		Relative MEK Activity (AR-CF:NL-CF)	
Cell Pair	**AR-RF(%)**	**MEK-4**	**MEK-7**
AR1 vs NL1	14	1.4:1	1.4:1
AR2 vs NL2	25	1.4:1	1.4:1
AR3 vs NL3	45	1.9:1	1.5:1
AR4 vs NL4	54	2.5:1	2.2:1
AR5 vs NL5	72	2.1:1	2.2:1

1067-136 Beta-Adrenergic Receptor Kinase Is Overexpressed in Patients With Chronic Mitral Regurgitation

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Background: Mitral regurgitation (MR) imposes a volume overload on the left ventricle (LV) during which LV ejection fraction remains normal, while LV contractility deteriorates. We have reported that LV contractile dysfunction is directly related to a decrease in responsivity of the β-adrenergic receptor (β-AR_1), but the mechanism for this reduced responsivity in *chronic* MR patients has not been explored. We hypothesized that this decrease in β-AR_1 responsivity may occur because of increased β-adrenergic receptor kinase (β-ARK_1) expression. **Methods**: Endomyocardial biopsy samples were obtained from four normal donor hearts and eight patients with *chronic* MR. Standard Affymetrix® chip technology was employed to analyze the samples for expression of β-ARK_1, β-ARK_2, β-AR_1, β-AR_2, and β-AR_3. The expression data were optimized to the standard, probe-pairs were quantile normalized, and the data were expressed as a fold-change for the MR patients compared to the normal donor hearts. Then, simplified t-tests were applied to the log transformed data. **Results**: Seven of the eight MR patients had LV contractile dysfunction but normal LV ejection fractions. Compared to the normal donor heart data, β-ARK_1 expression was 1.82 fold greater (p = 0.03), while β-ARK_2 and ß-arrestin expression were unchanged (1.00 and 0.94 fold change, p=0.27 and 0.31, respectively). The β-AR expression was not different between the two groups with β-AR_1 changing 0.56 fold (p=0.11), β-AR_2 changing 0.93 fold (p=0.72); and β-AR_3 changing 1.05 fold (p=0.79). **Conclusion**: β-ARK_1 expression is elevated in chronic MR patients with LV contractile dysfunction but normal LV ejection fractions, while β-AR expression is relatively unchanged. These data support the hypothesis that the decrease in β-AR_1 responsivity in these *chronic* MR patients may, in large part, be due to modification of β-AR_1 functionality through β-ARK_1 overexpression.

1067-137 Long-Term Afterload Reduction Halts Progression of Left Ventricular Dysfunction in Patients With Chronic Compensated Severe Mitral Regurgitation

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Background: Although afterload reduction is known to have favorable acute hemodynamic effects in patients with mitral regurgitation (MR), limited data exist concerning long-term effects. Our study examined whether afterload reduction slows progression of left ventricular (LV) dysfunction in stable asymptomatic patients with severe chronic MR.
Methods: A retrospective cohort study was conducted in patients with moderate-severe MR (3-4+) and an LV ejection fraction (EF) of ≥ 0.5, both determined by Doppler-echocardiographic visual estimate. The EF at 2 points in time from 48 patients not receiving afterload reduction during the interval (Group 1) and 45 patients receiving continuous afterload reduction both prior to and continuously during the observation period (Group 2) were compared.
Results: Groups 1 and 2 differed in age (69±17 years vs. 77±10, respectively, p=0.01) and EF (below, p=0.02), but not by gender, etiology of MR, symptoms, proportion treated with digoxin and beta blockade, chamber dimensions, severity of MR, blood pressure and heart rate. The average interval between examinations was 17±12 months (Group 1) and 20±14 (Group 2) p=0.2. Afterload reduction included ACE inhibitors (78%), calcium blockers (42%), angiotensin receptor blockers (20%), and vasodilators (4%). In Group 1, EF decreased from 62.0±7.5% to 59.7±6.7% (p=0.02) while Group 2 increased from 58.7±5.8% to 59.4±7.6%, (p=0.84). The changes observed in Group 1 (-2.3% over 17 months) was significantly different from Group 2 (+0.7 over 20 months) p=0.05. LV dimensions, MR severity, blood pressure and heart rate did not change.
Conclusions: In hemodynamically stable asymptomatic patients with severe chronic MR, long-term afterload reduction may halt progression of LV dysfunction.

1067-138 Dynamic Changes of the Tricuspid Annulus and Papillary Muscles During the Cardiac Cycle

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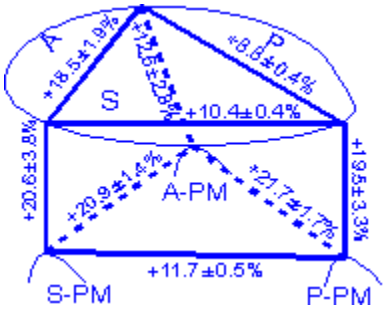
BACKGROUND: Knowledge of the normal dynamics of the cardiac valves is essential for understanding their pathologic changes and the design of surgical solutions. Although these geometric changes have been extensively studied in the aortic and mitral valves, the tricuspid valve has been largely ignored.
METHODS: Ten sonometric crystals were implanted in 7 sheep at midpoints of base of septal (S), anterior (A), and posterior (P) leaflets, tips of papillary muscles (PM), and apex.
RESULTS: Annulus area expanded from min 4.8± 0.3 cm^2 to max 6.1± 0.3 cm^2 (+28.6± 1.4%). Annulus perimeter expanded by 10.5± 0.5% (S), 13.0± 0.6% (A), and 14.0± 0.6% (P) leaflets. Increase in distance between commissures, PM, and commissures to PM are shown. The area from S-PM, A-PM, and P-PM expanded from 2.7± 0.2 cm^2 to 3.6± 0.2 cm^2 (+37.3± 3.8%). Angles between the annulus least squares plane and PM to the corresponding commissure axis changed at S-PM from 80.4± 3.3° to 94.3± 3.6° ; at A-PM from 67.8± 3.2° to 92.6± 3.4° , and at P-PM from 81.0± 2.3° to 90.4± 2.4° .
CONCLUSIONS: 1) the annulus' septal portion changes significantly during the cardiac cycle, and 2) at max displacement, all 3 PM were within the perimeter of the annulus. These findings should generate new tricuspid valve repair techniques.



1067-139 Is Visual Assessment a Valid Tool to Assess the Severity of the Mitral Regurgitation in Clinical Trials?

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Background: Although several semi-quantitative methods (SQM) for assessing the severity of mitral regurgitation (MR) have been validated, visual assessment (VA) of MR continues to be the easiest and the most popular means in clinical practice and clinical trials. This study aimed to validate VA by comparing it with the SQM in clinical trial that requires the assessment of MR. Methods: From the baseline data of Acorn cardiac support device trial, 111 cases with dilated cardiomyopathy and functional MR were identified. In these patients, the severity of MR was assessed by VA and compared with SQM including effective regurgitant orifice area (EROA), regurgitant volume (RV), MR area (MRA) by color Doppler test, MR area/left atrial area (MR/LA), MR distance (MRD), and vena contracta (VC). Results: The severity of MR by VA was grade I in 29, II in 22, III in 29, IV in 31 patients. The severity of MR by VA showed significant correlation with those by EROA (r = 0.75, p = 0.0006), RV (r = 0.76, p = 0.0004), MRA (r = 0.87, p < 0.0001), MR/LA (r = 0.91, p < 0.0001), MRD (r = 0.89, p < 0.0001), and VC (r = 0.88, p < 0.0001). With the increase of the MR severity by VA, the absolute values measured by SQM increased significantly.

	Grade I	Grade II	Grade III	Grade IV	p value
EROA (cm^2)	0.08±0.05	0.16±0.05	0.28±0.04	0.32±0.05	0.0150
RV (ml)	10±5.2	23±4.5	37±3.6	39±4.5	0.0024
MRA (cm^2)	3.7±0.6	6.3±0.6	9.1±0.6	14.8±0.5	< 0.0001
MR/LA (%)	15±2	26±2	37±2	53±2	< 0.0001
VC (mm)	2.0±0.3	2.5±0.2	3.6±0.2	5.8±0.2	< 0.0001

Conclusion: Visual assessment of the MR severity in patients with functional MR was consistent with those by various semi-quantitative methods. The semi-quantitative measures may serve as useful tools to assess the natural history of functional MR and the impact of medical and surgical interventions.

1067-140 Subnormal Tissue Inhibitor of Metalloproteinase Expression Modulates Matrix Metalloproteinase-2 Activity and Fibrosis in Aortic Regurgitation

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Background: Chronic aortic regurgitation (AR) is a predictable cause of heart failure. In our AR rabbit model, marked fibrosis is associated with hyperexpression of glycoproteins but not myocardial collagen content. We have shown that matrix metalloproteinase-2 (MMP-2), involved in collagen remodeling, is upregulated in AR and may suppress collagen content. MMP-2 activity can be modulated by endogenous tissue inhibitor metalloproteinases (TIMPs). To assess the role of TIMPs in regulating MMP-2 activity in AR, we assayed TIMP-1 and –2 expression by RT-PCR. Methods: Cardiac fibroblasts (CF) were cultured from NZW Rabbits without (NL)[n=3] and with surgically induced AR [n=3]. Total RNA was isolated [passage 6] from CF grown in triplicate. First-strand cDNA was synthesized from RNA using reverse transcriptase (RT) and was amplified by PCR using TIMP-1, TIMP-2 and GAPDH primers. The resulting products were resolved on ethidium bromide-stained agarose gels and scanned; band intensities were calculated using Kodak Digital Imaging and software. The TIMP band intensities for each sample were normalized to GAPDH and expressed as a ratio. Results: Quantitative analysis of TIMP-1[p=0.01] and TIMP-2 [p=0.06] gene expression show downregulation in AR-CF vs. NL-

CF. Conclusion: Increased MMP-2 activity in chronic AR may result in part from AR-induced downregulation of TIMPs, with subnormal inhibition of MMP. Pharmacological targeting of the MMP/TIMP-system may be effective in normalizing remodeling in AR.

Inhibitor	Regurgitant Fraction (%)	Inhibitor Band Intensity : GAPDH Band Intensity (n=6)		Ratio (NL:AR)
		NL	**AR**	
TIMP-1	14	0.9:1	0.6:1	1.5:1
	25	2.3:1	1.0:1	2.2:1
	45	2.4:1	1.7:1	1.4:1
			Avg Ratio	**1.7:1 (p=.01)**
TIMP-2	14	1.0:1	1.0:1	1.1:1
	25	2.6:1	1.6:1	1.6:1
	45	1.7:1	1.2:1	1.3:1
			Avg Ratio	**1.3:1 (p=.06)**

POSTER SESSION

1086 Valvular Heart Operations: New Procedures and Interventions

Monday, March 08, 2004, Noon-2:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 1:00 p.m.-2:00 p.m.

1086-135 The Modified Ross Procedure in Patients With Aortic Dilatation

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Background: The Ross Procedure (pulmonary autograft replacement of the aortic valve) has become a very useful option in young patients with isolated aortic valve disease. There has been concern about using this option in patients with ascending aortic dilatation or aneurysm. This study was designed to examine whether an aggressive approach to repairing or replacing the dilated ascending aorta could be safely combined with the modified Ross Procedure.
Methods: Fifty-six of 339 consecutive adult patients undergoing the modified Ross Procedure over 16 years had replacement (15) or reduction (41) of the ascending aorta. This included 47 men and 9 women with an average age of 43.8 years. Of the 15 graft replacement patients, the autograft root was supported with either an external “jacket” of graft material (10) or residual native aorta (3). Thirteen graft replacement patients required hypothermic circulatory arrest averaging 20 minutes. Thirty-seven patients had elliptical lateral aortorrhaphy and 4 had closed plication. Cardiac ischemic time averaged 180 minutes for graft replacement and 156 minutes for aortorrhaphy versus 145 minutes for patients without concomitant procedures.
Results: There was one operative death (from sepsis) for a 1.8% mortality compared to 2.2% (6/283) without ascending aortic surgery. Two other patients survived major complications – right ventricular failure and reversible neurologic deficit. Discharge echocardiograms of the 55 survivors revealed no or trace aortic regurgitation in 39 and mild in 16 patients. All returned to Class I functional status. No patients have required further surgery. Follow up echo data show only one patient (un-“jacketed”) with evidence of root dilatation.
Conclusion: The modified Ross Procedure can be safely extended to include patients with a dilated or aneurysmal ascending aorta using an aggressive approach to repair or replacement.

1086-136 Tissue Engineered Heart Valve Conduits of Porcine or Human Origin Differ Importantly in Chemotactic Activity for Monocytic Cells

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Background: To overcome the obstacles of conventional heart valve substitutes an already clinically applied approach is to decellularize xenogenous or allograft valves. As these prostheses are considered to be non-antigenic and thus superior to cryopreserved valve allografts, the aim of this study was to examine a remaining chemotactic activity of porcine and human acellular valve matrices.
Methods: Porcine and human pulmonary valves were decellularized using a detergent-based method. Soluble matrix proteins of the acellular tissue were extracted and chemotactic activity for U937 monocytic cells was examined in a transmigration-chamber. Native porcine and cryopreserved valve allograft tissue was used as positive control. To detect residual soluble proteins within the matrix, protein-electrophoresis was performed.
Results: A significantly reduced (p<0,05) cell migration was seen comparing the cryopreserved allograft tissue (746,4 ± 136,1 cells/µl ± SEM in lower chamber, n=10) and the decellularized porcine valve conduit tissue (183,6 ± 18,7, n=10). Surprisingly, the chemotactic activity of acellular human valve tissue (34,6 ± 8,6, n=10) was similar to the negative control (39,2 ±6,6 cells/µl, n=10) and significantly lower (p<0,001) than the decellularized porcine valve matrix. Electrophoresis of the acellular xenogeneic tissue revealed that considerable amounts of soluble proteins with different molecular weights remain in the porcine matrix which were not detected in the decellularized human valve tissue.
Conclusion: We describe for the first time that the remaining immunogenic activity strongly depends on the source of a tissue engineered heart valve. Whereas the acellular porcine pulmonary valve does not result in the considered inert heart valve scaffold and thus might induce an immunological response, the decellularization of a human pulmonary heart valve diminishes the chemotactic activity of the valve tissue. This findings will have an important impact on further investigations on tissue engineered heart valves.

1086-137 Impairment of Left Atrial Appendage Mechanical Function Following Electrical Isolation With Epicardial Radiofrequency Bipolar Ablation

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Background: Intraoperative, open-chest, beating heart epicardial radiofrequency ablation without atriotomy is an emerging technique for cure of atrial fibrillation. During these procedures, in order to replicate electrophysiologically the MAZE III procedure, an operator may ablate at the base of the left atrial appendage (LAA), rendering it electrically isolated, without physically removing or occluding it. Our experience suggests that this might be dangerous. **Methods:** In each of 5 large healthy pigs, electrical isolation of the LAA at its base (junction with left atrial body) was achieved without atriotomy in a beating heart/open chest preparation with a single application of energy via a bipolar ablation device. Post-mortem analysis demonstrated the ablation lesion to be transmural and very discrete, involving <10% of the total LAA volume. LAA, pulmonary vein, transmitral Doppler velocities and electromechanical properties were measured immediately prior to and after ablation using intracardiac echocardiography (ICE, AcuNav) and electromechanical mapping (NOGA, Biosense Webster). All animals were in sinus rhythm throughout the study. **Results:** There was a marked diminution of LAA peak flow velocity between pre (0.4 ± 0.2 meters.sec) and post (0.1 ± 0.08 meters/sec) ablation (p<0.05). There was no significant change in either pulmonary venous or transmitral velocity. NOGA-derived LAA local linear shortening was markedly diminished in the LAA region (8% ± 3% pre vs 2% ± 1% post-ablation; p<0.05). ICE also demonstrated spontaneous echo contrast not seen before. **Conclusions:** Electrical isolation of the LAA produces mechanical paralysis, dilatation, and blood stasis. It is reasonable to hypothesize that these changes would be clinically prothrombotic. If an electrically isolated LAA is not to be excised, its orifice should be carefully occluded.

1086-138 In Which Patients Does Artificial Renal Support Really Help After Cardiac Surgery?

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Objective: We developed a scoring system to predict outcome in patients who develop acute renal failure (ARF) requiring artificial renal support after cardiac surgery, thereby providing a tool to guide whether or not intensive artificial renal support therapy is justified.
Methods: From 01/92-07/01, 136/14,000 (0.9%) patients developed ARF requiring artificial renal support following cardiac surgery. Fifty-five (40%) underwent CABG/valve, 39 (29%) isolated CABG, 21 (15%) isolated valve, 12 (9%) heart transplant and 9 (6%) other procedures. Multivariate logistic regression, based on pre-dialysis parameters, was used to construct a prediction score for operative mortality for those patients with ARF requiring artificial renal support.
Results: The overall operative mortality (OM) was 58% (70/136). From the logistic regression model (Table) we assigned a score based on the presence of independent predictors of OM. Higher scores strongly predicted OM. Among the 54 patients with a score ≥3 prior to artificial renal support, OM was 85% (115/136) (Specificity 95%). The positive predictive value was 94%. In patients with score ≤1, OM was 18% (24/136).
Conclusions: The scoring system represents a simple and accurate tool for predicting OM in cardiac surgery patients who develop ARF prior to the institution of resource intensive artificial renal support. Thus, in patents with high scores, artificial renal support is associated with exceedingly high OM and may not be justified.

Multivariate Predictors of Operative Mortality

Patient Characteristics	OR	CI	P Value	Points Assigned
Pre Dialysis Coma	9.6	2.3-39	0.001	2
Preop Creatinine <1.5 mg/dL	5.0	2.0-12	0.0007	1
Preop Hypertension	4.4	1.6-12	0.004	1
Pre Dialysis Sepsis	6.4	2.2-18	0.0005	1
Pre Dialysis Total Bilirubin>2 mg/dL	5.6	2.1-15	0.0006	1