Exploring Development and Validation of an Accessible and Clinically Applicable Testing Method for Hypertrophic Cardiomyopathy

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Hypertrophic cardiomyopathy (HCM) is the most common heritable form of cardiovascular disease, affecting 1 in 500 individuals (Marion, 2002). Although typical age of onset is during the second and third decade of life, HCM has a wide range of clinical variability. Some individuals remain completely asymptomatic while others present throughout life with features ranging from palpitations to sudden cardiac death. Receiving a genetic diagnosis of HCM can provide information for at risk family members and alter medical management and surveillance. Currently, genetic testing is available through several clinical and research laboratories. Unfortunately, due to labor intensity of diagnostic methods, current testing is costly and has long turnaround times. In addition, the results from this testing requires the in depth analysis by a cardiology or genetics specialist which adds additional cost and time. A new testing platform designed to target only the most common pathogenic mutations eliminates many of these barriers to testing. The top 90 mutations were included on this test design. The mutations included in the panel were chosen by frequency and pathogenicity from a database of over 2,000 probands. The detection rate of the top mutation panel maintains half of the detection rate from current testing methods while the cost of testing is reduced to 15% of the current testing price. As the mutations on the panel meet the Laboratory for Molecular Medicine's criteria for pathogenic or likely pathogenic (http://pcpgm.partners.org/sites/default/files/LMM/Resources/Variant_Rules.pdf), the need for extensive interpretations of results is eliminated. This testing platform is validated to show analytical sensitivity of at least 98% and specificity of 100%, making it a viable new testing option in clinical laboratories. The HCM genotyping assay can be marketed to those who face financial barriers to testing or as a first-pass screening tool to decide if further genetic testing is warranted.