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2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy: web addenda

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

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Web addenda

Web Table 1: Summary of studies reporting prevalence and incidence of hypertrophic cardiomyopathy

First author (year)	Study design	HCM prevalence % or Incidence/100 000	Mean age at diagnosis (years)	Males (%)
Hada *et al* 1987[3]	Echocardiography after screening/clinical evaluation	0.17%	47	91%
Codd *et al* 1989[4]	Registry study	0.02%	59	60%
Maron *et al* 1995[5]	Population screened by echocardiography	0.17%	30	71%
Corrado *et al* 1998[6]	Echocardiography after screening/clinical evaluation	0.07%	20	91%
Maron *et al* 1999[7]	Echocardiography after screening/clinical evaluation	0.19%[a]	57[a]	51%[a]
Nistri *et al* 2003[8]	Echocardiography after screening/clinical evaluation	0.05%	19	Only males were studied
Zou *et al* 2004[9]	Population screened by echocardiography	0.16%	52	69%
Maron *et al* 2004[10]	Population screened by echocardiography	0.23%	64	50%
Maro *et al* 2006[11]	Echocardiography after screening/clinical evaluation	0.19%	55	68%
Ng *et al* 2011[12]	Echocardiography after screening/clinical evaluation	0.005%	19.5	Only males were studied
Lipshultz *et al* 2003[13]	Registry study	0.47/100 000	5.9	N/A
Nugent *et al* 2005[14]	Registry study	0.32/100 000	0.47	69

[a]Refers only to patients with *de novo* diagnosis.
N/A = not available.

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

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

Web Table 3: Other non-sarcomeric genetic disorders and syndromes associated with hypertrophic cardiomyopathy[21]

Disease	Gene	Inheritance	Clinical features
Disorders of carbohydrate metabolism			
Glycogen storage diseases			
Type II (Pompe)	GAA	AR	Hypotonia, failure to thrive
Type III (Cori or Forbes disease)	AGL	AR	Hypoglycaemia, failure to thrive, hepatomegaly
Type IX (cardiac phosphorylase kinase deficiency)	PHKA1	AR, X-linked	Hepatomegaly, growth retardation
Congenital disorder of glycosylation type 1a	PMM2	AR	Neurodevelopmental delay
Disorders of amino acid metabolism			
Type I tyrosinaemia	FAH	AR	Failure to thrive
Dihydrolipoamide dehydrogenase deficiency	DLD	AR	Maple syrup urine disease
Disorders of fatty acid metabolism			
Very long chain acyl Co-A dehydrogenase deficiency (VLCAD)	ACADVL	AR	Fatigue, muscle weakness, hepatomegaly, metabolic crisis
Malonyl-CoA decarboxylase deficiency	MLYCD	AR	Hypotonia, developmental delay, hypoglycaemia
Systemic primary carnitine deficiency	SLC22A5	AR	Variable – metabolic or cardiac presentation
Lysosomal storage diseases			
Mucolipidosis type II alpha/beta	GNPTAB	AR	Short stature, skeletal abnormalities
Mucopolysaccharidosis type VII (Sly syndrome)	GUSB	AR	Macrocephaly, hepatosplenomegaly
Gangliosidosis type 1	GLB1	AR	HCM or DCM
Mitochondrial disorders			
Complex I, II, III, IV and V deficiency	mtDNA various	Maternal AR	Variable presentations
ACAD9 deficiency (complex I)	ACAD9	AR	
ATP synthase deficiency (complex V)	ATPAF2, TMEM70	AR AR	Hypotonia, hypertrophic cardiomyopathy, lactic acidosis, hyperammonemia and 3-methylglutaconic aciduria.
Cytochrome C oxidase deficiency (complex IV)	COX6B1	AR	

Disease	Gene	Inheritance	Clinical features
Mitochondrial disorders			
Combined oxidative phosphorylation deficiency (types 3, 5, 8, 9 and 10)	MTO1, AARS2, TSFM, MRPS22, MRPL3, GFM1	AR	Fatal infantile HCM
Kearns-Sayre syndrome	TMEM70		Chronic progressive external ophthalmoplegia, bilateral pigmentary retinopathy, and cardiac conduction abnormalities
Leber's hereditary optic neuropathy	mtDNA	Maternal	Acute loss of central vision
Leigh syndrome (pyruvate dehydrogenase complex deficiency)	mtDNA SURF1 PDHA1	Maternal AR X-linked	Movement disorders
Friedreich's ataxia	FXN	AR	Commonest inherited ataxia, often non-ambulatory by the mid 20s, major cause of death is heart failure. Estimated carrier frequency 1/100. Due to mutation or trinucleotide repeat expansion (GAA)
Sengers syndrome	AGK	AR	Congenital cataracts, skeletal myopathy, lactic acidosis
Pyruvate dehydrogenase lipoic acid synthetase deficiency	LIAS	AR	Neonatal encephalomyopathy, lactic acidosis
Primary coenzyme Q10 deficiency	COQ2	AR	Encephalopathy, myopathy
Cardiocutaneous syndromes or RASopathies			
LEOPARD syndrome	PTPN11 RAF1	AD	Lentigines, ECG abnormalities, ocular hypertelorism, pulmonary valve stenosis, abnormalities of genitalia in males, retardation of growth, and deafness
Noonan syndrome	PTPN11, RAF1, SOS1, KRAS, NRAS, BRAF	AD	Pulmonary stenosis, atrial septal defect, short stature, learning difficulties, pectus excavatum, impaired blood clotting, webbed neck, flat nose bridge
Costello syndrome	HRAS	AD	Foetal overgrowth, postnatal growth retardation, coarse face, loose skin, developmental delay
Cardiofaciocutaneous syndrome	KRAS, BRAF, MEK1, MEK2	AD	Overlap with Costello and Noonan syndrome
Neurofibromatosis type 1	NF1	AD	Neurofibromas, café au lait patches, high blood pressure
Lipodystrophic syndromes			
Congenital generalized lipodystrophy			
Type 1 (Berardinelli-Seip syndrome)	AGPAT2	AR	Lipoatrophy, hepatomegaly, acromegaloid features, insulin resistance, skeletal muscle hypertrophy
Type 2 (Seip syndrome)	BSCL2	AR	
Neuromuscular disorders			
Myofibrillar myopathy type 2	CRYAB	AD	Early cataracts
Myofibrillar myopathy type 1	DES	AD/AR	HCM, DCM or RCM. Initially distal, then proximal muscle weakness. Onset in 2nd or 3rd decade
Myopathy, X-linked, with postural muscle atrophy or Emery Dreifuss muscular dystrophy 6	FHL1	X-linked recessive	Progressive muscular dystrophy with onset in adulthood. Patients may show muscle hypertrophy in the early stages of the disorder
Nemaline myopathy 3	ACTA1	AD	Skeletal myopathy of variable age of onset and severity. Also DCM
Amyloidosis			
Transthyretin-related amyloidosis	TTR	AD	Variable neurological and organ involvement related to TTR mutation and geographic area

AD = autosomal dominant; AR = autosomal recessive; CK = creatine kinase; DCM = dilated cardiomyopathy; ECG = electrocardiogram; HCM = hypertrophic cardiomyopathy; RCM = restrictive cardiomyopathy; WPW = Wolff-Parkinson-White syndrome.

Web Table 4: Prognostic significance of delayed contrast enhancement by cardiovascular magnetic resonance in hypertrophic cardiomyopathy

Study	Population - *n* - Mean age - LGE prevalence - Risk profile	LGE Quantification method	Outcome/s (mean FU duration)	Other classical RF considered	Conclusion	Comments
Prinz *et al* 2013[138]	- n = 87 - 50 years - 90% (30% with severe LGE) - High risk[a] cohort about to undergo implantation of ICD (1° or 2° SCD prophylaxis)	Semi-quantitative visual scoring	1) VF/sustained VT (3.5 years after CMR)	1) Cardiac arrest 2) VT 3) MWT ≥30 mm 4) Syncope 5) Abnormal BP response to exercise 6) Rest LVOTO	In subjects at high risk of SCD, severe LGE associates with arrhythmic events	MVA to test for independent association of LGE with malignant arrhythmic events
Bruder *et al* 2010[139]	- n = 243 - 58 years - 67% - Low risk/ asymptomatic[b] cohort by echocardiography presenting to Essen and Stuttgart for work-up	Automated counting of pixels >2 SD of nulled myocardium	1) All-cause mortality 2) Any cardiac death 3) SCD only (3 years after CMR)	1) Cardiac arrest 2) VT 3) MWT ≥30 mm 4) FH of SCD 5) Syncope 6) Rest LVOT gradient >30mmHg	LGE is an independent predictor of cardiac mortality	Underpowered for an MVA of LGE and SCD MVA done for independent association of LGE with cardiac mortality outcome only
O'Hanlon *et al* 2010[140]	- n = 217 - 52 years - 63% - Intermediate risk[c] cohort referred for CMR at Royal Brompton Hospital	Automated FWHM quantitation	Primary composite 1) CV death/ unplanned CV hospitalization/ VT or VF/ ICD discharge Secondary composites 1) HF 2) Arrhythmia (3.1 years post CMR)	As above	LGE is an independent predictor of major cardiovascular events, hospital stay and heart failure but not of arrhythmic outcomes NSVT only classical RF shown to have independent predictive ability (and only with the secondary arrhythmic outcome)	Underpowered to show predictive ability of LGE for CV death A large part of the difference in 1° outcome between LGE+/− is driven by differences in HF admissions
Rubinshtein *et al* 2010[141]	- n = 424 - 55 years - 56% - HCM patients who underwent CMR at Mayo Clinic (Incomplete data on classical RF; cannot define risk profile of study participants)	Manual tracing	1) SD or ICD therapy (3.6 years post CMR)	1) NSVT 2) MWT ≥30 mm 3) FH of SCD 4) Syncope	LGE is associated with SCD/ICD therapies	MVA for LGE association with outcomes not possible due to low event rates (serial bivariate analysis instead)
Adabag *et al* 2008[142]	- n = 177 - 41 years - 41% - HCM patients in the Minneapolis Heart Institute Foundation and Tufts Medical Centre (Incomplete data on classical RF; cannot define risk profile of study participants)	Automated counting of pixels ≥6 SD of myocardial mean	1) NSVT	1) MWT ≥30 mm 2) Syncope 3) Rest LVOT gradient >30 mmHg	LGE is an independent predictor for NSVT (>7 fold increased relative risk)	MVA performed
Maron *et al* 2008[143]	- n = 202 - 42 years - 55% - HCM patients presenting to Tufts Medical Center and Minneapolis Heart Institute Foundation (Incomplete data on classical RF; cannot define risk profile of study participants)	Automated counting of pixels ≥6 SD of myocardial mean	1) Composite: SD, ICD discharge + NYHA ≥1 (1.8 years post CMR)	1) MWT ≥30 mm 2) Rest LVOT gradient >30 mmHg	LGE not significantly associated with adverse outcomes	MVA not performed due to low incidence of events resulting from shortest FU duration

BP = blood pressure; CMR = cardiovascular magnetic resonance; CV = cardiovascular; FU = follow-up; FWHM = full width half maximum; HCM = hypertrophic cardiomyopathy; HF = heart failure; ICD = implantable cardioverter defibrillator; LGE = late gadolinium enhancement; LVOTO = left ventricular outflow tract obstruction; MVA = multivariable analysis; MWT = maximal wall thickness; NSVT = non-sustained ventricular tachycardia; NYHA = New York Heart Association functional class; PI = primary investigator; RF = risk factor; SD = standard deviation; SCD = sudden cardiac death; VF = ventricular fibrillation; VT = ventricular tachycardia.

[a]High risk due to presence of ≥2 RF (or 'malignant' family history).

[b]Low risk as >75% of patients did not have any recognized clinical RF for SCD; 1 RF in n= 43 (19.5%); 2 RF in n= 7; 3 RF in n= 3.

[c]Intermediate risk as 31.8% had 1 RF and 15.2% ≥2 RF.

Web Table 5: HCM Risk-SCD model: predictor variables for sudden cardiac death

Predictor Variable	Coding
Age at evaluation.	Continuous, years
History of sudden cardiac death in one or more first degree relatives under 40 years of age or SCD in a first degree relative with confirmed HCM at any age (post or ante-mortem diagnosis).	Binary (yes = 1/no = 0)
Maximal wall thickness: the greatest thickness in the anterior septum, posterior septum, lateral wall, and posterior wall of the LV, measured at the level of the mitral valve, papillary muscles and apex using parasternal short-axis plane using 2D echocardiography.	Continuous, mm
Left atrial diameter determined by M-Mode or 2D echocardiography in the parasternal long axis plane.	Continuous, mm
The maximum LV outflow gradient determined at rest and with Valsalva provocation (irrespective of concurrent medical treatment) using pulsed and continuous wave Doppler from the apical three and five chamber views. Peak outflow tract gradients were determined using the modified Bernouilli equation: Gradient= $4V^2$, where V is the peak aortic outflow velocity.	Continuous, mm Hg
NSVT: ≥3 consecutive ventricular beats at a rate of ≥120 beats per minute and <30s in duration on Holter monitoring (minimum duration 24 hours) at or prior to evaluation.	Binary (yes = 1/no = 0)
History of unexplained syncope at or prior to evaluation.	Binary (yes = 1/no = 0)

Web Table 6: Drugs during pregnancy and breastfeeding[427]

Drug	FDA category	Placenta permeable	Transfer to breast milk	Breastfeeding	Details
Antiplatelet and anticoagulants					
Abciximab	C	Unknown	Unknown	Not advised	No studies in humans. Use only on strict indication
Acenocoumarol, phenprocoumon, warfarin	X/D	Yes	Minimal	Foetal clotting time unchanged, no adverse effects	Embryopathy (first trimester) Intracranial bleeding throughout pregnancy. Use during first trimester contraindicated (except in mechanical valves). Vaginal delivery contraindicated
Acetylsalicylic acid	B	Yes	Yes (low dose)	No adverse effects (low dose)	Safe in dose up to 100 mg daily >100 mg: do not use in third trimester: risk of duct closure, inhibition of contractions
Clopidogrel	B	Unknown	Unknown	Not advised	Animal data: no foetal toxicity, no human data available. Do not use
Dabigatran	C	Probably	Unknown	Not advised	In animals toxic effects with high maternal dose; in humans unknown
Fondaparinux	B	Probably not	Probably in low dose	Limited data: preferably do not use during breastfeeding	Animal studies: no harm. Limited data in humans
Low molecular weight heparins	B	No	No	No adverse effects	Maternal effects with long term use: osteoporosis (rare), thrombocytopenia (less than unfractionated heparin)
Rivaroxaban	C	Yes	Yes (animals)	Not advised	In animals embryopathy; in humans no data
Unfractionated heparin	B	No	No	No adverse effects	Long term use: thrombocytopenia, osteoporosis
Antiarrhythmic drugs					
Adenosine	C	No	Unknown	Because of limited data do not use	Probably not toxic to the foetus, but only use on strict indication because human data are limited
Amiodarone	D	Yes	Yes	High dose in breast milk, do not use	Toxic for the foetus: hypothyroidism, hyperthyroidism, growth retardation, psychomotor retardation, bradycardia, structural cardiac abnormalities. Only use on strict indication for otherwise refractory severe arrhythmias
Flecainide	C	Yes	Yes	Low dose in breast milk, possibly compatible with breastfeeding	Limited experience in humans. Can be used for treatment of foetal tachycardia. Animal toxicity described: use on strict indication only

Drug	FDA category	Placenta permeable	Transfer to breast milk	Breastfeeding	Details
Antiarrhythmic drugs					
Disopyramide	C	Yes	Yes	Compatible with breastfeeding, no harmful effects described	No teratogenicity. Uterine contractions have been described in case reports and a small series. Should be given only when benefit clearly outweighs risk.
Lidocaine	B	Yes	Yes	Low dose in breast milk, compatible with breastfeeding	No harm in animals, limited data in humans. No harm demonstrated, but caution is advised
Mexiletine	C	Yes	Yes	Concentrates in breast milk but probably not harmful	Limited data in humans. No teratogenic effects. Foetal bradycardia has been demonstrated
Procainamide	C	Yes	Yes	Concentrates in breast milk, but low plasma concentrations in neonate expected. Limited data, use with caution	No animal studies, limited data in humans. No teratogenic effects demonstrated. Only use when necessary.
Propafenone	C	Yes	Yes	Limited data, use with caution	Animals: with high dose embryotoxic but no teratogenic effects. Humans: limited data, no harm demonstrated in 3rd trimester. Only use when necessary
Quinidine	C	Yes	Yes	Limited data, but therapeutic serum levels in neonates expected. Preferably do not use during breastfeeding	No data regarding harm in foetuses available. However, thrombocytopenia and ototoxicity can be expected.
Sotalol	B	Yes	Yes	Relatively high doses in breast milk. Monitoring of neonate (bradycardia, hypoglycaemia, QT time) advised	No harm in animal studies. Limited data in humans. Possibly bradycardia and hypoglycaemia in foetus/ neonate
ß-Blockers					
Atenolol	D	Yes	Yes	Concentrates in breast milk. Monitor neonate for hypoglycaemia and bradycardia when used during breastfeeding	In animals, fetotoxic. In humans, low birth weight and more bradycardia than other ß-blockers. Foetal hypoglycaemia.
Bisoprolol	C	Yes	Unknown	Monitor neonate for hypoglycaemia and bradycardia	No fetotoxicity in animal studies, foetal deaths at high dose. In humans limited data. Foetal/neonatal bradycardia or hypoglycaemia expected
Labetalol	C	Yes	Yes	Low dose in breast milk. Adverse effects unlikely	In animals, no fetotoxicity. In humans low birth weight, neonatal bradycardia and hypoglycaemia may occur
Metoprolol	C	Yes	Yes	Low dose in breast milk. Adverse effects unlikely	In animals, no fetotoxicity. In humans low birth weight, neonatal bradycardia and hypoglycaemia may occur
Propranolol	C	Yes	Yes	Transfers to breast milk but adverse effects unlikely. Use with caution.	No teratogenicity. In humans low birth weight. Neonatal bradycardia, hypoglycaemia. Monitoring of neonate is advisable
Diuretics					
Bumetanide	C	Yes	Unknown	Do not use	No teratogenicity in animals. No data in humans. Possible oligohydramnion and electrolyte disbalance in foetus
Furosemide	C	Yes	Yes	Milk production may be reduced. Use with caution	Animals: toxic effects with very high doses. Humans: no proof for fetotoxicity. Oligohydramnion and electrolyte disbalance in foetus possible. Do not use for hypertension, only for heart failure
Hydrochlorothiazide	B	Yes	Yes	Low dose in breast milk, adverse effects unlikely	Animals: no foetal harm. Humans: limited data, based on retrospective studies possibly harmful
Aldosterone antagonists					
Eplerenone	B	Unknown	Yes (animals)	Effects unknown, do not use	Animal studies: no teratogenicity Humans: no data. Only use when benefit outweighs risk
Spironolactone	C	Yes	Yes	Metabolites in breast milk may be tumorogenic, do not use	In rats, antiandrogenic effects and endocrine dysfunction. Only use when no alternatives available
ACE inhibitors, angiotensin II receptor blockers					
Candesartan	D	Yes	Unknown	Do not use	Use during pregnancy contraindicated. Details, see captopril
Captopril	D	Yes	Yes	Low dose in breast milk, but breastfeeding not advised	Neonatal skull and lung hypoplasia, renal failure, anuria, foetal death, limb contractures, craniofacial deformation
Enalapril	D	Yes	Yes	Low dose in breast milk, but breastfeeding not advised	Use contraindicated, see captopril
Ramipril	D	Yes	Yes	Unknown, breastfeeding not advised	Use contraindicated, see captopril

Drug	FDA category	Placenta permeable	Transfer to breast milk	Breastfeeding	Details
Calcium channel blockers					
Diltiazem	C	Yes	Yes	Breastfeeding not advised	Animal studies: teratogenicity demonstrated. Limited data in humans. Do not use
Nifedipine	C	Yes	Yes	Low dose in breast milk. Use with caution	Animal studies: teratogenicity demonstrated. In humans limited data, no birth defects. Tocolytic. May cause hypotension and placental hypoperfusion. Use with caution
Verapamil	C	Yes	Yes	Neonatal adverse effects unlikely, but use with caution	Animal studies; no teratogenicity; fetotoxicity only with high maternal dose. Foetal bradycardia and AV block possible. Tocolytic. Use with caution.
Other					
Digoxin	C	Yes	Yes	Low dose in breast milk. Neonatal adverse effects unlikely.	Animal studies no teratogenicity. Human data limited (no controlled studies). Probably not harmful but use with caution
Methyldopa	B	Yes	Yes	Low dose in breast milk, can be used with caution	In animal studies and in humans no teratogenicity or fetotoxicity
Statins	X	Yes	Unknown	Breastfeeding not advised	Congenital abnormalities in animals. On theoretical grounds, harmful in humans. Contraindicated during pregnancy
FDA category					
Pregnancy category A	Adequate and well-controlled human studies have failed to demonstrate a risk to the foetus in the first trimester of pregnancy (and there is no evidence of risk in later trimesters)				
Pregnancy category B	Animal reproduction studies have failed to demonstrate a risk to the foetus and there are no adequate and well-controlled studies in pregnant women OR animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the foetus in any trimester				
Pregnancy category C	Animal reproduction studies have shown an adverse effect on the foetus and there are no adequate and well-controlled studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks				
Pregnancy category D	There is positive evidence of human foetal risk based on adverse reaction data from investigational or marketing experience or studies in humans, but potential benefits may warrant use of the drug in pregnant women despite potential risks				
Pregnancy category X	Studies in animals or humans have demonstrated foetal abnormalities and/or there is positive evidence of human foetal risk based on adverse reaction data from investigational or marketing experience, and the risks involved in use of the drug in pregnant women clearly outweigh potential benefits				
Pregnancy category N	FDA has not classified this drug				

ACE = angiotensin converting enzyme; AV = atrioventricular; FDA = US Food and Drug Administration.

Web Table 7: Clinical features that favour the diagnosis of hypertrophic cardiomyopathy in elite athletes with maximal left ventricular wall thickness 12–15 mm

Category	Feature	Level of evidence	References
A. Demographics			
	Family history of hypertrophic cardiomyopathy in first degree relative(s)	B	9, 460
	Female gender	B	446, 447
	Family history of sudden cardiac death in first degree relative(s) ≤40 years	C	
	Cardiovascular symptoms (unexplained syncope, disproportionate dyspnoea on exertion, chest pain, palpitations)	C	
B. ECG			
	Abnormal Q waves in at least two leads from II, III, aVF (absence of left anterior hemiblock), V1–V4, I, aVL, V5–V6	B	450–452
	Inverted T–waves in two or more leads from lead groups II, III, aVF or/and I, aVL, V5-V6	B	450–452
	Inverted T–waves V2-V4 (>16 years old)[a]	B	450–452
	Giant negative T–waves in two contiguous leads (> 5mm)	B	450–452
	Inverted T–waves in leads V2–V4 (<16 years old)	B	450–452
	Complex ventricular arrhythmias at 24 h Holter rhythm recording or >2000 PVCs/24 h	B	448, 449
C. Structural			
	Asymmetrical interventricular septal hypertrophy (septal to posterior wall thickness ≥1.5)	B	445, 446, 455, 456
	Complete SAM of mitral valve	B	445, 446, 455, 456
	Left ventricular end diastolic diameter <45 mm	B	445, 446, 455, 456
	Late gadolinium enhancement on CMR	C	
	Resting intraventricular gradient	C	
	Incomplete SAM of mitral valve	B	445, 446, 455, 456
	Left ventricular hypertrophy of the anterior septum or the posterior wall ≥12 mm	B	445, 446, 455, 456
	Left atrium >45 mm	C	
	Right ventricular hypertrophy (right ventricular subcostal thickness >5 mm)	C	
	Myocardial crypts identified with CMR	C	
D. Functional			
	Mitral inflow pattern E<A (<20 years old)	B	453, 454
	Tissue Doppler Imaging: Ea <9 cm/sec	C	
	Tissue Doppler Imaging: Sa <9 cm/sec	C	
	Increased BNP	C	
	Ea 10–13 cm/sec	C	
	Diastolic radial strain <7 cm/sec	C	
	VO2max <50ml/kg/min or <120% of predicted VO2max (uncommon in endurance athletes)	C	
	Increased left ventricular torsion	C	
E. Detraining			
	No response to detraining for 3 months	B	453, 454
F. Genetics			
	Disease causing sarcomere mutation	B	455, 456

BNP = brain natriuretic peptide; CMR = cardiac magnetic resonance imaging; ECG = electrocardiogram; PVCs = premature ventricular contractions; SAM = systolic anterior motion.

[a]Exception to T wave inversion: elevated ST-segment with an upward ('domed') convexity, followed by a negative T wave in V1–V4, is a common pattern of early repolarisation seen in adult and adolescent athletes of African-Caribbean descent and it should be considered a minor criterion for this ethnic group. However, T wave inversion in the lateral or inferolateral leads (V5–V6, I and aVL, II and aVF), regardless of ethnicity, is considered a major criterion and requires additional testing to rule out hypertrophic cardiomyopathy.[452,457,458]