P2257 Extracellular matrix gene expression in left ventricular hypertrophy: controlled induction and remodelling after surgical therapy

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Introduction: Aim of this study was to assess extracellular matrix (ECM) gene expression (matrix metalloproteinases (MMP) and their tissue inhibitors (TIMP)) after controlled induction of left ventricular hypertrophy (LVH) and after ventricular remodeling due to surgical therapy.

Methods: Supracoronary banding of the ascending aorta was performed in 44 growing sheep (age 6-8 month, 2/3 of final bodyweight) using a left lateral thoracotomy (T1). After 8.3 ±1 months EAS was revised by debanding and/or end to end anastomosis (T2). The animals were sacrificed (T3) after another 10.1 ±2 months. At T1, T2 and T3 left ventricular biopsies were taken and echocardiographic examinations performed. Subtractive hybridisation and competitive PCR were applied for molecular biological analyses.

Results: At T2 echocardiography revealed significantly increased LV-mass (217 ±55g, p<0,05 versus 91 ±27g at T1) and severe myocardial cellular hypertrophy was diagnosed at histopathological examinations. At T3 LV-mass had significantly decreased (114 ±34g, p<0.05 versus T2). In parallel at T2 gene expression (mRNA level) was significantly increased for MMP 1, 2, 3, 9 and for TIMP 1 and 2. At T3 a significant regression of gene expression was found for MMP 1, 2, 3, 9 and for TIMP 1 and 2 as well.

Conclusion: ECM gene expression is significantly increased after controlled induction of LVH and significantly decreased after surgical therapy and left ventricular remodeling. Thus in LVH and after left ventricular remodeling close correlation exists between echocardiographic results and altered extracellular matrix gene expression.

P2258 Acute effects of DDD pacing over diastolic function in the obstructive hypertrophic cardiomyopathy

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We evaluated the hemodynamic and angiographic patterns of diastolic function in hypertrophic obstructive cardiomyopathy (HOC) immediately before and during DDD pacing.

Methods: 40 patients (mean age 64 ± 11 years, 31 to 83), 13 male, in NYHA functional class III-IV despite medical therapy, were treated with sequential DDD pacing. The hemodynamic study basally and after pacing evaluated left ventricle (LV) outflow tract peak and mean gradients, LV and RV end-diastolic pressures, mean capillary wedge, pulmonary diastolic and right atrial pressures, as well as cardiac output. The angiographic study included the early filling at 30% of diastole, the mean filling at 50% and the final LV filling, as well as the presence of mitral regurgitation. Student's Test was used for statistical comparisons.

Results: (See Table) Diastolic funcion improved after DDD pacing without worsening cardiac output.

Results

	At rest	After DDD pacing	p
Peak gradient	92 ± 37	36 ± 26	<0.001
Mean gradient	50 ± 21	18 ± 16	<0.001
LV end-diastolic P	22 ± 6	14 ± 5	<0.001
Mean wedge P	19 ± 7	14 ± 5	<0.001
Pulmonary sistolic P	44 ± 17	38 ± 16	<0.01
Pulmonary diastolic P	20 ± 7	16 ± 6	<0.001
RV end-diastolic P	8 ± 4	7 ± 3	<0.01
Mean right atrium P	7 ± 3	6 ± 4	< 0.05
Cardiac output	3.8 ± 1.2	4.1 ± 1.1	<0.01
30% early filling	41 ± 12	52 ± 10	<0.001
50% early filling	64 ± 10	75 ± 9	<0.001
50% late filling	36 ± 10	24 ± 9	<0.01
Mitral regurgitation (I-IV)	1.6 ± 1.2	0.83 ± 1	<0.001

Conclusions: Sequential A-V pacing improves LV diastolic function and achieves a decrease in biventricular filling pressures. Cardiac output is not reduced during pacing. This hemodynamic and angiographic patterns and the associated decrease in LV outflow tract gradients and mitral regurgitation do suggest a beneficial effect in NYHA functional class.

P2259 Microparticles for distal embolization of septal branches in hypertrofic obstructive cardiomyopathy

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Induced septal necrosis with alcohol in patients with hypertrophic obstructive cardiomyopathy (HOC) has been proved to significantly reduce the dynamic obstruction and improve the clinical condition. The microparticles may also obliterate the distal capillary bed and can be safely administered.

Methods: Since January 1999, we have treated 10 severely symptomatic patients with HOC by septal embolization with microparticles. The mean age was 45 ± 18 years, 7 were male and 3 female. The mean left ventricular outflow tract gradient, estimated by echocardiography was 78 ± 31 mmHg, and the mean thickness of the interventricular septum was 25 ± 6 mm. Various degrees of angiographic mitral insufficiency were observed (mild in 6 patients, moderate in 3 and severe in 1). Following the identification of the target septal branches, a monorail delivery catheter was selectively advanced and placed at different positions of the septal tree. Slow hand administration through the catheter of a mixture of microparticles (350–750 μ) and contrast material was continuously monitored by fluoroscopy to avoid undesirable embolization. In 4 patients more than one septal branches were embolized. The left ventricular to aortic gradient was continuously monitored throughout the procedure.

Results: The hemodynamic mean left ventricular to aortic gradient, decreased significantly from 81 ± 20 mmHg to 15 ± 22 mmHg (p < 0.001) after treatment. In seven patients a significant reduction of mitral regurgitation was observed. The mean CK-elevation was 818 ± 756 IU/L. All patients were discharged within 3 days after treatment, free of symptoms and without complications. At follow-up study (8 ± 3 months) all patients remain asymptomatic and the mean echo-Doppler gradient was 28 ± 35 mmHg. Mild mitral regurgitation persist in 3 patients.

Conclusions: This preliminary experience shows that septal tree embolization with microparticles is a safe and controlled procedure that provides sustained hemodynamic and clinical relief.

CLINICAL ASPECTS OF DILATED CARDIOMYOPATHY

P2260 Prognostic value of myocardial blood flow impairment in patients with idiopathic dilated cardiomyopathy

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Background: Impairment of myocardial blood flow (MBF) and of MBF reserve, due to abnormal coronary microcirculation, has been reported in patients with idiopathic dilated cardiomyopathy (DCM). It is not known whether the extent of MBF impairment may be an independent predictor of mortality and disease progression in these patients. To test this hypothesis we conducted a follow-up study in a population of patients with idiopathic DCM, with or without overt heart failure, in which MBF and MBF reserve were assessed by positron emission tomography (PET) at enrollement.

Methods and Results: Sixty-seven patients (52 males, mean age 52 ± 12 years) with idiopathic DCM (left ventricular ejection fraction < 0.50, mean 0.34 ± 0.10), in NYHA class I to III, underwent clinical evaluation, Holter recording, 2D-echocardiography and a PET study to measure absolute MBF at rest and after i.v. dipyridamole (0.56 mg/Kg in 4 min). During a mean follow up of 45 ± 37 months, 8 patients died of cardiac causes (7 suddenly) and 16 patients showed a progression of the disease with new or more severe episodes of heart failure leading to hospitalization in 8 cases and to heart transplantation in 2 cases. The 24 patients showing cardiac events at follow-up had higher incidence of intra-ventricular conduction delay (p<0.05), higher resting heart rate (p<0.001), larger left ventricular end-diastolic dimension (p<0.05), lower left ventricular ejection fraction (p<0.05), lower dipyridamole MBF (p<0.05) and lower MBF reserve (p<0.05) than event-free survivors. Multivariate analysis revealed dipyridamole MBF (Chi-sqare 11.3, p < 0.001), heart rate (Chi-square 7.0, p < 0.01), NYHA class > I (Chi-sqare 5.7, p < 0.05), left ventricular end-diastolic dimension (Chi-square 4.8, p < 0.05) and resting MBF (Chi-square 5.5, p < 0.05) as independent and additional predictors of subsequent cardiac events. Dipyridamole MBF lower than 1.36 ml*min-1*g-1 (median value in the whole population) was associated with an increase in relative risk of mortality or progression of the disease of 3.5 times.

Conclusions: The present study demonstrates that severely depressed MBF response to pharmacological vasodilation is the most powerful independent predictor of poor prognosis in patients with idiopathic DCM with or without overt heart failure. These results also suggest a possible pathogenetic role of coronary microcirculatory abnormalities in causing disease progression in this population and indicate PET as a valuable tool in the risk stratification of DCM patients.