MR with different degree of local and global LV remodeling, and characteristics of the regurgitant jet. Such, a complete characterization of the pattern of ischemic MR could aid to tailor the best treatment for the single patient

1084-22 Papillary Muscle Dysfunction Attenuates Ischemic Mitral Regurgitation in Patients With Localized Basal Inferior Left Ventricular Remodeling

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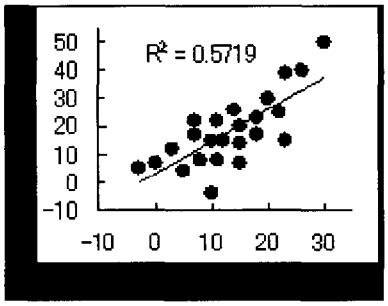
Background: In principle, papillary muscle (PM) dysfunction could be associated with less mitral regurgitation (MR) because of PM elongation, attenuating tethering. However, variability in the degree of left ventricular (LV) remodeling can influence the relation between PM dysfunction and MR. We, therefore, hypothesized that PM dysfunction attenuates MR in patients with comparable degree of segmental basal inferior LV remodeling.

Method: From 38 consecutive patients with previous inferior myocardial infarction, 2 patients with global LV remodeling and 12 with only modest inferior remodeling were excluded. In the remaining 24 patients with significant and localized basal inferior LV remodeling, LV volume, mitral annular area, PM tethering distance, % systolic thickening of middle portion of medial PM and MR fraction were quantified by 2-dimensional and Doppler echocardiography.

Results: % systolic PM thickening had positive and significant relation with % MR fraction (figure), which was best correlated with medial PM tethering distance.

Conclusion: Ischemic MR can be attenuated by PM dysfunction, reducing leaflet tethering, in patients with localized basal inferior LV remodeling.



1084-23 Inhibition of the c-Jun N-Terminal Kinase Pathway Minimizes Collagen Remodeling in Aortic Regurgitant Hearts

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Background: Fibrosis associated with aortic regurgitation (AR) shows abnormal fibronectin (FN) but normal collagen content. This pathologic fibrosis is important in genesis of heart failure (CHF) in AR; understanding fibrosis generation may enable specific therapy to retard CHF. We showed that increased FN expression by cardiac fibroblasts (CF) from rabbits with catheter-induced AR results from activation of the c-Jun N-terminal kinase (JNK) pathway, which also can upregulate collagen-specific metalloproteases (MMPs). To see if JNK activation of MMP is involved in minimizing collagen content in AR we assessed MMP-2 activity with SP600125, a specific JNK inhibitor. **Methods:** NL-CF vs AR-CF (3 pairs) from rabbits were grown in triplicate with and without 20μM SP600125. Media then were collected for 24 hr intervals over 5 days. Enzymes were separated by gelatin-containing zymograms, stained with coomassie blue, destained, and analyzed by videodensitometry. Band intensities were normalized to total cell protein concentrations. **Results:** MMP-2 activity was upregulated in AR-CF vs NL-CF (AR:NL=2.1:1, p< .03). When CF were grown with SP600125, MMP-2 activity was maximally downregulated by day 2 vs day 0 (NL, 1.0:0.4, p< .001; AR, 1.0:0.5, p< .001, Table). **Conclusion:** In AR myocardium, fibrotic myocardium featuring abnormal FN but normal collagen content results in part from AR-induced upregulation of MMP-2 by JNK stimulation. Inhibition of this reaction may help mitigate pathologic fibrosis and CHF.

	1	2	3	4	5
Exposure Day(N) →					
Cell Line ↓					
	Day 0: Day N				
NL1	1:0.4	1:0.5	1:0.7	1:0.7	1:0.6
NL2	1:0.8	1:0.3	1:0.6	1:0.8	1:0.8
NL3	1:0.7	1:0.3	1:0.4	1:0.4	1:0.5
Average	*1:0.6*	*1:0.4*	*1:0.5*	*1:0.7*	*1:0.6*
AR1	1:0.5	1:0.2	1:0.5	1:0.5	1:0.5
AR2	1:0.9	1:0.6	1:0.7	1:0.9	1:0.7
AR3	1:0.9	1:0.2	1:0.4	1:0.4	1:0.3
Average	*1:0.8*	*1:0.5*	*1:0.6*	*1:0.8*	*1:0.6*

1084-24 Heterogeneity of Response to Pressure Overload in Aortic Stenosis

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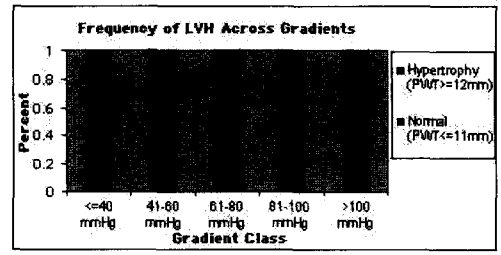
Left ventricular hypertrophy is a common response to the pressure overload conditions of aortic stenosis. The precise nature of this relationship, however has yet to be elucidated. **Methods:** We identified 285 patients referred for routine transthoracic echocardiography in the past 9 months who were found to have aortic stenosis with an aortic valve area <1.0 cm^2 and normal regional wall motion. Patients were excluded if they had LV cavity dilatation suggestive of eccentric hypertrophy (n=99) or inadequate echocardiography to perform the analysis(n=10). We assessed septal wall thickness(IVS), posterior wall thickness (PWT), chamber dimensions, ejection fraction, aortic gradients, aortic valve area, and calculated left ventricular mass. Correlation coefficients were calculated to examine the relationship between wall thicknesses and peak pressure gradients(PKGR). **Results:** Of the 175 patients included in this analysis, 49% were men, and the mean age was 74 +/- 0.9 years. While significant correlation coefficients were demonstrated for the relationship between IVS and PKGR (R=0.27, p<0.0003), between PWT and PKGR (R=0.30, p<0.0001), and between LV mass and PKGR (R=0.26, P<0.0005), a large percentage of patients failed to demonstrate hypertrophy at significant pressure gradients (Fig 1). **Conclusion:** The hypertrophic response to pressure overload in aortic stenosis appears heterogeneous. Other factors which influence ventricular remodeling may play a role in this process.



1084-25 Effect of Candesartan Cilexetil on Left Ventricular Remodeling in Mitral Regurgitation: A Randomized Clinical Trial

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Background: The effect of tissue angiotensin blockade in Mitral Regurgitation (MR) due to intrinsic valve disease is disputed due to lack of randomized clinical trials. Of particular importance is the effect of these medications on left ventricular (LV) remodeling, ie., on LV end-diastolic and end-systolic volume index (EDVI, ESVI). Candesartan Cilexetil is an angiotensin receptor blocker with insurmountable receptor attachment allowing prolonged clinical efficacy.

Methods: In 32 patients (age 69±14 years, 36% female) with organic MR of at least moderate degree, in functional Class I or II, with normal renal function (creatinine 1.1±0.2 mg/dL), patients were randomized between placebo (n=17) or Candesartan Cilexetil 32 mg/daily (n=15) treatment for 1 year. After one year the end-points of EDVI and ESVI were measured.

Results: At baseline, there was no difference between placebo and Candesartan groups for age, sex, systolic (141±19 vs. 144±18 mmHg, P=0.69) and diastolic (74±10 vs. 77±14 mmHg, P=0.48) blood pressure, regurgitant volume measured by 2 methods (73±25 vs. 77±14 mL/beat, P=0.97), EDVI (103±21 vs. 104±19 mL/m2,) and ESVI (26±9 vs. 25±10