Clinical Update

Adapted from: 2020 ACC/AHA Guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy
ACC/AHA Applying Class of Recommendation and Level of Evidence to Clinical Strategies, Interventions, Treatments, or Diagnostic Testing in Patient Care (Updated May 2019)*

### 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 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 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**
- Moderate-quality evidence† from 1 or more RCTs
- Meta-analyses of moderate-quality RCTs

**LEVEL B-NR**
- 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

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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.
Hypertrophic Cardiomyopathy (HCM) is a Globally Prevalent & Common Genetic Heart Disease

**Inheritance Pattern**
- Autosomal Dominant
  - +/-
  - +/-

**Sex Distribution**
- 50% Women
- 50% Men

**Disease Prevalence**
- Estimated 1:200 – 1:500

**Triggers for Evaluation**
- Symptoms
- Cardiac Event
- Heart Murmur
- Abnormal EKG
- Cardiac Imaging
- Family Studies

**LV Outflow Tract Obstruction (LVOTO)**
- ⅔ have LVOTO
- ⅓ do not have LVOTO

**Other non-HCM Causes of LV Hypertrophy**
- **Metabolic & Multi-organ Syndromes**
  - RASopathies
  - Mitochondrial myopathies
  - Glycogen / Lysosomal storage diseases
  - Amyloidosis
  - Sarcoidosis
  - Hemochromatosis
  - Danon disease

- **Secondary Causes**
  - Athlete’s heart
  - Hypertension
  - Valvular & subvalvular stenosis

Abbreviations: EKG, indicates electrocardiogram; RAS, reticular activating system.
Defining Hypertrophic Cardiomyopathy in 2020

- Morphologic expression confined solely to the heart
- Characterized by left ventricular (LV) hypertrophy
  *Basal anterior septum in continuity with the anterior free wall = most common*
- No other cardiac, systemic or metabolic disease capable of producing the magnitude of hypertrophy present
- Disease-causing sarcomere (or sarcomere-related) variant 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 in family member of HCM pt. or in conjunction with positive genetic test

**Other Nondiagnostic Morphologic Abnormalities Associated with HCM**

- Systolic anterior motion (SAM) of the mitral valve
- Hyperdynamic LV function
- Hypertrophied & apically displaced papillary muscles
- Myocardial crypts
- Anomalous papillary muscle insertion in anterior MV leaflet
- Elongated mitral valve leaflets
- Myocardial bridging
- Right ventricular hypertrophy

Abbreviations: 2D, indicates two dimensional; MRI, magnetic resonance imaging; mm, millimeter; pt, patient.
Genetic Etiology of Hypertrophic Cardiomyopathy (HCM)

~30-60% of HCM patients have an identifiable pathogenic or likely-pathogenic genetic variant.

Many others have no genetic evidence of disease and/or no other affected family members.

### Sarcomere Genes Implicated in HCM

<table>
<thead>
<tr>
<th>Gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>MYH7</td>
</tr>
<tr>
<td>MYBPC3</td>
</tr>
<tr>
<td>TNNI3</td>
</tr>
<tr>
<td>TNNT2</td>
</tr>
<tr>
<td>TPM1</td>
</tr>
<tr>
<td>MYL2</td>
</tr>
<tr>
<td>MYL3</td>
</tr>
<tr>
<td>ACTC1</td>
</tr>
</tbody>
</table>

Two most common genes that harbor pathogenic variants in HCM (70%).

Adverse Event Associated Hypertrophic Cardiomyopathy

Majority of patients with HCM have a normal life expectancy without limiting symptoms or the need for major treatments.

- Sudden Death
- Atrial Fibrillation
- Heart Failure
- Progressive Functional Limitation
- Thromboembolism

Hypertrophic Cardiomyopathy Mortality Rates Now < 1% per Year

Hypertrophic Cardiomyopathy: Now the greatest unmet treatment need in adults

Improvements in Risk Stratification

ICD Implantation

Abbreviations: ICD indicates implantable cardioverter-defibrillator.

Pathophysiologic Myocardial Changes in Hypertrophic Cardiomyopathy

Abbreviations: LVOT indicates left ventricular outflow tract.

Left Ventricular Outflow Tract Obstruction (LVOTO)

- Septal Hypertrophy
- Narrow Left Ventricular Outflow Tract
- Long Leaflets
- Anterior displacement of the papillary muscles & mitral valve apparatus
- Abnormal Flow Vectors
- Systolic Anterior Motion of the Mitral Valve
- LVOTO
- Contractility
- Preload
- Afterload
- LVOTO, either at rest or with provocation, is present in approximately 75% (2/3) of patients with HCM
- Peak gradient of ≥30 mm Hg is considered to be indicative of obstruction

- Stroke Volume
- Heart Failure
- Survival

- Left Ventricular Hypertrophy
- Myocardial Ischemia
- Prolonged ventricular relaxation
- Left Ventricular Systolic Pressure

- LVOTO
- Resting or provoked gradients ≥50 mm Hg generally considered to be the threshold for septal reduction therapy (SRT) in those patients with drug refractory symptoms.

Mitral Regurgitation
hypertrophied papillary muscles
compensatory mid-ventricular hyperkinesis after apical infarction
anomalous papillary muscle insertion

Dynamic LVOT
Combined
Mid-cavitary
Variable Location

Resting or provoked gradients ≥50 mm Hg generally considered to be the threshold for septal reduction therapy (SRT) in those patients with drug refractory symptoms.

A Closer Look at Left Ventricular Outflow Tract Obstruction (LVOTO)

Primary leaflet abnormalities

- Excessive leaflet length, anomalous papillary muscle insertion, & anteriorly displaced papillary muscles

Mitral Regurgitation (MR)

- Systolic Anterior Motion (SAM) of the Mitral Valve

Symptoms

- In MR caused by LVOTO, SAM of the mitral valve leads to loss of leaflet coaptation, and the jet is predominantly mid-to-late systolic and posterior or lateral in orientation. However, central and anterior jets may also result from SAM of the mitral valve.

- Factors that affect the severity of LVOTO also may affect the degree of MR. Thus, significant MR may not be evident without provocation for LVOTO and SAM of the mitral valve.

Left Ventricular Outflow Tract Obstruction (LVOT)

Pathophysiology of Diastolic Dysfunction in HCM

Impaired Cellular Mechanisms
- Abnormal intracellular Ca reuptake
- Altered systolic-diastolic coupling
- Impaired cardiac cellular energetics

Altered Ventricular Load
- High Intracavitary Pressures
- Non Uniformity in Contraction & Relaxation

Chamber Stiffness
- Myocardial Hypertrophy
- Ischemia
- Interstitial Fibrosis

Stroke Volume
- Left Ventricular Cavity Size

Atrial Fibrillation
- Left Atrial Fibrosis

Pathophysiologic Mechanisms of Myocardial Ischemia in HCM

- Increased Myocardial O$_2$ Demand
- Left Ventricular Outflow Obstruction
- Epicardial Coronary Artery Disease
- Micrvascular Dysfunction
- Medial Hypertrophy & Reduced Density of Arteries
- Impaired Coronary Flow Reserve
- Myocardial Hypertrophy
- Oxygen Demand-Supply Mismatch
- Myocardial Ischemia
- High Intracavitary Pressures
- Angina and/or Dyspnea
- Heart Failure
- Ventricular Arrhythmias
- Left Ventricular Aneurysm
- Diastolic Dysfunction

The prevalence of autonomic dysfunction in HCM is uncertain, although studies have described an abnormal blood pressure response to exercise in 25% of patients (1-3)


Recommendations for Shared Decision-Making in HCM

**Discussions should involve:**

-- Disclosure of risk and benefits
-- Anticipated outcomes of all options
-- Goals, concerns and preferences of the patient (and family if the patient is a minor)

**Shared decision discussions should be applied to:**

-- Genetic testing
-- Sudden death risk assessment and ICD implantation
-- Participation in high-intensity exercise and competitive sports
-- Medical and invasive therapies for LVOT obstruction

Teams Based Approach to Hypertrophic Cardiomyopathy Care

Cardiologists Working 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 and Procedures

Comprehensive HCM Centers:
- Complex Invasive Septal Reduction Therapies
- Catheter Ablation for Ventricular and Complex Atrial Tachyarrhythmias
- Advanced Heart Failure Therapies

Role of the Cardiologist

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
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Comprehensive HCM Centers:
- Complex Invasive Septal Reduction Therapies
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Recommendations for Septal Reduction Therapy

- Invasive septal reduction therapy is associated with increased morbidity and mortality at low volume centers defined as centers with the lowest tertiles of hospital volumes.

- Referral to a high volume HCM Center should be strongly considered for invasive septal reduction therapy.

- Centers performing invasive septal reduction therapies should aim for outcomes similar to comprehensive HCM Centers.

## 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>
<tbody>
<tr>
<td>Infants (0-12 months) and toddlers</td>
<td>Dysmorphic features, failure to thrive, metabolic acidosis</td>
<td>- RASopathies&lt;br&gt;- Glycogen storage diseases, other metabolic or mitochondrial diseases&lt;br&gt;- Infant of a mother with diabetes</td>
<td>- Geneticist assessment&lt;br&gt;- Newborn metabolic screening&lt;br&gt;- Specific metabolic assays&lt;br&gt;- Genetic testing</td>
</tr>
<tr>
<td>Early childhood</td>
<td>Delayed or abnormal cognitive development, visual or hearing impairment</td>
<td>- RASopathies&lt;br&gt;- Mitochondrial diseases</td>
<td>- Biochemical screening&lt;br&gt;- Genetic testing</td>
</tr>
<tr>
<td>School age and adolescence</td>
<td>Skeletal muscle weakness or movement disorder</td>
<td>- Friedrich ataxia, Danon disease&lt;br&gt;- Mitochondrial disease</td>
<td>- Biochemical screening&lt;br&gt;- Neuromuscular assessment&lt;br&gt;- Genetic testing</td>
</tr>
<tr>
<td>Adulthood</td>
<td>Movement disorder, peripheral neuropathy, renal dysfunction</td>
<td>- Anderson-Fabry disease, Friedrich ataxia, infiltrative disorders (e.g., amyloidosis), glycogen storage diseases</td>
<td>- Biochemical screening&lt;br&gt;- Neuromuscular assessment&lt;br&gt;- Genetic testing</td>
</tr>
</tbody>
</table>

Abbreviations: RAS indicates reticular activating system.
Recommended Evaluation and Testing for Suspected HCM or Family History of HCM

Phenotype Negative

Further clinical or genetic testing is not recommended (3: No Benefit)

Reassess variant classification (1)

Screening ECG and Echo (CMR if echo is inconclusive) at the intervals in the table below (1) (Slide 19)

Variant = P/LP

Variant downgraded to VUS

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.

## (1) Slide 19 - 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 genotype-positive families, and families with early onset disease</td>
<td>At the time HCM is diagnosed in another family member</td>
<td>Every 1-2 y</td>
</tr>
<tr>
<td>All other pediatric</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.

Recommended Evaluation and Testing of Phenotype Positive HCM

Phenotype Positive

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

Every 1-2 years or with change in symptoms* (1)
Serial evaluation for clinical status, SCD risk (if no ICD present), or sooner with change in symptoms:
- Clinical assessment
- Echo
- Holter

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

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

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

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.

### Echocardiography Recommendations in Hypertrophic Cardiomyopathy

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>B-NR</td>
<td>1. In patients with suspected HCM, a TTE is recommended in the initial evaluation.</td>
</tr>
<tr>
<td>1</td>
<td>B-NR children</td>
<td>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.</td>
</tr>
<tr>
<td>1</td>
<td>C-LD adults</td>
<td>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.</td>
</tr>
<tr>
<td>1</td>
<td>B-NR</td>
<td>3. For patients with HCM who experience a change in clinical status or a new clinical event, repeat TTE is recommended.</td>
</tr>
<tr>
<td>1</td>
<td>B-NR</td>
<td>4. For patients with HCM and resting LVOT gradient &lt;50 mm Hg, a TTE with provocative maneuvers is recommended.</td>
</tr>
</tbody>
</table>

Abbreviations: COR indicates classification of recommendation; LOE, level of evidence; B-NR, Level B nonrandomized; C-LD, Level C, limited data; TTE, transthoracic echocardiogram; LVOTO, left ventricular outflow tract obstruction; MR, mitral regurgitation; LVOT, left ventricular outflow tract.

# Cardiovascular Magnetic Resonance (CMR) Imaging
## Recommendations in HCM

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>B-NR</td>
<td>1. For patients suspected to have HCM in whom echocardiography is inconclusive, CMR imaging is indicated for diagnostic clarification</td>
</tr>
<tr>
<td>1</td>
<td>B-NR</td>
<td>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.</td>
</tr>
<tr>
<td>1</td>
<td>B-NR</td>
<td>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.</td>
</tr>
<tr>
<td>1</td>
<td>B-NR</td>
<td>4. For patients with obstructive HCM in whom the anatomic mechanism of obstruction is inconclusive on echocardiography, CMR imaging is indicated to inform the selection and planning of SRT.</td>
</tr>
</tbody>
</table>

**Abbreviations:** SCD indicates sudden cardiac death; ICD, implanted cardioverter-defibrillator; LV, left ventricular; LGE, late gadolinium enhancement; SRT, septal reduction therapy; COR, classification of recommendation; LOE, level of evidence; B-NR, Level B nonrandomized.

Risk Assessment of Sudden Cardiac Death (SCD) in HCM

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

Assess the following (Class I):

- 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, EF<=50%, apical aneurysm
- NSVT episodes on continuous ambulatory electrocardiographic monitoring; In select adult patients without major SCD risk factors, ICD may be considered in NSVT present on ambulatory monitoring (Class IIb).

IF none of the above:

CMR to help decision regarding ICD (Class I)

Reasonable to obtain echocardiographic LA diameter and LVOT gradient (Class IIa)

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.

Indications for ICD in HCM Patients

**Risk Factors**
- SCD, VF or sustained VT
- At least one of the following:
  - Massive LVH
  - FH of SCD
  - Unexplained syncope
  - Apical aneurysm
  - EF<=50%
- NSVT
- Significant LGE on CMR

**Recommendations**
- **If Yes**
  - An ICD is recommended (Class I)
- **If Yes in Children**
  - An ICD is reasonable (Class IIa)
- **If Yes in Adults**
  - An ICD may be considered (Class IIb)
- **If No Risk Factors**
  - An ICD is not indicated (Class III)

Consider using 5-year risk estimator tool for SCD to aid in decision making.

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; CMR, cardiac magnetic resonance imaging.

Pharmacologic Management Based on Type of HCM

**Obstructive**

**Symptoms r/t LVOTO**
- non-vasodilating β blockers
  - If not effective: CCBs *
  - If persistent severe symptoms: OR Add Disopyramide

**Persistent dyspnea with volume overload**

**Acute Hypotension**
- IV Fluids
- If no response: Phenylephrine ± β blockers

**Discontinue Vasodilators**
- Digoxin
- High dose diuretics

**Nonobstructive/Preserved EF**
- (symptoms of exertional angina or dyspnea)
  - ARBs/ACEi in symptomatic patients is not well established.
  - Therefore treatment includes: β blockers or CCBs*
    - If dyspnea continues: Diuresis
      - In persistent NYHA class III/VI + apical HCM
        - Treat with GDMT for HFpEF
        - Apical myectomy†

**Nonobstructive/Preserved EF**
- (asymptomatic)
  - The following is not well established: β blockers or CCBs if asymptomatic

*non-dihydropyridine calcium channel blockers (CCBs)

ILV end-diastolic volume <50 mL/m2 and LV stroke volume <30 mL/m2

**Abbreviations:** CCBs indicates calcium channel blockers; LVOTO, left ventricular outflow tract obstruction; IV, intravenous; EF, ejection fraction; ACEi, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; GDMT: goal-directed medical therapy; HFpEF: heart failure with preserved ejection fraction

Invasive Management of Obstructive HCM

**Alcohol septal ablation is recommended for eligible patients if surgery is contraindicated or the risk is considered unacceptable because of serious comorbidities or advanced age**

**Myectomy is recommended if associated conditions exist where surgical treatment is necessary (such as: associated anomalous papillary muscle, markedly elongated anterior mitral leaflet, intrinsic mitral valve disease, multivessel CAD, valvular aortic stenosis)**

**Obstructive HCM with NYHA class III/IV despite GDMT**

**SRT at an experienced center**

**For severely symptomatic patients, 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**

**Myectomy is reasonable in patients with NYHA class II if:**
- Severe and progressive pulmonary hypertension thought to be attributable to LVOTO or associated MR
- Left atrial enlargement with \( \geq 1 \) episodes of symptomatic AF
- Poor functional capacity attributable to LVOTO as documented on treadmill exercise testing
- Children and young adults with very high resting LVOT gradients (\( >100 \) mm Hg)

**For symptomatic patients in whom SRT is an option, mitral valve replacement should not be performed for the sole purpose of relief of LVOTO**

Abbreviations: GDMT indicates guideline directed medical therapy; NYHA, New York Heart Association; SRT, septal reduction therapy; CAD, coronary artery disease; MR, mitral regurgitation; LVOTO, left ventricular outflow tract obstruction; AF, atrial fibrillation.

Atrial Fibrillation (AF) in Hypertrophic Cardiomyopathy

✓ In patients with clinical AF or subclinical AF (duration ≥ 24 hours) DOACs are first line

✓ Vitamin K antagonists are second line Independent of CHA₂DS₂-VASc score

✓ For rate control strategy use either beta blockers, verapamil or diltiazem.

✓ In patients with poorly tolerated AF, a rhythm control strategy with cardioversion or anti-arrhythmic drugs can be beneficial

✓ AF catheter ablation can be effective when drug therapy is ineffective, contraindicated or not patient’s preference

✓ In patients with AF undergoing myectomy, surgical AF ablation can be beneficial

Abbreviations: DOACs indicates direct-acting oral anticoagulants.
Management of HCM and Ventricular Arrhythmias

Recurrence VT

Anti tachycardia pacing to minimize shocks

Despite AAD and ablation

Recurrence ICD shocks despite β-blockers

AAD
- Amiodarone
- Dofetilide*
- Mexiletine
- Sotalol

Heart transplant

Catheter ablation

If ineffective, not tolerated or not preferred

* Not in children

Abbreviations: AAD indicates antiarrhythmic drug therapy; VT, ventricular tachycardia; ICD, implantable cardioverter-defibrillator.

Hypertrophic Cardiomyopathy with Advanced Heart Failure

Consider discontinuing negative inotropic agents

If recurrent ventricular arrhythmias, refer for transplant

LVEF ≤50%

NYHA ≥ III

LVAD is reasonable bridge to transplant

LVEF ≤50%

ICD maybe beneficial

LBBB

Rule out

Other cause of LV systolic dysfunction

NYHA ≥ III

Despite medical therapy, consider CPET evaluation

NYHA ≥ III

Guideline-directed medical therapy similar to HFrEF

LVEF ≤50%

Abbreviations: LVEF indicates left ventricular ejection fraction; LV, left ventricular; HFrEF, heart failure reduced ventricular function; CPET, cardiopulmonary exercise testing; NYHA, New York Heart Association; LVAD, left ventricular assist device; ICD, implantable cardioverter defibrillator; LBBB, left bundle branch block; CRT, cardiac resynchronization therapy.

### Lifestyle Considerations in HCM

<table>
<thead>
<tr>
<th>Exercise Intensity</th>
<th>Recommendation</th>
<th>Class</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mild to moderate intensity exercise</strong> if beneficial</td>
<td>(Class I)</td>
<td></td>
</tr>
<tr>
<td>Comprehensive evaluation and shared discussion regarding sports participation are recommended</td>
<td>(Class I)</td>
<td></td>
</tr>
<tr>
<td>Patients with other comorbidities, prevention and management of atherosclerotic cardiovascular disease are recommended</td>
<td>(Class I)</td>
<td></td>
</tr>
<tr>
<td>It is reasonable to follow the Federal Motor Carrier Safety Guidelines that permit driving commercial vehicles for those who do not have ICD or any major risk for SCD</td>
<td>(Class IIa)</td>
<td></td>
</tr>
<tr>
<td>For pilots with HCM, it is reasonable to permit multi-crew flying duties if they are asymptomatic, low risk for SCD and complete a treadmill stress test</td>
<td>(Class IIa)</td>
<td></td>
</tr>
<tr>
<td>Moderate to high intensity exercise maybe considered after comprehensive evaluation and shared discussion</td>
<td>(Class IIb)</td>
<td></td>
</tr>
<tr>
<td>ICD placement for the sole purpose of participation in competitive athletics should not be performed</td>
<td>(Class III)</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** HCM indicates hypertrophic cardiomyopathy; ICD, implantable cardioverter defibrillator; SCD, sudden cardiac death. Oommen, SR et al. 2020 ACC/AHA Guideline for the Diagnosis and Treatment of Patients with Hypertrophic Cardiomyopathy. *Circulation.* XXX:XX-XX.
Recommendations for HCM in Pregnancy

In high risk HCM, consultation with a maternal-fetal medicine expert is recommended (Class I).

In patients with HCM and atrial fibrillation or other indications for anti-coagulation, low-molecular weight heparin or low dose warfarin are recommended (Class I).

Selected beta-blocker should be administered for symptoms of LVOT obstruction or arrhythmia, with continued fetal monitoring (Class I).

Vaginal delivery is the first-choice delivery option in HCM (Class I).

In clinically stable HCM, it is reasonable to advise pregnancy is generally safe as part of shared discussion (Class IIa).

Reasonable to cardiovert new or recurrent atrial fibrillation, especially if symptomatic (Class IIa).

Reasonable to perform serial echocardiography in the second or third trimester, or if symptoms develop (Class IIa).

Abbreviations: HCM indicates hypertrophic cardiomyopathy; LVOT, left ventricular outflow tract.
Unmet Needs

Randomized clinical trials are needed to prevent or attenuate disease progression, explore new therapies and gender-specific outcomes in HCM.

New risk factors to enhance the power of risk stratification algorithms, especially in children.

Pharmacological and catheter-based ablation for arrhythmia management, especially in young patients.

Greater access to genetic counseling and testing.

More data needed regarding potential risks of exercise and sports in patients with HCM.

Abbreviations: HCM indicates hypertrophic cardiomyopathy.
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