The identification of the first disease-causing mutation in hypertrophic cardiomyopathy (HCM) sparked tremendous interest in the potential correlation between genotype and clinical outcomes in these patients.1,2 To date, >1400 mutations have been identified in 18 genes, with 80% being identified in either myosin heavy chain (MYH7) or myosin-binding protein C (MYBPC3).3 It is well recognized that patients with HCM can develop adverse outcomes, including heart failure, sudden cardiac death (SCD), atrial fibrillation, and stroke. However, clinical expression of HCM is heterogeneous and disease penetrance may be incomplete throughout life.4 Studies evaluating specific correlations between genotype and clinical outcomes have reported conflicting findings.1,2,5–11 In a cohort of 203 patients, Olivotto et al 12 showed that adverse combined outcomes (cardiovascular death, nonfatal stroke, or progression to advanced heart failure symptoms) occurred more frequently in patients who tested positive for a pathogenic sarcomere mutation compared with those without pathogenic mutations. Although important, this study was limited by the small number of patients and the use of combined morbidity and mortality end points. Recently, studies have shown that patients with >1 mutation (homozygous or compound heterozygous) or rarely triple mutations seem to have more severe disease, suggesting a gene dosage effect.13,14 Because heart failure and SCD are both important yet distinct complications of HCM,15,16 we sought to further clarify the relationships between genotype status and specific clinical outcomes in patients with HCM using a large, single-center cohort of 558 proband patients.

**Background**—The aim of the study was to clarify the relationship between genotype status and major cardiovascular outcomes in a large cohort of patients with hypertrophic cardiomyopathy.

**Methods and Results**—Genetic testing was performed in 558 consecutive proband patients with hypertrophic cardiomyopathy. Baseline and follow-up (mean follow-up 6.3 years) clinical and echocardiographic data were obtained. Pathogenic mutations were identified in 198 (35.4%) patients. Genotype-positive patients were more likely to be women (44% versus 30%; \( P=0.001 \)), younger (39 versus 48 years; \( P<0.001 \)), and have a family history of hypertrophic cardiomyopathy (53% versus 20%; \( P<0.001 \)), as well as family history of sudden cardiac death (17% versus 7%; \( P=0.002 \)). There were no significant differences in the rates of atrial fibrillation, stroke, or septal reduction procedures. Multivariable analysis demonstrated that genotype-positive status was an independent risk factor for the development of combined heart failure end points (decline in left ventricular ejection fraction to <50%, New York Heart Association III or IV in the absence of obstruction, heart failure–related hospital admission, transplantation, and heart failure–related death; hazards ratio, 4.51; confidence interval, 2.09–9.31; \( P<0.001 \)). No difference was seen in heart failure events between the myosin heavy chain and myosin-binding protein C genotype-positive patients.

**Conclusions**—The presence of a pathogenic sarcomere mutation in patients with hypertrophic cardiomyopathy was associated with an increase in heart failure events, with no differences in event rates seen between myosin heavy chain and myosin-binding protein C genotype-positive patients. The presence of a disease-causing mutation seems more clinically relevant than the specific mutation itself. (Circ Cardiovasc Genet. 2014;7:416-422.)

**Key Words:** cardiomyopathy, hypertrophic ■ heart failure

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The identification of the first disease-causing mutation in hypertrophic cardiomyopathy (HCM) sparked tremendous interest in the potential correlation between genotype and clinical outcomes in these patients.1,2 To date, >1400 mutations have been identified in 18 genes, with 80% being identified in either myosin heavy chain (MYH7) or myosin-binding protein C (MYBPC3).3 It is well recognized that patients with HCM can develop adverse outcomes, including heart failure, sudden cardiac death (SCD), atrial fibrillation, and stroke. However, clinical expression of HCM is heterogeneous and disease penetrance may be incomplete throughout life.4 Studies evaluating specific correlations between genotype and clinical outcomes have reported conflicting findings.1,2,5–11 In a cohort of 203 patients, Olivotto et al 12 showed that adverse combined outcomes (cardiovascular death, nonfatal stroke, or progression to advanced heart failure symptoms) occurred more frequently in patients who tested positive for a pathogenic sarcomere mutation compared with those without pathogenic mutations. Although important, this study was limited by the small number of patients and the use of combined morbidity and mortality end points. Recently, studies have shown that patients with >1 mutation (homozygous or compound heterozygous) or rarely triple mutations seem to have more severe disease, suggesting a gene dosage effect.13,14 Because heart failure and SCD are both important yet distinct complications of HCM,15,16 we sought to further clarify the relationships between genotype status and specific clinical outcomes in patients with HCM using a large, single-center cohort of 558 proband patients.
Methods

Patient Selection

The study subjects were identified through the multidisciplinary clinic at Toronto General Hospital, which is a large tertiary referral center. Subjects in the cohort represent the first individual in the family (proband) to proceed with genetic testing between March 2005 and July 2011. Overall, a total of 558 probands with clinical expression of HCM underwent genetic testing after giving informed consent. Clinical diagnosis of HCM was based on the 2-dimensional echocardiographic finding of unexplained left ventricular (LV) hypertrophy with a maximum wall thickness ≥15 mm. Patients with concomitant arterial hypertension were required to have a ratio of maximum wall thickness to posterior wall thickness ≥1.5. This study was approved by the Research Ethics Board of the University Health Network.

Clinical Data

For all patients, detailed clinical data at baseline (defined as their first presentation to our HCM center) and follow-up visits, as well as detailed genetic, family history, and echocardiographic data, were collected. Disease-related complications were noted, including SCD, atrial fibrillation, heart failure events, stroke, syncope, septal reduction therapy, and the implantation of a permanent pacemaker or an automatic implantable cardioverter-defibrillator. Patients were classified as having arterial hypertension when either a blood pressure >140/90 mmHg on 2 separate clinic visits was documented or if a patient was diagnosed and medically treated for arterial hypertension by his or her primary physician. Heart failure events were defined as progression to New York Heart Association functional class III or IV in the absence of LV outflow tract obstruction, hospital admission for heart failure other than because of transient atrial fibrillation, decline in LV ejection fraction <50%, heart transplantation because of end-stage heart failure, or heart failure–related death. Of note, if a patient met >1 criteria for heart failure, then only the more severe event was counted. In cases where a patient’s advanced symptoms warranted septal reduction procedure (myectomy or septal alcohol ablation), the event was not counted toward a heart failure end point, given that symptoms were secondary to LV outflow tract obstruction. Combined SCD was defined as nonresuscitated SCD, successfully resuscitated cardiac death, or appropriate implantable cardioverter-defibrillator discharge. Family history was assessed by detailed pedigree analysis by genetic counselors specializing in cardiac genetics. A positive family history was defined as either documented evidence of HCM in a family member or by highly convincing patient report. Family history was considered positive for SCD if a first-degree relative had an SCD event at <50 years of age.

Genetic Testing

All 558 probands underwent genetic testing for HCM using a combination of oligonucleotide hybridization–based DNA sequencing and di-deoxy-based DNA sequencing. After February 2008, testing consisted of 8 HCM-associated myofilament genes involving MYBPC3, MYH7, essential and regulatory myosin light chains (MYL3, MYL2), cardiac troponin T (TNNT2), cardiac troponin I (TNNT3), α-tropomyosin (TPM1), cardiac actin (ACTC), as well as alpha-galactosidase for the Fabry disease, lysosomal-associated membrane protein 2 for Danon disease, and AMP-activated protein kinase γ2 for AMP-activated protein kinase γ2 cardiomyopathy. Testing before February 2008 did not include the alpha-galactosidase gene, and testing was initiated only in the setting of a clinical presentation suggestive of the Fabry disease.

Genetic tests were performed at the Harvard Partners HealthCare laboratory. Results of genetic testing were reported by the testing facility as pathogenic, presumed pathogenic, variant of unknown significance, probably benign, or negative. Variant designation was based on a combination of factors including reports in the medical literature, conservation across species, segregation studies, functional studies, and computer-based software prediction models with the help of GeneClinic program. In addition, all results were reviewed by a clinical genetics team including a geneticist and a genetic counselor, with expertise in cardiac genetics. Genotype-positive (G+) status was defined as having ≥2 variant that was deemed pathogenic or presumed pathogenic. Genotype-negative (G−) status was defined as the absence of any gene variants or the presence of a variant of unknown significance based on laboratory interpretation and expert clinical review. Because of the lack of a clear disease-causing role of the variant of unknown significance in HCM, patients with these mutations were classified as being G−.

Echocardiography

Each study patient underwent echocardiography according to the standards of the American Society of Echocardiography. The echocardiogram closest to the time of genetic testing was analyzed for each patient. For patients who had undergone septal reduction procedures (septal alcohol ablation and septal myectomy), the study before the procedure was used. Septal morphology was categorized as sigmoid, reversed curvature, neutral, and apical based on previously published criteria. In patients in whom the pattern of hypertrophy did not fall into one of these predefined categories, the subtype was defined as other. LV outflow tract obstruction was defined as either a resting or provokable gradient of ≥30 mmHg.

Statistical Analysis

Unpaired Student t test was conducted to compare continuous variables, and χ2 or Fisher exact test was used to assess categorical data. A value of P<0.05 was considered significant. Comparisons of various echocardiographic and clinical parameters between G+ and G− groups were made after adjusting for age and sex. For clinical end points, Kaplan–Meier survival analysis was performed, and the log-rank test was used to detect differences between MYH7 and MYBPC3 genopositive groups. For comparison between G+ and G− groups, the multivariable Cox model was constructed using a stepwise selection method, with criteria for entry and stay of P<0.20. The proportional hazards assumption was tested graphically and by using Schoenfeld residuals before proceeding. The following variables were thus entered into the multivariable model for heart failure events: genotype status, age at presentation, sex, LV ejection fraction, and hypertension.

Results

Mutation Spectrum

Overall, 198 (35.4%) of the 558 probands had ≥1 pathogenic mutation identified. After excluding patients with apical HCMs, the G+ rate was 40%. As expected, the most commonly identified disease-causing mutations occurred in the MYBPC3 (n=88; 44%) and MYH7 genes (n=74; 37%). Together, mutations in these 2 genes comprised 81% of all identified pathogenic mutations. The final distribution of sarcomere gene mutations is shown in Table 1. Twelve patients (6%) had double heterozygous, compound heterozygous, or homozygous mutations.

Clinical Characteristics

The G+ patients had a younger age at diagnosis compared with G− patients (39.5±15.2 versus 48.5±14.8 years; P<0.001). G+ patients were also more likely to be women (44% versus 30%; P=0.001), have a positive family history of HCM (52.8% versus 20%; P<0.001), and a family history of SCD (16.8% versus 7.2%; P=0.002). In addition, our patient cohort comprised an ethnically diverse group of patients with 74% whites, 6% Asians, 10% South Asians, 4% Afro-Caribbeans, and 6% mixed/other ancestries. There were no significant differences in the ethnic composition between G+ and G− groups. Patients with myofilament mutations were less likely to have risk factors for coronary artery disease (CAD), such as arterial hypertension (G+ 25.5% versus G− 46.9%; P<0.001) and hypercholesterolemia (G+ 25% versus G− 40.6%; P<0.001).

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Table 1. Distribution of Mutations

<table>
<thead>
<tr>
<th>Gene</th>
<th>No. of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>MYBPC3</td>
<td>88</td>
<td>44</td>
</tr>
<tr>
<td>MYH7</td>
<td>74</td>
<td>37</td>
</tr>
<tr>
<td>TNNT2</td>
<td>13</td>
<td>6.5</td>
</tr>
<tr>
<td>TNNT1</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>MYL3</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>TPM1</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>ACTC</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>MYL2</td>
<td>1</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Other data are given as patient numbers with percentages listed in parentheses. BMI indicates body mass index; FHHCM, family history of hypertrophic cardiomyopathy; FHSCD, family history of sudden cardiac death; FU years, follow-up time in years; and NYHA, New York Heart Association.

Echocardiographic Findings

Age- and sex-adjusted comparison of various echocardiographic parameters is shown in Table 3. As expected, the most common septal morphology types in the G+ group were reverse curvature and neutral types, representing 34.2% and 40.2% of all G+ patients, respectively (P<0.001). Sigmoid septum was the most commonly observed subtype in the G− patients (31.4%). Overall, a total of 89 patients (16%) in the cohort had apical morphology (12 patients in the G+ group and 77 patients in the G− group; Table 3).

Clinical Outcomes and Interventions

The mean follow-up period for the G+ and G− groups was 6.6±6.3 years and 6.2±5.6 years, respectively (P=0.433), from the time of initial presentation. The median follow-up period for the G+ and G− groups was 4.5 and 4.8 years, respectively (P=0.145).

After adjusting for age and sex, there were no significant differences between G+ and G− groups in terms of the incidence of atrial fibrillation, stroke, nonsustained ventricular tachycardia, rates of automated implantable cardioverter-defibrillator implantation, or septal reduction procedures (Table 4). There were a total of 44 stroke events, all of which were nonfatal. A total of 15 septal alcohol ablation procedures and 109 surgical myectomies were performed in our cohort of 558 patients. Only 8 patients had septal myectomy before initial presentation.

Heart Failure Outcome

During the follow-up period, there were 50 heart failure events in the cohort, with 30 events in the G+ group and 20 in the G− group (P<0.001). The breakdown of heart failure events is as follows: 22 of 50 (44%) patients had reduced LV ejection fraction, 8 patients had septal myectomy before initial presentation.

Table 2. Baseline Characteristics Based on Genotype Results

<table>
<thead>
<tr>
<th>Echo features</th>
<th>Genotype Positive (n=198)</th>
<th>Genotype Negative (n=360)</th>
<th>Adjusted P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left ventricular ejection fraction†</td>
<td>66.5±9.3</td>
<td>67.4±7.2</td>
<td>0.30</td>
</tr>
<tr>
<td>Left atrial diameter†</td>
<td>43.3±7.5</td>
<td>42.6±6.9</td>
<td>0.03</td>
</tr>
<tr>
<td>Left atrial volume index†</td>
<td>45.3±33.1</td>
<td>41±16.9</td>
<td>0.07</td>
</tr>
<tr>
<td>MWTH†</td>
<td>20.8±4.8</td>
<td>19.6±4.9</td>
<td>0.16</td>
</tr>
<tr>
<td>MVTH/PWTH ratio†</td>
<td>2.1±0.5</td>
<td>1.9±0.5</td>
<td>0.004</td>
</tr>
<tr>
<td>Patients with LVOT obstruction</td>
<td>89 (45)</td>
<td>181 (50)</td>
<td>0.69</td>
</tr>
</tbody>
</table>

Other data are given as patient numbers with percentages listed in parentheses. LVOT indicates left ventricular outflow tract; MWTH, maximum wall thickness; and MVTH/PWTH ratio, maximum wall thickness to posterior wall thickness ratio.

*Age- and sex-adjusted P values.

†Data are presented as median with 25th and 75th percentiles in parenthaseis.
Table 4. Follow-Up Clinical Data Based on Genotype Results

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Genotype Positive</th>
<th>Genotype Negative</th>
<th>Adjusted (P) Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFib (permanent or paroxysmal)</td>
<td>47 (23.9)</td>
<td>79 (21.9)</td>
<td>0.44</td>
</tr>
<tr>
<td>Stroke</td>
<td>16 (8.1)</td>
<td>28 (7.8)</td>
<td>0.55</td>
</tr>
<tr>
<td>nsVT</td>
<td>45 (23)</td>
<td>59 (16.4)</td>
<td>0.17</td>
</tr>
<tr>
<td>PPM</td>
<td>16 (8.1)</td>
<td>16 (4.4)</td>
<td>0.007</td>
</tr>
<tr>
<td>AICD</td>
<td>49 (24.9)</td>
<td>58 (16.1)</td>
<td>0.24</td>
</tr>
<tr>
<td>SEA</td>
<td>6 (3.1)</td>
<td>9 (2.5)</td>
<td>0.69</td>
</tr>
<tr>
<td>Septal reduction</td>
<td>44 (22.3)</td>
<td>65 (18.1)</td>
<td>0.30</td>
</tr>
<tr>
<td>(SEA or myectomy)</td>
<td>50 (25.4)</td>
<td>72 (20)</td>
<td>0.22</td>
</tr>
</tbody>
</table>

Data are given as patient numbers with percentages listed in parentheses. AFib indicates atrial fibrillation; AICD, automatic implantable cardioverter-defibrillator; nsVT, nonsustained ventricular tachycardia; PPM, permanent pacemaker; and SEA, septal ethanol ablation.

*Age- and sex-adjusted \(P\) values.

Discussion

To date, this is one of the largest single-center HCM cohorts with detailed genetic information and long-term follow-up data. The key findings from our study included the following: (1) a positive genotype status was associated with higher rates of heart failure events independent of age at presentation, sex, LV ejection fraction, or presence of arterial hypertension; (2) there was no difference in heart failure outcomes between MYBPC3 G+ patients and MYH7 G+ patients; and (3) G+ status was not an independent predictor of SCD in the present study, which may be related to the small number of events.

It is well recognized that a substantial proportion of patients with HCM could develop systolic dysfunction or advanced New York Heart Association symptoms that may eventually lead to heart transplantation or early cardiac death.20,21 The observed rates of heart failure complications in patients with HCM based on previous reports range from 2.4% to 20%, depending on the definition used in individual studies.3,42,32 Despite the considerable impact of heart failure on the morbidity and mortality of patients with HCM, the effect of a positive genetic test on heart failure outcome remains controversial to this day. The process by which a pathogenic sarcomere mutation leads to heart failure may be explained by previously proposed mechanisms including abnormal intracellular calcium handling and compromised cardiomyocyte energetic balance, which can lead to the development of myocardial disarray and fibrosis.42,45 These changes may eventually result in diastolic dysfunction, a quintessential pathophysiologic abnormality observed in HCM that contributes to symptoms and adverse clinical outcomes.28 Researchers have used mouse models containing various pathogenic MYH7 mutations and pluripotent stem cell cardiomyocytes from patients with MYH7 mutation to demonstrate that mutant cardiomyocytes exhibited increased...
calcium flux and delayed calcium reuptake by the sarcoplasmic reticulum. There is also evidence of increased active force generation along with increased ATP hydrolysis. Consequently, these intracellular changes may lead to upregulation of transcription factors such as myocyte enhancer factor 2 and transforming growth factor-β via a process known as mechanotransduction. The upregulation of these transcription factors plays a critical role in the formation of extracellular matrix, enhancement of hypertrophy, and development of interstitial fibrosis.

Over time, interstitial fibrosis and myocardial hypertrophy can result in microvascular ischemia and diastolic dysfunction, which are both early cardinal features of HCM. Indeed, G+ patients have been shown to have a significantly greater degree of ischemia using positron emission tomographic scans, and microvascular ischemia has been shown to be a predictor for long-term adverse outcomes. Of further note, microvascular dysfunction correlates well with the amount of delayed gadolinium on cardiac magnetic resonance imaging, which is a reflection of the degree of myocardial fibrosis. In addition to microvascular dysfunction, diastolic dysfunction is one of the key preclinical findings seen in G+ patients with HCM. Ho et al demonstrated that although the LV ejection fraction was normal or even increased in G+/left ventricular hypertrophy-HCM patients, the annular tissue Doppler velocities were significantly reduced. Abnormalities in longitudinal systolic strain have also been described in G+, phenotype-negative HCM patients with preserved ejection fraction. These findings are consistent with our results showing that the development of heart failure was predicted by the presence of pathogenic sarcomere mutations. Our results are important in light of recent evidence showing that patients with compound heterozygous or homozygous mutations have more aggressive clinical course with early disease onset, marked LV hypertrophy, and development of end-stage heart failure complications, suggesting a gene dosage effect. Of note, 12 patients in our cohort had multiple sarcomere mutations. Although this number is comparable with the 5% described in previous literature, we could not draw meaningful conclusions based on the small number of patients in this subgroup.

It is important to note that our G− group had a higher proportion of patients with sigmoid morphology than the G+ group. Although this pattern of distribution has been well described in the past, it is possible that a small group of patients with
nongenetically mediated hypertrophy were included in the cohort. This could partially account for some of the observed differences between the G+ and G− patients. Furthermore, we did not demonstrate any significant difference between the MYH7 G+ patients and MYBPC3 G+ patients. This finding may challenge the previous belief that missense mutations in MYH7 were implicated in reduced survival with early disease onset, and that MYBPC3 tended to be associated with delayed disease onset and better survival. However, some of the mutations in the MYBPC3 gene are implicated in haploinsufficiency and the formation of truncated protein products, which could lead to LV dysfunction through distinct mechanisms from the ones implicated in the missense mutations. Therefore, an alternative explanation for LV dysfunction in this group of patients with HCM includes a process whereby a truncated protein product causes a collapse of sarcomere stability followed by compensation by the residual MYBPC3 proteins in heterozygous patients.

Our study did not show a statistically significant relationship between genotype status and the risk of SCD. There are a few potential explanations for these findings. First, despite the large size of the cohort, the actual number of SCD events was low. This observation is consistent with the previously reported rate of SCD of ≤1% per year. Therefore, our study could be underpowered to draw a definitive conclusion. Second, sarcomere mutations may not be the sole determinant of risk for SCD outcome. Interestingly, of the 9 G+ patients with SCD in our study cohort, no patient tested positive for previously described malignant mutations such as MYH7-R403Q, R453C, G716R, or R719W. Numerous variables such as modifier genes and environmental factors could play important roles in influencing the natural history of this condition. For example, polymorphisms in the renin–angiotensin–aldosterone system such as the homozygous deletion subset of the angiotensin converting enzyme genotype was shown to promote the formation of microvascularopathy, fibrosis, and cardiac dysfunction compared with other genotypes. Another modifier is the presence of CAD. Our data showed that the G− group had a higher rate of epicardial CAD. The higher rate of CAD could contribute to the higher than expected SCD rate in the G− patients. Sorajja et al showed that patients with HCM and severe CAD had a hazard ratio of 2.77 for SCD compared with HCM patients without CAD, after controlling for variables such as age, stroke, and atrial fibrillation. Future studies involving multicenter HCM cohorts will be useful to clarify the true relationship between one’s genotype status and the risk of sudden death.

Limitations
This study was a retrospective analysis, which has its inherent biases. Genetic testing was performed between March 2005 and July 2011, and the earlier tests did not include all 11 genes that were part of the more recent tests. This might result in an underestimation of the number of patients with sarcomere gene mutations. The higher proportion of patients with apical HCM in the current cohort may also contribute to the lower G+ rate. In addition, the use of a maximum wall thickness of ≥15 mm rather than one corrected for body surface area may have led to the exclusion of some G+ as well as G− cases of HCM. The total number of SCD events was low in our cohort, and as such the study may be underpowered to detect a statistically significant relationship between genotype status and SCD events. Although a statistically significant difference in heart failure events was demonstrated between G+ and G− groups, there may be patients in the G− group who do not have true sarcomeric HCM. This should be taken into consideration when interpreting the results. Finally, additional magnetic resonance imaging data would be helpful to show any differences in the LV mass and late gadolinium enhancement between G+ and G− patients. This may provide more insights into the mechanism of heart failure in G+ patients.

Conclusions
The presence of a pathogenic sarcomere mutation in patients with HCM is associated with an increase in heart failure events, with no differences in event rates seen between MYH7 and MYBPC3 G+ subgroups. Although we demonstrated no statistically significant difference in the SCD outcome between G+ and G− groups, this may be related to the low number of events in the cohort. The presence of a disease-causing mutation seems more clinically relevant than the specific mutation itself.

Disclosures
None.

References
Hypertrophic cardiomyopathy (HCM) is one of the most common inherited cardiac conditions affecting 1 in 500 of the general population. More than 2 decades of research on the genetics of HCM has shown that HCM is caused by dominant mutations in various components of the sarcomere proteins or the adjacent Z disc proteins. The value of genetic testing has primarily been in the identification of disease-causing mutations. However, the implications and will allow clinicians to provide meaningful counseling and risk estimation for patients undergoing genetic testing.

Ploidy events (confidence interval, 2.09–9.31; $P<0.001$). Our study is the largest study to clearly demonstrate the association between pathogenic sarcomere mutations and adverse heart failure outcomes in patients with HCM. Our results have significant clinical implications and will allow clinicians to provide meaningful counseling and risk estimation for patients undergoing genetic testing.
Genotype-Positive Status in Patients With Hypertrophic Cardiomyopathy Is Associated With Higher Rates of Heart Failure Events
Qin Li, Christiane Gruner, Raymond H. Chan, Melanie Care, Katherine Siminovitch, Lynne Williams, Anna Woo and Harry Rakowski

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