2:30

SIGNAL-AVERAGED ELECTROCARDIOGRAPHY IMPROVES PATIENT CHARACTERIZATION IN HYPERTROPHIC CARDIOMYOPATHY AND AIDS LOCALIZATION OF A DISEASE GENE TO CHROMOSOME 2p IN A LINKAGE ANALYSIS STUDY

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We have previously reported that subjects who are obligate carriers of the gene for hypertrophic cardiomyopathy (HC) by virtue of their position in the pedigree, may have an abnormal signal-averaged ECG (SAE) but normal echocardiogram. To determine whether detection of late potentials (LPs) by SAE improves identification of patients with HC and thus assists localization of HC gene by linkage analysis studies, we performed SAE in 28 members of an HC family in whom multilocus linkage analysis had localized a disease gene to chromosome 2p (lod score 3.09 at θ=0). SAE was performed using a Corazonix Predictor with a 25 Hz bidirectional filter. LPs were present if the filtered QRS duration was $\geq$110 ms, Root-Mean-Square voltage was $\leq$25 μV, or Low Amplitude Signals (<40 μV) were $\geq$35 ms.

Eleven (39%) individuals were found to have late potentials. Nine of these 11 had normal 2-D echocardiograms. When these 11 individuals were scored as affected, a significant increase occurred in the odds in favor of linkage (from 1000:1 to 10,000:1; lod score 4.0 at θ=0), thus strengthening the evidence that the disease gene localizes to chromosome 2p in this family.

We conclude that this result lends credence to the ability of SAE to detect affected individuals without LV hypertrophy. Localization of an HC gene to chromosome 2p suggests several candidates for the critical gene, the most likely of which is β fodrin.

3:00

HETEROGENEOUS MYOCARDIAL FLUORODEOXYGLUCOSE UPTAKE IS ASSOCIATED WITH NONUNIFORM LEFT VENTRICULAR FUNCTION IN PATIENTS WITH HYPERTROPHIC CARDIOMYOPATHY

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Heterogeneity in regional hypertrophy and systolic function is frequently observed in pts with hypertrophic cardiomyopathy (HCM). Previous studies have also shown heterogeneous glucose utilization. To examine the relation between metabolic and functional heterogeneity, we studied 10 symptomatic HCM pts with gated magnetic resonance imaging (MRI) and PET with ^{18}F-deoxyglucose (FDG) and $H_2{}^{15}O$. Pts were divided into Group A (n=5) with and Group B (n=5) without homogeneous systolic regional wall thickening by MRI between the septum and lateral free wall. The 2 groups did not differ with respect to age, gender, severity of hypertrophy, or regional blood flow, which was quantitated from the $H_2{}^{15}O$ data. From matched MRI and PET transaxial tomograms, 176 myocardial regions were assessed in the septum and free wall. FDG activity (nCi/cc) was corrected for partial volume effects and normalized to blood flow. Regional systolic wall thickening and end-diastolic wall thickness were assessed by MRI (*p<0.01 compared to free wall):

	Group A		Group B	
	Free wall	Septum	Free wall	Septum
Thickening (mm)	3.2±4.1	2.6±3.1	6.9±3.7	2.2±4.7
Thickness (mm)	15±5	21±9*	16±5	24±8*
Flow (ml/g/m)	0.9±0.2	0.9±0.2	1.1±0.4	1.0±0.3
FDG/flow	125±38	114±30	164±29	95±26*

Thus, heterogeneity in glucose uptake in HCM is related not to severity of LV hypertrophy but to nonuniform LV regional systolic function.

2:45

MORPHOLOGIC DETERMINANTS OF THE MECHANISMS OF SUBAORTIC OBSTRUCTION IN HYPERTROPHIC CARDIOMYOPATHY

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To define the anatomic basis for a variety of mechanisms by which obstruction to left ventricular outflow occurs in pts with hypertrophic cardiomyopathy (HCM), we analyzed 61 mitral valve specimens removed at operation/necropsy and compared the findings to that of echocardiograms obtained in the same pts. Pts were divided into 2 groups according to the patterns of systolic anterior motion of mitral valve (SAM) on echo: 1) "Typical" SAM (32 pts) with acute anterior leaflet bending and localized septal contact of leaflet tip only; 2) "Atypical" SAM (29 pts) with mitral-septal contact, but without leaflet bending. Typical SAM valves were larger in area (13.7±3.8 vs 10.0±2.1 cm^2; p<0.001) and had longer leaflets (2.2±0.5 vs 1.8±0.3 cm; p<0.001). In contrast, pts with atypical SAM showed small mitral valves and a variety of mechanisms of outflow obstruction. These included SAM-septal contact due largely to posterior septal motion and associated with particularly small outflow tract and annular calcium, occurring predominantly in elderly women, and also papillary muscle-septal contact due to anomalous insertion of papillary muscle onto mitral valve. Conclusions, in HCM: 1) the precise mechanism of obstruction is the product of particular mitral valve structure; 2) typical dynamic SAM is associated with larger mitral valves; and 3) atypical obstruction occurs with normal-sized mitral valve and is due to a variety of alternative mechanisms.

3:15

DIPYRIDAMOLE-INDUCED ST SEGMENT DEPRESSION IN HYPERTROPHIC CARDIOMYOPATHY IS ASSOCIATED WITH A REDUCED CORONARY FLOW RESPONSE

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Stress testing frequently induces ischemic-like ST segment changes in pts with hypertrophic cardiomyopathy (HCM). To assess the pathophysiological meaning of these electrocardiographic (ECG) changes, we performed a high dose dipyridamole (DIP) test (2D echo and 12 lead ECG monitoring during DIP infusion up to 0.84 mg/kg over 10') in 20 pts with HCM. In addition, regional myocardial blood flow was measured by means of ^{13}N-Ammonia and dynamic PET in all pts at baseline (BAS) and after i.v. DIP (0.56 mg over 4'). Following high dose DIP test, 7/20 pts (group A) had ST segment depression >0.2 mVolt from BAS while 13/20 (group B) had not. However, echocardiographic monitoring during DIP test did not show regional or global dysfunction in any patient. The end-diastolic thickness of the septum (19±1.6, mean ± SE, vs 20±0.9 mm, p=ns), that of the posterior free wall (10±0.6 vs 10±0.2 mm, p=ns) and left ventricular end-diastolic diameter (45±2 vs 46±1.6 mm, p=ns) were comparable in the two groups. Coronary flow increment [(DIP-BAS/BAS)x100] was lower in group A than in B both in the septum (11±11% vs 75±15%, p<0.01) and in the left ventricular free wall (36±15% vs 100±21%, p=0.05). Coronary angiography performed in group A pts showed normal coronary arteries in all of them. In conclusion: 1) the ST segment depression elicited by DIP in HCM pts is associated with a depressed coronary flow reserve even in the absence of angiographically detectable coronary artery disease; 2) flow reserve seems to be reduced also in nonhypertrophied myocardium, suggesting a primary vascular abnormality.