

Myocardial deformation imaging identifies early phenotypic changes in children with HCM-causing sarcomere protein gene mutations

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Background: Hypertrophic cardiomyopathy (HCM) is caused by mutations in the cardiac sarcomere protein genes inherited as an autosomal dominant trait with age-related penetrance. We sought to analyse myocardial mechanics in mutation-positive children without overt left ventricular hypertrophy, using 2D speckle tracking echocardiography.

Methods: Offline 2D speckle tracking analysis was performed in 18 paediatric sarcomeric gene mutation-carriers (G) and compared with 30 phenotypically affected children with sarcomeric mutations (HCM) and 24 healthy controls (C).

Results: Global longitudinal strain (GLS%) was lower in hypertrophic cardiomyopathy (-15.8%) than controls (-24.8%) and mutation-carriers (-22.5%) ($p < 0.0005$ and 0.002 , respectively). In addition, significant ($p < 0.0005$) segmental changes were observed for HCM in peak longitudinal strain, predominantly at basal septum BS (HCM = -5.9%; C = -20.2%; G = -17.4%), mid septum MS (HCM = 7.9%; C = 22.1%; G = -20.8%), mid inferior segment MI (HCM = -9.7%; C = -22.6%; G = -21.2%), basal anterior septum BAS (HCM = -4.8%; C = -18.4%; G = -22.5%).

Strain rate was significantly ($p < 0.0005$) reduced at BS (HCM = -0.5/s; C = -1.5/s), BAS (HCM = -0.4/s; C = -1.3/s; G = -1.1/s), mid anterior septum (HCM = -0.9/s; C = -1.7/s), MI (HCM = -0.7/s; C = -1.6/s), MS (HCM = -0.6/s; C = -1.5/s; G = -1.2/s), apical inferior segment (HCM = -1.5/s; C = -2.1/s).

Post-systolic shortening was significantly ($p < 0.0005$) increased at BS (HCM = 8.4%; IQR 1.6-24.5; vs C = 0% IQR 0-1.2%), BAS (HCM = 6.9% IQR 0.2-36.9 vs C = 0% IQR 0-0), and MS (HCM = 4.7% IQR 0.4-22.8 vs C = 0% IQR 0-0). Moreover, mutation-carriers had slower strain rate than controls at BS (C = -1.5/s vs G = -1.1/s, $p = 0.015$) and MI (C = -1.6 vs G = -1.1/s, $p = 0.036$).

Mechanical dispersion was prolonged in hypertrophic cardiomyopathy (HCM = 67.7 IQR 54.1-101 ms vs C = 27.8 IQR 22.7-33.2ms and G = 31.6 IQR 27.3-47.2ms, $p < 0.0005$). Regression showed a 7.87ms increase in mutation-carriers as compared to controls, after adjusting for maximal wall thickness, LVOT gradient and history of VT.

Conclusions: Global and segmental systolic strain is significantly impaired in children with sarcomeric hypertrophic cardiomyopathy. Importantly, phenotype-negative mutation carriers have reduced global and regional strain parameters as well as mechanical dispersion as compared to controls, suggesting that impairment in myocardial mechanics could be an early phenotypic expression of sarcomeric disease.