

	Mild AS PG mean <30 mm Hg	Moderate AS PG mean >30 mm Hg	Severe AS PG mean > 50 mm Hg	AV R
n	11	18	39	17
NT-proBNP (pg/ml)	676	1508	3311	85 P < 4 0,01
PG mean (mm Hg)	15,3	37,8	64,3	15, P < 1 0,01
LVM (gr)	215	245	271	19 P < 9 0,05
Ejection fraction (%)	54.1	51.1	49.3	55 n.s.

Conclusions: NT-proBNP was closely linked to severity of aortic stenosis and therefore may be useful for therapeutic decision making.

1134-23

Is Mitral Regurgitation in Congestive Heart Failure Truly Functional? Evidence for Significant Biochemical Changes in the Valvular Extracellular Matrix

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Background: Mitral regurgitation (MR) is a complication for many patients with congestive heart failure (CHF). This MR was previously thought to be functional, due to alterations in the cardiac geometry rather than in the valvular microstructure. In contrast, we hypothesize that the geometric alterations found in CHF might be associated with biochemical changes in the extracellular matrix of the mitral valve.

Methods: Mitral valves were obtained post transplant from hearts with CHF (20 dilated cardiomyopathy, 14 ischemic, 3 other); all patients had undergone recent echocardiography. Left ventricular (LV) collagen and valvular DNA, collagen, glycosaminoglycan (GAG), and water content were measured, normalized to tissue weight, and compared with autopsy controls (n=12). Valvular and cardiac chamber dimensions and functional parameters were compared with biochemical parameters using a repeated measures generalized linear model.

Results: The mitral leaflets in CHF had 86% more DNA, 18% more GAGs, and 6% more collagen than normal (p<0.05). Mitral chordae in CHF had 83% more DNA, 42% more GAGs, and 8% less water (p<0.05). The elevated leaflet collagen concentration was significantly associated with increased anterior leaflet length and LV dimensions, and slightly associated with MR grade (p=0.06). Increased leaflet DNA, an indicator of cellularity, was associated with anterior leaflet thickening (p=0.002) and MR grade (p=0.01). Elevated leaflet GAGs were associated with left atrial diameter (p=0.002) and alterations in early and late diastolic flow (p<0.05). Chordal collagen, cellularity, and water concentrations were similarly associated with annular and ventricular dimensions as well as LV collagen concentration (p<0.04).

Conclusion: Mitral leaflets and chordae in CHF have significant biochemical differences from autopsy controls. These changes in the valvular extracellular matrix occur in proportion to the alterations in cardiac dimensions that accompany CHF. Our biochemical finding of leaflet and chordal remodeling suggests that MR in patients with CHF may not be purely functional, and that these mitral valves from failing hearts should not be considered "normal."

1134-24

Neurohormonal Activation Is Associated With Left Ventricular Remodeling in Chronic Asymptomatic Mitral Regurgitation and Normal Left Ventricular Ejection Fraction

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Background: Neurohormones are elevated in patients with chronic symptomatic mitral regurgitation (MR) and/or left ventricular (LV) dysfunction. There is little data regarding neurohormonal activation in asymptomatic MR with normal resting and exercise LV function.

Methods: We report our initial results of a prospective study. A total of 14 normal subjects and 7 asymptomatic MR patients were enrolled. Patients had at least 3+ MR, regurgitant orifice area of 0.43±0.12cm² and resting LV ejection fraction (LVEF) of 65±5.5%. Plasma epinephrine, norepinephrine, renin activity and N-terminal brain natriuretic peptide (N-BNP) were measured. Resting and stress exercise echocardiography were performed. LVEF, end-diastolic diameter (LVEDD), volume, end-systolic diameter and volume were measured. Exercise capacity was expressed as metabolic equivalents.

Results: Although MR patients presented with normal resting LVEF and normal exercise response (increased LVEF, decreased LV end-systolic diameter with excellent exercise capacity-metabolic equivalents, 12±1.7), neurohormones were elevated, especially N-BNP (table). Significant LV remodeling was seen in the MR group with increased resting and post-exercise LV diameters and volumes. **Conclusions:** Neurohormones, especially N-BNP, are elevated in asymptomatic MR patients with apparently normal resting and exercise LV function, but dilated LV. Neurohormonal activation may indicate ongoing LV remodeling due to volume overload.

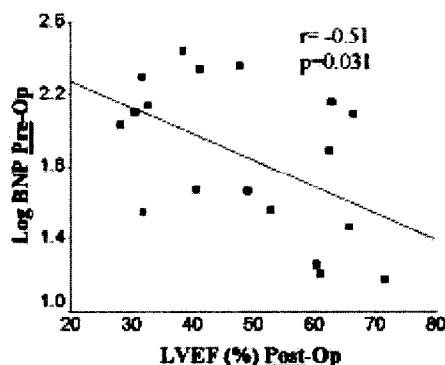
	Resting LVEDD (cm)	Resti ng LVED V (ml)	Resting LVEF (%)	N-BNP (fmol/ ml)	Epinephri ne (nM)	Nor- Epinephri ne (nM)	Renin (ng/ml/ h)
Normal	4.7±0.6	80±15	66±5	291±8 2	1.2±0.3	3.3±0.6	0.74±0. 7
MR group	5.5±0.6	164±2 9	65±5	435±1 13	1.5±0.5	3.6±0.9	1.7±2.0
P	<0.01	<0.00	>0.05	<0.01	=0.11	=0.44	=0.13

1134-25

B-Type Natriuretic Peptide Predicts Left Ventricular Response to Surgery in Patients With Severe Mitral Regurgitation in Asymptomatic Patients With Preserved Left Ventricular Function

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Background: BNP has been validated as marker of cardiac function and prognosis in a variety of settings. To date, the relationship of pre- and post-op BNP to cardiac structure and function in asymptomatic patients with severe mitral regurgitation (MR) has not been well defined. **Methods:** We prospectively studied 22 consecutive asymptomatic patients (mean age 56 ±13 yrs) with severe MR and LV ejection fraction (EF) =55% referred for mitral valve surgery. Patients underwent pre- and post-op 2D echo evaluation, with concurrent sampling of BNP (Biosite). LV volumes and EF were calculated by biplane Simpson's method. Cardiac dysfunction was defined as EF <50%. **Results:** Mean pre-op data included: regurgitant orifice area = 0.88 ±0.4 cm², EF = 61 ±6%, LVEDV = 177 ±44 ml, LVESV = 69 ±23 ml. BNP increased acutely from 92 ±73 pg/ml to 314 ±200 pg/ml following surgery. Pre-op logBNP correlated significantly with pre-op LA volume (r=0.49, p=0.04), post-op LVESV (r=0.50, p=0.04) and post-op EF (r=0.51, p=0.03), but not with other echo measures. Pre-op BNP was higher in patients who developed post-op cardiac dysfunction (141 ±85 pg/ml vs 57 ±51 pg/ml, p=0.03). A pre-op BNP of 50 pg/ml had a sensitivity of 83%, specificity of 60%, and negative predictive value of 91% for prediction of a post-op cardiac dysfunction (C=0.8). **Conclusion:** Pre-op plasma BNP correlates significantly with post-op EF and LVESV in our study population. A pre-op plasma BNP below 50 pg/ml maybe useful in excluding the likelihood of post-op cardiac dysfunction.



1134-26

Serum B-Type Natriuretic Peptide in Patients With Chronic Mitral Regurgitation Is Not Elevated

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Background: Chronic mitral regurgitation (MR) imposes a progressive hemodynamic burden upon the left ventricle (LV). Management is based on symptoms and LV size and function. To determine if B-Type natriuretic peptide (BNP), a hormone secreted by ventricular myocytes under strain, may be a useful marker of ventricular deterioration, we measured BNP levels in patients with chronic MR.

Methods: We studied 9 patients with moderate to severe MR and a range of symptoms (mean age 45 ±16.6) and five normal control subjects (mean age 42.2 ±11.1) by 2D echocardiography with Doppler. LV ejection fraction (EF), LV end diastolic volume (EDV), end systolic volume (ESV), and LV mass index (LVMI) were measured and severity of MR was assessed semiquantitatively using color Doppler. Patients were excluded if they had any other valve lesion. BNP levels were measured by the Shionogi assay.

Results: Patients and controls did not differ in age and had similar EF (63±12 vs 66±9%, p=ns). Seven of the 9 patients had severe MR and 6 had dyspnea, of whom 2 underwent valve surgery within 6 months. Compared to controls, the MR patients had significantly higher LVMI (109±30 vs 72±15 g/m², p=.02), ESV (53±25 vs 27±6 ml, p=.02) and EDV (132±42 vs 84±23 ml, p=.04). However, there was no significant difference in serum BNP levels (1±8 vs 6±4 pg/ml, p=0.20) between the two groups, and BNP did not relate to severity of MR or to symptoms.

Conclusion: These findings suggest that chronic MR is not associated with elevated lev-