2014 version

ESC Guidelines on

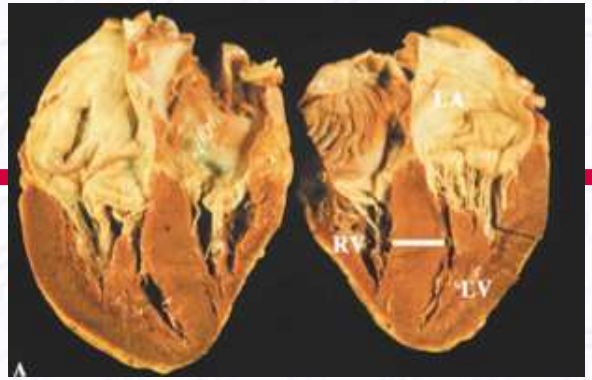
Hypertrophic Cardiomyopathy

Authors/Task Force members: Perry M. Elliott (Chairperson) (UK), Aris Anastasakis (Greece), Michael A. Borger (Germany), Martin Borggrefe (Germany), Franco Cecchi (Italy), Philippe Charron (France), Albert Alain Hagege (France), Antoine Lafont (France), Giuseppe Limongelli (Italy), Heiko Mahrholdt (Germany), William J. McKenna (UK), Jens Mogensen (Denmark), Petros Nihoyannopoulos (UK), Stefano Nistri (Italy), Petronella G. Pieper (Netherlands), Burkert Pieske (Austria), Claudio Rapezzi (Italy), Frans H. Rutten (Netherlands), Christoph Tillmanns (Germany), and Hugh Watkins (UK).
Additional Contributor: Constantinos O'Mahony (UK).

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®



Cardiomyopathy: Definition

- *"A myocardial disorder in which the heart muscle is structurally and functionally abnormal, in the absence of coronary artery disease, hypertension, valvular disease and congenital heart disease sufficient to cause the observed myocardial abnormality."*

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

HCM: Diagnostic criteria

Increased left ventricular wall thickness not solely explained by abnormal loading conditions

ADULTS:

- *LV wall thickness ≥15 mm in one or more LV myocardial segments measured by any imaging technique (echocardiography, cardiac magnetic resonance imaging (CMR) or computed tomography (CT) that is not explained solely by loading conditions.*

CHILDREN:

- *LV wall thickness more than two standard deviations above the predicted mean (z-score >2, where a z-score is defined as the number of standard deviations from the population mean)*

RELATIVES (adults)**:**

- *Unexplained increased LV wall thickness ≥13 mm in one or more LV myocardial segments measured by any imaging technique*

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

Management of HCM

Initial assessment

- Positive / differential diagnosis
- Diagnosis of aetiology
- Investigation of symptoms
- Risk stratification
- Genetic counselling and testing

Therapeutics

- Sport activity, life style
- TTT of symptoms
- SCD prevention
- TTT of complications
- Reproduction, maternal risk

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

AETIOLOGY

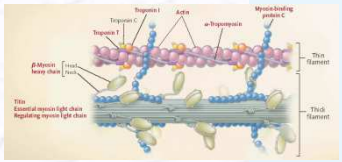
European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

HCM: Aetiological heterogeneity

Genetic and sarcomeric etiology

MYL3
TPM1
TNNI3
TNNT2
(Troponin T)
MYH7
(Beta myosin heavy chain)
MYBPC3
(Myosin binding protein C)



Unknown
~ 25–30%
~ 5–10%
Sarcomeric protein gene mutation 40–60%

The majority of cases in adolescents and adults are caused by mutations in sarcomere protein genes.

Other genetic and non-genetic causes

- Inborn errors of metabolism
  - Glycogen storage diseases:
    - Pompe
    - Danon
  - AMP-Kinase (PRKAG2)
  - Carnitine disorders
  - Lysosomal storage diseases
    - Anderson-Fabry
- Neuromuscular diseases
  - Friedreich's ataxia
  - FHL1
- Mitochondrial diseases
  - MELAS
  - MERFF
- Malformation Syndromes
  - Noonan
  - LEOPARD
  - Costello
  - CFC
- Amyloidosis
  - Familial ATTR
  - Wild type TTR (senile)
  - AL amyloidosis
- Newborn of diabetic mother
- Drug-induced
  - Tacrolimus
  - Hydroxychloroquine
  - Steroids

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

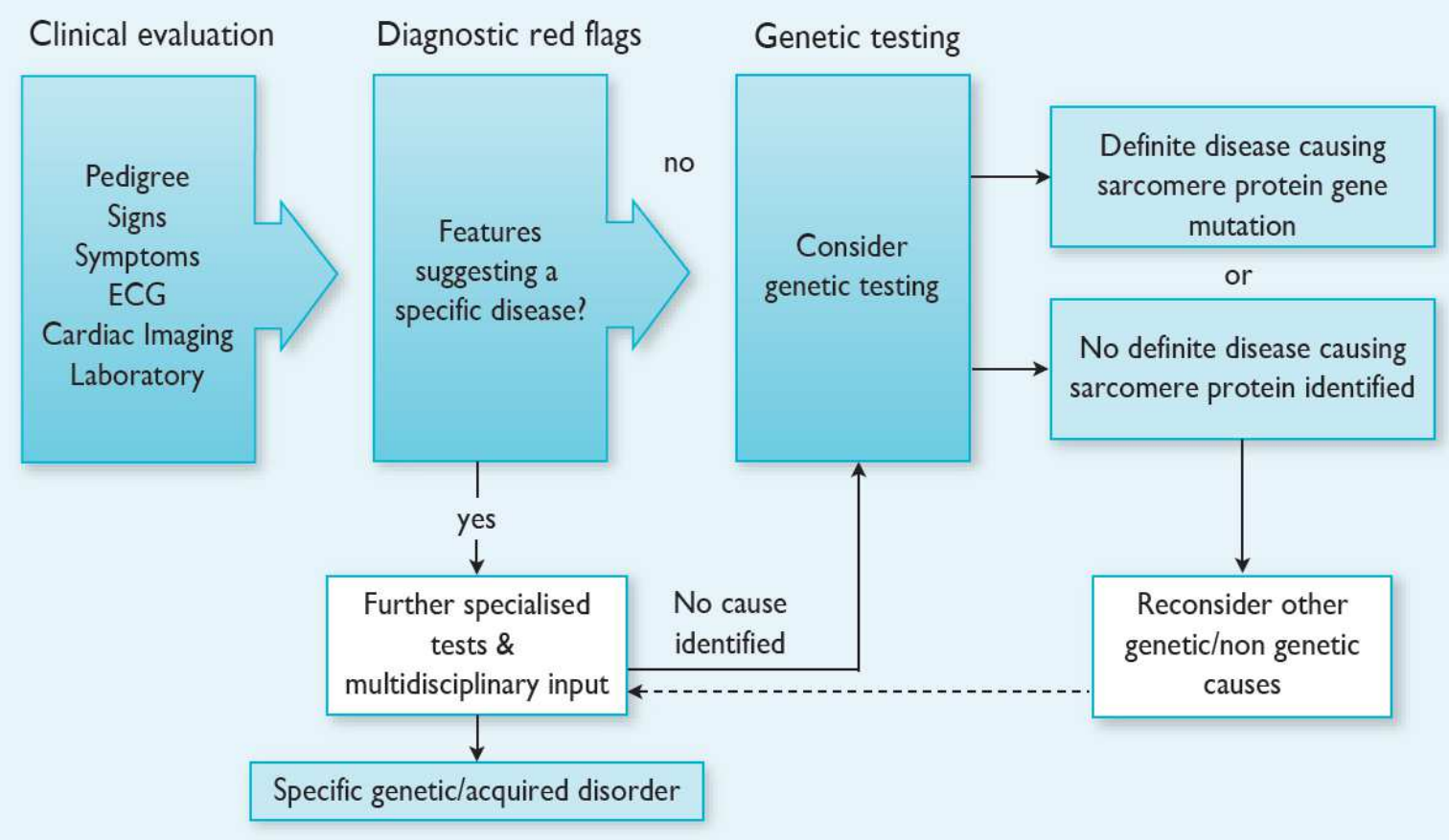
DIAGNOSIS

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

General approach to the diagnosis of hypertrophic cardiomyopathy

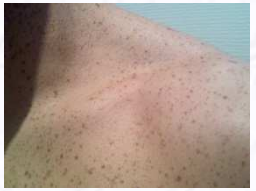


www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

History and Physical Examination

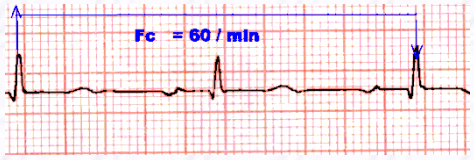


- **How old is the patient?**
- **Family history?**
- **Non-cardiac symptoms & signs?**

Symptom/sign	Diagnosis
Gait disturbance	• Friedreich's ataxia
Paraesthesia/sensory abnormalities/neuropathic pain	• Amyloidosis • Anderson-Fabry disease
Carpal tunnel syndrome	• TTR-related amyloidosis (especially when bilateral and in male patients)
Muscle weakness	• Mitochondrial diseases • Glycogen storage disorders • FHL1 mutations • Friedreich's ataxia
Palpebral ptosis	• Mitochondrial diseases • Noonan/LEOPARD syndrome • Myotonic dystrophy
Lentigines/café au lait spots	• LEOPARD/Noonan syndrome
Angiokeratomata, hypohidrosis	• Anderson-Fabry disease

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

Electrocardiographic abnormalities suggesting specific diagnoses



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.

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

Echocardiography: Differential Diagnosis

Interpret images in context of clinical features and other tests.

Echocardiographic features that suggest specific aetiologies[a]	
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 2-D 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

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

Cardiac Magnetic Resonance Imaging

CMR should be considered in patients with HCM at their baseline assessment if local resources and expertise permit.

Morphological evaluation:

- LV morphology and function

Etiological diagnosis:

Prognostic value:

- The extend of LGE has some utility in predicting cardiovascular mortality but current data do not support the use of LGE in sudden cardiac death prediction

CMR with LGE imaging should be considered in patients with suspected cardiac amyloidosis.	IIa	C

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

ASSESSMENT OF SYMPTOMS

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

Dyspnoea
Chest pain
Fatigue

- **LVOTO**
- **LV Diastolic failure**
- **LV Systolic failure**
- **Valve Disease**
- **Arrhythmia**
- **Microvascular dysfunction**

Syncope

- **LVOTO**
- **Arrhythmia**
- **Abnormal Vascular Function**

Assessment of LVOTO should be part of the routine evaluation of all symptomatic patients.

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

MANAGEMENT OF SYMPTOMS

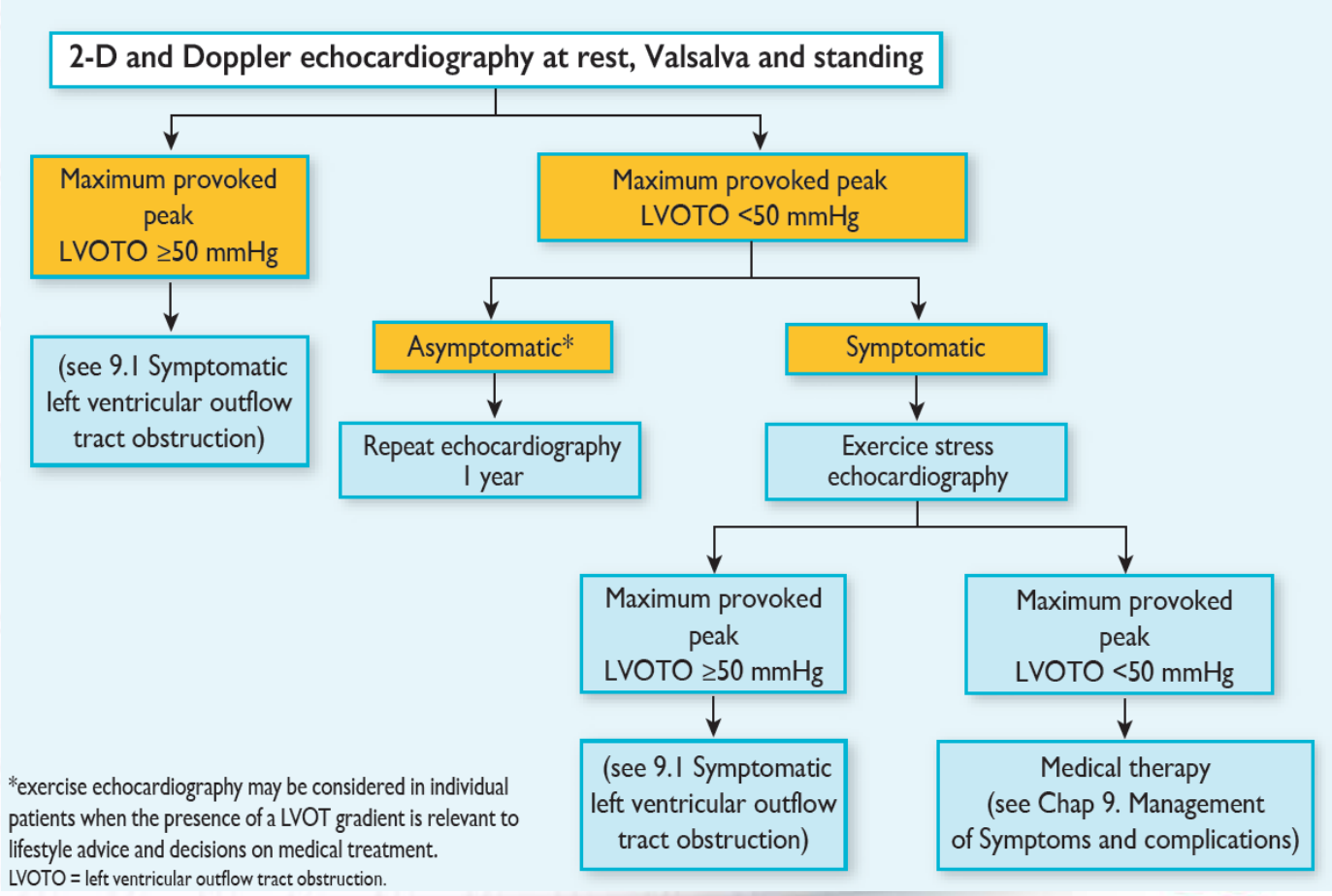
Beta BLOCKERS, as first line

If contra indication or second line: verapamil (Isoptine)

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

Echocardiography: LV Outflow Tract Obstruction

- ✓ **About 30% of patients have gradient at rest**
- ✓**About 30% of patients have latent obstruction** **(provoked by manoeuvres that reduce preload or afterload: standing from squat, Valsalva, exercise)**
- ✓**Clinically significant if ≥ 50 mmHg**



www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

Management of persistent symptoms (1)

LEFT VENTRICULAR OUTFLOW TRACT OBSTRUCTION

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

Treatment of Left Ventricular Outflow Tract Obstruction

- *By convention, LVOTO is defined as a peak instantaneous Doppler LV outflow tract gradient of ≥30 mm Hg, but the threshold for invasive treatment is usually considered to be ≥50 mm Hg.*

- *There are no data to support the use of invasive procedures to reduce LV outflow obstruction in asymptomatic patients, regardless of its severity.*

- *Arterial and veinous vasodilatators should be avoided, digoxin is not recommended*

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

Treatment of LV Outflow Tract Obstruction

Disopyramide, titrated to maximum tolerated dose,[c] is recommended in addition to a ß-blocker (or, if this is not possible, with verapamil) to improve symptoms in patients with resting or provoked[d] LVOTO.	I	B
Disopyramide, titrated to maximum tolerated dose,[c] may be considered as monotherapy to improve symptoms in patients with resting or provoked[d] LVOTO (exercise or Valsalva manoeuvre) taking caution in patients with—or prone to—AF, in whom it can increase ventricular rate response.	IIb	C

Disopyramide (Rythmodan): if persistent symptoms and LVOT

Low-dose loop- or thiazide diuretics may be used with caution in symptomatic LVOTO, to improve exertional dyspnoea.	IIb	C

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

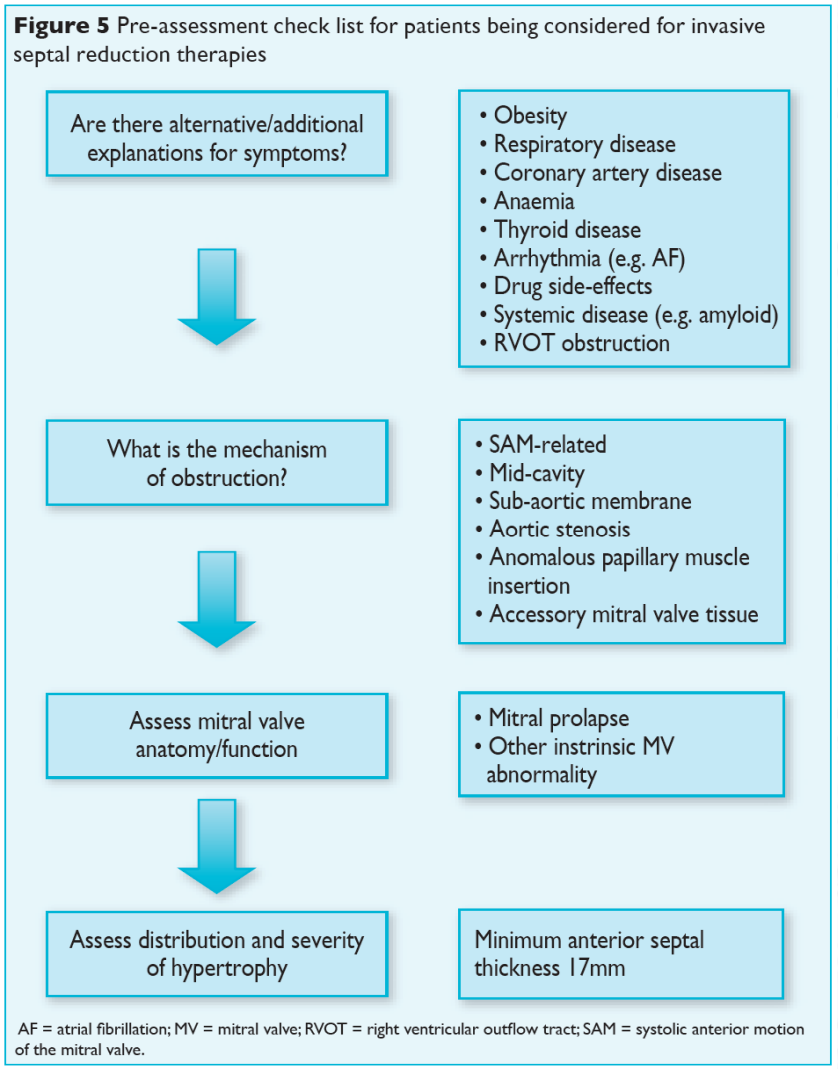
EUROPEAN SOCIETY OF CARDIOLOGY®

Invasive Treatment of LV Outflow Tract Obstruction

Experienced multidisciplinary teams should assess all patients before Intervention

Surgeons and cardiologists who perform invasive gradient reduction therapies should be trained in experienced centres and work as part of a multidisciplinary team experienced in the management of HCM.

Figure 5 Pre-assessment check list for patients being considered for invasive septal reduction therapies



AF = atrial fibrillation; MV = mitral valve; RVOT = right ventricular outflow tract; SAM = systolic anterior motion of the mitral valve.

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

Invasive Treatment of LV Outflow Tract Obstruction

Recommendations on septal reduction therapy	Class[a]	Level[b]
It is recommended that septal reduction therapies be performed by experienced operators, working as part of a multidisciplinary team expert in the management of HCM.	I	C
Septal reduction therapy to improve symptoms is recommended in patients with a resting or maximum provoked LVOT gradient of ≥50 mmHg, who are in NYHA functional Class III–IV despite maximum tolerated medical therapy.	I	B
Septal reduction therapy should be considered in patients with recurrent exertional syncope caused by a resting or maximum provoked LVOTO gradient ≥50 mmHg despite optimal medical therapy.	IIa	C
Septal myectomy, rather than SAA, is recommended in patients with an indication for septal reduction therapy and other lesions requiring surgical intervention (e.g. mitral valve repair/replacement, papillary muscle intervention).	I	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 not caused by SAM of the mitral valve alone.	IIa	C
Mitral valve repair or replacement may be considered in patients with a resting or maximum provoked LVOTO gradient ≥50 mmHg and a maximum septal thickness ≤16 mm at the point of the mitral leaflet–septal contact or when there is moderate-to-severe mitral regurgitation following isolated myectomy.	IIb	C

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

Cardiac Pacing for LV Outflow Tract Obstruction

Recommendations on indications for cardiac pacing in patients with obstruction	Class[a]	Level[b]
Sequential AV pacing, with optimal AV interval to reduce the LV outflow tract gradient or to facilitate medical treatment with ß-blockers and/or verapamil, may be considered in selected patients with resting or provocable LVOTO ≥50 mmHg, sinus rhythm and drug-refractory symptoms, who have contra-indications for septal alcohol ablation or septal myectomy or are at high-risk of developing heart block following septal alcohol ablation or septal myectomy.	IIb	C
In patients with resting or provocable 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 ß-blockers and/or verapamil.	IIb	C

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

Management of persistent symptoms (2)

NON-OBSTRUCTIVE HCM

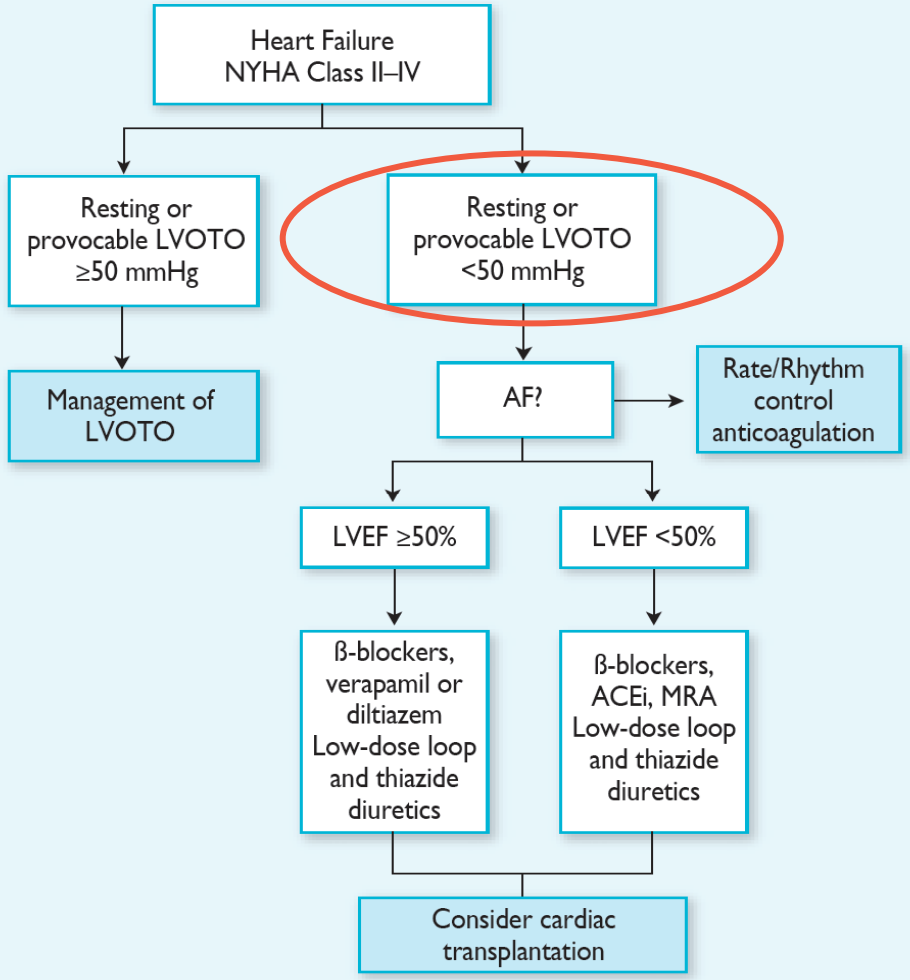
www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

Management of Heart Failure Symptoms in Non-Obstructive HCM

Figure 6 Algorithm for the treatment of heart failure in hypertrophic cardiomyopathy.



ACEi = angiotensin converting enzyme inhibitor; AF = atrial fibrillation; LVEF = left ventricular ejection fraction; LVOTO = left ventricular outflow tract obstruction; MRA = mineralocorticoid receptor antagonist; NYHA = New York Heart Association functional class.

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

SUDDEN CARDIAC DEATH

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

Sudden Cardiac Death in HCM

- *Annual incidence for cardiovascular death of 1–2%, with sudden cardiac death (SCD), heart failure and thromboembolism being the main causes of death.*

- *In adolescents and adults, the risk assessment should comprise of:*
  - ***clinical and family history,***
  - ***48-hour ambulatory ECG,***
  - ***TTE (or CMR in the case of poor echo windows)***
  - ***and a symptom-limited exercise test.***

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

Risk Factors for Sudden Cardiac Death (Adults)

- Non-sustained Ventricular Tachycardia
- Severity of LV wall thickness (>30 mm)
- Family History of Sudden Cardiac Death (age < 40y)
- Unexplained syncope (non vasovagal)
- Exercise Blood Pressure Response (delta PAS < 20-25 mmHg)
- Young Age
- Left Atrial Diameter
- Left Ventricular Outflow Tract Obstruction
- Some mutations etc…

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

Prevention of SCD in Hypertrophic Cardiomyopathy

- *There are no randomized trials or statistically validated prospective prediction models that can be used to guide ICD implantation in patients with HCM.*

O'Mahony C et al. Eur Heart J. 2014 Aug 7;35(30):2010-20

HCM Risk-SCD model for predicting 5 year risk

Probability $_{\text{SCD at 5 years}} = 1 - 0.998^{\exp(\text{prognostic index})}$

where Prognostic index = [0.15939858 x maximal wall thickness (mm)] – [0.00294271 x maximal wall thickness^2 (mm^2)] + [0.0259082 x left atrial diameter (mm)] + [0.00446131 x maximal (rest/Valsalva) left ventricular outflow tract gradient (mmHg)] + [0.4583082 x family history SCD] + [0.82639195 x NSVT] + [0.71650361 x unexplained syncope] – [0.01799934 x age at clinical evaluation (years)].

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

HCM Risk-SCD: Predictor variables

O'Mahony C et al. Eur Heart J. 2014 Aug 7;35(30):2010-20

Predictor Variable
Age at evaluation.
History of sudden cardiac death in one or more first degree relatives under 40 years of age or SCD in a first degree relative with confirmed HCM at any age (post or ante-mortem diagnosis).
Maximal wall thickness: the greatest thickness in the anterior septum, posterior septum, lateral wall, and posterior wall of the LV, measured at the level of the mitral valve, papillary muscles and apex using parasternal short-axis plane using 2-D echocardiography.
Left atrial diameter determined by M-Mode or 2D echocardiography in the parasternal long axis plane.
The maximum LV outflow gradient determined at rest and with Valsalva provocation (irrespective of concurrent medical treatment) using pulsed and continuous wave Doppler from the apical three and five chamber views. Peak outflow tract gradients were determined using the modified Bernouilli equation: Gradient= $4V^2$, where V is the peak aortic outflow velocity.
NSVT: ≥3 consecutive ventricular beats at a rate of ≥120 beats per minute and <30s in duration on Holter monitoring (minimum duration 24 hours) at or prior to evaluation.
History of unexplained syncope at or prior to evaluation.

On line calculator:

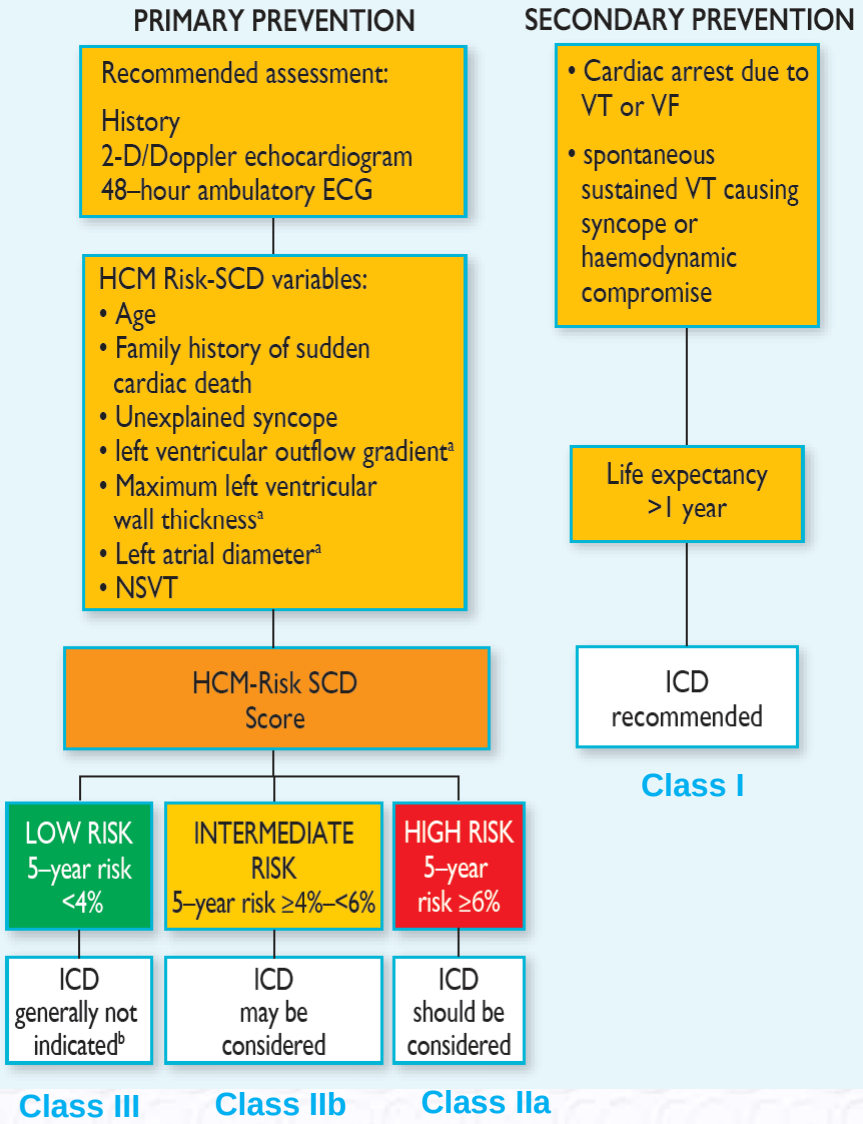
→ Absolute risk of SCD at 5 years

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

Figure 7 Flow chart for ICD implantation.



Prevention of Sudden Cardiac Death

Recommendations for ICD in each risk category take into account not only the absolute statistical risk, but also the age and general health of the patient, socio-economic factors and the psychological impact of therapy.

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

GENETIC COUNSELLING & TESTING

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

Genetic Counselling

Help the individual or the family to understand the options for dealing with the risk of recurrence and choose the action which is appropriate to them. *Godard et al. Eur J Hum Genet 2003*

- **Understand medical, psychological, social, professional, ethical & legal implications of a genetic diagnosis.**

Charron et al. ESC WG Statement. Eur Heart J 2010;31(22):2715

Recommendations on genetic counselling	Class[a]	Level[b]
Genetic counselling is recommended for all patients with HCM when their disease cannot be explained solely by a non-genetic cause, whether or not clinical or genetic testing will be used to screen family members.	I	B
Genetic counselling should be performed by professionals trained for this specific task working within a multidisciplinary specialist team.	IIa	C

Genetic Testing

Web Table 2: Main genes associated with familial hypertrophic cardiomyopathy (Online Mendelian Inheritance in Man OMIM phenotypic series, 192600)[21]

Protein	Gene	Location	MIM gene	Frequency
Myosin-7 (ß-myosin heavy chain)	MYH7	14q11.2	160760	10–20%
Myosin-binding protein C, cardiac-type	MYBPC3	11p11.2	600958	15–30%
Troponin T, cardiac muscle	TNNT2	1q32.1	191045	3–5%
Troponin I, cardiac muscle	TNNI3	19q13.42	191044	<5%
Tropomyosin alpha-1 chain	TPM1	15q22.2	191010	<5%
Myosin regulatory light chain 2, ventricular/cardiac muscle isoform	MYL2	12q24.11	160781	
Myosin light chain 3	MYL3	3p21.31	160790	1%
Actin, alpha cardiac muscle 1	ACTC1	15q14	102540	
Cysteine and glycine-rich protein 3, muscle LIM protein	CSRP3	11p15.1	600824	
Titin	TTN	2q31.2	188840	<5%
Cardiac phospholamban	PLN	6q22.31	172405	
5'-AMP-activated protein kinase subunit gamma-2	PRKAG2	7q36.1	602743	1%
Alpha galactosidase A (Anderson Fabry disease)	GLA	Xq22.1	300644	1–3%
Lysosome membrane associated protein 2 (Danon disease)	LAMP2	Xq24	309060	0.7%–2.7%

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

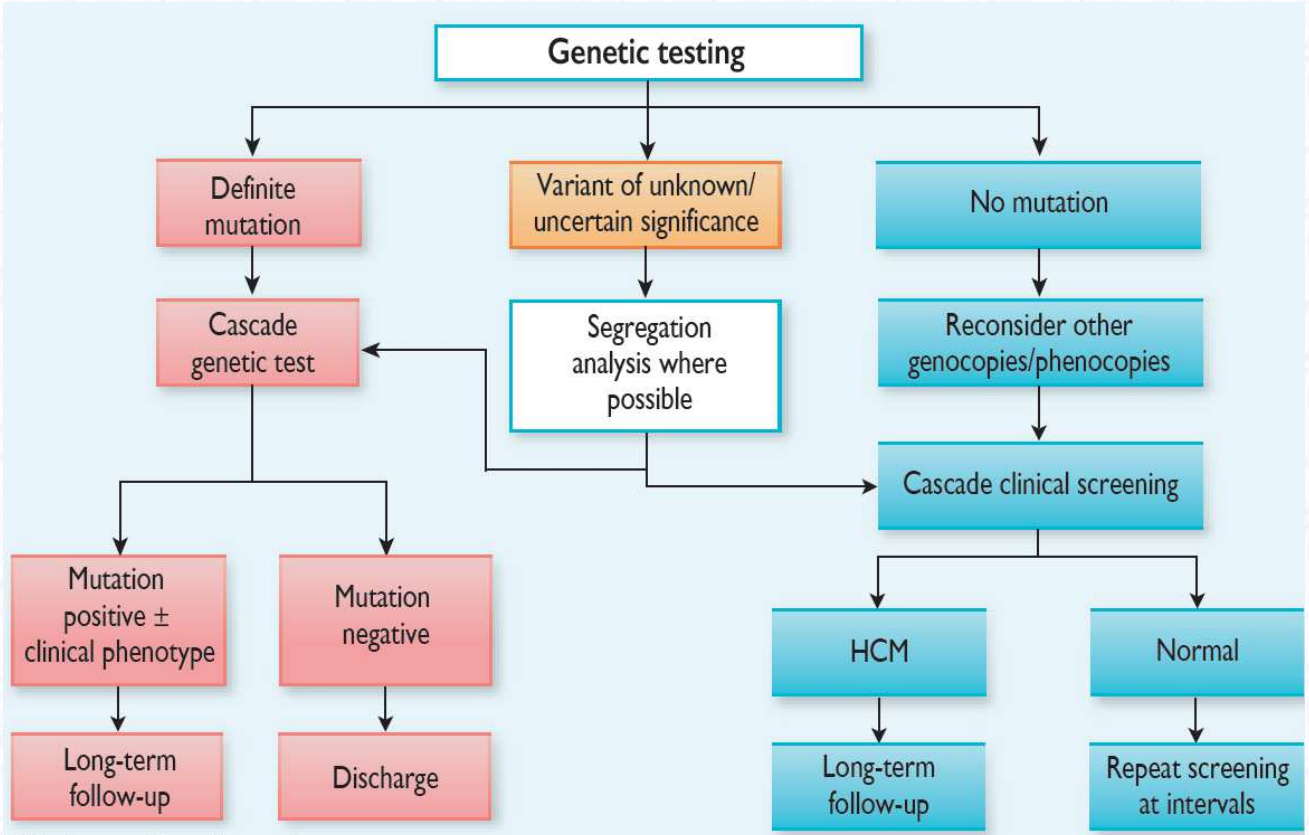
Genetic Testing

- *Genetic testing is recommended in patients fulfilling diagnostic criteria for HCM to enable cascade genetic screening of their relatives*

- *When a definite causative genetic mutation is identified in a patient, his or her relatives should first be genetically tested, and then clinically evaluated if they are found to carry the same mutation*

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

Flow chart for genetic and clinical screening of probands and relatives.



HCM = hypertrophic cardiomyopathy.
Cascade genetic test = screening of first degree relatives of patients already diagnosed with HCM.

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

Other potential indications for genetic testing in probands

- **Accurate diagnosis of HCM subtype (non sarcomeric)**
- **Accurate diagnosis in ambiguous situations (e.g. borderline phenotype, SCD and preclinical stage)**
- **Manage procreative issues (prenatal diagnosis, pre-implantation diagnosis)**
- **Prognostic evaluation** (some phenotype-genotype correlations, sarcomeric versus non sarcomeric HCM, multiple mutations)

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

ESC Guidelines on HCM

Authors/Task Force members: Perry M. Elliott (Chairperson) (UK), Aris Anastasakis (Greece), Michael A. Borger (Germany), Martin Borggrefe (Germany), Franco Cecchi (Italy), Philippe Charron (France), Albert Alain Hagege (France), Antoine Lafont (France), Giuseppe Limongelli (Italy), Heiko Mahrholdt (Germany), William J. McKenna (UK), Jens Mogensen (Denmark), Petros Nihoyannopoulos (UK), Stefano Nistri (Italy), Petronella G. Pieper (Netherlands), Burkert Pieske (Austria), Claudio Rapezzi (Italy), Frans H. Rutten (Netherlands), Christoph Tillmanns (Germany), and Hugh Watkins (UK).
Additional Contributor: Constantinos O'Mahony (UK).

Pr Philippe Charron
philippe.charron@psl.aphp.fr

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY

Classes of recommendations

Classes of recommendations	Definition	Suggested wording to use
Classe I	Evidence and/or general agreement that a given treatment or procedure is beneficial, useful, effective.	Is recommmended/ is indicated.
Class II	Conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of the given treatment or procedure.	
Class IIa	*Weight of evidence/opinion is in favour of usefulness/efficacy.*	*Should be considered.*
Class IIb	*Usefulness/efficacy is less well established by evidence/opinion.*	May be considered.
Class III	Evidence or general agreement that the given treatment or procedure is not useful/effective, and in some cases may be harmful.	Is not recommended.

www.escardio.org/guidelines

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®

Levels of evidence

Level of Evidence A	Data derived from multiple randomized clinical trials or meta-analyses.
Level of Evidence B	Data derived from a single randomized clinical trial or large non-randomized studies.
Level of Evidence C	Consensus of opinion of the experts and/ or small studies, retrospective studies, registries.

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

Acknowledgements

ESC Committee for Practice Guidelines (CPG): Jose Luis Zamorano (Chairperson) (Spain), Stephan Achenbach (Germany), Helmut Baumgartner (Germany), Jeroen Bax (Netherlands), Héctor Bueno (Spain), Veronica Dean (France), Christi Deaton (UK), Çetin Erol (Turkey), Robert Fagard (Belgium), Roberto Ferrari (Italy), David Hasdai (Israel), Arno W. Hoes (Netherlands), Paulus Kirchhof (Germany/UK), Juhani Knuuti (Finland), Philippe Kolh (Belgium), Patrizio Lancellotti (Belgium), Ales Linhart (Czech Republic), Petros Nihoyannopoulos (UK), Massimo F. Piepoli (Italy), Piotr Ponikowski (Poland), Per Anton Sirnes (Norway), Juan Luis Tamargo (Spain), Michal Tendera (Poland), Adam Torbicki (Poland), William Wijns (Belgium), and Stephan Windecker (Switzerland).

Document Reviewers: David Hasdai (Israel) (CPG Review Coordinator), Piotr Ponikowski (Poland) (CPG Review Coordinator), Stephan Achenbach (Germany), Fernando Alfonso (Spain), Cristina Basso (Italy), Nuno Miguel Cardim (Portugal), Juan Ramón Gimeno (Spain), Stephane Heymans (Netherlands), Per Johan Holm (Sweden), Andre Keren (Israel), Paulus Kirchhof (Germany/UK), Philippe Kolh (Belgium), Christos Lionis (Crete), Claudio Muneretto (Italy), Silvia Priori (Italy), Maria Jesus Salvador (Spain), Christian Wolpert (Germany), and Jose Luis Zamorano (Spain).

National Cardiac Societies document reviewers

European Heart Journal (2014):doi:10.1093/eurheartj/ehu284

EUROPEAN SOCIETY OF CARDIOLOGY®