2014 version

ESC Guidelines on Hypertrophic Cardiomyopathy

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Chairperson
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2014 ESC Guidelines for the Diagnosis & Management of Hypertrophic Cardiomyopathy

The Task Force for the Diagnosis and Management of Hypertrophic Cardiomyopathy of the European Society of Cardiology (ESC)

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Classes of recommendations

Classes of recommendations	Definition	Suggested wording to use
Class 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**

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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.

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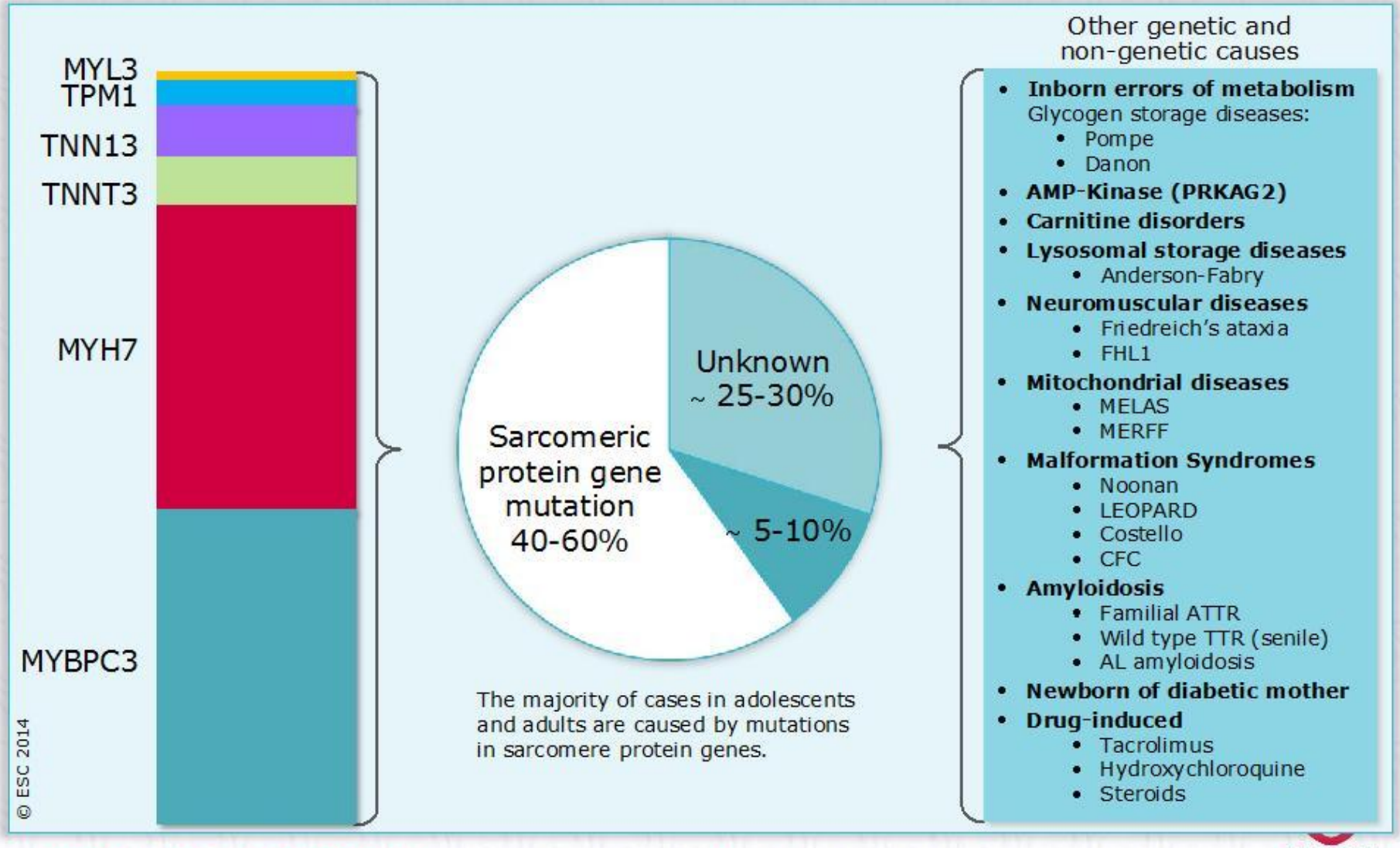
Diverse aetiology of hypertrophic cardiomyopathy



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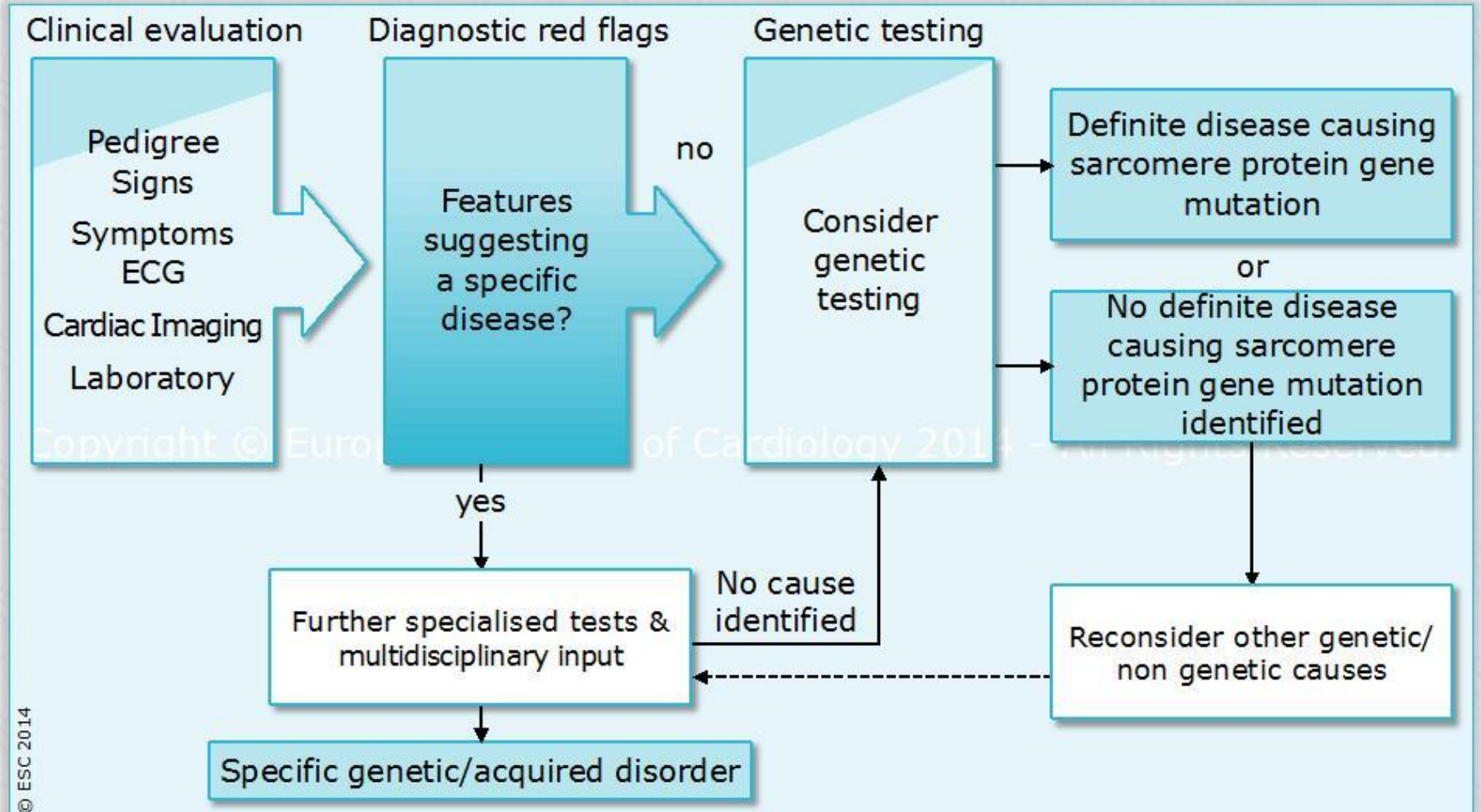
Schematic summarising the general approach to the diagnosis of hypertrophic cardiomyopathy



Notes: 1. Counselling is essential before and after testing for genetic disease. 2. Genetic testing is recommended in patients fulfilling diagnostic criteria for HCM to enable cascade genetic screening of their relatives. 3. For recommendations on individual investigations see relevant sections.

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Examples of signs and symptoms suggestive of specific diagnoses

Symptom/sign	Diagnosis
Learning difficulties, mental retardation	• Mitochondrial diseases • Noonan/LEOPARD/Costello syndrome • Danon disease
Sensorineural deafness	• Mitochondrial diseases (particularly with diabetes) • Anderson-Fabry disease • LEOPARD syndrome
Visual impairment	• Mitochondrial diseases (retinal disease, optic nerve atrophy) • TTR-related amyloidosis (cotton wool type vitreous opacities) • Danon disease (retinitis pigmentosa) • Anderson-Fabry disease (cataracts, corneal opacities)

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Examples of signs and symptoms suggestive of specific diagnoses *(Cont.)*

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

FHL1 = four and a half LIM domains 1; LEOPARD = lentigines, ECG abnormalities,ocular hypertelorism, pulmonary stenosis, abnormal genitalia, retardation of growth and sensorineural deafness; TTR = transthyretin.

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

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.

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Electrocardiographic abnormalities suggesting specific diagnoses or morphological variants (Cont.)

Finding	Comment
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 ≥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 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-segment in the lateral chest leads.

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.

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Electrocardiography

Recommendations	Class	Level
Standard 12-lead electrocardiography is recommended in patients with suspected hypertrophic cardiomyopathy to aid diagnosis and provide clues to underlying aetiology.	I	B
48-hour ambulatory ECG monitoring is recommended in patients at their initial clinical assessment to detect atrial and ventricular arrhythmia.	I	B

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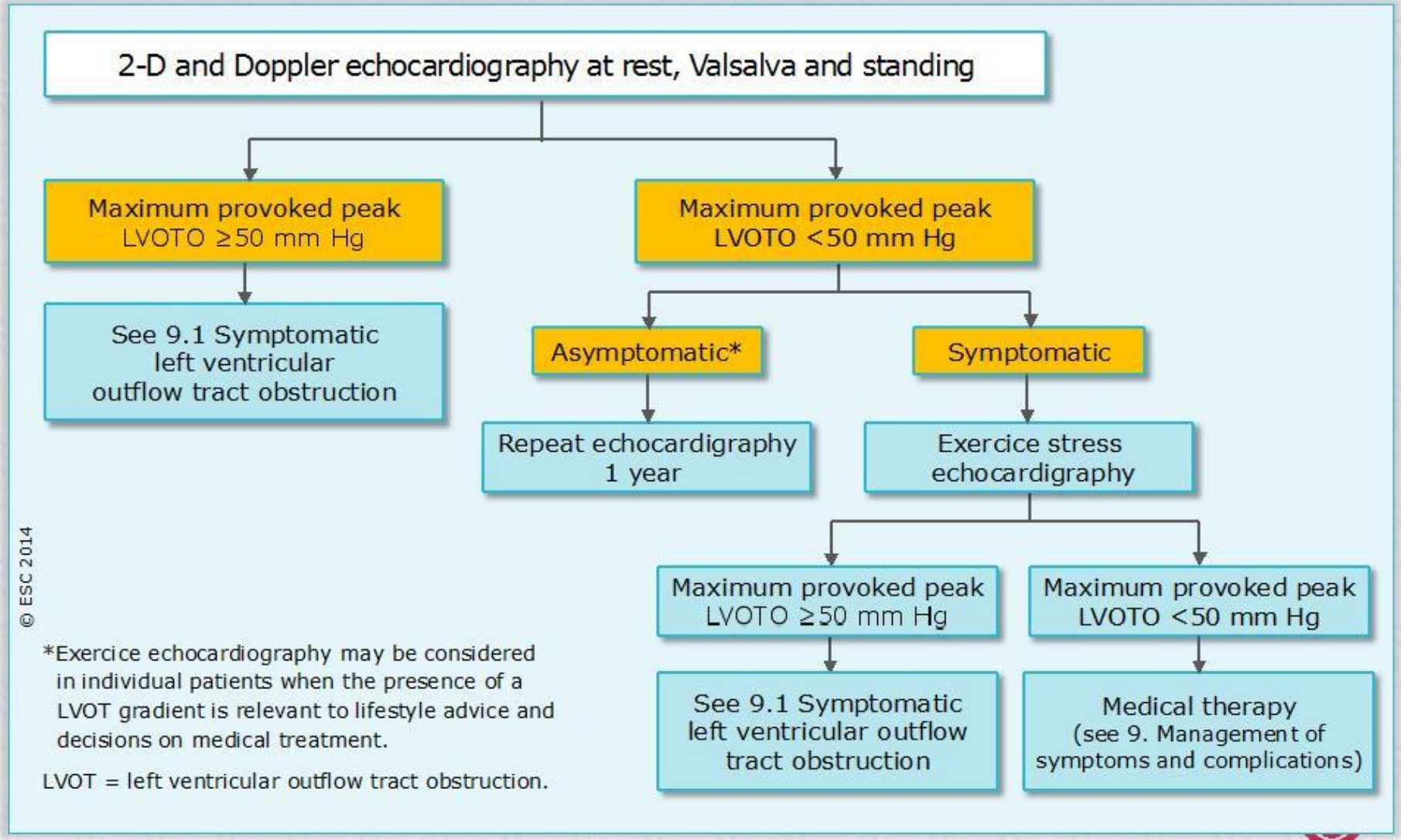
Protocol for the assessment and treatment of left ventricular outflow tract obstruction



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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 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

PRKAG2 = gamma-2 subunit of the adenosine monophosphate-activated protein kinase;

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Transthoracic echocardiography evaluation in hypertrophic cardiomyopathy

Recommendations	Class	Level
In all patients with HCM at initial evaluation, transthoracic 2-D and Doppler echocardiography are recommended, at rest and during Valsalva manœuvre in the sitting and semi-supine positions—and then on standing if no gradient is provoked.	I	B
Measurement of maximum diastolic wall thickness is recommended, using 2-D short-axis views in all LV segments, from base to apex.	I	C
A comprehensive evaluation of LV diastolic function is recommended, 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
In *symptomatic* patients with a resting or provoked peak instantaneous LV outflow tract gradient <50 mm Hg, 2-D and Doppler echocardiography *during exercise* in the standing, sitting or semi-supine position is recommended to detect provocable LVOTO and exercise induced mitral regurgitation.	I	B

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Transthoracic echocardiography evaluation in hypertrophic cardiomyopathy *(Cont.)*

Recommendations	Class	Level
In *asymptomatic* patients with a resting or provoked peak instantaneous LV outflow tract gradient <50 mm Hg, 2-D and Doppler echocardiography *during exercise*—in the standing, sitting or semi-supine positions—may be considered when the presence of a LVOT gradient is relevant to lifestyle advice, and decisions on medical treatment.	**IIb**	**C**
In patients with sub-optimal images or with suspected LV apical hypertrophy or aneurysm, TTE with LV cavity opacification—using intravenous echocardiographic contrast agents—should be considered as an alternative to CMR imaging.	**IIa**	**C**
Intracoronary contrast echocardiography is recommended in all patients undergoing SAA, to ensure correct localization of alcohol.	**I**	**B**

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Transoesophageal echocardiography

Recommendations	Class	Level
Perioperative TOE is recommended in patients undergoing septal myectomy, to confirm the mechanism of LVOTO, to guide the surgical strategy, to assess post-surgical complications and to detect residual LV outflow tract obstruction.	I	C
TOE should be considered in patients with LVOTO 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 should be considered to guide septal alcohol ablation when transthoracic windows are insufficient for proper visualization of echo-contrast within the myocardium.	IIa	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Cardiovascular magnetic resonance evaluation in hypertrophic cardiomyopathy

Recommendations	Class	Level
It is recommended that CMR studies be performed and interpreted by teams experienced in cardiac imaging and in the evaluation of heart muscle disease.	I	C
In the absence of contra-indications, CMR with LGE is recommended in patients with suspected HCM who have inadequate echocardiographic windows, in order to confirm the diagnosis.	I	B
In the absence of contra-indications, CMR with LGE should be considered in patients fulfilling diagnostic criteria for HCM, to assess cardiac anatomy, ventricular function, and the presence and extent of myocardial fibrosis.	IIa	B
CMR with LGE imaging should be considered in patients with suspected apical hypertrophy or aneurysm.	IIa	C
CMR with LGE imaging should be considered in patients with suspected cardiac amyloidosis.	IIa	C
CMR with LGE may be considered before septal alcohol ablation or myectomy, to assess the extent and distribution of hypertrophy and myocardial fibrosis.	IIb	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Nuclear scintigraphy

Recommendations	Class	Level
Bone scintigraphy (particularly with 99mTc-DPD) should be considered in patients with symptoms, signs and non-invasive tests consistent with TTR-related amyloidosis.	IIa	B
Cardiac CT should be considered in patients who have inadequate echocardiographic imaging and contra-indications for CMR.	IIa	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Endomyocardial biopsy

Recommendations	Class	Level
Endomyocardial biopsy may be considered when the results of other clinical assessments suggest myocardial infiltration, inflammation or storage that cannot be confirmed by other means.	IIb	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Laboratory tests in adult patients with hypertrophic cardiomyopathy (HCM)

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 ß-oxidation defects.
Creatine phosphokinase	• Serum creatine phosphokinase is raised in metabolic disorders such as Danon and mitochondrial disease.

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Laboratory tests in adult patients with HCM *(Cont.)*

Test	Comment
Plasma/leucocyte alpha galactosidase A (in men aged >30 years)	• Low (<10% normal values) or undetectable plasma and leucocyte alpha galactosidase A is present in male patients with Anderson-Fabry disease[a]. • 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 and 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.

[a]Pseudo-deficiency may be seen in some genetic variants such as D313Y

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Genetic counselling

Recommendations	Class	Level
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

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Genetic testing in probands

Recommendations	Class	Level
Genetic testing is recommended in patients fulfilling diagnostic criteria for HCM, when it enables cascade genetic screening of their relatives.	I	B
It is recommended that genetic testing be performed in certified diagnostic laboratories with expertise in the interpretation of cardiomyopathy-related mutations.	I	C
In the presence of symptoms and signs of disease suggestive of specific causes of HCM, genetic testing is recommended to confirm the diagnosis.	I	B
Genetic testing in patients with a borderline[a] diagnosis of HCM should be performed only after detailed assessment by specialist teams.	IIa	C
Post-mortem genetic analysis of stored tissue or DNA should be considered in deceased patients with pathologically confirmed HCM, to enable cascade genetic screening of their relatives.	IIa	C

[a]Borderline: left ventricular wall thickness 12 – 13 mm in adults; left ventricular hypertrophy in the presence of hypertension, athletic training, valve disease.

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Genetic and clinical testing of adult relatives

Recommendations	Class	Level
Cascade genetic screening, after pre-test counselling, is recommended in first-degree adult relatives of patients with a definite disease-causing mutation.	I	B
Clinical evaluation, employing ECG and echocardiography and long-term follow-up, is recommended in first-degree relatives who have the same definite disease-causing mutation as the proband.	I	C
First-degree relatives who do not have the same definite disease-causing mutation as the proband should be discharged from further follow-up but advised to seek re-assessment if they develop symptoms or when new clinically relevant data emerge in the family.	IIa	B
When no definite genetic mutation is identified in the proband or genetic testing is not performed, clinical evaluation with ECG and echocardio-graphy should be considered in first-degree adult relatives and repeated every 2-5 years (or 6-12 monthly if non-diagnostic abnormalities are present).	IIa	C

Proband = usually the first family member to be diagnosed with the condition.

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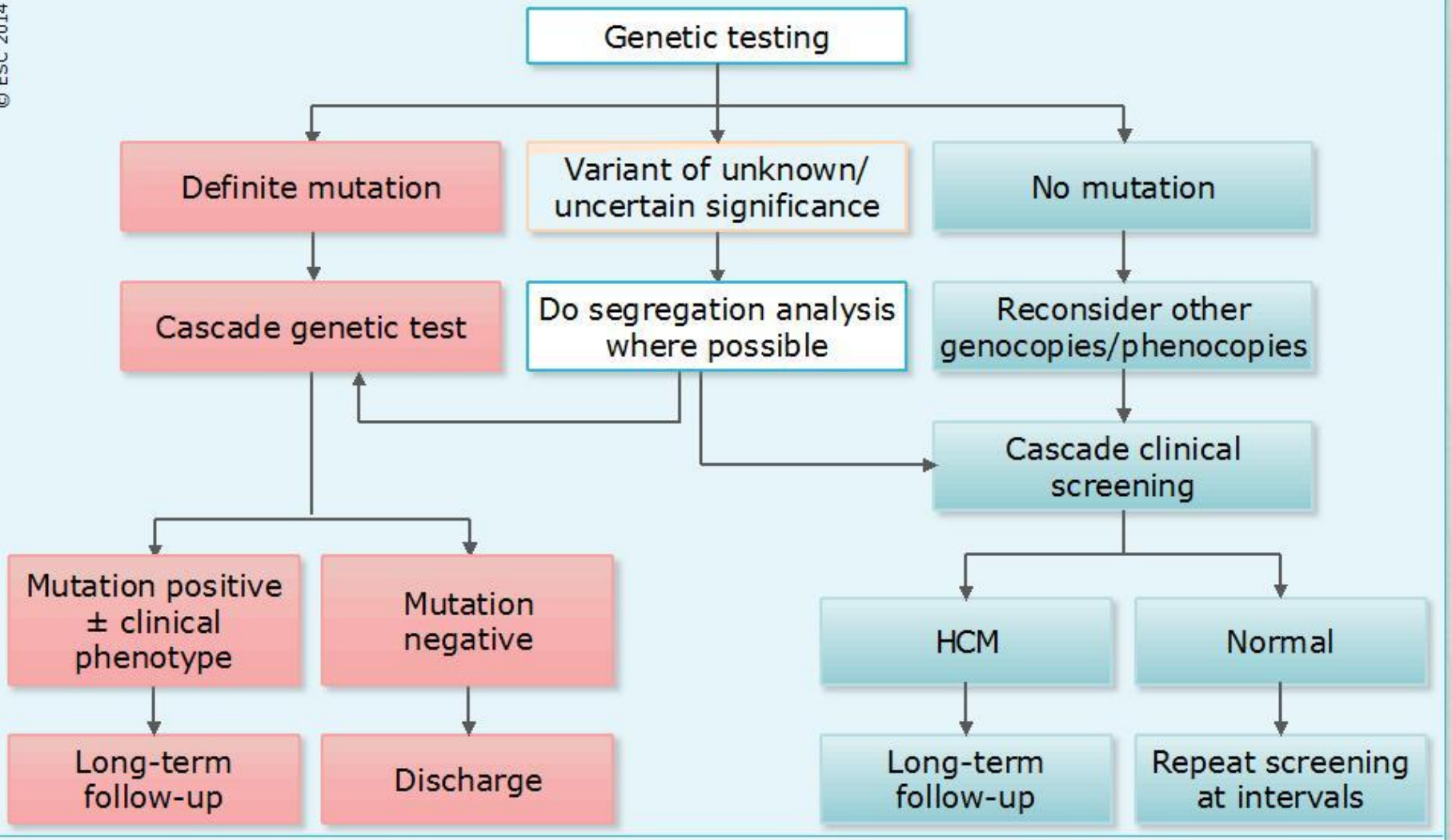
Flow chart for the genetic and clinical screening of probands and relatives



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

Genetic and clinical screening in children

Recommendations	Class	Level
The children of patients with a definite disease-causing mutation should be considered for predictive genetic testing—following pre-test family counselling—when they are aged 10 or more years and this should be carried out in accordance with international guidelines for genetic testing in children.	IIa	C
In first-degree child relatives aged 10 or more years, in whom the genetic status is unknown, clinical assessment with ECG and echocardiography should be considered every 1–2 years between 10 and 20 years of age, and then every 2–5 years thereafter.	IIa	C
If requested by the parent(s) or legal representative(s), clinical assessment with ECG and echocardiography may precede or substitute for genetic evaluation after counselling by experienced physicians and when it is agreed to be in the best interest of the child.	IIb	C
When there is a malignant family history in childhood or early-onset disease or when children have cardiac symptoms or are involved in particularly demanding physical activity, clinical or genetic testing of first-degree child relatives before the age of 10 years may be considered.	IIb	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Follow-up of mutation carriers without a phenotype

Recommendations	Class	Level
In definite mutation carriers who have no evidence of disease expression, sports activity may be allowed after taking into account the underlying mutation and the type of sport activity, and the results of regular and repeated cardiac examinations.	IIb	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Delivery of care

Recommendations	Class	Level
It is recommended that individuals who have an uncertain diagnosis, severe symptoms or increased risk for disease-related complications, be referred to specialist teams for further investigation and management.	I	C
Irrespective of symptom status, regular clinical surveillance of patients —and, when appropriate, their first-degree relatives—is recommended.	I	C
In all cases of HCM, clinicians should consider evaluation of patients in centres with multidisciplinary teams, with expertise in the diagnosis, genetics, risk stratification and management of heart muscle disease.	IIa	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Coronary angiography

Recommendations	Class	Level
Invasive coronary angiography is recommended in adult survivors of cardiac arrest, in patients with sustained ventricular tachyarrhythmia and in patients with severe stable angina (Canadian Cardiovascular Society (CCS) Class ≥3).	I	C
Invasive or CT coronary angiography should be considered 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 aged 40 years or more, invasive or CT coronary angiography should be considered before septal reduction therapy, irrespective of the presence of typical exertional chest pain.	IIa	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Invasive haemodynamic studies

Recommendations	Class	Level
Cardiac catheterization—to evaluate right and left heart function and pulmonary arterial resistance—is recommended in patients being considered for heart transplantation or mechanical circulatory support.	I	B
In symptomatic patients with 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.	IIb	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Cardiopulmonary exercise testing

Recommendations	Class	Level
Cardiopulmonary exercise testing, with simultaneous measurement of respiratory gases, is recommended in severely symptomatic patients with systolic and/or diastolic LV dysfunction being evaluated for heart transplantation or mechanical support.	I	B
Irrespective of symptoms, cardiopulmonary exercise testing with simultaneous measurement of respiratory gases (or standard treadmill or bicycle ergometry when unavailable) should be considered to assess the severity and mechanism of exercise intolerance and change in systolic blood pressure.	IIa	B
Cardiopulmonary exercise testing, with simultaneous measurement of respiratory gases (or standard treadmill or bicycle ergometry when unavailable), should be considered in symptomatic patients undergoing septal alcohol ablation and septal myectomy to determine the severity of exercise limitation.	IIa	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Investigation of syncope

Recommendations	Class	Level
12–lead ECG, upright exercise test, resting and exercise 2-D and Doppler echocardiography, and 48–hour ambulatory ECG monitoring are recommended in patients with unexplained syncope, to identify the cause of their symptoms.	I	C
An ILR should be considered in patients with recurrent episodes of unexplained syncope, who are at low risk of SCD.	IIa	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Palpitations

Recommendations	Class	Level
For patients with frequent or sustained palpitations,48–hour ambulatory ECG monitoring is recommended, to identify the likely cause.	I	C
An ILR may be considered in patients with frequent palpitations, in whom no cause is identified following prolonged ECG monitoring.	IIb	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Electrophysiologic testing

Recommendations	Class	Level
Invasive electrophysiological study is recommended in patients with documented persistent or recurrent supraventricular tachycardia (atrial flutter, atrial tachycardia, atrioventricular nodal re-entry tachycardia, accessory atrioventricular pathway mediated tachycardias) and in patients with ventricular pre-excitation, in order to identify and treat an ablatable substrate.	I	C
Invasive electrophysiological study may be considered in selected patients with documented, symptomatic, monomorphic, sustained (>30 s) ventricular tachycardia in order to identify and treat an ablatable arrhythmia substrate.	IIb	C
Invasive electrophysiological study with programmed ventricular stimulation is not recommended for sudden cardiac death risk stratification.	III	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Treatment of left ventricular outflow tract obstruction: General measures

Recommendations	Class	Level
Arterial and venous dilators, including nitrates and phosphodiesterase inhibitors, should be avoided if possible in patients with resting or provocable LVOTO.	IIa	C
Restoration of sinus rhythm or appropriate rate control should be considered before considering invasive therapies in patients with new-onset or poorly controlled atrial fibrillation.	IIa	C
Digoxin is not recommended in patients with resting or provocable LVOTO.	III	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Medical treatment of left ventricular outflow tract obstruction

Recommendations	Class	Level
Non-vasodilating ß-blockers, titrated to maximum tolerated dose, are recommended as first-line therapy to improve symptoms in symptomatic patients with resting or provoked LVOTO.	I	B
Verapamil, titrated to maximum tolerated dose, is recommended to improve symptoms in symptomatic patients with resting or provoked[a] LVOTO, who are intolerant or have contra-indications to ß-blockers.	I	B
Disopyramide, titrated to maximum tolerated dose[b], is recommended in addition to a ß-blocker (or, if this is not possible, with verapamil) to improve symptoms patients with resting or provoked[a] LVOTO.	I	B
Disopyramide, titrated to maximum tolerated dose[b], may be considered as monotherapy to improve symptoms in symptomatic patients with resting or provoked[a] LVOTO (exercise or Valsalva manoeuvre) taking caution in patients with–or prone to–AF, in whom it can increase ventricular rate response.	IIb	C
ß-Blockers or verapamil may be considered in children and *asymptomatic* adults with resting or provoked[a] LVOTO, to reduce left ventricular pressures.	IIb	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Medical treatment of left ventricular outflow tract obstruction *(Cont.)*

Recommendations	Class	Level
Low-dose loop–or thiazide diuretics may be used with caution in symptomatic LVOTO, to improve exertional dyspnoea.	IIb	C
Diltiazem, titrated to maximum tolerated dose, should be considered in symptomatic patients with resting or provoked[a] LVOTO, who are intolerant or have contra-indications to ß-blockers and verapamil to improve symptoms.	IIa	C
Oral or i.v. ß-blockers and vasoconstrictors should be considered in patients with severe provocable LVOTO presenting with hypotension and pulmonary oedema.	IIa	C

[a]Provocation with Valsalva manoeuvre, upright exercise or oral nitrates if unable to exercise.
[b]QTc interval should be monitored during up-titration of disopyramide and the dose reduced if it exceeds 480 ms.

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Septal reduction therapy

Recommendations	Class	Level
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 mm Hg, 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 mm Hg 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 mm Hg 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 mm Hg 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

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Indications for cardiac pacing in patients with obstruction

Recommendations	Class	Level
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 mm Hg, 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 mm Hg, 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**

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

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

Are there alternative/additional explanations for symptoms?

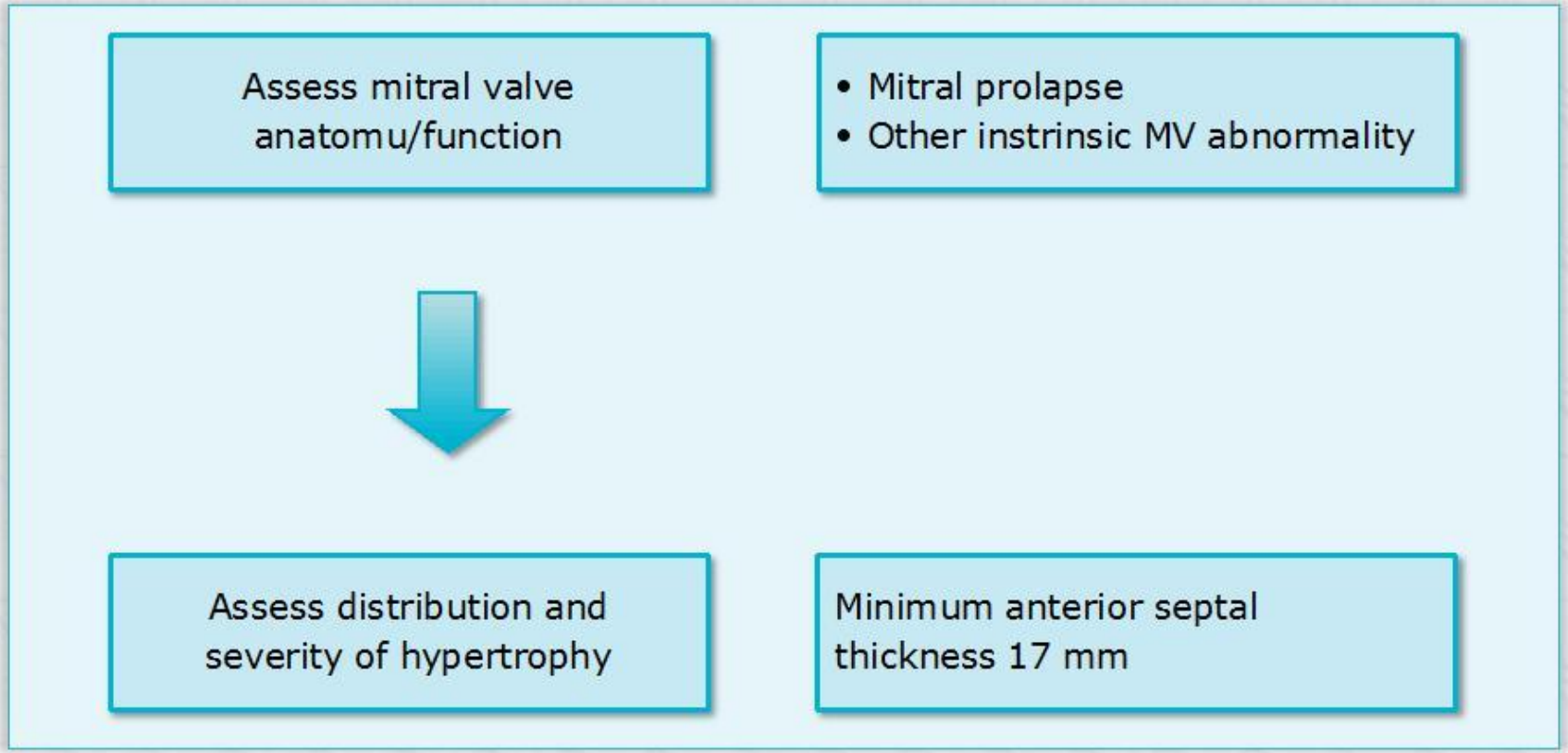
- Obesity
- Respiratory Disease
- Coronary artery disease
- Anaemia
- Thyroid disease
- Arrhythmia (e.g. AF)
- Drug side-effects
- Systemic disease (e.g. amyloid)
- RVOT obstruction

What is the mechanism of obstruction?

- SAM-related
- Mid-cavity
- Sub-aortic membrane
- Aortic stenosis
- Anomalous papillary muscle insertion
- Accessory mitral valve tissue

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Pre-assessment check list for patients being considered for invasive septal reduction therapies *(Cont.)*



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Patients with heart failure and preserved LV ejection fraction (≥50%)

Recommendations	Class	Level
In patients in NYHA functional Class II–IV with an LVEF ≥50% and no evidence for resting or provocable LVOTO, ß-blockers, verapamil or diltiazem should be considered, to improve heart failure symptoms.	IIa	C
Low-dose loop and thiazide diuretics should be considered in patients in NYHA functional Class II–IV with an EF ≥50%, and no evidence for resting or provocable LVOTO, to improve heart failure symptoms.	IIa	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Patients with heart failure and reduced LV ejection fraction (<50%)

Recommendations	Class	Level
An ACE-inhibitor (or ARB if ACE inhibitor not tolerated) should be considered, in addition to a ß-blocker, for patients without LVOTO who have an LVEF <50%, to reduce the risk of HF hospitalization and risk of premature death[a].	IIa	C
A ß-blocker should be considered, in addition to an ACE-inhibitor (or ARB if ACE-inhibitor not tolerated), for patients without LVOTO who have an LVEF <50% to improve symptoms and reduce the risks of HF hospitalization and premature death[a].	IIa	C
Low-dose loop diuretics should be considered for symptomatic patients in NYHA functional Class II–IV with an LVEF <50%, to improve symptoms and reduce the risk of HF hospitalization[a].	IIa	C
For all patients with persisting symptoms (NYHA functional Class II–IV) and an LVEF <50%—despite treatment with an ACE-inhibitor (or an ARB if an ACE-inhibitor is not tolerated) and a ß-blocker—a mineralocorticoid receptor antagonist (MRA) should be considered, to reduce the risks of HF hospitalization and premature death[a].	IIa	C
Low-dose digoxin may be considered for patients without LVOTO who are in NYHA functional Class II–IV and have an LVEF <50% and permanent atrial fibrillation to control heart rate response.	IIb	C

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

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Cardiac resynchronization therapy

Recommendations	Class	Level
Cardiac resynchronization therapy to improve symptoms may be considered in patients with HCM, maximum LVOTG <30 mmHg, drug refractory symptoms, NYHA functional Class II–IV, LVEF<50% and LBBB with a QRS duration >120 ms.	IIb	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

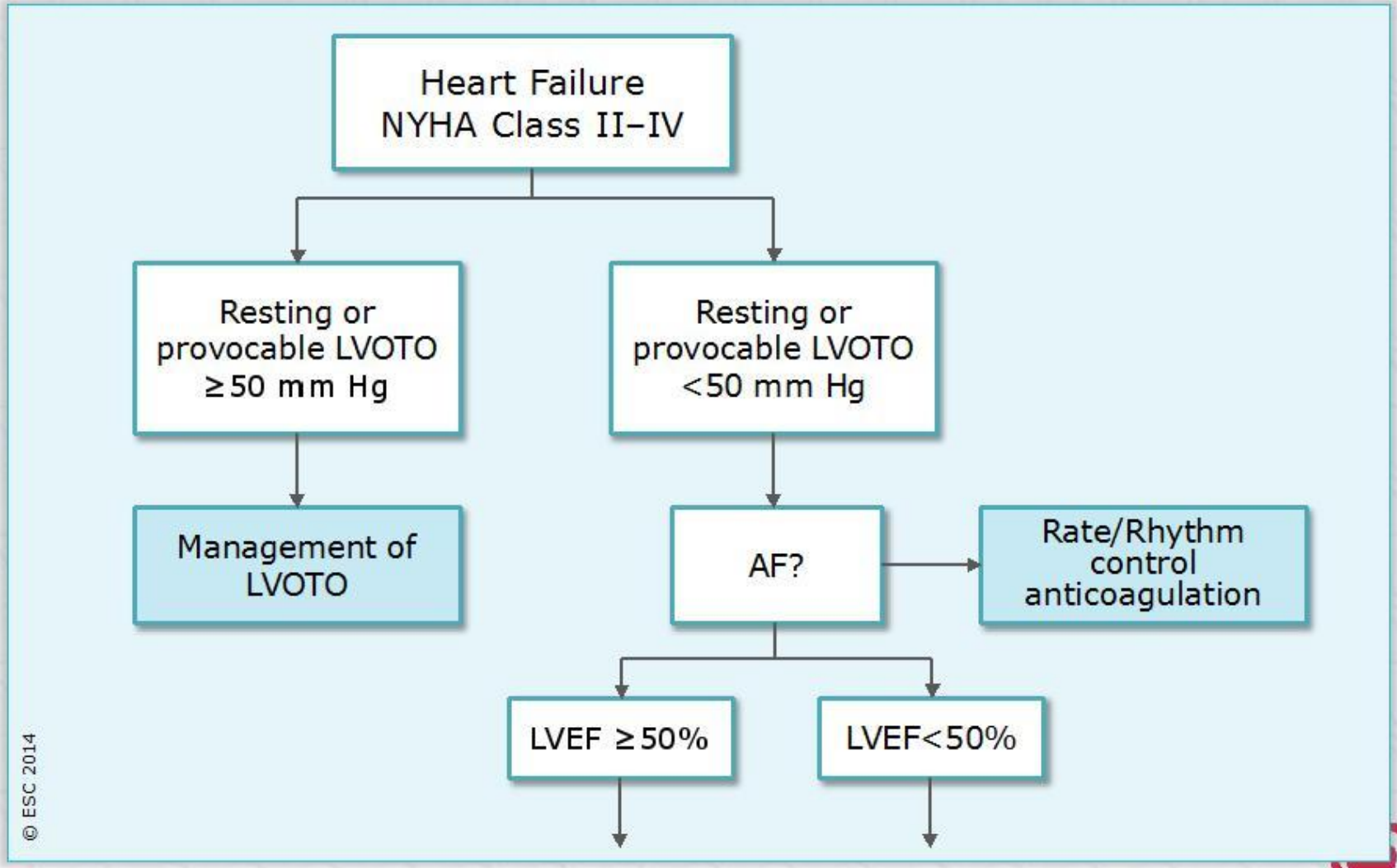
Cardiac transplantation

Recommendations	Class	Level
Orthotopic cardiac transplantation should be considered in eligible patients who have an LVEF <50% and NYHA functional Class III–IV symptoms despite optimal medical therapy or intractable ventricular arrhythmia.	**IIa**	**B**
Orthotopic cardiac transplantation may be considered in eligible patients with normal LVEF (≥50%) and severe drug refractory symptoms (NYHA functional Class III–IV) caused by diastolic dysfunction.	**IIb**	**B**

Left ventricular assist devices

Recommendations	Class	Level
Continuous axial flow LVAD therapy may be considered in selected 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.	**IIb**	**C**

Algorithm for the treatment of heart failure in hypertrophic cardiomyopathy



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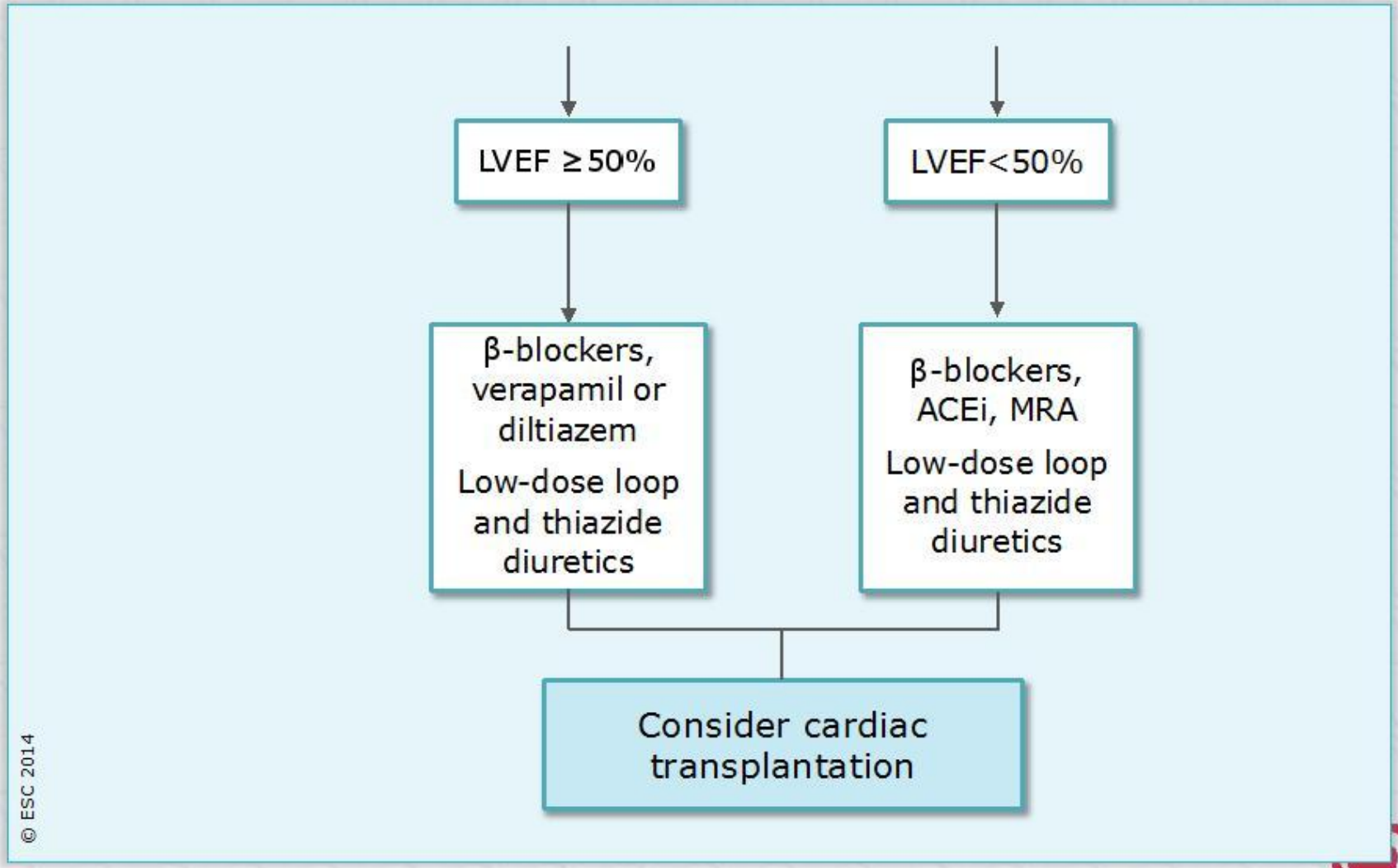
Algorithm for the treatment of heart failure in hypertrophic cardiomyopathy *(Cont.)*



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Chest pain on exertion in patients without left ventricular outflow tract obstruction

Recommendations	Class	Level
ß-Blockers and calcium antagonists should be considered, to improve symptoms in patients with angina-like chest pain and no evidence for LVOTO or obstructive coronary artery disease.	**IIa**	C
Oral nitrates may be considered, to improve symptoms in patients with angina-like chest pain and no evidence for LVOTO or obstructive coronary artery disease.	**IIb**	C

Atrial fibrillation/atrial flutter

Recommendations	Class	Level
Unless contra-indicated, oral anticoagulation with VKA (target INR 2.0–3.0) is recommended in patients who develop persistent, permanent or paroxysmal AF, to prevent thromboembolism.	I	B
Antithrombotic therapy is recommended for patients with atrial flutter, as for those with AF.	I	C
Assessment of the risk of bleeding with the HAS-BLED score should be considered when prescribing antithrombotic therapy (whether with VKA or antiplatelet therapy).	IIa	B
Restoration of sinus rhythm, by DC or pharmacological cardioversion with intravenous amiodarone, should be considered in patients presenting with recent-onset AF.	IIa	C
Amiodarone should be considered for achieving rhythm control and to maintain sinus rhythm after DC cardioversion.	IIa	B
ß-Blockers, verapamil and diltiazem are recommended to rate control in patients with permanent or persistent AF.	I	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Atrial fibrillation/atrial flutter *(Cont.)*

Recommendations	Class	Level
Catheter ablation for AF should be considered 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 may be considered 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 dual-chamber (DDD) pacemaker with mode-switch function is recommended for patients with paroxysmal AF and a single-chamber (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 may be considered after AV node ablation.	IIb	C
48-Hour ambulatory ECG monitoring every 6–12 months to detect AF should be considered in patients who are in sinus rhythm and have an LA diameter of ≥45 mm.	IIa	C

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Atrial fibrillation/atrial flutter *(Cont.)*

Recommendations	Class	Level
Ablation procedures during septal myectomy may be considered in patients with HCM and symptomatic AF.	IIb	C
Antiplatelet therapy using aspirin 75-100 mg *plus* clopidogrel 75 mg daily (where there is a low-risk of bleeding) should be considered 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—a direct thrombin inhibitor (dabigatran) or an oral factor Xa inhibitor (e.g. rivaroxaban, apixaban) is recommended.	I	B
Unless there is a reversible cause of AF, lifelong OAC therapy with a VKA (INR 2.0-3.0) is recommended, even if sinus rhythm is restored.	I	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

5-year risk of SCD using the HCM Risk-SCD model

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

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 (mm Hg)] + [0.4583082 x family history SCD] + [0.82639195 x NSVT] + [0.71650361 x unexplained syncope] – [0.01799934 x age at clinical evaluation (years)].

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Prevention of sudden cardiac death

Recommendations	Class	Level
Avoidance of competitive sports is recommended in patients with HCM.	I	C
ICD implantation is recommended in patients who have survived a cardiac arrest due to VT or VF, or who have spontaneous sustained VT causing syncope or haemodynamic compromise, and have a life expectancy of >1 year.	I	B
HCM Risk-SCD is recommended as a method of estimating risk of sudden death at 5 years in patients aged ≥16 years without a history of resuscitated VT/VF or spontaneous sustained VT causing syncope or haemodynamic compromise.	I	B
It is recommended that the 5-year risk of SCD be assessed at first evaluation and re-evaluated at 1–2 yearly intervals or whenever there is a change in clinical status.	I	B
ICD implantation should be considered in patients with an estimated 5-year risk of sudden death of ≥6% and a life expectancy of >1 year, 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.	IIa	B

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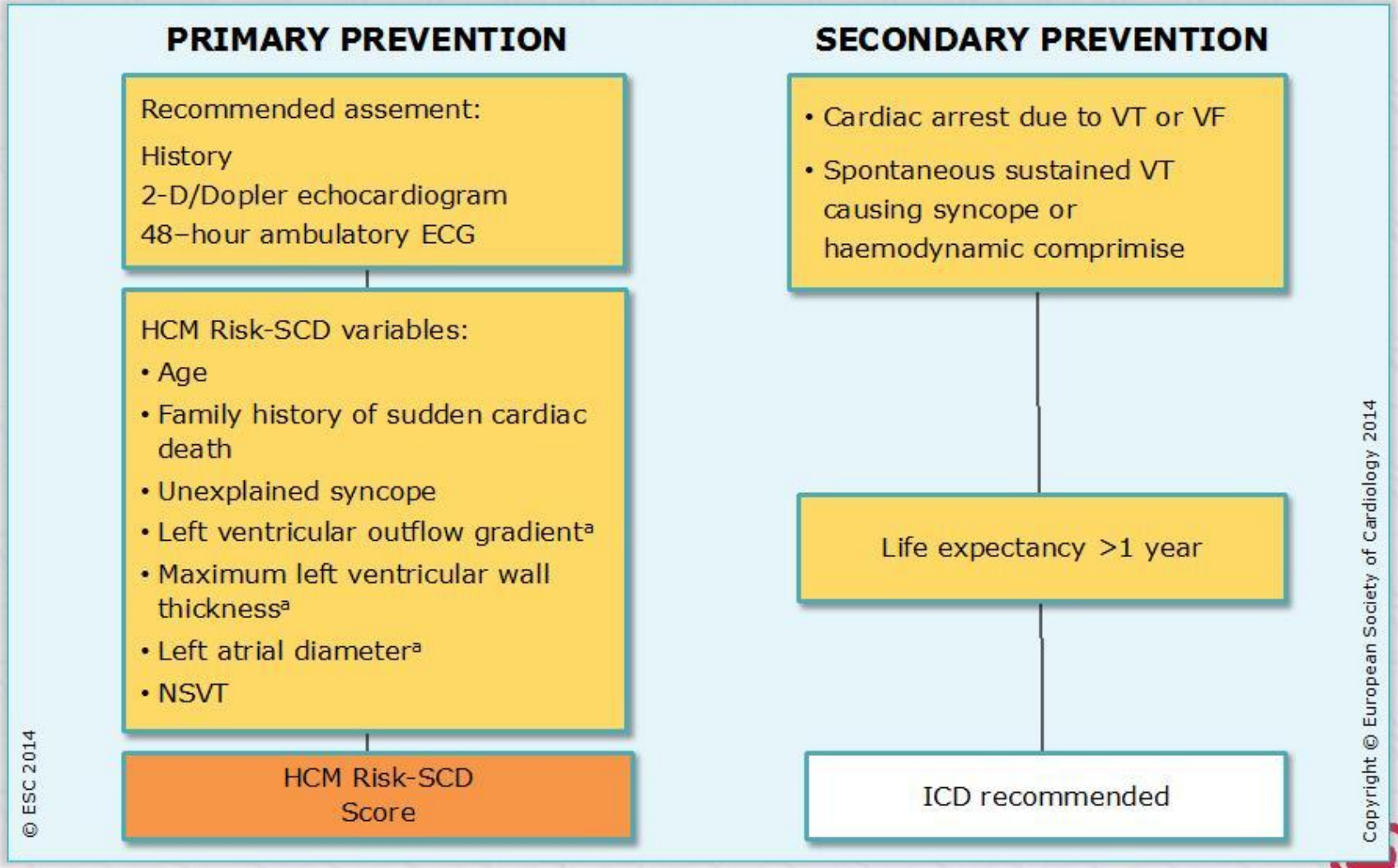
Prevention of sudden cardiac death *(Cont.)*

Recommendations	Class	Level
ICD implantation may be considered in individual patients with an estimated 5–year risk of SCD of between ≥4% and <6% and a life expectancy of >1 year 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.	**IIb**	**B**
ICD implantation may be considered in individual patients with an estimated 5–year risk of SCD of <4% only when they have clinical features that are of proven prognostic importance, and when an assessment of the lifelong risk of complications and the impact of an ICD on lifestyle, socio-economic status and psychological health suggests a net benefit from ICD therapy.	**IIb**	**B**
ICD implantation is not recommended in patients with an estimated 5–year risk of SCD of <4% and no other clinical features that are of proven prognostic importance.	**III**	**B**

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Flow chart for ICD implantation



[a]Use absolute values for LVOT gradient, MLVWT and left atrial dimension.

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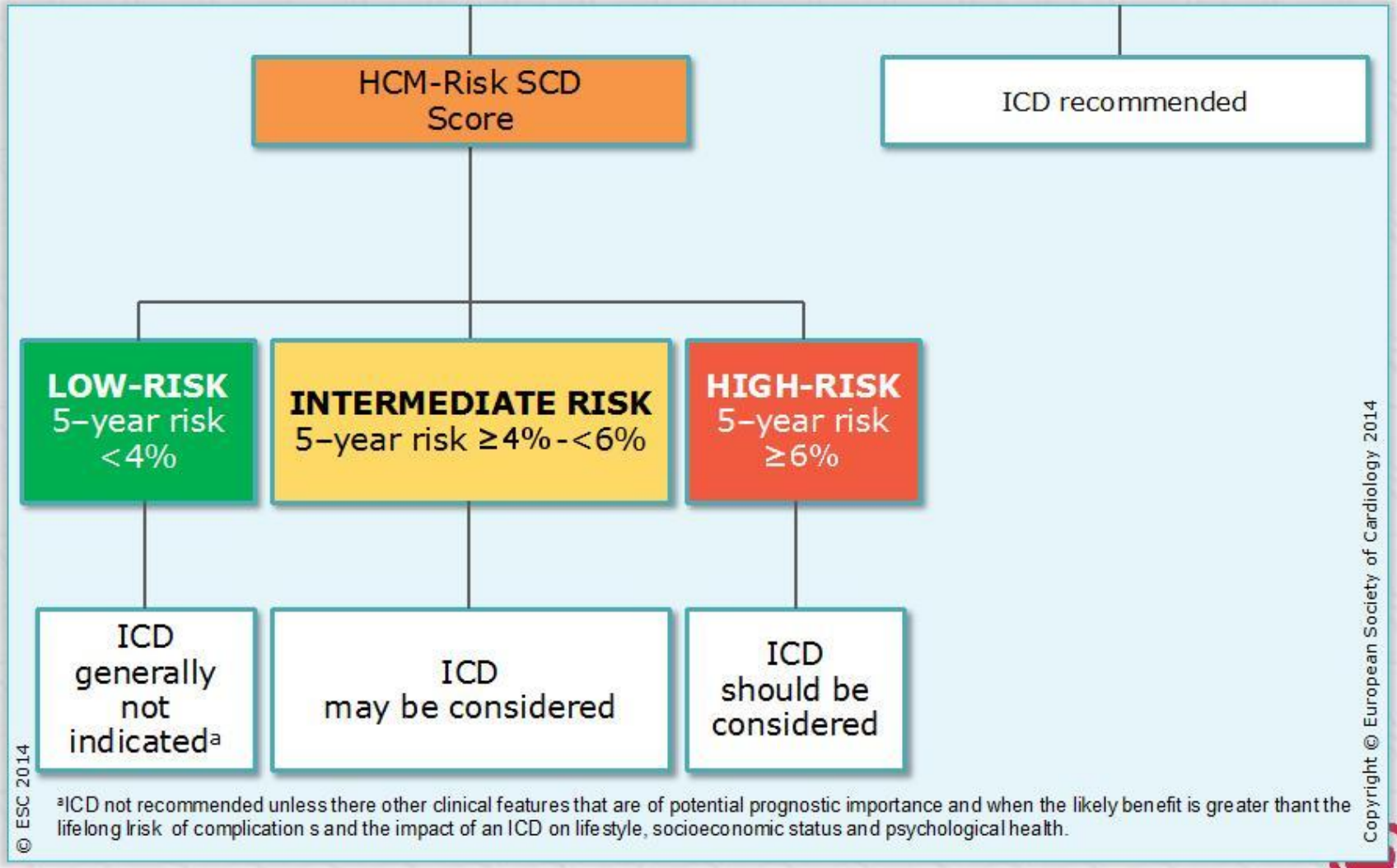
Flow chart for ICD implantation



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Practical aspects of implantable cardioverter defibrillator therapy

Recommendations	Class	Level
Prior to ICD implantation, patients should be counselled on the risk of inappropriate shocks, implant complications and the social, occupational, and driving implications of the device.	I	C
ß-Blockers and/or amiodarone are recommended in patients with an ICD, who have symptomatic ventricular arrhythmias or recurrent shocks despite optimal treatment and device re-programming.	I	C
Electrophysiological study is recommended in patients with ICD, and inappropriate shocks due to regular supraventricular tachycardias, to identify and treat any ablatable arrhythmia substrate.	I	C
A subcutaneous ICD lead system (S-ICD™) may be considered in HCM patients who do not have an indication for pacing.	IIb	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

ICD implantation in children

Recommendations	Class	Level
ICD implantation is recommended in children who have survived a cardiac arrest or experienced documented sustained ventricular tachycardia.	I	B
ICD implantation should be considered in children with two or more major paediatric risk factors* after appropriate counselling and when an assessment of the lifelong risk of complications and the impact of an ICD on lifestyle and psychological health suggests a net benefit from ICD therapy.	IIa	C
ICD implantation may be considered in children with a single major paediatric risk factor* after appropriate counselling and when an assessment of the lifelong risk of complications and the impact of an ICD on lifestyle and psychological health suggests a net benefit from ICD therapy.	IIb	C

Major paediatric risk factors: Maximum left ventricular wall thickness ≥ 30 mm or a Z-score ≥ 6, unexplained syncope, non-sustained ventricular tachycardia (≥3 consecutive ventricular beats at ≥ 120 BPM lasting,30 seconds), family history of SCD (one or more first-degree relatives with SCD aged, 40 years with or without the diagnosis of HCM, or SCD in a first-degree relative at any age with an established diagnosis of HCM).

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Routine flollow-up

Recommendations	Class	Level
A clinical evaluation, including 12-lead ECG and TTE, is recommended every 12–24 months in clinically stable patients.	I	C
A clinical evaluation, including 12-lead ECG and TTE, is recommended whenever there is a change in symptoms.	I	C
48-Hour ambulatory ECG is recommended 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 may be considered every 5 years in clinically stable patients, or every 2–3 years in patients with progressive disease.	IIb	C
Symptom-limited exercise testing should be considered every 2–3 years in clinically stable patients, or every year in patients with progressive symptoms.	IIa	C
Cardiopulmonary exercise testing (when available) may be considered every 2–3 years in clinically stable patients, or every year in patients with progressive symptoms.	IIb	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Reproductive issues in women with HCM

Recommendations	Class	Level
Pre-pregnancy risk assessment and counselling is indicated in all women.	I	C
Counselling on safe and effective contraception is indicated in all women of fertile age.	I	C
Counselling on the risk of disease transmission is recommended for all men and women before conception.	I	C
β-Blockers (preferably metoprolol) should be continued in women who used them before pregnancy.	IIa	C
β-Blockers (preferably metoprolol) should be started in women who develop symptoms during pregnancy.	I	C
Whenever β-blockers are prescribed, monitoring of foetal growth and of the condition of the neonate is recommended.	I	C
Scheduled (induced) vaginal delivery is recommended as first choice in most patients.	I	C
Therapeutic anticoagulation with LMWH or vitamin K antagonists depending on the stage of pregnancy is recommended for atrial fibrillation.	I	C
Cardioversion should be considered for persistent atrial fibrillation.	IIa	C

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Clinical features that assist in the differential diagnosis of hypertensive heart disease and hypertrophic cardiomyopathy

Clinical features favouring hypertension only
Normal 12-lead ECG or isolated increased voltage without repolarisation abnormality.
Regression of LVH over 6–12 months tight systolic blood pressure control (<130 mmHg).
Clinical features favouring hypertrophic cardiomyopathy
Family history of HCM.
Right ventricular hypertrophy.
Late gadolinium enhancement at the RV insertion points or localized to segments of maximum LV thickening on CMR.
Maximum LV wall thickness ≥15 mm (Caucasian); ≥20 mm (black).
Severe diastolic dysfunction.
Marked repolarisation abnormalities, conduction disease or Q-waves on 12-lead ECG.

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

General lifestyle considerations for patients with hypertrophic cardiomyopathy

Topic	General guidance
Exercise	• Patients with HCM should avoid competitive sports activities, but should maintain a healthy lifestyle. • Advice on recreational activities should be tailored to symptoms and the risk of disease-related complications including sudden cardiac death.
Diet, alcohol and weight	• Patients should be encouraged to maintain a healthy body mass index. • Large meals can precipitate chest pain, particularly in patients with LVOTO. Smaller, more frequent meals may be helpful. • Avoid dehydration and excess alcohol, particularly in patients with LVOTO. • Constipation is a frequent side-effect of verapamil/disopyramide and should be managed with diet and if necessary aperients.
Smoking	• There are no data that show an interaction between tobacco smoking and HCM, but patients should be provided with general advice on the health risks associated with smoking and, when available, information on smoking cessation.

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

General lifestyle considerations for patients with hypertrophic cardiomyopathy *(Cont.)*

Topic	General guidance
Sexual activity	• Patients should be given the opportunity to discuss their concerns about sexual activity. Anxiety and depression following a diagnosis are frequent and some patients may express guilt or fear about their genetic diagnosis and the risk of transmission to offspring. • Patients should be counselled on the potential effect of their medication on sexual performance. • In general, patients should avoid PDE inhibitors, particularly when they have LVOTO.
Medication	• Patients should be provided with information about their medication, including potential side-effects and interactions with prescribed medications, over-the-counter remedies and other complementary therapies. • Where possible, peripheral vasodilators should be avoided in patients, particularly when they have LVOTO.
Vaccination	• In the absence of contra-indications, symptomatic patients should be advised to have yearly influenza vaccination.

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

General lifestyle considerations for patients with hypertrophic cardiomyopathy *(Cont.)*

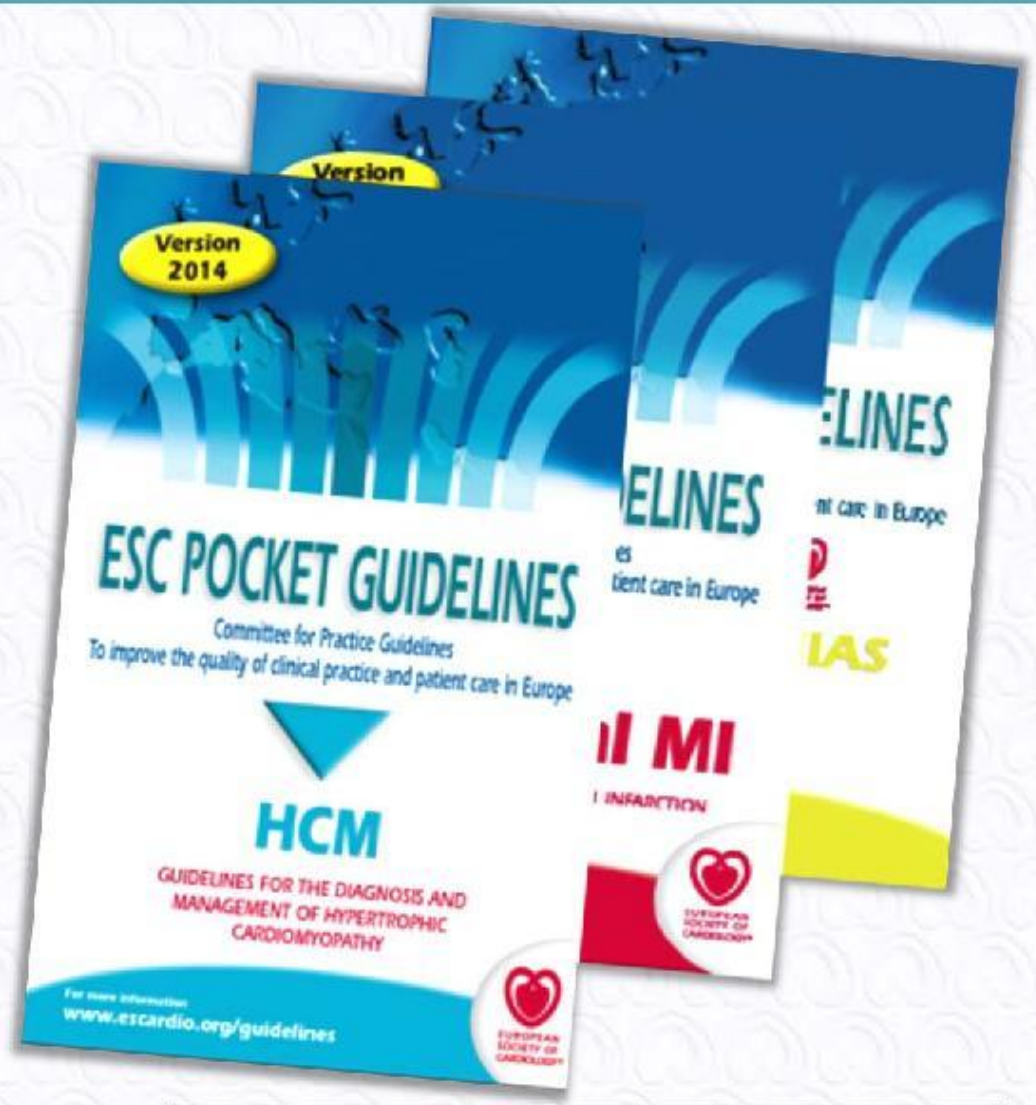
Topic	General guidance
Driving	• Most patients should be eligible for an ordinary driving licence and can continue driving unless they experience distracting or disabling symptoms. • Advice on driving licences for heavy goods or passenger-carrying vehicles should be in line with local legislation. • For further advice on driving with ICD see EHRA guidance and local rules.
Occupation	• Most people with HCM will be able to continue in their normal job. The implications of heavy manual jobs that involve strenuous activity should be discussed with the appropriate specialist • For some occupations such as pilots, and military and emergency services, there are strict guidelines on eligibility. • The social and financial implications of a diagnosis of HCM should be included in the counselling of relatives before clinical or genetic screening.

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

General lifestyle considerations for patients with hypertrophic cardiomyopathy *(Cont.)*

Topic	General guidance
Holidays and travel insurance	• Most asymptomatic or mildly symptomatic patients can fly safely. For further advice see Fitness to fly for passengers with cardiovascular disease. • Insurance companies may charge more for travel insurance. In some countries, patient support organizations can provide further advice about obtaining reasonable insurance.
Life insurance	• The diagnosis fo HCM will result in difficulty obtaining life insurance or mortgages. Advice on the rules that apply in different countries should be provided to patients at diagnosis.
Pregnancy and childbirth	• See Reproduction and contraception (section II).
Education/ schooling	• Teachers and other carers should be provided with advice and written information relevant to the care of children with HCM. • In the absence of symptoms and risk factors, children should be allowed to perform low to moderate level aerobic physical activity, in accordance with advice from their cardiologist. • Provision should be made for children with learning difficulties and other special needs.

European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284



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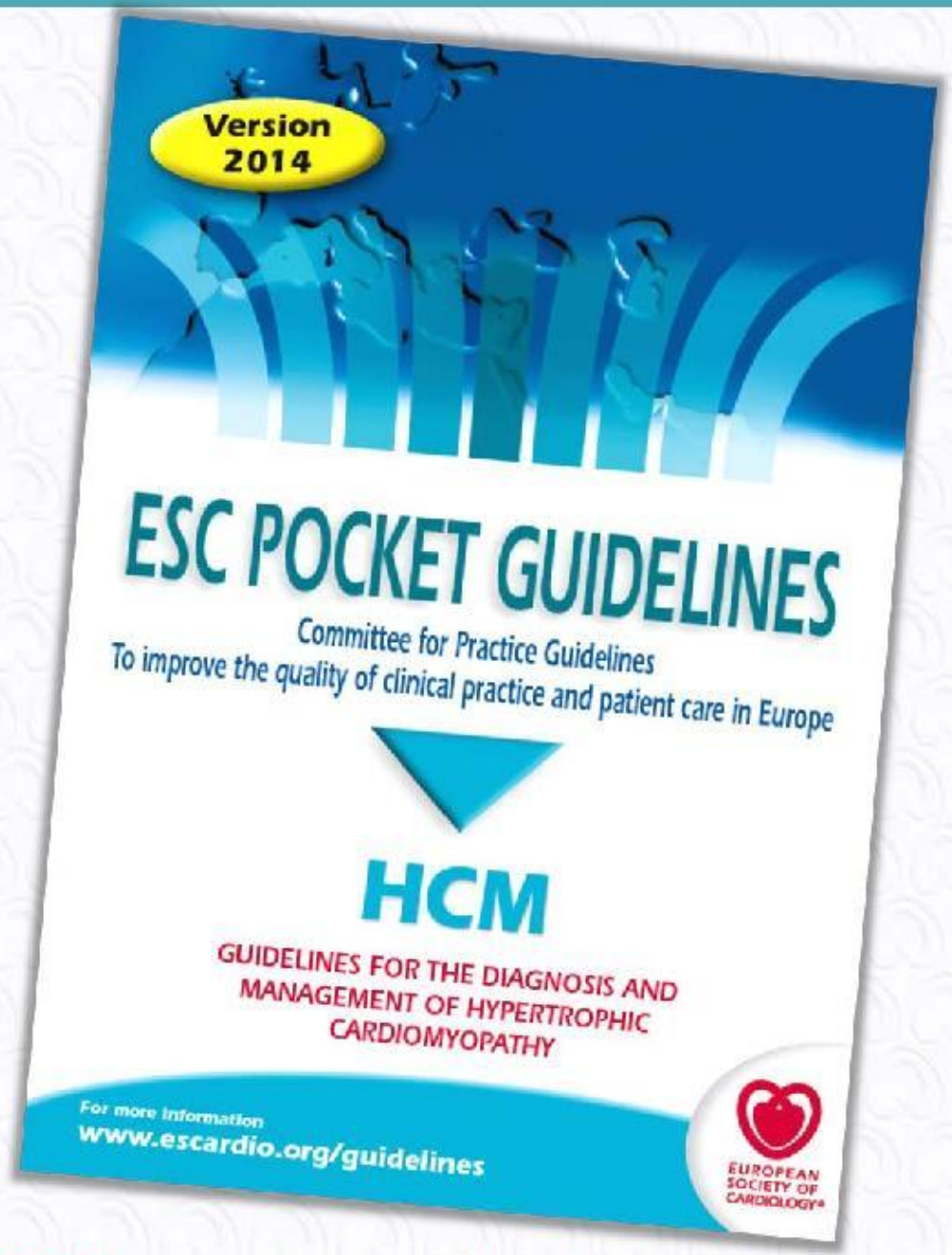

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