right heart catheterization.
Results: TNFa and IL-6 were detected in 8 and 6 patients in CS respectively with absence in PV. IL-6 and TNFaR1, 2 level in PV was significantly correlated with that of CS(r=0.92, 1.0, 1.0:p<0.001). The level of IL-6 and TNFaR1, 2 in CS have positive correlations with the severity of decompensation(r=0.47, 0.49, 0.52:p<0.001), along with trans-myocardial gradient of IL-6 (r=0.58: p=0.01).
Conclusion: The magnitude of a trans-myocardial gradient of cytokines depends on the severity of heart failure decompensation and therefore, increased plasma level of cytokines in heart failure might be the result of myocardial production.

Mean±SEM, *p<0.05 compared to peripheral vein.

(pg/ml)	Peripheral vein	Coronary sinus
TNFa	0.4±0.2	1.5±0.3*
TNFaR1	1717.2±216.3	1788.4±229.2*
TNFaR2	3226.6±411.1	3347.1±420.5*
IL-6	2.2±1.0	5.44±1.4*

1110-143 Limited Diastolic Response to Afterload in Mice

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Background: The passive diastolic pressure-volume relationship of the left ventricle (LV) is nonlinear. Therefore, use of preload reserve should move the end-diastolic (ED) working point to a less compliant portion of the filling curve. Whether this occurs in mice, where exceedingly high heart rates diminish time for diastolic filling, is unknown. Accordingly, we assessed diastolic properties in hearts of open chest mice in response to sustained afterload.
Methods: Mice (C57B, n = 6) were sedated, intubated, and via a sternotomy had a dual frequency pressure sensitive conductance catheter placed into the LV via the apex. A flow probe was placed around the thoracic aorta. Baseline LV pressure-volume relationships were recorded at steady state and during occlusion of the inferior vena cava. The hearts were exposed to sustained aortic occlusion for 7 minutes and recordings were repeated. LVED pressure and volume, Tau, and chamber compliance (dP/dV) were determined.
Results: As shown in the Table, afterload augmentation led to an increase in maximum pressure (Pmax) and LVEDV, but Tau, LVEDP and dP/dV did not change.
Conclusions: Although afterload stress caused an increase in LVEDV, there was no attendant rise in LVEDP, indicating that the ventricles are operating on the flat portion of the PV curve. At the high operating heart rates of mice, short diastolic filing periods preclude LV filling sufficient to raise LVEDP.

*** p < 0.05 Baseline vs. Afterload**

	HR (bpm)	Pmax (mm Hg)	LVEDV (ul)	LVEDP (mm Hg)	Tau (msec)	dP/dV (1/ul)
Baseline	522 +/- 26	91 +/- 6	28 +/- 8	5 +/- 1	11 +/- 2	.053 +/- .017
Afterload	470 +/- 36	119 +/- 2*	34 +/- 12*	4 +/- 2	16 +/- 7	.077 +/- .066

1110-144 Dynamic Expressions of eNOS, iNOS, and TNF-a in Canine Myocardium In Response to Pacing-Induced Dilated Cardiomyopathy

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Background: Nitric oxide (NO) and tumor necrosis factor α (TNF-α) have been implicated in the pathogenesis of dilated cardiomyopathy. Whether and to what extend the failing heart of large mammals expresses these cytokines in the absence of inflammation is unclear.
Methods: We investigated the expressions of the constitutive endothelial nitric oxide synthase (eNOS), the inducible NOS (iNOS), and TNF-α in adult dogs under control conditions (conscious but chronically instrumented), following pacing-induced heart failure, and recovery from left ventricular failure using immunohistochemical (IHC) staining technique and Western blotting analysis.
Results: In control myocardium, prominent eNOS staining was seen in endothelium of blood vessels of varying sizes within the myocardium, with weak but positive staining in the myocardium. No IHC signal was detected for either iNOS or TNF-α in the control hearts. Following pacing for *22 to 36 days* when hemodynamically significant heart failure developed (LVdP/dt, C: 2670±81, CHF: 1298±89; LVEDP, C: 14±1, CHF: 34±2; HR, C: 80±5, CHF: 121±6; n=6) there was a marked decrease in the eNOS staining while both iNOS and TNF-α were detectable in the myocardial cytoplasm (n=5), as compared to controls (n=3). In four additional dogs, a moderate increase in eNOS and a concomitant decrease in iNOS and TNF-α were observed one week after the pacing was stopped. Western blotting experiments confirmed the decrease in eNOS (140kd) and increase in TNF-α (51kd) protein levels in the myocardium of heart failure dogs. Further analysis using densitometry showed a 74% decrease in eNOS and 250% increase in TNF-α.
Conclusions: Our results suggest that loss of cardiac eNOS protection and emerging cytotoxic influence from increased myocardial TNF-α and iNOS expressions may be pathogenic in the development of dilated cardiomyopathy and congestive heart failure. The influence of these cytokines is reversible following cessation of pacing and correlates with hemodynamic recovery.

1110-145 Analysis of Gene Expression During Induction and Regression of Cardiac Hypertrophy Using cDNA Microarray Technology

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Background; Recent advances in the production of cDNA microarrays have made it possible to analyze gene expression of tens of thousands of genes simultaneously. We compared gene expression profiling in the rat models of cardiac hypertrophy-regression using cDNA microarrays in order to evaluate whether the altered gene expression during regression is a simple reversal of the hypertrophy induction program or the activation of a separate transcriptional program.
Methods; Pressure-overload left ventricular hypertrophy (LVH) was generated by transverse aortic constriction (TAC) and regression of LVH was induced by the elimination of pressure gradient (untying) at 2 weeks after TAC. ^{33}P-labeled cDNAs prepared from total RNA extracted from LV samples before and after TAC and at days 1, 3, and 7 after untying were hybridized to Rat GeneFilters Microarrays (GF300 and GF301, Research Genetics, USA).
Results; Of 10,330 genes initially screened, 83 known genes and 1,060 uncharacterized expressed sequence tags (ESTs) had a level of expression 2 times or more in response to pressure overloading. Among them, transcription level of 269, 50 and 8 genes was continuously increased at days 1, 3 and 7 after untying, respectively. Interestingly, gene expression of PLCδ-4 and 11 ESTs was abruptly declined after induction of regression and maintained up to 3 days after untying but expression of 6 genes including PLCδ-4 was normalized at day 7. In contrast, transcription level of 132 genes (16 known genes, 116 ESTs) was significantly declined after induction of pressure-overload LVH. One day after untying, expression of 40 ESTs were upregulated but 35 genes including 16 known genes showed depressed expression up to 7 days after untying.
Conclusion; This study identified both known and novel genes whose expression is affected at different stages of cardiac hypertrophy and regression and demonstrates the applicability of cDNA microarray technology for identification of novel candidate genes.

POSTER SESSION

1111 Heart Failure: Pacing/Implantable Cardiac Defibrillator

Monday, March 18, 2002, Noon-2:00 p.m.
Georgia World Congress Center, Hall G
Presentation Hour: Noon-1:00 p.m.

1111-137 Impact of Underlying Heart Disease on Success of Resynchronization in Severe Heart Failure

Barbara Lamp, Johannes Heintze, Bert Hansky, Leon Krater, Lothar Faber, Frank Warzok, Dieter Horstkotte, Reiner Koerfer, Juergen Vogt, *Heart Center North Rhine-Westphalia, Bad Oeynhausen, Germany.*

Severe heart failure in coronary artery disease (CAD) is mainly caused by large myocardial scars and left ventricular (LV) remodeling, in dilated cardiomyopathy (DCM) by progressive diffuse myocardial fibrosis. The origin of left bundle branch block (LBBB) in both entities is different: in DCM diffuse conduction delay with typical LBBB, in CAD central LBBB and often arborisation. Whether these pathophysiological differences result in a different outcome in resynchronisation therapy (RT) is not known.
We analysed the 161 consecutive pts. (mean age 61 years (y), (93 DCM, 56 CAD, 12 other) who received RT with respect to the underlying heart disease. Mean follow-up (FU) was 9.9 months (m) (1-38). We found significant differences (p<0.05, unpaired t-test) between in LVEDD (83.7±11 versus 77.7±10 mm) and VO2AT (11.3±2.5 versus 10.1±2.4 ml/kg/min. NYHA class, VO2 peak, 6 min walk, quality of life (Minnesota), EF and QRS did not differ. During FU at 3, 6 and 12 m DCM pts. had an ongoing improvement of all measured parameters. In contrast the CAD pts. improved only during the first 3 m and then stayed stable. (Fig. 1).
These data of a large patient cohort show for the first time, that pts. with CAD seem to respond less to RT than pts. with DCM during mid term FU. This is probably due to a more advanced scaring of the myocardium in CAD and a different pattern of asynchroy. Special indicators of RT-response for CAD pts. have not been identified yet, but will be very important.