2014 version

ESC Guidelines on

Hypertrophic Cardiomyopathy

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European Heart Journal
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2014 ESC Guidelines on diagnosis and management of hypertrophic cardiomyopathy

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Cardiomyopathy: Definition

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

ESC Working Group on Myocardial Pericardial Diseases (Elliott P et al. EHJ 2007)

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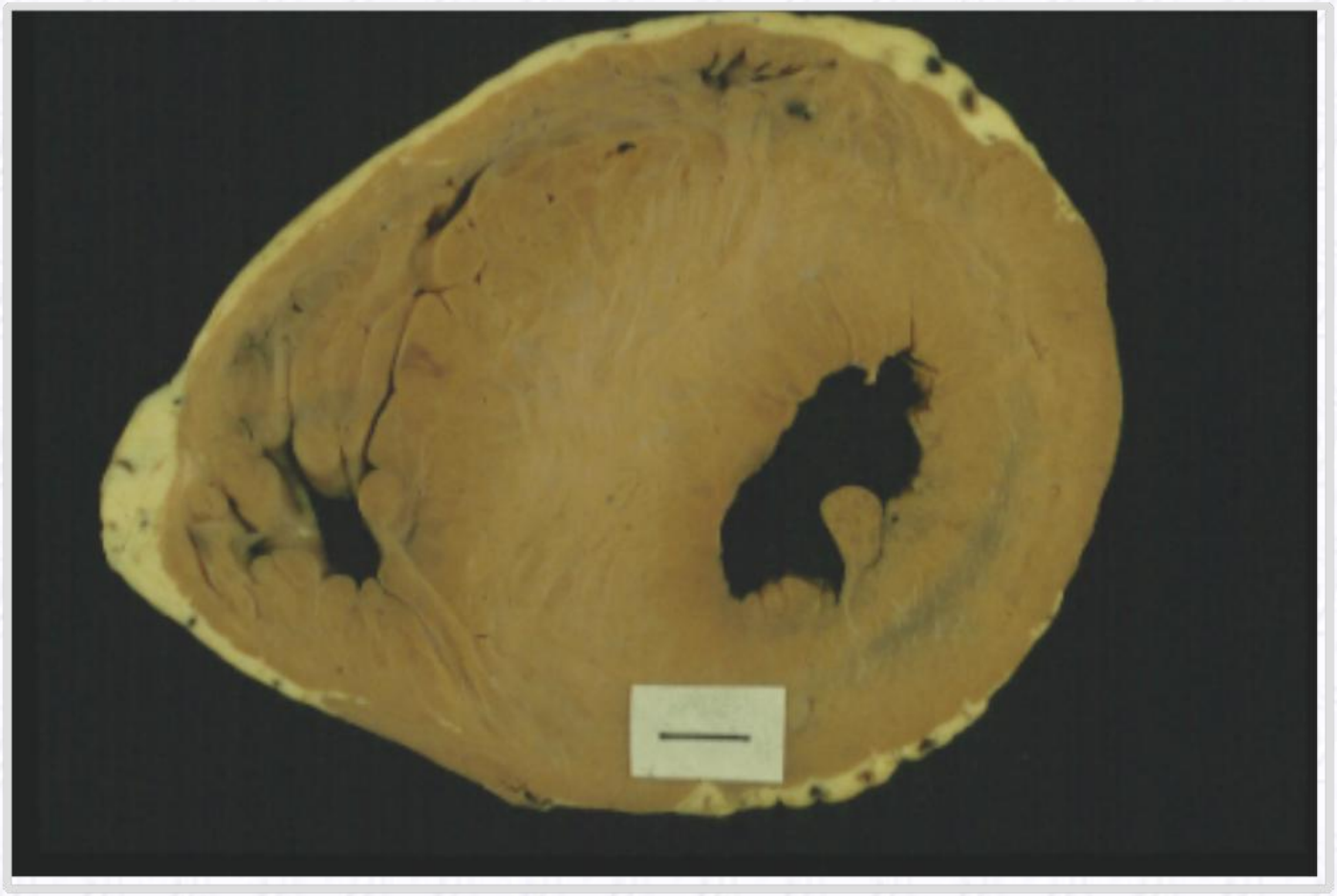
Hypertrophic Cardiomyopathy



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HCM: Definitions

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

ADULTS:

- *LV wall thickness ≥15 mm in one or more LV myocardial segments measured by any imaging technique*

CHILDREN:

- *LV wall thickness more than two standard deviations above the predicted mean (z-score >2)*

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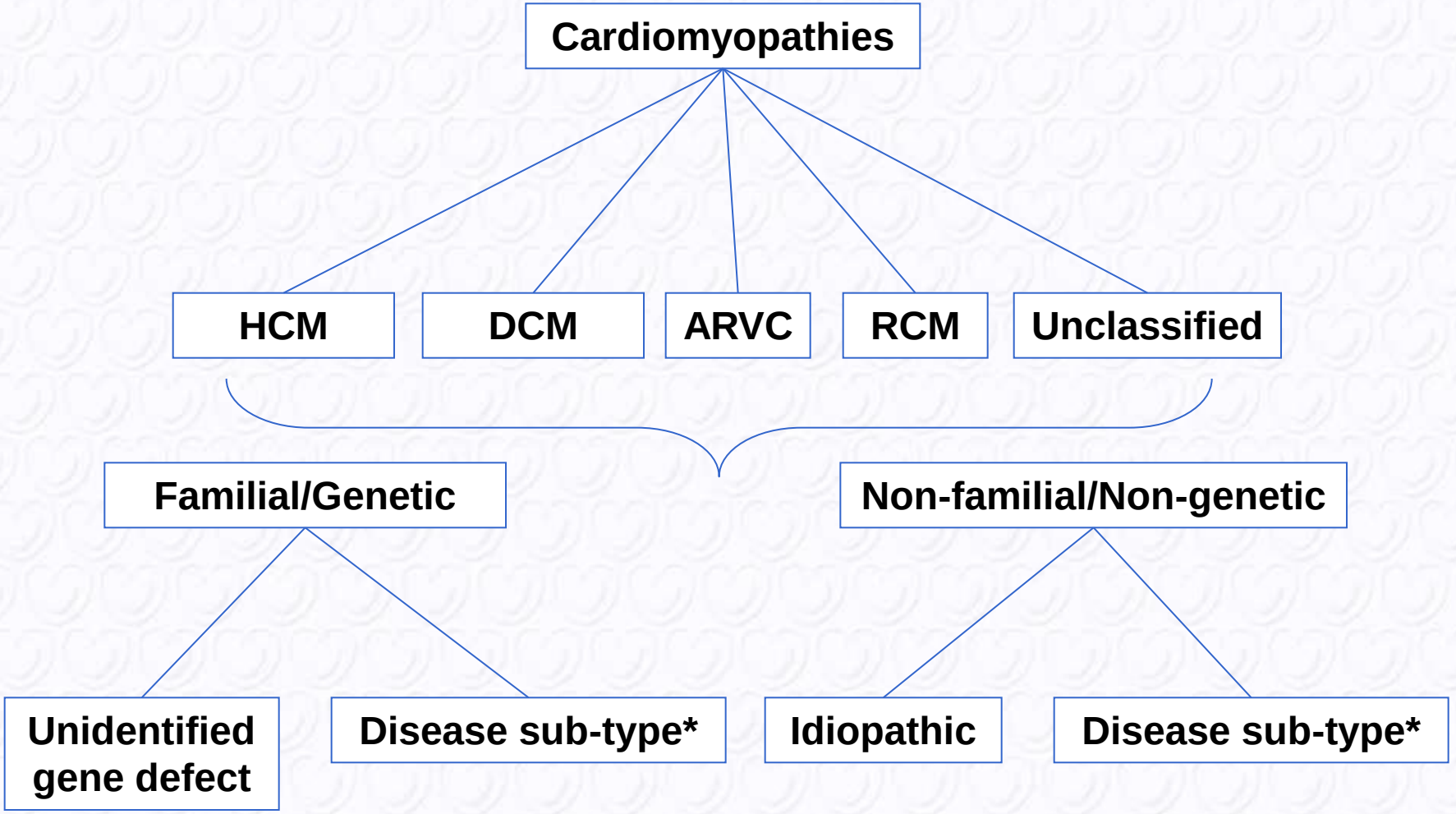

European WG on Myocardial and Pericardial Diseases (Elliott P et al. EHJ 2007)

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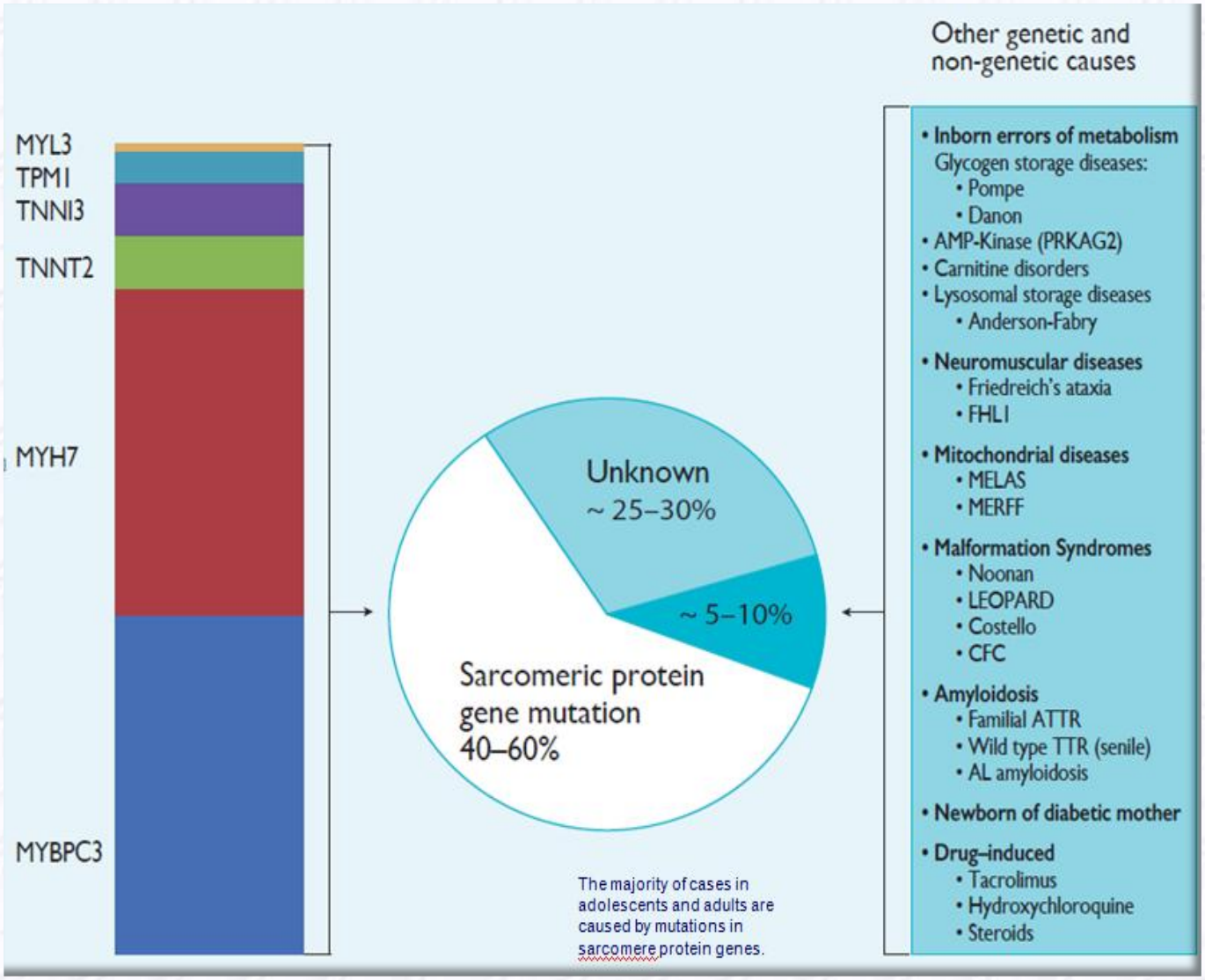

The majority of cases in adolescents and adults are caused by mutations in sarcomere protein genes.

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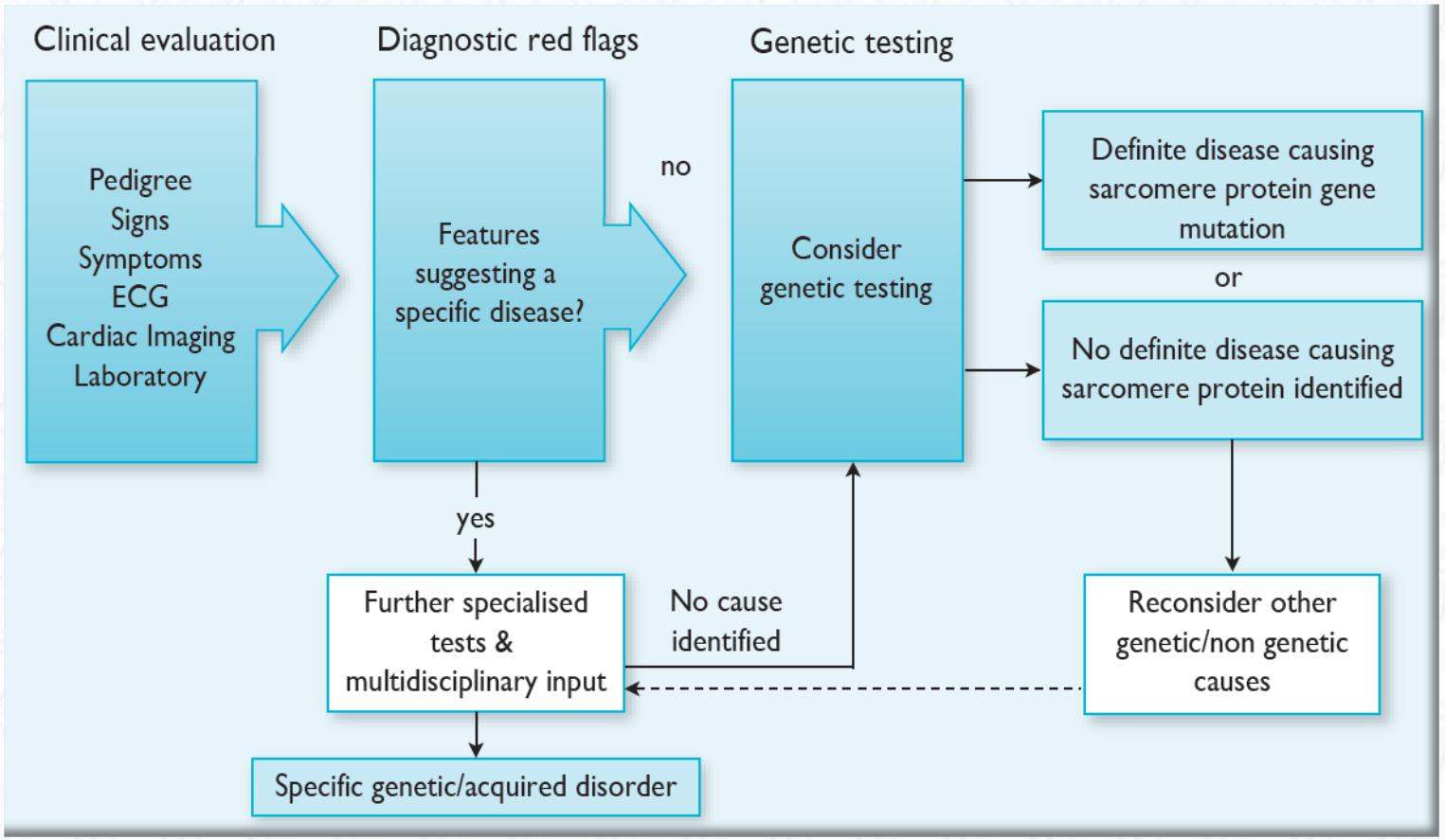
General approach to the diagnosis of hypertrophic cardiomyopathy



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History and Physical Examination

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

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History & physical examination

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

Table 3 Examples of signs and symptoms suggestive of specific diagnoses (modified from Rapezzi et al.[67])

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) • TTR-related amyloidosis (cotton wool type vitreous opacities) • Danon disease (retinitis pigmentosa) • Anderson-Fabry disease (cataracts, corneal opacities)
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

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Electrocardiogram

- **Value of ECG**
  - Distribution of hypertrophy
  - Myocardial fibrosis
  - Early diagnosis in relatives
  - Diagnostic red flags

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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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ECHOCARDIOGRAPHY

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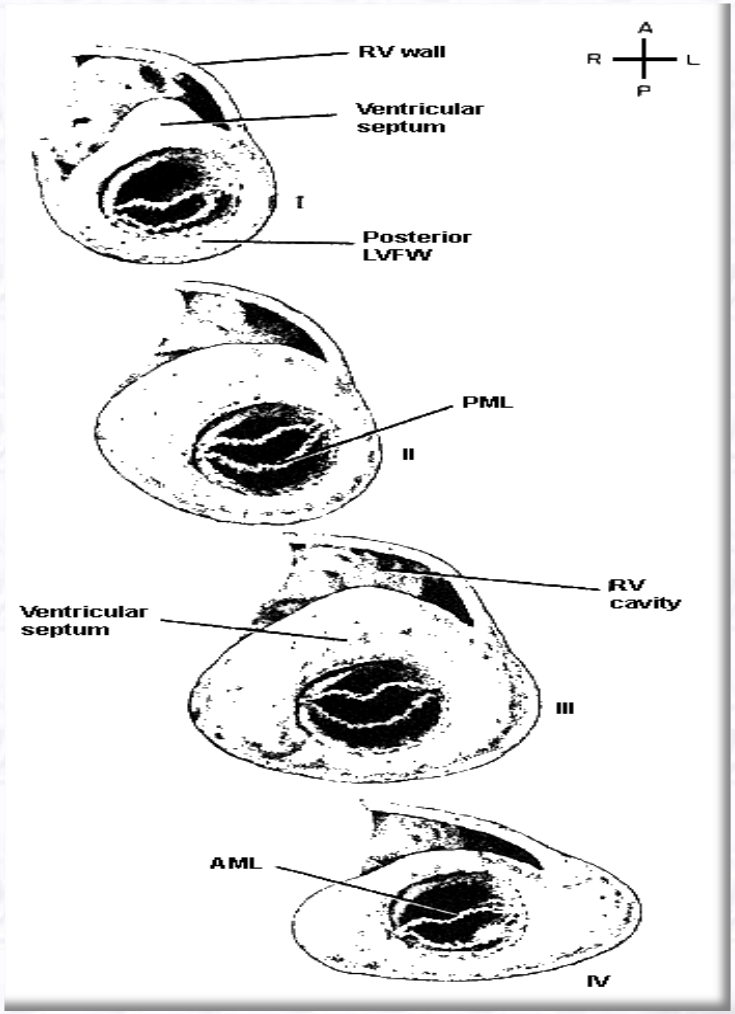
Echocardiography

- *All LV segments from base to apex should be examined, ensuring that the wall thickness at mitral, mid-LV and apex is recorded.*



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Echocardiography: Differential Diagnosis

Interpret images in context of clinical features and other tests

Echocardiographic features that suggest specific aetiologies[a]	
Finding	**Specific diseases to be considered**
Increased interatrial septum thickness	Amyloidosis
Increased AV valve thickness	Amyloidosis; Anderson-Fabry disease
Increased RV free wall thickness	Amyloidosis, myocarditis, Anderson-Fabry disease, Noonan syndrome and related disorders
Mild to moderate pericardial effusion	Amyloidosis, myocarditis
Ground-glass appearance of ventricular myocardium on 2-D echocardiography	Amyloidosis
Concentric LVH	Glycogen storage disease, Anderson-Fabry disease, PRKAG2 mutations
Extreme concentric LVH (wall thickness ≥30 mm)	Danon disease, Pompe disease
Global LV hypokinesia (with or without LV dilatation)	Mitochondrial disease, TTR-related amyloidosis, PRKAG2 mutations, Danon disease, myocarditis, advanced sarcomeric HCM, Anderson-Fabry disease
Right ventricular outflow tract obstruction	Noonan syndrome and associated disorders

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CARDIAC MRI

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Cardiac Magnetic Resonance Imaging

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

Value of Cardiac CMR:

- LV morphology and function
- Myocardial fibrosis
- Differential Diagnosis

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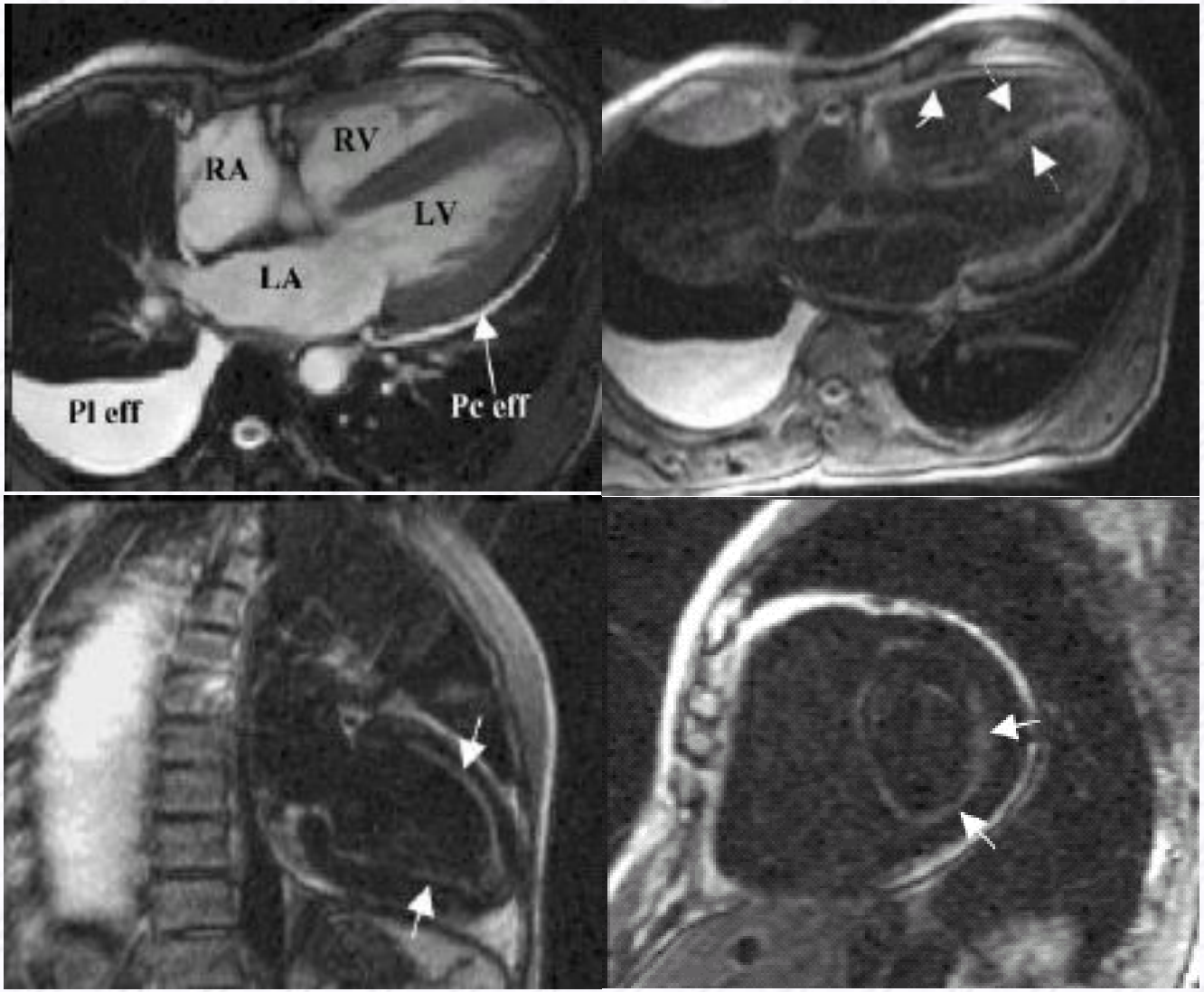

Circulation 2005;111:186-93

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LABORATORY TESTS

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Value of laboratory testing

- **Assessment of extra-cardiac disease/complications**
  - (e.g. renal function)
- **Severity of LV dysfunction**
  - (e.g. natriuretic peptides)
- **Diagnostic Red Flags**
  - (e.g. creatine kinase)
- **Confirmatory tests in phenocopies**

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Recommended Laboratory Tests

Recommended laboratory tests in adult patients with hypertrophic cardiomyopathy	
Test	**Comment**
Haemoglobin	Anaemia exacerbates chest pain and dyspnoea and should be excluded whenever there is a change in symptoms.
Renal function	Renal function may be impaired in patients with severe left ventricular impairment. Impaired GFR and proteinuria may be seen in amyloidosis, Anderson-Fabry disease and mitochondrial DNA disorders.
Liver transaminases	Liver tests may be abnormal in mitochondrial disorders, Danon disease and ß-oxidation defects.
Creatine phosphokinase	Serum creatine phosphokinase is raised in metabolic disorders such as Danon and mitochondrial disease.

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Recommended Laboratory Tests

Recommended laboratory tests in adult patients with hypertrophic cardiomyopathy (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.

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GENETIC COUNSELLING & TESTING

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Genetic Counselling

Genetic counselling is recommended in all patients when HCM cannot be explained solely by a non-genetic cause

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

- Gather information on other family members that helps to determine probability of genetic disease and possible aetiology.

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Genetic Testing

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

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

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Genetic Testing

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

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

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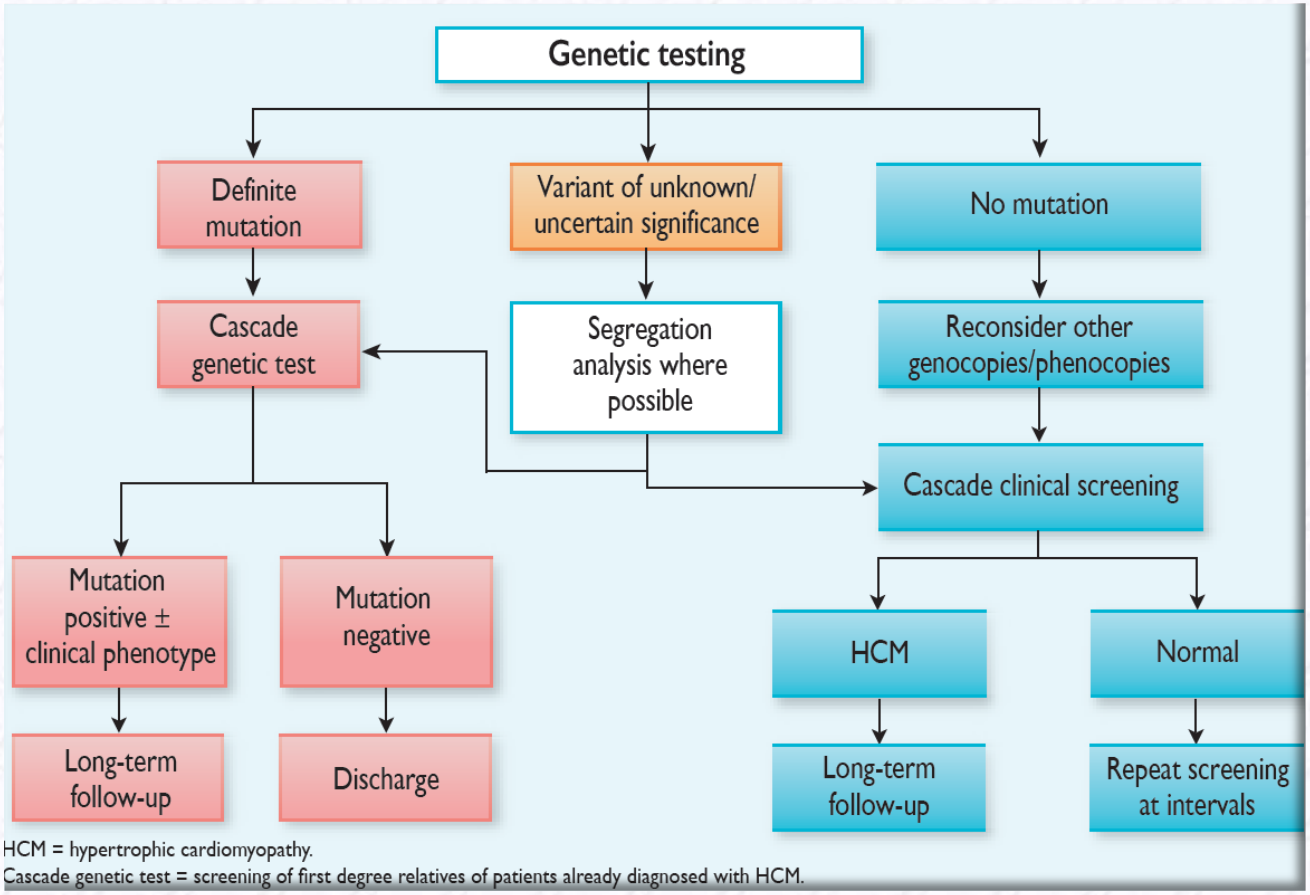
Flow chart for genetic and clinical screening of probands and relatives.



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

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ASSESSMENT OF SYMPTOMS

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Chest pain
Dyspnoea
Fatigue
Palpitations

- LVOT Obstruction
- Arrhythmia
- LV Diastolic failure
- LV Systolic failure
- Valve Disease
- Microvascular dysfunction

Syncope

- LVOT Obstruction
- Arrhythmia
- Abnormal Vascular Function

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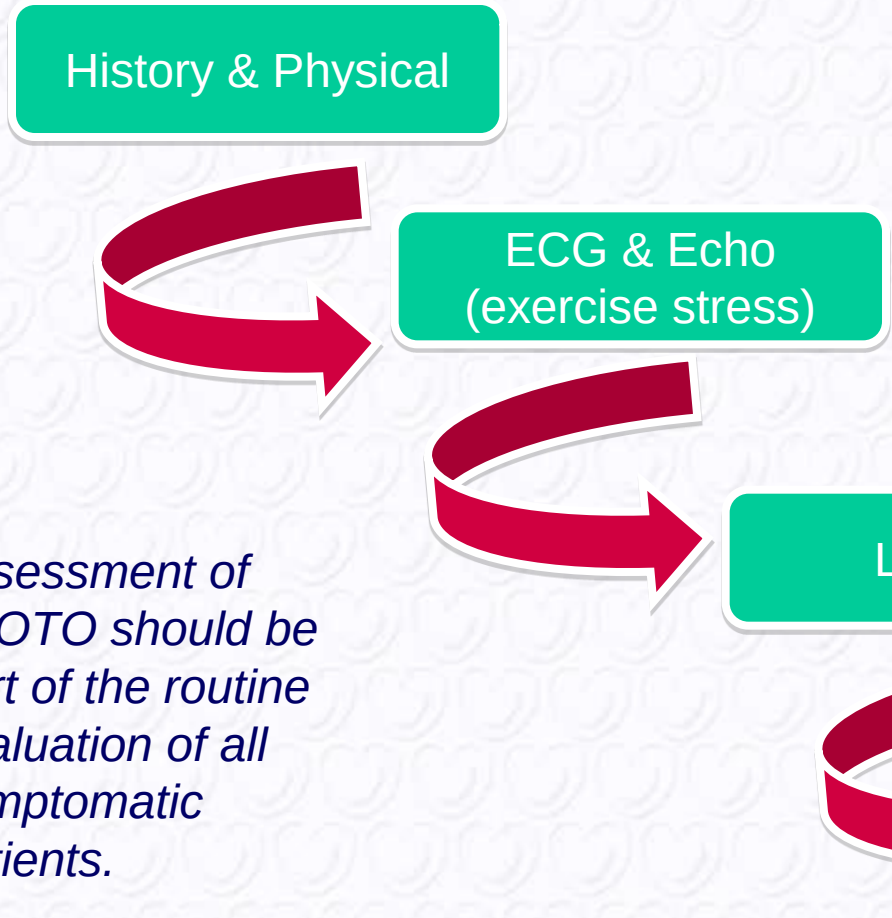
Investigation of Heart Failure Symptoms



When facilities are available, cardiopulmonary exercise testing… should be considered at the initial clinical evaluation

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

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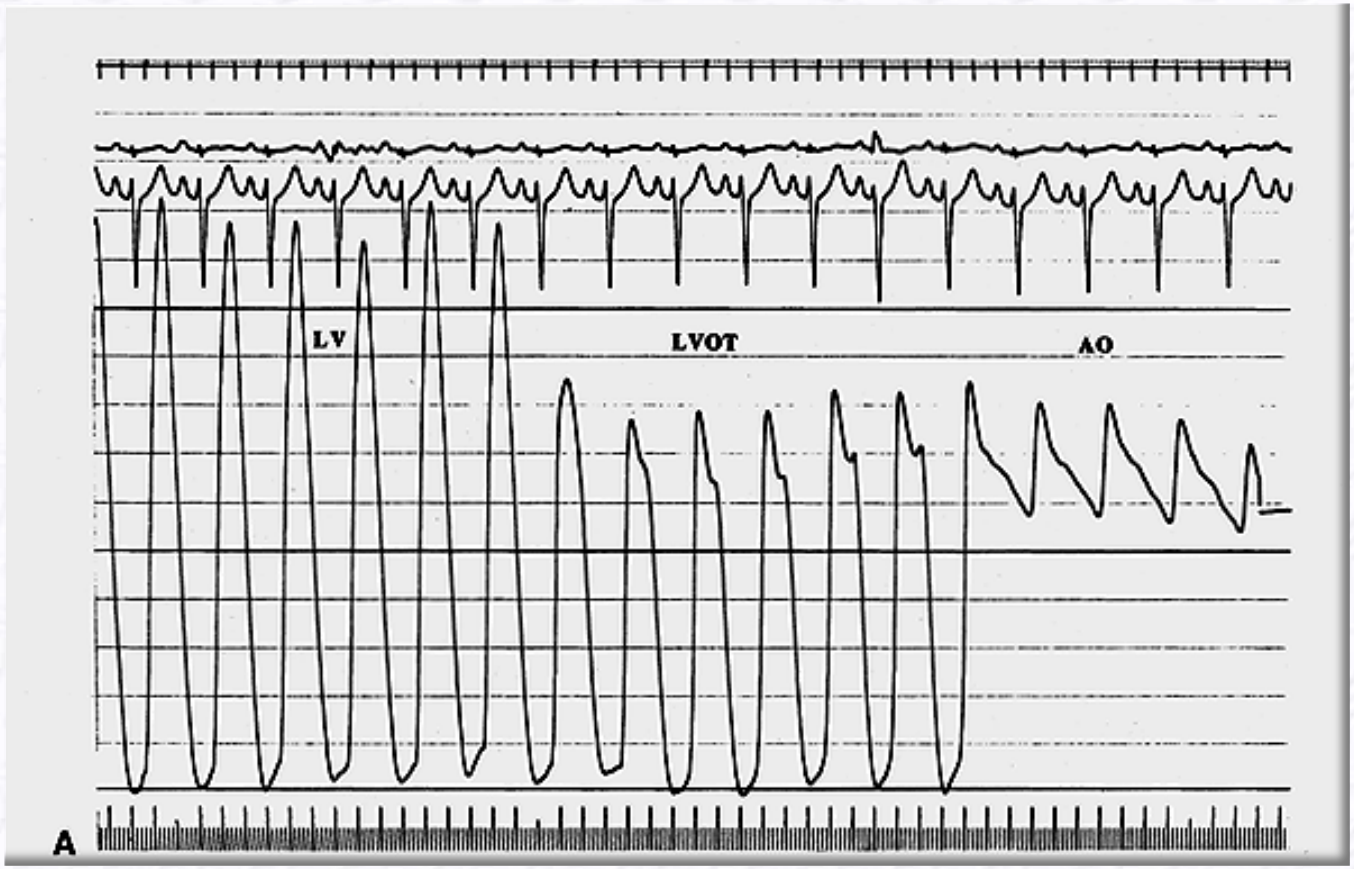
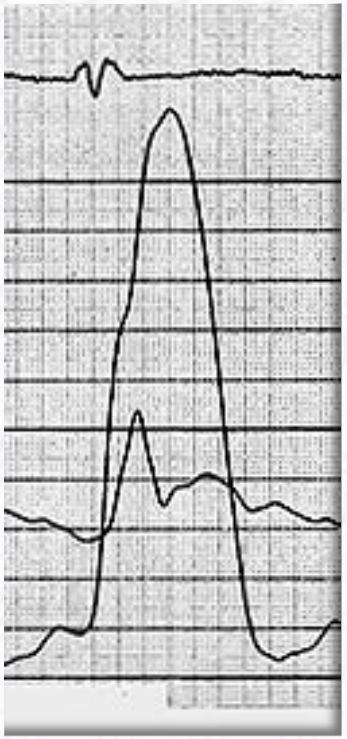
LV Outflow Tract Obstruction





Elliott & McKenna: Textbook of Cardiology (Topol ed.)

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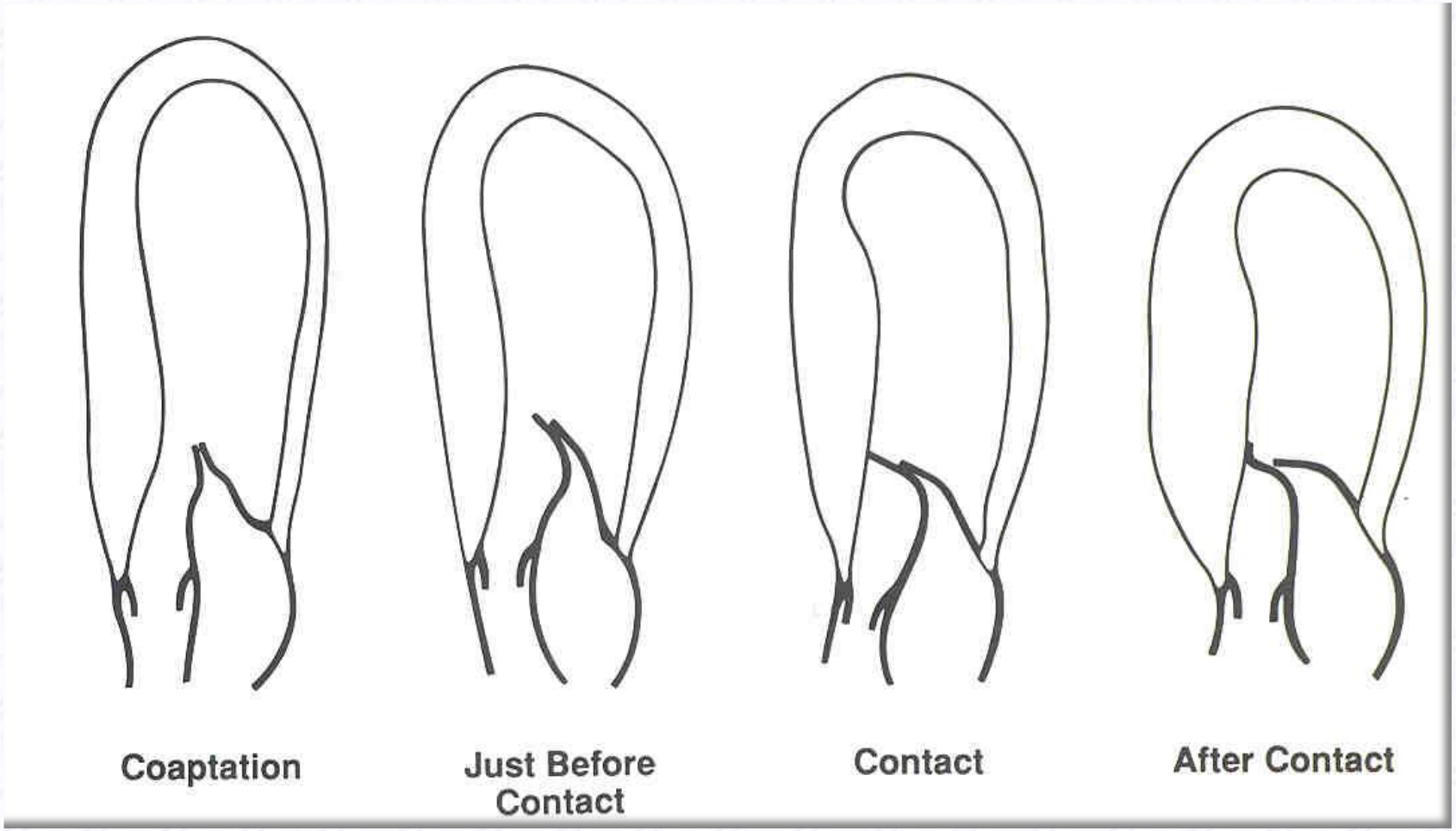

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Echocardiography: LV Outflow Tract Obstruction

- *Systematically exclude obstruction unrelated to SAM, including sub-aortic membranes, mitral valve leaflet abnormalities and mid-cavity obstruction.*

- *The presence of a central- or anteriorly directed jet of mitral regurgitation should raise suspicion of an intrinsic mitral valve abnormality and prompt further assessment.*

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Echocardiography: Latent Obstruction

- About 30% of symptomatic patients without resting gradients
- Provoked by manoeuvres that reduce preload or afterload (standing from squat, Valsalva)
- Clinically significant if ≥ 50 mmHg

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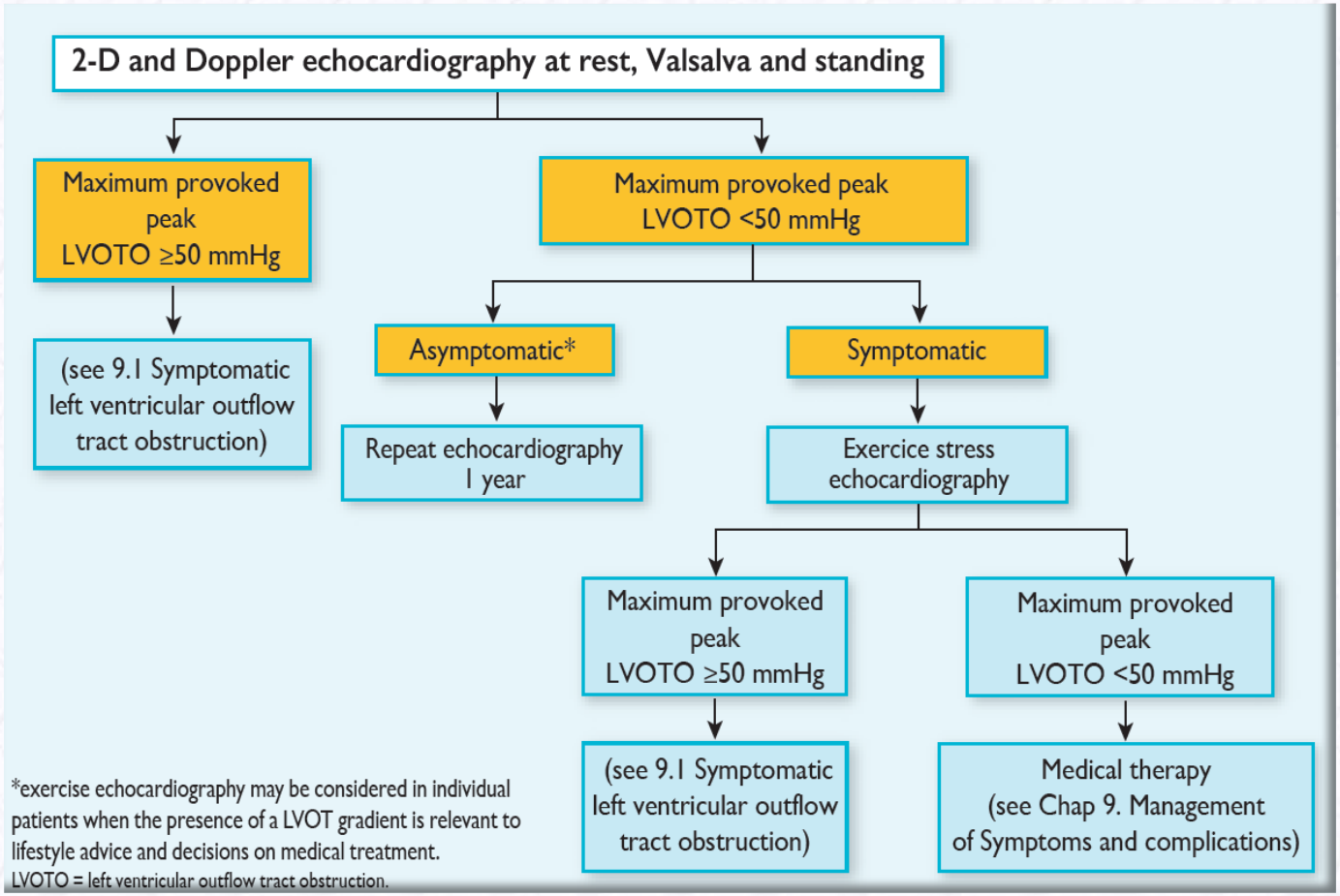
Protocol for the assessment and treatment of left ventricular outflow tract obstruction



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SYNCOPE

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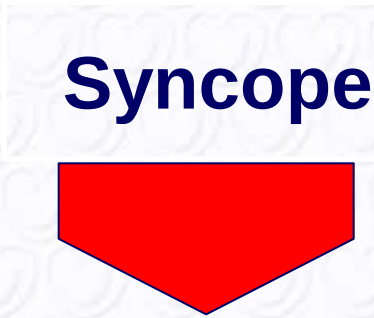
Syncope in HCM



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

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

Recommendations	Class[a]	Level[b]	Ref.[c]
For patients with frequent or sustained palpitations,48-hour ambulatory ECG monitoring is recommended, to identify the likely cause.	I	C	250,253
An ILR may be considered for patients with frequent palpitations, in whom no cause is identified following prolonged ECG monitoring.	IIb	C	250

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Syncope

- *The routine use of electrophysiological studies (EPS) in patients with syncope or symptoms suggestive of arrhythmia is not recommended.*

- *As unexplained non-vasovagal syncope is a risk factor for sudden cardiac death… treatment with a prophylactic implantable cardioverter defibrillator (ICD) may be appropriate in individuals with other features indicative of high sudden death risk...*

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MANAGEMENT OF SYMPTOMS & COMPLICATIONS

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Left ventricular outflow tract obstruction

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Treatment of Left Ventricular Outflow Tract Obstruction

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

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

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Treatment of LV Outflow Tract Obstruction

Recommendations for treatment of left ventricular outflow tract obstruction: General measures		
	Class[a]	Level[b]
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

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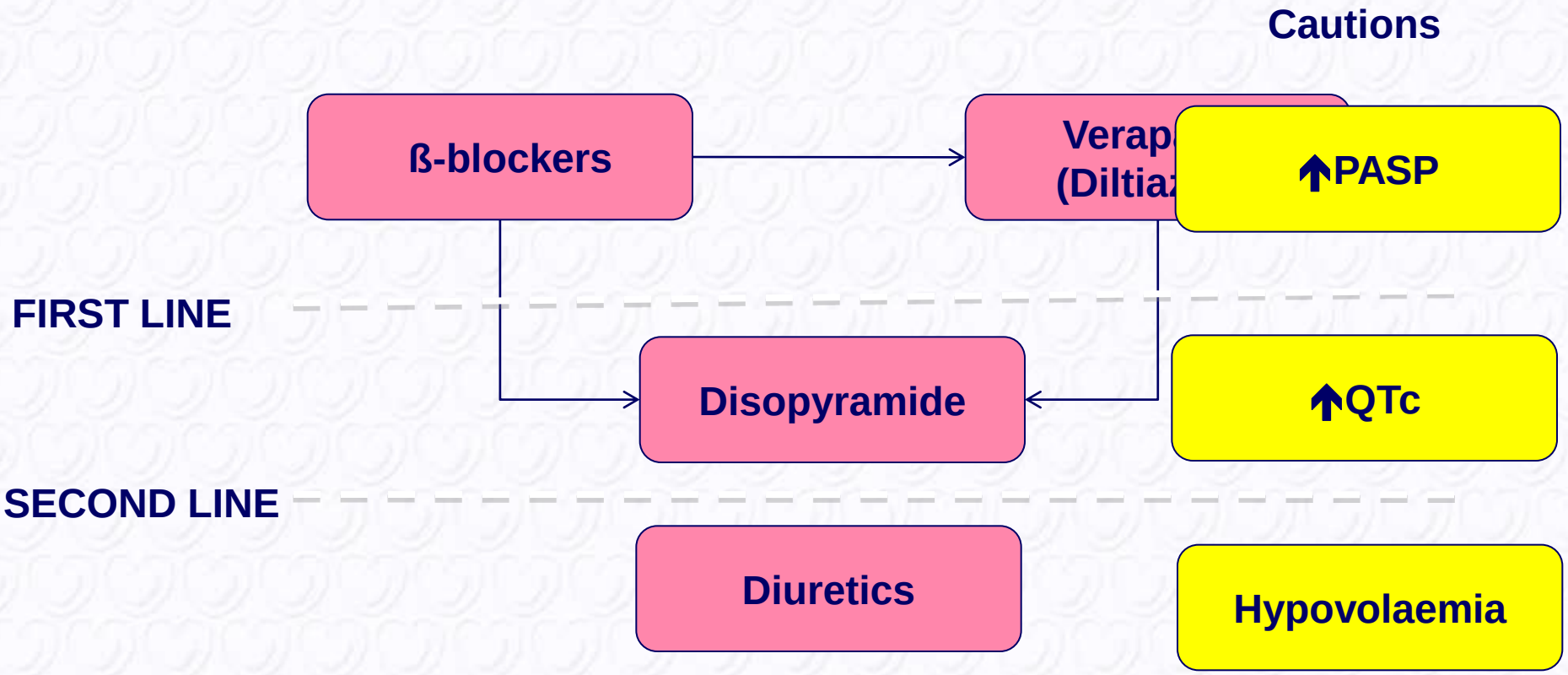
Drug treatment of LVOTO



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Invasive Treatment of LV Outflow Tract Obstruction

Experienced multidisciplinary teams should assess all patients before intervention

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

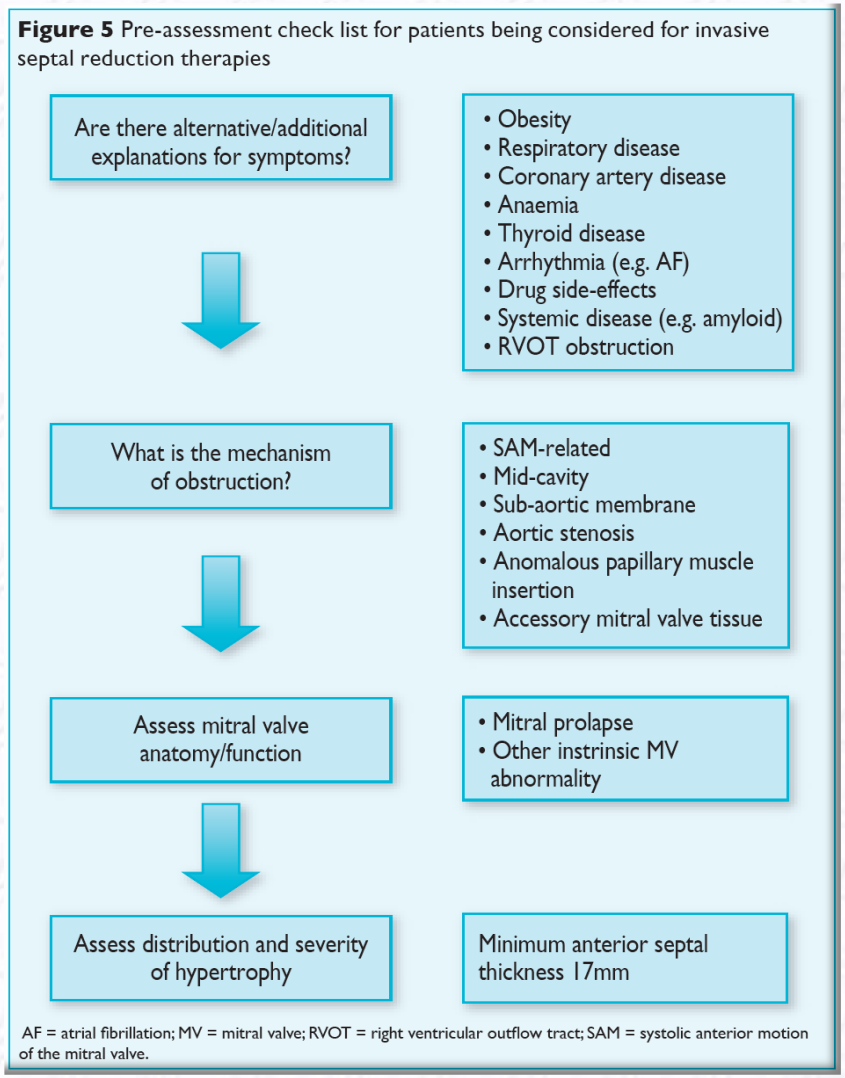

Figure 5 Pre-assessment check list for patients being considered for invasive septal reduction therapies

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

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Non-obstructive HCM

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Management of Heart Failure Symptoms in Non-Obstructive HCM

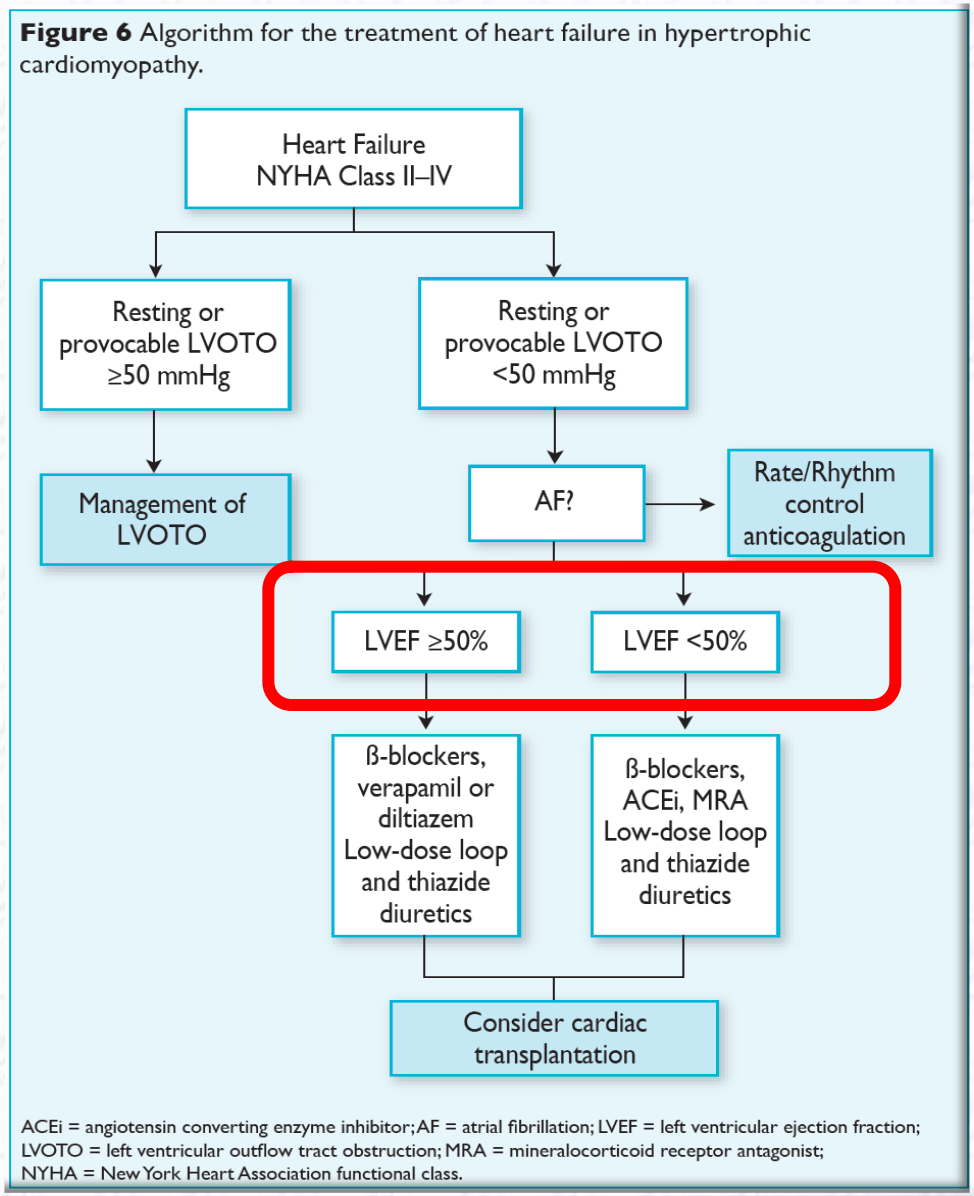

Figure 6 Algorithm for the treatment of heart failure in hypertrophic cardiomyopathy.

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

EF Threshold of 50%

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ATRIAL ARRHYTHMIA

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Atrial Fibrillation: Key Points

- *Use of the CHA_2DS_2-VASc score to calculate stroke risk is NOT recommended.*
- *In general, lifelong therapy with oral anticoagulants is recommended, even when sinus rhythm is restored.*
- *As left atrial size is a consistent predictor for AF and stroke in patients with HCM, patients in sinus rhythm with LA diameter ≥45mm should undergo 6–12 monthly 48-hour ambulatory ECG monitoring to detect AF.*

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SUDDEN CARDIAC DEATH

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Sudden Cardiac Death in HCM

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

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

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Risk Factors for Sudden Cardiac Death (Adults)

- Young Age
- Non-sustained Ventricular Tachycardia
- Severity of LV wall thickness
- Family History of Sudden Cardiac Death (age < 40y)
- Unexplained syncope
- Left Atrial Diameter
- Left Ventricular Outflow Tract Obstruction
- Exercise Blood Pressure Response

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FASTTRACK CLINICAL RESEARCH

A novel clinical risk prediction model for sudden cardiac death in hypertrophic cardiomyopathy (HCM Risk-SCD)

Constantinos O'Mahony[1], Fatima Jichi[2], Menelaos Pavlou[8], Lorenzo Monserrat[3], Aristides Anastasakis[4], Claudio Rapezzi[5], Elena Biagini[5], Juan Ramon Gimeno[6], Giuseppe Limongelli[7], William J. McKenna[1], Rumana Z. Omar[2,8] and Perry M. Elliott[1]*, for the Hypertrophic Cardiomyopathy Outcomes Investigators

O'Mahony, C et al. Eur Heart J. 2013 Oct 14. [Epub ahead of print]

HCM Risk-SCD: Predictor variables

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

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

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

HCM Risk-SCD model for predicting 5 year risk

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

where Prognostic index = [0.15939858 x maximal wall thickness (mm)] – [0.0029427I x maximal wall thickness^2 (mm^2)] + [0.0259082 x left atrial diameter (mm)] + [0.00446131 x maximal (rest/Valsalva) left ventricular outflow tract gradient (mmHg)] + [0.4583082 x family history SCD] + [0.82639195 x NSVT] + [0.71650361 x unexplained syncope] – [0.01799934 x age at clinical evaluation (years)].

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

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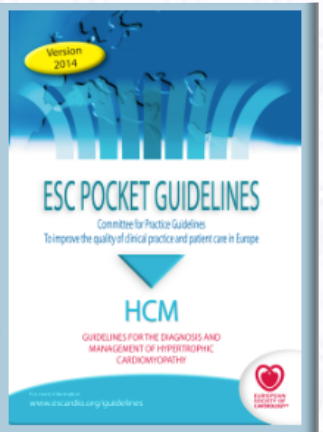
HCM Risk-SCD Calculator

Age	**Years**	*Age at evaluation*
Maximum LV wall thickness	**mm**	*Transthoracic Echocardiographic measurement*
Left atrial size	**mm**	*Left atrial diameter determined by M-Mode or 2D echocardiography in the parasternal long axis plane at time of evaluation*
Max LVOT gradient	**mmHg**	*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 should be determined using the modified Bernouilli equation: Gradient= $4V^2$, where V is the peak aortic outflow velocity*
Family History of SCD	○ No ○ Yes	*History of sudden cardiac death in 1 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).*
Non-sustained VT	○ No ○ Yes	*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.*
Unexplained syn-cope	○ No ○ Yes	*History of unexplained syncope at or prior to evaluation.*
Risk of SCD at 5 years (%)		
Recommendations		

Reset



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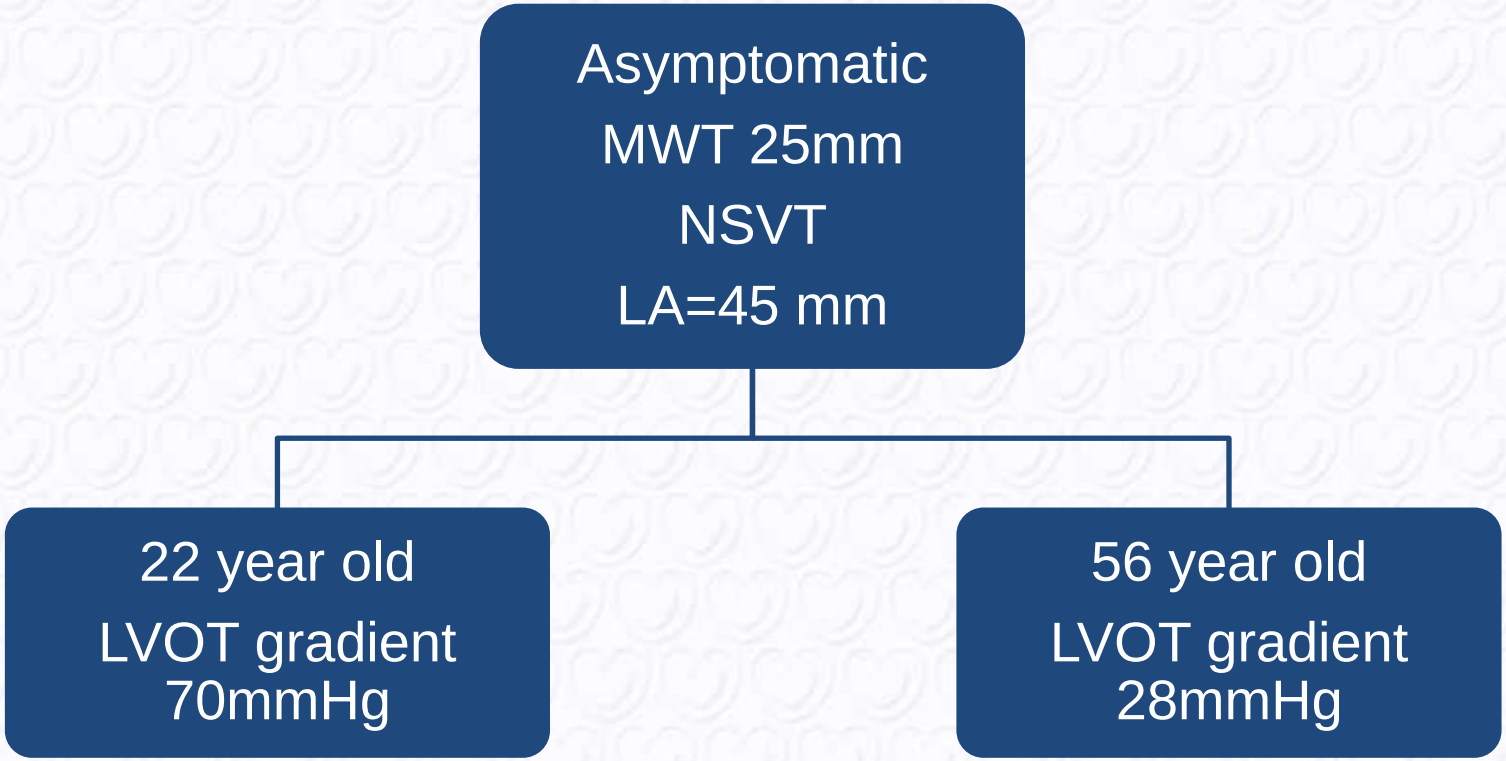

5-year SCD probability: 10.9% 5-year SCD probability: 5.1%

CURRENT GUIDELINES TREAT THESE 2 PATIENTS THE SAME

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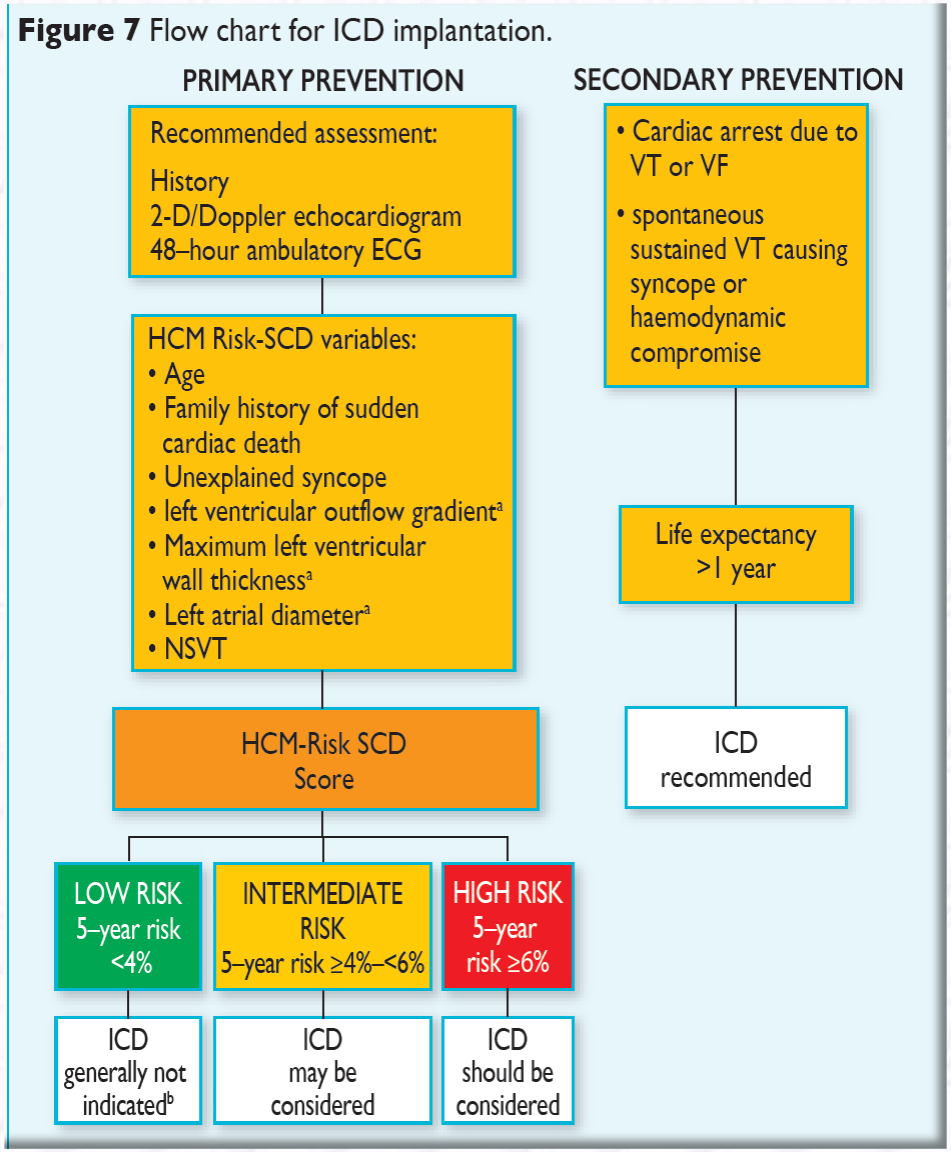

Figure 7 Flow chart for ICD implantation.

Prevention of Sudden Cardiac Death

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

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Caveats

- > 16 years
- Resting/Valsalva gradients
- Myectomy/PTSMA?
- Severe (≥35mm) LVH?

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Key Innovations

- Emphasis on specific diagnoses
- Guidance on genetic counselling and testing in adults and children
- Systematic approach to evaluation of symptoms
- Stepwise approach to the management of LVOTO and heart failure
- Advice on reproduction
- Tailored advice to patients and carers

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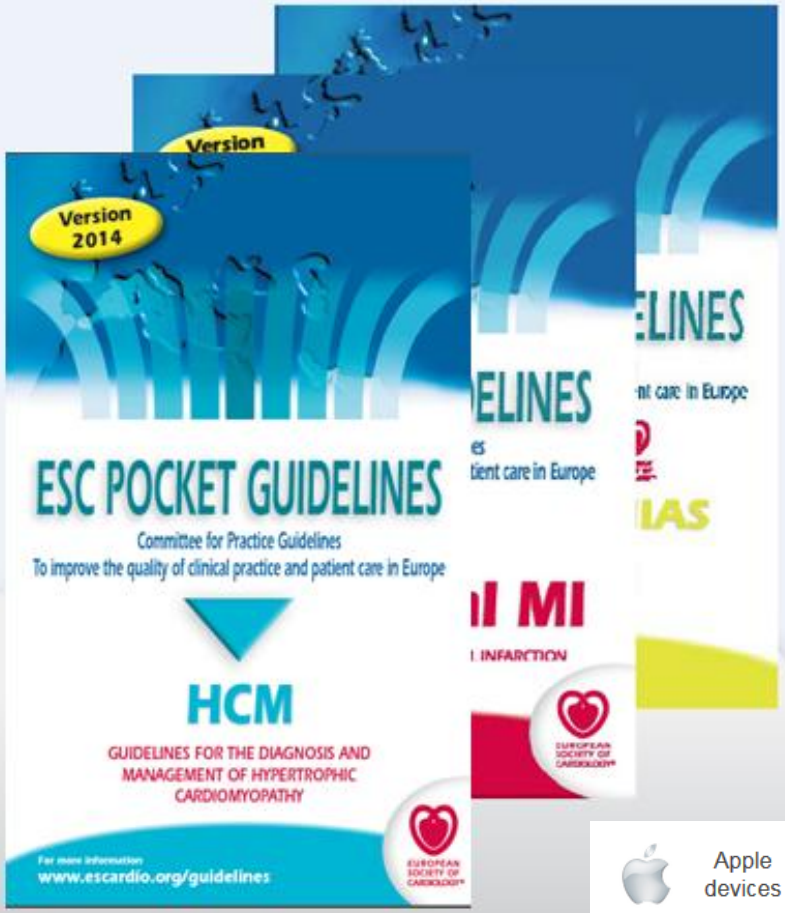

Apple devices

Available on the App Store

Android devices

Google play

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CMR and Sudden Death Risk

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 ≥I (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

"On balance, the extent of LGE on CMR has some utility in predicting cardiovascular mortality, but current data do not support the use of LGE in prediction of SCD risk."

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REPRODUCTION & CONTRACEPTION

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Maternal Risk

Table 8 Modified WHO classification of maternal cardiovascular risk: principles and application

Risk class	Risk of pregnancy	Application to HCM
I	No detectable increased risk of maternal mortality and no/mild risk of morbidity	-
II	Small increased risk of maternal mortality or moderate increase in morbidity	Most women with HCM: mild to moderate LVOTO; asymptomatic with or without medication, well-controlled arrhythmia, normal systolic LV function or mild LV dysfunction
III	Significantly increased risk of maternal mortality or severe morbidity	Severe LVOTO, symptoms or arrhythmias despite optimal medication, moderate systolic LV dysfunction
IV	Extremely high risk of maternal mortality or severe morbidity; pregnancy contraindicated	Severe systolic LV dysfunction, severe symptomatic LVOTO

HCM = hypertrophic cardiomyopathy; LV = left ventricle; LVOTO = left ventricular outflow tract obstruction; WHO = World Health Organization.

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Reproduction & Contraception

Recommendations on reproductive issues in women with HCM	Class[a]	Level[b]
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
ß-blockers (preferably metoprolol) should be continued in women who used them before pregnancy.	IIa	C
ß-blockers (preferably metoprolol) should be started in women who develop symptoms during pregnancy.	I	C
Whenever ß-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

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