

**Table 1. EHRA/HRS/APHRS/LAHS 2022 Consensus Statement on genetic testing.
Genes implicated in hypertrophic cardiomyopathy**

Gene	Locus	Syndrome	Protein (functional effect)	Frequency	ClinGen classification
<i>MYBPC3</i>	11p11.2	Familial HCM	↓contractility due to ↓Ca ²⁺ sensitivity	40–45%	Definite
<i>MYH7</i>	14q11.2-q12	Familial HCM	↓contractility due to ↓Ca ²⁺ sensitivity	15–25%	Definite
<i>TNNI3</i>	19q13.4	Familial HCM	Loss of function (inhibitory)	1–7%	Definite
<i>TNNT2</i>	1q32.1	Familial HCM	Increase oxygen consumption	1–7%	Definite
<i>TPM1</i>	15q22.2	Familial HCM	Loss-of-function of the thin filament	1–2%	Definite
<i>ACTC1</i>	15q.14	Familial HCM	Gain-of-function causing high contractile phenotype	1–2%	Definite
<i>MYL2</i>	12q24.11	Familial HCM	Loss-of-function	1–2%	Definite
<i>MYL3</i>	3p21.31	Familial HCM	Loss-of-function	1–2%	Definite
Intrinsic cardiomyopathy genes					
<i>ACTN2</i>	1q43	LVH, LVNC, DCM, and idiopathic VF	Loss-of-function	<1%	Moderate
<i>PLN</i>	6q22.31	HCM, DCM, and ARVC	Loss-of-function of SERCA (Ca ²⁺ overload) mitochondrial disease	<1%	Definite
<i>JPH2</i>	20q13.12	Familial HCM/DCM	Unknown	<1%	Moderate

<i>FHOD3</i>	18q12.2	Familial HCM/ DCM	Actin filament polymerization disruption	0.5–2%	Not curated by ClinGen
<i>CSRP3</i>	11p15.1	Late onset familial HCM, DCM	Unknown (non-sarcomeric gene)	<1%	Moderate
<i>TNNC1</i>	3p21.1	Familial HCM	Disruption of Ca ²⁺ handling	<1%	Moderate
Syndromic genes, where isolated LVH may be seen					
<i>CACNA1C</i>	12p13.33	Timothy syndrome, BrS, LQTS	Intracellular Ca (2+) overload	<1%	Definite
<i>DES</i>	2q35	Desminopathy (DCM), myofibrillar myopathy	Dysfunction through Z-disk and myofibril disintegration, followed by abnormal accumulation of intracellular proteins	<1%	Definite
<i>FHL1</i>	Xq26.3	Emery-Dreifuss MD, cardiac conduction abnormalities, arrhythmias, HCM	Dysfunction through Z-disk and myofibril disintegration, followed by abnormal accumulation of intracellular proteins	<1%	Definite
<i>FLNC</i>	7q32.1	Myofibrillar myopathy, HCM, RCM, distal myopathy	Dysfunction through Z-disk and myofibril disintegration, followed by abnormal accumulation of intracellular proteins	<1%	Not curated by ClinGen
<i>GLA</i>	Xq22.1	Fabry disease	Loss-of-function	<1%	Definite
<i>LAMP2</i>	Xq24	Danon disease	Loss-of-function	<1%	Definite
<i>PRKAG2</i>	7q36.1	PRKAG2 cardiomyopathy	Dysfunction of AMPK	1–2%	Definite
<i>PTPN11</i>	12q24.13	Noonan syndrome	RASopathy	<1%	Definite
<i>RAF1</i>	3p25.2	Noonan syndrome	RASopathy	<1%	Definite
<i>RIT1</i>	1q22	Noonan syndrome	RASopathy	<1%	Definite
<i>TTR</i>	18q12.1	Transthyretin amyloidosis	Loss-of-function causing amyloid deposition in peripheral nerves and heart	1–2%	Definite
<i>ALPK3</i>	15q25.3	Infant-onset HCM/ DCM	Biallelic loss-of-function	<1%	Strong
Syndromic genes, where LVH is occurs together with other syndromic features					
<i>ABCC9</i>	12p12.1	Cantu syndrome	Reduce ATP-mediated potassium channel inhibition (gain-of-function)	<1%	Definite
<i>BAG3</i>	10q26.11	Myofibrillar myopathy	Dysfunction through Z-disk and myofibril disintegration, followed by abnormal accumulation of intracellular proteins	<1%	Definite
<i>CAV3</i>	3p25.3	Caveolinopathy	Disruption of caveolae formation	<1%	Definite
<i>COX15</i>	10q24.2	Leigh syndrome	Loss-of-function of SERCA (Ca ²⁺ overload) mitochondrial disease	<1%	Strong
<i>CRYAB</i>	15	Alpha-B crystallinopathy	Dysfunction through Z-disk and myofibril disintegration, followed by abnormal accumulation of intracellular proteins	<1%	Definite
<i>FXN</i>	9q21.11	Friedreich ataxia	Loss-of-function of mitochondrial protein	<1%	Definite
<i>GAA</i>	17q25.3	Pompe disease	Loss-of-function	<1%	Definite
<i>LDB3/ZASP</i>	10q23.2	Myofibrillar myopathy	Dysfunction through Z-disk and myofibril disintegration, followed by abnormal accumulation of intracellular proteins	<1%	Moderate
<i>MYO6</i>	6q14.1	Bilateral hearing loss	Disruption of the structural integrity of inner ear hair cells	<1%	Definite
<i>SLC25A4</i>	4q35.1	Mitochondrial disease	RASopathy	<1%	Definite

ACM, arrhythmogenic cardiomyopathy; BrS, Brugada syndrome; DCM, dilated cardiomyopathy; HCM, hypertrophic cardiomyopathy; LQTS, long QT syndrome.

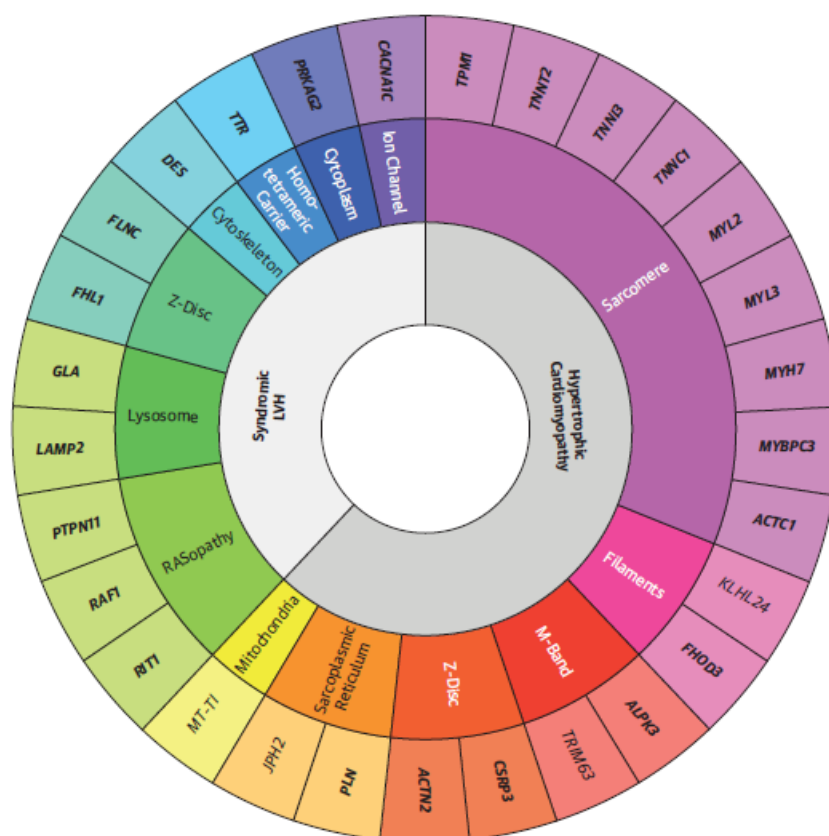


Figure 1. Updated List of Genes With Moderate, Strong, or Definitive Hypertrophic Cardiomyopathy Association

Genetic architecture of hypertrophic cardiomyopathy or genocopies causing left ventricular hypertrophy (LVH) (innermost circle), spanning numerous gene ontologies (middle circle). Genes classified as definitive or strong evidence are emphasized in bold type.

Hespe S, et al. Genes Associated With Hypertrophic Cardiomyopathy: A Reappraisal by the ClinGen Hereditary Cardiovascular Disease Gene Curation Expert Panel. *J Am Coll Cardiol.* 2025;85:727-740.

Table 2. Initial Evaluation**AHA/ACC 2024 GL on HCM.****Recommendation for Shared Decision-Making**

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 and caregivers to express their goals and concerns. ¹⁻⁵
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Recommendations for Multidisciplinary HCM Centers

In patients 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.

1 C-LD

Consultation with or referral to a comprehensive or primary HCM center to aid in complex disease-related management decisions.

2a C-LD

Recommendation for Clinical Diagnosis

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
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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 children and adolescents	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 (eg, 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.

ESC 2014 GL on HCM. Recommended laboratory tests in adult patients with hypertrophic cardiomyopathy

Test	Comment
Haemoglobin	• Anaemia exacerbates chest pain and dyspnoea and should be excluded whenever there is a change in symptoms.
Renal function	• Renal function may be impaired in patients with severe left ventricular impairment. • Impaired GFR and proteinuria may be seen in amyloidosis, Anderson–Fabry disease and mitochondrial DNA disorders.
Liver transaminases	• Liver tests may be abnormal in mitochondrial disorders, Danon disease and β -oxidation defects.
Creatine phosphokinase	• Serum creatine phosphokinase is raised in metabolic disorders such as Danon and mitochondrial disease.
Plasma/leucocyte alpha galactosidase A (in men aged >30 years)	• Low (<10% normal values) or undetectable plasma and leucocyte alpha galactosidase is present in male patients with Anderson–Fabry disease.* • Plasma and leucocyte enzyme levels are often within the normal range in affected females and so genetic testing may be considered if clinically suspected.
Serum immunoglobulin free light chain assay, serum and urine immunofixation, and urine electrophoresis	• Should be considered if amyloidosis is suspected from history and non-invasive tests. Confirmation of the diagnosis usually requires histological analysis.
Fasting glucose	• May be elevated in some mitochondrial DNA disorders • May be low in fatty acid and carnitine disorders.
Brain natriuretic peptide and troponin T	• Elevated plasma levels of BNP, NT-proBNP, and troponin T are associated with higher risk of cardiovascular events, heart failure and death.
Thyroid function tests	• Should be measured at diagnosis and monitored every 6 months in patients treated with amiodarone.
Plasma lactate	• Elevated in some patients with mitochondrial disorders.

BNP = brain natriuretic peptide; DNA = deoxyribonucleic acid; GFR = glomerular filtration rate; NT-proBNP = N-terminal pro brain natriuretic peptide.

* Pseudo-deficiency may be seen in some genetic variants such as D313Y

ESC 2014 Guidelines on diagnosis and management of hypertrophic cardiomyopathy, *Eur Heart J.* 2014;**35**:2733–79, with permission from Oxford University Press.

Table 3. Electrocardiography**ESC 2014 GL on HCM****Electrocardiography**

Standard 12-lead ECG in suspected HCM	I-B
48-hour ambulatory ECG monitoring at initial clinical assessment, to detect atrial and ventricular arrhythmia.	I-B

Palpitations

48-hour ambulatory ECG monitoring for frequent or sustained palpitations	I-C
Implantable loop recorder for frequent palpitations, when no cause is identified following prolonged ECG monitoring.	IIb-C

Unexplained syncope

12-lead ECG, upright exercise test, resting and exercise 2D and Doppler echocardiography, and 48-hour ambulatory ECG monitoring	I-C
Implantable loop recorder in patients with recurrent episodes of syncope, who are at low risk of SCD.	IIa-C

Electrocardiographic abnormalities suggesting specific diagnoses or morphological variants

Finding	Comment
Short PR interval/pre-excitation	Pre-excitation is a common feature of storage diseases (Pompe, PRKAG2, and Danon) and mitochondrial disorders (MELAS, MERFF). A short PR interval without pre-excitation is seen in Anderson-Fabry disease.
AV block	Progressive atrioventricular conduction delay is common in mitochondrial disorders, some storage diseases (including Anderson-Fabry disease), amyloidosis, desminopathies and in patients with PRKAG2 mutations.
Extreme LVH (Sokolow score ≥ 50)	Extremely large QRS voltage is typical of storage diseases such as Pompe and Danon disease, but can be caused by pre-excitation alone.
Low QRS voltage (or normal voltages despite increased LV wall thickness)	Low QRS voltage in the absence of pericardial effusion, obesity and lung disease is rare in HCM (limited to cases with end-stage evolution) but is found in up to 50% of patients with AL amyloidosis and 20% with TTR amyloidosis. Differential diagnosis between HCM and cardiac amyloidosis is aided by measuring the ratio between QRS voltages and LV wall thickness.
Extreme superior ("North West") QRS axis deviation	Seen in patients with Noonan syndrome who have severe basal hypertrophy extending into the RV outflow tract.
Giant negative T wave inversion (>10 mm)	Giant negative T wave inversion in the precordial and/or inferolateral leads suggests involvement of the LV apex.
Abnormal Q waves ≥ 40 ms in duration and/or $\geq 25\%$ of the R wave in depth and/or ≥ 3 mm in depth in at least two contiguous leads except aVR	Abnormally deep Q waves in the inferolateral leads, usually with a positive T wave, are associated with an asymmetrical distribution of LVH. Q waves of abnormal duration (≥ 40 ms) are associated with areas of replacement with fibrosis.
Coved ST segment elevation in lateral chest leads	Some patients with apical or distal hypertrophy develop small apical aneurysms, sometimes associated with myocardial scarring. These may only be detectable on CMR, ventriculography or contrast echo, and are occasionally associated with ST elevation in the lateral chest leads.

AV = atrioventricular; AL = amyloid light chain; CMR = cardiac magnetic resonance; HCM = hypertrophic cardiomyopathy; LV = left ventricular; LVH = left ventricular hypertrophy; MELAS = mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes; MERFF = myoclonic epilepsy with ragged red fibres; PRKAG2 = gamma-2 subunit of the adenosine monophosphate-activated protein kinase; RV = right ventricular; TTR = transthyretin.

ESC 2014 Guidelines on diagnosis and management of hypertrophic cardiomyopathy, *Eur Heart J.* 2014;**35**:2733–79, with permission from Oxford University Press.

AHA/ACC 2024 GL on HCM. Heart Rhythm assessment

A 12-lead ECG in the initial evaluation and as part of periodic follow-up (every 1 to 2 years) I-B-NR

24- to 48-hour ambulatory electrocardiographic monitoring in the initial evaluation and as part of periodic follow-up (every 1 to 2 years) to identify patients who are at risk for SCD and guide management of arrhythmias I-B-NR

In patients who develop palpitations or lightheadedness, extended (>24 hours) electrocardiographic monitoring or event recording, which should not be considered diagnostic unless patients have had symptoms while being monitored.	I-B-NR
In first-degree relatives of patients with HCM, a 12-lead ECG as a component of the screening algorithm.	I-B-NR
Extended ambulatory monitoring to screen for AF as part of initial evaluation and periodic follow-up (every 1 to 2 years), in patients who have additional risk factors for AF, such as left atrial dilatation, advanced age, and NYHA) class III to class IV HF, and who are eligible for anticoagulation	IIa-B-NR
Extended ambulatory monitoring to assess for asymptomatic paroxysmal AF as part of initial evaluation and periodic follow-up (every 1 to 2 years), in adult patients without risk factors for AF and who are eligible for anticoagulation,	IIb-B-NR

Table 4. ESC 2023 GL on Cardiomyopathies. Imaging evaluation in hypertrophic cardiomyopathy

Item to assess	Primary imaging modality	Comments
LV wall thickness	ECHO/CMR	- All LV segments from base to apex examined in end-diastole, preferably in the 2D short-axis view, ensuring that the wall thickness is recorded at mitral, mid-LV, and apical levels. - CMR is superior in the detection of LV apical and anterolateral hypertrophy, aneurysms,⁵⁸⁰ and thrombi,⁵⁸¹ and is more sensitive in the detection of subtle markers of disease in patients with sarcomeric protein gene variants (e.g. myocardial crypts, papillary muscle abnormalities).^{159,582,583}
Systolic function (global and regional)	ECHO/CMR	- Ejection fraction is a suboptimal measure of LV systolic performance when hypertrophy is present. - Doppler myocardial velocities and deformation parameters (strain and strain rate) are typically reduced at the site of hypertrophy despite a normal EF and may be abnormal before the development of increased wall thickness in genetically affected patients.
Diastolic function	ECHO	Routine examination should include mitral inflow assessment, tissue Doppler imaging, pulmonary vein flow velocities, pulmonary artery systolic pressure, and LA size/volume.
Mitral valve	ECHO	Assess presence and degree of SAM and mitral regurgitation. The presence of a central- or anteriorly directed jet of mitral regurgitation should raise suspicion of an intrinsic/primary mitral valve abnormality and prompt further assessment.
LVOT	ECHO	See Figure 12.
LA dimensions	ECHO/CMR	- Provides important prognostic information.^{365,525,584} - Most common mechanisms of LA enlargement are SAM-related mitral regurgitation and elevated LV filling pressures.
Myocardial fibrosis/LGE	CMR	The distribution and severity of interstitial expansion can suggest specific diagnoses. Anderson-Fabry disease is characterized by a reduction in non-contrast T1 signal and the presence of posterolateral LGE.^{134,155} In cardiac amyloidosis, there is often global, subendocardial or segmental LGE and a highly specific pattern of myocardial and blood-pool gadolinium kinetics caused by similar myocardial and blood T1 signals.^{585,586}

2D, two-dimensional; CMR, cardiac magnetic resonance; ECHO, echocardiogram; EF, ejection fraction; LA, left atrium; LGE, late gadolinium enhancement; LV, left ventricular; LVOT, left ventricular outflow tract; SAM, systolic anterior motion; SCD, sudden cardiac death.

Table 5. Echocardiography

ESC 2014 GL on HCM	
Transthoracic echocardiography	
In all patients with HCM at initial evaluation 2D and Doppler echocardiography at rest and during Valsalva in the sitting and semi-supine positions-and then on standing if no gradient is provoked.	I-B
Measurement of maximum diastolic wall, using 2D short-axis views in all LV segments, from base to apex.	I-C
Comprehensive evaluation of LV diastolic function, Including pulsed Doppler of mitral valve inflow, tissue Doppler velocities at the mitral annulus, pulmonary vein flow velocities, pulmonary artery systolic pressure, and measurement of LA size and volume.	I-C
Detect provokable LVOT obstruction and exercise-induced mitral regurgitation in symptomatic patients with a resting or provoked* peak instantaneous LV outflow tract gradient <50 mm Hg, 2D and Doppler echocardiography during exercise in the standing, sitting or semi-supine position.	I-B
2D and Doppler echocardiography during exercise-in the standing, sitting or semi-supine positions when the presence of an LVOT gradient is relevant to lifestyle advice and decisions on medical treatment, in asymptomatic patients with a resting or provoked* peak instantaneous LV outflow tract gradient <50 mm Hg	IIb-C
In patients with sub-optimal images or with suspected LV apical hypertrophy or aneurysm, TTE with IV echocardiographic contrast as an alternative to CMR	IIa-C
Intracoronary contrast echocardiography in all patients undergoing septal alcohol ablation, to ensure correct localization of alcohol.	I-B
Transoesophageal echocardiography	
Perioperative TOE for septal myectomy, to confirm the mechanism of LVOT obstruction, to guide the surgical strategy, to assess post-surgical complications and to detect residual LV outflow tract obstruction.	I-C
TOE in patients with LVOT obstruction if the mechanism is unclear, or when assessing the mitral valve apparatus before a septal reduction procedure, or when severe mitral regurgitation, caused by intrinsic valve abnormalities, is suspected.	IIa-C
TOE with intracoronary contrast injection of the candidate septal perforator artery to guide septal alcohol ablation when transthoracic windows are insufficient for proper visualization of echo-contrast	IIa-C
Echocardiographic features that suggest specific aetiologies	
Finding	Specific diseases to be considered
Increased interatrial septum thickness	Amyloidosis
Increased AV valve thickness	Amyloidosis; Anderson-Fabry disease
Increased RV free wall thickness	Amyloidosis, myocarditis, Anderson-Fabry disease, Noonan syndrome and related disorders
Mild to moderate pericardial effusion	Amyloidosis, myocarditis
Ground-glass appearance of ventricular myocardium on 2D echocardiography	Amyloidosis
Concentric LVH	Glycogen storage disease, Anderson-Fabry disease, PRKAG2 mutations
Extreme concentric LVH (wall thickness ≥30 mm)	Danon disease, Pompe disease
Global LV hypokinesia (with or without LV dilatation)	Mitochondrial disease, TTR-related amyloidosis, PRKAG2 mutations, Danon disease, myocarditis, advanced sarcomeric HCM, Anderson-Fabry disease
Right ventricular outflow tract obstruction	Noonan syndrome and associated disorders

* provocation with Valsalva, standing, or oral nitrate.

2D = two-dimensional; AV = atrioventricular; HCM = hypertrophic cardiomyopathy; LV = left ventricular; LVH = left ventricular hypertrophy; PRKAG2 = gamma-2 subunit of the adenosine monophosphate-activated protein kinase; RV = right ventricle; TTR = transthyretin.

ESC 2023 GL on Cardiomyopathies. Recommendation for evaluation of left ventricular outflow tract obstruction

In all patients with HCM, at initial evaluation, transthoracic 2D and Doppler echocardiography are recommended, at rest and during Valsalva manoeuvre in the sitting and semi-supine positions—and then on standing if no gradient is provoked—to detect LVOTO. ^{84,86,365,525,584,587,589–594}	I	B
In symptomatic patients with HCM and a resting or provoked ^c peak instantaneous LV outflow tract gradient <50 mmHg, 2D and Doppler echocardiography during exercise in the standing, sitting (when possible), or semi-supine position are recommended to detect provokable LVOTO and exercise-induced mitral regurgitation. ^{588,595–598}	I	B
Transoesophageal echocardiography should be considered in patients with HCM and LVOTO if the mechanism of obstruction is unclear or when assessing the mitral valve apparatus before a septal reduction procedure, or when severe mitral regurgitation caused by intrinsic valve abnormalities is suspected. ^{599–602}	IIa	C
In symptomatic patients with HCM and inconclusive non-invasive cardiac imaging, left and right heart catheterization may be considered to assess the severity of LVOTO and to measure LV filling pressures. ⁶⁰³	IIb	C

cProvocation with Valsalva, standing, or oral nitrate.

ESC 2023 GL on Cardiomyopathies. Echocardiographic features that suggest specific aetiologies in hypertrophic cardiomyopathy

Finding	Specific diseases to be considered
Increased interatrial septum thickness	Amyloidosis
Increased AV valve thickness	Amyloidosis; Anderson–Fabry disease
Increased RV free wall thickness	Amyloidosis, myocarditis, Anderson–Fabry disease, Noonan syndrome, and related disorders
Mild-to-moderate pericardial effusion	Amyloidosis, myocarditis/myopericarditis
Ground-glass appearance of ventricular myocardium on 2D echocardiography	Amyloidosis
Concentric LVH	Glycogen storage disease, Anderson–Fabry disease, <i>PRKAG2</i> variants, Friedreich ataxia
Extreme concentric LVH (wall thickness ≥ 30 mm)	Danon disease, Pompe disease
Global LV hypokinesia (with or without LV dilatation)	Mitochondrial disease, TTR-related amyloidosis, <i>PRKAG2</i> variants, Danon disease, myocarditis, advanced sarcomeric HCM, Anderson–Fabry disease, Friedreich ataxia
RVOTO	Noonan syndrome and associated disorders
Apical sparing pattern on longitudinal strain imaging	Amyloidosis

2D, two-dimensional; AV, atrioventricular; HCM, hypertrophic cardiomyopathy; LV, left ventricular; LVH, left ventricular hypertrophy; *PRKAG2*, protein kinase AMP-activated non-catalytic subunit gamma 2; RV, right ventricular; RVOTO, right ventricular outflow tract obstruction; TTR, transthyretin.

AHA/ACC 2024 GL on HCM. Recommendations for echocardiography

TEE in patients with suspected HCM	I-B-NR
In patients with no change in clinical status or events, repeat TTE every 1 to 2 years to assess the degree of myocardial hypertrophy, dynamic LVOTO, MR, and myocardial function.	I-B-NR (children) I-C-LD (adults)
TTE for patients who experience a change in clinical status or a new clinical event	I-B-NR
TTE with provocative maneuvers in resting LVOT gradient <50 mm Hg	I-B-NR
Exercise TTE for the detection and quantification of dynamic LVOTO in the absence of a resting or provokable outflow tract gradient $\geq$ 50 mm Hg in symptomatic patients	I-B-NR
Intraoperative transesophageal echocardiogram (TEE) to assess mitral valve anatomy and function and adequacy of septal myectomy.	I-B-NR
TTE or intraoperative TEE with intracoronary ultrasound-enhancing contrast injection of the candidate's septal perforator(s) for alcohol septal ablation.	I-B-NR
TTE within 3 to 6 months after the procedure to evaluate the procedural results of septal reduction therapy.	I-B-NR
Screening: In first-degree relatives of patients with HCM, a TTE as part of initial family screening and periodic follow up	I-B-NR
Screening: In individuals who are genotype positive or phenotype-negative, serial echocardiography 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	I-B-NR
TEE 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.	IIa-C-LD
Use of an intravenous ultrasound-enhancing agent, when the diagnoses of apical HCM, apical aneurysm, or atypical patterns of hypertrophy are inconclusive on TTE, particularly if other imaging modalities such as CMR are not readily available or contraindicated.	IIa-B-NR
Exercise TTE for the detection and quantification of dynamic LVOTO for asymptomatic patients without a resting or provokable outflow tract gradient $\geq$ 50 mm Hg.	IIa-C-LD

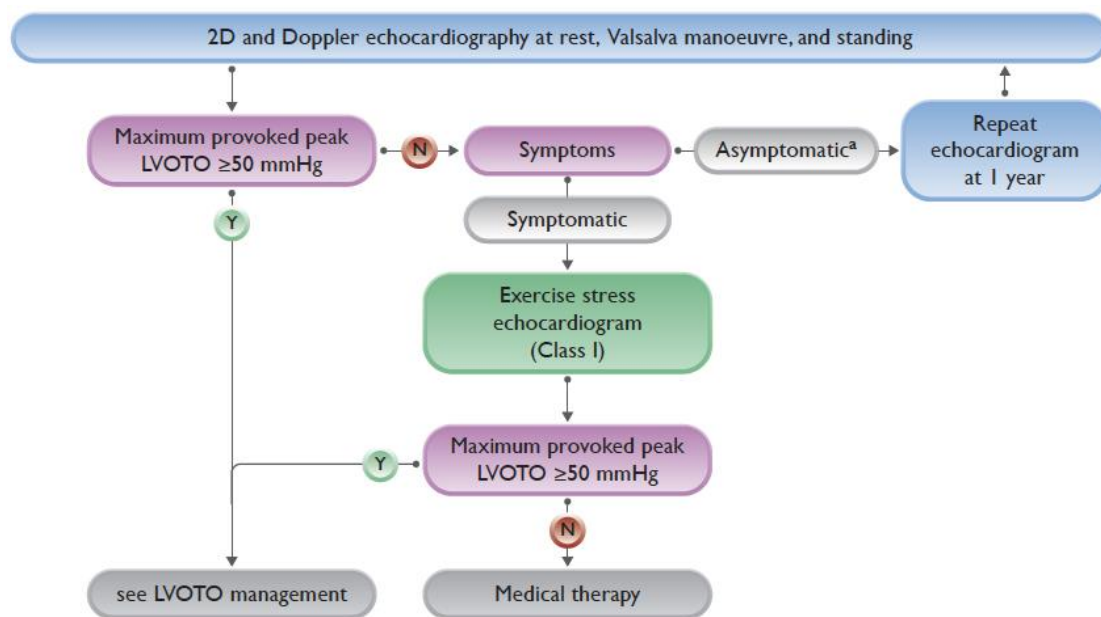


Figure 2. ESC 2023 GL on cardiomyopathies. Protocol for the assessment and treatment of left ventricular outflow tract obstruction.

2D, two-dimensional; LVOTO, left ventricular outflow tract obstruction.

^a Exercise echocardiography may be considered in individual patients when the presence of an left ventricular outflow tract gradient is relevant to lifestyle advice and decisions on medical treatment.

Table 6. Cardiac magnetic resonance.**ESC 2014 GL on HCM**

Invasive coronary angiography in adult survivors of cardiac arrest, in patients with sustained ventricular tachyarrhythmia and in patients with severe stable angina (CCS Class ≥ 3)	I-C
Invasive or CTA in patients with typical exertional chest pain (CCS Class <3) who have an intermediate pre-test probability of atherosclerotic coronary artery disease based on age, gender and risk factors for atherosclerosis, or a history of coronary revascularization.	IIa-C
In all patients ≥ 40 years, invasive or CTA before septal reduction therapy	IIa-C

CTA = computed tomographic coronary angiography; CCS = Canadian Cardiovascular Society

AHA/ACC 2024 GL on HCM. CMR imaging.

Suspicion of HCM and inconclusive echocardiography.	I-B-NR
LVH and suspicion of alternative diagnoses, including infiltrative or storage disease as well as athlete's heart.	I-B-NR
To assess maximum LV wall thickness, EF, LV apical aneurysm, and extent of myocardial fibrosis with LGE in patients 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,	I-B-NR
CMR to inform the selection and planning of septal reduction therapy when the anatomic mechanism of obstruction is inconclusive on echocardiography.	I-B-NR
Repeat contrast-enhanced CMR imaging on a periodic basis (every 3 to 5 years) for the purpose of SCD risk stratification to evaluate changes in LGE and other morphologic changes, including EF, development of apical aneurysm, or LV wall thickness.	IIb-C-EO

ESC 2023 GL on Cardiomyopathies. Additional recommendation for cardiovascular magnetic resonance evaluation in hypertrophic cardiomyopathy

Contrast-enhanced CMR may be considered before ASA or myectomy to assess the extent and distribution of hypertrophy and myocardial fibrosis. IIb C

ASA, alcohol septal ablation; CMR, cardiac magnetic resonance

Table 7. Exercise testing.

ESC 2014 GL on HCM	
Cardiopulmonary exercise testing	
Cardiopulmonary exercise testing, with simultaneous measurement of respiratory gases, in severely symptomatic patients with systolic and/or diastolic LV dysfunction evaluated for heart transplantation or mechanical support.	I-B
Cardiopulmonary exercise testing with simultaneous measurement of respiratory gases (or standard treadmill or bicycle ergometry when unavailable)	
Irrespective of symptoms to assess the severity and mechanism of exercise intolerance and change in systolic blood pressure.	IIa-B
In symptomatic patients undergoing septal alcohol ablation and septal myectomy to determine the severity of exercise limitation.	IIa-C

AHA/ACC 2024 GL on HCM. Exercise stress testing.

Exercise TTE for the detection and quantification of dynamic LVOTO in symptomatic patients with HCM who do not have resting or provokable outflow tract gradient ≥ 50 mm Hg.	I-B-NR
Cardiopulmonary exercise stress testing to quantify the degree of functional limitation and aid in selection of patients for heart transplantation or mechanical circulatory support in nonobstructive HCM and advanced HF (NYHA III-IV despite GDMT).	I-B-NR
In pediatric patients, exercise stress testing to determine functional capacity and to provide prognostic information, regardless of symptom status	I B-NR
In adult patients exercise stress testing to determine functional capacity and to provide prognostic information as part of initial evaluation.	IIa-B-NR
Exercise TTE for the detection and quantification of dynamic LVOTO for asymptomatic patients who do not have a resting or provokable outflow tract gradient ≥ 50 mm Hg.	IIa-C-LD
Exercise stress testing to guide therapy in patients with obstructive HCM and ambiguous functional capacity	IIb C-LD
Exercise stress testing every 2 to 3 years in patients for whom it is unclear if their functional capacity has declined	IIb C-EO

Table 8. Coronary angiography and invasive haemodynamic assessment**ESC 2014 GL on HCM****Coronary Angiography**

Invasive coronary angiography in adult survivors of cardiac arrest, in patients with sustained ventricular tachyarrhythmia and in patients with severe stable angina (CCS Class ≥ 3)	I-C
Invasive or CTA in patients with typical exertional chest pain (CCS Class < 3) who have an intermediate pre-test probability of atherosclerotic coronary artery disease based on age, gender and risk factors for atherosclerosis, or a history of coronary revascularization.	IIa-C
In all patients ≥ 40 years, invasive or CTA before septal reduction therapy	IIa-C

CTA = computed tomographic coronary angiography; CCS = Canadian Cardiovascular Society

Invasive haemodynamic studies

Cardiac catheterization-to evaluate right and left heart function and pulmonary arterial resistance-in patients considered for heart transplantation or mechanical circulatory support.	I-B
In symptomatic patients with inconclusive, non-invasive cardiac imaging, left and right heart catheterization to assess the severity of LVOT obstruction and to measure LV filling pressures	IIb-C

AHA/ACC 2024 GL on HCM. Angiography and invasive hemodynamic assessment.

Invasive hemodynamic assessment with cardiac catheterization for patients who are candidates for septal reduction therapy SRT and for whom there is uncertainty regarding the presence or severity of LVOTO on noninvasive imaging studies I-B-NR

Coronary angiography (CT or invasive) in symptoms or evidence of myocardial ischemia I-B-NR

Coronary angiography (CT or invasive) before surgical myectomy at risk of coronary atherosclerosis. I-B-NR

Table 9. ESC 2014 GL on HCM**Invasive electrophysiological study**

In documented persistent or recurrent supraventricular tachycardia (atrial flutter, atrial tachycardia, AVNRT, AVRT) and in patients with ventricular pre-excitation, to guide ablation.	I-C
In documented, symptomatic, monomorphic, sustained (> 30 s) ventricular tachycardia to guide ablation	IIb-C
Programmed ventricular stimulation is not recommended for sudden cardiac death risk stratification.	III-C

ESC 2014 Guidelines on diagnosis and management of hypertrophic cardiomyopathy, *Eur Heart J.* 2014;**35**:2733–79, with permission from Oxford University Press.

Table 10. ESC 2014 GL on HCM Other potentially necessary tests**Nuclear scintigraphy**

Bone scintigraphy (particularly with ^{99m}Tc-DPD) in symptoms, signs and non-invasive tests consistent with transthyretin-related amyloidosis. IIa-B

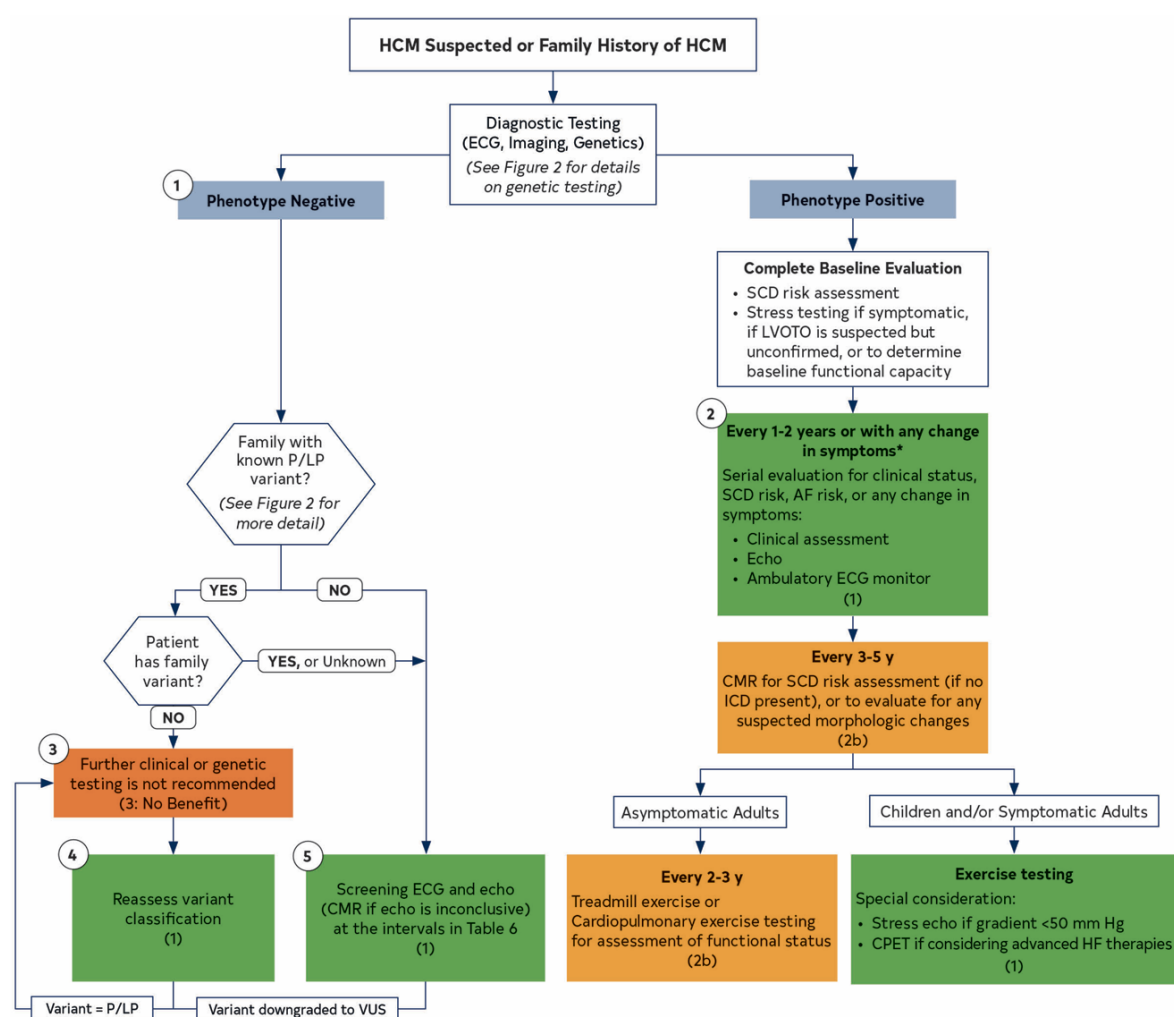
Cardiac CT in patients with inadequate echocardiographic imaging and contraindications for CMR IIa-C

Endomyocardial biopsy

When the results of other clinical assessments suggest myocardial infiltration, inflammation or storage that cannot be confirmed by other means. IIb-C

^{99m}Tc-DPD: ^{99m}Technetium-3,3-diphosphono-1,2-propano-di-carboxylic acid

ESC 2014 Guidelines on diagnosis and management of hypertrophic cardiomyopathy, *Eur Heart J.* 2014;35:2733–79, with permission from Oxford University Press.

**Figure 3. AHA/ACC 2024 GL on HCM.** Recommended evaluation and testing for HCM.

*The interval may be extended, particularly in adult patients who remain stable after multiple evaluations.

AF indicates atrial fibrillation; CMR, cardiovascular magnetic resonance; CPET, cardiopulmonary exercise test; ECG, electrocardiography/electrocardiogram; echo, echocardiography/echocardiogram; 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.

Table 11. Specific aspects of diagnosis**ESC 2021 GL on HF. Hypertrophic cardiomyopathy: specific aspects of diagnosis and treatment. Differential diagnosis**

It might be difficult with physiological hypertrophy induced by intense athletic training, severe hypertension or aortic stenosis and with isolated septal hypertrophy. Consider a genetic HCM if the degree of LV hypertrophy is disproportionate with respect to the acquired trigger.

Consider amyloidosis as a cause when increased thickness of the interatrial septum, AV valve and/or RV free wall are detected.

AV=atrio-ventricular

2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur Heart J

Table 12. AHA/ACC 2024 GL on HCM. 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 diseases	Biochemical screening Genetic testing
Youth and adolescence	Skeletal muscle weakness or movement disorder	Friedreich's ataxia Danon disease Mitochondrial disease	Biochemical screening Neuromuscular assessment Genetic testing
Adulthood	Movement disorder, peripheral neuropathy, renal dysfunction	Anderson-Fabry disease Friedreich's ataxia infiltrative disorders (eg, amyloidosis) Glycogen storage diseases Mitochondrial disease	Biochemical screening Neuromuscular assessment Genetic testing

Table 13. Genetic testing and family screening.**AHA/ACC 2024 GL on HCM. Genetics and family screening.**

Evaluation of familial inheritance in patients with HCM, including a 3-generation family history, as part of the initial assessment.	I-B-NR
Genetic testing in patients with HCM to elucidate the genetic basis to facilitate the identification of family members at risk for developing HCM (cascade testing).	I-B-NR
A work-up including genetic testing for HCM and other genetic causes of unexplained cardiac hypertrophy (“HCM phenocopies”) in patients with an atypical clinical presentation of HCM or when another genetic condition is suspected.	I-B-NR
Pre- and post test genetic counselling by an expert in the genetics of cardiovascular disease so that risks, benefits, results, and their clinical significance can be reviewed and discussed with the patient in a shared decision-making process.	I-B-NR
When performing genetic testing in a HCM proband, the initial tier of genes tested should include genes with strong evidence to be disease-causing in HCM.*	I-B-NR
Offer both clinical screening (ECG and 2D echocardiogram) and cascade genetic testing (when a pathogenic/likely pathogenic variant has been identified in the proband) in first-degree relatives of patients with HCM.	I-B-NR
Postmortem genetic testing to facilitate cascade genetic testing and clinical screening in first-degree relatives, in families where a sudden unexplained death has occurred with a postmortem diagnosis of HCM	I-B-NR
Serial reevaluation of the clinical significance of the variant(s) identified to assess for variant reclassification which may impact diagnosis and cascade genetic testing in family members, in patients who have undergone genetic testing	I-B-NR
Preconception and prenatal reproductive and genetic counseling in affected families with HCM	I-B-NR
In patients with HCM, the usefulness of genetic testing in the assessment of risk of SCD is uncertain.	IIb-B-NR
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.	IIb-B-NR
For patients with HCM who have undergone genetic testing and were found to have no pathogenic variants (ie, harbor only benign/ likely benign variants), cascade genetic testing of the family is not useful.	III-B-NR No benefit
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.	III-B-NR No benefit

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

AHA/ACC 2024 GL on HCM. Individuals Who Are Genotype-Positive, Phenotype-Negative

Serial clinical assessment, electrocardiography, and cardiac at periodic intervals depending on age (every 1 to 2 years in children and adolescents, and every 3 to 5 years in adults) and change in clinical status	I-B-NR
Participation in competitive athletics of any intensity	IIa-B-NR
ICD is not recommended for primary prevention	III-B-NR No benefit

EHRA/HRS/APHRS/LAHRs 2022 Consensus Statement on genetic testing.

Impact of genetic testing for the index case

Disease	Diagnostic	Prognostic	Therapeutic
HCM	+++	++	++

Recommendations

Should do

For genetic testing in a proband with HCM (including those cases diagnosed post-mortem), the initial tier of genes tested should include genes with definitive or strong evidence of pathogenicity (currently MYH7, MYBPC3, TNNI3, TPM1, MYL2, MYL3, ACTC1, and TNNT2).

In patients with HCM, genetic testing for identification of family members at risk of developing HCM. Genetic testing is recommended for patients with atypical clinical presentation of HCM, or when another genetic condition associated with unexplained hypertrophy is suspected (e.g. HCM phenocopy).

Predictive genetic testing in related children is recommended in those aged >10–12 years.

In patients with HCM who harbour a variant of uncertain significance, testing of affected family members for the purpose of variant classification.

May do

For genetic testing in a proband with HCM, the initial tier of genes tested may include genes with moderate evidence of pathogenicity (CSRP3, TNNC1, JPH2).

In patients with HCM who harbour a variant of uncertain significance, the usefulness of genetic testing of phenotype-negative relatives for the purpose of variant reclassification is uncertain.

Predictive genetic testing in related children aged below 10–12 years may be considered, especially where there is a family history of early-onset disease.

Do not do

For patients with HCM in whom genetic testing found no LP/P variants, cascade genetic testing of family relatives is not recommended.

Ongoing clinical screening is not recommended in genotype-negative relatives in most families with genotype-positive HCM.

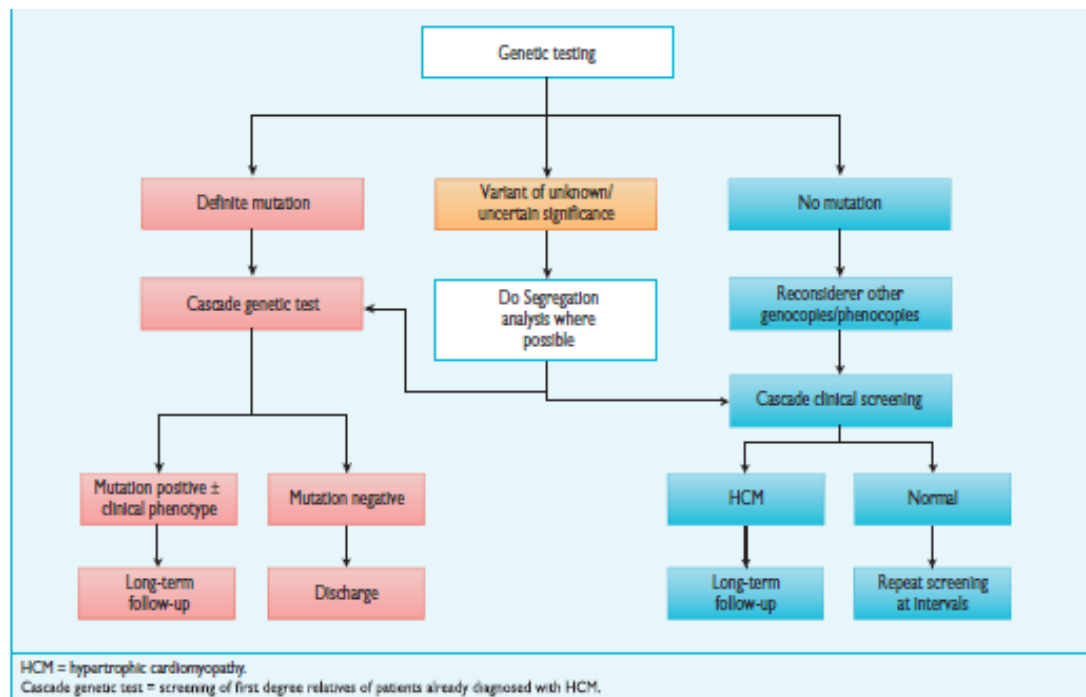


Figure 4. ESC 2014 GL on HCM. Flow chart for the genetic and clinical screening of probands and relatives.

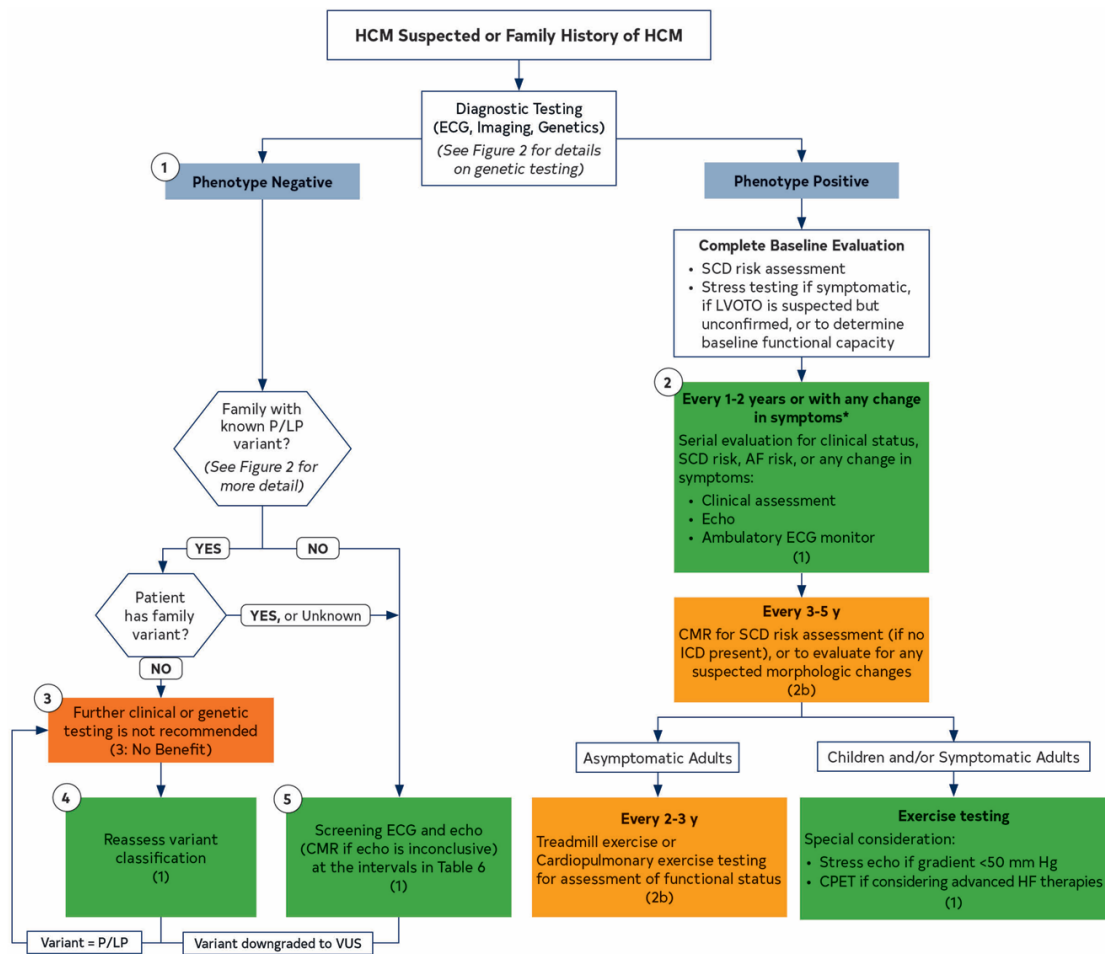


Figure 5. AHA/ACC 2024 GL on HCM Genetic testing process in HCM.

*The interval may be extended, particularly in adult patients who remain stable after multiple evaluations.

AF indicates atrial fibrillation; CMR, cardiovascular magnetic resonance; CPET, cardiopulmonary exercise test; ECG, electrocardiography/electrocardiogram; echo, echocardiography/echocardiogram; 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.

Table 14. Risk stratification

ESC 2023 GL on Cardiomyopathies. Major clinical features associated with an increased risk of sudden cardiac death

Risk factor	Comment
Age	- The effect of age on SCD has been examined in a number of studies^{86,525,584,760–764} and two have shown a significant association, with an increased risk of SCD in younger patients.^{525,584} - Some risk factors appear to be more important in younger patients, most notably NSVT,⁷⁶⁵ severe LVH,⁷⁶⁶ and unexplained syncope.⁵⁸⁴ - Sudden cardiac death is very rare below the age of 6 years,^{535,767} and there are some data to suggest a peak of SCD in childhood HCM between 9 and 15 years;⁷⁵⁷ however, the association between age at diagnosis and SCD risk in childhood HCM remains unclear.
NSVT	- NSVT (defined as ≥ 3 consecutive ventricular beats at ≥ 120 b.p.m. lasting <30 s) occurs in 20–30% of patients during ambulatory ECG monitoring and is an independent predictor of SCD.^{81,525,535,590,764,765,768–773} - There is no evidence that the frequency, duration, or rate of NSVT influences the risk of SCD.^{765,774} - NSVT occurring during or immediately following exercise is very rare, but may be associated with a high risk of SCD.⁷⁶⁸
Maximum LV wall thickness	- The severity and extent of LVH measured by TTE are associated with the risk of SCD.^{81,535,592,593,763,765,770–772,775–780} - Several studies have shown the greatest risk of SCD in patients with a maximum wall thickness of ≥ 30 mm; however, there are few data in patients with extreme hypertrophy (≥ 35 mm).^{525,592,763,765,769,781–784}
Family history of sudden cardiac death at a young age	- While definitions vary,^{525,592,762,782} a family history of SCD is usually considered clinically significant when one or more first-degree relatives have died suddenly aged <40 years with or without a diagnosis of HCM, or when SCD has occurred in a first-degree relative at any age with an established diagnosis of HCM. - Family history of SCD does not appear to be an independent risk factor for SCD in childhood HCM.^{81,535} This may be due to a higher prevalence of <i>de novo</i> variants in childhood HCM, the inclusion of non-sarcomeric disease, and/or under-reporting of family history in paediatric cohorts.
Syncope	- Syncope is common in patients with HCM but is challenging to assess, as it has multiple causes.⁷⁸⁵ - Non-neurocardiogenic syncope for which there is no explanation after investigation is associated with an increased risk of SCD.^{81,525,535,584,590,755,761,768,769,781,786–788} - Episodes within 6 months of evaluation may be more predictive of SCD.⁵⁸⁴
Left atrial diameter	Several studies have reported a positive association between LA size and SCD.^{81,525,535,584,772,789} There are no data on the association between SCD and LA area or volume. Measurement of LA size is also important in assessing the risk of AF (see Section 6.10.3).
LV outflow tract obstruction	- A number of studies have reported a significant association between LVOTO and SCD risk.^{86,525,590,762,768,790} Several unanswered questions remain, including the prognostic importance of provokable LVOTO and the impact of treatment (medical or invasive) on SCD. - In childhood HCM, there are conflicting data on the association between LVOTO and SCD risk.^{81,535,772,777}

AF, atrial fibrillation; b.p.m., beats per minute; ECG, electrocardiogram; HCM, hypertrophic cardiomyopathy; LA, left atrium; LV, left ventricular; LVH, left ventricular hypertrophy; LVOTO, left ventricular outflow tract obstruction; NSVT, non-sustained ventricular tachycardia; SCD, sudden cardiac death; TTE, transthoracic echocardiogram.

ESC 2022 GL on VA and SCD. Recommendations for risk stratification, sudden cardiac death prevention, and treatment of ventricular arrhythmias in hypertrophic cardiomyopathy

Diagnostic evaluation and general recommendations

CMR with LGE in HCM patients for diagnostic work-up.	I B
Genetic counselling and testing are recommended in HCM patients.	I B
Participation in high-intensity exercise for asymptomatic adult HCM patients without risk markers.	IIb C

AHA/ACC 2024 GL on HCM. Clinical Sudden Death Risk Factors for Adults and Children With HCM

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 y of age. Close relatives would generally be second-degree relatives; however, multiple SCDs in tertiary relatives should also be considered relevant. ^{30,31}
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 thickness that corresponds to a z-score ≥ 20 (and >10 in conjunction with other risk factors) appears reasonable. ^{32,33}
Unexplained syncope	≥ 1 unexplained episodes involving acute transient loss of consciousness, judged by history unlikely to be of neurocardiogenic (vasovagal) etiology, not attributable to LVOTO, and especially when occurring within 6 mo of evaluation (events beyond 5 y in the past do not appear to have relevance). ³⁴
HCM with LV systolic dysfunction	Systolic dysfunction with EF $<50\%$ by echocardiography or CMR imaging. ^{24,27}
LV apical aneurysm	Apical aneurysm defined as a discrete thin-walled dyskinetic or akinetic segment with transmural scar or LGE of the most distal portion of the LV chamber, independent of size. (In children, apical aneurysm is uncommon, and the risk has not been studied.) ^{15,16}
Extensive LGE on CMR imaging	Extensive LGE, representing replacement fibrosis, either quantified or estimated by visual inspection, comprising $\geq 15\%$ of LV mass (extent of LGE conferring risk has not been defined in children). ^{9–11,20–22,25}
NSVT on ambulatory monitor	≥ 3 beats at ≥ 120 bpm has generally been used in studies. It would seem most appropriate to place greater weight on NSVT as a risk marker when runs are frequent (eg, ≥ 3), longer (eg, ≥ 10 beats), or faster (eg, ≥ 200 bpm) occurring usually over 24 to 48 h of monitoring. For pediatric patients, a VT rate that exceeds the baseline sinus rate by $>20\%$ is considered significant. ^{35–37}
Genotype status	Genotype-positive status (ie, harboring a putatively disease-causing pathogenic/likely pathogenic variant) is associated with higher SCD risk in pediatric patients with HCM. ^{12,14}

bpm indicates beats/min; CMR, cardiovascular magnetic resonance; EF, ejection fraction; HCM, hypertrophic cardiomyopathy; LGE, late gadolinium enhancement; LV, left ventricular; LVH, left ventricular hypertrophy; LVOTO, left ventricular outflow tract obstruction; NSVT, nonsustained ventricular tachycardia; SCD, sudden cardiac death; and VT, ventricular tachycardia.

AHA/ACC 2024 GL on HCM. SCD risk assessment in adults with HCM

A comprehensive, systematic noninvasive SCD risk assessment at initial evaluation and every 1 to 2 years thereafter, and should include evaluation of these risk factors: I-B-NR

- Personal history of cardiac arrest or sustained ventricular arrhythmias
- Personal history of syncope suspected by clinical history to be arrhythmic
- Family history in close relative of premature HCM-related sudden death, cardiac arrest, or sustained ventricular arrhythmias
- Maximal LV wall thickness, EF, LV apical aneurysm
- NSVT episodes on continuous ambulatory electrocardiographic monitoring

For patients who are not otherwise identified as high risk for SCD, or in whom a decision to proceed with ICD placement 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. I-B-NR

For patients who are ≥ 16 years of age 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 IIa-B-NR

SCD: sudden cardiac death

AHA/ACC 2024 GL on HCM. SCD risk assessment in children and adolescents with HCM

A comprehensive, systematic noninvasive SCD risk assessment at initial evaluation and every 1 to 2 years thereafter, and should include evaluation of these risk factors: I-B-NR

- 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

When there is a borderline risk for SCD, or a decision to proceed with ICD placement remains uncertain after clinical assessment that includes personal and family history, echocardiography, and ambulatory electrocardiographic monitoring, CMR imaging to assess for extent of myocardial fibrosis with LGE I C-LD

For patients <16 years of age with HCM, calculate an estimated 5-year sudden death risk that includes echocardiographic parameters (interventricular septal thickness in diastole, LV posterior wall thickness in end-diastole, left atrial diameter, maximal LVOT gradient) and genotype, which may be useful during shared decision-making for ICD placement IIa B-NR

SCD: sudden cardiac death

Table 15. Medical Therapy**AHA/ACC 2020 GL on HCM. Pharmacologic management of patients with obstructive HCM**

Non-vasodilating beta-blockers, titrated to effectiveness or maximally tolerated doses, for patients with symptoms* attributable to LVOTO. I-B-NR

Verapamil I-B-NR
or diltiazem I-C-LD
for patients with symptoms* attributable to LVOTO,
for whom beta-blockers are ineffective or not tolerated.

A myosin inhibitor (adult patients only) or isopyramide in combination I-B-R
(with an atrioventricular blocking agent) or SRT performed at experienced centers,†
for patients who have persistent severe symptoms* attributable to LVOTO
despite beta-blockers or non-dihydropyridine calcium channel blockers.

IV phenylephrine (or other vasoconstrictors without inotropic I-C-LD
activity), alone or in combination with beta blocking drugs,
for patients with acute hypotension who do not respond
to fluid administration.

Cautious use of low-dose oral diuretics for persistent dyspnea with clinical evidence I Ib-C-EO
of volume overload and high left- sided filling pressures despite other HCM GDMT.

Discontinuation of vasodilators (eg, angiotensin converting I Ib-C-EO
enzyme inhibitors, angiotensin receptor blockers, dihydropyridine calcium
channel blockers) or digoxin, because these agents can worsen
symptoms caused by dynamic outflow tract obstruction.

Verapamil is potentially harmful in patients with obstructive HCM and severe III-C-LD
dyspnea at rest, hypotension, very high resting gradients (eg, >100 mm Hg), Harm
as well as all children <6 weeks of age.

*Symptoms include effort-related dyspnea or chest pain; and occasionally other exertional symptoms (eg, 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.

SRT: septal reduction therapy

GDMT: guideline-directed management and therapy

LVOTO: left ventricular outflow tract obstruction

AHA/ACC 2020 GL on HCM. Management of patients with nonobstructive HCM with preserved LVEF

Beta-blockers or nondihydropyridine calcium channel blockers for exertional angina or dyspnea.	I-C-LD
Add oral diuretics when exertional dyspnea persists despite the use of beta-blockers or non-dihydropyridine calcium channel blockers.	IIa-C-EO
The usefulness of angiotensin converting enzyme inhibitors and angiotensin receptor blockers in the treatment of symptoms (angina and dyspnea) is not well established.	IIb-C-LD
Apical myectomy by experienced surgeons at comprehensive centers to reduce symptoms of 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 (LV end-diastolic volume <50 mL/m ² and LV stroke volume <30 mL/m ² . ¹²	IIb-C-LD
In asymptomatic patients, the benefit of beta-blockers or calcium channel blockers is not well established.	IIb-C-EO
Valsartan to slow adverse cardiac remodeling in younger (eg, ≤45 years of age) patients with nonobstructive HCM due to a pathogenic or likely pathogenic cardiac sarcomere genetic variant, and a mild phenotype.*	IIb B-R

*Mild phenotype indicates NYHA functional class I or II, maximal LV wall thickness 13 to 25 mm, no secondary prevention ICDs, no history of appropriate ICD shocks, and no AF.

ESC 2023 GL on Cardiomyopathies. Recommendations for treatment of left ventricular outflow tract obstruction (general measures)

Avoidance of digoxin and arterial and venous dilators, including nitrates and phosphodiesterase inhibitors, should be considered, if possible, in patients with resting or provokable LVOTO. ^{626,627}	IIa	C
Restoration of sinus rhythm or appropriate rate control should be considered before invasive management of LVOTO in patients with new-onset or poorly controlled AF. ^{629,630}	IIa	C

AF, atrial fibrillation; LVOTO, left ventricular outflow tract obstruction.

ESC 2023 GL on Cardiomyopathies. Recommendations for medical treatment of left ventricular outflow tract obstruction

Non-vasodilating beta-blockers, titrated to maximum tolerated dose, are recommended as first-line therapy to improve symptoms in patients with resting or provoked ^c LVOTO. ^{631-633,648-650}	I	B
Verapamil or diltiazem, titrated to maximum tolerated dose, are recommended to improve symptoms in symptomatic patients with resting or provoked ^c LVOTO who are intolerant or have contraindications to beta-blockers. ^{633,637-641}	I	B
Disopyramide, ^d titrated to maximum tolerated dose, is recommended in addition to a beta-blocker (or, if this is not possible, with verapamil or diltiazem) to improve symptoms in patients with resting or provoked ^c LVOTO. ⁶³²⁻⁶³⁴	I	B
Cardiac myosin ATPase inhibitor (mavacamten), titrated to maximum tolerated dose with echocardiographic surveillance of LVEF, should be considered in addition to a beta-blocker (or, if this is not possible, with verapamil or diltiazem) to improve symptoms in adult patients with resting or provoked ^c LVOTO. ^{622,642-646}	IIa	A
Cardiac myosin ATPase inhibitor (mavacamten), titrated to maximum tolerated dose with echocardiographic surveillance of LVEF, should be considered as monotherapy in symptomatic adult patients with resting or provoked ^c LVOTO (exercise or Valsalva manoeuvre) who are intolerant or have contraindications to beta-blockers, verapamil/diltiazem, or disopyramide. ^{622,644-646}	IIa	B
Oral or i.v. beta-blockers and vasoconstrictors should be considered in patients with severe provokable ^c LVOTO presenting with hypotension and acute pulmonary oedema who do not respond to fluid administration. ⁶²⁷	IIa	C
Disopyramide, titrated to maximum tolerated dose, may be considered as monotherapy in patients who are intolerant to or have contraindications to beta-blockers and verapamil/diltiazem to improve symptoms in patients with resting or provoked ^c LVOTO. ⁶³²	IIb	C
Beta-blockers or verapamil may be considered in selected cases in <i>asymptomatic</i> patients with resting or provoked ^c LVOTO to reduce LV pressures. ^{623,639}	IIb	C
The cautious use of low-dose diuretics may be considered in symptomatic LVOTO to improve exertional dyspnoea.	IIb	C

ATPase, adenosine triphosphatase; i.v., intravenous; LV, left ventricular; LVEF, left ventricular ejection fraction; LVOTO, left ventricular outflow tract obstruction.

c Provocation with Valsalva manoeuvre, upright exercise, or oral nitrates if unable to exercise.

d QTc interval should be monitored during up-titration of disopyramide and the dose reduced if it exceeds 500 ms.

ESC 2023 GL on Cardiomyopathies. Recommendations for chest pain on exertion in patients without left ventricular outflow tract obstruction

Beta-blockers and calcium antagonists (verapamil or diltiazem) should be considered to improve symptoms in patients with angina-like chest pain even in the absence of LVOTO or obstructive CAD. ⁷⁴⁰⁻⁷⁴⁴	IIa	C
Oral nitrates may be considered to improve symptoms in patients with angina-like chest pain, even in the absence of obstructive CAD, if there is no LVOTO.	IIb	C
Ranolazine may be considered to improve symptoms in patients with angina-like chest pain even in the absence of LVOTO or obstructive CAD. ^{738,739}	IIb	C

CAD, coronary artery disease; LVOTO, left ventricular outflow tract obstruction.

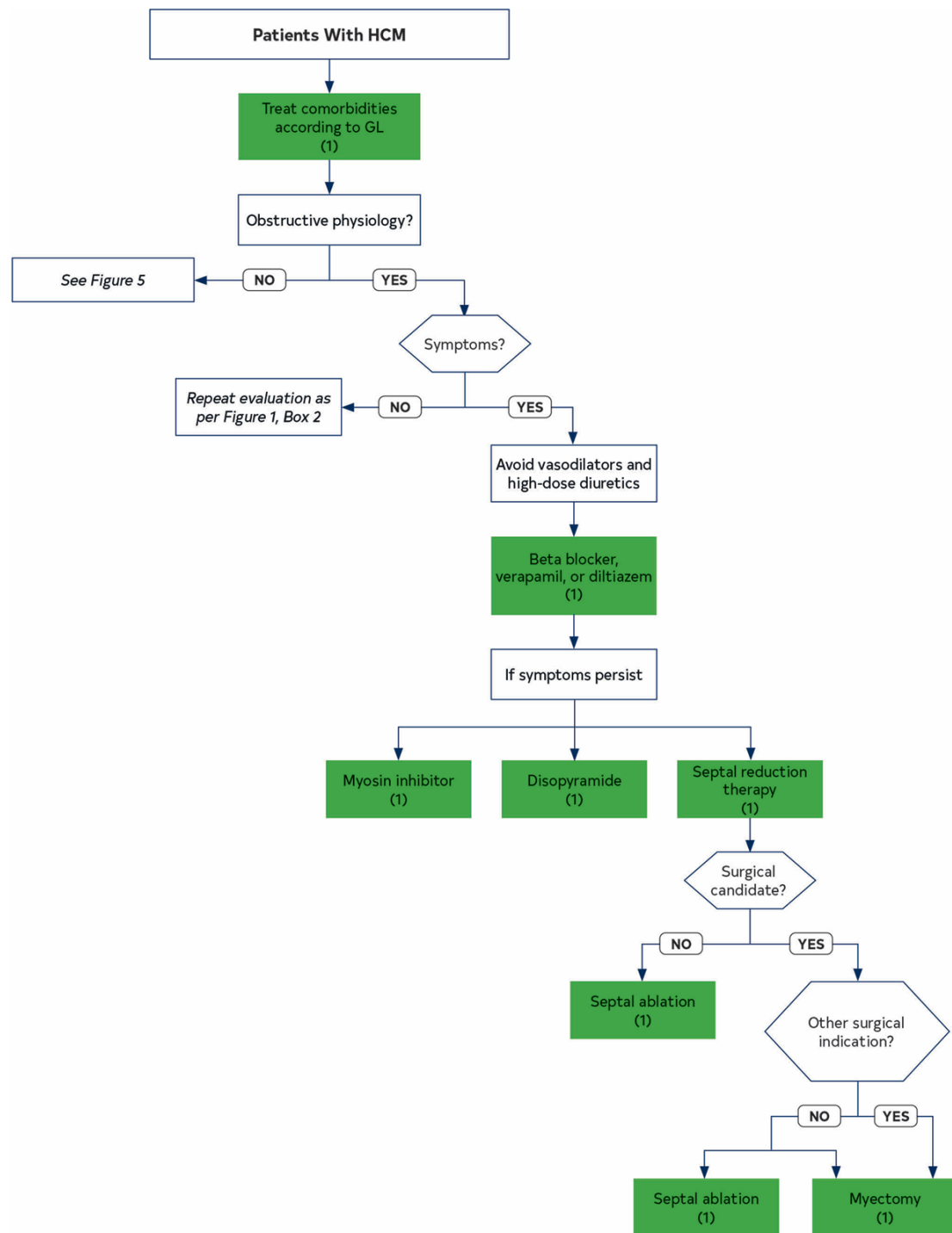


Figure 6. AHA/ACC 2024 GL on HCM. Management of symptoms in patients with HCM.

GL indicates guideline; HCM, hypertrophic cardiomyopathy

Please change:

“See Figure 5” to: “See Figure 11”

“Repeat evaluation as per Figure 1, Box 2” to: “Repeat evaluation as per Figure 3”

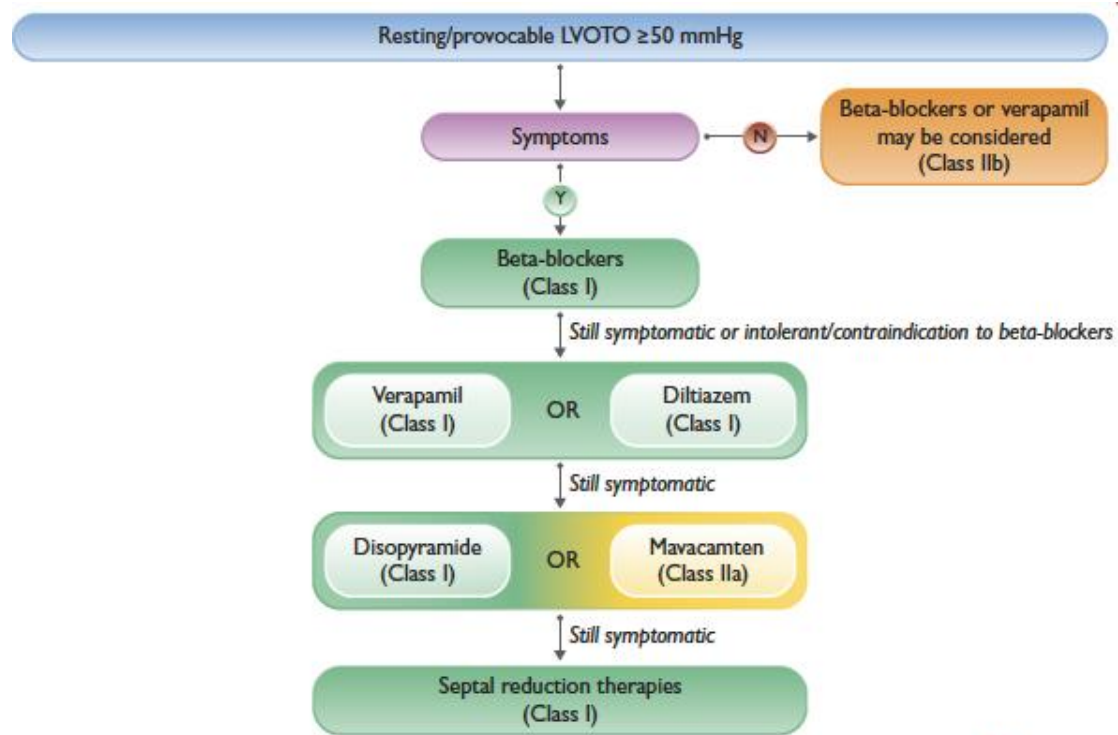


Figure 7. ESC 2023 GL on Cardiomyopathies. Flow chart on the management of left ventricular outflow tract obstruction.

LVOTO, left ventricular outflow tract obstruction.

Table 16. Septal reduction therapies**AHA/ACC 2020 GL on HCM. Invasive treatment of symptomatic patients with obstructive HCM.**

In patients who remain severely symptomatic despite GDMT, SRT in eligible patients,* performed at experienced centers,† for relieving LVOTO.	I-B-NR
Surgical myectomy, performed at experienced centers,† in associated cardiac disease requiring surgical treatment (eg, associated anomalous papillary muscle, markedly elongated anterior mitral leaflet, intrinsic mitral valve disease, multivessel CAD, valvular aortic stenosis).	I-B-NR
Alcohol septal ablation in eligible patients,* performed at experienced centers,† in adult patients 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.	I-C-LD
Earlier (NYHA class II) surgical myectomy performed at comprehensive HCM centers, 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).	IIB-B-NR
SRT in eligible patients,* performed at experienced centers† for severely symptomatic patients, as an alternative to escalation of medical therapy after shared decision-making including risks and benefits of all treatment options.	IIB-C-LD
For patients who are asymptomatic and have normal exercise capacity, SRT is not recommended.	III-C-LD Harm
When SRT is an option, mitral valve replacement should not be performed for the sole purpose of relief of LVOTO.	III-B-NR Harm

*General eligibility criteria for septal reduction therapy:

- Clinical: Severe dyspnea or chest pain (usually NYHA functional class III or class IV), or occasionally other exertional symptoms (eg, syncope, near syncope), when attributable to LVOTO, that interferes with everyday activity or quality of life despite optimal medical therapy.
- 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.
- 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.

ESC 2023 GL on Cardiomyopathies. Recommendations for septal reduction therapy

It is recommended that SRT be performed by experienced operators working as part of a multidisciplinary team expert in the management of HCM. ^{664,665,687,695,696,708–710}	I	C
SRT to improve symptoms is recommended in patients with a resting or maximum provoked LVOT gradient of ≥ 50 mmHg who are in NYHA/Ross functional class III–IV, despite maximum tolerated medical therapy. ^{697–702}	I	B
Septal myectomy, rather than ASA, is recommended in children with an indication for SRT, as well as in adult patients with an indication for SRT and other lesions requiring surgical intervention (e.g. mitral valve abnormalities). ⁶⁷³	I	C
SRT should be considered in patients with recurrent exertional syncope caused by a resting or maximum provoked LVOTO gradient ≥ 50 mmHg despite optimal medical therapy. ^{686,711–713}	IIa	C
Mitral valve repair or replacement should be considered in symptomatic patients with a resting or maximum provoked LVOTO gradient ≥ 50 mmHg and moderate-to-severe mitral regurgitation that cannot be corrected by SRT alone. ^{661,669–672,714}	IIa	C
Mitral valve repair should be considered in patients with a resting or maximum provoked LVOTO gradient ≥ 50 mmHg when there is moderate-to-severe mitral regurgitation following isolated myectomy.	IIa	C
SRT may be considered in expert centres with demonstrable low procedural complication rates in patients with mild symptoms (NYHA class II) refractory to medical therapy who have a resting or maximum provoked (exercise or Valsalva) gradient of ≥ 50 mmHg and: • moderate-to-severe SAM-related mitral regurgitation; or • AF; or • moderate-to-severe left atrial dilatation.^{653,715}	IIb	C
Mitral valve replacement may be considered in patients with a resting or maximum provoked LVOTO gradient ≥ 50 mmHg when there is moderate-to-severe mitral regurgitation following isolated myectomy. ^{661,674,714,716}	IIb	C
Surgical AF ablation and/or left atrial appendage occlusion procedures during septal myectomy may be considered in patients with HCM and symptomatic AF. ^{717,718}	IIb	C

AF, atrial fibrillation; ASA, alcohol septal ablation; HCM, hypertrophic cardiomyopathy; LVOT, left ventricular outflow tract; LVOTO, left ventricular outflow tract obstruction; NYHA, New York Heart Association; SAM, systolic anterior motion; SRT, septal reduction therapy.

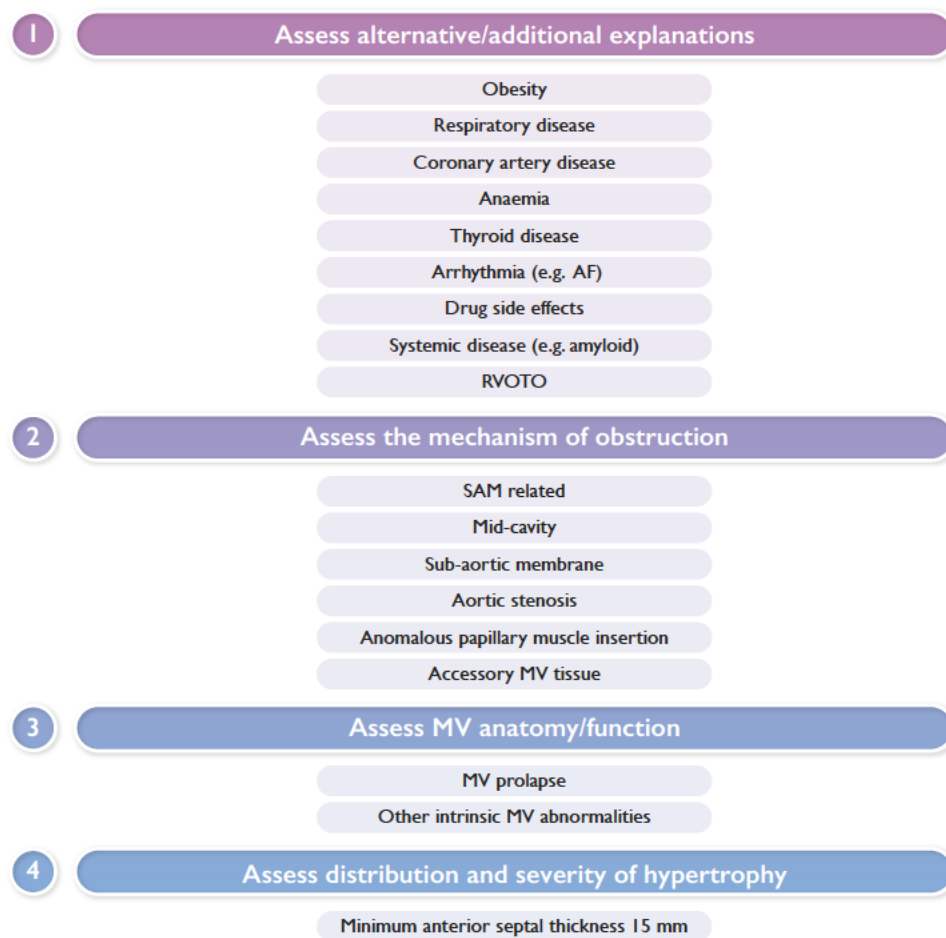


Figure 8. ESC 2023 GL on Cardiomyopathies. Pre-assessment checklist for patients being considered for invasive septal reduction therapies.

AF, atrial fibrillation; MV, mitral valve; RVOTO, right ventricular outflow tract obstruction; SAM, systolic anterior motion.

Table 17. Pacing

ESC 2023 GL on Cardiomyopathies. Recommendations for indications for cardiac pacing in patients with obstruction

Sequential AV pacing, with optimal AV interval to reduce the LV outflow tract gradient or to facilitate medical treatment with beta-blockers and/or verapamil, may be considered in selected patients with resting or provokable LVOTO ≥ 50 mmHg, sinus rhythm, and drug-refractory symptoms, who have contraindications for ASA or septal myectomy or are at high risk of developing heart block following ASA or septal myectomy. ^{633,719–724}	IIb	C
In patients with resting or provokable LVOTO ≥ 50 mmHg, sinus rhythm, and drug-refractory symptoms, in whom there is an indication for an ICD, a dual-chamber ICD (instead of a single-lead device) may be considered, to reduce the LV outflow tract gradient or to facilitate medical treatment with beta-blockers and/or verapamil. ^{633,719–724,726}	IIb	C

ASA, alcohol septal ablation; AV, atrioventricular; ICD, implantable cardioverter defibrillator; LV, left ventricular; LVOTO, left ventricular outflow tract obstruction.

TABLE 18. Implantable Cardioverter Defibrillator**AHA/ACC 2024 GL on HCM. Patient selection for ICD placement**

Application of individual clinical judgment 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.	I-C-EO
ICD in previous documented cardiac arrest or sustained VT	I-B-NR
ICD for adult patients with ≥ 1 major risk factors for SCD. 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 (ie, unlikely to be of neurocardiogenic [vasovagal] etiology, or related to LVOTO); d. LV apical aneurysm, independent of size; e. LV systolic dysfunction (EF $< 50\%$).	Ila-B-NR
ICD placement in children who have ≥ 1 conventional risk factors, including unexplained syncope, massive LVH, NSVT, or family history of early HCM-related SCD, after considering the relatively high complication rates of long-term ICD placement in younger patients	Ila-B-NR
For patients with HCM with ≥ 1 major SCD risk factors, discussion of the estimated 5-year suddendeath risk and mortality rates during the shared decision-making process for ICD placement	Ila B-NR
ICD in extensive LGE by contrast-enhanced CMR imaging or NSVT on ambulatory monitoring, in adult patients without major SCD risk factors after clinical assessment, or in whom the decision to proceed remains otherwise uncertain.	Iib-B-NR
In pediatric patients in whom risk stratification is otherwise less certain, consider additional factors such as extensive LGE on contrast-enhanced CMR imaging and systolic dysfunction in risk stratification.	Iib-B-NR
In patients without risk factors, ICD placement should not be performed	III-B-NR Harm
ICD placement for the sole purpose of participation in competitive athletics should not be performed.	III-B-NR Harm

AHA/ACC 2024 GL on HCM. ICD device selection considerations

A single chamber transvenous or a subcutaneous ICD after a shared decision-making discussion that takes into consideration patient preferences, lifestyle, and expected potential need for pacing for bradycardia or VT termination.	I-B-NR
Single-coil in preference to dual-coil leads if defibrillation threshold is adequate	I-B-NR
Dual-chamber ICDs 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).	IIa-B-NR
Cardiac resynchronization therapy (CRT) for symptom reduction in adult patients with nonobstructive HCM receiving an ICD who have NYHA class II to ambulatory class IV HF, LBBB), and LVEF <50%	IIa-C-LD
Dual-chamber ICD in patients in whom a decision has been made for ICD implantation and who have paroxysmal atrial tachycardias or AF, but this decision must be balanced against higher complication rates of dual-chamber devices.	IIb-C-LD

ESC 2023 GL on Cardiomyopathies. Additional recommendations for prevention of sudden cardiac death in patients with hypertrophic cardiomyopathy

Secondary prevention		
Implantation of an ICD is recommended in patients who have survived a cardiac arrest due to VT or VF, or who have spontaneous sustained VT with haemodynamic compromise. ^{532,534,726,831,832}	I	B
Primary prevention		
The HCM Risk-SCD calculator is recommended as a method of estimating risk of sudden death at 5 years in patients aged ≥ 16 years for primary prevention. ^{525,821–824}	I	B
Validated paediatric-specific risk prediction models (e.g. HCM Risk-Kids) are recommended as a method of estimating risk of sudden death at 5 years in patients aged < 16 years for primary prevention. ^{81,833}	I	B
It is recommended that the 5-year risk of SCD be assessed at first evaluation and re-evaluated at 1–2 year intervals or whenever there is a change in clinical status. ⁵²⁵	I	B
Implantation of an ICD should be considered in patients with an estimated 5-year risk of sudden death of $\geq 6\%$, following detailed clinical assessment that considers: (i) the lifelong risk of complications; (ii) competing mortality risk from the disease and comorbidities; AND (iii) the impact of an ICD on lifestyle, socio-economic status, and psychological health. ^{81,521,525,726,832,833}	IIa	B
In patients with LV apical aneurysms, decisions about primary prevention ICD based on an assessment of risk using the HCM Risk-SCD or a validated paediatric risk-prediction (e.g. HCM Risk-Kids) tool and not solely on the presence of the aneurysm should be considered. ^{580,726,737,791,792}	IIa	B
Implantation of an ICD may be considered in individual patients with an estimated 5-year risk of SCD of between $\geq 4\%$ and $< 6\%$, following detailed clinical assessment that takes into account the lifelong risk of complications and the impact of an ICD on lifestyle, socio-economic status, and psychological health. ^{81,521,525,726,832,833}	IIb	B
For patients who are in the low-risk category ($< 4\%$ estimated 5-year risk of SCD), the presence of extensive LGE ($\geq 15\%$) on CMR may be considered in shared decision-making with patients about prophylactic ICD implantation, acknowledging the lack of robust data on the impact of scar quantification on the personalized risk estimates generated by HCM Risk-SCD or a validated paediatric model (e.g. HCM Risk-Kids). ^{141,796,797,834–841}	IIb	B
For patients who are in the low-risk category ($< 4\%$ estimated 5-year risk of SCD), the presence of LVEF $< 50\%$ may be considered in shared decision-making with patients about prophylactic ICD implantation, acknowledging the lack of robust data on the impact of systolic dysfunction on the personalized risk estimates generated by HCM Risk-SCD or a validated paediatric model (e.g. HCM Risk-Kids). ^{89,315,841–844}	IIb	B

CMR, cardiac magnetic resonance; HCM, hypertrophic cardiomyopathy; ICD, implantable cardioverter defibrillator; LGE, late gadolinium enhancement; LV, left ventricular; LVEF, left ventricular ejection fraction; SCD, sudden cardiac death; VF, ventricular fibrillation; VT, ventricular tachycardia.

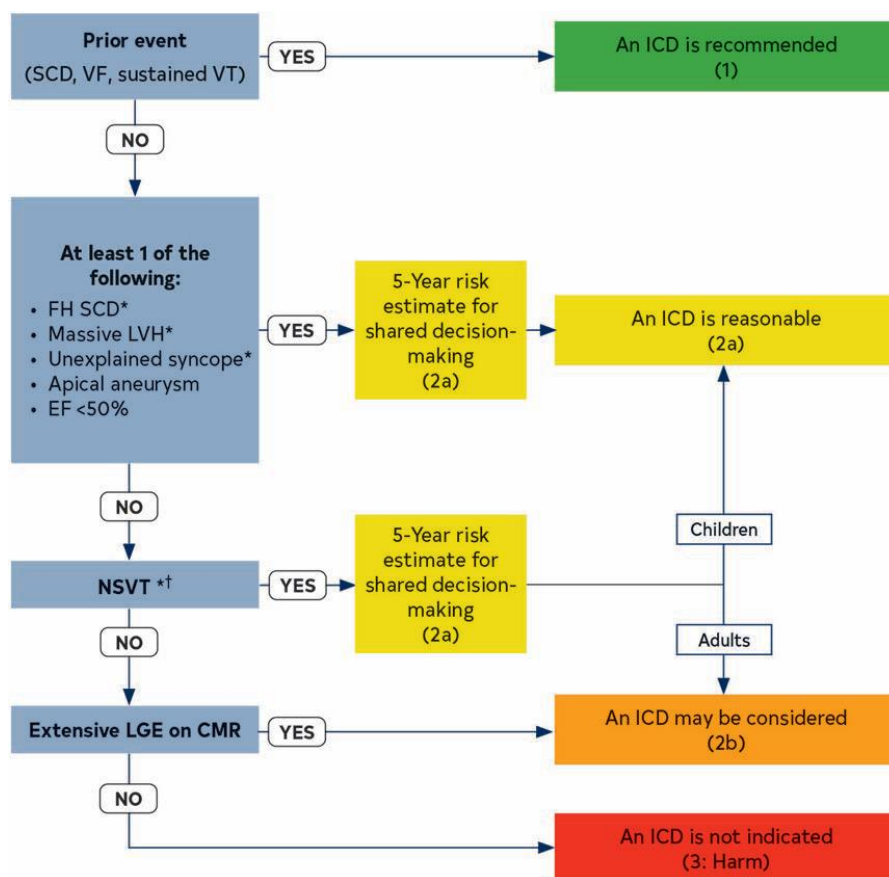


Figure 9. AHA/ACC 2024 GL on HCM Patient selection for ICD use

*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.

†5-year risk estimates can be considered to fully inform patients during shared decisionmaking 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.

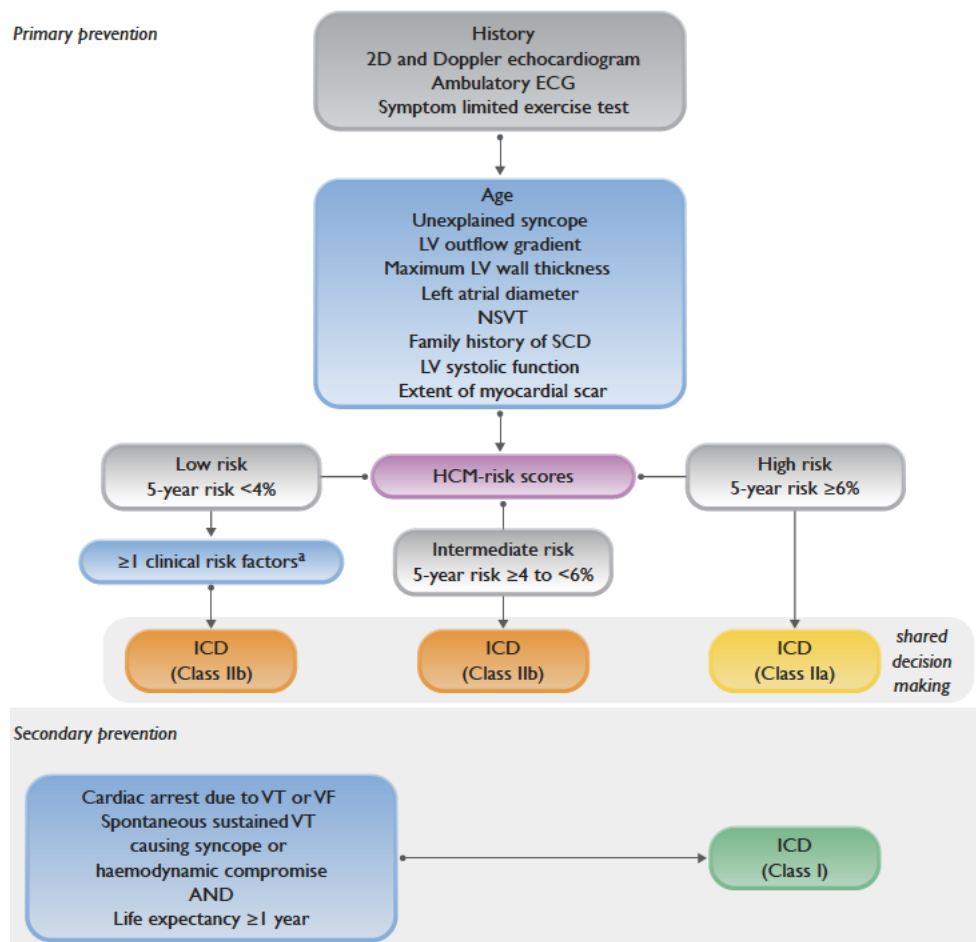


Figure 10. ESC 2023 GL on Cardiomyopathies. Flow chart for implantation of an implantable cardioverter defibrillator in patients with hypertrophic cardiomyopathy.

2D, two-dimensional; CMR, cardiac magnetic resonance; ECG, electrocardiogram; HCM, hypertrophic cardiomyopathy; ICD, implantable cardioverter defibrillator; LGE, late gadolinium enhancement; LV, left ventricular; LVEF, left ventricular ejection fraction; NSVT, non-sustained ventricular tachycardia; SCD, sudden cardiac death; VF, ventricular fibrillation; VT, ventricular tachycardia.

^a Clinical risk factors: extensive LGE ($>15\%$) on CMR; LVEF $<50\%$.

Table 19. Table. Atrial arrhythmias

ESC 2014 GL on HCM. Atrial fibrillation/atrial flutter	
Unless contraindicated, oral anticoagulation with VKA (target INR 2.0–3.0) in patients who develop persistent, permanent or paroxysmal AF	I-B
Antithrombotic therapy for patients with atrial flutter, as for those with AF.	I-C
Assessment of the risk of bleeding with the HAS-BLED score when prescribing antithrombotic therapy (whether with VKA or antiplatelet therapy).	IIa-B
Restoration of sinus rhythm, by DC or pharmacological cardioversion with IV amiodarone in patients presenting with recent-onset AF.	IIa-C
Amiodarone for achieving rhythm control and to maintain sinus rhythm after DC cardioversion.	IIa-B
β-Blockers, verapamil and diltiazem for controlling ventricular rate in permanent or persistent AF.	I-C
48-Hour ambulatory ECG monitoring every 6–12 months to detect AF in patients who are in SR and have an LA diameter of 45 mm	IIa-C
Catheter ablation for AF in patients without severe left atrial enlargement, who have drug refractory symptoms or are unable to take anti-arrhythmic drugs.	IIa-B
Ablation of the AV node to control heart rate when the ventricular rate cannot be controlled with drugs and when AF cannot be prevented by anti-arrhythmic therapy or is associated with intolerable side-effects.	IIb-C
Following AV node ablation in patients with an LVEF <50%, implantation of a DDD pacemaker with mode-switch function for patients with paroxysmal AF and a VVIR pacemaker for those in persistent or permanent AF.	I-C
In patients with any type of AF and LVEF <50%, implantation of a CRT pacemaker after AV node ablation.	IIb-C
Ablation procedures during septal myectomy in patients with symptomatic AF.	IIb-C
Antiplatelet therapy using aspirin 75–100 mg plus clopidogrel 75 mg daily (where there is a low risk of bleeding) when patients refuse the use of any OAC (whether VKAs or NOACs*).	IIa-B
When adjusted-dose VKA (INR 2–3) cannot be used in a patient with AF-due to failure to maintain therapeutic anticoagulation, side-effects of VKAs, or inability to attend or undertake INR monitoring-use a direct thrombin inhibitor (dabigatran) or an oral factor Xa inhibitor (e.g. rivaroxaban)	I-B
Unless there is a reversible cause of AF, lifelong OAC therapy with a VKA (INR 2.0–3.0), even if sinus rhythm is restored.	I-C

AHA/ACC 2020 GL on HCM. Management of AF

Anticoagulation with direct-acting oral anticoagulants (DOAC) as first-line option and vitamin K antagonists as second-line option, independent of CHA2DS2-VASc score.	I-B-NR
Anticoagulation, independent of CHA2DS2-VASc score, in subclinical AF detected by internal or external cardiac device or monitor of >24 hours' duration for a given episode	I-C-LD
For rate control, either beta-blockers, verapamil, or diltiazem.	I-C-LD
Anticoagulation for subclinical AF detected by internal or external device or monitor, of >5 minutes' but <24 hours' duration for a given episode, taking into consideration duration of AF episodes, total AF burden, underlying risk factors, and bleeding risk.	IIa-C-LD
A rhythm control strategy with cardioversion or antiarrhythmic drugs for poorly tolerated AF, with the choice of an agent according to AF symptom severity, patient preferences, and comorbid conditions.	IIa-B-NR
Catheter ablation as part of an AF rhythm control strategy can be effective when drug therapy is ineffective, contraindicated, or not the patient's preference.	IIa-B-NR
Concomitant surgical AF ablation when surgical myectomy is required. procedure can be beneficial for AF rhythm	IIa-B-NR

AHA/ACC 2024 GL on HCM. Antiarrhythmic Drug Therapy Options for Patients With HCM and AF

Antiarrhythmic Drug	Efficacy for AF	Adverse Effects	Toxicities	Use in HCM
Disopyramide	Modest	Anticholinergic HF	Prolonged QTc TdP	Particularly with early onset AF Generally used in conjunction with atrioventricular nodal blocking agents
Flecainide and propafenone	...	Prolonged QRS	Proarrhythmia Typical atrial flutter	Not generally recommended in the absence of an ICD
Sotalol	Modest	Fatigue Bradycardia	Prolonged QTc TdP	Reasonable
Dofetilide	Modest	Headache	Prolonged QTc TdP	Reasonable
Dronedarone	Low	HF	Prolonged QTc	...
Amiodarone	Modest-high	Bradycardia	Liver, lung, thyroid, skin, neurologic Prolonged QTc	Reasonable

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

Table 20. Ventricular arrhythmias

AHA/ACC 2024 GL on HCM. Management of Patients With HCM and Ventricular Arrhythmias

Heart transplantation assessment in accordance with current listing criteria, I-B-NR
in recurrent poorly tolerated life-threatening ventricular tachyarrhythmias
refractory to maximal antiarrhythmic drug therapy and ablation.

In symptomatic ventricular arrhythmias or recurrent ICD shocks despite beta-blocker
use, antiarrhythmic drug therapy with the choice of agent guided by age, underlying comorbidities,
severity of disease, patient preferences, and balance between efficacy and safety.

Amiodarone I-B-NR

Dofetilide I-C-LD1

Mexiletine I-C-LD2

Sotalol I-C-CD3

In children with recurrent ventricular arrhythmias despite betablocker I-C-LD
use, antiarrhythmic drug therapy (amiodarone, mexiletine, sotalol) is
recommended, with the choice of agent guided by age, underlying
comorbidities, severity of disease, patient preferences, and balance of efficacy and safety.

Programming antitachycardia pacing to minimize risk of shocks I-C-LD
In patients with pacing-capable ICDs.

Catheter ablation for reducing arrhythmia burden in recurrent symptomatic IIa-C-LD
sustained monomorphic VT, or recurrent ICD shocks despite optimal
device programming, and when antiarrhythmic drug therapy is either ineffective,
not tolerated, or not preferred.

Table 21. Heart failure

ESC 2014 GL on HCM	
Patients with heart failure NYHA II-IV, LVEF $\geq$50%, and no evidence for resting or provokable LVOT obstruction	
β -blockers, verapamil or diltiazem	Ila-C
Low-dose loop and thiazide diuretics	Ila-C
Patients with heart failure and LVEF <50%	
In patients without LVOT obstruction to reduce the risks of HF hospitalization and premature death. ^a	
An ACE inhibitor (or ARB if ACE inhibitor not tolerated), in addition to a β -blocker	Ila-C
A β -blocker in addition to an ACE inhibitor (or ARB if ACE inhibitor not tolerated)	Ila-C
Low-dose loop diuretics for symptomatic patients in NYHA II-IV, to improve symptoms and reduce the risk of HF hospitalization. ^a	Ila-C
A mineralocorticoid receptor antagonist to reduce the risks of HF hospitalization and premature death, ^a if NYHA Class II-IV and symptoms despite ACE inhibitor (or an ARB) and a β -blocker	Ila-C
Low-dose digoxin for patients without LVOTO who are NYHA II-IV and have AF to control heart rate response.	Ilb-C
Left ventricular assist devices	
Continuous axial flow LVAD in patients with end-stage HF despite optimal pharmacological and device treatment, who are otherwise suitable for heart transplantation, to improve symptoms, and reduce the risk of HF hospitalization from worsening HF and premature death while awaiting a transplant.	Ilb-C
Orthotopic cardiac transplantation	
Eligible patients with LVEF <50% and NYHA III-IV despite optimal medical therapy, or intractable ventricular arrhythmia.	Ila-B
Eligible patients with normal LVEF (50%) and severe drug refractory symptoms (NYHA III-IV) caused by diastolic dysfunction.	Ilb-B

a: In the absence of randomized trials in HCM, the benefit on hospitalization, symptoms and mortality is assumed but unproven.

AHA/ACC 2024 GL on HCM. HCM and advanced heart failure.

Guideline directed therapy for HF with reduced EF for patients who develop systolic dysfunction with an LVEF <50%	I-C-LD
Diagnostic testing to assess for concomitant causes of systolic dysfunction (such as CAD) in patients with systolic dysfunction.	I-C-LD
In nonobstructive HCM and advanced HF (NYHA III - IV despite GDMT), cardiopulmonary exercise test to quantify the degree of functional limitation and aid in selection of patients for heart transplantation or mechanical circulatory support.	I-B-NR
In nonobstructive HCM and advanced HF (NYHA III - IV despite GDMT)) or with life-threatening ventricular arrhythmias refractory to maximal guideline-directed therapy, assessment for heart transplantation in accordance with current listing criteria.	I-B-NR
In systolic dysfunction (LVEF <50%), discontinue previously indicated negative inotropic agents (specifically, verapamil, diltiazem, or disopyramide).	Ila-C-EO
In patients with nonobstructive HCM and advanced HF (NYHA III - IV despite GDMT) who are candidates for heart transplantation, continuous-flow LVAD therapy as a bridge to heart transplantation.	Ila-B-NR
ICD placement in LVEF <50%	Ila-C-LD
CRT in LVEF <50%, HF (NYHA III - IV despite GDMT), and LBBB	Ila-C-LD

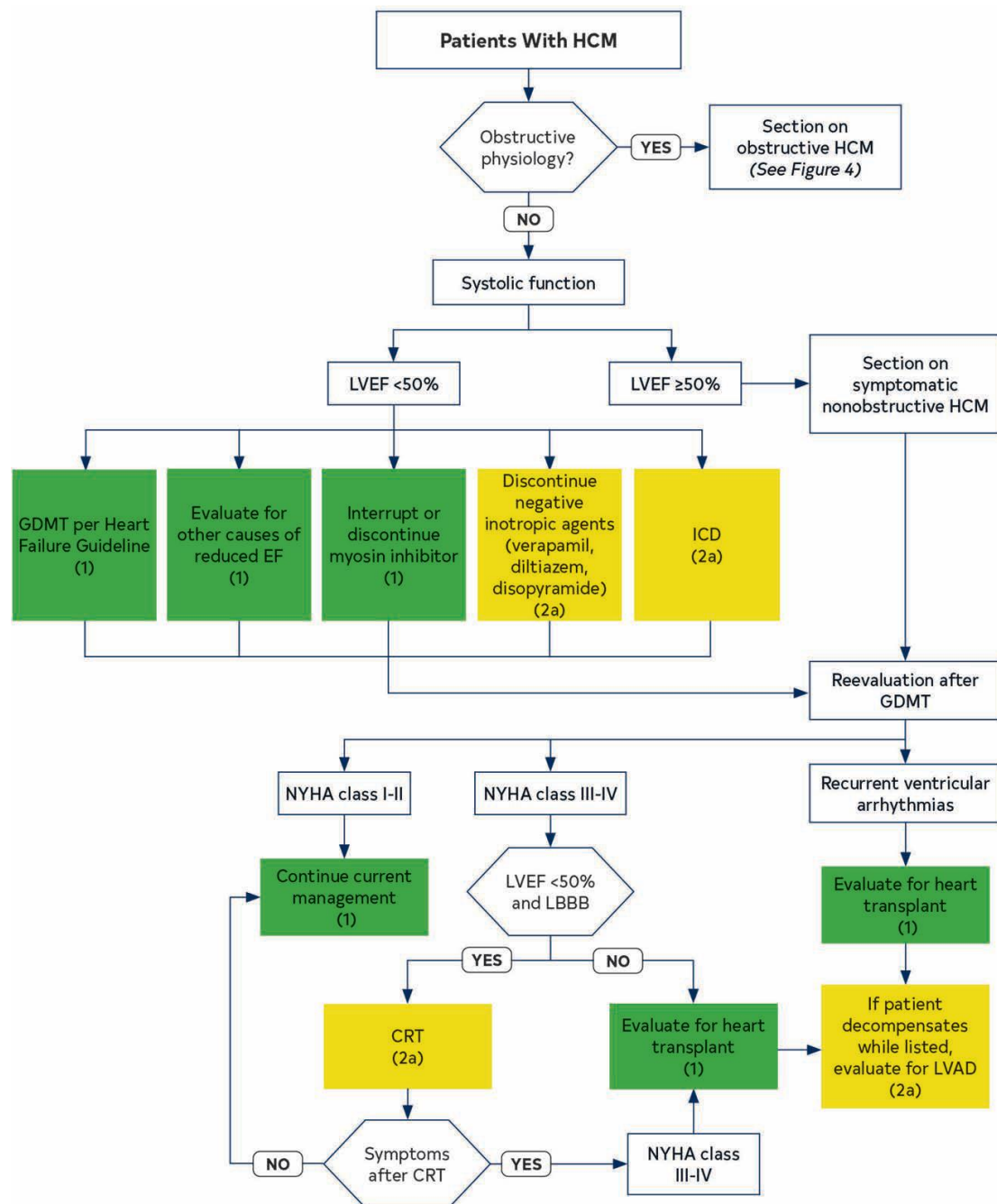


Figure 11. AHA/ACC 2024 GL on HCM. Heart failure algorithm.

Cardiac myosin inhibitor should be discontinued if LVEF <50% and can be restarted at a lower dose if the LVEF recovers.

CRT indicates cardiac resynchronization therapy; EF, ejection fraction; GDMT, guideline-directed management and therapy; HCM, hypertrophic cardiomyopathy; ICD, implantable cardioverter-defibrillator; LBBB, left bundle branch block; LVAD, left ventricular assist device; LVEF, left ventricular ejection fraction; and NYHA, New York Heart Association.

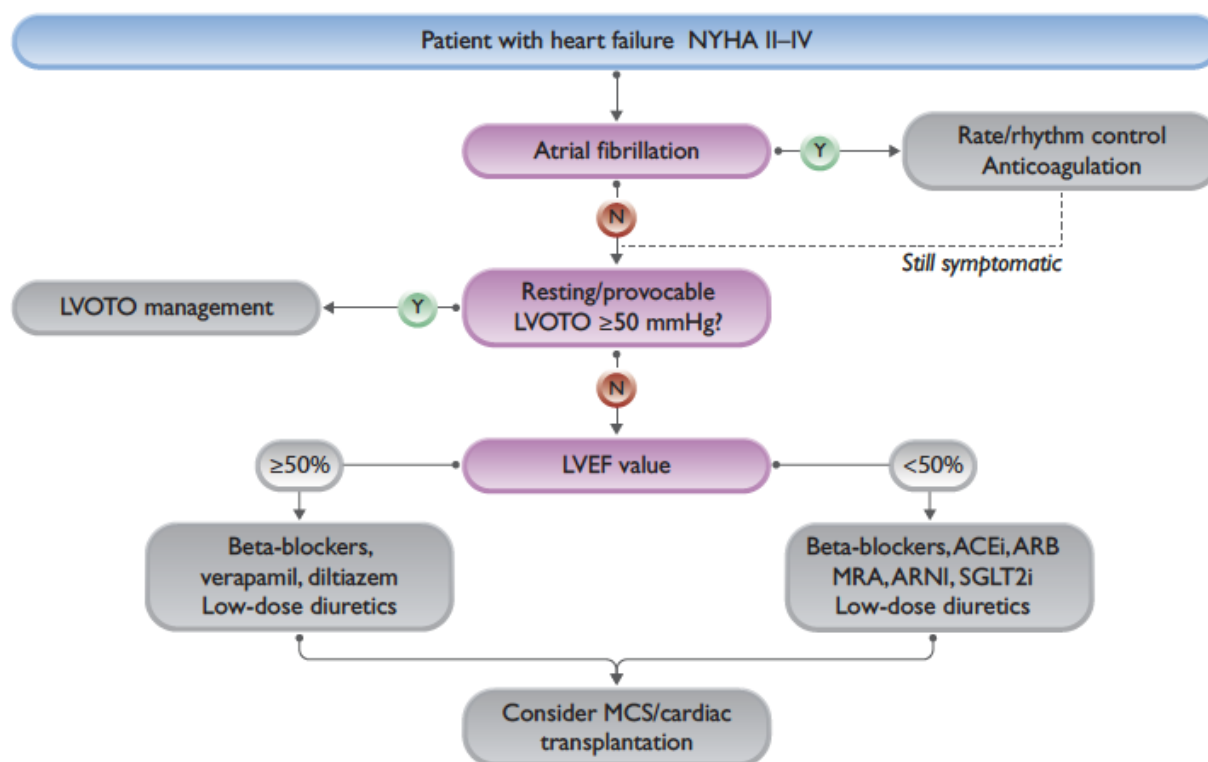


Figure 12. ESC 2023 GL on Cardiomyopathies. Algorithm for the treatment of heart failure in hypertrophic cardiomyopathy.

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNI, angiotensin receptor neprilysin inhibitor; LVEF, left ventricular ejection fraction; LVOTO, left ventricular outflow tract obstruction; MCS, mechanical circulatory support; MRA, mineralocorticoid receptor antagonist; NYHA, New York Heart Association; SGLT2i, sodium–glucose cotransporter 2 inhibitor.

Table 22. AHA/ACC 2024 GL on HCM. Other comorbidities

Adherence to the guidelines on the prevention of atherosclerotic cardiovascular disease to reduce risk of cardiovascular events.	I-C-EO
In overweight or obese patients, counseling and comprehensive lifestyle interventions for achieving and maintaining weight loss ¹ and possibly lowering the risk of developing LVOTO, HF, and AF.	I-B-NR
In patients with hypertension, lifestyle modifications and medical therapy for hypertension are, ¹ with preference for beta-blockers and non-dihydropyridine calcium channel blockers in patients with obstructive HCM.	I-C-LD
Assessment for symptoms of sleep-disordered breathing and, if present, referral to a sleep medicine specialist for evaluation and treatment.	I-C-LD

Table 23. Sports activity**AHA/ACC 2024 GL on HCM. Recreational physical activity and competitive sports**

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.	I -B-NR
A comprehensive evaluation and shared discussion about of sports participation with an expert provider for athletes with HCM	I-C-EO
Participation in competitive sports of any intensity of individuals who are genotype-positive, phenotype-negative for HCM	IIa B-NR
Participation in vigorous* recreational activities after an annual comprehensive evaluation and shared decision-making with an expert professional who balances potential benefits and risks, with this process being repeated annually.	IIa B-NR
For patients with HCM who are capable of a high level of physical performance, participation in competitive sports† after review by an expert provider with experience managing athletes with HCM who conducts an annual comprehensive evaluation and shared decision making that balances potential benefits and risks.	IIb B-NR
For most patients with HCM, universal restriction from vigorous physical activity or competitive sports is not indicated	III B-NR No benefit
ICD placement for the sole purpose of participation in competitive athletics should not be performed.	III-C-EO Harm
*Exercise intensity can be gauged by metabolic equivalents (METs): light <3 METs, moderate 3-6 METs, and vigorous >6 METs, by percentage of maximum heart rate achieved (light 40%-50%, moderate 50%-70%, vigorous >70%), or by level of perceived exertion on the Borg scale (light 7-12, moderate 13-14, vigorous ≥15).	
**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. Competitive sports involve systematic training for the primary purpose of competition against others, at multiple levels, including high school, collegiate, master's level, semiprofessional, or professional sporting activities.	

ESC 2023 GL on Cardiomyopathies. Exercise recommendations for patients with cardiomyopathy

High-intensity exercise and competitive sport should be considered in genotype-positive/phenotype-negative individuals who seek to do so. IIa C

High-intensity exercise and competitive sport may be considered in asymptomatic low-risk individuals with morphologically mild hypertrophic cardiomyopathy in the absence of resting or inducible left ventricular outflow obstruction and exercise-induced complex ventricular arrhythmias IIb C

High-intensity exercise, including competitive sport, is not recommended in high-risk individuals and in individuals with left ventricular outflow tract obstruction and exercise-induced complex ventricular arrhythmias. III C

Table 24. Occupation

AHA/ACC 2024 GL on HCM. Occupation in patients with HCM.

For patients with HCM, follow Federal Motor Carrier Safety Administration cardiovascular disease guidelines that permit driving commercial motor vehicles, if they do not have an ICD or any major risk factors for SCD and are following a guideline-directed management plan. IIa-C-EO

For pilot aircrew with a diagnosis of HCM, follow Federal Aviation Administration guidelines that permit consideration of multicrew flying duties, provided they are asymptomatic, are deemed low risk for SCD, and can complete a maximal treadmill stress test at 85% peak heart rate. IIa-C-EO

Patients with HCM may consider occupations that require manual labor, heavy lifting, or a high level of physical performance after a comprehensive clinical evaluation, risk stratification for SCD, and implementation of guideline-directed management in the context of shared decision-making. IIb-C-EO

Table 25. AHA/ACC 2024 Guideline on Noncardiac Surgery.**Recommendation for Hypertrophic Cardiomyopathy**

3: Harm	C-LD	1. For patients with hypertrophic cardiomyopathy (HCM) undergoing NCS, factors that aggravate or trigger dynamic outflow obstructions (eg, positive inotropic agents, tachycardia, or reduced preload) are harmful and should be avoided to reduce the risk of hemodynamic instability. ^{1,2}
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Preoperative and Intraoperative Management Considerations in Patients With Hypertrophic Cardiomyopathy**Management Considerations**

Continue beta blockers and/or nondihydropyridine calcium channel blockers without interruption in the perioperative period

Avoid hypovolemia and reduced preload (can worsen LVOT obstruction)

Avoid hypotension and reduced afterload (can worsen LVOT obstruction)

Avoid tachycardia to ensure adequate LV filling

If hypotension develops:

- Prioritize intravenous fluid administration to correct hypovolemia
- Use alpha-agonists, such as phenylephrine or vasopressin,⁷ rather than beta-agonists, which can worsen LVOT obstruction
- Consider intraoperative echocardiography to evaluate LVOT obstruction in the setting of hypotension
- In selected cases, intravenous beta-blockade may be necessary to reduce LV myocardial contractility and relieve LVOT obstruction

LV indicates left ventricular; and LVOT, left ventricular outflow tract.

Table 26. ESC 2014 GL on HCM. Routine follow-up

A clinical evaluation, including 12-lead ECG and TTE, every 12–24 months in clinically stable patients or whenever there is a change in symptoms.	I-C
48-Hour ambulatory ECG every 12–24 months in clinically stable patients, every 6–12 months in patients in sinus rhythm with left atrial dimension ≥45 mm, and whenever patients complain of new palpitations.	I-C
CMR every 5 years in clinically stable patients, or every 2–3 years in patients with progressive disease.	IIb-C
Symptom-limited exercise testing every 2–3 years in clinically stable patients, or every year in patients with progressive symptoms.	IIa-C
Cardiopulmonary exercise testing (when available) every 2–3 years in clinically stable patients, or every year in patients with progressive symptoms.	IIb-C

Table 27. Pregnancy.**AHA/ACC 2024 GL on HCM. Pregnancy**

For AF or other indications for anticoagulation, low molecular-weight heparin or vitamin K antagonists (at maximum therapeutic dose of <5 mg daily)	I-B-NR
Selected beta blockers for symptoms related to outflow tract obstruction or arrhythmias, with monitoring of fetal growth.	I-C-LD
In most pregnant women with HCM, vaginal delivery is the first-choice delivery option.	I-C-LD
Preconceptional and prenatal reproductive and genetic counseling in affected families with HCM	I-B-NR
Care should be coordinated between their cardiologist and an obstetrician. For high risk patients, consultation with an expert in maternal-fetal medicine.	I-C-EO
Pregnancy is generally safe women with clinically stable HCM. Advice as part of a shared discussion regarding potential maternal and fetal risks, and initiation of guideline-directed therapy.	IIa-C-LD
Cardioversion for new or recurrent AF, particularly if symptomatic	IIa-C-LD
General or epidural anesthesia, with precautions to avoid hypotension.	IIa-C-LD
Serial echocardiography, particularly during the second or third trimester when hemodynamic load is highest, or if clinical symptoms develop.	IIa-C-EO
Fetal echocardiography for diagnosis of fetal HCM in the context of prenatal counseling.	IIb-C-EO
In pregnant women, use of mavacamten is contraindicated due to potential teratogenic effects.	III C-EO Harm

ESC 2025 GL on Pregnancy. Hypertrophic Cardiomyopathy

It is recommended to use the same risk stratification protocol for ventricular arrhythmias in pregnant women with HCM as for non-pregnant women with HCM. ⁴³	I	C
It is recommended to start beta-blockers ^c in women with HCM who develop symptoms due to outflow tract obstruction or arrhythmia during pregnancy. ⁴³	I	C
It is recommended that women with HCM with symptomatic LV dysfunction (EF <50%) and or severe LVOTO (≥ 50 mmHg) wishing to become pregnant are counselled by the Pregnancy Heart Team regarding the high risk of pregnancy-related adverse events. ^{294,295}	I	C
Cardioversion for AF should be considered in pregnant women with HCM. ^{43,305}	IIa	C
Disopyramide may be considered in pregnant women with HCM only when the potential benefits outweigh the risk of uterine contractions. ^{305,306}	IIb	C
Myosin inhibitors are not recommended in women during pregnancy due to lack of safety data. ^{303,304}	III	C

AF, atrial fibrillation; EF, ejection fraction; HCM, hypertrophic cardiomyopathy; LVOTO, left ventricular outflow tract obstruction

^cExcept for atenolol.