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Hypertrophic cardiomyopathy in childhood show difference in degree of hypercontractility between MYH7 mutations and MYBPC3 mutations

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BACKGROUND MYH7- and MYBPC3-mutations are the most common causes of HCM in Northern Europe. HCM due to MYH7-mutations has been reported to have earlier penetrance of overt disease than MYBPC3-mutations. It thus seemed interesting to study if there were any systematic differences in cardiac function measures on cardiac ultrasound that might be utilized for early detection of mutation carriers.

METHODS Among consecutive patients attending the Queen Silvia Childrens Hospital in Gothenburg with HCM caused by pathogenic mutations, and with clearly pathological hypertrophy <19 yrs of age, we identified 11 patients with MYH7-mutations, and 13 with MYBPC3-mutations. Patients with compound heterozygosity were excluded.

RESULTS Median age at presentation with pathological hypertrophy within this pediatric cohort were 11.0yr for MYH7 and 13.6yr for MYBPC3 (p=0.49). There were no significant differences in degree of septal or posterior wall hypertrophy with median Detroit Z-score for septal thickness 2.68 for MYH7 and 2.60 for MBPC3 (p=0.23), and for posterior wall 1.87 versus 1.80. Circumferential contractility as measured by fractional shortening was notably higher in MYH7, median 53% [IQR 44-60%] versus 42% [40-46%] in MYBPC3, p=0.008. Related to that systolic wall-to-cavity ratio was also higher in MYH7: median 1.00 [0.72-1.34] versus 0.63 [0.58-0.85], p=0.010. There were no significant differences in left atrial-to aortic ratio, median 1.39 and 1.34 respectively, but nevertheless there were clear differences in diastolic function with trans-mitral E:A ratio 1.28 [1.11-1.52] in MYH7 versus 1.80 [1.63-2.21; p=0.005] in MYBPC3. Tissue-Doppler also differed with E:e ratio 12.8 [10.6-14.3] and 8.2 [7.25-10.40; p=0.006], and e:a ratio 1.30 [0.80-1.86] and 2.10 [1.70-2.40; p=0.034] respectively. Pulmonary venous SD-ratio tended to be higher in MYH7: 1.3 [0.9-1.9] versus 0.8 [0.7-1,2; p=0.051]. There was also a trend for a lower LV end-diastolic volume measured with 3-D ultrasound, but with some missing values it did not reach significance: 28.3ml/m2 BSA [24.2-39.9ml] for MYH7 versus 44.3 ml/m2 BSA [28.9-45.8, p=0.07] in MYBPC3.

CONCLUSIONS It may be possible to diagnose mutation carriers with MYH7-mutations early in situations where genetic testing cannot be offered or is declined by looking for high fractional shortening, unusually small cavity and for age-inappropriate values in diastolic function.