

ORAL PRESENTATION

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Preclinical alterations in cardiac energetics amongst sarcomere mutation carriers in hypertrophic cardiomyopathy

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Background

Hypertrophic cardiomyopathy (HCM) is characterised by reduced myocardial tissue oxygenation (assessed using blood oxygen level dependent (BOLD) CMR imaging) during stress, as well as reduced myocardial perfusion reserve (MPRI) due to coronary microvascular dysfunction. In HCM gene carriers without the HCM phenotype, it has been suggested that only oxygenation is impaired. [1] It remains unclear whether this relates to early cardiac remodelling/ diastolic dysfunction, or whether oxygen consumption is intrinsically altered with sarcomere mutations. We sought to assess the BOLD signal change during vasodilator stress in a homogenous group of MYPBC3 positive HCM patients (some with clinical HCM, and some with no phenotypic features of HCM), and normal controls.

Methods

A total of 21 subjects with MYPBC3 mutations (11 with (G+P+) and 10 without (G+P-) phenotypic evidence of HCM on MRI or echocardiogram), and 6 normal controls underwent CMR scanning at 3.0 T. Myocardial function, as well as oxygenation (BOLD signal intensity change) during rest and adenosine stress was performed.

All HCM (both G+ P+ and G+P-) patients had transthoracic echocardiography performed, including evaluation of diastolic function using pulsed-wave and tissue Doppler.

Results

Mean age (yrs) was similar across the groups (40 for G+P+, 39.5 for G+P- and 45 for normal controls). Maximal septal

thickness was 21mm in the G+P+ group, vs 9.2 for the G+P- group. As expected, the G+P+ group had a blunted oxygenation response during stress (BOLD SI change $-4.8 \pm 10.3\%$ vs controls 11.1 ± 8.1 , $p = 0.003$). The G+P- group also showed reduced oxygen response during stress (BOLD SI change $2.5 \pm 4.8\%$ vs controls, $p = 0.009$). 8 of the 11 (73%) G+P+ HCM patients had diastolic dysfunction, vs none of the G+P- group. Mean E/E' was 13.3 ± 2.8 for the G+P+ group vs 8 ± 1.9 for the G+P- group, $p = <.00001$.

Conclusions

HCM gene carriers without hypertrophy show reduced myocardial oxygenation during vasodilator stress compared to normal controls. Our findings support the hypothesis that alterations in cardiac energetics may be due to the presence of sarcomere mutations rather than cardiac remodelling or diastolic dysfunction which occur at a later stage.

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