Appendix 5: The use of mutation analysis in hypertrophic cardiomyopathy

Mutation analysis is most helpful when family evaluation is appropriate. The use of genotype to predict outcome has generally failed to be helpful.[1] While the presence of any sarcomere mutation indicates increased risk over the absence of any mutation, this does not represent actionable information for any given patient and, as such, does not represent a reasonable clinical target.[2] Relatively uncommon (3%–5% of the overall population with hypertrophic cardiomyopathy) but identifiable mutations (i.e., troponin T mutations) are associated with adverse outcomes and may indicate the need to consider placement of an implantable defibrillator even in the setting of minimal hypertrophy.[3] In such cases, abnormal electrocardiography and imaging (diastolic dysfunction, atrial enlargement, scar tissue on cardiac MRI) will often be present. Although placement of an implantable defibrillator based on genotype alone is not recommended, in the presence of minimal hypertrophy and important family history of sudden death, testing for troponin T may be clinically useful.

Guidelines released by the Heart Rhythm Society support the routine use of mutation analysis for patients with clinical hypertrophic cardiomyopathy, in large part to enable cascade screening of the family.[4] As a corollary to these guidelines, it is important to understand the limitations of DNA testing, and how the results will be of use. It is critical that thorough genetic counselling be offered both before testing is initiated and once the results are available. As such, genetic testing should be undertaken within structured programs specializing in diagnosis and treatment of inherited cardiomyopathies.

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Appendix to: Jacoby DL, DePasquale EC, McKenna WJ. Hypertrophic cardiomyopathy: diagnosis, risk stratification and treatment. *CMAJ* 2012. DOI:10.1503/cmaj.120138.