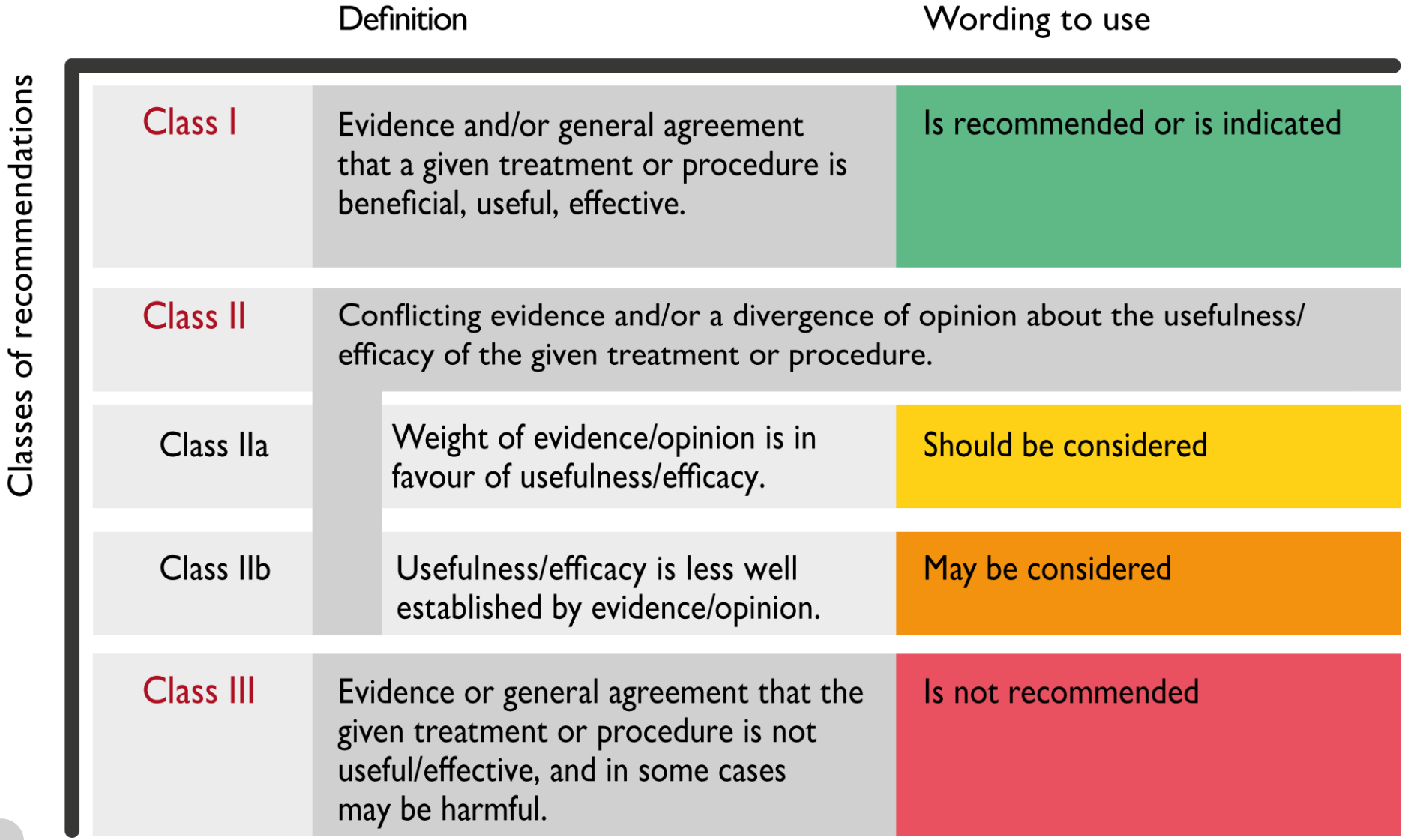
2023 ESC Guidelines for the management of cardiomyopathies

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ESC Classes of recommendations



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ESC 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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Hypertrophic Cardiomyopathy : Diagnostic Criteria

Defined by an LV wall thickness ≥ 15mm

If 13-15mm → ECG, family history, genetics

In 1st degree relatives : ≥ 13mm

Hypertrophic Cardiomyopathy and signal MR vs LVOT

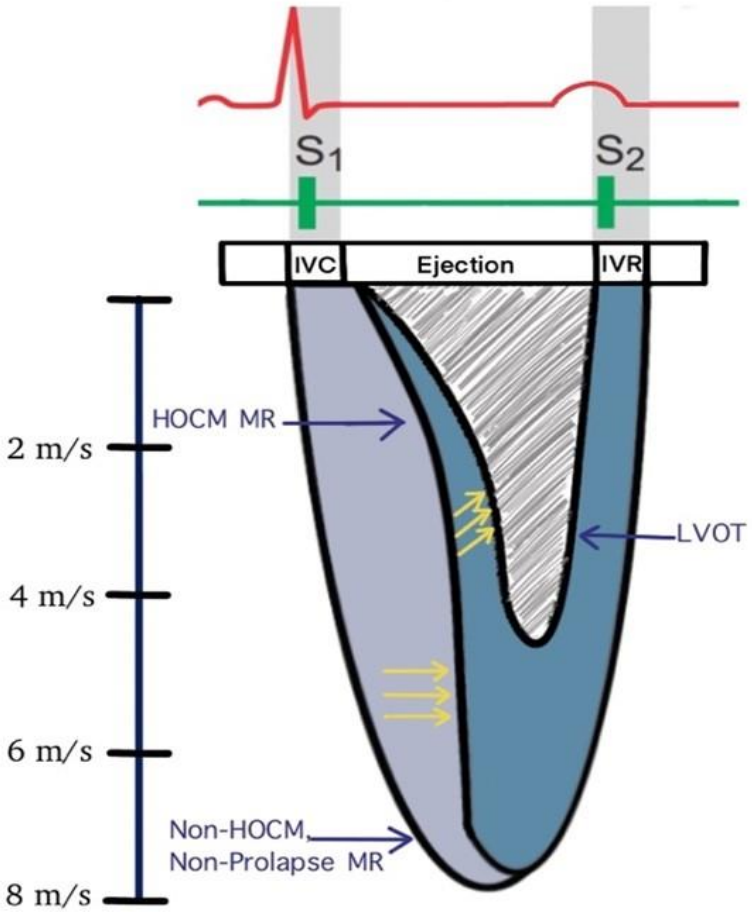
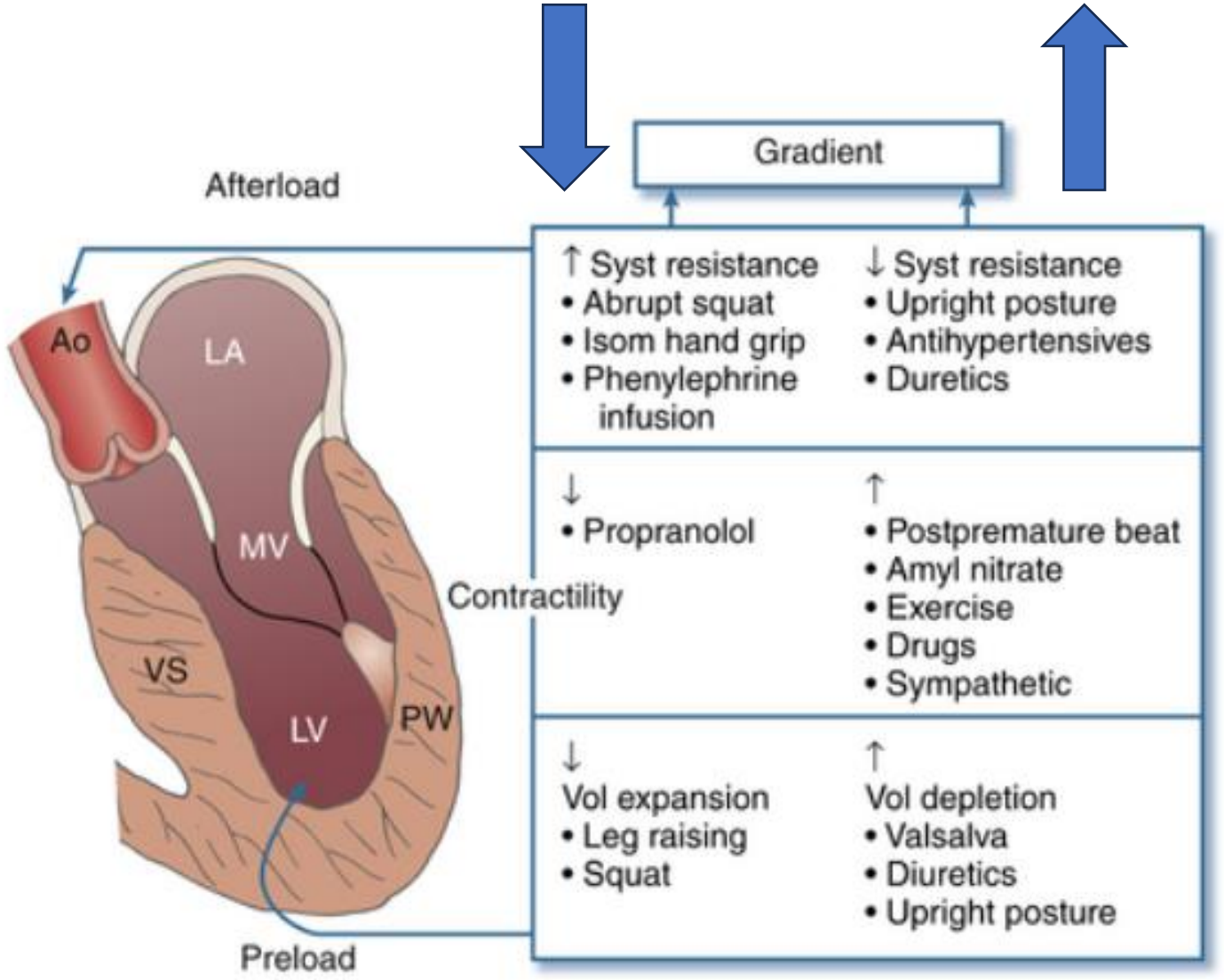


Table 1

HOCM MR Signal	LVOT Signal
• MR signal velocity is always higher because it gives the LV-to-LA gradient	• LVOT signal velocity is lower
• HOCM MR envelope is wider, begins after the onset of ejection, and terminates at the end of IVR	• LVOT signal is narrower and spans the ejection time
• Curved initially but then straightens out (perpendicular to baseline) by midsystole	• Characteristic late peaking, dagger shaped, and continues to show rightward curvature in mid-late systole

Hypertrophic Cardiomyopathy and obstruction



Imaging evaluation in hypertrophic cardiomyopathy (1)

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, and thrombi, 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).
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.

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Imaging evaluation in hypertrophic cardiomyopathy (2)

Item to assess	Primary imaging modality	Comments
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 in the guidelines.
LA dimensions	ECHO/CMR	Provides important prognostic information. Most common mechanisms of LA enlargement are SAM-related mitral regurgitation and elevated LV filling pressures.

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Imaging evaluation in hypertrophic cardiomyopathy (3)

Item to assess	Primary imaging modality	Comments
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. 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.

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Hypertrophic Cardiomyopathy and MRI

Better in apical / lateral hypertrophy, LV apical aneurysms, LV thrombi

LGE : present in 65% of patients

LGE Patchy mid-wall pattern in areas of hypertrophy and in RV insertion points

LGE is absent in athletes, young HCM patients, and mild-HCM patients

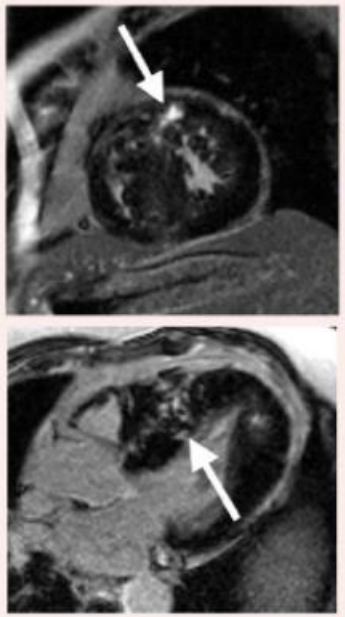
LGE is associated with adverse remodeling / RWMA / diastolic dysfunction

Cardiac MRI of Hereditary Cardiomyopathy

Late gadolinium enhancement (LGE) patterns

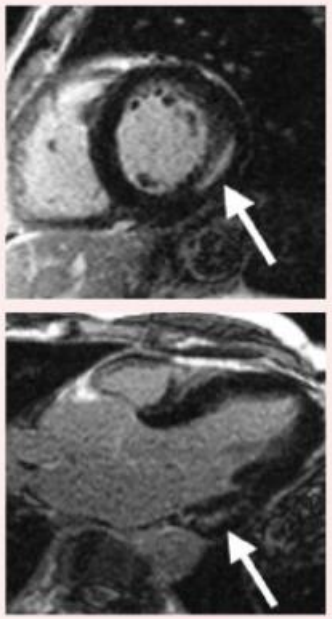
Hypertrophic cardiomyopathy

Right ventricle septal insertion sites and areas of hypertrophy



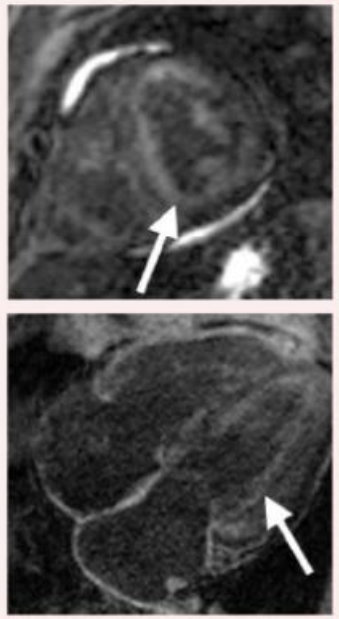
Fabry disease

Basal inferolateral wall, with sparing of the endocardium



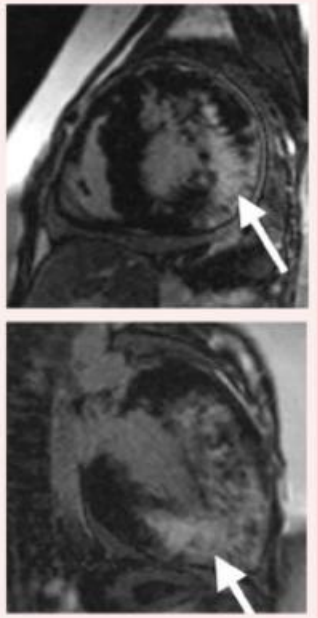
Amyloidosis

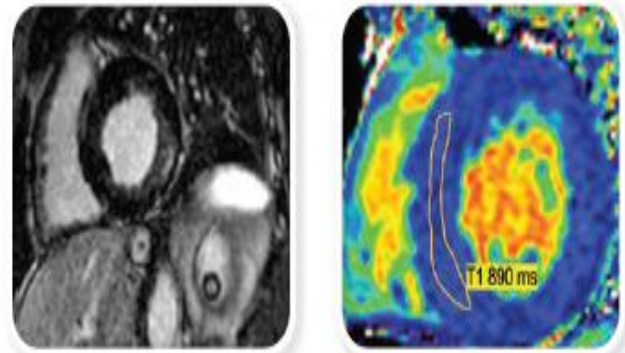
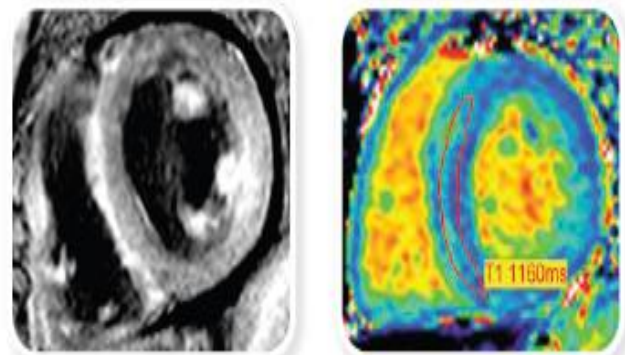
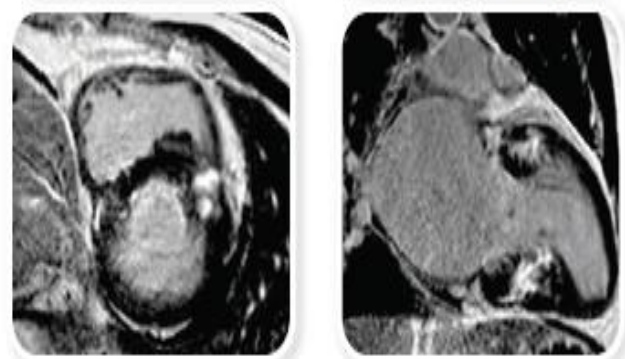
Diffuse subendocardial enhancement



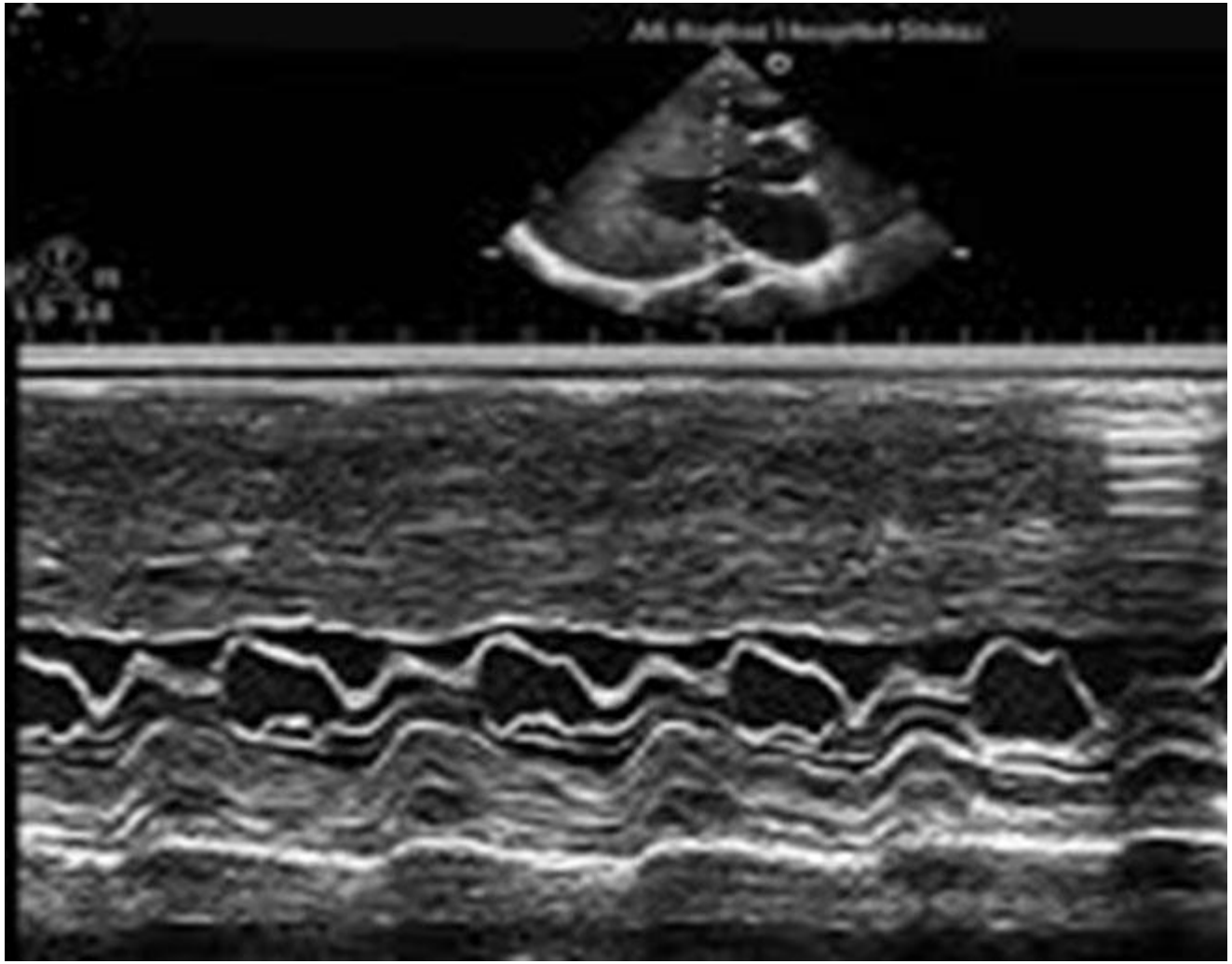
Danon disease

Extensive LGE with relative sparing of the midseptum



Cardiomyopathy phenotype	Finding	Cardiac CMR examples	Specific diseases to be considered
HCM	Posterolateral LGE and concentric LVH Low native T1		Anderson–Fabry disease
	Diffuse subendocardial LGE, high native T1		Amyloidosis
	Patchy mid-wall in hypertrophied areas		Sarcomeric HCM

Hypertrophic Cardiomyopathy and SAM-MR



Echocardiographic features that suggest specific aetiologies in hypertrophic cardiomyopathy (1)

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, *PRKAG2* variants, Friedreich ataxia
Extreme concentric LVH (wall thickness ≥30 mm)	Danon disease, Pompe disease

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Echocardiographic features that suggest specific aetiologies in hypertrophic cardiomyopathy (2)

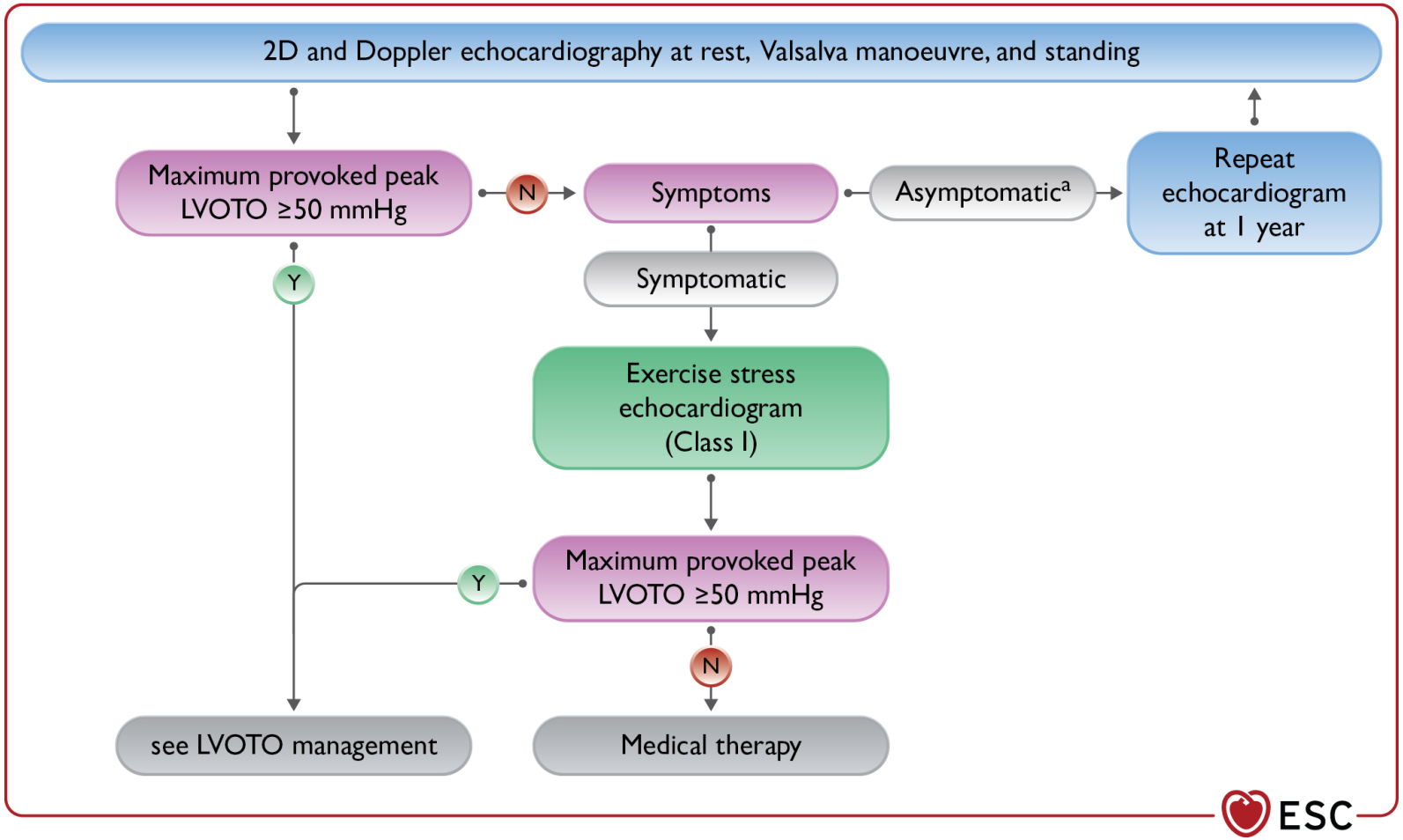
Finding	Specific diseases to be considered
Global LV hypokinesia (with or without LV dilatation)	Mitochondrial disease, TTR-related amyloidosis, *PRKAG2* variants, Danon disease, myocarditis, advanced sarcomeric HCM, Anderson–Fabry disease, Friedreich ataxia
RVOTO	Noonan syndrome and associated disorders
Apical sparing pattern on longitudinal strain imaging	Amyloidosis

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Figure 12

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



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

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Recommendation for evaluation of left ventricular outflow tract obstruction

Recommendations	Class	Level
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.	I	B
In symptomatic patients with HCM and a resting or provoked 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 provocable LVOTO and exercise-induced mitral regurgitation.	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.	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.	IIb	C

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Additional recommendation for cardiovascular magnetic resonance evaluation in hypertrophic cardiomyopathy

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

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Hypertrophic Cardiomyopathy and Genetics

	HCM
Genetic origin (Mendelian)	Nearly certain
Mode of inheritance	AD (usually) AR, mitochondrial and X-linked (rare forms)
Penetrance	Age-related Nearly complete at 50–60 years
Genetic heterogeneity[b]	High (>15 genes; >400 mutations)
Mutation screening efficiency (proband)	High (40–70%)
Phenotype/genotype correlations	Yes but few (high risk vs. low risk or delayed onset)

Hypertrophic Cardiomyopathy and Genetics

In 50% HCM patients → autosomal dominant [Sarcomeric]

Gene identification in 40-60% patients (more common young patients with family history)

<5% in adults (25% in children) – Phenocopies

- Inborn errors of metabolism [Lysosmal storage diseases (Fabry-Anderson), Glycogen Storage Disease (Pompe D., Danon D., PRKAG2 cardiomyopathy), Amyloidosis, Sarcoidosis]
- Malformation syndromes (Noon S.)
- Neuromascular disorders (Friedrich Ataxia)

Hypertrophic Cardiomyopathy and Genetics

Cardiomyopathy phenotype		AD	AR	X-linked	Matrilineal
HCM	Sarcomeric	X			
	Anderson–Fabry			X	
	Danon			X	
	TTR amyloidosis	X			
	RASopathy	X	(X)		
	Friedreich ataxia		X		
	Mitochondrial				
	Mitochondrial DNA				X
	Nuclear DNA	X	X	X	

Hypertrophic Cardiomyopathy and Genetics

Cardiomyopathies	Genes
HCM	*MYBPC3* (myosin-binding protein C), *MYH7* (bêta myosin heavy chain), *TNNT2* (troponin T), *TNNI3* (troponin I), *MYL2* (regulatory myosin light chain) ± *TPM1* (alpha tropomyosin), *MYL3* (essential myosin light chain), *ACTC* (actin)
With particular phenotype	*PRKAG2* (AMP-activated protein kinase), *LAMP2* (lysosome-associated membrane protein2), *GLA* (alpha galactosidase), mitochondrial DNA

Hypertrophic Cardiomyopathy and Symptoms (Dx)

	HCM
Learning difficulties, developmental delay	Mitochondrial diseases
	Noonan syndrome
	Danon disease
Sensorineural deafness	Mitochondrial diseases
	NSML
Visual impairment	Mitochondrial diseases
	ATTRv or hereditary ATTR
	Danon disease
	Anderson–Fabry disease[a]
Gait disturbance	Friedreich ataxia
Myotonia	
Paraesthesia/sensory abnormalities/neuropathic pain	Amyloidosis
	Anderson–Fabry disease
Carpal tunnel syndrome	TTR-related amyloidosis
Muscle weakness	Mitochondrial diseases
	Glycogenoses
	FHL1 variants
Palpebral ptosis	Mitochondrial diseases
Lentigines	NSML
Angiokeratomata	Anderson–Fabry disease
Pigmentation of skin and scars	
Palmoplantar keratoderma and woolly hair	

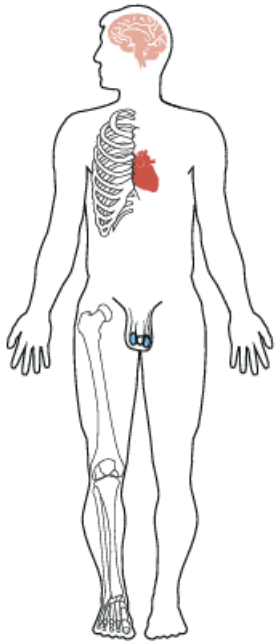
Hypertrophic Cardiomyopathy and Symptoms (Dx)

Cardiomyopathy phenotype	Finding	Specific diseases to be considered
HCM	Short PR interval/pre-excitation	Glycogenosis Danon disease *PRKAG2* cardiomyopathy Anderson–Fabry disease Mitochondrial disease
	AV block	Amyloidosis Anderson–Fabry disease (late stage) Danon disease Sarcoidosis *PRKAG2* cardiomyopathy
	Extreme LVH	Danon disease Glycogenosis (e.g. Pompe disease) *PRKAG2* cardiomyopathy
	Low QRS voltage[a]	Amyloidosis Friedreich ataxia
	Superior QRS axis ('northwest axis')	Noonan syndrome
	Q waves/pseudoinfarction pattern	Amyloidosis

Hypertrophic Cardiomyopathy and Noonan S.

Features highly suggestive of NS (2 or more)

1. Dysmorphic facial features
2. Heart defect
3. Short stature
4. Chest deformity
5. First-degree relative who has NS or any of the above features
6. Developmental delay/learning issues
7. Cryptorchidism
8. Lymphatic dysplasia
9. Delayed puberty



Other potential features

Thick curly or sparse thin hair

Vision/eye problems

Dental/oral issues

Feeding issues

Failure to thrive

Kidney problems

Lymphoedema

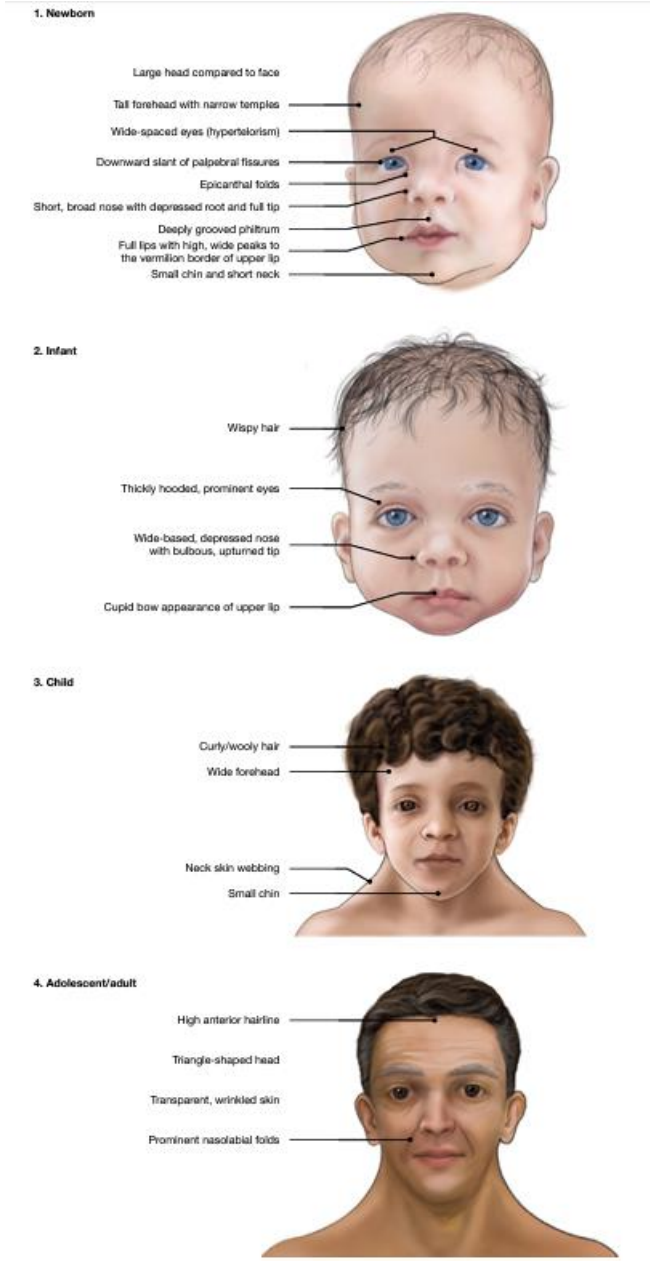
Bleeding/clotting problems

Skin conditions

Behavioural issues

Speech disorders

Hearing problems



<u>Cardiac Abnormalities</u>

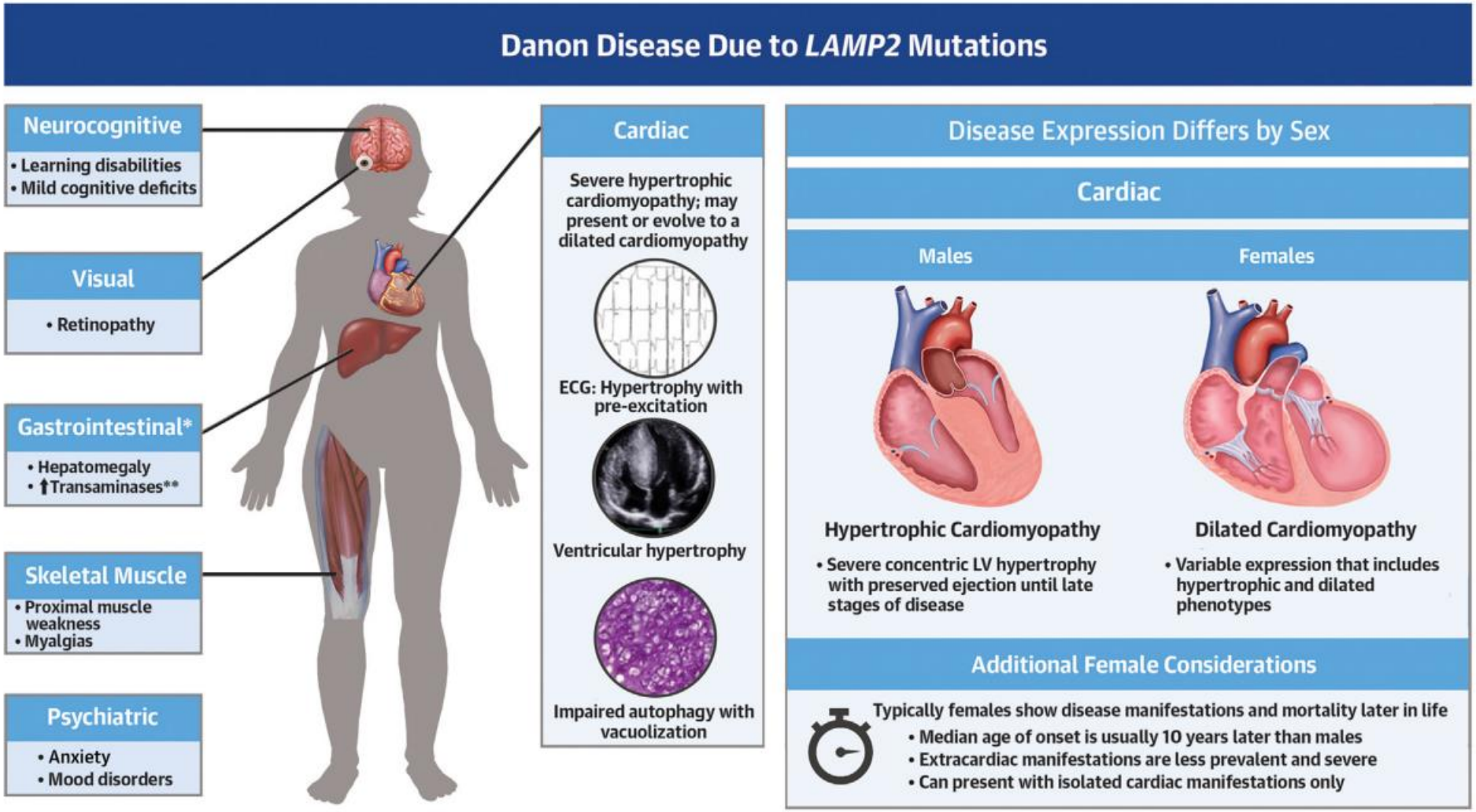
Pulmonary Valve Stenosis

ASD

VSD / HCM

PDA

Hypertrophic Cardiomyopathy and Danon S.



Hong KN, et al. J Am Coll Cardiol. 2023;82(16):1628-1647.

Hypertrophic Cardiomyopathy and Fabry-Anderson

Table 1 Anderson Fabry disease main features
X-linked lysosomal storage disease - glycosphingolipidosis (Xq22 locus, deficiency of α-galactosidase A)
Stored substance • Mainly globotriaosylceramide - Gb_3 • Deacylated form - lyso-Gb_3 or globotriaosylsphingosine - potentially toxic, causing secondary damage and representing one of the biomarkers of the disease severity
Clinical phenotypical presentations • Classical multisystemic disease - early onset of symptoms within first two decades of life • Late-onset variants - predominantly cardiac, manifesting after the 3rd decade of life
Prevalence and incidence • Classical forms 1:30-40 000 in males (raw estimate from the rate between classical and late-onset variants detected by neonatal screenings) • Late-onset forms (based on neonatal screenings) 1: 1 250 - 1: 7 800 males
Prevalence among patients with unexplained LVH or diagnosed as hypertrophic cardiomyopathy ~ 1%
Factors influencing disease severity • Mutation type (classical forms associated with truncating mutations and absent residual enzyme activity, late-onset forms usually due to missense mutations and preserved residual enzyme activity) • Gender - hemizygous males are affected earlier and having more severe disease than heterozygous females • Random vs. skewed X-chromosome inactivation in females • Age - the disease is progressive with severe organ damage manifesting in adult patients, life expectancy is reduced particularly in untreated males

Table 3 Main cardiac manifestations	
Cardiac hypertrophy	
• Mostly diffuse, in some cases may be asymmetrical mimicking obstructive hypertrophic cardiomyopathy • LVOT obstruction may be present both at rest and provoked by exercise (less frequent than in sarcomeric HCM)	• Papillary muscle hypertrophy • Right ventricular hypertrophy • Posterolateral mid-myocardial fibrosis development, wall thinning and akinesia
Cardiac function	
• EF preserved, scar and hypo/akinesia may develop within posterolateral basal segment • Global longitudinal strain is reduced, postsystolic shortening detectable in cases with basal fibrosis	• Mild-to-moderate diastolic dysfunction, restrictive filling only in very advanced stages, diastolic dysfunction is the main cause of heart failure symptoms • Right ventricular function usually preserved
Arrhythmias	
• Short PR interval without preexcitation • Conduction abnormalities, AV block, bundle branch blocks • Bradycardia, chronotropic incompetence	• Atrial fibrillation • Ventricular arrhythmias with an increased risk of sudden cardiac death
Valvular changes	
• Mitral and aortic valve thickening, mild-to moderate regurgitations (does not predispose to development of any valvular stenotic lesions)	• Mitral valve prolapse / mitral valve systolic restriction in cases with extensive posterolateral fibrosis • Mild-to-moderate aortic dilatation, aortic dissection risk not reported
Vascular changes	
• Carotid and radial intima-media thickening. coronary wall thickening	• Microvascular dysfunction, reduction of coronary flow reserve

Hypertrophic Cardiomyopathy and Fabry-Anderson

Table 1 Extracardiac manifestations of Anderson Fabry disease
Neurological • Peripheral neuropathy – pain within extremities, painful (febrile crises) • Autonomous nervous dysfunction • Premature stroke (mostly ischemic, intracerebral bleeding risk is also increased) • White matter lesions, pulvinar sign, tortuous vertebral and basilar arteries • Tinnitus, hearing loss, vertigo
Gastrointestinal • Diarrhea / constipation, abdominal pain, irritable-bowel syndrome-like manifestations • Normal endoscopy findings, w/o bleeding risk
Skin • Angiokeratomas • Hypo / anhidrosis (in some cases hyperhidrosis) • Lymphoedema, periorbital oedema, coarse facial features
Kidney • Albuminuria – proteinuria • Glomerular filtration decline, end-stage kidney disease
Eye • Cornea verticillata • Fabry cataract • Tortuous conjunctival and retinal vessels
Other non-specific findings • Mild anemia • Osteoporosis • General fatigue, weakness, reduced exercise capacity • Depression

Hypertrophic Cardiomyopathy and Investigations

Level	HCM
First	• CK • Liver function • NT-proBNP[a] • Proteinuria • Renal function • Troponin
Second	• Alpha-galactosidase A levels (males) and lyso-Gb3 • Carnitine profile • Free fatty acids • Immunofixation and free light chains • Lactic acid • Myoglobinuria • Pyruvate • PTH • Urine and plasma protein • Urine organic acids and plasma amino acids

Mitochondrial disease

Hypertrophic Cardiomyopathy and Treatment

Treatment in HCM : improve functional capacity and reduce symptoms

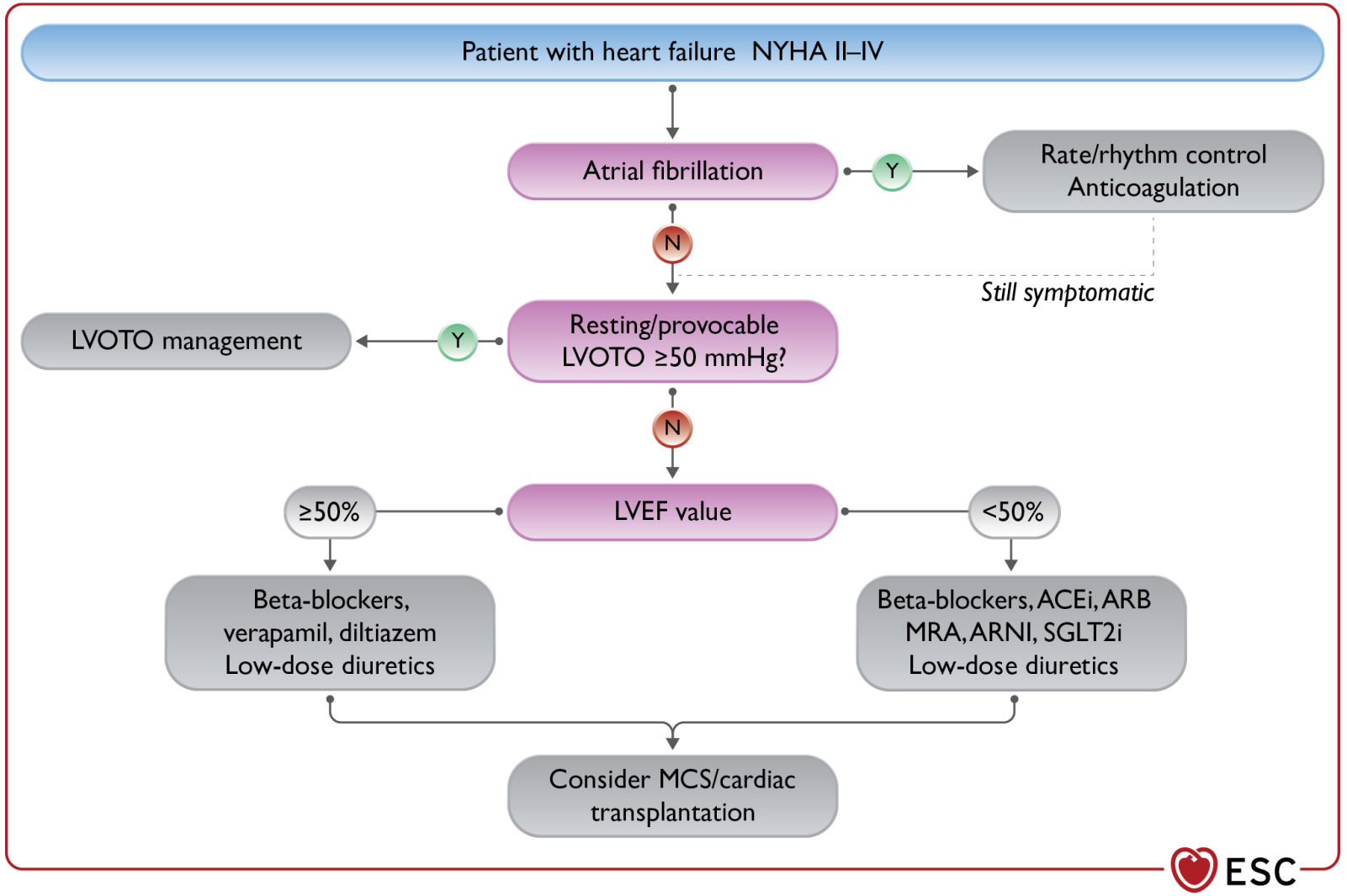
Treatment in Symptomatic Patient with LVOT : (drugs, surgery, ASA): improve symptoms

Treatment in Symptomatic Patient without LVOT: management of arrhythmias, reduction of LV filling pressures and treatment of angina

Candidates for LVAD Bridge to Tx / Transplantation

Figure 13

Algorithm for the treatment of heart failure in hypertrophic cardiomyopathy



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Hypertrophic Cardiomyopathy and Treatment

Recommendation Table 9 — Recommendations for cardiac transplantation in patients with cardiomyopathy

Recommendations	Class[a]	Level[b]
Orthotopic cardiac transplantation is recommended for eligible cardiomyopathy patients with advanced heart failure (NYHA class III–IV) or intractable ventricular arrhythmia refractory to medical/invasive/device therapy, and who do not have absolute contraindications.[317–319]	I	C

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Recommendation Table 10 — Recommendation for left ventricular assist device therapy in patients with cardiomyopathy

Recommendation	Class[a]	Level[b]
Mechanical circulatory support therapy should be considered in selected cardiomyopathy patients with advanced heart failure (NYHA class III–IV) despite optimal pharmacological and device treatment, who are otherwise suitable for heart transplantation, to improve symptoms and reduce the risk of heart failure hospitalization from worsening heart failure and premature death while awaiting a transplant.[320–324]	IIa	B
Mechanical circulatory support therapy should be considered in selected cardiomyopathy patients with advanced heart failure (NYHA class III–IV) despite optimal pharmacological and device therapy, who are not eligible for cardiac transplantation or other surgical options, and without severe right ventricular dysfunction, to reduce the risk of death and improve symptoms.[321,325–330]	IIa	B

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Hypertrophic Cardiomyopathy and Treatment

Condition	AF epidemiology		AF management			
	Prevalence	Annual incidence	Anticoagulation	Long-term rate control	Long-term rhythm control	
HCM	17–39%[331–334,365,413,421–428]	2.8–4.8%[332,333,365]	Always (if no contraindication)[371,429]	Beta-blockers (preferred) Verapamil or diltiazem (only if preserved LVEF) Digoxin AV node ablation + CRT or physiological pacing[388–390]	Rhythm control is preferred	
					Amiodarone, dofetilide disopyramide, sotalol,[a] dronedarone[b]	Ablation[397,412,415,416,418,430–435]

Hypertrophic Cardiomyopathy and Treatment

Recommendations	Class[a]	Level[b]
Anticoagulation		
Oral anticoagulation in order to reduce the risk of stroke and thrombo-embolic events is recommended in all patients with HCM or cardiac amyloidosis and AF or atrial flutter (unless contraindicated).[332,365,369,371,373,378,413,427,428,456–464]	I	B

Irrespective of CHADs-VASC score

Hypertrophic Cardiomyopathy and Treatment

Rhythm Control > Rate Control

Catheter Ablation (Rhythm Control)

- Symptoms not controlled AAD I/III
- Tachy-myocardiopathy
- Early-Stage w/o major risk factors
- Preferred over AAD I/III due to complications or contra-indications (prolonged QTc)
- And Heart Failure for LVEF or QoL improvement, and improve prognosis

Control of symptoms and heart failure		
Atrial fibrillation catheter ablation is recommended for rhythm control after one failed or intolerant class I or III AAD to improve symptoms of AF recurrences in patients with paroxysmal or persistent AF and cardiomyopathy.[335,397–399,412,415–420,430–435,447,451,473–498]	I	B
Atrial fibrillation catheter ablation is recommended to reverse LV dysfunction in AF patients with cardiomyopathy when tachycardia-induced component is highly probable, independent of their symptom status.[405,407,408,499–501]	I	B
Maintenance of sinus rhythm rather than rate control should be considered at an early stage for patients with a cardiomyopathy and AF without major risk factors for recurrence, regardless of symptoms.[402]	IIa	C
Atrial fibrillation catheter ablation should be considered as first-line rhythm control therapy to improve symptoms in selected patients with cardiomyopathy and paroxysmal or persistent AF without major risk factors for recurrences as an alternative to class I or III AADs, considering patient choice, benefit, and risk.[392,393,480,502–506]	IIa	C
Atrial fibrillation catheter ablation should be considered in selected patients with cardiomyopathy, AF, and heart failure and/or reduced LVEF to prevent AF recurrences and improve QoL, LVEF, and survival and reduce heart failure hospitalization.[399–401,403–408,499–501,507]	IIa	B

Hypertrophic Cardiomyopathy and Treatment

Rate Control

- ❑ Beta blockers > Digoxin (esp. in CM and HF not with LVOT)
- ❑ CCBs (in LV EF > 40%)
- ❑ AV ablation and PM (CRT)
  - Symptomatic persistent AF (>6 months) unsuitable for AF ablation
  - In which AF ablation had failed
  - Narrow QRS
  - At least one admission for heart failure
  - Not for PM (HBP)

Hypertrophic Cardiomyopathy and Treatment

Rhythm Control

- ❑ Catheter ablation > AADs
- ❑ AADs have shown
  - limited success in maintaining SR
  - high rates of withdrawal due to intolerance,
  - are associated with significant side effects, including pro-arrhythmia and extracardiac side effects
  - in some cases (sotalol and class IA drugs, such as quinidine and disopyramide), increased mortality
- ❑ Class III (amiodarone / sotalol) > I
  - Sotalol not in HFrEF, LVH, prolonged QT, asthma, hypokalaemia, or creatinine clearance (CrCl) <30 ml/min
  - Dronedarone not in HFrEF

Hypertrophic Cardiomyopathy w/o LVOT and Treatment

Should follow HFrEF / HFpEF drug treatment

The aim of drug therapy is to reduce **LV diastolic pressures and improve LV filling** by slowing the heart rate with beta-blockers, verapamil, or diltiazem (ideally monitored by ambulatory ECG recording), and cautious use of loop diuretics

Beta-blockers or calcium antagonists should be considered in patients with exertional or prolonged episodes of **angina- like pain** even in the absence of resting or provocable LVOTO or obstructive CAD.

In the absence of LVOTO, cautious use of **oral nitrates** may be considered.

Ranolazine may also be considered to improve symptoms in patients with angina-like chest pain and no evidence for LVOTO.

Recommendations for chest pain on exertion in patients without left ventricular outflow tract obstruction

Recommendations	Class	Level
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.	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.	IIb	C

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Hypertrophic Cardiomyopathy w/o LVOT and Treatment

CRT

While acknowledging this as an area of unmet research need, the Task Force suggests a more pragmatic approach in which CRT might be considered in individual symptomatic patients **with LV impairment (LVEF <50%)** that meet current ESC ECG criteria (LBBB, QRS 130– 149 ms)

Cardiac resynchronization therapy might also be considered in patients with HCM and impaired systolic function **who require permanent ventricular pacing**

Hypertrophic Cardiomyopathy w LVOT and Treatment

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

- Most patients with a maximum resting or provoked LV outflow tract gradient <50 mmHg should be managed in accordance with the recommendations **for non-obstructive HCM**

- Between 30 and 50 mmHg and no other obvious cause of symptoms, invasive gradient reduction may be considered

Recommendations for treatment of left ventricular outflow tract obstruction (general measures)

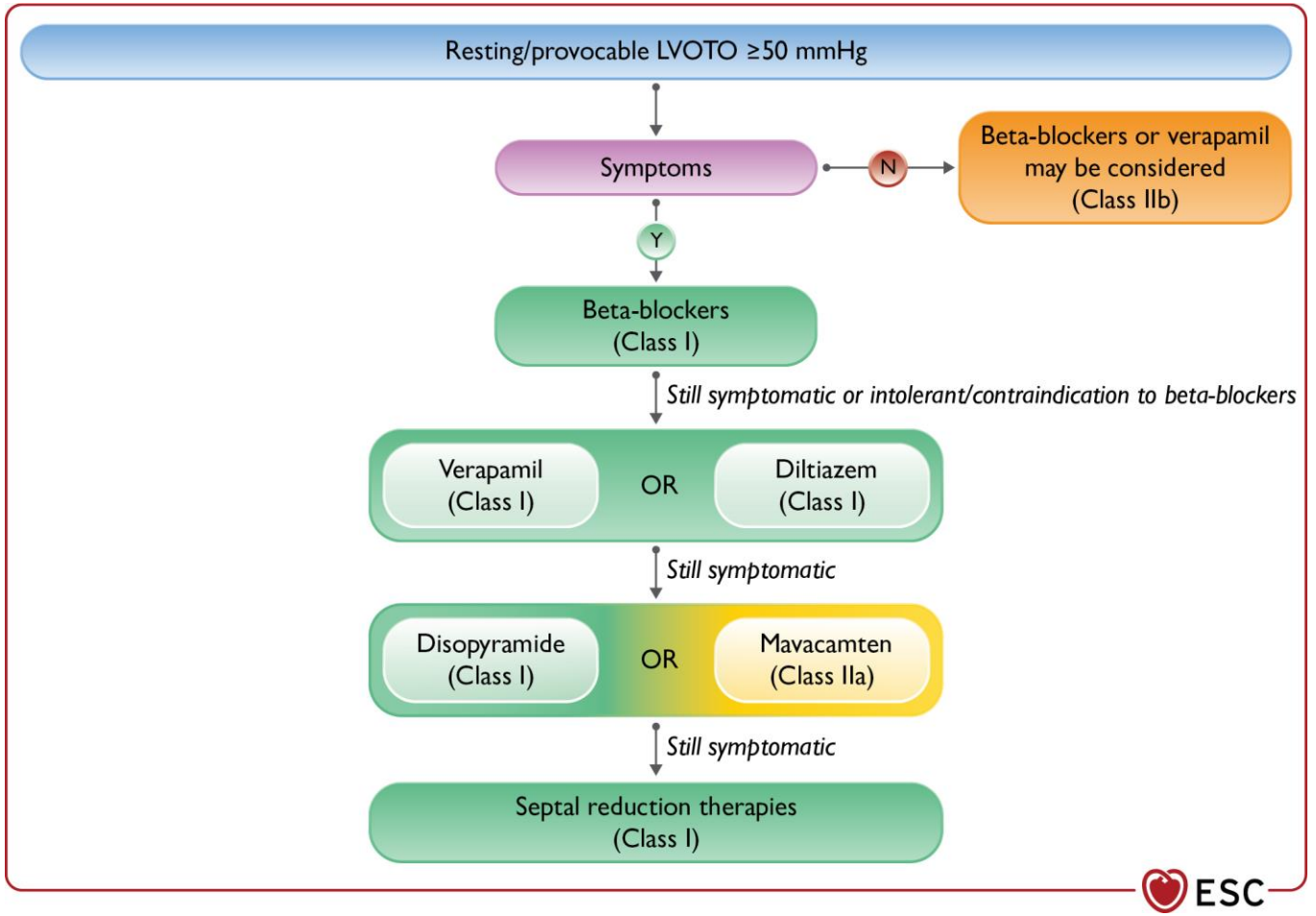
Recommendation	Class	Level
Avoidance of digoxin and arterial and venous dilators, including nitrates and phosphodiesterase inhibitors, should be considered, if possible, in patients with resting or provocable LVOTO.	IIa	C
Restoration of sinus rhythm or appropriate rate control should be considered before invasive management of LVOTO in patients with new-onset or poorly controlled AF.	IIa	C

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Figure 14

Flowchart on the management of left ventricular outflow tract obstruction



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Hypertrophic Cardiomyopathy w LVOT and Treatment

Beta Blockers (non-vasodilating) > CCBs (verapamil / diltiazem) or Disopyramide > Diuretics

Disopyramide (AAD IA)
- Anticholinergic side effects
- QTc prolonging
- Not in glaucoma, prostate hyperplasia, other QTc prolonging drugs

Calcium Channel Blockers
- not in severe LVOT (>100mmHg)
- not in increased sPAP

Diuretics
- avoid hypovolemia

Cardiac Myosin ATP inhibitors (Mavacamten)
- only as a second line therapy with LV EF echo surveillance
- only in symptomatic LVOT obstruction
- not with disopyramide

Recommendations for medical treatment of left ventricular outflow tract obstruction (1)

Recommendations	Class	Level
Non-vasodilating beta-blockers, titrated to maximum tolerated dose, are recommended as first-line therapy to improve symptoms in patients with resting or provoked LVOTO.	I	B
Verapamil or diltiazem, titrated to maximum tolerated dose, are recommended to improve symptoms in symptomatic patients with resting or provoked LVOTO who are intolerant or have contraindications to beta-blockers.	I	B
Disopyramide, 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 LVOTO.	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 LVOTO.	IIa	A

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Recommendations for medical treatment of left ventricular outflow tract obstruction (2)

Recommendations	Class	Level
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 LVOTO (exercise or Valsalva manoeuvre) who are intolerant or have contraindications to beta-blockers, verapamil/diltiazem, or disopyramide.	IIa	B
Oral or i.v. beta-blockers and vasoconstrictors should be considered in patients with severe provocable LVOTO presenting with hypotension and acute pulmonary oedema who do not respond to fluid administration.	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 LVOTO.	IIb	C

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Recommendations for medical treatment of left ventricular outflow tract obstruction (3)

Recommendations	Class	Level
Beta-blockers or verapamil may be considered in selected cases in *asymptomatic* patients with resting or provoked LVOTO to reduce LV pressures.	IIb	C
The cautious use of low-dose diuretics may be considered in symptomatic LVOTO to improve exertional dyspnoea.	IIb	C

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Hypertrophic Cardiomyopathy w LVOT and Treatment

Invasive Treatment

Not in asymptomatic patients

Indications

In patients

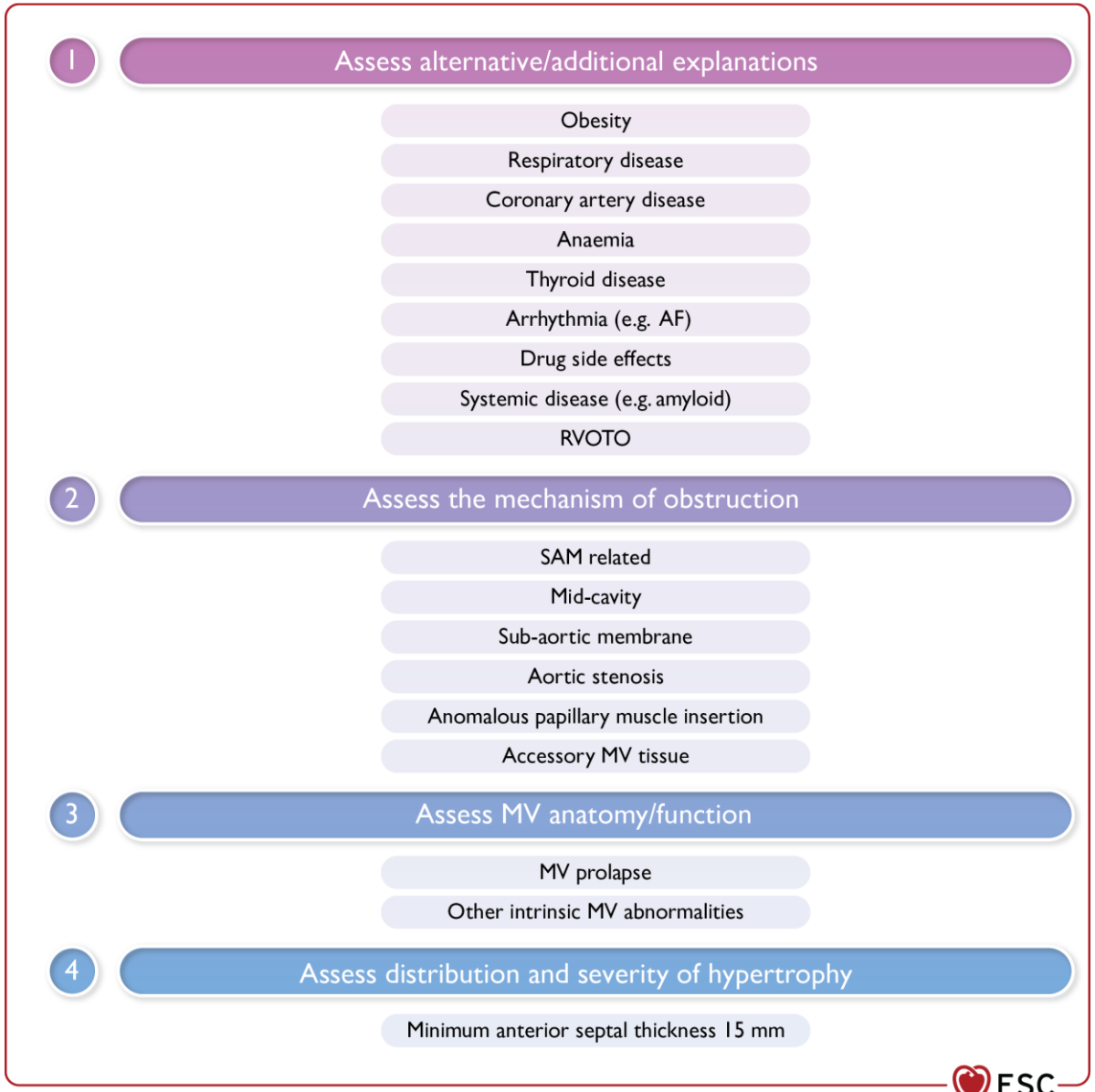
- with a LVOTO gradient ≥50 mmHg,
- severe symptoms (NYHA functional class III–IV),
- and/or exertional or unexplained recurrent syncope

in spite of maximally tolerated drug therapy

Invasive therapy *may also be considered* in patients with mild symptoms (NYHA class II) refractory to medical therapy who have a resting or maximum provoked gradient of ≥50 mmHg (exercise or Valsalva) and moderate-to-severe systolic anterior motion-related mitral regurgitation, AF, or moderate-to-severe left atrial dilatation

Figure 15

Pre-assessment checklist for patients being considered for invasive septal reduction therapies



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Hypertrophic Cardiomyopathy w LVOT and Treatment

Invasive Treatment

Surgery

- Success rate >80%
- **Good predictors :** age < 50 years, LAD < 46mm, absence of AF, male sex
- **Complications :** AV nodal block, LBBB, VSD, AR
- When primary MV disease exists or moderate to severe MR → MV repair / replacement

Alcohol Septal Ablation

- Complications : AV block
- Larger residual gradients
- Repeat procedures 7-20%
- Poor results if LVH > 30mm

Recommendations for septal reduction therapy (1)

Recommendations	Class	Level
It is recommended that SRT be performed by experienced operators working as part of a multidisciplinary team expert in the management of HCM.	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.	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).	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.	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.	IIa	C

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Recommendations for septal reduction therapy (2)

Recommendations	Class	Level
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 gradient of ≥50 mmHg (exercise or Valsalva) and: • moderate-to-severe SAM-related mitral regurgitation; or • AF; or • moderate-to-severe left atrial dilatation.	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.	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.	IIb	C

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Recommendations for 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 beta-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 contraindications for ASA or septal myectomy or are at high risk of developing heart block following ASA 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 beta-blockers and/or verapamil.	IIb	C

Last resort for symptom control or if another implantation is warranted (CRT or ICD)

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Major clinical features associated with an increased risk of sudden cardiac death (1)

Risk factor	Comment
Age	• The effect of age on SCD has been examined in a number of studies and two have shown a significant association, with an increased risk of SCD in younger patients. • Some risk factors appear to be more important in younger patients, most notably NSVT, severe LVH, and unexplained syncope. • Sudden cardiac death is very rare below the age of 6 years, and there are some data to suggest a peak of SCD in childhood HCM between 9 and 15 years; however, the association between age at diagnosis and SCD risk in childhood HCM remains unclear.

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Major clinical features associated with an increased risk of sudden cardiac death (2)

Risk factor	Comment
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. • There is no evidence that the frequency, duration, or rate of NSVT influences the risk of SCD. • NSVT occurring during or immediately following exercise is very rare, but may be associated with a high risk of SCD.
Maximum LV wall thickness	• The severity and extent of LVH measured by TTE are associated with the risk of SCD. • 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).

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Major clinical features associated with an increased risk of sudden cardiac death (3)

Risk factor	Comment
Family history of sudden cardiac death at a young age	• While definitions vary, 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. This may be due to a higher prevalence of de novo 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. • Non-neurocardiogenic syncope for which there is no explanation after investigation is associated with an increased risk of SCD. • Episodes within 6 months of evaluation may be more predictive of SCD.

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Major clinical features associated with an increased risk of sudden cardiac death (4)

Risk factor	Comment
Left atrial diameter	• Several studies have reported a positive association between LA size and SCD. There are no data on the association between SCD and LA area and volume. Measurement of LA size is also important in assessing the risk of AF.
LV outflow tract obstruction	• A number of studies have reported a significant association between LVOTO and SCD risk. Several unanswered questions remain, including the prognostic importance of provocable 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.

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Additional recommendations for prevention of sudden cardiac death in patients with hypertrophic cardiomyopathy (1)

Recommendations	Class	Level
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.	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.	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.	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.	I	B

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Additional recommendations for prevention of sudden cardiac death in patients with hypertrophic cardiomyopathy (2)

Recommendations	Class	Level
Primary prevention (continued)		
Implantation of an ICD should be considered in patients with an estimated 5-year risk of sudden death of ≥6%, following detailed clinical assessment that considers: (i) the lifelong risk of complications; (ii) competing mortality risk from the disease and comorbidities; AND (i) the impact of an ICD on lifestyle, socio-economic status, and psychological health.	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.	IIa	B

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Additional recommendations for prevention of sudden cardiac death in patients with hypertrophic cardiomyopathy (3)

Recommendations	Class	Level
Primary prevention (continued)		
Implantation of an ICD may be considered in individual patients with an estimated 5-year risk of SCD of between ≥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.	IIb	B
For patients who are in the low-risk category (<4% estimated 5-year risk of SCD), the presence of extensive LGE (≥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).	IIb	B

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Additional recommendations for prevention of sudden cardiac death in patients with hypertrophic cardiomyopathy (4)

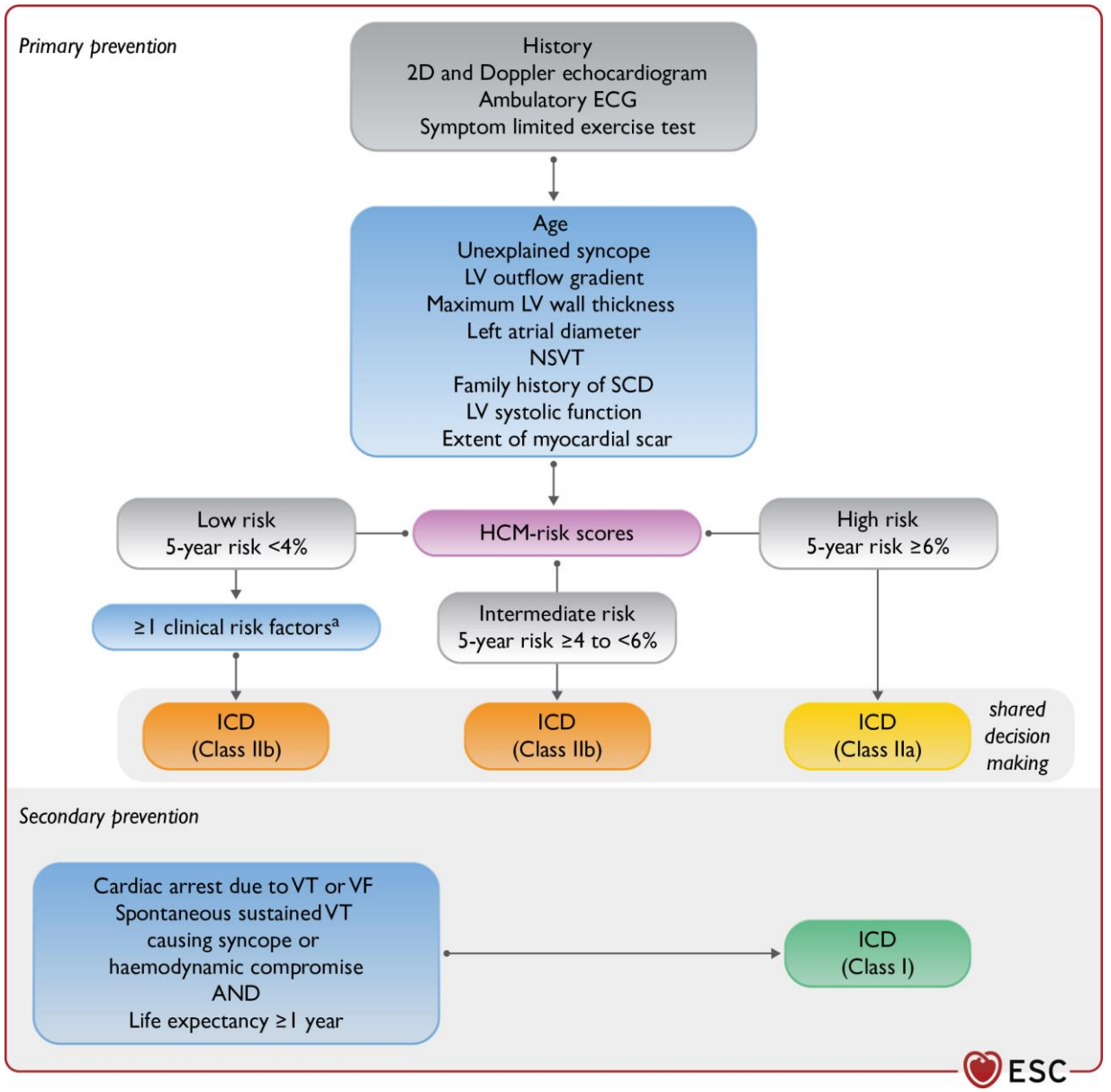
Recommendations	Class	Level
Primary prevention (continued)		
For patients who are in the low-risk category (<4% estimated 5-year risk of SCD), the presence of LVEF <50% may be considered in shared decision-making with patients about prophylactic ICD implantation, acknowledging the lack of robust data 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).	**IIb**	**B**

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Figure 16

Flow chart for implantation of an implantable cardioverter defibrillator in patients with hypertrophic cardiomyopathy



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