

Identifying carriers of a mutation causing hypertrophic cardiomyopathy in childhood – M-mode echocardiography still the best simple technique

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BACKGROUND First-degree relatives of patients with hypertrophic cardiomyopathy (HCM) have a 50% risk of having inherited the same mutation and, as DNA analysis is expensive, simple screening measures that could estimate risk of mutation carriage at young age would aid determining clinical follow-up.

PATIENTS AND METHODS 60 individuals, mean age 8.4 years (SD=6.0) from families with familial HCM with a known mutation and a confirmed DNA status were recruited. 30 mutation-positive (MP) and 30 mutation-negative (MN) children matched for gender and age, were compared in regards to ECG-features and echocardiographic measures, including tissue Doppler and 3D-left ventricular (LV) volume.

RESULTS ECG-findings: pathological Q-waves were present in 20% of MP, and 11% of MN individuals ($p=n.s.$), and there were no significant differences in 12-lead amplitude sums or 12-lead amplitude-times-duration products either. Echocardiography: There were no significant differences in diastolic function (E:A ratio, IVRT, E:e ratio, e:a ratio) or left atrial size, or in systolic function (fractional shortening). The LV cavity was however significantly smaller in MP than in MN (LV end-diastolic diameter Z-score $p=0.014$; LV end-diastolic 3-D volume/m²BSA $p=0.028$). M-mode septal thickness was significantly greater in MP than in MN group (Septum Z-score $p=0.0005$; septum-to-cavity ratio (sepcavr) $p=0.00005$; septum-to-posterior LV wall ratio (sepLVR) $p=0.0025$) with some overlap between the groups in all measures. Screening performance was best in the last two measures. Sepcavr >95th centile for age (defined in Östman-Smith, Devlin, Eur J Echocardiography 2001;2:22) gave a sensitivity of 50%, specificity of 93%, positive predictive value of 88% and negative predictive value of 66%, with corresponding figures for sepLVR >1.5 below three years of age, and >1.25 above three years of age being 43%, 83%, 72% and 60%.

CONCLUSIONS Long-axis M-mode is the best simple technique to predict mutation carriers. A sepcavr >0.27 at birth, >0.24 by one year of age, >0.22 after two years of age, and >0.23 after eleven years of age has a high specificity of 93% for identification of mutation carriers, but sensitivity is only 50% since many children do not develop a pathological phenotype during childhood. The smaller LV cavities make sepcavr more sensitive than septum Z-scores.