2020 Guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy

GUIDELINES MADE SIMPLE

A Selection of Tables and Figures

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AMERICAN COLLEGE of CARDIOLOGY

2020 Guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy

A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines

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The ACC/AHA Joint Committee on Clinical Practice Guidelines has commissioned this guideline to address comprehensive evaluation and management of adults and children with hypertrophic cardiomyopathy (HCM). Diagnostic modalities such as electrocardiography, imaging and genetic testing, and management of patients include medical therapies, septal reduction therapies, sudden cardiac death (SCD) risk assessment/prevention, and lifestyle considerations such as participation in activities/sports, occupation, and pregnancy.

The following resource contains tables and figures from the 2020 Guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy. The resource is only an excerpt from the Guideline and the full publication should be reviewed for more tables and figures as well as important context.

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Class of Recommendation (COR)/ Level of Evidence (LOE) Table

CLASS (STRENGTH) OF RECOMMENDATION	
CLASS 1 (STRONG)	**Benefit >>> Risk**
Suggested phrases for writing recommendations: • Is recommended • Is indicated/useful/effective/beneficial • Should be performed/administered/other • Comparative-Effectiveness Phrases†: – Treatment/strategy A is recommended/indicated in preference to treatment B – Treatment A should be chosen over treatment B	
CLASS 2a (MODERATE)	**Benefit >> Risk**
Suggested phrases for writing recommendations: • Is reasonable • Can be useful/effective/beneficial • Comparative-Effectiveness Phrases†: – Treatment/strategy A is probably recommended/indicated in preference to treatment B – It is reasonable to choose treatment A over treatment B	
CLASS 2b (WEAK)	**Benefit ≥ Risk**
Suggested phrases for writing recommendations: • May/might be reasonable • May/might be considered • Usefulness/effectiveness is unknown/unclear/uncertain or not well-established	
CLASS 3: No Benefit (MODERATE) **(Generally, LOE A or B use only)**	**Benefit = Risk**
Suggested phrases for writing recommendations: • Is not recommended • Is not indicated/useful/effective/beneficial • Should not be performed/administered/other	
Class 3: Harm (STRONG)	**Risk > Benefit**
Suggested phrases for writing recommendations: • Potentially harmful • Causes harm • Associated with excess morbidity/mortality • Should not be performed/administered/other	

LEVEL (QUALITY) OF EVIDENCE‡	
LEVEL A	
• High-quality evidence‡ from more than 1 RCT • Meta-analyses of high-quality RCTs • One or more RCTs corroborated by high-quality registry studies	
LEVEL B-R	**(Randomized)**
• Moderate-quality evidence‡ from 1 or more RCTs • Meta-analyses of moderate-quality RCTs	
LEVEL B-NR	**(Nonrandomized)**
• Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies • Meta-analyses of such studies	
LEVEL C-LD	**(Limited Data)**
• Randomized or nonrandomized observational or registry studies with limitations of design or execution • Meta-analyses of such studies • Physiological or mechanistic studies in human subjects	
LEVEL C-EO	**(Expert Opinion)**
• Consensus of expert opinion based on clinical experience	

COR and LOE are determined independently (any COR may be paired with any LOE).

A recommendation with LOE C does not imply that the recommendation is weak. Many important clinical questions addressed in guidelines do not lend themselves to clinical trials. Although RCTs are unavailable, there may be a very clear clinical consensus that a particular test or therapy is useful or effective.

* The outcome or result of the intervention should be specified (an improved clinical outcome or increased diagnostic accuracy or incremental prognostic information).

† For comparative-effectiveness recommendations (COR 1 and 2a; LOE A and B only), studies that support the use of comparator verbs should involve direct comparisons of the treatments or strategies being evaluated.

‡ The method of assessing quality is evolving, including the application of standardized, widely-used, and preferably validated evidence grading tools; and for systematic reviews, the incorporation of an Evidence Review Committee.

COR indicates Class of Recommendation; EO, expert opinion; LD, limited data; LOE, Level of Evidence; NR, nonrandomized; R, randomized; and RCT, randomized controlled trial.

(Updated May 2019)

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Master Abbreviation List

Abbreviation	Meaning/Phrase
AF	atrial fibrillation
CAD	coronary artery disease
CMR	cardiovascular magnetic resonance
CPET	cardiopulmonary exercise test
CRT	cardiac resynchronization therapy
DOAC	direct-acting oral anticoagulants
EF	ejection fraction
GDMT	guideline-directed management and therapy
HCM	hypertrophic cardiomyopathy
HF	heart failure
ICD	implantable cardioverter-defibrillator
LAMP2	lysosome-associated membrane protein-2
LBBB	left bundle branch block
LGE	late gadolinium enhancement
LV	left ventricular
LVAD	left ventricular assist device
LVEF	left ventricular ejection fraction
LVH	left ventricular hypertrophy

Abbreviation	Meaning/Phrase
LVOT	left ventricular outflow tract
LVOTO	left ventricular outflow tract obstruction
MET	metabolic equivalent
MR	mitral regurgitation
NSVT	nonsustained ventricular tachycardia
NYHA	New York Heart Association
RCT	randomized controlled trial
RV	right ventricular
SAM	systolic anterior motion
SCAF	subclinical AF
SCD	sudden cardiac death
SRT	septal reduction therapy
TEE	trans-esophageal echocardiogram
TTE	transthoracic echocardiogram
VF	ventricular fibrillation
VT	ventricular tachycardia

Top 10 Take-Home Messages *(1 of 2)*

1 **Shared decision-making,** a dialogue between patients and their care team that includes full disclosure of all testing and treatment options, discussion of the risks and benefits of those options and, importantly, engagement of the patient to express their own goals, is particularly relevant in the management of conditions such as hypertrophic cardiomyopathy (HCM).

2 Athough the primary cardiology team can initiate evaluation, treatment, and longitudinal care, **referral to multidisciplinary HCM centers** with graduated levels of expertise can be important to optimizing care for patients with HCM. Challenging treatment decisions—where reasonable alternatives exist, where the strength of recommendation is weak (e.g., any Class 2b decision) or is particularly nuanced, and for invasive procedures that are specific to patients with HCM—represent crucial opportunities to refer patients to these HCM centers.

3 Counseling patients with HCM regarding the potential for **genetic transmission of HCM** is one of the cornerstones of care. Screening first-degree family members of patients with HCM, using either genetic testing or an imaging/electrocardiographic surveillance protocol, can begin at any age and can be influenced by specifics of the patient/family history and family preference. As screening recommendations for family members hinge on the pathogenicity of any detected variants, the reported pathogenicity should be reconfirmed every 2 to 3 years

4 Optimal care for patients with HCM requires **cardiac imaging** to confirm the diagnosis, characterize the pathophysiology for the individual, and identify risk markers that may inform decisions regarding interventions for left ventricular outflow tract obstruction and sudden cardiac death (SCD) prevention. Echocardiography continues to be the foundational imaging modality for patients with HCM. Cardiovascular magnetic resonance imaging will also be helpful in many patients, especially those in whom there is diagnostic uncertainty, poor echocardiographic imaging windows, or where uncertainty persists regarding decisions around implantable cardioverter-defibrillator (ICD) placement.

5 Assessment of an **individual patient's risk for SCD** continues to evolve as new markers emerge (e.g., apical aneurysm, decreased left ventricular systolic function, and extensive gadolinium enhancement). In addition to a full accounting of an individual's risk markers, communication with patients regarding not just the presence of risk markers but also the magnitude of their individualized risk is key. This enables the informed patient to fully participate in the decision-making regarding ICD placement, which incorporates their own level of risk tolerance and treatment goals.

"Top Ten Messages" is continued in the next page.

Top 10 Take-Home Messages *(2 of 2)*

6 The risk factors for **SCD in children with HCM** carry different weights than those observed in adult patients; they vary with age and must account for different body sizes. Coupled with the complexity of placing ICDs in young patients with anticipated growth and a higher risk of device complications, the threshold for ICD implantation in children often differs from adults. These differences are best addressed at primary or comprehensive HCM centers with expertise in children with HCM.

7 **Septal reduction therapies** (surgical septal myectomy and alcohol septal ablation), when performed by experienced HCM teams at dedicated centers, continue to improve in safety and efficacy such that earlier intervention may be possible in select patients with drug-refractory or severe outflow tract obstruction causing signs of cardiac decompensation. Given the data on the significantly improved outcomes at comprehensive HCM centers, these decisions represent an optimal referral opportunity.

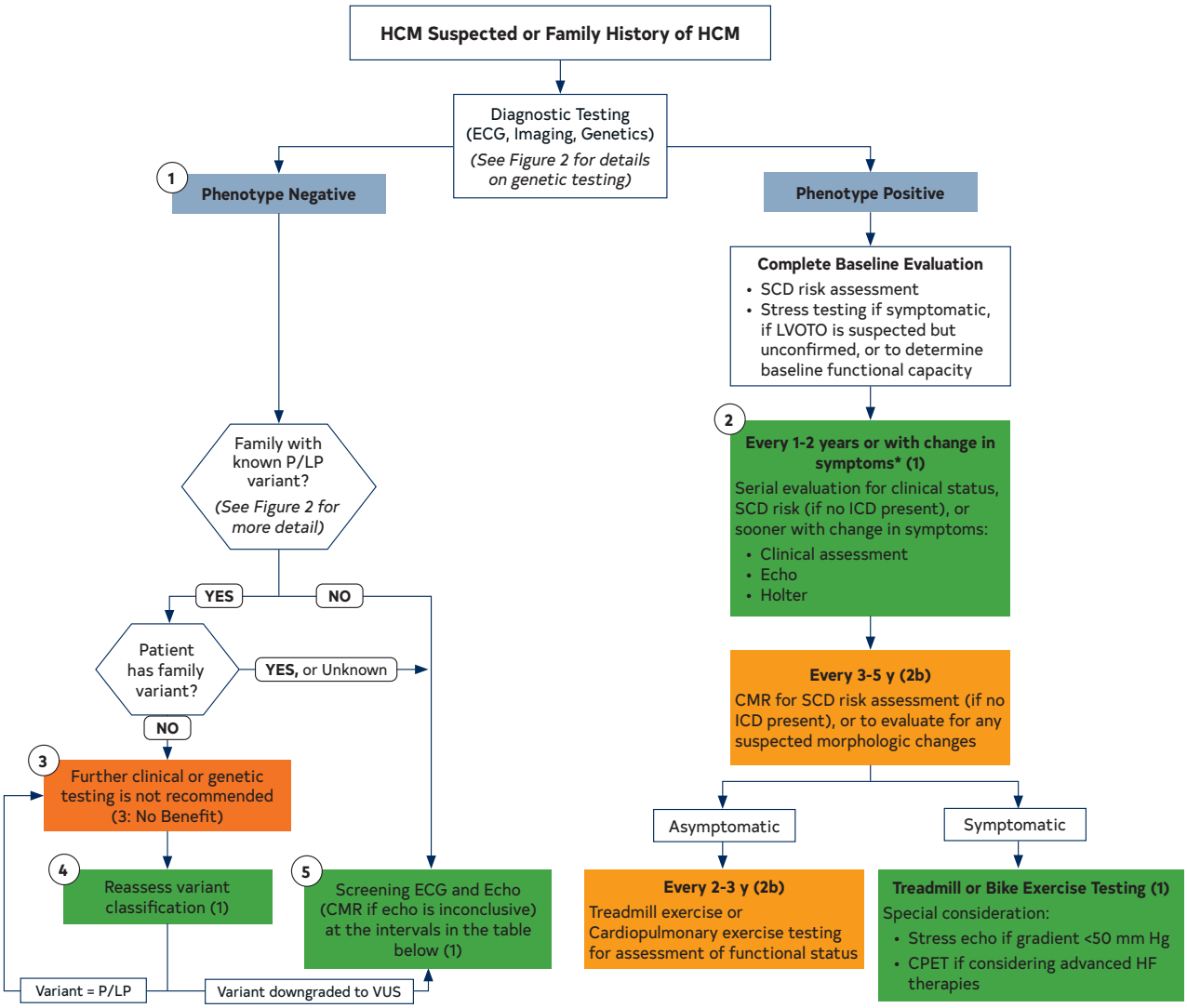
8 **Patients with HCM and persistent or paroxysmal atrial fibrillation** have a sufficiently increased risk of stroke such that oral anticoagulation with direct oral anticoagulants (or alternatively warfarin) should be considered the default treatment option independent of the CHA2DS2VASc score. As rapid atrial fibrillation is often poorly tolerated in patients with HCM, maintenance of sinus rhythm and rate control are key pursuits in successful treatment.

9 **Heart failure symptoms in patients with HCM,** in the absence of left ventricular outflow tract obstruction, should be treated similarly to other patients with heart failure symptoms, including consideration of advanced treatment options (e.g., cardiac resynchronization therapy, left ventricular assist device, transplantation). In patients with HCM, an ejection fraction <50% connotes significantly impaired systolic function and identifies individuals with poor prognosis and who are at increased risk for SCD.

10 Increasingly, data affirm that the **beneficial effects of exercise** on general health can be extended to patients with HCM. Healthy recreational exercise (moderate intensity) has not been associated with increased risk of ventricular arrhythmia events in recent studies. Whether an individual patient with HCM wishes to pursue more rigorous exercise/training is dependent on a comprehensive shared discussion between that patient and their expert HCM care team regarding the potential risks of that level of training/participation but with the understanding that exercise-related risk cannot be individualized for a given patient.

Genetic Testing and Evaluation

Figure 1. Recommended Evaluation and Testing for HCM



Screening Asymptomatic First-Degree Relatives of Patients With HCM		
Age of First-Degree Relative	**Initiation of Screening**	**Surveillance Interval**
Children and adolescents from genotype-positive family and/or family with early onset HCM	At the time of diagnosis in another family member	Every 1-2 y
All other children and adolescents	At any time after the diagnosis in the family, but no later than puberty	Every 2-3 y
Adults	At the time of diagnosis in another family member	Every 3-5 y

Table 6. Screening With Electrocardiography and 2D Echocardiography in Asymptomatic Family Members*

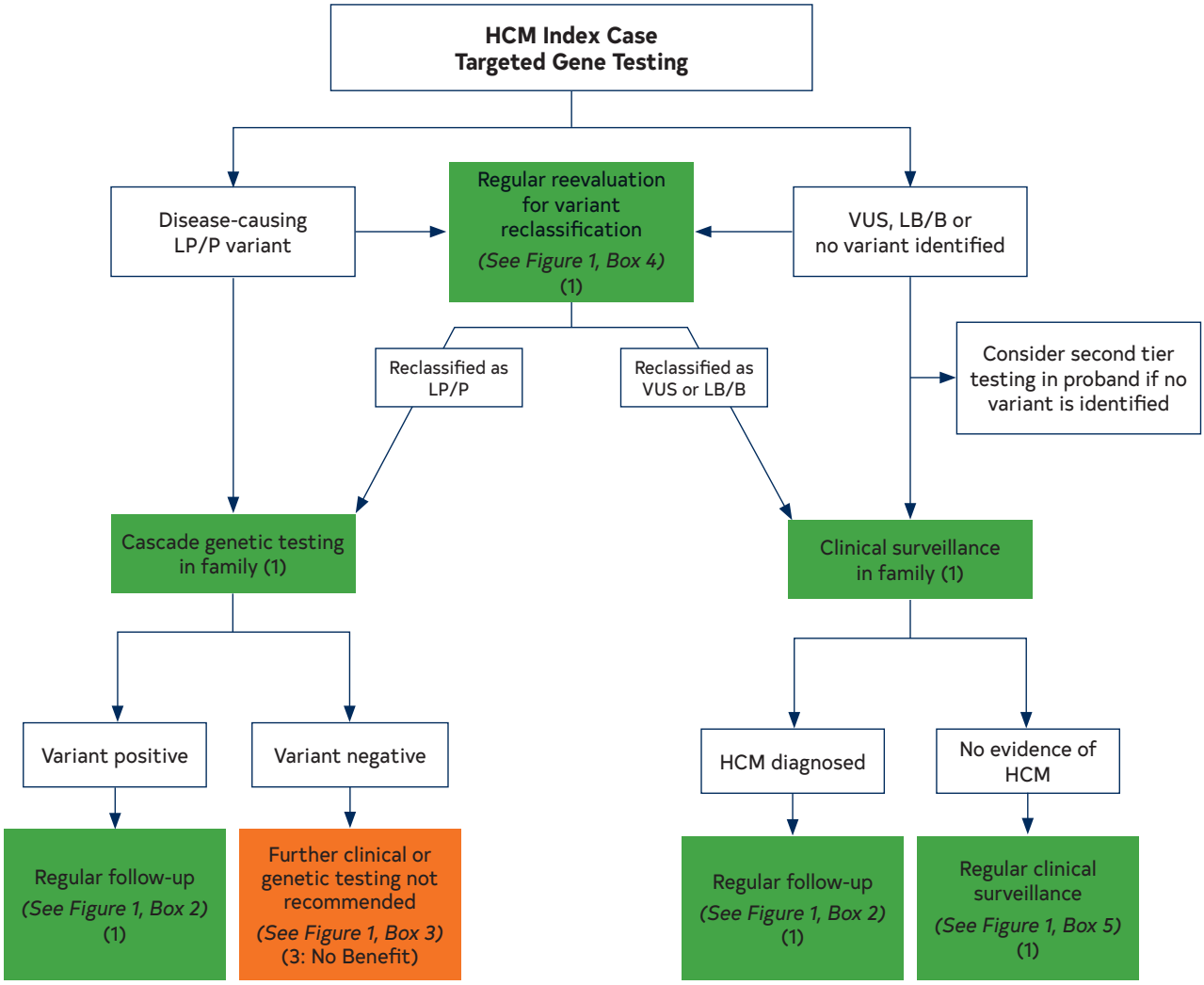
Age of First-Degree Relative	Initiation of Screening	Repeat ECG, Echo
Pediatric		
Children and adolescents from genotype-positive families, and families with early onset disease	At the time HCM is diagnosed in another family member	Every 1-2 y
All other pediatric	At any time after HCM is diagnosed in a 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 judgment. Screening interval may be modified (e.g., at onset of new symptoms or in families with a malignant clinical course or late-onset HCM).

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

Determining pathogenicity of variants relies on a weight of collective evidence based on American College of Medical Genetics and Genomics criteria and may change over time.

Figure 2. Genetic Testing Process in HCM



Diagnosis

Table 5. Clinical Features in Patients With "HCM Phenocopies (Mimics)"

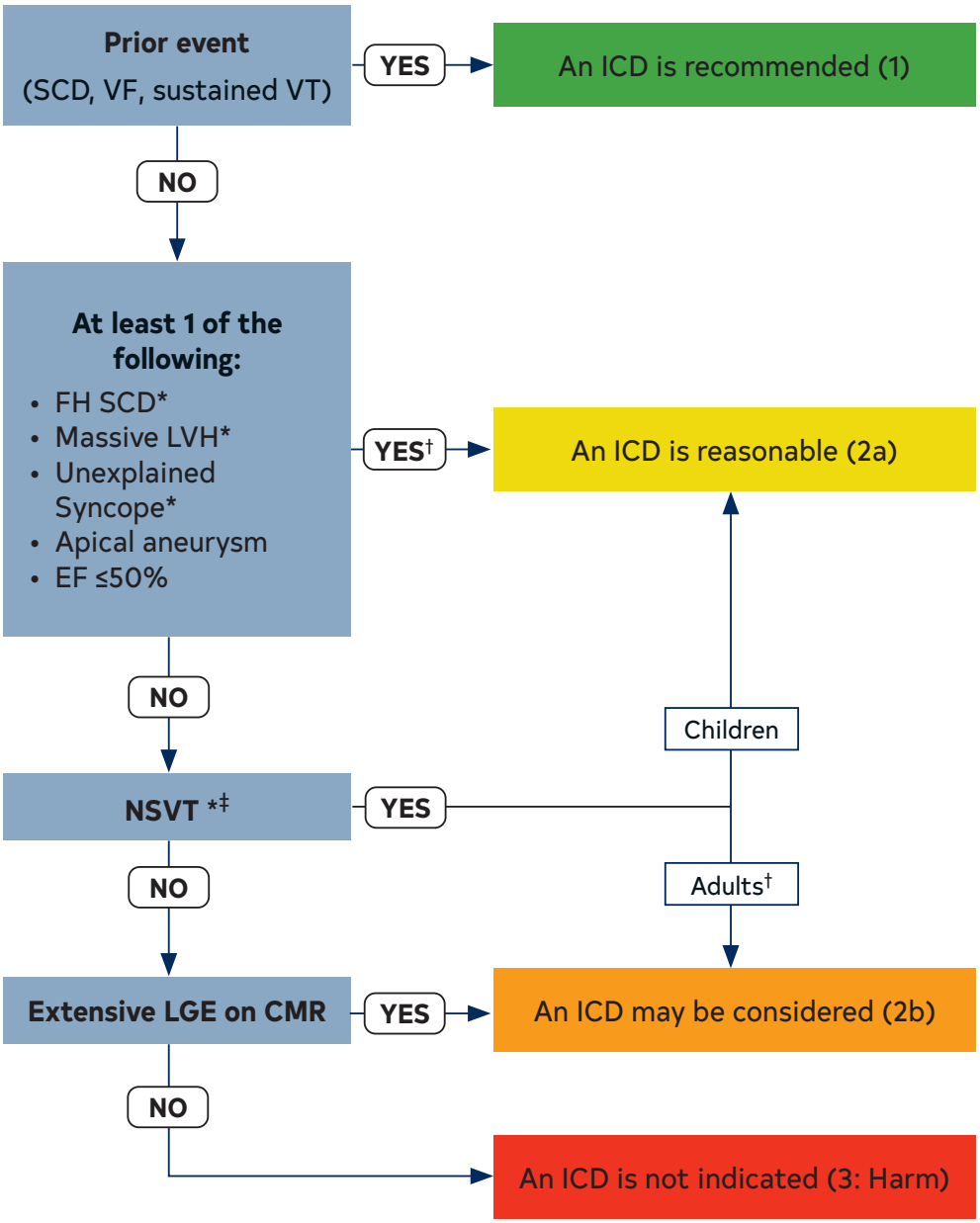
Typical Presentation Age	Systemic Features	Possible Etiology	Diagnostic Approach
Infants (0-12 mo) and toddlers	Dysmorphic features, failure to thrive, metabolic acidosis	· RASopathies · Glycogen storage diseases, other metabolic or mitochondrial diseases · Infant of a mother with diabetes	· Geneticist assessment · Newborn metabolic screening · Specific metabolic assays · Genetic testing
Early childhood	Delayed or abnormal cognitive development, visual or hearing impairment	· RASopathies · Mitochondrial diseas	· 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

Sudden Cardiac Death Risk Assessment

Table 7. Established Clinical Risk Factors for HCM Sudden Death Risk Stratification

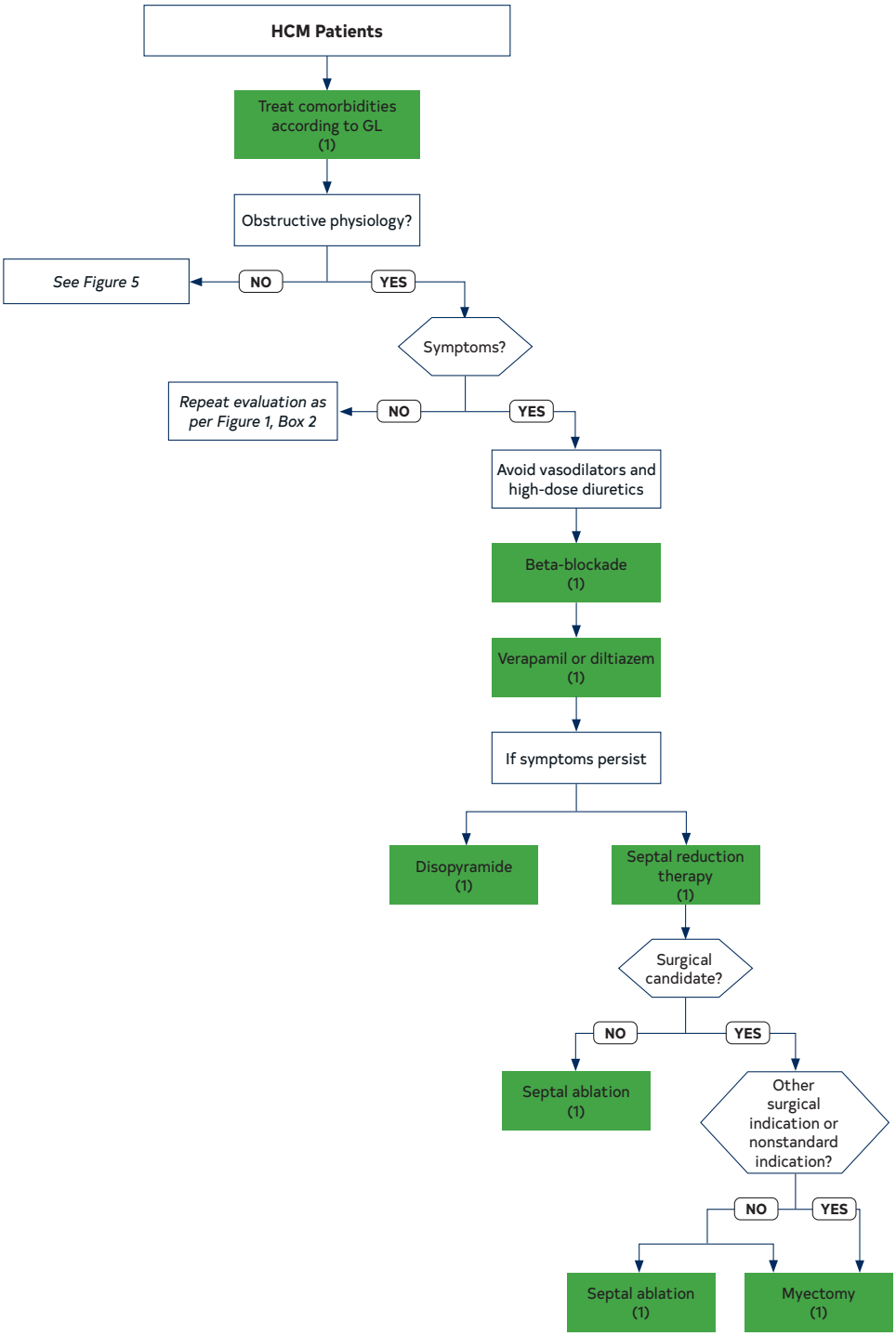
Family history of sudden death from HCM	Sudden death judged definitively or likely attributable to HCM in ≥1 first-degree or close relatives who are ≤50 years of age. Close relatives would generally be second-degree relatives; however, multiple SCDs in tertiary relatives should also be considered relevant.
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	Apical 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.

Figure 3. ICD Patient Selection



Management of Symptoms

Figure 4. Management of Symptoms in Patients With HCM



Recommendations for Pharmacologic Management of Patients With Obstructive HCM

COR	LOE	Recommendations
1	B-NR	1. In patients with obstructive HCM and symptoms* attributable to LVOTO, nonvasodilating beta-blockers, titrated to effectiveness or maximally tolerated doses, are recommended.
1	Verapamil B-NR Diltiazem C-LD	2. In patients with obstructive HCM and symptoms* attributable to LVOTO, for whom beta-blockers are ineffective or not tolerated, substitution with non-dihydropyridine calcium channel blockers (e.g., verapamil, diltiazem) is recommended.
1	B-NR	3. For patients with obstructive HCM who have persistent severe symptoms* attributable to LVOTO despite beta-blockers or non-dihydropyridine calcium channel blockers, either adding disopyramide in combination with 1 of the other drugs, or SRT performed at experienced centers,† is recommended.
1	C-LD	4. For patients with obstructive HCM and acute hypotension who do not respond to fluid administration, intravenous phenylephrine (or other vasoconstrictors without inotropic activity), alone or in combination with beta-blocking drugs, is recommended.
2b	C-EO	5. For patients with obstructive HCM and persistent dyspnea with clinical evidence of volume overload and high left- sided filling pressures despite other HCM GDMT, cautious use of low-dose oral diuretics may be considered.
2b	C-EO	6. For patients with obstructive HCM, discontinuation of vasodilators (e.g., angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, dihydropyridine calcium channel blockers) or digoxin may be reasonable because these agents can worsen symptoms caused by dynamic outflow tract obstruction.
3: Harm	C-LD	7. For patients with obstructive HCM and severe dyspnea at rest, hypotension, very high resting gradients (e.g., >100 mm Hg), as well as all children <6 weeks of age, verapamil is potentially harmful.

*Symptoms include effort-related dyspnea or chest pain; and occasionally other exertional symptoms (e.g., syncope, near syncope) that are attributed to LVOTO and interfere with everyday activity or quality of life.

†Comprehensive or primary HCM centers with demonstrated excellence in clinical outcomes for these procedures (Table 3 and 4).

Table 3. 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.

Table 4. 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%

Sports Participation

Recommendations for Sports and Activity

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.

Heart Failure Symptoms in Patients with HCM

Figure 5. Heart Failure Algorithm