1086-139 Comparison Between Successful and Unsuccessful Mitral Valve Repair of Ischemic Mitral Regurgitation: An Echocardiographic Follow-Up Study

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Ischemic mitral regurgitation (IMR) is commonly treated by ring annuloplasty, but it is unclear what factors contribute to the success of annular reduction surgery. This study aimed to investigate predictive echo factors for the success of mitral valve (MV) repair.
Methods: 437 patients underwent MV repair for IMR at Cleveland Clinic Foundation between April 1990 and November 2002. 76 patients were excluded from this study due to insufficient or inconsistent echo reports or clinical information. Pre-operative echo data in the remaining 361 patients were analyzed, including ejection fraction (EF), left atrial diameter (LAD), left ventricular end-diastolic diameter (LVDD) and end-systolic diameter (LVSD). Severity of mitral regurgitation (MR) was graded on a scale of 0 to 4.
Results (Table): 298 patients (83%) had satisfactory outcomes with <2+ MR, while 63 (17%) had recurrent significant MR (≥2+) during follow-up. There was no significant difference in age, sex, EF and follow up period between the 2 groups. The success group was found to have a smaller LAD, LVDD, and LVSD pre-operatively than the recurrent MR group. The most striking difference between the two groups was the severity of MR before repair.

	No Recurrent MR	Recurrent MR	P-value
Data Availability (N)	298	63	
Days of Follow-up	262±546	190±384	NS
Age (years)	66±9	67±8	NS
Male/Female	193/105	39/24	NS
EF (%)	33±11	32±10	NS
LAD (cm)	4.56±0.8	4.89±0.6	0.01
LVDD (cm)	5.77±0.86	6.06±0.71	0.04
LVSD (cm)	4.09±1.03	4.85±0.74	0.03
Pre-Op MR (0~4+)	2.67±0.84	3.15±0.86	<0.0001

Conclusion: LAD, LVDD, LVSD and especially MR severity in preoperative 2D echo were larger or worse in the recurrent MR group as compared to the success one. Accordingly, MV repair should be carefully selected in IMR patients with larger left atrium/left ventricle and more severe MR.

POSTER SESSION

1107 Pathophysiologic Aspects of Calcium Deposition in Valvular Heart Disease

Monday, March 08, 2004, 3:00 p.m.-5:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 3:00 p.m.-4:00 p.m.

1107-135 Neoangiogenesis via Vascular Endothelial Growth Factor Expression Is Associated With an Osteoblast-like Bone Formation in Calcified Rheumatic Heart Valves

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Intro: Rheumatic fever is the most common cause of valvular heart disease in developing countries. Despite its high prevalence, the inflammatory-immune and fibrocalcific mechanisms leading to progressive valvular dysfunction are not well characterized. We hypothesized that calcification is associated with osteoblastic bone formation and angiogenesis.
Methods: To test this hypothesis we examined human rheumatic valves (RV) replaced at surgery (n=23) and normal human valves (nl) (n=20). Micro computed tomography was used to assess mineralization fronts to reconstruct the 2 dimensional and 3 dimensional extent of mineralization. Hematoxylin and eosin, Masson trichrome stains were performed. Immunohistochemistry was used to localize osteopontin protein, alpha actin, CD34, Vascular Endothelial Growth Factor (VEGF), von willebrand factor (VWF), and CD68 stains (human macrophage). Quantification of PCNA was performed by computer analysis (Quantification of Proliferation Index Baccus, Inc, Lombard, IL). **Results:** H and E, and Masson Trichrome stains confirmed the presence of mineralization in areas of intense calcification of the calcified rheumatic heart valves as compared to normal valves. Immunohistochemistry localized osteopontin to smooth muscle cells within the microvessels within the valves. MicroCT demonstrated calcification with complex formations developing within the mineralized tissues. Immunohistochemistry markers including VEGF and CD34 for angiogenesis were positive in areas of inflammation (CD68). In cells staining for alpha-actin, PCNA index was positive in 5 of 22 cardiac valves in the alpha actin staining cells (1.26+/-0.32 (nl) versus 37.64 (RV)). The amount of new vessels present were positive in 19 of 22 valves (0 (nl) versus 21.55+/-22.08(RV)). These markers were present minimally in the normal valves. **Conclusions:** These findings strongly suggest that rheumatic valve calcification results from ongoing osteoblast bone formation and neoangiogenesis. Neither of those cellular processes are passive or random; both are active and regulated by multiple inflammatory mediators which are important in bone formation.

1107-136 Progression of Aortic Valve Calcification Measured by Electron Beam Computed Tomography: A Population-Based Study

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Background: Calcification of the aortic valve has been recently linked to poor outcome. However, prevalence, progression and association to cardiovascular risk factors and subclinical atherosclerosis are unknown
Methods: Between 1996 and 1999, 262 research participants ≥60 years (68±5 years, 43% male) enrolled in a prospective population-based study underwent Electron Beam Computed Tomography (ECBT) for assessment of aortic valve (AVC) and coronary artery (CAC) calcifications
Results: *Prevalence:* Prevalence of AVC was 30% and increased with age (<65 years: 15%; 65-70 years: 35% and ≥70 years: 42%; p<0.01) *Association to cardiovascular risk factors and CAC:* History of diabetes and hypertension, serum glucose and body mass index were significantly associated with AVC (all p<0.05). Patients with AVC had higher CAC (441±802 vs. 265±566, p<0.01) independent of age *Progression:* After a mean follow-up of 3.8±0.9 years, AVC increased (baseline: 54±173, follow-up: 94±271, p<0.01) and more so in patients with than without baseline AVC (+37±53 vs. +1±4 /year, p<0.01). Overall, independent predictors of AVC progression were baseline AVC (p<0.01) and LDL-C (p<0.01). Compared to the 173 AVC-free participants (baseline and follow-up), total and LDL-C and CAC progression (adjusted for baseline score) were higher in the 19 with AVC-acquisition at follow-up (respectively 235±39 vs. 209±33 mg/dL; 141±31 vs. 121±27 mg/dL; +78±87 vs. +28±47 /year, all p<0.01) but not in the 70 with established AVC at baseline (respectively 205±35; 120±31; +53±58; all p>0.40). LDL-C was the only independent determinant of acquisition of AVC and baseline AVC of progression of AVC in the AVC established group
Conclusion: In the population, AVC 1) is frequent and increases with age, 2) is associated with atherosclerotic risk factors, 3) is a marker of more severe coronary artery disease a potential mechanism for poor outcome 4) appears de novo in a context of progressive atherosclerosis 5) whereas established AVC progresses independently of atherosclerotic risk factors and faster with increasing AVC loads. These data underscore the importance of AVC measurement by EBCT and of evaluating strategies to slow the disease progression

1107-137 Influence of C-Reactive Protein on Matrix Remodeling in Calcific Aortic Stenosis

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Background: Calcific aortic stenosis (AS) is based on an inflammatory process leading to marked remodeling of the extracellular matrix. We have shown that matrix metalloproteinase (MMP)-1 contributes to this process. Recent studies showed that serum levels of the inflammatory mediator C-reactive protein (CRP) are elevated in patients with calcific AS, however, its the role during the pathogenesis of calcific aortic stenosis is unknown.
Methods: Human tricuspid aortic valves with calcific AS (n=11) were obtained at valve replacement, sclerotic valves without stenosis (n=5) and normal valves (n=4) at autopsy. CRP immunostaining was performed using monoclonal antibodies, and staining intensities were assessed by semiquantitative scoring. Human aortic valve myofibroblasts were cultured with and without addition of CRP. MMP-1 expression was assessed by Western blotting.
Results: No staining for CRP was detectable in normal valves. Sclerotic valves showed moderate staining, stenotic valves intense staining (p<0.05 by Kruskal-Wallis test). Stimulation of human aortic valve myofibroblasts with CRP lead to a time-dependent increase in MMP-1 as compared to unstimulated controls.
Conclusion: CRP staining is absent in normal valves, present in sclerotic valves and strong in stenotic valves. Stimulation of cultured human aortic valve myofibroblasts with CRP leads to increased expression of MMP-1. These results suggest a pathogenetic influence of CRP on tissue remodeling during calcific AS, further supporting the concept of calcific AS as an inflammatory disorder.

1107-138 Statin Therapy Does Not Affect Bioprosthetic Valve Degeneration

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Background: Several recent studies have suggested that statins reduce the hemodynamic progression of calcific aortic stenosis. Similarly, a slower rate of bioprosthetic valve degeneration has recently been reported for statin-treated patients. However, the differences in underlying pathophysiolgical mechanisms of these two disorders question such positive statin effects. Thus, further retrospective analyses are required before prospective randomized trials can be justified.
Methods: 202 pts (71±11 years, 118 female) with bioprosthetic aortic valves, normal left ventricular function and no other significant valvular lesion who were examined between 2000 and 2002 and who had two echocardiograms separated by at least 6 months were studied (mean interval 28±17 months). Of these, 84 pts (42%) were on statin therapy. The change in peak transprosthetic velocity (TP-Vel) during follow-up was assessed.