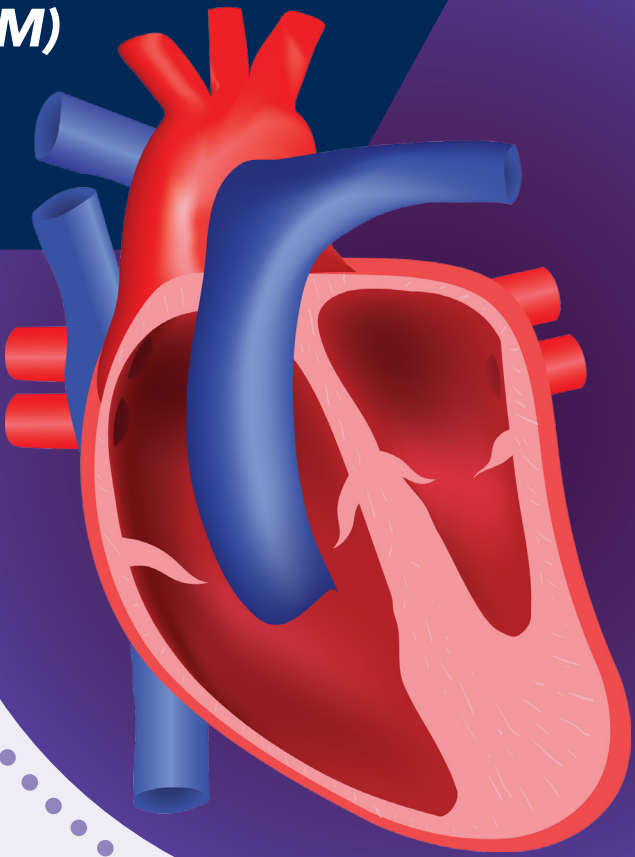
ACCELERATING INNOVATION FOR MEDICAL EXCELLENCE IN HYPERTROPHIC CARDIOMYOPATHY *(AIME HCM)*

Pocket Guide



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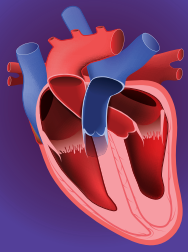
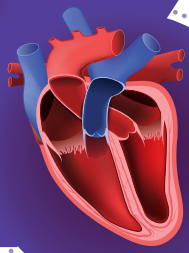
HCM INTRODUCTION

Hypertrophic Cardiomyopathy *(HCM)* **happens when the walls of the heart's ventricles thicken and become stiff, preventing the heart from being properly filled, making it more difficult for the heart to pump blood to the body.**





HCM is the most common ***genetic heart disease*** and the most common cause of non-traumatic sudden death.

- Estimates of asymptomatic HCM in the U.S. ranges from 1:200 to 1:500.*
- Estimates of heart failure (HF) in the U.S. is 1,915 per 100,000 people (about 10:500).**
- Death due to HCM is usually sudden (i.e., unexpected death of young adult jogger or athlete during game).
- Patients with HCM tend to have comorbidities such as HF, atrial fibrillation, and ventricular arrythmias.

**Source:*

***Source:*

HCM INTRODUCTION *(Continued)*

HCM is most often caused by a spontaneous genetic mutation or an inherited genetic defect. First-degree family members should be screened every 2 to 3 years with genetic testing or imaging/ECG.

Symptoms (most seen in ages 20-40):	Diagnosis:	Imaging helps to:
• Fainting (often suddenly) • Chest pain • Shortness of breath • Palpitations	• Symptoms, physical exam, ECG and CXR • Echocardiography and/or magnetic resonance imaging (MRI) of the heart is used to confirm	• Establish the diagnosis (and differential diagnoses) • Inform treatment options • Inform sudden cardiac death (SCD) risk stratification

POCKET GUIDE OVERVIEW

This pocket guide is a practical, streamlined resource for clinicians regarding HCM awareness and pathology. It includes key information from the *2020 AHA/ACC Guideline for the Diagnosis and Treatment of Patients With Hypertrophic Cardiomyopathy*.

This resource is only an excerpt from the manuscript published in *Journal of the American College of Cardiology (JACC)* and the full publication should be reviewed for important context and additional information.

To access the full manuscript, please scan this QR code.

TOP 10 TAKE-HOME MESSAGES

1 Shared decision-making is particularly relevant in the management of HCM because treatment decisions are not clear cut.

Recommendation for Shared Decision-Making Referenced studies that support the recommendation are summarized in the Online Data Supplement 1		
COR	**LOE**	**RECOMMENDATION**
1	B-NR	1. For patients with HCM or at-risk for HCM, shared decision-making is recommended in developing a plan of care (including but not limited to decisions regarding genetic evaluation, activity, lifestyle, and therapy choices) that includes a full disclosure of the risks, benefits, and anticipated outcomes of all options, as well the opportunity for the patient to express their goals and concerns.

2 Referral to multidisciplinary HCM centers can be important to optimizing care for patients with HCM, like in valvular heart disease.

Recommendations for Multidisciplinary HCM Centers		
COR	**LOE**	**RECOMMENDATIONS**
1	C-LD	1. In patients with HCM in whom SRT is indicated, the procedure should be performed at experienced centers (comprehensive or primary HCM centers) with demonstrated excellence in clinical outcomes for these procedures.
2a	C-LD	2. In patients with HCM, consultation with or referral to a comprehensive or primary HCM center is reasonable to aid in complex disease-related management decisions.

Table: Example Targets for Invasive Septal Reduction Therapies Outcomes

	Rate	
	Myectomy	Alcohol Septal Ablation
30-d mortality	≤1%	≤1%
30-d adverse complications (tamponade, LAD dissection, infection, major bleeding)	≤10%	≤10%
30-d complete heart block resulting in need for permanent pacemaker	≤5%	≤10%
Mitral valve replacement within 1 year	≤5%	
More than moderate residual mitral regurgitation	≤5%	≤5%
Repeat procedure rate	≤3%	≤10%
Improvement ≥ NYHA class	>90%	>90%
Rest and provoked LVOT gradient <50 mm Hg	>90%	>90%

LAD indicates left anterior descending; NYHA, New York Heart Association; and LVOT, left ventricular outflow tract.

Table: Suggested Competencies of Comprehensive and Primary HCM Centers

Potential HCM Care Delivery Competencies	Comprehensive HCM Center	Primary HCM Center	Referring Centers/ Physicians
Diagnosis	X	X	X
Initial and surveillance TTE	X	X	X
Advanced echocardiographic imaging to detect latent LVOTO	X	X	
Echocardiography to guide SRT	X	*	
CMR imaging for diagnosis and risk stratification	X	X	
Invasive evaluation for LVOTO	X	*	*
Coronary angiography	X	X	X
Stress testing for elicitation of LVOTO or consideration of advanced HF therapies/transplant	X	X	
Counseling and performing family screening (imaging and genetic)	X	X	X
Genetic testing/counseling	X	X	*
SCD risk assessment	X	X	X
Class 1 and Class 2a ICD decision-making with adult patients	X	X	X
Class 2B ICD decision-making with adult patients	X		
ICD implantation (adults)	X	X	*
ICD decision-making and implantation with children/adolescents and their parents	X	*	
Initial AF management and stroke prevention	X	X	X
AF catheter ablation	X	X	*
Initial management of HFrEF and HFpEF	X	X	X
Advanced HF management (e.g., transplantation, CRT)	X	*	
Pharmacologic therapy for symptomatic obstructive HCM	X	X	X
Invasive management of symptomatic obstructive HCM	X	†	
Counseling occupational and healthy living choices other than high-intensity or competitive activities	X	X	X
Counseling options on participation in high-intensity or competitive athletics	X		
Managing women with HCM through pregnancy	X	*	
Management of comorbidities	X	X	X

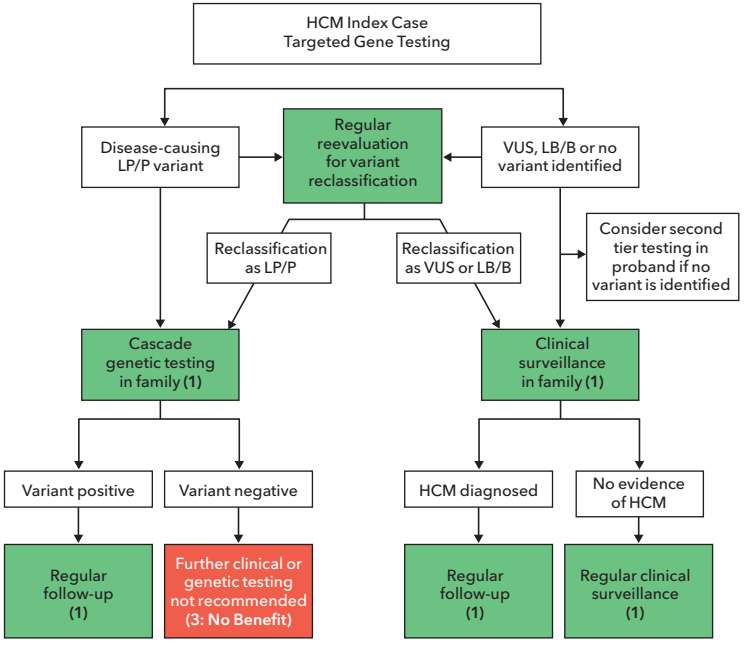
*Optional depending on the core competencies of the institution.
†If these procedures are performed, adequate quality assurance should be in place to demonstrate outcomes consistent with that achieved by comprehensive centers.
AF indicates atrial fibrillation; CMR, cardiovascular magnetic resonance; CRT, cardiac resynchronization therapy; HCM, hypertrophic cardiomyopathy; HF, heart failure; HFrEF, heart failure with reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; ICD, implantable cardioverter-defibrillator; LVOTO, left ventricular outflow tract obstruction; SCD, sudden cardiac death; TTE, transesophageal echocardiography.

3 Counseling patients with HCM regarding the potential for genetic transmission of HCM is one of the cornerstones of care.

Recommendations for Genetics and Family Screening Referenced studies that support the recommendations are summarized in Online Data Supplements 8 and 9		
COR	**LOE**	**RECOMMENDATIONS**
1	B-NR	1. In patients with HCM, evaluation of familial inheritance, including a 3-generation family history, is recommended as part of the initial assessment.
1	B-NR	2. In patients with HCM, genetic testing is beneficial to elucidate the genetic basis to facilitate the identification of family members at-risk for developing HCM (cascade testing).
1	B-NR	3. In patients with an atypical clinical presentation of HCM or when another genetic condition is suspected to be the cause, a work-up including genetic testing for HCM and other genetic causes of unexplained cardiac hypertrophy ("HCM phenocopies") is recommended.
1	B-NR	4. In patients with HCM who choose to undergo genetic testing, pre- and posttest genetic counseling by an expert in the genetics of cardiovascular disease is recommended so that risks, benefits, results, and their clinical significance can be reviewed and discussed with the patient in a shared decision-making process.
1	B-NR	5. When performing genetic testing in an HCM proband, the initial tier of genes tested should include genes with strong evidence to be disease-causing in HCM*.
1	B-NR	6. In first-degree relatives of patients with HCM, both clinical screening (ECG and 2D echocardiogram) and cascade genetic testing (when a pathogenic/likely pathogenic variant has been identified in the proband) should be offered.
1	B-NR	7. In families where a sudden unexplained death has occurred with a postmortem diagnosis of HCM, postmortem genetic testing is beneficial to facilitate cascade genetic testing and clinical screening in first-degree relatives.
1	B-NR	8. In patients with HCM who have undergone genetic testing, serial reevaluation of the clinical significance of the variant(s) identified is recommended to assess for variant reclassification, which may impact diagnosis and cascade genetic testing in family members.
1	B-NR	9. In affected families with HCM, preconception and prenatal reproductive and genetic counseling should be offered.
2b	B-NR	10. In patients with HCM, the usefulness of genetic testing in the assessment of risk of SCD is uncertain.
2b	B-NR	11. In patients with HCM who harbor a variant of uncertain significance, the usefulness of clinical genetic testing of phenotype-negative relatives for the purpose of variant reclassification is uncertain.
3: No benefit	B-NR	12. For patients with HCM who have undergone genetic testing and were found to have no pathogenic variants (i.e., harbor only benign/likely benign variants), cascade genetic testing of the family is not useful.
3: No benefit	B-NR	13. Ongoing clinical screening is not indicated in genotype-negative relatives in families with genotype-positive HCM, unless the disease-causing variant is downgraded to variant of uncertain significance, likely benign, or benign variant during follow-up.

*Strong evidence HCM genes include, at the time of this publication: *MYH7, MYBPC3, TNNI3, TNNT2, TPM1, MYL2, MYL3,* and *ACTC1.*

Figure: Genetic Testing Process in HCM



HCM indicates hypertrophic cardiomyopathy; LB/B, likely benign/benign; LP/P, likely pathogenic or pathogenic; and VUS, variant of unknown significance.

4 Many patients with HCM are asymptomatic and identified as a result of screening so cardiac imaging (echocardiography) is especially important.

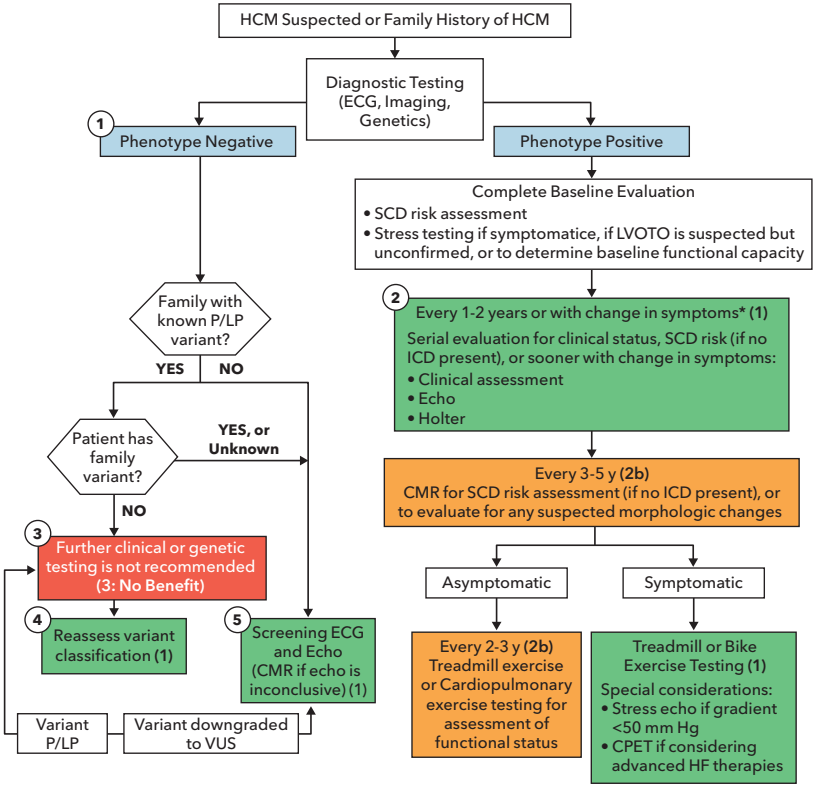
Recommendation for Diagnosis, Initial Evaluation, and Follow-up Referenced studies that support the recommendation are summarized in Online Data Supplement 2.		
COR	**LOE**	**RECOMMENDATION**
1	B-NR	1. In patients with suspected HCM, comprehensive physical examination and complete medical and 3-generation family history is recommended as part of the initial diagnostic assessment.

Table: Clinical Features in Patients With "HCM Phenocopies (Mimics)"

Typical Presentation Age	Systemic Features	Possible Etiology	Diagnostic Approach
Infants (0-12 mo) and toddlers	Dysmorphic features, failure to thrive, metabolic acidosis	• RASopathies • Glycogen storage diseases, other metabolic or mitochondrial diseases • Infant of a mother with diabetes	• Genetic assessment • Newborn metabolic screening • Specific metabolic assays • Genetic testing
Early childhood	Delayed or abnormal cognitive development, visual or hearing impairment	• RASopathies • Mitochondrial diseases	• Biochemical screening • Genetic testing
School age and adolescence	Skeletal muscle weakness or movement disorder	• Friedrich ataxia, Danon disease • Mitochondrial disease	• Biochemical screening • Neuromuscular assessment • Genetic testing
Adulthood	Movement disorder, peripheral neuropathy, renal dysfunction	Anderson-Fabry disease, Friedrich ataxia, infiltrative disorders (e.g., amyloidosis), glycogen storage diseases	• Biochemical screening • Neuromuscular assessment • Genetic testing

*see next page for HCM Suspected or Family History of HCM

Figure: Recommended Evaluation and Testing for HCM



*The interval may be extended, particularly in adult patients who remain stable after multiple evaluations. CMR indicates cardiovascular magnetic resonance; CPET, cardiopulmonary exercise test; ECG, electrocardiography/electrocardiogram; HCM, hypertrophic cardiomyopathy; HF, heart failure; ICD, implantable cardioverter-defibrillator; LVOTO, left ventricular outflow tract obstruction; P/LP, pathogenic or likely pathogenic variant; SCD, sudden cardiac death; and VUS, variant of unknown significance.

*see next page: Recommendations for Echocardiography

Recommendations for Echocardiography Referenced studies that support the recommendations are summarized in Online Data Supplement 3		
COR	**LOE**	**RECOMMENDATIONS**
1	B-NR	1. In patients with suspected HCM, a TTE is recommended in the initial evaluation.
1	B-NR children C-LD adults	2. In patients with HCM with no change in clinical status or events, repeat TTE is recommended every 1 to 2 years to assess the degree of myocardial hypertrophy, dynamic LVOTO, MR, and myocardial function.
1	B-NR	3. For patients with HCM who experience a change in clinical status or a new clinical event, repeat TTE is recommended.
1	B-NR	4. For patients with HCM and resting LVOT gradient <50 mm Hg, a TTE with provocative maneuvers is recommended.
1	B-NR	5. For symptomatic patients with HCM who do not have a resting or provocable outflow tract gradient ≥50 mm Hg on TTE, exercise TTE is recommended for the detection and quantification of dynamic LVOTO.
1	B-NR	6. For patients with HCM undergoing surgical septal myectomy, intraoperative transesophageal echocardiogram (TEE) is recommended to assess mitral valve anatomy and function and adequacy of septal myectomy.
1	B-NR	7. For patients with HCM undergoing alcohol septal ablation, TTE or intraoperative TEE with intracoronary ultrasound-enhancing contrast injection of the candidate's septal perforator(s) is recommended.
1	B-NR	8. For patients with HCM who have undergone SRT, TTE within 3 to 6 months after the procedure is recommended to evaluate the procedural results.
1	B-NR	9. Screening: In first-degree relatives of patients with HCM, a TTE is recommended as part of initial family screening and periodic follow-up.
1	B-NR	10. Screening: In individuals who are genotype-positive or phenotype-negative, serial echocardiography is recommended at periodic intervals depending on age (1 to 2 years in children and adolescents, 3 to 5 years in adults) and change in clinical status.
2a	C-LD	11. For patients with HCM, TEE can be useful if TTE is inconclusive in clinical decision-making regarding medical therapy, and in situations such as planning for myectomy, exclusion of subaortic membrane or MR secondary to structural abnormalities of the mitral valve apparatus, or in the assessment of the feasibility of alcohol septal ablation.
2a	B-NR	12. For patients with HCM in whom the diagnoses of apical HCM, apical aneurysm, or atypical patterns of hypertrophy is inconclusive on TTE, the use of an intravenous ultrasound-enhancing agent is reasonable, particularly if other imaging modalities such as CMR are not readily available or contraindicated.
2a	C-LD	13. For asymptomatic patients with HCM who do not have a resting or provocable outflow tract gradient ≥50 mm Hg on standard TTE, exercise TTE is reasonable for the detection and quantification of dynamic LVOTO.

*see next page for Screening With Electrocardiography and 2D Echocardiography in Asymptomatic Family Members

Table: Screening With Electrocardiography and 2D Echocardiography in Asymptomatic Family Members

Age of First-Degree Relative	Initiation of Screening	Repeat ECG, Echo
Pediatric: Children and adolescents from genotype-positive families, and families with early onset disease	At the time HCM is diagnosed in another family member	Every 1-2 y
Pediatric: All other children and adolescents	At any time after HCM is diagnosed in another family member but no later than puberty	Every 2-3 y
Adults	At the time HCM is diagnosed in another family member	Every 3-5 y

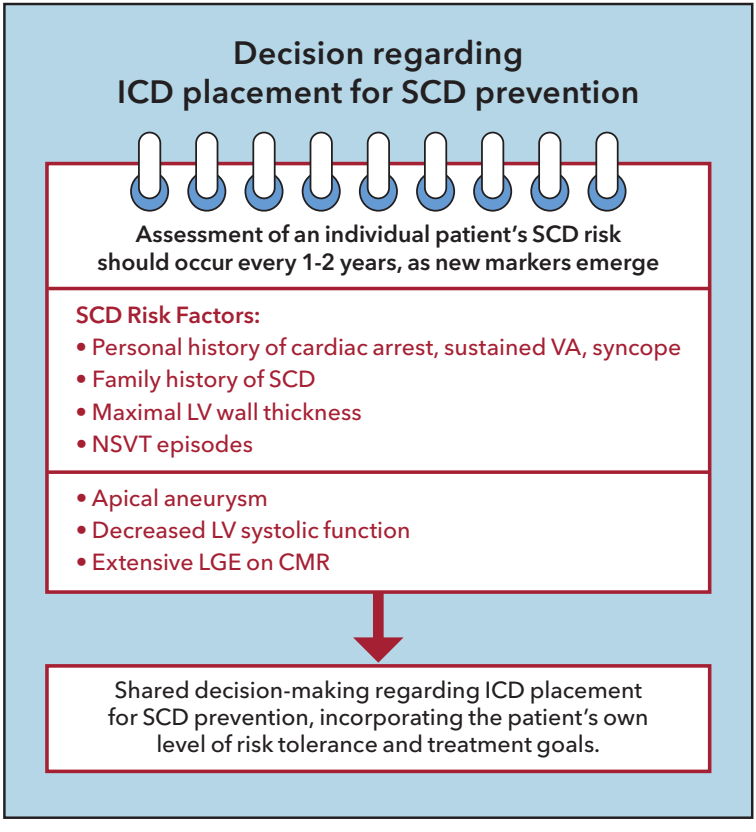
*Includes all asymptomatic, phenotype-negative first-degree relatives deemed to be at-risk for developing HCM based on family history or genotype status and may sometimes include more distant relatives based on clinical judgement. Screening interval may be modified (e.g., at onset of new symptoms or in families with a malignant clinical course or late-onset HCM). ECG indicates electrocardiogram; Echo, echocardiogram; and HCM, hypertrophic cardiomyopathy.

Recommendations for CMR Imaging
Referenced studies that support the recommendations are summarized in Online Data Supplement 4.

COR	LOE	RECOMMENDATIONS
1	B-NR	1. For patients suspected to have HCM in whom echocardiography is inconclusive, CMR imaging is indicated for diagnostic clarification.
1	B-NR	2. For patients with LVH in whom there is a suspicion of alternative diagnoses, including infiltrative or storage disease as well as athlete's heart, CMR imaging is useful.
1	B-NR	3. For patients with HCM who are not otherwise identified as high risk for SCD, or in whom a decision to proceed with ICD remains uncertain after clinical assessment that includes personal/family history, echocardiography, and ambulatory electrocardiographic monitoring, CMR imaging is beneficial to assess for maximum LV wall thickness, ejection fraction (EF), LV apical aneurysm, and extent of myocardial fibrosis with LGE.
1	B-NR	4. For patients with obstructive HCM in whom the anatomic mechanism of obstruction is inconclusive on echocardiography, CMR imaging is indicated in order to inform the selection and planning of SRT.
2b	C-EO	5. For patients with HCM, repeat contrast-enhanced CMR imaging on a periodic basis (every 3 to 5 years) for the purpose of SCD risk stratification may be considered to evaluate changes in LGE and other morphologic changes, including EF, development of apical aneurysm, or LV wall thickness.

5 There are new individual risk markers for sudden cardiac death (SCD) which can help identify patients who may need an ICD (i.e., identify at-risk patients earlier to prevent SCD).

Central Illustration: 2020 AHA/ACC Guideline for the Diagnosis and Treatment of Patients With Hypertrophic Cardiomyopathy



Ommens S. et al. J Am Coll Cardiol. 10.1016/j.jacc.2020.08.045

Recommendations for ICD Placement in High-Risk Patients With HCM
Referenced studies that support the recommendations are summarized in Online Data Supplement 12

COR	LOE	RECOMMENDATIONS
1	C-EO	1. In patients with HCM, application of individual clinical judgment is recommended when assessing the prognostic strength of conventional risk marker(s) within the clinical profile of the individual patient, as well as a thorough and balanced discussion of the evidence, benefits, and estimated risks to engage the fully informed patient's active participation in ICD decision-making.
1	B-NR	2. For patients with HCM, and previous documented cardiac arrest or sustained VT, ICD placement is recommended.
2a	B-NR	3. For adult patients with HCM with ≥1 major risk factors for SCD, it is reasonable to offer an ICD. These major risk factors include: a. Sudden death judged definitively or likely attributable to HCM in ≥1 first-degree or close relatives who are ≤50 years of age; b. Massive LVH ≥30 mm in any LV segment; c. ≥1 recent episodes of syncope suspected by clinical history to be arrhythmic (i.e., unlikely to be of neurocardiogenic [vasovagal] etiology, or related to LVOTO); d. LV apical aneurysm, independent of size; e. LV systolic dysfunction (EF <50%).
2a	B-NR	4. For children with HCM who have ≥1 conventional risk factors, including unexplained syncope, massive LVH, NSVT, or family history of early HCM-related SCD, ICD placement is reasonable after considering the relatively high complication rates of long-term ICD implantation in younger patients.
2a	B-NR	5. For patients ≥16 years of age with HCM and with ≥1 major SCD risk factors, discussion of the estimated 5-year sudden death risk and mortality rates can be useful during the shared decision-making process for ICD placement.
2b	B-NR	6. In select adult patients with HCM and without major SCD risk factors after clinical assessment, or in whom the decision to proceed with ICD placement remains otherwise uncertain, ICD may be considered in patients with extensive LGE by contrast-enhanced CMR imaging or NSVT present on ambulatory monitoring.
2b	C-LD	7. In select pediatric patients with HCM in whom risk stratification is otherwise less certain, it may be useful to consider additional factors such as extensive LGE on contrast-enhanced CMR imaging and systolic dysfunction in risk stratification.
3: Harm	B-NR	8. In patients with HCM without risk factors, ICD placement should not be performed.
3: Harm	B-NR	9. In patients with HCM, ICD placement for the sole purpose of participation in competitive athletics should not be performed.

Table: Established Clinical Risk Factors for HCM Sudden Death Risk Stratification

Family history of sudden death from HCM	Sudden death judged definitively or likely attributable to HCM in ≥1 first-degree or close relatives who are ≤50 years of age. Close relatives would generally be second-degree relatives; however, multiple SCDs in tertiary relatives should also be considered relevant.
Massive LVH	Wall thickness ≥30 mm in any segment within the chamber by echocardiography or CMR imaging; consideration for this morphologic marker is also given to borderline values of ≥28 mm in individual patients at the discretion of the treating cardiologist. For pediatric patients with HCM, an absolute or z-score threshold for wall thickness has not been established; however, a maximal wall that corresponds to a z-score ≥20 (and >10 in conjunction with other risk factors) appears reasonable.
Unexplained syncope	≥1 Unexplained episodes involving acute transient loss of consciousness, judged by history unlikely to be of neurocardiogenic (vasovagal) etiology, nor attributable to LVOTO, and especially when occurring within 6 months of evaluation (events beyond 5 years in the past do not appear to have relevance).
HCM with LV systolic dysfunction	Systolic dysfunction with EF <50% by echocardiography or CMR imaging.
LV apical aneurysm	Atypical aneurysm defined as a discrete thin-walled dyskinetic or akinetic segment of the most distal portion of the LV chamber; independent of size.
Extensive LGE on CMR imaging	Diffuse and extensive LGE, representing fibrosis, either quantified or estimated by visual inspection, comprising ≥15% of LV mass (extent of LGE conferring risk has not been established in children.)
NSVT on ambulatory monitor	It would seem most appropriate to place greater weight on NSVT as a risk marker when runs are frequent (≥3), longer (≥10 beats), and faster (≥200 bpm) occurring usually over 24 to 48 hours of monitoring. For pediatric patients, a VT rate that exceeds the baseline sinus rate by >20% is considered significant.

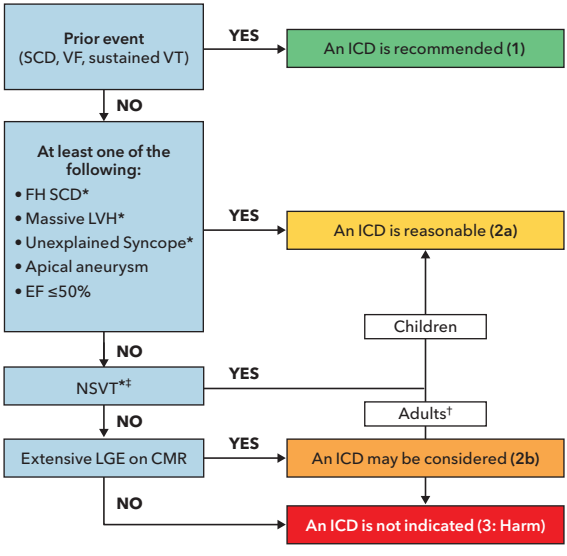
CMR indicates cardiovascular magnetic resonance; ICD, implantable cardioverter-defibrillator; LGE, late gadolinium enhancement; LV, left ventricular; LVH, left ventricular hypertrophy; LVOTO, left ventricular outflow tract obstruction; NSVT, nonsustained ventricular tachycardia; and SCD, sudden cardiac death.

Recommendations for SCD Risk Assessment Referenced studies that support the recommendations are summarized in Online Data Supplement 11.		
COR	**LOE**	**RECOMMENDATIONS**
1	B-NR	1. In patients with HCM, a comprehensive, systematic noninvasive SCD risk assessment at initial evaluation and every 1 to 2 years thereafter is recommended and should include evaluation of these risk factors: a. Personal history of cardiac arrest or sustained ventricular arrhythmias; b. Personal history of syncope suspected by clinical history to be arrhythmic; c. Family history in close relative of premature HCM-related sudden death, cardiac arrest, or sustained ventricular arrhythmias; d. Maximal LV wall thickness, EF, LV apical aneurysm; e. NSVT episodes on continuous ambulatory electrocardiographic monitoring.
1	B-NR	2. For patients with HCM who are not otherwise identified as high risk for SCD, or in whom a decision to proceed with ICD implantation remains uncertain after clinical assessment that includes personal/family history, echocardiography, and ambulatory electrocardiographic monitoring, CMR imaging is beneficial to assess for maximum LV wall thickness, EF, LV apical aneurysm, and extent of myocardial fibrosis with LGE.
2a	B-NR	3. For patients who are ≥ 16 years of age with HCM, it is reasonable to obtain echocardiography-derived left atrial diameter and maximal LVOT gradient to aid in calculating an estimated 5-year sudden death risk that may be useful during shared decision-making for ICD placement.

Recommendations for Selection of ICD Device Type Referenced studies that support the recommendations are summarized in Online Data Supplement 13.		
COR	**LOE**	**RECOMMENDATIONS**
1	B-NR	1. In patients with HCM who are receiving an ICD, either a single chamber transvenous ICD or a subcutaneous ICD is recommended after a shared decision-making discussion that takes into consideration patient preferences, lifestyle, and expected potential need for pacing for bradycardia or VT termination.
1	B-NR	2. In patients with HCM who are receiving an ICD, single-coil ICD leads are recommended in preference to dual-coil leads.
2a	B-NR	3. In patients with HCM who are receiving an ICD, dual-chamber ICDs are reasonable for patients with a need for atrial or atrioventricular sequential pacing for bradycardia/conduction abnormalities, or as an attempt to relieve symptoms of obstructive HCM (most commonly in patients >65 years of age).
2a	C-LD	4. In selected adult patients with nonobstructive HCM receiving an ICD who have NYHA class II to ambulatory class IV HF, left bundle branch block (LBBB), and LV ejection fraction (LVEF) <50%, cardiac resynchronization therapy (CRT) for symptom reduction is reasonable.
2b	C-LD	5. In patients with HCM in whom a decision has been made for ICD implantation and who have paroxysmal atrial tachycardias or AF, dual-chamber ICDs may be reasonable, but this decision must be balanced against higher complication rates of dual-chamber devices.

5 *(Continued)*

Figure: ICD Patient Selection



*ICD decisions in pediatric patients with HCM are based on ≥1 of these major risk factors: family history of HCM SCD, NSVT on ambulatory monitor, massive LVH, and unexplained syncope.
†In patients >16 years of age, 5-year risk estimates can be considered to fully inform patients during shared decision-making discussions.
‡It would seem most appropriate to place greater weight on frequent, longer, and faster runs of NSVT. CMR indicates cardiovascular magnetic resonance; EF, ejection fraction; FH, family history; HCM, hypertrophic cardiomyopathy; ICD, implantable cardioverter-defibrillator; LGE, late gadolinium enhancement; LVH, left ventricular hypertrophy; NSVT, nonsustained ventricular tachycardia; SCD, sudden cardiac death; VF, ventricular fibrillation; and VT, ventricular tachycardia.

6 Several newer studies have found that not all adult SCD risk factors are important for children but ICD implantation decisions in children are still best addressed at HCM centers.

COR	LOE	RECOMMENDATIONS
2a	B-NR	4. For children with HCM who have ≥1 conventional risk factors, including unexplained syncope, massive LVH, NSVT, or family history of early HCM-related SCD, ICD placement is reasonable after considering the relatively high complication rates of long-term ICD implantation in younger patients.
2b	C-LD	7. In select pediatric patients with HCM in whom risk stratification is otherwise less certain, it may be useful to consider additional factors such as extensive LGE on contrast-enhanced CMR imaging and systolic dysfunction in risk stratification.

7 Procedures to reduce heart thickness (SRT, septal reduction therapies) are getting safer and more effective when performed by experienced HCM teams at dedicated centers.

COR	LOE	RECOMMENDATIONS
1	C-LD	1. In patients with HCM in whom SRT is indicated, the procedure should be performed at experienced centers (comprehensive or primary HCM centers) with demonstrated excellence in clinical outcomes for these procedures.

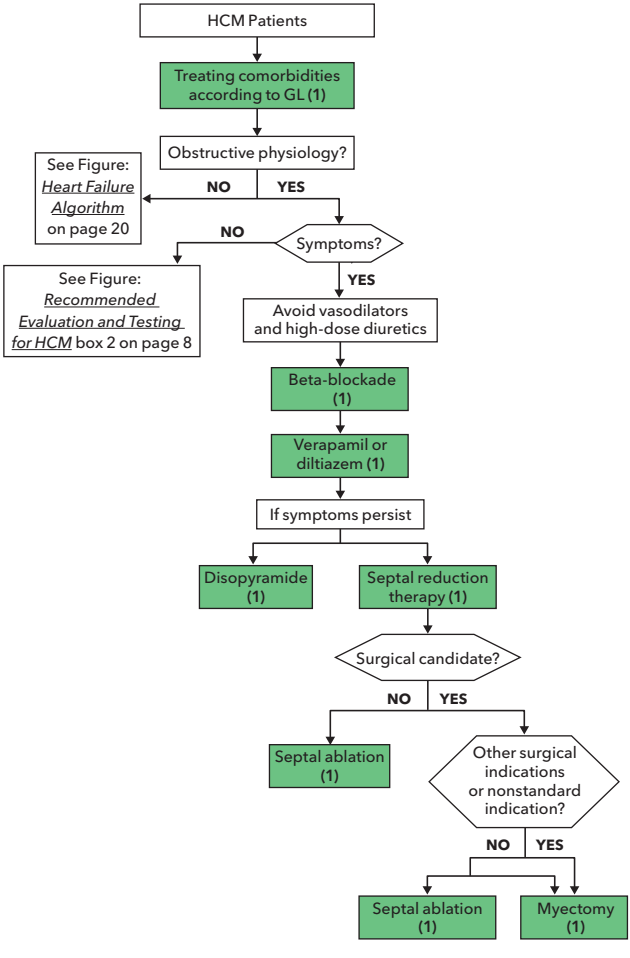
Recommendations for Invasive Treatment of Symptomatic Patients with Obstructive HCM
Referenced studies that support the recommendations are summarized in Online Data Supplement 15

COR	LOE	RECOMMENDATIONS
1	B-NR	1. In patients with obstructive HCM who remain severely symptomatic despite GDMT, SRT in eligible patients,* performed at experienced centers,† is recommended for relieving LVOTO.
1	B-NR	2. In symptomatic patients with obstructive HCM who have associated cardiac disease requiring surgical treatment (e.g., associated anomalous papillary muscle, markedly elongated anterior mitral leaflet, intrinsic mitral valve disease, multivessel CAD, valvular aortic stenosis), surgical myectomy, performed at experienced centers,† is recommended.
1	C-LD	3. In adult patients with obstructive HCM who remain severely symptomatic, despite GDMT and in whom surgery is contraindicated or the risk is considered unacceptable because of serious comorbidities or advanced age, alcohol septal ablation in eligible patients,* performed at experienced centers,† is recommended.
2b	B-NR	4. In patients with obstructive HCM, earlier (NYHA class II) surgical myectomy performed at comprehensive HCM centers may be reasonable in the presence of additional clinical factors, including: a. Severe and progressive pulmonary hypertension thought to be attributable to LVOTO or associated MR; b. Left atrial enlargement with ≥1 episodes of symptomatic AF; c. Poor functional capacity attributable to LVOTO as documented on treadmill exercise testing; d. Children and young adults with very high resting LVOT gradients (>100 mm Hg).
2b	C-LD	5. For severely symptomatic patients with obstructive HCM, SRT in eligible patients,* performed at experienced centers†, may be considered as an alternative to escalation of medical therapy after shared decision-making including risks and benefits of all treatment options.
3: Harm	C-LD	6. For patients with HCM who are asymptomatic and have normal exercise capacity, SRT is not recommended.
3: Harm	B-NR	7. For symptomatic patients with obstructive HCM in whom SRT is an option, mitral valve replacement should not be performed for the sole purpose of relief of LVOTO.

*General eligibility criteria for septal reduction therapy: a) Clinical: Severe dyspnea or chest pain (usually NYHA functional class III or class IV), or occasionally other exertional symptoms (e.g., syncope, near syncope), when attributable to LVOTO, that interferes with everyday activity or quality of life despite optimal medical therapy. b) Hemodynamic: Dynamic LVOT gradient at rest or with physiologic provocation with approximate peak gradient of ≥50 mm Hg, associated with septal hypertrophy and SAM of mitral valve. c) Anatomic: Targeted anterior septal thickness sufficient to perform the procedure safely and effectively in the judgment of the individual operator.

†Comprehensive or primary HCM centers with demonstrated excellence in clinical outcomes for these procedures.

Figure: Management of Symptoms in Patients with HCM



GL indicates guideline; HCM, hypertrophic cardiomyopathy; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; and SRT, septal reduction therapy.

8 Patients with both HCM and atrial fibrillation are at an increased risk of stroke so anticoagulants (DOACs) should be the default treatment option regardless of risk scores.

Recommendations for Management of Atrial Fibrillation
Referenced studies that support the recommendations are summarized in Online Data Supplement 16.

COR	LOE	RECOMMENDATIONS
1	B-NR	1. In patients with HCM and clinical AF, anticoagulation is recommended with direct-acting oral anticoagulants (DOAC) as first-line option and vitamin K antagonists as second-line option, independent of CHA_2DS_2-VASc score.
1	C-LD	2. In patients with HCM and subclinical AF detected by internal or external cardiac device or monitor of >24 hours' duration for a given episode, anticoagulation is recommended with DOAC as first-line option and vitamin K antagonists as second-line option, independent of CHA_2DS_2-VASc score.
1	C-LD	3. In patients with AF in whom rate control strategy is planned, either beta-blockers, verapamil, or diltiazem are recommended, with the choice of agents according to patient preferences and comorbid conditions.
2a	C-LD	4. In patients with HCM and subclinical AF detected by internal or external device or monitor, of >5 minutes' but <24 hours' duration for a given episode, anticoagulation with DOAC as first-line option and vitamin K antagonists as second-line option can be beneficial, taking into consideration duration of AF episodes, total AF burden, underlying risk factors, and bleeding risk.
2a	B-NR	5. In patients with HCM and poorly tolerated AF, a rhythm control strategy with cardioversion or antiarrhythmic drugs can be beneficial with the choice of an agent according to AF symptom severity, patient preferences, and comorbid conditions.
2a	B-NR	6. In patients with HCM and symptomatic AF, as part of a AF rhythm control strategy, catheter ablation for AF can be effective when drug therapy is ineffective, contraindicated, or not the patient's preference.
2a	B-NR	7. In patients with HCM and AF who require surgical myectomy, concomitant surgical AF ablation procedure can be beneficial for AF rhythm control.

Table: Antiarrhythmic Drug Therapy Options for Patients With HCM and AF

Arrhythmic Drug	Efficacy for AF	Side Effects	Toxicities	Use in HCM
Disopyramide	Modest	-Anticholinergic -HF	Prolonged QTc	Particularly with early onset AF
Flecainide and propafenone	?		Proarrhythmia	Not generally recommended in the absence of an ICD
Sotalol	Modest	-Fatigue -Bradycardia	Prolonged QTc Prolonged QTc Proarrhythmia	Reasonable
Dofetilide	Modest	Headache	Proarrhythmia	Reasonable
Dronedarone	Low	HF	Prolonged QTc	?
Amiodarone	Modest-high	Bradycardia	Liver, lung, thyroid, skin, neurologic	Reasonable

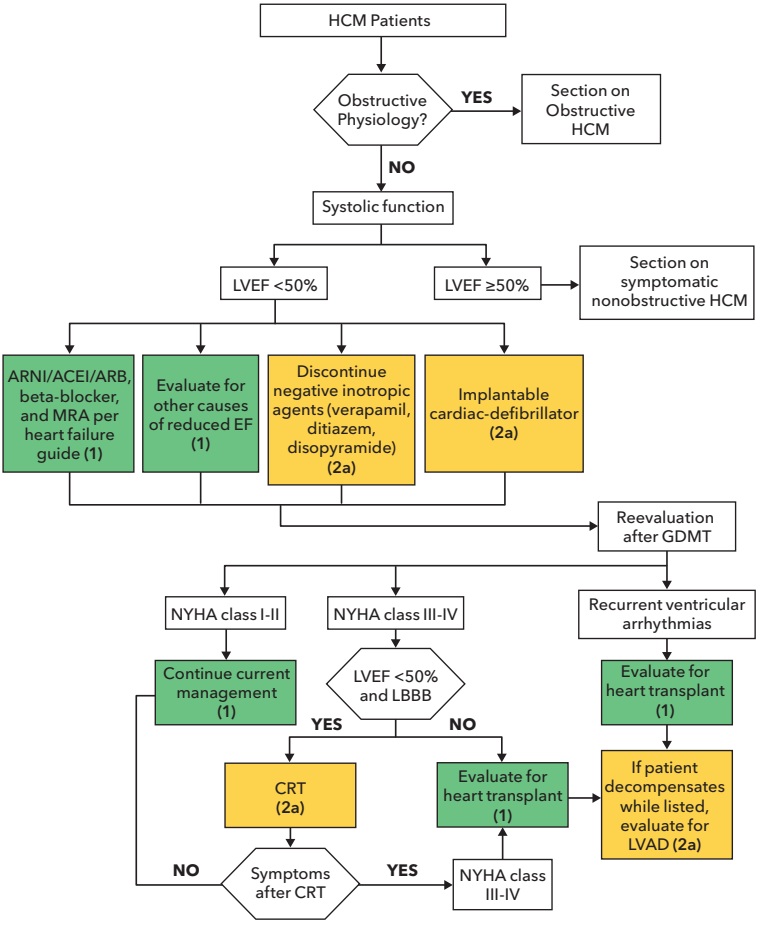
AF indicates atrial fibrillation; HCM, hypertrophic cardiomyopathy; HF, heart failure; and ICD, implantable cardioverter-defibrillator.

9 Patients with HCM and an ejection fraction (EF) of <50% are at increased risk for SCD so GDMT should be initiated at LVEF<50% instead of LVEF<40% as is done in other HF populations.

Recommendations for Patients With HCM and Advanced HF
Referenced studies that support the recommendations are summarized in Online Data Supplements 18.

COR	LOE	RECOMMENDATIONS
1	C-LD	1. In patients with HCM who develop systolic dysfunction with an LVEF <50%, guideline-directed therapy for HF with reduced EF is recommended.
1	C-LD	2. In patients with HCM and systolic dysfunction, diagnostic testing to assess for concomitant causes of systolic dysfunction (such as CAD) is recommended.
1	B-NR	3. In patients with nonobstructive HCM and advanced HF (NYHA functional class III to class IV despite guideline-directed therapy), CPET should be performed to quantify the degree of functional limitation and aid in selection of patients for heart transplantation or mechanical circulatory support.
1	B-NR	4. In patients with nonobstructive HCM and advanced HF (NYHA class III to class IV despite guideline-directed therapy) or with life-threatening ventricular arrhythmias refractory to maximal guideline-directed therapy, assessment for heart transplantation in accordance with current listing criteria is recommended.
2a	C-EO	5. For patients with HCM who develop systolic dysfunction (LVEF <50%), it is reasonable to discontinue previously indicated negative inotropic agents (specifically, verapamil, diltiazem, or disopyramide).
2a	B-NR	6. In patients with nonobstructive HCM and advanced HF (NYHA functional class III to class IV despite GDMT) who are candidates for heart transplantation, continuous-flow LVAD therapy is reasonable as a bridge to heart transplantation.
2a	C-LD	7. In patients with HCM and LVEF <50%, ICD placement can be beneficial.
2a	C-LD	8. In patients with HCM and LVEF <50%, NYHA functional class II to class IV symptoms despite guideline-directed therapy, and LBBB, CRT can be beneficial to improve symptoms.

Figure: Heart Failure Algorithm



ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitors; CRT, cardiac resynchronization therapy; EF, ejection fraction; GDMT, guideline-directed management and therapy; HCM, hypertrophic cardiomyopathy; LBBB, left bundle branch block; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; MRA, mineralocorticoid receptor antagonist; and NYHA, New York Heart Association.

10 New evidence shows that moderate exercise is not harmful for patients with HCM. In addition, participation in competitive sports may be considered after a comprehensive evaluation and shared decision-making conversation.

Recommendations for Sports and Activity
Referenced studies that support the recommendations are summarized in Online Data Supplement 19

COR	LOE	RECOMMENDATIONS
1	B-NR	1. For most patients with HCM, mild- to moderate-intensity recreational* exercise is beneficial to improve cardiorespiratory fitness, physical functioning, and quality of life, and for their overall health in keeping with physical activity guidelines for the general population.
1	C-EO	2. For athletes with HCM, a comprehensive evaluation and shared discussion of potential risks of sports participation by an expert provider is recommended.
2a	C-EO	3. For most patients with HCM, participation in low-intensity competitive sports is reasonable.
2a	C-LD	4. In individuals who are genotype-positive, phenotype-negative for HCM, participation in competitive athletics of any intensity is reasonable.
2b	C-LD	5. For patients with HCM, participation in high-intensity recreational activities or moderate- to high-intensity competitive sports activities may be considered after a comprehensive evaluation and shared discussion, repeated annually with an expert provider who conveys that the risk of sudden death and ICD shocks may be increased, and with the understanding that eligibility decisions for competitive sports participation often involve third parties (e.g., team physicians, consultants, and other institutional leadership) acting on behalf of the schools or teams.
3: Harm	B-NR	6. In patients with HCM, ICD placement for the sole purpose of participation in competitive athletics should not be performed.

*Recreational exercise is done for the purpose of leisure with no requirement for systematic training and without the purpose to excel or compete against others.

The Accelerating Innovation for Medical Excellence in Hypertrophic Cardiomyopathy *(AIME HCM)* initiative is designed to increase the awareness and understanding of HCM, activate clinicians and optimize disease management to improve outcomes.

For additional information related to ***Accelerating Innovation for Medical Excellence in Hypertrophic Cardiomyopathy (AIME HCM)***, scan this QR code or visit: ***ACC.org/HCM.***

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