – thorax radiography and TRE to investigate non-coronary causes.

Treatment

a) ***Oxygen therapy*** – In UA and AMINEST there can be hypoxemia which favors the increase of myocardial lesion. Oxygen (O_2) administration can limit the acute ischemic lesion. However, its use must be monitored by O_2 plasma saturation and maintained up to approximately 4 h after the pain subsides.

b) ***Analgesia and sedation*** – Prechordalgia and anxiety are frequently present in SCA episodes, contributing to the increase of sympathetic activity, increasing the myocardial consumption of oxygen and predisposes to ventricular tachyarrhythmias. Thus, intravenous morphine sulfate is recommended when necessary to halt prechordal pain. On the other side, the use of anxiolytics (usually benzodiazepines) must be reserved for especial occasions.

c) ***Nitrates*** – Despite its routine use in UA and AMINEST patients, nitrates have not been evaluated yet in randomized studies in such situations. Treatment with nitrates usually begins with sublingual followed by intravenous route.

These products are counter-indicated in case of blood hypotension or use of sildenafil within the last 24 h.

d) ***Beta-blockers*** – Its use in UA patients is based on results from small clinical studies, and especially, inferrence on findings from AMI studies, given the

large pathophysiological similarity between both conditions. Except when counter-indicated, BB must be initiated by intravenous route, and subsequently used orally, with adequate doses to maintain heart rate at approximately 60 bpm.

e) ***Calcium channel antagonists*** – There are favorable evidence to the use of verapamil and diltiazen in ACS patients with no ST drop and without LV dysfunction. On the other hand, short action dihydropiridines (nifedipine) are counter-indicated due to the increase of adverse cardiac events.

f) ***Aspirin*** – Aspirin blockades platelet cyclooxigenase preventing the forming of A_2 thromboxane, hindering platelet aggregation and interfering with thromb formation, which has an important role on triggering and evolvement of ACS.

g) ***Thienepiridine derivatives*** – Tychlopidine and clopidogrel exert a platelet anti-aggregating action by blocking the activation of adenosine diphsophate (ADP). The benefits of clopidogrel in the reduction of cardiovascular events in UA and AMINEST patients were confirmed by the CURE study[23], in which the group that took clopidogrel + ASA presented a smaller incidence of AMI, stroke and cardiac death than the group that took ASA + placebo.

h) ***Inhibitors of angiotensin converting enzyme (IECA)*** – The Hope study[24] showed that CAD patients presented significant reductions of death, AMI and stroke five years after the use of ramipril (10 mg/day). The results in patients older than 65 years were better than in younger ones.

i) ***Inhibitors of HMG-CoA reductase*** - The MIRACL study[25] showed that early and aggressive reduction of LDL cholesterol with atorvastatin (80 mg/day) significantly decreased the incidence of recurrent ischemic events in the first 16 weeks of ACS without raising the ST segment. This study selected 3,086 patients with mean age of 65 years.

j) ***Glucoprotein IIb/IIIa receptor blockers*** – GP IIb/IIIa blockers are a new class of potent anti-platelet drugs, which act on the final and mandatory mechanism of platelet activation, regardless of the route used[26]. Abciximab is a monoclonal antibody with high affinity for the GP IIb/IIIa receptor and biological half-life of 6-12h. It must be given in a bolus dose of 0.25 mg/kg, followed by a

continuous supply of 0.125 μg/kg for 12 h. This product was specifically evaluated in UA patients not submitted to the PCI in the GUSTO IV study, and who could not show a reduction of cardiac events, even on those who presented ST elevation. On the other hand, as confirmed in the CAPTURE study[27], abciximab is useful only in UA patients who will be submitted to PCI within the next 24h.

Tirofiban is a synthetic derivative of low affinity for GP IIb/IIIa, and consequently, has a short plasma half-life (approximately 2h). The recommended dose is 10 μg/kg given as a bolus, followed by continuous infusion of 0.15 μg/kg/min, during 48h. This drug is used as a pre-treatment in UA patients in the TATICS-TIMI 18[28], contributing to improve the evolution of patients who had an early intervention.

k) ***Heparin*** – Non-fractionated Heparin (NFH) has been successfully used in the treatment of CSA without ST elevation; however, it has important pharmacokinetic limitations related to its capacity to bind non-specifically to proteins and cells.

Low molecular weight heparins (LMWH), on the other hand, present the following advantages: may be given subcutaneously, do not require monitorization and anti-coagulation parameters, and are less associated with heparin-induced thrombocytopenia. Several studies demonstrate the benefits of LMWH use in CSA patients without ST elevation. Nonetheless, since enoxparin in the subgroup of elderly presented excellent performance, as demonstrated in the ESSEN-CE and TIMI 11B studies[29], this may be the indirect anti-thrombosis drug of choice for this age range.

l) ***Myocardial revascularization*** – myocardial revascularization (OCI or MRS) is an effective procedure to relieve symptoms, prevent ischemic complications, and improve the functional capacity and prognosis in coronary patients. Recent studies (FRISC II and TATIC-TIMI 18) showed greater advantage in the use of early invasive strategy in CSA patients without ST elevation.

Degrees of recommendation for the use of pharmacotherapy in UA and AMINEST patients – **degree of recommendation A, level of evidence 1** – aspirin without contra-indication, aspirin + clopidogrel without contra-indication, ACE inhibitors in patients with LV dysfunction, GP IIb/IIIa blockers (tirofiban); **degree of recommendation A, level of evidence 2** – beta-blockers, non-fractionated heparin, low molecular weight heparin, HGM-CoA reductase inhibitors; **degree of**

recommendation A, level of evidence 3 – sublingual and intravenous nitrates; **degree of recommendation A, level of evidence 4** – oxygen therapy in case of respiratory discomfort and arterial oxygen saturation < 90%, morphine in persistent pain after medication with verapamil without contra-indication; **degree of recommendation B2, level of evidence 2** – ticlopidine or clopidogrel; **degree of recommendation B2, level of evidence 4** – oral or topic nitrate; **degree of recommendation C, level of evidence 1** – oral GP IIb/IIIa fibrinolytic blockers; **degree of recommendation C, level of evidence 2** – short action dihydropiridines direct thrombin inhibitors.

Degrees of recommendations for performing myocardial revascularization (PCI or MRS) in UA and AMINEST patients: **degree of recommendation A, level of evidence 1** – abciximab followed by immediate PCI; tirofiban in the first 24h, followed by PCI in the third and fourth days; MRS for patients with unfavorable anatomy for PCI and without satisfactory response to medication therapy.

3) Acute Myocardial Infarct

Currently, AMI is still one the main cause of death. According to the specialized literature, 80% of the deaths attributed to AMI occur in individuals older than 65 years[30]. Rechannelling of the damaged coronary, by means of fibrinolytics and PCI procedures, caused a significant impact on AMI treatment, reducing mortality to less than 10%. The GUSTO V study[31] recorded an incidence of death < 6% in 30 days for infarct victims submitted to this approach. The elderly AMI bearers are usually classified as a subgroup of high risk, therefore associated to higher indexes of morbidity and mortality[32,33].

Myocardial reperfusion in AMI

A) **Fibrinolytics** – The use of fibrinolytics for treatment of AMI is proven beneficial in elderly patients[34,35]. The only exception refers to individuals older than 75 years with a higher incidence of hemorragic stroke, especially when the agent used is t-PA[36]. For this age range, careful evaluation of the cost-benefit therapy is recommended, and also the preferential use of streptokinase (at a dose of 1.5 million units in 30 to 60 min), which correlates less intensely with hemorragic stroke.

B) **Primary angioplasty/*Stent*** – PCI is a useful procedure for the treatment of AMI in the elderly[37-39], and must be performed by experienced staff and centers, preferrably within 90 minutes of hospital admission.

Degrees of recommendation for the use of thrombolytics/PCI in the elderly - **degree of recommendation A, level of evidence 2** – percutaneous coronary intervention; **degree of recommendation B1, level of evidence 2** – thrombolytic, preferrably streptokinase.

Medication associated to the acute phase of the infarct

Despite the high incidence of AMI in the elderly, most of the large randomized study that deals with this issue include few aged participants. Therefore, most of the available information derives from the analysis of relatively small subgroups of patients older than 65 years of age.

a) **Platelet anti-aggregating drugs** – The ISIS – 2 study[40] showed that ASA is as effective as streptokinase to reduce AMI-induced early mortality, even in a population > 70 years (20%). Therapy has also been proved a late benefit of this; however, ASA continues to be under used in elderly subjects. ASA use is recommended at 200 mg/day, beginning immediately upon patient's hospitalization[41]. In those patients with counterindication to ASA use, trifusal was shown to be a safe therapeutic option as demonstrated in TIM study[42].

b) **Heparin** – Conventional heparin must be used intravenously, in full doses, in infarct patients submitted to reperfusion with t-PA or alteplase and in patients with high risk of systemic embolism (previous extensive infarct, presence of ventricular thrombus or atrial fibrillation and history of embolism)[43]. On the other hand, there is no evidence to recommend the routine use of non-fractionated heparin for AMI treatment.

c) **Beta-blockers (BB)** – The use of BB is fully indicated in AMI patients, since increased sympathetic activity may aggravate myocardial ischemia, stimulate platelet aggregation and predispose to cardiac arrhythmias[44]. Therefore, several studies demonstrate reduction of sudden death and recurrent infarct in patients with or without LV dysfunction treated with BB[45].

d) **Inhibitors of the angiotensin converting enzyme (IACE)** – The SAVE study demonstrated benefits with the early use of captopril in AMI patients, regardless of age, sex and left ventricular function. Therefore, it is recommended to begin IACE within the first 24 h of the onset of the event in patients with previous AMI or heart failure, in the absence of significant hypotension or counterindication for the use of this medication[46].

e) **Nitrates** – The early use of i.v. nitrate is recommended in patients with pump failure, extensive AMI, persistent ischemia or SAH. After 48h, use oral or topic formula. Nitrates are counterindicated for patients with clinical and/or electrocardiographic commitment in right ventricle AMI, hypotension and bradycardia.

Levels of recommendation for the use of medication in acute phase AMI – **degree of recommendation A, level of evidence 1** – ASA in the absence of contra-indication; BB as initial therapy when not counter-indicated; **degree of recommendation A, level of evidence 2** – IACE in case of LV dysfunction; trifusal when ASA is absolutely counter-indicated; non-fractionated heparin when thombolytic used is rt-PA and derivatives; **degree of recommendation A, level of evidence 4** – clopidogrel or tychlopidine when ASA is absolutely counter-indicated; **degree of recommendation B1, level of evidence 2** – nitrate in previous AMI and recurrent angina; **degree of recommendation B2, level of evidence 2** – diltiazen when BB is counter-indicated; **degree of recommendation B2, level of evidence 4** – clopidogrel or tychlopidine + ASA.

IV - Systemic Arterial Hypertension

Although there is a tendency for blood pressure to increase with age, levels of systolic pressure > 140 mm Hg and/or diastolic pressure > 90 mm Hg must not be considered physiological for the elderly[1]. Brazilian epidemiological studies (Multicentric Study in the Elderly – "E.M.I. Study") showed that the prevalence of arterial hypertension among the elderly is very high. Approximately 65% are hypertensive and, among women older than 75 years, the prevalence of hypertension may reach 80%[2,3].

Isolated systolic hypertension is more prevalent among the elderly, and appears to be more associated to cardiovascular events than diastolic hypertension

or systolic and diastolic. Special attention must be given to the presence of pseudo-hypertension, to the presence of auscultation hiatus and to possibility of white coat hypertension[4], which will be described later.

The purpose of the treatment must be the reduction of blood pressure to levels < 140/90 mm Hg. In patients with very high systolic pressure it must be maintained at levels up to 160 mm Hg. In the latter group of patients, treatment must begin with half of the lowest dose recommended, and slowly increase it until the therapeutic dose is reached[5-9].

The overall analysis of several randomized studies documented a mean reduction of 34% of strokes, 19% of coronary events and 23% of vascular deaths after an average follow-up of five years, after a reduction of 12 to 14 mm Hg of systolic arterial pressure and of 5 to 6 mm Hg of diastolic arterial pressure compared with placebo[10-19].

Diagnostic and classification

The diagnostic of arterial hypertension is basically established by the observation of pressure levels permanently above the normal levels, when blood pressure is determined by appropriate methods and conditions. Therefore, measurement of blood pressure is the key-element for the diagnosis of arterial hypertension.

Assessment of blood pressure must be stimulated and accomplished in every health evaluation, by doctors of all specialties and other health professionals. Mercuric sphygmomanometer is ideal for this measurement. When used, aneroid-type devices must be periodically tested and adequately calibrated. Assessment of blood pressure must be carried out in the sitting or standing position[7].

In the elderly population three major variables must be considered. The first one refers to the auscultation hiatus, which leads to underestimation of systolic blood pressure. In these cases, after auscultation of the 1st noise (Korotkoff's phase I) it will disappear, and its reappearance will occur only after reduction of up to 40 mm Hg. If not identified, this situation may lead to the underestimation of systolic pressure (SBP) or overestimation of diastolic pressure. In face of this situation, systolic pressure must be considered as the value obtained when radial pulse appears at palpation after cuff disinflation.

Another extremely common situation identified by William Osler in 1892 is the *pseudo-hypertension*. Elderly with high arteriosclerosis and calcification of

arterial walls have such a prominent vessel stiffening that cuff insufflation is insufficient to collapse the brachial artery. To identify this condition, the Osler's maneuver is used, which is inflating the cuff to levels above the systolic pressure (SBP) and, concomitantly palpating the radial artery. In case it remains palpable, artery rigidity is proven, indicating that the index obtained by auscultation does not express the true systolic blood pressure, if compared to the index obtained by intra-arterial measurement.

Measurement of BP in the standing position is also important. The predisposition of the elderly to present orthostatic hypotension makes them vulnerable to falls and to bone fractures and/or subdural hematoma due to cranial trauma. The best known factors associated to this event are: lower efficiency of regulatory mechanisms of blood pressure by baroreceptors, frequent use of medication, such as diuretics, tranquilizers, vasodilators and beta-blockers, as well as higher frequency of cerebral vascular failure. The prevalence of this phenomenon increases with age and is present in 15.7% of the SHEP (Systolic Hypertension in the Elderly Program) study[14].

Finally, the *white coat* or *office hypertension*, must be also mentioned, which according to some authors may occur in 20% of the hypertensive patients[20]; it can be minimized by repeated measurements in the office or at home.

Home measurement and self-control of blood pressure – These are useful procedures to identify isolated office hypertension (white coat hypertension), to evaluate the efficacy of anti-hypertensive therapy, to stimulate compliance to treatment and to reduce costs. Electronic devices appropriately validated and calibrated are the most indicated for home checking of blood pressure. Mercury column devices and aneroids may be used, provided they are calibrated and after appropriate training. Finger devices for blood pressure checking are not recommended.

Although there is still no consensus regarding normal values for home measurement of blood pressure, values as 135/85 mmHg[7] are considered normal **(degree of recommendation B2, level of evidence 4)**.

Ambulatory measurement of blood pressure (AMBP) – AMBP is an automatic method of indirect and intermittent 24h blood pressure checking, while the patient performs daily routine activities, including sleep[21]. Studies have shown that this method shows a better correlation with cardiovascular risk than office

measurement of blood pressure. The main indications for using this method are isolated office hypertension and autonomic dysfunction-related hypertension.

It is important to emphasize that there is still no evidence that this method must be used for the patients´ routine evaluation, and therefore, does not replace the clinical evaluation and office measurement of blood pressure[7] **(degree of recommendation B2, level of evidence 2)**.

Diagnostic criteria and classification – Normal values accepted are < 130 mmHg for systolic pressure and 85 mmHg for diastolic pressure[7]. Levels between 130-139 mmHg and 85-89 mmHg are considered in the limit of normality. As mentioned, levels > 140/90 mmHg must not be considered physiological. However, in the elderly with very high systolic pressure, levels of 160 mmHg may be targeted.

In fact, despite any number being arbitrary and any classification insufficient, the need for systematization forces an operational definition to separate healthy and sick patients. There may be a higher or lower cardiovascular risk, either above or below the borderline value when the patient is considered individually. Therefore, extreme caution is required before labeling someone as hypertensive, either because of the risk of false-positive or due to the repercussion on the individual's health and the resulting social cost (Table I).

Including in the group individuals with normal borderline pressure values of 130-139 mmHg/85-89 mmHg is due to the fact that these individuals will benefit from preventive measurements.

According to the present clinical situation, we recommend that the measurements be repeated at least twice. Measurements in the first evaluation must be obtained on both arms and also in the orthostatic position[5-7].

Table I – Diagnostic classification of blood pressure

DBP (mmHg)	SBP (mmHg)	Classification
< 85	< 130	Normal
85-89	130-139	Borderline normal
90-99	140-159	Mild hypertension (stage 1)
100-109	160-179	Moderate hypertension (stage 2)
> 110	> 180	Severe hypertension (stage 3)
< 90	> 140	Isolated systolic hypertension

Clinical-laboratory investigation – Detailed clinical history and physical examination must be carried out, associated to laboratory evaluation: urine exam (biochemistry and sediment), creatinine, potassium, glicemia, total cholesterol, electrocardiogram at rest (**degree of recommendation A, level of evidence 4)**.

Nonetheless, the frequent association of other risk factors and lesions in target-organs in this age range often lead to complementary laboratory evaluation: echodopplercardiography, chest radiography, HDL-cholesterol (if total cholesterol/ glicemia are high), triglycerides, uric acid, TSH, calcium, 24h proteinuria, hematocrit and hemoglobin **– degree of recommendation B1, level of evidence 3**; AMBP **– degree of recommendation B2, level of evidence 2**; effort test (elderly with coronary risk) **– degree of recommendation B2, level of evidence 3**.

Most of the elderly patients present essential or primary hypertension, with high prevalence of isolated systolic hypertension. Evidence of secondary hypertension must be investigated by means of clinical history well-addressed to the most frequent causes and specific diagnostic methods. Among the secondary causes of hypertension, we emphasize aorta failure, hipertireoidism, total atrioventricular blockade, use of drugs which increase blood pressure and renal vascular arteriosclerosis are emphasized.

On the other hand, healthy elderly individuals show a progressive reduction of renal mass, renal flow and glomerular filtration rate, that may not occur together with increase of serum creatinine. The reason is that with age there is also a progressive loss of muscle mass, which is the main determinant of creatinine production. Consequently, creatinine serum levels above 1.5 mg/dl are considered abnormal for this population. The real possibility of an associated uni- or bilateral stenosis of the renal artery aggravate the problem, since renal ischemia induced by this mechanism leads to increased blood pressure and to the deterioration of renal function. The association of elevated serum creatinine with arterial hypertension, even at a moderate level, but with evidence of arteriosclerosis in other vascular sites or, still hypertension of difficult therapeutic control, suggests renal vascular cause. The diagnostic of lesion can be done non-invasively, using ultra-sound with Doppler of the renal arteries, searching for a flow gradient between the aorta and the renal artery **(degree of recommendation B1, level of evidence 3)**. If the Doppler is negative and clinical suspicion persists, the magnetic angioressonance **(degree of recommendation B1, level of evidence 4)** or computerized tomography **(degree of recommendation B1, level of evidence 4)** should be indicated. The

echo-Doppler may be false-positive if the examiner is not an expert, if the equipment is not good quality or if the elderly is obese. If the test is positive, the patient must be addressed to a bilateral renal arteriography **(degree of recommendation A, level of evidence 3)**, an important exam for the diagnostic and planning of the therapeutic approach.

Therapeutic Decision

In addition to taking blood pressure into account, the therapeutic decision must consider the presence or abscence of lesions in target-organs and associated cardiovascular risk factors. The next Table shows the components for stratification of individual risk for patients in view of risk factors and lesion in target-organs.

Major risk factors are: smoking, dislipidemia, diabetes mellitus, lesions in target-organs or cardiovascular diseases, cardiac diseases (left ventricular hypertrophy or previous myocardial infarct, previous myocardial revascularization, heart failure), ischemic episode or stroke, nephropathy, peripheral artery vascular disease and hypertensive retinopathy[22,23].

Based on this information, patients may be classified in three groups: Group A – no risk factors and no lesions in target-organs; group B – presence of risk factors (not including diabetes mellitus) and no lesions in target-organs; group C – presence of lesions in target-organs, cardiovascular disease clinically identifiable and/or diabetes mellitus.

Table II deals with the therapeutic orientation based on risk stratification and blood pressure levels. Life style changes may be recommended to the general population as a way to promote health. Patients on arterial hypertension stages 2 and 3 must receive initial drug treatment, which is also recommended to hypertensive patients with lesions in target-organs, or cardiovascular disease, or diabetes mellitus, regardless of the stage of arterial hypertension. Patients with blood pressure within the normal borderline range, belonging to risk group C, must receive drug treatment in case they present heart failure, renal failure, or diabetes mellitus. In the mild hypertension (stage 1), patients from risk groups A and B are eligible to be treated only with life style changes for 6 to 12 months. If blood pressure is not controlled within this follow-up period, drug treatment must be considered. Advanced age or isolated high systolic pressure does not alter the therapeutic decision.

Table II – Therapeutic decision based on risk stratification and pressure levels			
Blood pressure	Group A	Group B	Group C
Normal borderline (130-139 mmHg/88-89 mmHg)	Life style changes	Life style changes	Life style changes*
Mild hypertension (stage 1) (140-159 mmHg/90-99 mmHg)	Life style changes (up to 12 months)	Life style changes (up to 6 months)**	Drug therapy
Moderate and severe hypertension (stages 2 and 3) (160 mmHg/> 100 mmHg)	Drug therapy	Drug therapy	Drug therapy
* Drug therapy must be implemented in case of heart failure, renal failure or diabetes mellitus; ** Patients with multiple risk factors may be considered for initial drug therapy			

Multiprofessional approach to the hypertensive patient: Because arterial hypertension is multicausal, multifactorial, most of the times assymptomatic, and involving orientations directed to several objectives, reaching these goals successfully is quite limited when only one professional acts. Maybe this justifies the low success and compliance rates obtained when the patient is cared by only one health professional, generally the physician. Multiple objectives require different approaches and, therefore, a multiprofessional team[7] **(degree of recommendation A, level of evidence 3)**.

Treatment

Non-pharmacological treatment: life style changes – The main goal of the non-pharmacological treatment is to reduce cardiovascular morbidity and mortality by means of life style changes that lower blood pressure. It is indicated to all hypertensive and to normotensive individuals with high cardiovascular risk. Among these modifications are those proven to reduce blood pressure: reduction of body weight, of salt intake and alcoholic beverages, practice of regular physical exercise, and no use of drugs that raise blood pressure[24-29]. The reasons for these life style changes to be useful are: low cost and minimum risk; reduction of blood pressure, and control of other risk factors; increased efficacy of pharmacological treatment; and reduction of cardiovascular risk.

Life style changes are indicated to all hypertensive as an initial approach, or together with the drug therapy. Considering the natural physical and social constraints resulting from aging, the health professional must also be concerned with therapeutic interventions that may alter further the hypertensive patient's well-being. This type of treatment for arterial hypertension must be encouraged in the elderly, specially because they often present comorbidities, implying in more side effects of drugs and hospitalizations.

Patients with mild or moderate hypertension without lesions in target-organs or risk factors, may be observed for four to six months only with life style changes. Among these, the main measures are weight control, control of fat, and salt intake, consumption of alcoholic beverages, control of smoking and physical activity. Control of diabetes mellitus and dislipidemias are extremely important and are dealt with in separate items. Calcium or magnesium supplementation are not recommended to reduce blood pressure, except when there is a deficiency, although maintenance of adequate calcium intake is recommended to prevent osteoporosis[30-34].

There is evidence of possible effects of psychosocial stress on blood pressure related to "stressful conditions", such as poverty, social dissatisfaction, low education level, unemployment, physical inactivity and, specially, those professional activities characterized by high psychological demands and low control of these situations. Even so, the role of anti-stress treatment and the use of techniques that aim to alter behavioral responses for the treatment of hypertensive patients are still undefined.

Several drugs can present hypertensive effects, and must be avoided or discontinued. Among these are non-steroid anti-inflammatories, decongestant anti-histamine, tricyclic antidepressants, corticosteroids, anabolic steroids, nasal vasoconstrictors, carbenoxolone, cyclosporin, monoamineoxidase inhibitors (MAOI), lead, cadmium, thallium, ergot-derivative alkaloids, appetite controllers, thyroid hormones (high doses), sodium-rich anti-acids, erithopoietin, cocaine, caffeine (?).

It becomes evident that almost all non-pharmacological measures depend on permanent life style changes. Due to the hypertensive approach directed towards several goals, the medical action benefits from a multiprofessional proposition. It is worth mentioning the vital importance of the hypertensive patient's family members getting involved in order to reach the goals targeted by the life style changes.

Non-pharmacological procedures to control hypertension and cardiovascular risk.

Procedures with higher anti-hypertensive efficacy: **degree of recommendation A, level of evidence 1**: body weight reduction, reduction of salt intake, increased intake of potassium-rich foods, reduction of alcohol intake, regular physical exercise.
Procedures without definitive evaluation: **degree of recommendation B2, level of evidence 4**: calcium and magnesium supplementation, vegetarian diets rich in fibers, anti-stress measures.
Associated procedures: **degree of recommendation B2, level of evidence 3**: quit smoking, control of dislipidemias, control of diabetes mellitus, avoiding drugs which increase blood pressure.

Pharmacological treatment – The main goal of the arterial hypertension treatment is to reduce cardiovascular morbidity and mortality in the hypertensive patient, increased because of the high pressure levels. In order to do so, isolated non-pharmacological procedures are used, or associated to anti-hypertensive drugs. Anti-hypertensive drugs should not only lower the pressure levels, but also reduce morbid fatal and non-fatal cardiovascular events. Until the present, the reduction of cardiovascular morbidity and mortality in mild and moderate hypertensive patients was consistently demonstrated in several studies only with diuretics and beta-blockers.

As emphasized, drug treatment aims to reduce pressure values lower than 140 mmHg for systolic pressure and 90 mmHg for diastolic pressure, according to the patient's individual characteristics, co-morbidity, and quality of life. Reducing pressure to levels < 130/85 mmHg may be useful in specific situations, such as for patients with proteinuric nephropathy and to prevent strokes [35-37].

Drug treatment must be individualized and its general principles must be[38] oral efficacy and good tolerance, in addition to allowing fewer daily takings, preferably those of single dose posology. The beginning should be with the lowest effective doses recommended for each clinical situation, gradually increasing them and/or associating them to another hypotensor of a different pharmacological class (it should be taken into consideration that the higher the dose, the more likely

the undesirable effects); respecting a minimum period of four weeks before increasing the dose and/or the association of drugs, except in special situations; instructing the patient about the drug, side effects, therapeutic planning and objectives; considering the patient´s socio-economic conditions.

Currently used anti-hypertensive drugs can be divided in six groups: *diuretics, beta-blockers, inhibitors of the angiotensin converting enzyme, calcium channel antagonists, angiotensin II receptor antagonists,* and *direct vasodilators*.

The efficacy of thiazide diuretics, beta-blockers (propranolol, atenolol) and calcium channel antagonists (nitrendipine, felodipine) for the control of blood pressure and reduction of morbidity and mortality was proven in controlled studies and should be the first choice agents. However, considering the co-morbidities common in this population, any group of medications, except direct action vasodilators, must be appropriate for the control of blood pressure in initial monotherapy, specially for mild to moderate hypertension patients who do not respond to non-pharmacological procedures[9,10,13,14,16,17,19,33,37-39].

Diuretics

The anti-hypertensive mechanism of diuretics is related, in the first place, to volume depletion, and subsequently, to the reduction of peripheral vascular resistance. They are efficient as monotherapy for treatment of arterial hypertension and present proven efficacy in the reduction of cardiovascular morbidity and mortality. The preferred anti-hypertensive diuretics are thiazides and similar. Loop diuretics are reserved for hypertensive situations associated to kidney and heart failure. Potassium sparing diuretics present small diuretic potency, but when associated to thiazides and loop diuretics are useful in the prevention and treatment of hypopotassemia. The use of potassium sparing diuretics in patients with reduction of kidney function may result in hyperpotassemia.

Among the undesirable effects of diuretics, we emphasize hypopotassemia, sometimes accompanied by low serum levels of magnesium (which may induce ventricular arrhythmias), and hyperuricemia. They can also cause glucose intolerance and temporary increase of triglycerides serum levels, usually dose-dependent. The clinical importance of such fact is not proven yet. In many cases, diuretics cause sexual dysfunction. The side effects are usually related to the dose of diuretics **(degree of recommendation A, level of evidence 1)**.

Beta-blockers

The benefits of beta-blockers as monotherapy for arterial hypertension in the elderly are less evident than those of diuretics. They control blood pressure in approximately 50% of the patients and may reach 80% when associated to low doses of diuretics. In the elderly, beta-blockers reduce cardiovascular morbidity and mortality, specially by strokes; nonetheless more than half of the patients treated used beta-blockers associated to diuretics, being it difficult to appraise the real beneficial effects of these drugs used isolatedly. In hypertensive elderly patients with previous myocardial infarct, beta-blockers must be used as first choice, when there are no contra-indications.

More selective and less liposoluble beta-blockers are the most adequate because they affect less the central nervous system, the bronchial muscles, and the peripheral circulation. They should be avoided in sleep apnea patients, because they inhibit the reflex tachycardia that occurs after an apnea episode.

Degree of recommendation:
- as monotherapy: **Degree A, level of evidence 2**.
- associated to a diuretic: **Degree A, level of evidence 1**.
- after infarct: **Degree A, level of evidence 1**.

Calcium channel antagonists

Calcium channel antagonists are included among the most used SAH due to their efficacy, absence of adverse effects on lipid profile, for not interfering with glucose tolerance, with serum electrolytes, with sexual function, and for the benefits on target-organs, such as kidneys. They present one of the lowest side effects-related treatment drop out indices in anti-hypertensive therapy.

Their main action is the selective blockade of voltage-dependent calcium channels (type L), of the smooth muscle cells, of contractile myocardium fibers and of node cells (sinoatrial and atrioventricular nodes), reducing ion influx and, consequently, the cytoplasm calcium concentration. Despite the common mechanism of action, calcium channel blockers have an heterogeneous chemical structure, responsible for marked differences in their preferred acting locations and

in receptor binding characteristics, pharmacokinetic and pharmacodynamic properties. Regarding their chemical structure, calcium channel blockers belong to three different groups: phenylalkilamines (prototype is verapamil); benzotyazepines (prototype is diltiazem) and dihydropiridines (prototype is niphedipine), including the larger number of available agents for clinical use in the latter group, such as nitrendipine isradipine, felodipine, amlodipine, lacidipine, among others.

They are efficient as monotherapy, and preferred to those of long time action for the treatment of SAH. Nitrendipine has been associated to the reduction of cardiovascular and brain morbidity and mortality in the *Syst-Eur* study[13] **(degree of recommendation A, level of evidence 2)**. Felodipine and isradipine have been efficient in reducing pressure levels and cardiovascular mortality in the elderly, being similar to conventional drugs (diuretic and beta-blocker): **degree of recommendation B1, level of evidence 2**. Calcium channel blockers of short duration are not indicated for the anti-depressive treatment because they can induce an increased risk for strokes and acute myocardial infarct **(degree of recommendation C, level of evidence 3)**.

Inhibitors of angiotensin converting enzyme

The mechanism of action of these drugs depends basically on the inhibition of the converting enzyme, thus blocking the transformation of angiotensin I to II in the blood and tissues. The inhibitors of the converting enzyme may be used in the elderly for the treatment of arterial hypertension. Although there is no direct clinical evidence of effects on mortality in hypertensive elderly, they are similarly efficient to diuretics and beta-blockers in the reduction of cardiovascular mortality (STOP-II)[39]. When evaluating anti-hypertensive drugs, the analysis of non-fatal effects, such as the development of lesions in target-organs and respective prevention or even regression, may suggest the inference of the probable beneficial effect on mortality, although such statement is not always correct and possible to be made.

JNC IV also recommends the use of the inhibitors of the converting enzyme as anti-hypertensive monotherapy in the elderly, because they are effective and well tolerated. However, JNC IV emphasizes that the direct effect of these drugs on cardiovascular mortality has not been proved yet. In this group of patients, the

choice of anti-hypertensive medication must be based on individualization and presence of co-morbidities.

The employment of inhibitors of the converting enzyme is indicated for the hypertensive elderly with associated heart failure and/or diabetes mellitus[40]. Recently, a study on secondary prevention (PROGRESS) demonstrated the reduction of strokes with the use of perindopril[41].

Degree of recommendation and level of evidence: captopril, elanapril and lisinopril – **degree of recommendation A, level of evidence 2**; captopril for diabetic nephropathy - **degree of recommendation A, level of evidence 1**; benazepril - **degree of recommendation A, level of evidence 1 –** in nephropathy of any etiology (except of polycystic kidneys); perindopril - **degree of recommendation A, level of evidence 1**; all others - **degree of recommendation B1, level of evidence 2**.

Angiotensin II receptor antagonists

These drugs oppose angiotensin II action by specific blockade of its AT-1 receptors. They are efficient as monotherapy for the treatment of hypertension. They are effective in reducing morbidity and mortality of elderly patients with heart failure. They present a good tolerance profile. Precautions for its use are similar to those described for ACE inhibitors **(degree of recommendation B2, level of evidence 3)**.

Other anti-hypertensive medication

Central and peripheral sympatholytics – There are no randomized clinical trials demonstrating that these drugs improve cardiovascular morbidity and mortality. Besides, they present potentially harmful side effects to the elderly. In a comparative study with clortalidone in patients older than 55 years, the alpha blocker doxazosin specifically showed higher risk of stroke and heart failure[42].

Direct action vasodilators – Can be used in association for the stage 3 hypertensive elderly. Due to their potential effects of reflex tachycardia and sodium and water retention, they should preferrably be used in association with diuretics and/or beta-blockers. **Degree of recommendation B2, level of evidence 3** (except for doxazosin, whose **degree of recommendation is C, level of evidence 2**).

Summarizing, the treatment must be individualized and the initial choice of medication as monotherapy must be based on the predominant physiopathogenic mechanism, on the individual characteristics, on associated diseases, on the socioeconomic conditions and on the drug´s influence on the cardiovascular morbidity and mortality. Finally, as has been mentioned before, the implemented therapeutic schedules must preserve the patient's quality of life, resulting in better following the medical recommendations. Indications specific for some anti-hypertensive drugs are included in the item concerning treatment of arterial hypertension in special situations.

Drug associations must follow a rationale, according to the premise that no drugs with similar mechanism of action should be associated, except for the association between thiazide and potassium sparing diuretics.

As a rule, we do not recommend beginning a treatment with fixed drug associations. All associations between different classes of anti-hypertensive drugs are efficient. However, low dose diuretics as a second drug have been universally used with good clinical results. Some fixed drug associations are available in the market. Its application after unsuccessful monotherapy may be useful to simplify the posologic schedule, reducing the amount of tablets administered.

For hypertension resistant to double therapy, three or more drugs may be prescribed. In this case, the use of diuretics is essential. In cases of more resistance, the association of minoxidil to the therapeutic schedule has been shown useful.

The elderly patient presents different pharmacokinetics and pharmacodynamics from the young adult and is more prone to side effects. Drug interactions should also be taken into account, and must be evaluated with other non-cardiovascular medications which may have an important influence on the elderly[7].

Treatment of hypertension in special situations

Hypertensive crisis and emergency – The hypertensive crisis is divided in hypertensive urgency and emergency. In the hypertensive urgencies, as high as blood pressure may be, it is not associated to acute clinical features, such as faintness, vomiting, dyspnea, etc., and therefore, it does not represent an immediate vital risk or damage to target-organs (as, for instance, accelerated hypertension and perioperative hypertension). In this situation, blood pressure control must be done in 24h. Initially, blood pressure must be monitorized for 30 min. In case it remains in the same level, we recommend oral administration of one

of the following drugs: loop diuretic, beta-blocker, ACE inhibitor or calcium channel antagonist. Although sublingual administration of rapid action nifedipine has been widely used for this purpose, severe side effects have been described. The difficulty to control the rhythm or reduction levels of blood pressure and the existence of efficient and better tolerated alternatives make the use of this agent (nifedipine of short action and duration) not recommended for this situation.

In hypertensive emergencies, the crisis occurs with signs indicating evolving lesions in target-organs, such as hypertensive encephalopathies, strokes, acute lung edema, myocardial infarct and evidence of malignant hypertension or of acute aorta dissection. In these cases, there is an impeding vital risk or risk of irreversible organic lesion, and the patients must be hospitalized and submitted to treatment with e.v. vasodilators, such as sodium nitroprussiate or hydralazine. After the immediate reduction of pressure levels, maintenance anti-hypertensive therapy must begin and parenteral medication halted.

In the two situations mentioned, the approach to the elderly patient must be very careful, because of the many associations with other potentially severe clinical situations that may be aggravated by the abrupt blood pressure reduction.

Treatment of renovascular hypertension – Stent angioplasty may show 80% of success in expert hands. Most of the failures occur in patients with severe and ostial lesion. At the end of one year, approximately 20% of the patients present stenosis. In successful cases, improvement of blood pressure and of kidney function reach up to 75% of the patients, thus postponing the evolution of patients to dialysis programs.

Surgical revascularization is reserved for cases that evolve to complications during angioplasty, not appropriate anatomy for angioplasty, and in cases that evolve to repetitive re-stenosis.

Comorbidities – The elderly patient often presents associated diseases that require individualized treatments, such as:

Chronic obstructive pulmonary disease or bronchial asthma – The only drug restriction in this group is limited to beta-blockers because they may elicit bronchospasm, regardless of the agent's cardioselectivity. One should watch for occasional sympathomimetics, such as theophyline and ephedrine which, associated or not to corticosteroids, can make the adequate control of blood pressure difficult. However, when these drugs are indicated, they can and should

be used carefully. Sodium chromoglicate, ipratropic bromide or corticosteroids by inhalation may be used safely with hypertensive individuals.

Depression – Depression may be a difficulty for those on to arterial hypertension treatment, as well as in the treatment of other cardiovascular risk factors. On the other hand, several hypotensor agents (alphametyldopa, clonidine and central action beta-blockers) can also cause depression. Thiazide diuretics can increase serum lithium levels. The use of tricyclic antidepressants, monoaminoxidase inhibitors (MAOI) and venlaphaxine requires attention to pressure levels.

Obesity – Arterial hypertension and obesity are frequently associated conditions. Diet and physical activity are essential for weight loss. Anorexigenics must be avoided when possible, because they may increase blood pressure. Excess weight reduction, dietary sodium restriction and practice of regular physical exercise are vital for pressure control and can, by themselves, normalize pressure levels. Association between obesity and sleep apnea must always be considered a difficult factor for blood pressure control.

ACE inhibitors are beneficial to the obese patient because they increase sensitivity to insulin, whereas calcium channel antagonists can be recommended by its natriuretic action and for being neutral on lipids and carbohydrates metabolism. On the other hand, diuretics and beta-blockers must be used carefully because of the possibility of increasing insulin resistance and determining glucose intolerance.

Diabetes mellitus – In patients with diabetes, high blood pressure is at least twice as prevalent as in the general population. In type I diabetes (insulin-dependent), high blood pressure is clearly associated with diabetic kidney disease. In these patients, the control of high blood pressure is crucial to delay the loss of renal function. In type II diabetes (not insulin-dependent), high blood pressure is commonly associated with other cardiovascular risk factors, such as dyslipidemia, obesity, left ventricular hypertrophy, and hyperinsulinemia. For these patients, a non-medication treatment (regular exercising and appropriate diet) is mandatory. Any drugs can be used. Diuretic drugs may alter the insulin release, or even increase the resistance to it, thus damaging the control of glycemia in some patients, although the medication can be used in low doses, as currently recommended. Betablockers may interfere with the insulin release, and increase

the resistance to endogenous insulin as well. In type I diabetics under insulin use, betablockers may mask the symptoms of hypoglycemia, thus prolonging hypoglycemic crises. However, these agents should be given preference in situations with a specific indication (angina and post-myocardial infarction). Adrenergic inhibitors and vasodilators may aggravate neuropathic symptoms, such as sexual dysfunction or postural hypotension. ACE inhibitors become particularly useful, as they do not interfere with the glucose metabolism and improve the resistance to insulin. In addition to that, they were proven to have a renal protection effect in patients with diabetic kidney disease, characterized by micro or macroalbuminuria. If the treatment with ACE inhibitors is impossible to maintain, the angiotensin II receptor antagonists are a promising alternative. In cases of difficult blood pressure control, calcium channel antagonists, alphablockers, and hydralazin can be useful.

Hyporeninemic hypoaldosteronism is not uncommon in diabetics; therefore, the serum potassium levels must be monitored, due to the possibility of hyperpotassemia, especially during the use of ACE inhibitors, angiotensin II receptor antagonists, potassium-saving diuretics, and betablockers. Given the greater prevalence and severity of retinopathy in hypertensive diabetics, the performance of regular ocular funduscopy is mandatory.

Dyslipidemia – The association between dyslipidemia and high blood pressure is frequent; when they are present, both affections must be aggressively treated. The non-medication approach (regular exercising and appropriate diet) is necessary for both conditions. ACE inhibitors, calcium channel antagonists, and alpha-2-agonists do not interfere with lipidemia, whereas alphablockers can improve the lipid profile. Low-dose diuretics do not interfere with the lipid serum levels. Betablockers may temporarily increase the triglyceride levels and reduce HDL-cholesterol. However, in myocardial infarction patients, the benefits granted by betablockers outweigh their possible disadvantages. More recent studies have shown that the aggressive reduction of serum lipids achieved by using vastatin grants protection against coronary disease.

Encephalic vascular disease – High blood pressure is the main risk factor for encephalic vascular disease. This risk is in higher correlation with the systolic pressure levels, increasing in the presence of other causal factors. When encephalic vascular accidents occur in hypertensive patients, it is recommended to maintain

the patients under observation for a few hours, before intervening in their blood pressure, unless extremely high blood pressure levels occur. Chronic hypertensive patients are known to undergo a deviation to the right of their brain flow self-regulation curve. Thus, a reduction of more than 20% in the diastolic blood pressure can damage the encephalic perfusion, and should therefore be avoided. The reduction of the blood pressure should be slow and gradual, with continuous observation of the clinical parameters of the neurological picture. It is worth recalling that in many situations, like, for example, in subarachnoid hemorrhage, the elevation of blood pressure is an important hemodynamic factor for the maintenance of cerebral perfusion in vasospasm conditions. Drugs which act on the central nervous system (clonidine, alpha-methyl-dopa, guanabenzo, and monoxidine) should be avoided. Particularly indicated are ACE inhibitors, calcium channel antagonists, and diuretics.

Ischemic heart disease - In such patients, blood pressure has to be controlled in a gradual manner, until it reaches levels below 140/90 mmHg, keeping in mind that very pronounced reductions may jeopardize the coronary blood flow. In addition to that, it is also indicated to control other present risk factors, and to use low doses of acetylsalicylic acid. Among the hypotensive drugs, betablockers are the most indicated ones, because of their anti-ischemic action. If betablockers are ineffective or contraindicated, calcium channel antagonists may be used, except for the fast-acting ones. Hypotensive agents which increase the heart rate should be avoided. In patients who already had an acute myocardial infarction, betablockers without an intrinsic sympathomimetic activity and ACE inhibitors should be preferred, especially if a ventricular systolic dysfunction is present. In patients with preserved ventricular function, ramipril proved to be of benefit to the reduction of infarction, stroke, and death of cardiovascular origin. In cases of acute myocardial infarction without a Q-wave and with preserved systolic function, diltiazem or verapamil can be used.

Heart failure – High blood pressure can produce structural alterations in the left ventricle, accompanied or not by coronary ischemia, contributing to the development of heart failure, with or without preserved systolic function. Among the different agents, the first recommended choice are the ACE inhibitors, followed by vasodilators such as hydralazine combined with nitrates. The isolated use of such agents, or combined with diuretics and digitalins, reduces cardiovascular

morbidity and mortality. It was recently demonstrated that the angiotensin II receptor antagonists are also effective in reducing the mortality of elderly patients with heart failure. Betablockers such as carvedilol, metoprolol, and bisoprolol have proven to produce a significant reduction in morbidity-mortality, with an obvious improvement in quality of life.

Hypertrophy of the left ventricle – Hypertrophy of the left ventricle (HLV) may be associated with high blood pressure, and is an important risk indicator for arrhythmias and sudden death, independently from hypertension itself. Drug treatment is mandatory. All drugs, except directly acting vasodilators, are effective in the reduction of left ventricular hypertrophy.

Algorithm for the treatment of high blood pressure

Continuous life style changes

ξ

Target blood pressure (140/90 mmHg) was not reached

Lower target levels for patients with diabetes or kidney disease

ξ

Initial choice of drugs (see degree of recommendation and level of evidence)

Uncomplicated hypertension:

Diuretics
Betablockers

Specific indications:

Evaluate co-morbidities and individualize treatment:
calcium channel antagonists,
ACE inhibitors, or angiotensin II receptor antagonists.

ξ

Target blood pressure was not reached

ξ

Absence of response or important side effects

ξ

Replace by another drug of a different class

ξ

ξ

Inadequate but well tolerated response

ξ

Add a second agent of different class (diuretic, if not yet used)

ξ

Target blood pressure was not reached

ξ

Continue adding agents of different classes

Consider referral to specialist in high blood pressure

Nephropathies – High blood pressure may result from any kind of kidney disease that reduces the number of operational nephrons, leading to the retention of sodium and water. Hypertensive nephrosclerosis is the most common cause of progressive kidney disease, particularly in African Americans. Prospective studies in male patients showed conclusive and direct evidence of the relationship between blood pressure and end-stage kidney disease. Early detection of the kidney damage associated with hypertension has shown to be essential for the prophylaxis of the kidney lesion progression, including a serum creatinine evaluation, urine test, and, as a complement, an ultrasound of kidneys and urinary ways, to detect obstructive renal disease, polycystic kidney disease, and to determine kidney size. Small creatinine elevations may indicate significant functional losses of the renal function. Blood pressure levels must be reduced to 130/85 mmHg (or 125/75 mmHg), especially in patients with proteinuria over 1g/24hrs, by using the required anti-hypertensive therapy. Among the therapeutic measures considered to be important, a dietary sodium intake of less than 100mEq/day (salt-free general diet) is pointed out. It is recommended that patients with serum creatinine levels above 3mg/dl should be careful with their potassium intake.

All classes of hypotensive medications can be used. The use of angiotensin-converting enzyme inhibitors is recommended for patients with creatinine levels under 3mg/dl, particularly in the presence of proteinuria and/or diabetes mellitus. In patients with creatinine levels over 3mg/dl, ACE inhibitors have to be used with caution. The introduction of ACE inhibitors to any kind of patient requires an evaluation of serum potassium and creatinine levels after one week. Serum creatinine elevations above 1mg/dl may be suggestive of renal artery stenosis, bilaterally or affecting a single kidney. Thiazide diuretics are ineffective in patients with creatinine > 2.5mg/dl. In these patients, if necessary, loop diuretics can be used. Potassium-saving diuretics like amyloride, spironolactone, and triamterene are formally contraindicated in these patients, due to the risk of inducing hyperpotassemia.

Peripheral arterial vascular disease – Arterial hypertension is an important risk factor for atherosclerosis and peripheral arterial vascular disease. In these patients, the use of betablockers can lead to a worsening of the clinical picture, so vasodilators, calcium channel antagonists, and ACE inhibitors have to be indicated. There is a rare possibility of co-existence of bilateral renal artery stenosis, and, in this case, renal function may be reduced by the latter. The benefits of quitting smoking have to be emphasized, as it surely represents an important risk factor for the severity of the crippling peripheral arterial vascular disease.

Other diseases – Arterial hypertension may predispose elderly persons to dementia, and controlling the blood pressure, along with the treatment of other risk factors, seems to prevent it. In gout cases, caution is recommended in the use of diuretics. On the other hand, hyperuricemia induced by diuretics does not require treatment, if gout or uric lithiasis are absent. For migraine, betablockers and clonidine may be useful, whereas hydralazine is contraindicated. In patients with chronic liver disease, alphamethyldopa is contraindicated, and liposoluble betablockers (propanolol, methoprolol) should be used with caution. In patients with liver disease, the association of betablockers with hydralazine, cimetidine, and chlorpromazine should be avoided. In glaucoma cases, betablockers are useful. However, in susceptible patients, even eyewash containing betablockers may cause a bronchospasm. In the presence of cardiac arrhythmia, especially in cases of supraventricular tachyarrhythmia, betablockers or verapamil are preferable. In cases of atrioventricular conduction blocks, the use of betablockers, verapamil, and dilthiazem should be avoided. Non-hormonal anti-inflammatory drugs reduce the anti-hypertensive effectiveness of diuretics, betablockers, ACE inhibitors, and angiotensin II receptor antagonists. Moreover, the use of non-hormonal anti-inflammatory drugs in dehydrated patients like, for example, those using diuretics, may lead to renal function loss. For hypertension associated with chronic use of cyclosporine, all agents can be used, although the ACEI are less effective. Dihydropyridine calcium channel antagonists are indicated as well. Dilthiazem and verapamil raise the blood levels of cyclosporine and digoxin. The use of human recombinant erythropoietin can cause a blood pressure elevation that is more related to an increase in peripheral vascular resistance than to an increase of the hematocrit or of viscosity. Adequate control has to be kept on the circulating volume and on the antihypertensive agents. In some cases, the erythropoietin dose may be reduced, and its way of administration changed from

intravenous to subcutaneous. In patients with essential tremor or anxiety, the use of a betablocker should be considered. Erectile dysfunction is frequent, especially in patients with risk factors for vascular disease. On the other hand, anti-hypertensive drugs may cause or worsen it. The use of sildenafil has proven effective and safe, even in association with hypotensive agents.

V – Valvopathies

Valvopathies are the third most frequent cause of congestive heart failure in elderly persons, after myocardial ischemia and systemic arterial hypertension [1].

In the elderly, degenerative calcifications develop in several cardiac structures, the common areas being the fibrous heart skeleton and the fibrous portion of the valve cusps. It is possible that an atherosclerosis-like process takes part in determining some of these degenerative processes [2]. Valvar calcium degeneration has shown to be a characteristic process of aging, that is responsible for the dramatic increase in surgical interventions in elderly persons, mainly over the last two decades [3]. Extensive degenerative processes may cause hemodynamic and electrical dysfunctions, worsening the clinical picture even more. Calcified or degenerative aortic valvopathy is the lesion most commonly found in elderly patients [2]. The calcification of the mitral ring is another one of these manifestations [4]. In elderly people, rheumatic cases – congenital and myxomatous degenerative – are also found, besides the valvopathies resulting from ischemic processes, and those which are secondary to the dilation of the radix of the aorta.

A remarkable peculiarity of the geriatric population is the frequent presence of co-morbidities. Affections like coronary artery disease, high blood pressure, chronic obstructive pulmonary disease, cerebrovascular disease, peripheral vascular disease, diabetes mellitus, and renal failure are frequently diagnosed in elderly patients with a valvopathy, mainly after the age of 75 [3,5]. These associations have an influence on the therapeutic decisions and on the prognosis of this population, regarding correction procedures of their valvopathies.

Symptomatic Manifestations

It is difficult to recognize valvar disease in elderly patients due to a complex picture, characterized by atypical manifestations and by the presence of associated diseases. Thus, symptoms like chest pain, difficulties to breathe, dizziness,

syncope, and intolerance to exercise, which reflect a drop in cardiac output, are frequently not considered for the diagnosis of a valvopathy, in spite of their clinical compatibility with this picture. Due to the presence of multiple diseases, the clinical history does not always show the symptoms in a chronologically accurate manner, reflecting the difficulties frequently experienced by elderly people to describe their symptoms [6]. As the disease progresses, the symptoms may become more pronounced, and nocturnal paroxysmal dyspnea, acute pulmonary edema, and hemoptysis may appear. In other cases, the disease remains silent, being clinically recognized by a sudden onset, due to a picture of heart failure.

The overlap of unspecific symptoms and findings jeopardizes recognition. They are frequently not considered as indicative of hemodynamically important valvar lesions, but rather usually considered manifestations of aging and its expected decreasing physical fitness, or even as resulting from other morbidities [7].

On the other hand, cardiac murmurs which are very representative expressions of valvar lesions are common in elderly populations, being therefore less valued, besides the fact that occasionally they really are absent in cases of severe valvopathies, mainly in this age range.

Moreover, modifications altering the elasticity characteristics of the arteries, which are peculiar to the aging process, may attenuate or enhance peripheral manifestations which can be attributed to hemodynamic disorders of valvopathies, thus making them more difficult to recognize.

Therapeutic and prognostic perspectives

The inevitable co-morbidities which are inherent to old-age constrain the functional reserves and consequently reduce the capacity to react to surgical aggressions and to the disease itself. Therefore, the therapeutic conducts for elderly persons have to be individualized down to every detail. Whereas the indication for surgery in young patients is based on well-established criteria, taking into account symptoms, ventricular diameters, ejection fraction, and wall stress, for elderly patients the criteria are less clear-cut [8]. It is worth noticing, however, that, in spite of the fact that new treatment options, both surgical and by medication, are becoming increasingly efficient in the elderly age group, mainly up to 75 years, more modern and invasive techniques remain underutilized [9].

In patients with ages $\geq$75 years and a concomitant heart disease, surgical mortality is higher and survival is lower [5,7,10].

Mitral failure

Calcification of the mitral ring is common in old-age, mainly in women, its prevalence being 18% between 62 and 70 years, and 89% after 91 years of age. In men aged >62 years, the prevalence is 47% [5-7]. Some degree of regurgitation is found in approximately 50% of patients with mitral ring calcification. In this age range, the lesion is typically mild, with an unlikely indication for surgery [3].

Etiology – The causes of mitral regurgitation are innumerable. In addition to the calcification process, there are myxomatous degeneration with prolapse of the mitral valve (PMV), ischemic heart disease, and, less frequently, infectious endocarditis [1,10]. Differently from young patients, in the elderly the more prevalent manifestation of PMV is heart failure. On the other hand, acute cases may occur, mainly in connection with acute coronary disease, due to papillary muscle dysfunction or resulting from a rupture of the tendinous cordage.

Diagnosis – The *symptoms*, when present, are related to progressive dyspnea, feebleness, cough, edema of the lower limbs, and sometimes palpitations. It is worth recalling the difficulties which are inherent to the diagnosis of such symptoms in elderly patients, either because of the lack of demand to make them show, or because they may mimic other clinical pictures. In acute cases, the symptoms present themselves in a more dramatic manner, with pictures of acute congestive heart failure, with intense dyspnea, sweating, and sometimes states of hypotension.

The *physical examination* findings are related to the presence of mitral focus systolic murmur of varying intensity, and displaced ictus with characteristics of volumetric overload. On the other hand, chest deformities like kyphosis or kyphoscoliosis, which are common at this age, may modify ictus, noises, and murmurs.

The *electrocardiogram* is useful in revealing signs of overload of the left chambers, yet with less specificity than in young subjects.

X-ray of the chest helps to detect co-morbidities, to evaluate the state of pulmonary congestion, and to distinguish between acute and chronic cases. In the first ones, the chest X-ray shows congestion and a normal or slightly enlarged heart area, whereas in chronic, hemodynamically important cases, the heart area is enlarged.

The *echocardiogram* is a very valuable test in the diagnosis of mitral failure, as it can help to quantify it, and to analyze its etiology and its hemodynamic repercussion.

In association with Doppler, it offers a better perspective to the evaluation of the severity of the mitral reflux. According to the relationship between the area of the regurgitating spurt/ left atrium, spurt length and actual reflux orifice, mitral failure is classified as mild, moderate, or severe. It also analyzes the hemodynamic repercussion, according to the alterations of the left ventricle and the left atrium. A trans-thoracic echocardiogram may be sufficient, but it is often necessary to resort to the use of a trans-esophageal echocardiogram, due to the difficulties commonly found in this age range, related to the adequacy of an echocardiographic window. Its use in the follow-up of asymptomatic patients is recommended on an annual basis for moderate cases, and every six months for severe cases. With the new diagnostic techniques, the echocardiogram is sufficient for the diagnosis of mitral failure in most cases. Thus, heart catheterization is only justified when there are persistent doubts about the severity of the lesion, for the diagnosis of coronary lesion when there is a clinical suspicion, or for cinecoronariography, which is mandatory in all cases referred for surgical correction.

Treatment – ***Clinical:*** In cases of acute mitral failure, the indicated treatment until the final correction procedure depends on the intensity of the hemodynamic manifestations. In cases of major damage, such as acute lung edema, intravenous vasodilators (i.e., sodium nitroprusside), vasopressor amines, and even an intra-aortic balloon can be used.

In cases of severe chronic mitral failure, drug treatment can be carried out using vasodilators like hydralazine and minoxidil. Nifedipine has already been used for this purpose. More recently, the use of angiotensin-converting enzyme inhibitors has been preferred. However, further studies are needed to prove their effectiveness in the treatment of mitral failure.

Surgical: Surgery should be considered in symptomatic patients, despite clinical treatment.

In asymptomatic patients, up to 72 years of age, surgery should be considered whenever there are demonstrations of a left ventricle dysfunction or, if it is severe, whenever there is an indication for myocardial revascularization surgery. Surgery usually consists of valve replacement, but, in some situations, mitral plasty can be performed, mainly in cases of mitral valve prolapse, or papillary muscle dysfunction, or rupture of the tendinous cordage.

In patients over the age of 75, the presence of symptoms indicates surgery [11, 12].

Mitral stenosis

Importance – Among elderly persons, mitral stenosis has a lower prevalence than mitral failure. Nevertheless, when occasionally found, its manifestations are the same as those of congestive heart failure, exposing the patient to the risk of a stroke due to an embolic phenomenon, mainly in the presence of atrial fibrillation, a common occurrence in this situation.

Etiology – Its etiology is attributed to a sequel of rheumatic fever, although in some cases it results from an intense calcification process of the mitral valve system.

Diagnosis – The *symptoms,* when present, are characterized by dyspnea and cough, occasionally hemoptysis and lower limb edema. Chest pain with a feeling of weight can be mistaken for angina pectoris secondary to coronary artery disease, which is not an uncommon association.

On *physical examination*, an atrial fibrillation rhythm can be found, its more characteristic findings being associated with the presence of hyperphonetic B1, mitral opening snap, and mitral focus diastolic flutter. It is worth pointing out that, as a result of a more intense degree of calcification of the mitral valve in elderly patients, a less intense expression of these auscultation findings is common.

The intensity of B2 is in good correlation with the severity of the disease. Chest deformities, like kyphosis or kyphoscoliosis, common at this age, may modify ictus, noises, and murmurs.

The *electrocardiogram* is useful to reveal left atrial overload or right ventricular overload, or atrial fibrillation rhythm. The presence of a left ventricular overload indicates the presence of another process associated with mitral stenosis, such as the presence of ischemic alterations. The ECG is less specific in elderly than in young persons.

X-ray of the chest is very useful to detect co-morbidities, and to evaluate the state of pulmonary congestion.

The *echocardiogram* is a fundamentally important test in the initial evaluation and in the follow-up of patients with mitral stenosis. A trans-thoracic echocardiogram may be sufficient to provide information, such as the state of the valve, by the analysis of its mobility, the degree of thickening, of calcification, of

affectedness of the mitral valve system, thus allowing to establish the score known as Wilkins' score (varying from 0 to 16). In addition, the severity of the stenosis itself can be assessed, aided by Doppler, determining the transmitral gradient, the pulmonary artery pressure (PAP), and the size of the chambers, besides verifying the presence of a thrombus in the left atrium or in the atrial appendix. Occasionally, not all this information can be obtained by this method, requiring the use of a trans-esophageal echocardiogram. Echocardiographic follow-up is of major importance and should be performed on an annual basis in asymptomatic patients with moderate mitral stenosis, and every six months in asymptomatic patients with the severe form of the disease, to detect any significant elevation of PAP.

Treatment

Clinical – The follow-up of patients with mitral stenosis intends to relieve congestion symptoms, which can be achieved by the adequate use of diuretics. In cases of sinusoidal rhythm, betablockers can be useful, if there are no contraindications to their use. Digoxin is used to control the heart rate in cases of atrial fibrillation, when the use of anticoagulants is indicated.

Interventional – In symptomatic patients whose echocardiograms show a favorable Wilkins' score (up to 8) and without a left atrium thrombus or any other limitation to its use, percutaneous valvotomy is currently acceptable as a method of choice for treatment. However, in the elderly population, the finding of valves with a favorable echocardiographic score is not as frequent as it is in younger individuals.

Surgical – Surgery is indicated for symptomatic patients who are unable to benefit from the percutaneous valvotomy procedure, or who present concomitant coronary lesions requiring myocardial revascularization.

Aortic failure

The incidence of aortic failure (AoF) increases with age, mainly as a result of degenerative alterations of the aortic valve and of the walls of the aorta itself. This should be taken into account when treating patients with mild or pronounced AoF.

Etiology – In a casuistic of elderly patients with AoF who underwent surgical treatment, the rheumatic etiology prevailed in 39%, disease of the aorta in 28%, isolated alterations of the aortic valve including rheumatoid disease in 22%, and infectious endocarditis in 11% [13].

Diagnosis – In patients with aortic failure, the characteristic *clinical findings* are cardiac murmur and modifications of the peripheral pulses. The murmur is diastolic, protodiastolic, decreasing, aspirative, and of high rate, better heard at the left sternal rim or at the aortal focus. Its severity is more related with the duration of the murmur than with its intensity. It is worth reminding that, in more severe situations, both duration and intensity of the murmur may be reduced.

Ictus is displaced, revealing a volumetric overload of the left ventricle. Its dimension is proportional to the severity of the lesion, except for the acute cases in which the dimensions of the left ventricle are not yet too altered.

Peripheral alterations characteristic of severity in young patients (increased pulse pressure, arterial pulsation in neck arteries, systolic pulsation of the head, Duroziez' symptom) may be heightened in the elderly and, when they are milder, losing their indication of severity, since the very alterations resulting from the loss of elasticity of the large arteries in old-age can enhance them.

The *electrocardiogram* is relatively useful, as it can reveal an overload of the left ventricle, but its prognosis estimate capacity is limited.

Chest X-ray is very useful to detect co-morbidities, to evaluate the state of pulmonary congestion, and to distinguish between acute and chronic cases. In acute cases, the chest X-rays show congestion and a normal or slightly enlarged cardiac area, whereas in chronic and hemodynamically important cases, the heart area is enlarged.

The *ergometric test* has been used, mainly in association with spirometry, as an aid in the evaluation of functional capacity. The stress test with radioisotopes for the assessment of EF to stress has a less defined position in the diagnostic evaluation of the severity of aortic failure.

The *echocardiogram* is very useful for diagnostic clarification, estimate of lesion severity, and also as a follow-up element in patients with aortic failure. Echodopplercardiography has added images and indexes (for example, the so-called ventricular function indexes), and has perfected the screening for the complex adaptive remodeling of the ventricle [14,15].

It is known that, as it occurs in younger patients, the enlargement of the ventricular cavity with a final diastolic volume index >150ml/m^2 or a diastolic diameter > 70mm, and a final diastolic volume index >60ml/m^2 or a diastolic diameter > 55mm are associated with imminent arising of symptoms [16,17]. These indexes have already been used to make surgical decisions in asymptomatic patients. Nowadays, based on repeated observations, they are taken as signs of alert for a more careful clinical follow-up of such cases, where a decision for surgery is based mainly on the development of symptoms. Echocardiographic follow-up is recommended annually for moderate cases, and every six months for asymptomatic patients with a severe lesion.

Cardiac catheterization is only justified for cineangiocoronariography, mandatory in all cases referred for surgical correction.

Treatment

Clinical – Clinical treatment is reserved for asymptomatic patients, usually including those with mild to moderate aortic failure, or those presenting a more severe form of aortic failure with preserved ejection fraction.

The utilization of LV dimension indexes as a criterion for surgical indication, regardless of symptoms, is not supported by recent observations which clearly show that the arising of ventricular dysfunction is immediately accompanied by the appearing of symptoms [18,19]. The best option is to use angiotensin-converting enzyme inhibitors.

Other options are the direct vasodilators and the calcium channel antagonists [20,21].

Surgical – Surgery should be considered in symptomatic patients, despite clinical treatment or, in severe cases, whenever there is an indication for myocardial revascularization surgery.

Aortic Stenosis

This is the most frequent valvopathy, occurring in approximately 2% of the elderly population. Many patients with severe aortic stenosis develop symptoms and need surgery. Among the most frequent symptoms, dyspnea, angina, and syncope stand out. Sudden death is rare as an event devoid of previous symptoms [22]. After the symptoms appear, the survival average is less than 2 to 3 years. So,

there is a need for strict monitoring of clinical symptoms, in order to take the necessary measures to maintain life and its quality in elderly patients with aortic stenosis (AoS) [23].

Etiology – Calcified or degenerative stenosis is the most frequent cause of aortic stenosis. Other causes include calcified bicuspid valve, rheumatic aortic stenosis, and other less common affections.

Diagnosis – The main symptoms are dyspnea, angina, and syncope; the latter is considered the most feared, for it announces the possibility of sudden death, and is usually preceded by the first ones.

The diagnosis of severe AoS can usually be made by the presence of ejective systolic murmur in aortic position, carotid *parvus* and *tardus* pulses, *ictus cordis* of the impulsive type, and a hypophonetic second noise. A murmur with apex predominance is more common in elderly patients (Gallavardin's phenomenon).

It should be stressed that, in elderly patients, *parvus* and *tardus* pulse may not be present, since the effect of age on the blood vessels may increase their rigidity, expediting the transmission of the pulse wave.

The *electrocardiogram* is useful to detect left ventricular overload, left atrial overload, atrial fibrillation, and fascicular blocks. It has a good sensitivity for more severe cases, but its specificity is low. It is important for the assessment of heart rhythm, mainly of atrial fibrillation, which is of prognostic relevance.

Stress tests have been very little performed on patients with AoS, and should never be done on symptomatic patients. When they are performed, it has to be done under observation by specialized personnel, with blood pressure and ECG monitoring. A stress test can provide information on the intensity of exercise to be made during physical activities, or even induce symptoms in patients with a negative medical history. Although the alterations in segment ST have no prognostic signification, an abnormal hemodynamic response, like low blood pressure in patients with severe AoS, indicates the need for surgical intervention.

Chest X-ray is very useful to detect co-morbidities, and to evaluate the state of pulmonary congestion.

The *echocardiogram* is an important test and should be included in the follow-up routine of elderly patients with aortic stenosis, for, in addition to making the differential diagnosis of murmur possible, it can assess the evolution of the disease and even suggest a prognosis in asymptomatic patients [24]. An echocardiogram

with dobutamine should be considered in patients with a low output, for a better evaluation of their gradient. An echocardiogram should be performed annually in asymptomatic patients with severe aortic stenosis, every 2 years in moderate cases, and every 3 years in mild cases, except for cases in which symptoms appear, requiring it to be performed immediately.

Heart catheterization can be requested to verify the possibility of an associated coronary disease, and to clarify the clinical diagnosis.

Treatment

Clinical – Prophylaxis with antibiotics should be recommended to prevent infectious endocarditis. Patients with associated high blood pressure should be cautiously treated with adequate anti-hypertensive agents.

If atrial fibrillation is present, the sinusoidal rhythm has to be restored, or the heart rate controlled. Except for this one, there is no other clinical treatment for asymptomatic patients, and for symptomatic patients only surgical treatment is indicated.

Valvotomy by balloon catheter – Its use in elderly patients is limited, because this procedure presents a high degree of morbidity and mortality [24-30], and within approximately 12 months re-stenosis and a worsening of the clinical picture occur [25]. This procedure should be used as a bridge to the valve replacement surgery in such critical patients who would certainly not survive surgery, for example, patients in cardiogenic shock or with an acute lung edema resistant to clinical treatment; after catheter valvotomy, such patients would present better hemodynamic conditions for valve replacement [26,27].

Other special conditions include non-cardiac emergency surgery, dementia, inoperable coronary disease, severe pulmonary hypertension, and the patient's definite refusal of surgical procedure.

Surgical – In the absence of relevant co-morbidities, all symptomatic patients with AoS should be submitted to valve replacement.

There is no evidence so far that valve replacement brings any benefit to asymptomatic patients, for, despite the low morbidity and mortality associated with this surgery, it is clear that over the years carriers of valve prostheses will have an increased need for surgery [28].

Patients with severe AoS, whether symptomatic or asymptomatic, who will undergo myocardial revascularization have to undergo valve replacement. The same applies to patients who will be submitted to other valve surgeries, or to an intervention at the radix of the aorta. It is accepted that patients with moderate AoS who will be submitted to myocardial revascularization surgery also undergo aortic valve replacement, but there are not many data to support this indication.

The choice of the prosthesis

In elderly patients, the choice of the prosthesis faces two important and determinant variables: lesser durability of biological prostheses, and the risk of bleeding of mechanical prostheses, due to the use of anticoagulants. It is nevertheless still a fully established indication that the tissue valve should be used more in elderly patients, given their lower life expectancy, lower risk of failure in this group, and the difficulty of anticoagulation in old-age. However, a mechanical prosthesis is sometimes indicated in view of the increasing longevity of the population. Thus, bioprostheses are usually chosen for patients over 70 or, at age <70 years, for its mitral position, or if it is the patient's choice.

Mechanical prostheses are usually used in patients under the age of 70 who are in good anticoagulation conditions, or by the patient's decision.

Prophylaxis of bacterial endocarditis

Elderly patients with a valvopathy represent a group that is particularly susceptible to the risks of endocarditis, because they are more subject to invasive procedures like vesicular catheterization and others. In 75% of these cases, the underlying structural disease is degenerative. Atheromatous deposits may be the site of endarteritis, and valve prostheses are highly predisposing to infection. It should be mentioned that myxomatous degeneration of the mitral valve is also more subject to endocarditis, mainly when associated with mitral regurgitation. On the other hand, although infrequently, pacemaker wires are an increasing cause of endocarditis.

The main predisposing events are: dental procedures, instrumentation (cystoscopy), débridement of decubital ulcers, infected gastrointestinal surgeries, biliary tract surgeries, infected catheters, and others.

Prophylaxis is performed by means of amoxacillin 2g, taken one hour prior to dental procedures or, if it cannot be given orally, ampicillin 2g, 30 minutes before the procedure. In patients who are allergic to penicillin, the option is clindamycin 600mg, one hour before, or cephalexin or cefadroxil 2.0g, one hour before, or azitromycin 500mg, one hour before the procedure. Where it cannot be given orally: clindamycin 600mg I.V. 30 min before, or cephazolin 1.0g I.M. 30 min before the procedure.

For genitourinary or gastrointestinal procedures, a combination of ampicillin and aminoglycoside is preferred.

VI – Cardiovascular Prevention

The doubt in a doctor's mind facing an elderly patient is: "Is it worth to investigate and treat the patient to prevent cardiovascular disease?", i. e., would there be any benefit for the patient in changing a deep-rooted lifestyle he/she has been used to for decades? Studies have shown that, if on one hand the presence of risk factors decreases in patients over the age of 75, probably due to the natural selection that has occurred, on the other hand, cardiovascular diseases are still more prevalent in old-age [1-3]. It has also been observed that, although the relative risk for cardiovascular disease decreases with age, the absolute morbidity and mortality risk increases.

The control of risk factors provides cardiovascular protection, both regarding the evolution of the disease and the outcome of acute events and, at least in theory, there is no reason for depriving elderly patients of this protection. The way prevention is handled should consider the patient's cost/benefit and risk/benefit rates and his/her quality of life [4-6].

In the present guidelines, the classical risk factors and the more recently assessed risk factors will be considered.

Table I – Infectious endocarditis prophylaxis in elderly patients
Dental processes, oral cavity, respiratory system, and esophagus

Situation	Agent	Administration
Prophylaxis	Amoxacillin Ampicillin	2.0g O 1hr before 2.0g I.M. or I.V. 30 min before
Allergic to penicillin	Clindamycin, or	600mg 1hr before
Cephalexin, or Cefadroxil, or	2.0g 1hr before	
Azitromycin, or Claritromycin	500mg 1hr before	
Clindamycin, or Cefazolin	600mg I.V. 30 min before	

Dajani AS, et al. JAMA 1997; 277: 1794-1801.

Table II – Endocarditis prophylaxis in elderly patients
Genitourinary and gastrointestinal (except for esophageal) processes

Situation	Agent	Administration
High-risk	Ampicillin + Gentamycin	Ampi 2.0g I.M. or IV + Genta 1.5mg/kg 30 min before (max. 120mg). 6hrs after: Amp 1g I.M. or I.V. or Amoxi 1g oral
Allergic to Ampi/ Amoxi	Vancomycin + Gentamycin	Vanco 1.0g I.V. for 1-2hrs + Genta 1.5mg/kg I.V./I.M. (max. 120mg) within 30 min before procedure
Moderate-risk	Amoxicillin, or	Amoxi 2.0g oral 1hr prior or

Ampicillin	Ampi 2.0g I.V./I.M. within 30 min before procedure	
Allergic to Ampi/ Amoxi	Vancomycin	Vanco 1.0g I.V. for 1-2hrs, completing infusion within 30 min before procedure

Dajani AS, et al. JAMA 1997; 277: 1794-1801.

Smoking

Smoking is, according to the WHO, the most important preventable cause of disease, passive smoking being classified as the third most important cause, preceded by inadequate dietary habits and followed by alcoholism.

Quitting smoking reduces cardiovascular mortality and morbidity, improves quality of life and fitness in *all age ranges* [7,8], besides reducing the risk for lung cancer and others, both in men and in women. Thus, it is recommended for elderly patients to quit smoking (**degree of recommendation A**). Medical counseling is fundamental for the success of withdrawal. The doctor can also resort to aid methods such as nicotine pads (**degree of recommendation A, level of evidence 2**) and/or the use of antidepressants, like nortryptiline or bupropione (**degree of recommendation 1, level of evidence 3**), or even psychotherapic methods [9,10]. Co-morbidities should be investigated and treated, so that the full benefits of quitting smoking may be reached. Members of the smokers' families who were exposed to cigarette smoke (passive smokers) have similar risks.

Dyslipidemias

The relationship between cholesterol fractions, especially the total/HDL cholesterol rate, and triglyceride levels as risk factors in old-age seem to have been confirmed by epidemiological studies [11]. Treatment is therefore justified even in the more advanced age brackets [12].

Hypertriglyceridemia

High triglyceride levels also have to be considered as risk factors in elderly patients [13-15]. In primary prevention, the normal value is < 200mg/dl. The ideal

value to be reached in patients with diabetes, with plurimetabolic syndrome or lipid triad, is 150mg/dl, especially in secondary prevention.

Evidence indicates that hypertriglyceridemia is a risk factor especially in female patients with lipid triad (HDL< 35mg/dl, total cholesterol/HDL cholesterol >5, and triglyceride levels >200mg/dl) (**degree of recommendation A, level of evidence 2**) [12].

In primary prevention, the initial recommendations are a change of dietary habits, weight loss, exercising, and restriction to alcohol consumption (**degree of recommendation A, level of evidence 2**).

If there is no adequate response, drug treatment is started. If, along with hypertriglyceridemia, LDL cholesterol is elevated, vastatins are indicated; if the increased triglycerides are accompanied by low HDL, fibrates are recommended (**degree of recommendation A, level of evidence 2**) [16]. Caution is recommended for the association of fibrates with vastatins.

For secondary prevention, the recommendations are the same, keeping in mind the goals to be achieved (**degree of recommendation B, level of evidence 2**) [17].

Hypercholesterolemia

Hypercholesterolemia is an absolute risk factor for the population in general, and especially for elderly patients. A low dosage of the HDL cholesterol fraction is a better coronary risk predictor than high LDL levels, especially in women [18].

Primary prevention should be encouraged, even in elderly patients. Studies have shown that the results obtained in adults are similar to those obtained in elderly subpopulations [19,20]. **Degree of recommendation A, level of evidence 2.**

The ideal recommended goals to be achieved are: total cholesterol <200mg/dl, LDL cholesterol <100mg/dl, and HDL >40mg/dl.

Treatment should be started by introducing adequate dietary habits, loss of weight in overweight or obese patients, and exercising during 4 months. If the non-pharmacological approach is unsuccessful, drug therapy is indicated. As a first option, vastatins are indicated, fibrates remaining as an alternative [21-24].

Secondary prevention is indicated in patients with clinical expression of atherosclerotic disease, in high-risk patients, and in diabetics. **Degree of recommendation A, level of evidence 2.** The recommended objective of the treatment is to reach levels of total cholesterol <160, and of LDL cholesterol <100.

The initial treatment includes the introduction of adequate dietary habits, loss of weight in overweight or obese elderly patients, and exercising for 2 months. If the non-pharmacological therapy is unsuccessful, vastatins are indicated as a first choice, fibrates remaining as an alternative [25-28].

It is recommended to always investigate secondary causes of hypercholesterolemia, such as hypothyroidism, renal failure, and diabetes.

The analysis of blood lipids should be done jointly (total cholesterol, fractions, and triglycerides), in association with other risk factors and with a global clinical evaluation of the patient. The result of all this information is crucial for the decision to treat or not to treat, and which is the best individual therapy [29].

Hyperuricemia

The significance of hyperuricemia in the evaluation of cardiovascular risk is still controversial. Several studies have demonstrated the relationship between serum uric acid levels and cardiovascular death [30,31], and the development of high blood pressure (26). On the other hand, there are many studies which did not show any relationship between serum uric acid levels and cardiovascular disease [32-34]. Thus, hyperuricemia should only be considered as a risk marker for cardiovascular disease, but not as an independent risk factor for cardiovascular disease. Elevated uric acid is also found in association with other risk factors, like old age, male gender, high blood pressure, diabetes, dyslipidemia, hyperinsulinemia, and renal function decay [35-37].

Uric acid measurement should be performed upon the initial evaluation as a risk marker for cardiovascular and/or renal disease, in addition to guiding the treatment of associated diseases, such as high blood pressure.

The treatment of hyperuricemia with the purpose of preventing cardiovascular disease is not indicated (**degree of recommendation C, level of evidence 3**), for there are no reliable data showing that the treatment of high uric acid levels changes the natural history of atherosclerotic disease [38,39].

Hormone replacement

The benefits brought by hormone replacement therapy (HRT) to the health of menopausal women are clear. Among others, there is a reduction in hot flashes, insomnia, depression, genitourinary atrophy, and a smaller risk for fractures

resulting from osteoporosis [40]. In spite of the countless experimental and human studies proving the beneficial effects of estrogens on the cardiovascular system, only observational studies showed that HRT causes a reduction in mortality rates by cardiovascular disease in women without a previous coronariopathy [41]. Regarding secondary prevention, HRT (the use of 0.625mg/day of conjugated equine estrogen, associated with 2.5mg/day medroxyprogesterone acetate) is contraindicated (**degree of recommendation C, level of evidence 2**). In patients which have been using HRT for over a year, this medication can be maintained (**degree of recommendation B2, level of evidence 2**) [42,43]. The results of the *Women's Health Initiative*, a randomized, double-blind, prospective, placebo-controlled study, to be concluded in 2005, will certainly answer the questions involving steroids and primary and secondary prevention of CAD.

Diabetes mellitus

This is a highly prevalent disease among elderly people, so that the doctors should pay attention to its presence upon first evaluation, even in asymptomatic patients.

The diagnosis of diabetes had its criteria established by the WHO and the Brazilian Diabetes Society [44] as being the presentation of diabetes symptoms and random glycemia >200mg/dl (the diagnosis having to be confirmed by ulterior glucose dosage $\geq$126mg/dl following 8hs fasting); glycemia $\geq$200mg/dl following a 75g glucose overload. Fasting glycemia $\geq$110mg/dl indicates glucose intolerance.

Diabetes is a risk factor for coronary artery disease [45,46], and is prognosis-determining for diabetics with coronary disease [47].

Glycemia control has shown to be effective regarding microcirculation-dependent complications, but the same benefits are not observed in controlling the large and medium vessel disease [48-50] (**degree of recommendation A, level of evidence 1**). The level recommended as a goal for fasting glycemia is $\leq$110mg/dl, but 126mg/dl is acceptable (level of evidence 2). Postprandial glycemia levels are $\leq$126mg/dl (**degree of recommendation A, level of evidence 2**). In elderly diabetics, the objective to be reached is 140mg/dl, although levels <160mg/dl are acceptable (**degree of recommendation A, level of evidence 2**). Glycosylated hemoglobin up to one percent above the upper limit of normality for the method is acceptable (**degree of recommendation B1, level of evidence 2**). In elderly patients, the risk/benefit of intensive treatment should be considered, in view of the risk for hypoglycemia (**degree of recommendation A, level of evidence 4**).

Doctors should also watch out for postprandial hyperglycemia, which is related to cardiovascular complications (**degree of recommendation A, level of evidence 2**).

Diabetes in elderly patients is usually type 2. Initially, non-pharmacological measures are recommended, followed by drug use, if necessary. Non-pharmacological measures include changes in dietary habits, directed by a doctor or by a nutritionist, and guided exercising. Weight loss is recommended for the obese. If the initial measures are insufficient, oral monotherapy is indicated and, if necessary, according to glycemic control tests, a combination of oral medications with different pharmacological actions. If control is not achieved, insulin therapy, isolated or in association with oral medication, is started [51]. Diabetes treatment is found to be dynamic, requiring regular control tests and possible changes in conduct.

Based on our current knowledge, it can be concluded that a strict glycemia control is hard to achieve, and its benefits regarding macrovascular disease are small. The ideal treatment should include the control of associated risk factors [52].

Homocystein

Routine measurement of homocystein levels is not recommended, but it is recommended in cases of patients with atherosclerotic disease antecedents which cannot be attributed to the traditional risk factors and/or diffuse atherosclerotic disease, or diabetics [53] with or without renal failure (**degree of recommendation B2, level of evidence 4**). In elderly patients, the intake of food that is rich in folic acid and vitamins B6 and B12 (citric fruits and vegetables) is recommended.

Exercising

Exercising is recommended with the purpose of providing physical well-being and self-confidence (**degree of recommendation A, level of evidence 1**). It should be preceded by medical evaluation to detect diseases which were previously unsuspected, but which may increase the risks of exercising. Exercise prescription is individualized, according to the clinical conditions and goals of each patient.

The exercising period should be divided into a warming-up phase, aerobic fitness exercise, muscular training, recovery. The starting duration should be 20 min, and the frequency 3 times a week. Exercising intensity should be 60% of the maximum heart rate for elderly patients with good functional capacity, and 40%

for those with a deficit. Maximum heart rate is the one reached on the previously performed ergometric test, or determined by the formula 220-age.

I) ***Training*** **–** 1) Warming-up (10 to 15 min); 2) stretching; 3) low-level aerobic activity.

II) ***Muscular fitness workout (15 to 20 min)*** **–** 1) Calisthenic exercises; 2) static exercises of low to moderate intensity.

III) ***For correction of muscle feebleness*** **–** 1) Series of 8 to 12 repeats (isotonic muscle workout); 2) slower and longer-lasting recovery (to remove lactate and prevent hypotension); 3) stretching for 20 to 30 s, to reduce rigidity and increase flexibility.

IV) ***Aerobic period*** **–** 1) Spending 250/300 Kcal/session, 1,200Kcal/week; 2) low-impact activity; 3) fractioned hiking greater compliance.

V) ***Cooling down (10 to 15 min)*** **–** 1) Light dynamic activities, and flexibility and stretching exercises.

VI) ***Frequency***: 3 to 4 times a week, alternating with resting days.

VII) ***Modality*** **–** Low shock/impact risk, hiking, volleyball, tennis doubles, and biodance.

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