Mechanisms of adaptation to high intensity exercise in hypertrophic cardiomyopathy


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Background: Many individuals with hypertrophic cardiomyopathy (HCM) demonstrate exercise limitation. For a proportion this may be related to their overall cardiorespiratory fitness influenced by physical activity habits, body mechanics, or habitus. In others there is evidence of central and/or peripheral pathophysiology. However, some individuals with HCM demonstrate favourable adaptation to exercise. In the SAFE-HCM study, participants who underwent 12 weeks of high intensity exercise showed significant improvement in exercise indices including peak VO2, VO2/kg at anaerobic threshold (AT), time to AT, and overall exercise time compared to a usual care group.

Purpose: There have been no studies investigating the mechanistic adaptation(s) to exercise in HCM. This sub-study aimed to identify whether the observed improvements in exercise indices were attributable to central or peripheral adaptation.

Methods: Eighty patients with HCM (45.7 ± 8.6 years) underwent baseline clinical, quality of life and psychological assessment. Individuals were randomised to a 12-week high intensity exercise programme (n=40) or usual care (n=40). Baseline evaluation was repeated at 12 weeks. The Fick equation (oxygen uptake (VO2) = cardiac output (CO) X (arterial-venous oxygen content (a-vO2 difference))) was used to assess whether central and/or peripheral adaptation was responsible for observed improvements. 2D speckle tracking imaging was utilised to calculate left ventricular longitudinal strain from the apical 2-, 3- and 4 chamber views (EchoPAC, V202, GE Healthcare).

Results: 12-weeks of high intensity exercise training produced a statistically significant increase in CO (1.1 ± 0.4 L/min, CI (0.2,2.0), p=0.016) compared with the usual care group. There was no difference in the change in a-vO2 difference between groups (p=0.682) suggesting central adaptation to high intensity exercise. This was driven by an increase in stroke volume (SV) (6.1 ± 3.0ml, CI (0.1,12.2), p=0.047) rather than an increase in heart rate (0.6 ± 3.6 bpm, CI (-6.6,7.7), p=0.874). However, there was no change in resting myocardial deformation to account for the observed improvement in CO. Analysis of strain data demonstrated no difference in resting regional 4Ch (-0.7 ± 0.9, CI (-1.9, 0.5), p=0.270) 3Ch (-1.1 ± 0.9, CI (-2.8, 0.6), p=0.201), 2Ch (-1.3 ± 0.9, CI (-3.1, 0.5), p=0.162) or average global longitudinal strain (0.9 ± 0.6, CI (-2.2,0.3), p=0.144) between groups at 12 weeks.

Conclusion: Favourable central adaptations, predominantly driven by an increase in SV, enable improvements in exercise capacity following a high intensity exercise programme. Further studies are required to understand the physiological processes underlying this adaptation including assessment of myocardial deformation at peak exercise.