	SR	Afib	P
LV EF (%)	57 ± 17	56 ± 12	0.58
LAVol (mL)	111 ± 52	129 ± 66	0.14
RAVol (mL)	58 ± 26	93 ± 36	0.001
S PAP (mmHg)	44 ± 14	40 ± 13	0.70
ET-1 (pg/mL)	13.5 ± 7	13.5 ± 7	0.97
N-ANP (pg/mL)	1655 ± 1323	2613 ± 1681	0.003

both idiopathic and secondary Afib, therefore 3) limiting the value of N-ANP level as a marker of LV Dysfunction.

1222 Anatomic Factors in Valvular Heart Disease

Wednesday, April 1, 1998, 3:00 p.m.–5:00 p.m.
Georgia World Congress Center, West Exhibit Hall Level
Presentation Hour: 3:00 p.m.–4:00 p.m.

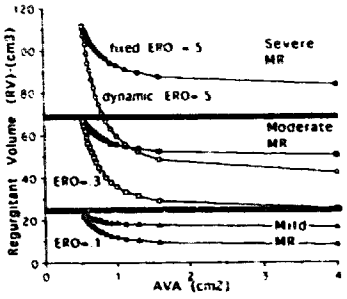
1222-18 Computer Simulations of the Change in Mitral Regurgitant Volume After Repair of Concomitant Aortic Stenosis: Significance of Pressure Dependent Mitral Effective Orifice Area

R.Y. Grimes, A.P. Yoganathan, R.A. Levine. *Massachusetts General Hospital, Boston, MA, USA*

A common issue where both significant aortic stenosis (AS) and mitral regurgitation (MR) exist is whether the MR will improve after the AS is relieved. It is commonly assumed that it will because of the reduced left ventricular pressures (LVP). However, the MR effective regurgitant orifice (ERO-cm2) may also decrease with lower LVP.

Methods: The relative roles of these two possibilities were explored in a mathematical model of the aorta and left heart that produces physiologic pressures and flows. The maximal MR ERO was varied from 0.1 to 0.5 and aortic valve area (AVA-cm2) = 4–0.5. MR ERO was kept fixed or varied proportional to LVP. At each AVA and ERO, LVP was adjusted to a achieve a forward CO of 5 l/min at a HR of 70.

Results: With fixed EROs, as AVA increased from 0.5 to 4, peak LVP decreased from 210 to 120 mmHg, and MR volume decreased by only an average of 25%, without a change in the MR grade (moderate/severe corresponding to regurgitant fraction = 25/50%). With dynamic EROs, MR volume decreased by 61%, with severe converting to moderate MR.



Conclusions: If the orifice remains fixed, only modest decreases in MR occur with relief of AS, because the RV is proportional to the *square root* of LVP. However, with a dynamic orifice, severe MR resolves if AS is relieved. This observation underscores the importance of knowing the mechanism of MR in patients undergoing AS surgery: fixed or rheumatic MR may remain severe, whereas dynamic forms, such as prolapse, may be largely relieved without direct repair.

1222-19 Progression of Aortic Stenosis Is Related to an Echocardiographic Index of Aortic Leaflet Pathology

D.R. Desser, M.E. Yousseff, S.J. Brener, R.S. Finkelhor, R.C. Bahler. *Case Western Reserve University at MetroHealth Medical Center, Cleveland, Ohio, USA*

Background: The rate of progression of aortic stenosis (AS) is variable and it is unclear if any clinical or echo factors predict a more rapid progression.

Methods: We identified from an echo database 98 patients with AS, who had 2 or more technically adequate studies separated by ≥6 months. From the first study we measured standard M-mode, 2-D and Doppler variables. An index of aortic leaflet pathology (ALP) was determined from review blinded to AS severity. ALP = calcification + mobility with each rated on a numerical scale. Clinical and ECG variables were abstracted from records closest in time to the first echo.

Results: The mean age was 68 years (range 29–89) and females predominated (66:32). Severity of AS at first study ranged from a peak gradient of 6 to 95 mmHg (median 26.4 mmHg) and aortic valve area (AVA) of 0.6 to 2.2 cm^2 (median 1.3 cm^2). Mean follow-up was 1.8 years (range 0.5–4.25). Change in severity of AS (Δ AS) was expressed as terciles of Δ peak gradient/year. The mean Δ AS was 4.4 mmHg/year. More rapid Δ AS occurred in males ($p = 0.05$), patients with elevated serum creatinine ($p = 0.03$), greater LV mass ($p = 0.01$), and higher ALP scores ($p = 0.0003$). No significant differences were found for: initial peak or mean gradients, AVA, ejection fraction, valvular regurgitation, or ECG variables. In multivariable regression analysis only ALP score remained significant ($r = 0.38$, $p < 0.01$).

Conclusions: Δ AS is independent of initial AVA or clinical parameters but associated with an echocardiographic index of aortic leaflet pathology.

1222-20 Bone Formation and Osteoclast Remodeling in Calcified Cardiac Valves: A Clinical and Pathologic Analysis

E.R. Mohler, F.H. Gannon, C. Reynolds, F.S. Kaplan. *University of Pennsylvania, Philadelphia, PA, USA*

Calcification of native and bioprosthetic cardiac valves is the leading reason for surgical valve replacement. Recently, Bone Morphogenetic Proteins have been found associated with valve calcification implicating an active and not degenerative process. Ossification (bone formation) has not been studied in a large series of valve specimens. We studied 206 consecutive patients (122 men and 84 women) who underwent valve replacement between the years 1994–1997 at the Hospital of the University of Pennsylvania. Clinical records were reviewed for cardiovascular risk factors as well as the presence of atherosclerosis. Histologic material was analyzed by light microscopy. Immunohistochemical studies for lymphocyte subset markers, neural markers, vascular markers and several bone formation proteins were performed on all valves. The mean age was 68 years with a history of hypertension in 48%, smoking in 51%, hypercholesterolemia in 23% and diabetes in 17%. Atherosclerosis of the coronaries was reported in 46%, in the carotid 11% and in the lower extremity 9%. Rheumatic fever was reported in 22% and hyperparathyroidism in 9%. A total of 228 valves (180 aortic and 48 mitral) were examined. Mineralized tissue was present in 25% of all valves. Lamellar bone was identified in 30 valves (both aortic and mitral) and cartilagenous tissue in 4 valves. Lymphocytes were seen in 54 valves and showed a mixed population of B- and T- cells. Osteoclasts were seen in 11 valves and neoangiogenesis was seen in 1 valve. Thus, this report identifies features of bone formation and remodeling in mineralized aortic and mitral valves.

Conclusion: These novel findings establish valvular ossification as a fundamental pathologic process in valve stenosis and suggests new avenues for investigating the molecular pathophysiology of osteogenesis in an intravascular environment.

1222-21 Mechanism of Ischemic Mitral Regurgitation With Ventricular Remodeling After Myocardial Infarction: Demonstration of Leaflet Tethering by Three-dimensional Echocardiography

Y. Otsuji, M.D. Handschumacher, N. Liel-Cohen, H. Tanabe, J.L. Guerrero, L.A. Nicholls, G.J. Vlahakes, R.A. Levine. *Massachusetts General Hospital, Boston, MA, USA*

Competing hypotheses for ischemic mitral regurgitation (MR) include ischemic dysfunction of the LV and papillary muscles (PMs) per se, vs. geometric distortion of the mitral apparatus by LV dilatation, tethering the leaflets and restricting closure. We studied these possibilities by analyzing mitral apparatus geometry in 7 sheep *right after left circumflex obtuse marginal 2 & 3 ligation* with no LV remodeling *and 8 weeks later.* The mitral apparatus was reconstructed by 3D echo from rotated midsystolic views, and MR stroke volume (SV) calculated as LV ejection volume - aortic SV.