

More than 95% of positive genetic results for inherited cardiomyopathies and arrhythmias have medical management implications

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There is growing evidence supporting the value of genetic testing for improved diagnostic and management decisions for individuals with inherited cardiovascular disorders. These conditions may present as isolated cardiac findings or as part of a systemic syndrome, such as the RASopathies. Numerous consensus statements recommend genetic testing in the setting of suspicion of an inherited cardiovascular disorder based on clinical findings or family history. By identifying the molecular etiology of disease, genetic testing can improve diagnostic accuracy, guide personalized medical management recommendations, distinguish genotype-specific cardiac event triggers to avoid, and identify at-risk family members for appropriate cascade testing. While these benefits are well described, the proportion of individuals who receive a diagnostic finding with an associated treatment consideration and the overall types of medical management recommendations following genetic testing have not been thoroughly defined.

Here, we retrospectively reviewed the genetic testing outcomes for an unselected cohort of individuals undergoing evaluation for personal or family history of inherited cardiomyopathy, arrhythmia, or RASopathy. In total, 47 genes with one or more treatment considerations were identified and grouped into the following categories: (1) tailored therapies, (2) earlier ICD implantation, (3) medical specialist referrals, (4) lifestyle modifications, and (5) enhanced family surveillance.

Overall, 18.55% (2,861/15,420) of the arrhythmia and cardiomyopathy testing cohort had a diagnostic finding on genetic testing. Of these positive cases, 95.14% (2,722/2,861) had at least one pathogenic or likely pathogenic alteration in a gene with medical management implications, accounting for 17.65% of all individuals tested. 95 individuals had more than one reported finding with management implications, bringing the total number of reported findings to 2,818. Enhanced family surveillance was the most common resulting treatment consideration (50.18%). For 939 individuals tested, there was a gene-based tailored therapy available following molecular diagnosis.

Determining a genetic cause for inherited arrhythmias and cardiomyopathies can provide clinicians with specific guidance for optimizing patient outcomes and follow-up surveillance of at-risk family members. As the field of precision medicine and gene-based tailored therapies continues to grow, the importance of an accurate molecular diagnosis is increasingly more vital.