ORAL CONTRIBUTIONS

807 Hypertrophic Cardiomyopathy: Basic and Clinical II

Monday, March 31, 2003, 9:15 a.m.-10:30 a.m.
McCormick Place, Room S402

9:15 a.m.

807-1 The Long-Term Outcome of Patients With Hypertrophic Cardiomyopathy and Coronary Artery Disease

Paul Sorajja, Steve R. Ommen, Rick A. Nishimura, Robert B. McCully, A. Jamil Tajik, Bernard J. Gersh, Mayo Clinic and Mayo Foundation, Rochester, MN

Background. Hypertrophic cardiomyopathy (HCM) and coronary artery disease (CAD) both confer an increased risk of sudden and other cardiac death. However, there is a paucity of data on the long-term outcomes of patients with HCM who have acquired CAD.
Methods and Results. We examined 475 patients with HCM who underwent coronary angiography at the Mayo Clinic. Patients who were aged <55 years, had a prior history of surgical revascularization, or had abnormal systolic function (left ventricular ejection fraction or EF<50%) were excluded, leaving a final study population of 299 patients (median age, 70 yrs; 131 men). CAD (i.e., luminal stenosis of 50% or more in left main artery or 70% or more in other epicardial branches) was present in 95 patients. Of the HCM patients with CAD, revascularization was undertaken with coronary artery bypass grafting in 21 and percutaneous coronary intervention in eight. There were no significant differences between HCM patients with CAD and those without CAD with respect to age, EF, functional class, or prior medical history. In the entire study population (n=299), there were 85 deaths during a mean follow-up of 5.8 yrs. Fifty-seven deaths were cardiac in origin, including 22 sudden cardiac deaths. In comparison to HCM patients without CAD, those with concomitant disease demonstrated markedly reduced survival. For HCM patients with CAD and those without CAD, ten-year survival free of all-cause mortality was 43.3% (95% CI, 30.4 to 56.1%) and 69.9% (61.8 to 78%), respectively (p=0.0003, log-rank). For the endpoint of cardiac death, this survival was 59.1% (45.6 to 72.5%) vs. 78.2% (70.7 to 85.8%) (p=0.005). For the endpoint of sudden death, this survival was 78.3% (66.4 to 90.3%) vs. 91.7% (86.2 to 97.1%) (p=0.01). The presence of CAD also was predictive of these events in multivariate models that additionally identified prior stroke and atrial fibrillation as co-variates with statistical significance (p<0.05).
Conclusions. Patients with HCM who have acquired CAD are at markedly increased risk of sudden death, other causes of cardiac death, and overall mortality.

9:30 a.m.

807-2 Prevalence, Spectrum, and Phenotype of Beta Myosin Heavy Chain Mutations in Patients With Hypertrophic Cardiomyopathy

Michele A. Jaeger, Sara L. Van Driest, Melissa L. Will, Bernard J. Gersh, Steve R. Ommen, Michael J. Ackerman, Mayo Clinic, Rochester, MN

Background: Beta myosin heavy chain (*MYH7*) mutations are reportedly pathogenic in 25-30% of cases of Hypertrophic Cardiomyopathy (HCM). Approximately 10 specific mutations have been designated as either "malignant" or "benign." However, the frequency, spectrum, and phenotype of *MYH7* mutations in a single large cohort are unknown. We analyzed such a cohort of HCM patients for mutations in *MYH7* and determined the genotype-phenotype correlations for this subset.
Methods: DNA from 395 unrelated HCM patients was obtained and analyzed. Mutational analysis of all 38 protein coding exons of *MYH7* was performed using polymerase chain reaction, denaturing high performance liquid chromatography, and DNA sequencing. Clinical data were archived independent of patient genotype.
Results: Overall, the mean age at diagnosis was 41.2 ± 19 years. Over half had left ventricular outflow tract obstruction. One-third had a family history of HCM and 14% had a family history of sudden cardiac death. In all, 54 patients (14%) were identified with *MYH7* mutations. Thirty-eight different mutations were identified including 24 (63%) previously unpublished, novel mutations. When compared to the remaining cohort of HCM patients without a *MYH7* mutation, patients with *MYH7* mutations were younger at diagnosis (33.1 ± 18 vs 41.3 ± 19 years, $p = 0.0004$), were more likely to have a first degree relative with HCM (40% vs 31%, $p = 0.009$), had greater left ventricular wall thickness (24.3 ± 8 vs 21.5 ± 6 mm, $p = 0.0007$), and received a myectomy more frequently (59% vs 41%, $p = 0.004$). However, there was no difference in frequency of sudden death (3.7% vs 2.9%, p = NS).
Conclusions: This study represents a comprehensive mutational analysis of the *MYH7* gene in a large cohort from a single tertiary referral center for HCM. The profound genetic heterogeneity is underscored as nearly two-thirds of the mutations discovered were novel. Here, *MYH7* mutations accounted for less than 15% of HCM. Interestingly, patients with *MYH7*-HCM had an earlier diagnosis, more family history of HCM, more hypertrophy, and more need for myectomy than patients with non-*MYH7*-HCM. However, these patients did not experience more sudden cardiac death.

9:45 a.m.

807-3 Prognosis of Patients With Hypertrophic Obstructive Cardiomyopathy After Transcoronary Ablation of Septal Hypertrophy

Thorsten Lawrenz, Frank Lieder, Frank Gietzen, Udo Goetsch, Horst Kuhn, Bielefeld Klinikum, Bielefeld, Germany

Background and Methods: Transcoronary Ablation of Septal Hypertrophy (TASH) constitutes a new catheter based therapeutic option for symptomatic patients with hypertrophic obstructive cardiomyopathy (HOCM). Regarding the prognosis after TASH only few data are available. Based on a validated quality of life questionnaire (QoL) and serial control examinations we analysed the clinical course of all patients treated in our institution up to December 2001.
Results: Since 1995 329 pts were treated by TASH in our institution (pressure/angiography guided technique, age 60.0 ± 13.1 years, male/female (155/174 pts), 98.8% follow up (325/329 pts), mean follow up time 2.1 ± 1.6 years, maximum 6.2 years, Kaplan-Meier calculations). The TASH related total in hospital mortality amounts to 1.8% (6/329pts). Sudden out of hospital death occurred in 4 pts and not sudden, not TASH related death in 19 pts (Table). An ethanol amount of more than 2.0 ml was an independent predictor of an increased risk for cardiac death (p = 0.047, Cox regression analysis), without a significant difference in the QoL-benefit rate (≤ 2.0 ml vs. > 2.0 ml ethanol). Advanced age (> 61 years) was another independent predictor of increased prognostic risk (p = 0.002).

Cause of Death in 329 pts After TASH (98.8% Follow up)	Death (pts)
HOCM-related	**10**
TASH-related in hospital death	6
Sudden cardiac death during follow up	4
HOCM-related death with respect to the amount of ethanol injected	**10**
Low ethanol subset (≤ 2.0 ml)	2
High ethanol subset (> 2.0 ml)	8
Not HOCM-, not TASH-related death (e.g. carcinoma)	**19**
Total in hospital mortality	**1.8%**
Total in hospital mortality (pts without severe comorbidity)	**0.3%**
Total annual mortality	**4.3% per year**
Annual cardiac mortality (pts with sudden death)	**1.5% per year**
Annual cardiac mortality after hospital discharge	**0.6% per year**

Conclusions: For the first time annual mortality rates after TASH are communicated. The prognosis compares favourable with the good prognosis after surgery for HOCM. It turned out to be significantly better in pts treated with small amounts of ethanol (without reduction of clinical benefit).

10:00 a.m.

807-4 Upper Limits and Clinical Significance of Left Atrium Dilatation in Trained Athletes

Antonio Pelliccia Fernando M. Di Paolo, Franco Culasso, Filippo M. Quattrini, Stefano Caselli, Barry J. Maron, Institute Sports Science, Rome, Italy, Minneapolis Heart Institute Foundation, Minneapolis, MN

Background. Left atrium (LA) dimension may be increased in trained athletes, raising the question of differential diagnosis between athlete's heart and structural cardiac disease.
Methods. We prospectively examined LA transverse dimension by echocardiography, and determinants of LA size were assessed in 1,823 competitive athletes (1,298 men), aged 10-56 years (mean 24), participating in 38 different sports, with multivariate analysis.
Results. LA dimension showed a wide range, 23-50 mm (mean 36.8±4.2) in men, and 20-46 mm (mean 32.0±4.0) in women, and was enlarged (based on arbitrary clinical cut-point of ≥40 mm) in 362 (20%) subjects (343 male, 19 female), including 38 (2%) with markedly dilated LA (≥45 mm). Of these 362, only 9 (2%) showed structural cardiac diseases potentially responsible for LA enlargement, including mitral or aortic valve disease with regurgitation in 5, hypertrophic and dilated cardiomyopathy, ischemic heart disease and atrial septal defect in 1, respectively. Of the remaining 353 athletes with enlarged LA, 305 (86%) showed increased left ventricular (LV) cavity dimension (≥ 55 mm) and/or wall thickness (≥ 13 mm), with normal systolic function and transmitral diastolic filling pattern, compatible with physiologic LV hypertrophy. Stepwise regression analysis showed that most of the variability in LA size was explained by LV cavity dimension, wall thickness, age and BSA (multiple $R^2 = 0.59$). Furthermore, sports such as cycling, rowing rugby and ice hockey showed the greatest effect on LA enlargement. Each athlete remained free of symptoms and without ventricular dysfunction, over 4±2 years.
Conclusions. In a population of trained athletes, LA shows a broad range of dimension and is increased (i.e. ≥40 mm) in 20% of subjects, including 2% with marked dilated LA (≥45 mm) compatible with primary cardiac disease. In the presence of normal LV systolic function and filling and in the absence of symptoms or clinical events, left atrial dilatation likely represents an extreme physiologic adaptation to intensive athletic conditioning and, therefore, another component of the "athlete's heart".