Reduction of the LVOT gradient post PTSMA was determined by echocardiographic.
Results: All patients demonstrated regional myocardial hyperenhancement of the interventricular septum, exclusively located on the right ventricular side of the septum in 7. In patients with exclusively right sided hyperenhancement, the LVOT gradient reduction was 30± 28 mmHg versus 78± 22 mmHg in the remaining patients (p<0.001). Myocardial injury size in the right sided group was significantly lower (10± 4 g vs. 23± 8 g, p<0.001). In these patients the volume of ethanolinjected was lower (2.6± 1.2 ml versus 3.6± 1.8 ml, p = 0.19) and the ethanol was infused distal of a bi- or trifurcation in 4 out of 7 patients. In the remaining patients ethanol was injected proximally in the septal branch.
Conclusion: In patients with HOCM, size and location of myocardial injury induced by PTSMA can be determined using contrast-enhanced MRI. An exclusively right sided location of myocardial injury is associated with lesser reduction of the LVOT gradient.

1014-86 Progressive Left Ventricular Impairment in Hypertrophic Cardiomyopathy Patients Is Determined by Functional Location of Mutation

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Background: More than 70 mutations affecting β-myosin heavy chain (β-MHC coded by *MYH7*), the commonest cause of familial hypertrophic cardiomyopathy (FHC), are reported. Mutation-specific natural history contributes to patient management, but most mutations are uncharacterized. We sought to determine if the affected functional domain influences outcome, allowing domain-specific prognosis. Several *MYH7* mutations affect the converter (CD), which functions as a fulcrum for force leverage. Methods: Residues of the CD were predicted from β-MHC's 3-D structure. Echo and clinical data from unrelated FHC patients with a CD mutation (CD+) were compared with 98 unrelated patients without CD mutations (CD-), a subset of whom had other *MYH7* mutations. Results: There were 9 CD mutations in 22 patients. Compared to all CD- patients, CD+ patients were diagnosed with FHC at younger age (22±10 vs 35±18 years, p<0.001) and more frequently had a family history of HCM (15/22 vs 42/98, p<0.05). Magnitude of left ventricular (LV) hypertrophy and LV gradients were similar. CD+ patients had lower fractional shortening (FS; 36±14 vs 42±7, p<0.005) despite a lower mean age (34±14 vs 47±18 years, p<0.005). FS was <30% in 7/21 CD+ patients and only 4/83 CD- patients, p<0.001. CD+ patients with FS<30 were older than those with FS>30 (43±9 vs 30±14 years, p<0.05). *MYH7* mutations other than CD were found in 17/98 CD- patients; FHC was diagnosed at a younger age in CD+ patients (22±10 vs 31±17 years, p<0.05), left atrial (LA) size was smaller (45±10 mm vs 54±10; P=0.01) and FS lower (42±7 vs. 47±7, p=0.01) compared to patients with non-CD *MYH7* mutations. Conclusions: Despite similar magnitude of LV hypertrophy and LV obstruction, there are differences between FHC associated with CD mutations, non CD *MYH7* mutations and non-*MYH7* causes. (1) CD mutations result in higher penetrance and presentation at a younger age; (2) CD mutations are more likely to cause progressive LV systolic dysfunction; (3) LA distension associated with non CD *MYH7* mutations may reflect greater diastolic dysfunction. Identification of mutant functional domain will contribute to the management of FHC patients with *MYH7* mutations of undetermined natural history.

1014-87 Factors Associated With Increased Risk of Sudden Death in Young Patients With Hypertrophic Cardiomyopathy

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Background: Hypertrophic cardiomyopathy (HCM) in the young is associated with increased risk for sudden death (SD). We determined outcomes in a cohort of children attending a tertiary referral center, and prognostic significance of the presenting clinical findings. METHODS: Study comprised of 260 children aged <20 years (mean, 10±6 years) with HCM: 13 (5%) presented with cardiac arrest, 52 (20%) had syncope, 34 (13%) had presyncope, 91 (35%) had chest pain, 84 (32%) had dyspnea, and 80(31%) were asymptomatic. Studies included echocardiography, Holter, treadmill exercise test, exercise thallium scintigraphy, cardiac catheterization, and electrophysiology study (EPS). Results: 240 children, or 92%, had one or more risks for SD, Table. Therapy included implantable defibrillators (ICD) in 56, pacemakers in 97, cardiac surgery for obstructive HCM in 22, and cardiac transplantation in 6 (3 died post-operatively). Thirty-five adverse events: 20 deaths (13 SD); 8 cardiac arrests; and 7 ICD therapies. The 5-year survival rate was 92±2%,and the 5-year event-free rate was 87±2%. Conclusions: (1) Traditional risk factors are common in young patients who presented to a tertiary referral center, and therefore as a group, have a poor predictive value. (2) Despite this high prevalence of risk factors associated with increased risk for SD, therapy directed at relieving symptoms and correcting identified abnormalities was associated with a prognosis similar to that reported from non-tertiary centers.

Risk factors associated with poor prognosis

Parameter	Prevalence
Cardiac arrest or syncope	65/260(25%)
LV outflow obstruction (cardiac cath)	110/210 (52%)
LV wall thickness ³20 mm	132/260(51%)
Non-sustained ventricular tachycardia VT during 24-48 hr Holter	43/234 (18%)
Myocardial ischemia by exercise thallium	135/175(77%)
Abnormal BP response to exercise	74/224 (33%)
Family History of sudden death	72/230 (31%)
Genetic mutation associated with poor prognosis	20/48 (42%)
Sustained ventricular tachycardia induced at EPS	37/139 (27%)

1014-88 Progression of Hypertrophic Cardiomyopathy to Dilated Cardiomyopathy: Three New Mutations in Genes Encoding Sarcomeric Proteins With Two Cases of Double Heterozygosity

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Background: About 10% of cases of hypertrophic cardiomyopathy (HCM) develop a dilated cardiomyopathy (DCM). The molecular mechanisms of this evolution are still unknown. The genes accounting for approximately 2/3 of all HCM cases are β-myosin heavy chain (MyH7), myosin-binding protein C (MyBPC) and cardiac troponin T (cTnT). In order to investigate if specific gene mutations are consistently associated with HCM progressing to DCM we have performed mutational analysis of these genes in 10 unrelated affected patients (pts).
Methods: We enrolled 10 unrelated pts with HCM who progressed to DCM, symptomatic and with left ventricular dilatation and impaired contractile function but no ouflow tract gradient. Mutational analysis was performed for the entire coding region and exon-intron boundaries of the MyH7, MyBPC and cTnT genes using direct sequencing.
Results: In these 3 genes a total of 5 missense mutations were found in 5 pts; 2 of these were previously described mutations and 3 were new mutations. The already known mutations were a MyH7 mutation (R453C) affecting the actin binding property and a variation in the cTnT gene (K236R). The first new MyH7 mutation (L517M) occurred in the head-rod junction of myosin, lying close to a reactive cysteine (Cys-695). The second MyH7 mutation (Q734E) occurred in the light chain-binding site following the reactive cysteines. A new MyBPC mutation (S236G) was found in the IG-like C2-type domain 1 of the protein and is likely to disrupt the phosphorylation site. The simultaneous presence of two missense mutations in two different genes was observed in two pts, one carrying the newly discovered MyH7 (L517M) and MyBPC mutations and one carrying the MyBPC and the cTnT mutations.
Conclusion: We identified 3 formerly unreported mutations and the simultaneous presence of mutations in two different genes in 2 pts. However we failed to identify a specific mutation in our pts with HCM who progressed to DCM. Thus the action of multiple gene mutations, the presence of modifier genes and post-transcriptional mechanisms appear to play a major role in the progression from HCM to DCM.

POSTER SESSION

1038 Heart Failure: Spectrum and Prognostic Factors

Sunday, March 30, 2003, Noon-2:00 p.m.
McCormick Place, Hall A
Presentation Hour: 1:00 p.m.-2:00 p.m.

1038-68 Left Ventricular Systolic Function and Survival in a Contemporary Cohort of Patients With Heart Failure

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Background: Although preserved left ventricular systolic function (LVSF) reportedly confers a better prognosis than impaired LVSF in patients with heart failure, it is unclear if this pattern exists in current practice. Our goal was to describe the independent relationship between LVSF and survival in a cohort of patients with heart failure.
Methods: We used data from the CMS-sponsored National Heart Failure (NHF) Project, a national sample of Medicare beneficiaries hospitalized with a principal diagnosis of heart failure in 1998 and 1999. We studied patients at least 65 years old who were discharged alive (n=31,991). Multivariable Cox proportional hazards regression with mean follow-up of one year was employed, adjusting for patient factors and differences in ACE-inhibitor prescription at discharge.
Results: Crude mortality rates and fully adjusted hazard ratios for mortality among ACE-treated and non-ACE-treated patients are presented below. In the multivariable model, there was a graded inverse relationship between LVSF and mortality. Although ACE-