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1145-117 **Reduction in Regional Myocardial Function Is Associated With Concentric Left Ventricular Remodeling: Multi-Ethnic Study of Atherosclerosis**

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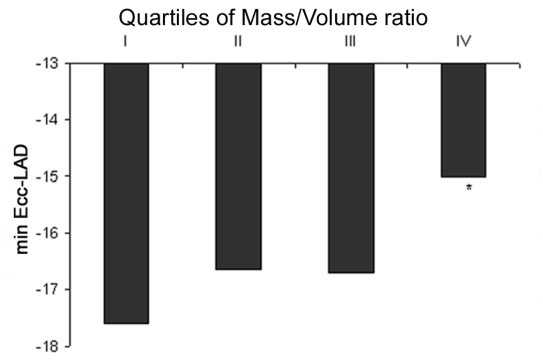
Background: Left ventricular hypertrophy is a risk factor for heart failure, but the transition from regional myocardial dysfunction, compensatory remodeling and global dysfunction has not been thoroughly clarified. Therefore, we investigated the association between LV remodeling and regional LV function expressed as peak systolic circumferential strain (Ecc) in participants of the Multi-Ethnic Study of Atherosclerosis (MESA).
Methods: Peak Ecc from 441 tagged MR studies was determined by Harmonic Phase (HARP) tool, and its relationship with the degree of concentric remodeling expressed by LV mass/ end diastolic volume (M/V) ratio was studied. Regions were defined by coronary territories.
Results: In both genders, reduced strain was seen in the highest quartile of M/V ratio when compared to lower quartiles (-13.2 vs -15.3, p<0.01). This decrease was regionally nonuniform and was more pronounced in the left anterior descending (LAD) region (figure, *p<0.01). However, it was statistically significant in all regions. Decrease from the first three quartiles to the fourth quartile in LAD, right (RCA)and left circumflex (LCX) regions was 15.3%, 12.3% 10.3%, respectively (p<0.05 for all regions).
Conclusion: Concentric remodeling is associated with reduced systolic regional function in asymptomatic individuals. Decrease in function is more prominent in the LAD territory but is also present in the RCA and LCX regions. It may reflect transition from compensatory remodeling to myocardial failure.



1145-118 **Torasemide Inhibits Transcardiac Extraction of Aldosterone in Patients With Congestive Heart Failure**

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Background. We reported that mineralocorticoid receptor antagonist spironolactone inhibits the transcardiac extraction of aldosterone (ALD) in patients with congestive heart failure (CHF). In the TORIC (TORasemide In patients with Congestive heart failure in NYHA class II and III) study, torasemide had more beneficial effect on mortality and morbidity of CHF patients than furosemide. However, the mechanism of the beneficial effect of torasemide remains unknown. Method. To evaluate whether the torasemide has an aldosterone (ALD) receptor antagonist, we studied 50 CHF patients who had been randomly administered furosemide (n=25) or torasemide (n=25). Patients who received spironolactone were excluded in this study. Results. There was no difference of patients characteristics and other treatments between the two groups. There was no difference of NYHA functinal class, left ventricular ejection fraction (35±9 vs. 33±10%), or plasma levels of ALD and brain natriuretic peptide (BNP) (372±91 vs. 315±74 pg/mL) in the aortic root (AO) between the two groups. In the furosemide group, plasma ALD was significantly lower in the coronary sinus (CS) than in the AO (96±11 vs. 75±12 pg/mL, p<0.001), suggesting that ALD is extracted through the heart. In contrast, there was no difference of plasma ALD between the AO and CS in the torasemide group (83±11 vs. 78±12 pg/mL, p=0.17) and the transcardiac gradient of ALD[ALD (AO-CS)] was significantly lower in the torasemide group than the furosemide group (4.6±3 vs. 16±4 pg/mL, p<0.05), suggesting that the extraction of ALD through the heart is inhibited by torasemide. In addition, plasma procollagen type III aminoterminal peptide, a biochemical marker of fibrosis, level in the CS is significantly lower in in the torasemide group than the furosemide group (0.5±0.03 vs. 0.65±0.08 U/mL, p<0.05). Conclusion. These findings suggest that torasemide has an ALD receptor antagonist in the failing heart in patients with CHF.

1145-119 **Tissue Inhibitor of Matrix Metalloproteinase-1 Is a Marker of Left Ventricular Diastolic Dysfunction in Diabetic Heart Disease**

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Background: The high prevalence of diastolic dysfunction in diabetes may be related to abnormal cardiac extracellular matrix composition, regulated by matrix metalloproteinases (MMP) and tissue inhibitors of metalloproteinases (TIMP). We hypothesised that plasma MMP-9, TIMP-1 & -2 are related to diastolic dysfunction in patients with diabetes.
Methods: We measured plasma MMP-9, TIMP-1 & -2 by ELISA in 56 patients with diabetes and 16 comparable controls. Early (E) and atrial (A) diastolic mitral inflow velocity was measured with pulse wave Doppler and early mitral annular velocity (E'), an index of diastolic relaxation, with tissue Doppler on transthoracic echocardiogram. The ratio of E to A (E/A) and E to E' (E/E', an index of left ventricular filling pressure) were derived from these measurements.
Results: Patients with diabetes had lower E', higher E/E' ratio and higher TIMP-1 levels (Table). There was no significant difference in E/A ratio, MMP-9 and TIMP-2 levels between patients and controls. E' (r = -0.31, p=0.02) but not the ratio of E/E' (p=0.061) correlated negatively with TIMP-1. There were no significant correlations between TIMP-1 with age, systolic or diastolic blood pressure and HbA1c. TIMP-1 remained a predictor of E' on multivariate regression analysis (p=0.002).
Conclusion: In diabetes, raised circulating levels of TIMP-1 is associated with abnormal diastolic function. This suggests that TIMP-1 may be involved in abnormal cardiac extracellular matrix turnover in diabetes.

Table: data as mean ± SD or median (IQR)

	Patients (n=56)	Controls (n=16)	P value
Age (years)	68 ± 6	65 ± 7	0.23
SBP (mmHg)	139 ± 17	128 ± 16	0.02
DBP (mmHg)	76 ± 9	78 ± 8	0.63
HbA1c (%)	7.6 ± 1.5	5.5 ± 0.2	<0.001
E' (cm/s)	0.07 ± 0.01	0.09 ± 0.02	0.007
E/A	0.87 ± 0.19	0.89 ± 0.15	0.21
E/E'	10.8 ± 1.2	9.3 ± 1.9	0.002
MMP-9 (ng/ml)	45 (32 – 50)	37 (31 – 42)	0.48
TIMP-1 (ng/ml)	450 (370 – 525)	380 (300 – 479)	0.037
TIMP-2 (ng/ml)	140 (140 – 185)	150 (130 – 178)	0.78

1145-120 **Left Ventricular Mass Reduction in Type 1 Diabetes Mellitus**

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Background: Improvement in glucose control of patients with type 1diabetes (DM1) has been demonstrated to blunt the progression of microvascular complications (retinopathy, nephropathy). A relationship between renal dysfunction, level of advanced glycated end products (AGE) and microvascular complications has recently been shown. Last year we reported that a fall in HbA1c was also associated with a reduction in left ventricular mass (LVM) and LV septal thickness (LVS). We now postulate that reduction of LVM and AGE is less likely to occur when renal dysfunction progresses.
Method: 17 DM1 patients (pts) with proteinuria were followed for 12 months on an intensive glycemia/hypertension control program with repeated ambulatory blood pressure monitoring, echocardiogram, serum creatinine, creatinine clearance and AGE.
Results: Of the 17, ten pts decreased LV mass (LVM) >= 20 g (mean = 46 ± 7 g), during the study, 7 did not (mean increase = 20 ± 12 g, p = 0.0002). These two LVM groups differed with respect to change in AGE (p = 0.01), but not HbA1c. MAP (94, 107 baseline, p = 0.0045; 98, 103 12 months, p = ns; delta 4.45, -3.79, p = 0.0186) was similar in all groups at the end of the study. Eight pts decreased septal (LVS) thickness >= 1mm during the study, 9 did not (-1.75 ± 0.25 vs. 0.56 ± 0.18, p = 0.0001). These two LVS groups differed with respect to change in HbA1c (p < 0.05), but not in AGE or MAP.
The 10 pts with a decrease in LVM maintained creatinine clearance (Ccreat) at 63 ml/min. The 7 pts without a decrease in LVM changed Ccreat from 54 to 40 (p < 0.02). The 8 pts with decreased LVS changed Ccreat from 65 to 57 ml/min. The 9 pts without a decrease in LVS changed Ccreat from 54 to 50 ml/min (p = ns)
Conclusion: Decreases in LVM and LVS as a result of glycemic and blood pressure control appear to be related to preservation of renal function in DM1. In a total group of patients that diminished LVM with glycemic and blood pressure control, we noted that LVM decreased preferentially in pts with stable renal function.

1145-121 **Prognostic Value of Plasma Erythropoietin on Mortality in Patients With Chronic Heart Failure**

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Background
Anemia is common and is associated with mortality in chronic heart failure (CHF). Erythropoietin (EPO) is a hematopoietic growth factor, upregulated in anemic conditions. Its prognostic value in CHF patients is unknown.
Methods and results
In 74 patients with CHF (age 60±7 years, Left Ventricular Ejection Fraction (LVEF) 0.32±0.01, peak oxygen consumption (VO_2) 19.1±0.6, (mean±SEM) and in 15 control patients, plasma concentrations of EPO were prospectively assessed. During a mean follow-up of 2.6 years, 22 patients (30%) died. Anemia (hemoglobin levels <12 g/dl) was present in 12.9% of the patients. We observed only a mild inverse correlation between the logarithm of EPO log(EPO) and hemoglobin levels (r^2=0.08, p = 0.02), which was much more pronounced in the control group r^2=0.44, p=0.007). There was a significant association between log(EPO) and BNP levels (r^2=0.27, p < 0.001). Multivariate analysis showed that plasma EPO (p=0.02), hemoglobin levels (p=0.002) and age (p=0.02) were independent predictors of survival in this CHF population.
Conclusion