AHA Clinical Update

ADAPTED FROM:

2024 AHA/ACC/AMSSM/HRS/PACES/SCMR Guideline for the Management of Hypertrophic Cardiomyopathy
Table 1. Applying Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care

<table>
<thead>
<tr>
<th>CLASS (STRENGTH) OF RECOMMENDATION</th>
<th>Benefit &gt;&gt;&gt; Risk</th>
<th>LEVEL (QUALITY) OF EVIDENCE‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (STRONG)</td>
<td>Benefit &gt;&gt;&gt; Risk</td>
<td>LEVEL A</td>
</tr>
<tr>
<td>Suggested phrases for writing recommendations:</td>
<td>• Is recommended</td>
<td>• High-quality evidence from more than 1 RCT</td>
</tr>
<tr>
<td>• Is indicated/useful/effective/beneficial</td>
<td></td>
<td>• Meta-analyses of high-quality RCTs</td>
</tr>
<tr>
<td>• Should be performed/administered/other</td>
<td></td>
<td>• One or more RCTs corroborated by high-quality registry studies</td>
</tr>
<tr>
<td>• Comparative-Effectiveness Phrases†:</td>
<td>• Treatment/strategy A is recommended/indicated in preference to treatment B</td>
<td>• Moderate-quality evidence from 1 or more RCTs</td>
</tr>
<tr>
<td>- Treatment/strategy A should be chosen over treatment B</td>
<td></td>
<td>• Meta-analyses of moderate-quality RCTs</td>
</tr>
<tr>
<td>2a (MODERATE)</td>
<td>Benefit &gt;&gt; Risk</td>
<td>LEVEL B-R (Randomized)</td>
</tr>
<tr>
<td>Suggested phrases for writing recommendations:</td>
<td>• Is reasonable</td>
<td>• Moderate-quality evidence from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies</td>
</tr>
<tr>
<td>• Can be useful/effective/beneficial</td>
<td></td>
<td>• Meta-analyses of such studies</td>
</tr>
<tr>
<td>• Comparative-Effectiveness Phrases†:</td>
<td>• Treatment/strategy A is probably recommended/indicated in preference to treatment B</td>
<td></td>
</tr>
<tr>
<td>- It is reasonable to choose treatment A over treatment B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2b (Weak)</td>
<td>Benefit ≥ Risk</td>
<td>LEVEL B-NR (Nonrandomized)</td>
</tr>
<tr>
<td>Suggested phrases for writing recommendations:</td>
<td>• May/might be reasonable</td>
<td>• Moderate-quality evidence from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies</td>
</tr>
<tr>
<td>• May/might be considered</td>
<td></td>
<td>• Meta-analyses of such studies</td>
</tr>
<tr>
<td>• Usefulness/effectiveness is unknown/unclear/uncertain or not well-established</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3: No Benefit (MODERATE)</td>
<td>Benefit = Risk</td>
<td>LEVEL C-LD (Limited Data)</td>
</tr>
<tr>
<td>Suggested phrases for writing recommendations:</td>
<td>• Not recommended</td>
<td>• Randomized or nonrandomized observational or registry studies with limitations of design or execution</td>
</tr>
<tr>
<td>• Is not indicated/useful/effective/beneficial</td>
<td></td>
<td>• Meta-analyses of such studies</td>
</tr>
<tr>
<td>• Should not be performed/administered/other</td>
<td></td>
<td>• Physiological or mechanistic studies in human subjects</td>
</tr>
<tr>
<td>3: Harm (STRONG)</td>
<td>Risk &gt; Benefit</td>
<td>LEVEL C-EO (Expert Opinion)</td>
</tr>
<tr>
<td>Suggested phrases for writing recommendations:</td>
<td>• Potentially harmful</td>
<td>• Consensus of expert opinion based on clinical experience.</td>
</tr>
<tr>
<td>• Causes harm</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Associated with excess morbidity/mortality</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Should not be performed/administered/other</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* 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 recommendation (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.
Hypertrophic Cardiomyopathy Prevalence and Characteristics

Inheritance Pattern

Autosomal Dominant

Sex Distribution

Women are diagnosed less often and later

Disease Prevalence

Estimated 1:500

Triggers for Evaluation

Symptoms
Heart Murmur
Abnormal EKG or Imaging
Family history

Differential Diagnosis: Non-HCM Causes of LV Hypertrophy

Underlying SDOH likely drive differences in prevalence, genetic testing, and cardiovascular outcomes by race and ethnicity

Metabolic & Multi-organ Syndromes

RASopathies (Noonan Syndrome)
Glycogen / Lysosomal storage diseases
Cardiac Amyloidosis
Sarcoidosis
Danon disease

Secondary Causes

Athlete’s heart
Uncontrolled Hypertension
Valvular & subvalvular aortic stenosis

Abbreviations: EKG indicates electrocardiogram; SDOH, social determinants of health; and RAS, reticular activating system.
Defining Hypertrophic Cardiomyopathy in 2024

- Characterized by left ventricular hypertrophy
  *Asymmetric septal hypertrophy is most characteristic*
- No other cardiac, systemic or metabolic disease capable of producing the magnitude of increased LV wall thickness present
- Disease-causing variant in a sarcomere gene identified or genetic etiology unresolved

### Diagnostic Criteria in Adults

*2D echocardiography or cardiac MRI*

- Maximal end-diastolic LV wall thickness > 15 mm
- Maximal end-diastolic LV wall thickness 13-14 mm if there is a family history of HCM or a pathogenic sarcomere gene is present

### Diagnostic Criteria in Children

*2D echocardiography or cardiac MRI*

- LV wall thickness z-score > 2.5
- LV wall thickness z-score > 2 if there is a family history of HCM or a pathogenic sarcomere gene is present

**Abbreviations:** 2D indicates two dimensional; MRI, magnetic resonance imaging; mm, millimeter

Adverse Events Associated Hypertrophic Cardiomyopathy

Although some patients with HCM have a normal life expectancy without limiting symptoms, many will have important consequences.

**Abbreviations:** HCM indicates hypertrophic cardiomyopathy.
Pathophysiology of Hypertrophic Cardiomyopathy

- Dynamic LVOT Obstruction
- Myocardial Ischemia
- Atrial and Ventricular Arrhythmias
- Mitral Regurgitation
- Metabolic/Energetic Dysfunction
- Diastolic Dysfunction

Abbreviations: LVOT indicates left ventricular outflow tract.
Pathophysiology of HCM: LV Outflow Tract Obstruction

LVOTO, either at rest or with provocation, is present in many patients with HCM and primarily caused by systolic anterior motion of the mitral valve.

Peak gradient of $\geq 30$ mm Hg is considered indicative of obstruction

Resting or provoked gradients $\geq 50$ mmHg generally considered to be the threshold for advanced pharmacologic or septal reduction therapy in those patients with symptoms refractory to standard management.

LVOTO in HCM is primarily caused by basal septal hypertrophy and systolic anterior motion of the mitral valve

LVOTO in HCM is dynamic and sensitive to ventricular preload, afterload, and contractility

**Abbreviations:** HCM indicates hypertrophic cardiomyopathy; and LVOTO, left ventricular outflow tract.

Pathophysiology of HCM: Diastolic Dysfunction

Features of HCM that contribute to Diastolic Dysfunction

- Abnormal intracellular Ca reuptake
- Excess actin-myosin binding
- Microvascular ischemia
- Altered energetics
- Altered Ventricular Load with High Intracavitary Pressures
- Impaired LV compliance

Diastolic Dysfunction can contribute to:

- Decreased Exercise Capacity
- Heart Failure
- Dyspnea
- Adverse prognosis independent of LVOTO

Abbreviations: HCM indicates hypertrophic cardiomyopathy.

Pathophysiology of HCM: Mitral Valve Abnormalities

Common abnormalities of the Mitral Valve in HCM

- Excessive leaflet length
- Anomalous papillary muscle insertion
- Anteriorly displaced papillary muscles

Mitral Regurgitation occurs

Primarily from leaflet abnormalities

Secondarily from Systolic Anterior Motion

Factors that affect the severity of LVOTO also may affect the degree of MR. Thus, imaging should be performed at rest and with provocation.

Abbreviations: HCM indicates hypertrophic cardiomyopathy; LVOTO, left ventricular outflow tract; MR, mitral regurgitation.

Shared Decision-Making in HCM

Discussions should involve:
- Disclosure of risk and benefits of all screenings and therapies
- Anticipated outcomes of all options
- Goals, concerns and preferences of the patient (and family if the patient is a minor) (Class 1)

Shared decision discussions should be applied to:
- Genetic testing
- Medical and invasive therapies for LVOT obstruction
- Sudden death screening and ICD Implantation
- Participation in high-intensity exercise and competitive sports
- Pregnancy

Abbreviations: HCM indicates hypertrophic cardiomyopathy, and LVOT, left ventricular outflow tract.
Patient Centered Team-Based Care

Cardiologists Outside of HCM Centers:
- Initial and Surveillance Testing
- Initial Treatment Recommendations
- Rapid Assessment for Change in Disease Course

HCM Centers:
- Confirmation of Diagnosis
- Genetic Counseling and Testing
- Advanced Treatment Decisions

Comprehensive HCM Centers:
- HCM Center Activities, Plus
- Invasive Septal Reduction Therapies
- Catheter Ablation for Ventricular and Complex Atrial Tachyarrhythmias
- Advanced Heart Failure Therapies
- Management during Pregnancy

Abbreviations: HCM indicates hypertrophic cardiomyopathy.
Septal Reduction Therapy

- Referral to a comprehensive HCM Center with expertise in invasive septal reduction therapy to ensure optimal outcomes
- Invasive septal reduction therapy performed at centers with lower volumes and less expertise may be associated with worse outcomes

Abbreviations: HCM indicates hypertrophic cardiomyopathy.
Diagnosis and Initial Evaluation

In suspected HCM comprehensive exam and 3-generation family history (1)

Consider “mimics” (see next slide)

Diagnostic evaluation: ECG, Imaging, Genetics

ECG → Genetics → Imaging

• 12-Lead ECG is recommended in initial evaluation and every 1-2 years (1)

ECG

Diagnostic evaluation: ECG, Imaging, Genetics

Imaging

Genetics

In patients with HCM, genetic testing is beneficial for identification of family members at risk

• Genetic counseling recommended to facilitate shared decision-making (1)

In suspected HCM comprehensive exam and 3-generation family history (1)

Abbreviations: CMR indicates cardiac magnetic resonance; CT, computed tomography; ECG, electrocardiography; echo, echocardiography; EF, ejection fraction; HCM, hypertrophic cardiomyopathy; ICD, implantable cardiac defibrillator; IV, intravenous; LVH, left ventricular hypertrophy; SCD, sudden cardiac death; and TTE, transthoracic echo.
## Clinical Features in Patients with “HCM Mimics”

<table>
<thead>
<tr>
<th>LIFE STAGE</th>
<th>SYSTEMIC FEATURES</th>
<th>POSSIBLE ETIOLOGY</th>
<th>DIAGNOSTIC APPROACH</th>
</tr>
</thead>
</table>
| Infants (0-12 months) and toddlers | Dysmorphic features, failure to thrive, metabolic acidosis | • RASopathies (e.g. Noonan Syndrome)  
• 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 (e.g. Noonan Syndrome)  
• 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 |

**Abbreviations:** RAS indicates reticular activating system.
**Guidance for Family Management**

**Family with known disease-causing variant?**

- Yes
  - Patient has family variant?
    - Yes, or Unknown
      - Further clinical or genetic testing is not recommended (3:No Benefit)
      - Periodically Reassess variant classification (1)
    - No
      - Relatives should present for evaluation if clinical change
  - No
    - Screening ECG and Echo (CMR if echo is inconclusive) at the intervals in the next slide (1)

**Patient has family variant?**

- Yes
  - Periodically Reassess variant classification (1)
- No
  - No

**Abbreviations:** 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.
Guidance for Individuals Diagnosed with Clinical HCM

**Phenotype Positive**

**Complete Baseline Evaluation**
- SCD risk assessment
- Exercise echo testing if symptomatic, if LVOTO is suspected but unconfirmed, or to determine baseline functional capacity

**Every 1-2 years or with any change in symptoms**
- Serial evaluation for clinical status, SCD risk, AF risk, or any change in symptoms (1):
  - Clinical assessment
  - Echo

**Exercise Testing**
- Special consideration (1):
  - Stress echo if gradient <50 mm Hg
  - CPET if considering advanced HF therapies

**Every 3-5 y**
- CMR for SCD risk assessment (if no ICD present), or to evaluate for any suspected morphologic changes (2b)

**Every 2-3 y**
- Treadmill exercise or Cardiopulmonary exercise testing for assessment of functional status (2b)

**Asymptomatic Adults**

**Children and/or Symptomatic Adults**

**Abbreviations: 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.**
## Screening with Electrocardiography and 2D Echocardiography Recommendations in Asymptomatic Family Members*

<table>
<thead>
<tr>
<th>AGE OF FIRST-DEGREE RELATIVE</th>
<th>INITIATION OF SCREENING</th>
<th>REPEAT ECG, ECHO</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pediatric</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Children and adolescents from families with a disease-causing sarcomere variant, and families with early onset disease</td>
<td>At the time HCM is diagnosed in a family member</td>
<td>Every 1-2 y</td>
</tr>
<tr>
<td>All other children</td>
<td>At any time after HCM is diagnosed in a family member but no later than puberty</td>
<td>Every 2-3 y</td>
</tr>
<tr>
<td><strong>Adults</strong></td>
<td>At the time HCM is diagnosed in another family member</td>
<td>Every 3-5 y</td>
</tr>
</tbody>
</table>

* 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).

**Abbreviations:** ECG indicates electrocardiogram; Echo, echocardiogram; and HCM, hypertrophic cardiomyopathy.
Initiate Diagnostic Genetic Testing in Proband with HCM

- Disease-causing LP/P variant identified
  - Regular reevaluation for variant reclassification (See Figure 1, Box 4) (1)
  - Reclassified as LP/P
  - Variant positive: Cascade genetic testing in family (1)
  - Variant negative: Further clinical or genetic testing not recommended (See Figure 1, Box 3) (3: No Benefit)

- VUS, LB/B or no variant identified
  - Reclassified as VUS or LB/B
  - HCM diagnosed: Regular follow-up (See Figure 1, Box 2) (1)
  - No evidence of HCM: Regular clinical surveillance (See Figure 1, Box 5) (1)
  - Consider second tier testing in probrand if no variant is identified

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

Figure 1 refers to figure on slide 18 (two slides prior).

Heart Rhythm Assessment in HCM

<table>
<thead>
<tr>
<th>COR</th>
<th>RECOMMENDATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24- to 48-hour ambulatory ECG monitoring is recommended in the initial evaluation and as part of periodic follow-up (every 1-2 years) to identify patients at risk for SCD and guide management of arrhythmias (Class 1)</td>
</tr>
<tr>
<td>1</td>
<td>In patients with HCM who develop palpitations or lightheadedness, extended (&gt;24h) ECG monitoring or event recording is recommended (Class 1)</td>
</tr>
<tr>
<td>1</td>
<td>In patients with HCM who are deemed high risk for AF based on risk factors or risk score, and who are eligible for anticoagulation, extended ambulatory monitoring is recommended to screen for AF as part of initial evaluation and annual follow-up. (Class 1)</td>
</tr>
<tr>
<td>2b</td>
<td>In adult patients with HCM without risk factors for AF and who are eligible for anticoagulation, extended ambulatory monitoring may be considered to assess for asymptomatic paroxysmal AF as part of initial evaluation and periodic follow-up (every 1-2 years) (Class 2b)</td>
</tr>
</tbody>
</table>

**Abbreviations:** AF indicates atrial fibrillation; ECG, electrocardiography; HCM, hypertrophic cardiomyopathy; and SCD, sudden cardiac death.
Risk Assessment of Sudden Cardiac Death (SCD) in HCM

At initial evaluation and every 1-2 years (Class 1)

Assess the following (Class 1):
- Personal history of cardiac arrest, sustained ventricular arrhythmia, OR unexplained syncope suspected to be arrhythmic
- Family history of premature SCD in a close relative
- Maximal LV wall thickness ≥30mm, EF ≤50%, LV apical aneurysm
- NSVT or VT episodes on continuous ambulatory electrocardiographic monitoring

CMR imaging to help decision regarding ICD if risk remains “unresolved” or if the patient is unsure about ICD placement (Class 1)

≥16 years old, reasonable to obtain echocardiographic LA diameter and maximal LVOT gradient to assist in shared decision making for ICD placement (Class 2a)

< 16 years of age it is reasonable to calculate an estimated 5-year sudden death risk that includes echocardiographic parameters and genotype that may be useful during shared decision-making for ICD placement (Class 2a)

Abbreviations: EF indicates ejection fraction; NSVT, non-sustained ventricular tachycardia; CMR, cardiovascular magnetic resonance; ICD, implantable cardioverter-defibrillator; LA, left atrium; LVOT, left ventricular outflow tract.
ICD Placement in High-Risk Patients with HCM

**Cardiac Arrest, or sustained VT**

- An ICD is recommended (Class 1)

- At least one major risk factor for SCD:
  - FH of SCD
  - Massive LVH ≥30mm
  - Unexplained syncope
  - LV Apical aneurysm
  - EF ≤50%

**At least one major risk factor for SCD:**

- FH of SCD
- Massive LVH ≥30mm
- Unexplained syncope
- LV Apical aneurysm
- EF ≤50%

**An ICD may be considered (2b)**

- Consider additional factor of LGE on CMR or NSVT

**An ICD is reasonable (Class 2a)**

- At least one conventional risk factor:
  - Unexplained syncope
  - Massive LVH
  - NSVT
  - FH of SCD

**An ICD is not indicated (3: Harm)**

- No major risk factors for SCD with LGE on CMR or NSVT

**Children**

- At least one conventional risk factor:
  - Unexplained syncope
  - Massive LVH
  - NSVT
  - FH of SCD

- Consider additional factor of LGE on CMR or NSVT

**No risk factors**

- No major risk factors for SCD with LGE on CMR or NSVT

**Abbreviations:** ICD indicates implantable cardioverter defibrillator; SCD, sudden cardiac death; VF, ventricular fibrillation; VT, ventricular tachycardia; LVH, left ventricular hypertrophy; FH, family history; EF, ejection fraction; NSVT, non-sustained ventricular tachycardia; LGE, late gadolinium enhancement; and CMR, cardiac magnetic resonance imaging.

Pharmacologic Management of Obstructive and Non-Obstructive HCM

**Obstructive**

Symptoms r/t LVOTO

- Step-Wise Approach:
  1. Non-Vasodilating β-Blocker
  2. If not effective or not tolerated, switch to Non-Dihydropyridine CCBs
  3. If persistent severe symptoms, consider Low Dose Diuretics (Class 2b)

- If persistent severe symptoms, add Myosin Inhibitor (ie Mavacamten)
- If persistent severe symptoms, add Disopyramide
- Septal Reduction Therapy performed at experienced centers (Class 1)

- Consider Discontinuing:
  - Vasodilators
  - Digoxin
  - High Dose Diuretics (Class 2b)

**Acute Hypotension**

1. Intravenous Fluids
2. Phenylephrine + β-Blocker (without inotropic activity) (Class 1)

**Non-Obstructive HCM**

Preserved LVEF

Symptomatic:

- β-Blocker or Non-Dihydropyridine CCBs (Class 1)

- Oral Diuretic if evidence of congestion (Class 2a)

- Usefulness of ACEi / ARBs in symptomatic patients with LVEF≥50% is not well established (Class 2b)

- Verapamil potentially HARMFUL in:
  - Severe Dyspnea at Rest
  - Very High Gradients (>100 mmHg)
  - Children < 6 Weeks (Class 3: Harm)

- In highly selected patients with apical HCM with severe dyspnea or angina (NYHA class III or class IV) despite maximal medical therapy, and with preserved EF and small LV cavity size, apical myectomy by experienced surgeons at comprehensive centers may be considered to reduce symptoms (Class 2b)

Asymptomatic:

- ≤45 years
- Asymptomatic
- Pathogenic sarcomere variant carrier
- Mild phenotype

Benefits of β-Blocker or CCBs is not well established (Class 2b)

Valsartan may be considered to potentially slow adverse cardiac remodeling (Class 2b)

Abrreviations: ACEi indicates angiotensin-converting enzyme inhibitors; ARB, angiotensin receptor blockers; CCBs, calcium channel blockers; GDMT, guideline-directed medical therapy; HCM, hypertrophic cardiomyopathy; LVOTO, left ventricular outflow tract obstruction; and r/t, related to symptom
Invasive Management of Obstructive HCM

**Obstructive HCM**
NYHA Class III / IV or symptoms attributable to LVOTO

Despite GDMT

**Septal Reduction Therapy** at experienced centers (Class 1)

Alcohol Septal Ablation in eligible patients is recommended in patients whom:
- Surgery is contraindicated or declined
- Risk is considered unacceptable due to comorbidities or advanced age (Class 1)

Surgical Myectomy is recommended in patients with associated cardiac disease requiring surgical treatment:
- Associated anomalous papillary muscle
- Markedly elongated anterior mitral valve leaflet
- Intrinsic mitral valve disease
- Multivessel coronary artery disease
- Valvular aortic stenosis (Class 1)

Mitral Valve Replacement should not be performed for sole purpose of relieving LVOTO (Class 3:Harm)

Septal Reduction Therapy should not be performed in asymptomatic patients with normal exercise capacity (Class 3:Harm)

Septal Reduction Therapy may be considered as alternative to escalation of medical therapy after shared-decision making (Class 2b)

Surgical Myectomy is reasonable in NYHA Class II if:
- Severe PH attributable to LVOTO or MR
- LAE with ≥1 episodes of symptomatic AF
- Poor functional capacity attributable to LVOTO
- Children or young adults Class with very high LVOT gradients (> 100 mmHg) (Class 2b)

**Abbreviations:** AF indicates atrial fibrillation; GDMT, guideline-directed medical therapy; LVOTO, HCM, hypertrophic cardiomyopathy; LAE, left atrial enlargement; left ventricular outflow tract obstruction; NYHA, New York Heart Association; and MR, mitral regurgitation;
Hypertrophic Cardiomyopathy with Advanced Heart Failure

**If systolic dysfunction:**
Rule out alternative etiologies (eg CAD) (Class 1)

**If persistent systolic dysfunction:**
Discontinue Cardiac Myosin Inhibitors (eg Mavacamten) (Class 1)

**If persistent systolic dysfunction:**
Reasonable to Discontinue negative inotropic agents:
- Verapamil
- Diltiazem
- Disopyramide (Class 2a)

**NYHA II – IV despite GDMT with LBBB**

- Cardiac Resynchronization Therapy can be beneficial (Class 2a)
- ICD Implantation can be beneficial (Class 2a)

**If non-obstructive and NYHA III / IV despite GDMT:**
- Cardiopulmonary Exercise Testing should be performed to quantify functional limitations
- Heart Transplantation Assessment
  - Also consider if ventricular arrhythmias refractory to GDMT (Class 1)

**If non-obstructive and NYHA III / IV:**
Continuous-Flow LVAD therapy is a reasonable bridge to heart transplantation (Class 2a)

Abbreviations: CAD indicates coronary artery disease; GDMT, guideline-directed medical therapy; LBBB, left bundle branch block; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; and NYHA, New York Heart Association

Management of Atrial Fibrillation in Patients with HCM

<table>
<thead>
<tr>
<th>COR</th>
<th>RECOMMENDATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>In patients with clinical AF or subclinical AF (≥ 24 hours), anticoagulation with <strong>direct-acting oral anticoagulants (DOACs)</strong> is <strong>first line</strong></td>
</tr>
<tr>
<td>1</td>
<td>Anticoagulation with <strong>Vitamin K Antagonists</strong> is <strong>second line</strong></td>
</tr>
<tr>
<td>1</td>
<td><strong>ß-Blocker, Verapamil, or Diltiazem</strong> is recommended if pursuing rate control strategy</td>
</tr>
<tr>
<td>2α</td>
<td>In patients with subclinical AF, lasting &gt; 5 minutes but &lt; 24 hours for a given episode, anticoagulation with <strong>DOAC</strong> as <strong>first line</strong>, and <strong>vitamin K Antagonist</strong> as <strong>second line</strong> can be beneficial</td>
</tr>
<tr>
<td>2α</td>
<td>Patients with poorly tolerated AF, a <strong>rhythm control strategy</strong> with cardioversion or anti-arrhythmic drugs can be beneficial</td>
</tr>
<tr>
<td>2α</td>
<td><strong>AF catheter ablation</strong> can be effective when drug therapy is 1) ineffective, 2) contraindicated or 3) not patient’s preference</td>
</tr>
<tr>
<td>2α</td>
<td>In patients with AF undergoing myectomy, <strong>concomitant surgical AF ablation</strong> can be beneficial</td>
</tr>
</tbody>
</table>

**Abbreviations:** AF indicates atrial fibrillation; and DOACs, direct-acting oral anticoagulants

HCM-AF Risk Calculator: Risk for Atrial Fibrillation in Hypertrophic Cardiomyopathy

Risk For Atrial Fibrillation in Hypertrophic Cardiomyopathy

This score provides patients who have an HCM diagnosis with individualized estimates of their risk for developing new-onset atrial fibrillation in the five-year period following their evaluation. These predictions are based on the previously published risk model from Canick et al. (2021).

Citation: [https://professional.heart.org/en/guidelines-and-statements/hcm-af-risk-calculator](https://professional.heart.org/en/guidelines-and-statements/hcm-af-risk-calculator)

Abbreviations: AF indicates atrial fibrillation; and HCM, hypertrophic cardiomyopathy

Management of Ventricular Tachycardia in Patients with HCM

**Recurrent Ventricular Tachycardia**

- Despite β-Blocker Use
  - **ADULTS***
    - Amiodarone
    - Dofetilide
    - Mexiletine
    - Sotalol (Class 1)
  - **CHILDREN***
    - Amiodarone
    - Mexiletine
    - Sotalol (Class 1)
- If AAD is ineffective, not tolerated, or not preferred
  - Catheter Ablation can be useful for reducing arrhythmia burden (Class 2a)
- Despite AAD and Ablation
  - Anti-Tachycardia Pacing to minimize risk of shocks (Class 1)
  - Heart Transplantation Assessment (Class 1)

* Choice of agent guided by age, underlying comorbidities, severity of disease, patient preferences, and balance of efficacy and safety

**Abbreviations:** AADs indicates anti-arrhythmic drugs; and HCM, hypertrophic cardiomyopathy

Recreational Physical Activity and Competitive Sports in HCM

<table>
<thead>
<tr>
<th>COR</th>
<th>RECOMMENDATIONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Mild- to moderate-intensity recreational exercise is encouraged for all patients with HCM.</td>
</tr>
<tr>
<td>1</td>
<td>Elite athletes engaging in competition should undergo comprehensive evaluation with an expert provider.</td>
</tr>
<tr>
<td>2a</td>
<td>In individuals who are genotype-positive, phenotype-negative for HCM, participation in competitive sports is reasonable.</td>
</tr>
<tr>
<td>2a</td>
<td>Vigorous recreational activities are reasonable for patients with HCM accompanied by annual evaluations.</td>
</tr>
<tr>
<td>2b</td>
<td>Competitive sports may be considered after annual comprehensive evaluation and shared decision-making that includes an expert in HCM and sports cardiology.</td>
</tr>
<tr>
<td>3: No Benefit</td>
<td>Universal restriction from vigorous physical activity or competitive sports is not indicated</td>
</tr>
<tr>
<td>3: Harm</td>
<td>ICD placement for the sole purpose of participation in competitive athletics should not be performed.</td>
</tr>
</tbody>
</table>

Abbreviations: HCM indicates hypertrophic cardiomyopathy; ICD, implantable cardioverter defibrillator; and SCD, sudden cardiac death.
# Occupation Recommendations in HCM

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>2a</td>
<td>Follow the Federal Motor Carrier Safety Guidelines for those without ICD or major risk factors for SCD and are using a GDMT plan.</td>
</tr>
<tr>
<td>2a</td>
<td>For pilots, follow Federal Aviation Administration guidelines for multicrew flying duties if they are asymptomatic, low risk for SCD and complete a treadmill stress test at 85% of peak heart rate.</td>
</tr>
<tr>
<td>2b</td>
<td>Occupations that require manual labor, heavy lifting, or a high level of physical performance may be reasonably considered after annual comprehensive evaluation, SCD risk assessment, and GDMT in the context of shared decision-making.</td>
</tr>
</tbody>
</table>

**Abbreviations:** GDMT indicates guideline-directed management and therapy; HCM, hypertrophic cardiomyopathy; ICD, implantable cardioverter defibrillator; and SCD, sudden cardiac death.
## Pregnancy in HCM

<table>
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<tbody>
<tr>
<td>1</td>
<td>In high risk HCM, consultation with a maternal-fetal medicine expert is recommended.</td>
</tr>
<tr>
<td>1</td>
<td>In families affected by HCM, preconception and prenatal reproductive and genetic counseling recommended.</td>
</tr>
<tr>
<td>1</td>
<td>In patients with HCM and AF low molecular weight heparin or low dose warfarin are recommended.</td>
</tr>
<tr>
<td>1</td>
<td>Beta-blocker for symptoms of LVOT obstruction or arrhythmia, with monitoring of fetal growth.</td>
</tr>
<tr>
<td>1</td>
<td>Vaginal delivery is the first-choice in HCM.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
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</tr>
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<tbody>
<tr>
<td>2a</td>
<td>Reasonable to cardiovert new or recurrent atrial fibrillation, especially if symptomatic.</td>
</tr>
<tr>
<td>2a</td>
<td>Reasonable to use general or epidural anesthesia, with precautions to avoid hypotension.</td>
</tr>
<tr>
<td>2a</td>
<td>Reasonable to perform serial echocardiography in the second or third trimester, or if symptoms develop.</td>
</tr>
<tr>
<td>3: Harm</td>
<td>Use of mavacamten is contraindicated due to potential teratogenic effects.</td>
</tr>
</tbody>
</table>

**Abbreviations:** GDMT indicates guideline-directed management and therapy; HCM, hypertrophic cardiomyopathy; and LVOT, left ventricular outflow tract.
Unmet Needs and Future Directions

Expanding access to genetic counseling and testing, as well as improving interpretation of results (particularly pertaining to variants of unknown significance)

Refining criteria for HCM to improve diagnostic accuracy and facilitate potential targeted therapies

Improving management and risk stratification of arrhythmias in patients with HCM

Developing safe and effective therapies that attenuate and prevent disease progression

Incorporating new risk factors and tools to improve screening, risk stratification, and disease monitoring

Advancing care for patients with non-obstructive HCM

Abbreviations: HCM indicates hypertrophic cardiomyopathy
Acknowledgments

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The American Heart Association requests this electronic slide deck be cited as follows: