HYPERTROPHIC CARDIOMYOPATHY: DETECTION AND INTERVENTION

Hypertrophic cardiomyopathy (HCM) is defined by the presence of increased left ventricular (LV) wall thickness not solely explained by abnormal loading conditions

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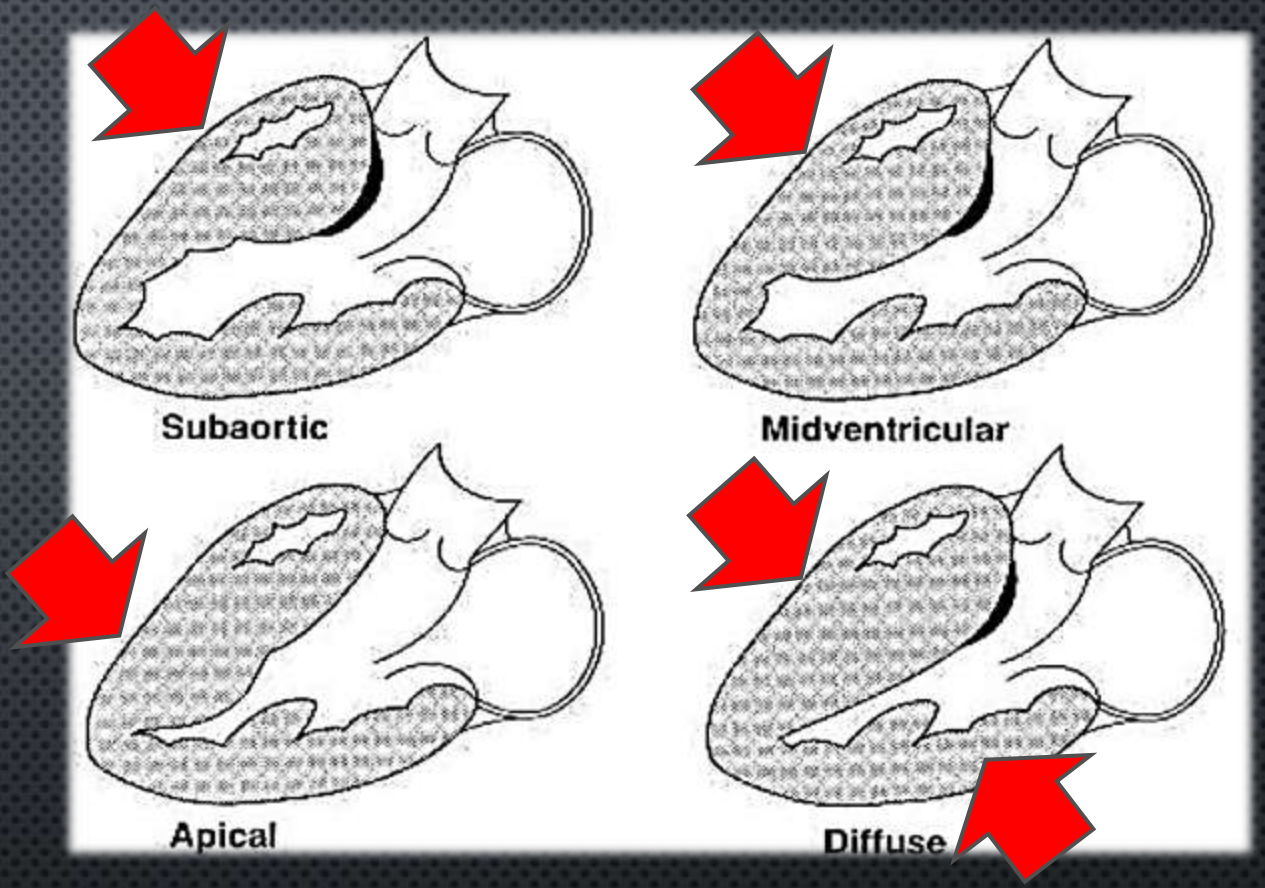
2019

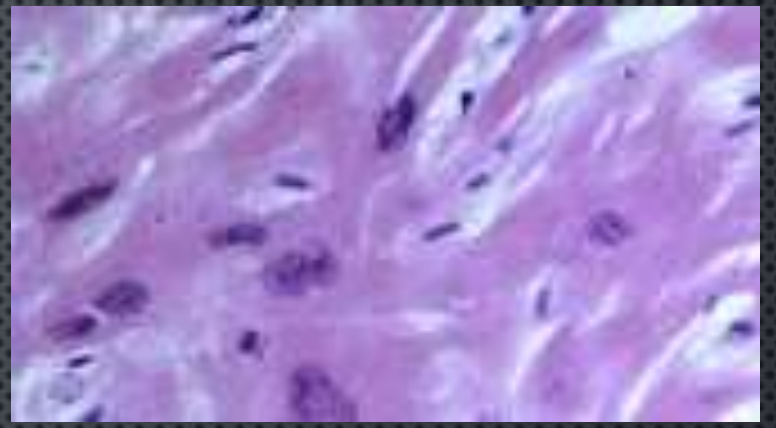


Eur Heart J 2014;35:2711
Circ 2011;124:2761-2766
Radiology 2014;271:329-348

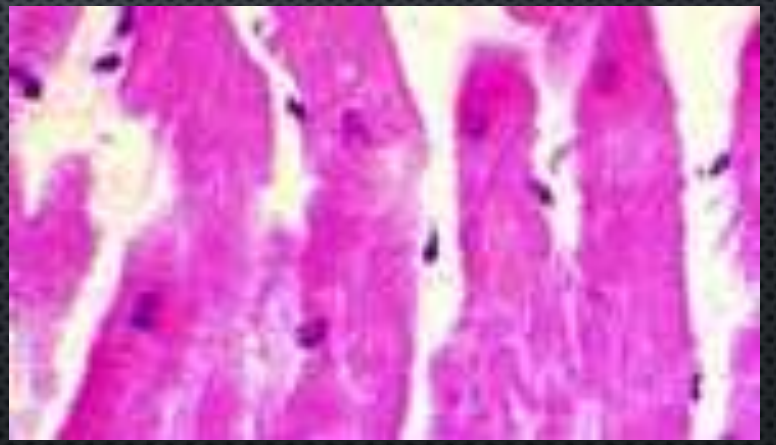
OUTLINE

- Definition
- Epidemiology / etiology
- Diagnosis
  - Genetic testing
- Clinical evaluation / treatment of symptoms
- Treatment follow up
- Special problems

Irregular arrangement
Abnormal shaped myocyte disarray with increased connective tissue



Endomyocardial biopsy

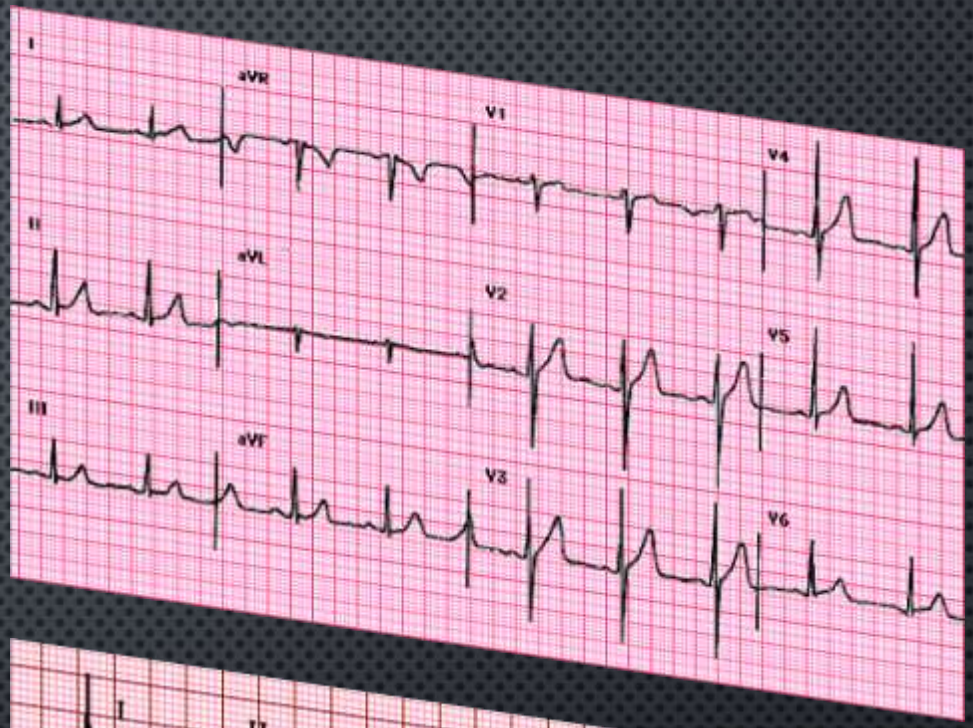


Normal

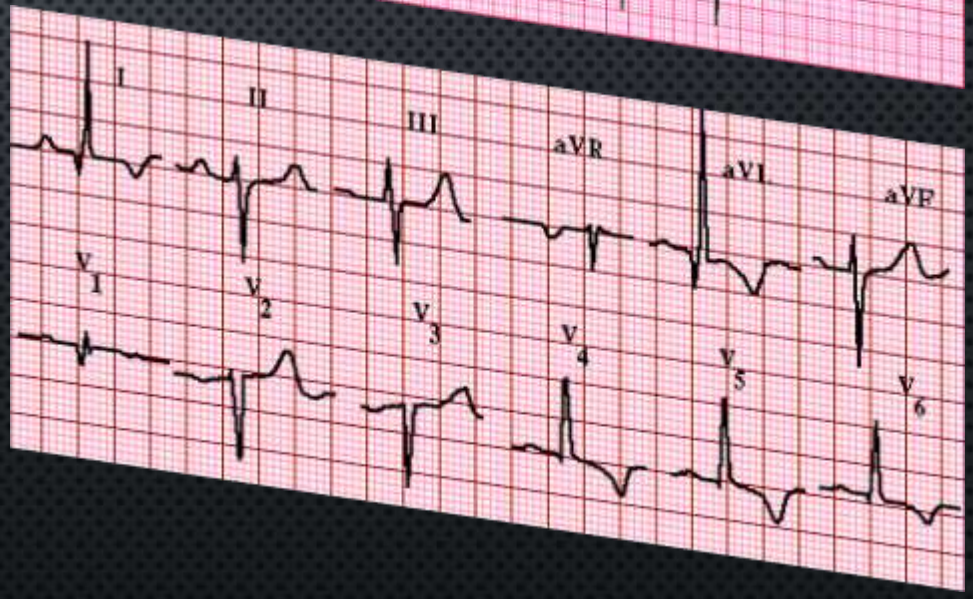
DIAGNOSIS

- LV myocardial segment >15 mm
- Dynamic obstruction >30 mm HG
- Relatives: One or more LV segments >13
- Special considerations
  - Athlete heart – LVH
  - Hypertension – LVH
  - Aortic stenosis- LVH
  - Elderly – Basal hypertrophy
  - Infiltrative disease- LVH
  - Apical HCM vs LV noncompaction

Normal

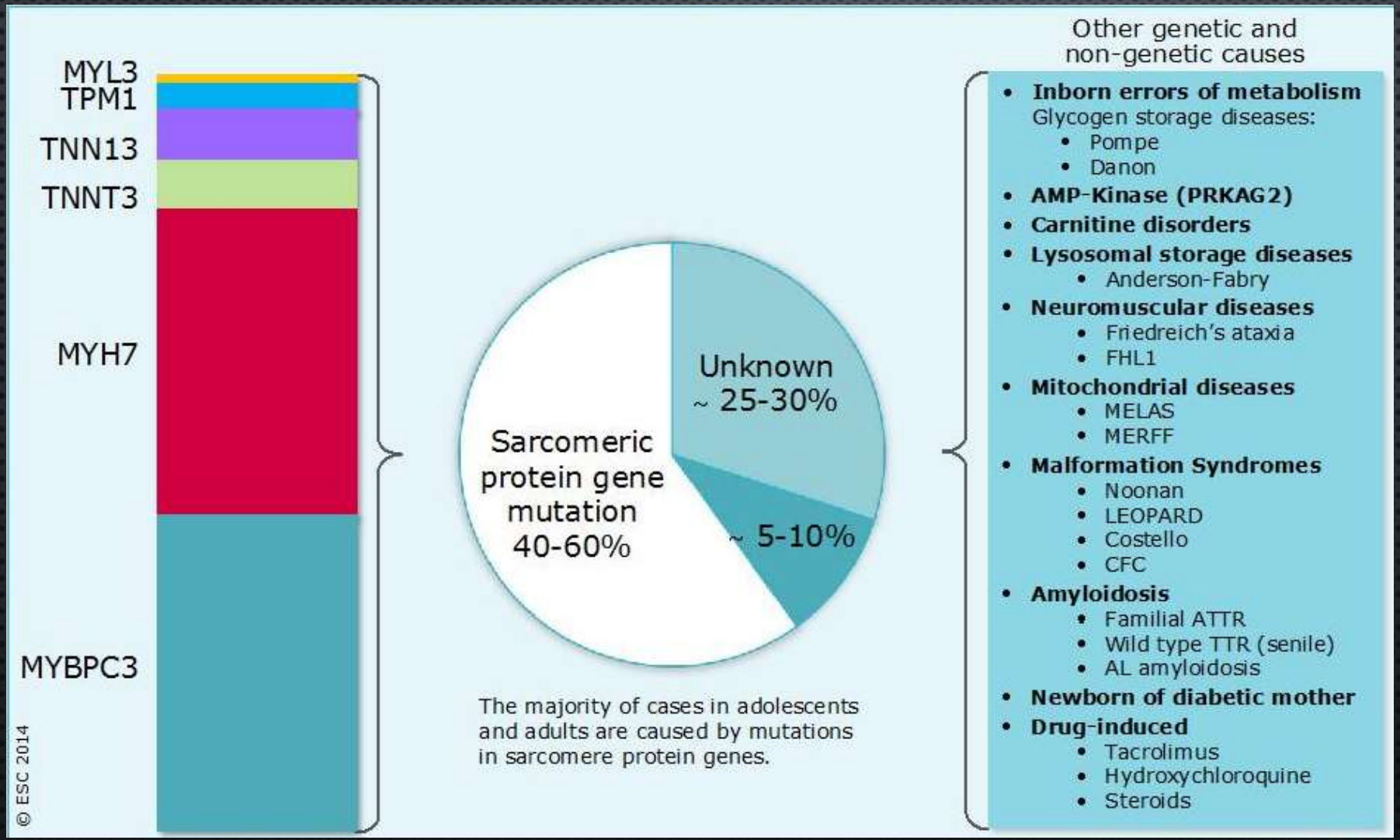


LVH with strain



Epidemiology

>60% caused from mutations in genes encoding sarcomere



Genetic testing per guidelines

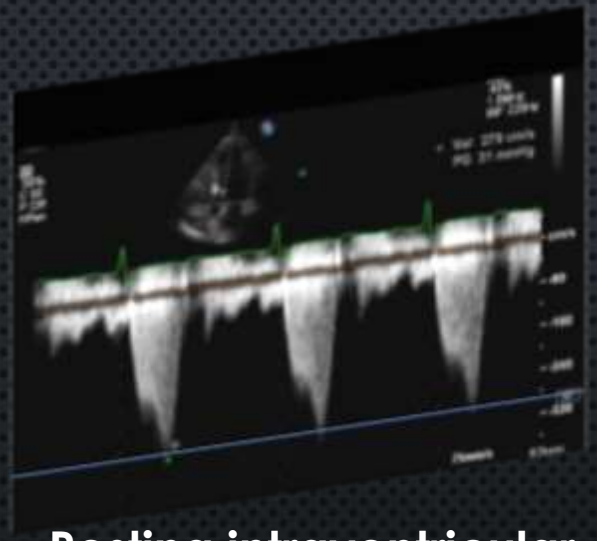
- Class 1: All patients with HCM when it enables genetic testing of relatives
- Class 1: Cascade genetic screening after pre test counseling of all first degree relatives
- Class II: All children >10 y/o and first degree relatives

Cascade screening -process of testing their immediate biological relatives to figure out which other members of the family also have the FH gene.

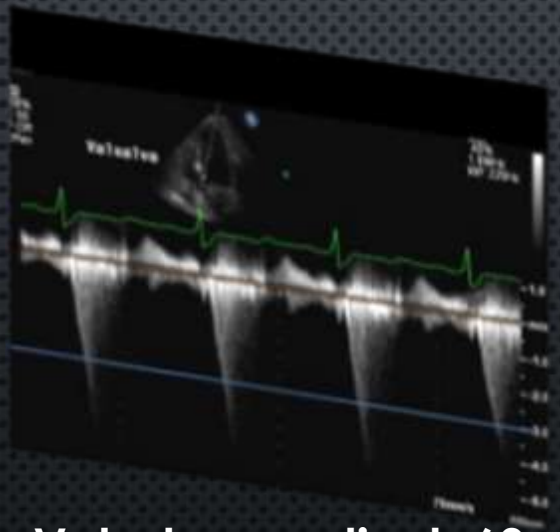
Class 1: Serial echo/EKG/Exam each year in children
Adults every 5 years

Class II: Holter for palpations

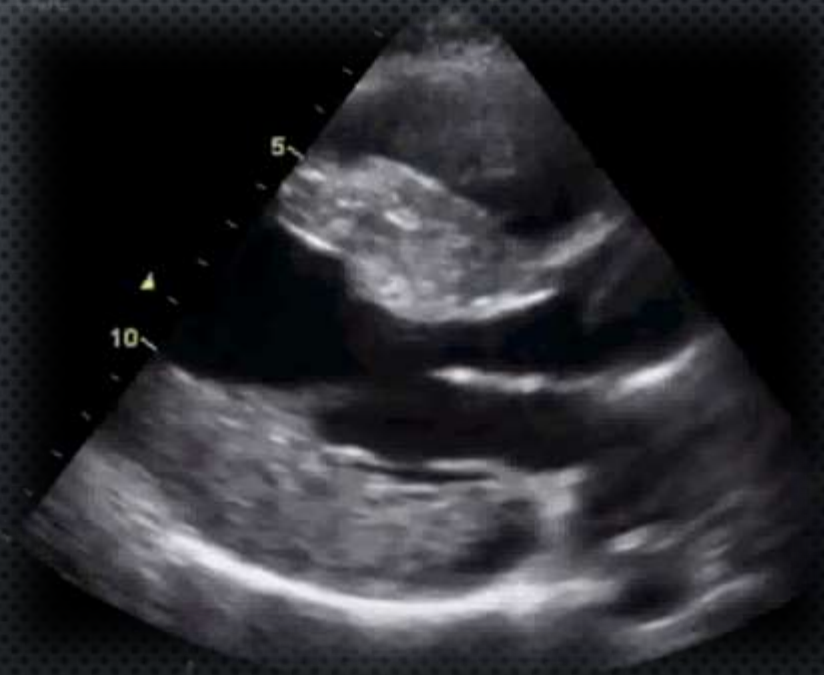
Outflow gradient



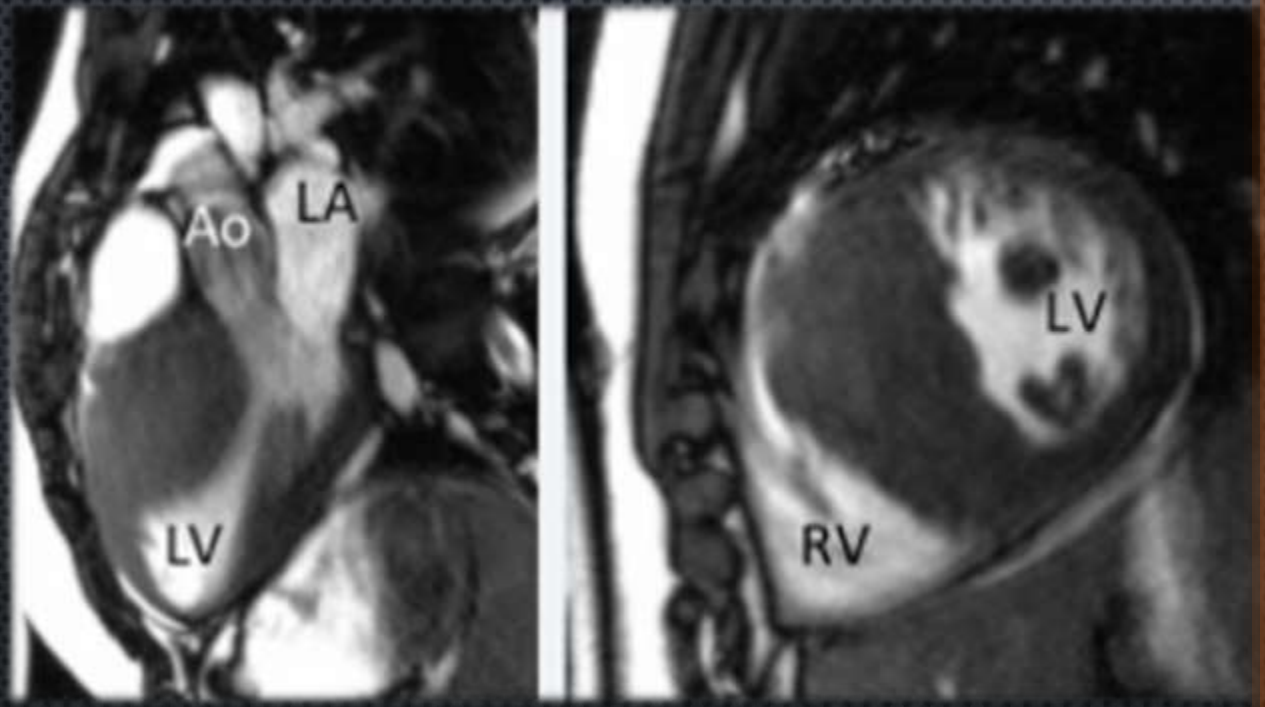
Resting intraventricular gradient=31 mmHg

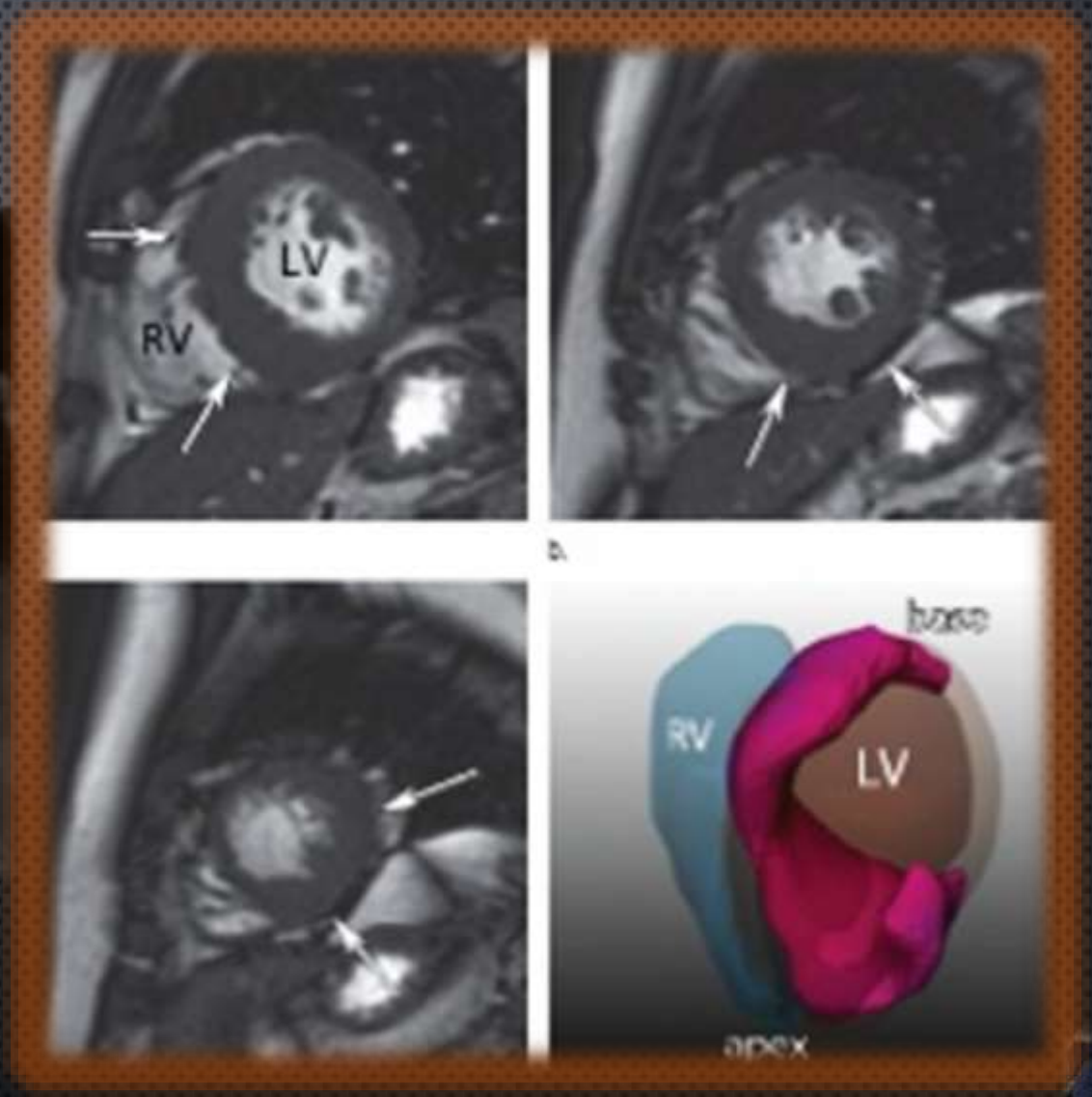


Valsalva gradient=60 mmHg



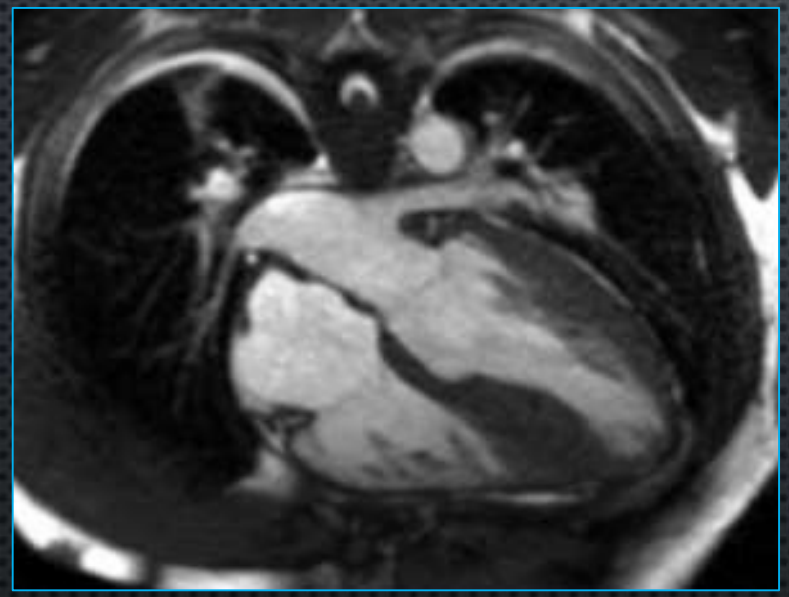
MRI- marked septal hypertrophy



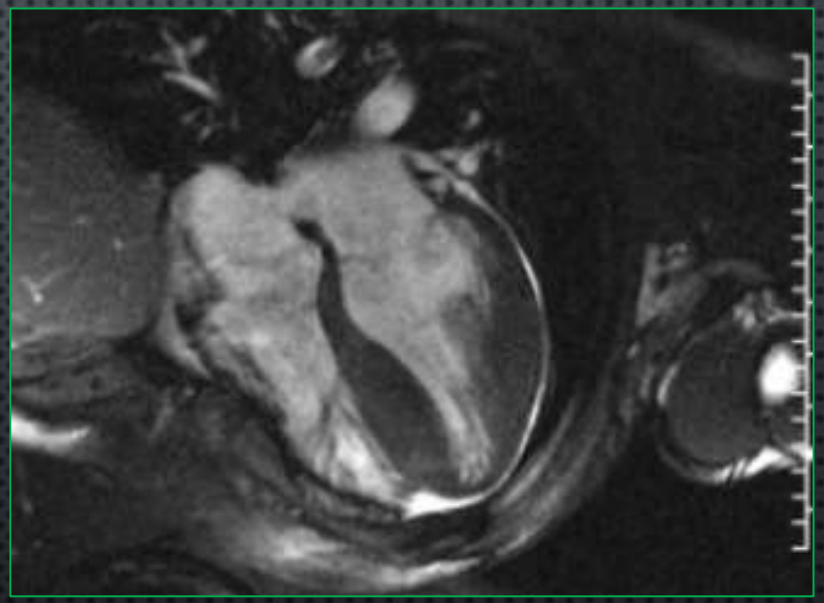


MRI: location of HCM

Mid-ventricular HCM



Apical HCM



Apical HCM

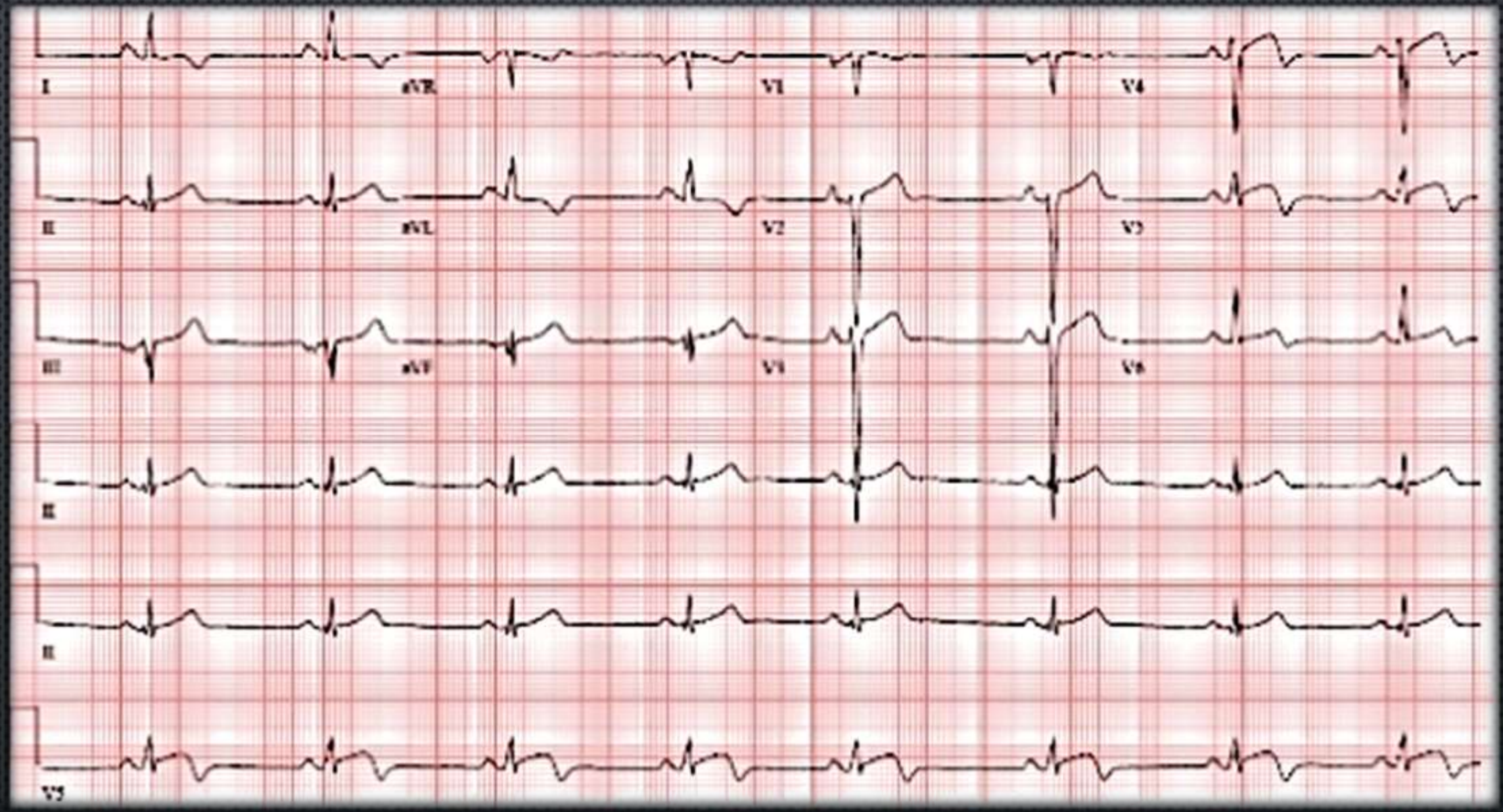
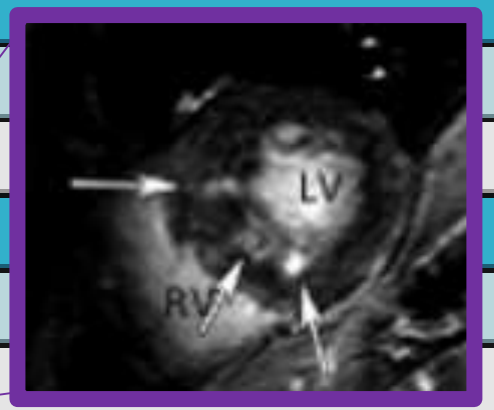


Table 9 **Clinical features that assist in the differential diagnosis of hypertensive heart disease and hypertrophic cardiomyopathy**

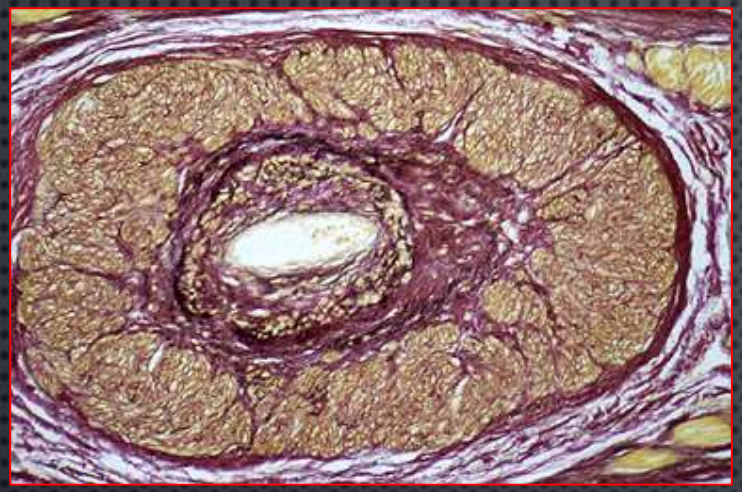
Clinical features favouring hypertension only
Normal 12 lead ECG or isolated increased voltage without repolarisation abnormality
Regression of LVH over 6–12 months tight systolic blood pressure control (<130 mm Hg)[166]
Clinical features favouring hypertrophic cardiomyopathy
Family history of HCM
Right ventricular hypertrophy
Late gadolinium enhancement at the RV insertion points or localized to segments of maximum LV thickening on CMR
Maximum LV wall thickness ≥15 mm (Caucasian); ≥20 mm (black)
Severe diastolic dysfunction
Marked repolarisation abnormalities, conduction disease or Q-waves on 12 lead ECG

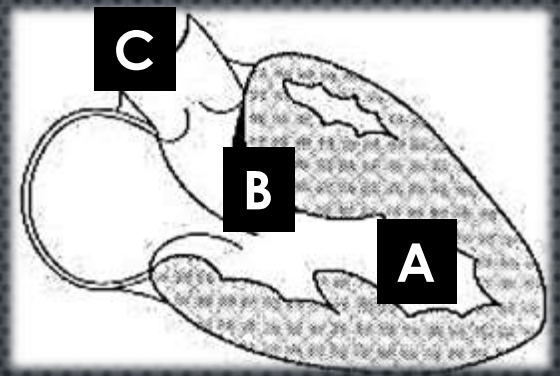


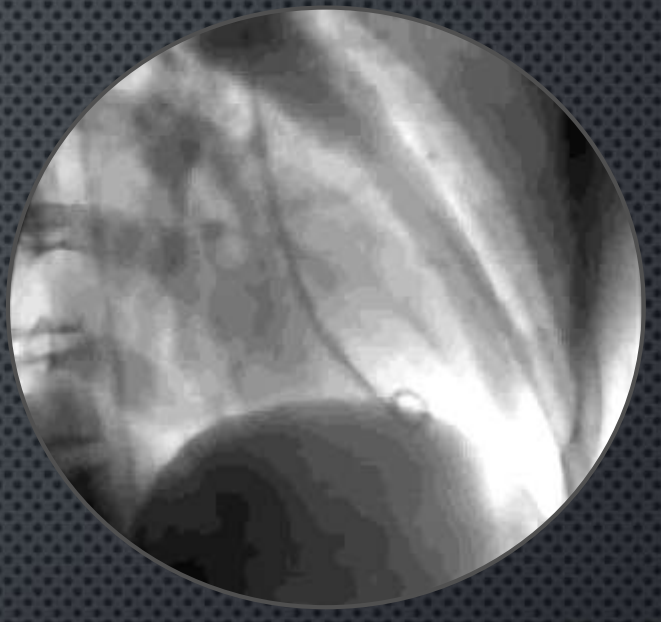
ECG = electrocardiogram; CMR = cardiac magnetic resonance imaging; HCM = hypertrophic cardiomyopathy; LV = left ventricle; LVH = left ventricular hypertrophy; RV = right ventricle.

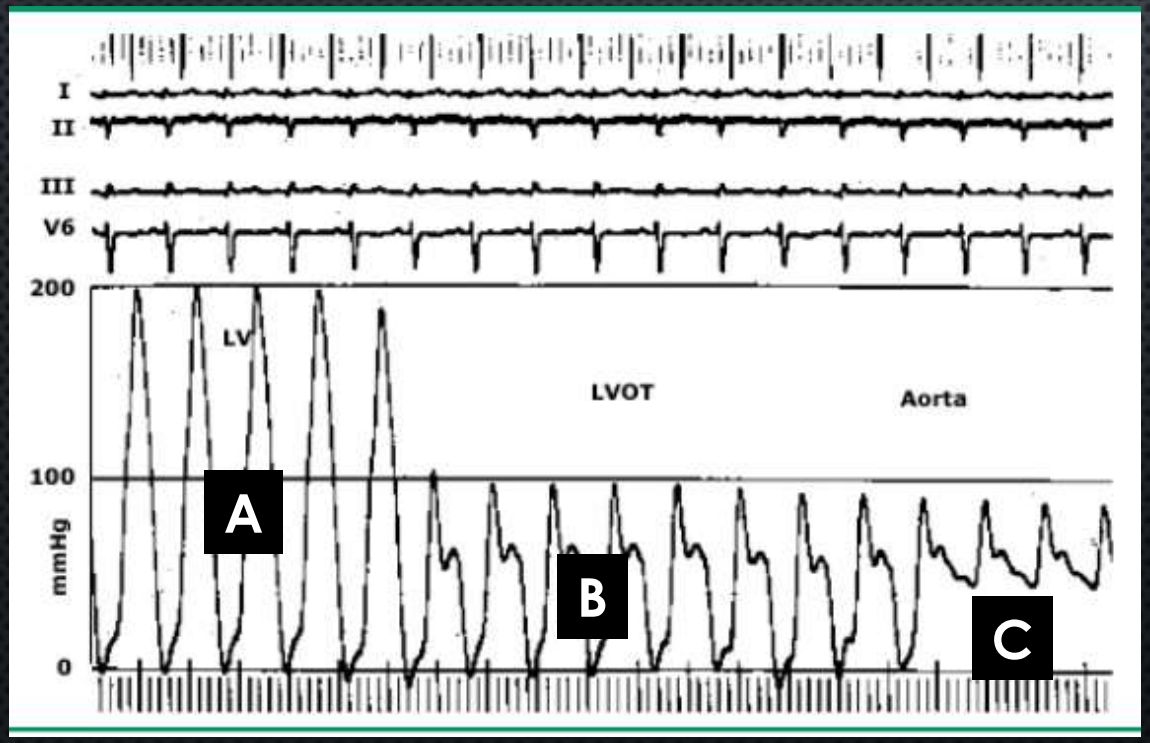
European Heart Journal (2014) 35, 2733–2779

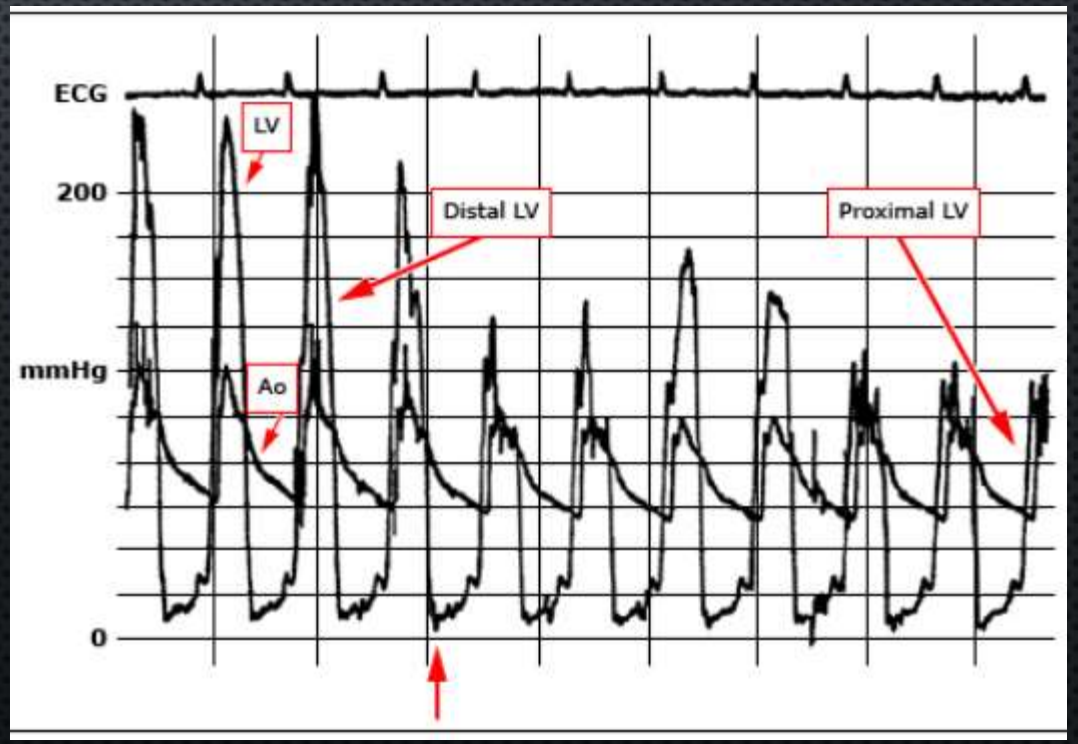
HOCM PATIENTS HAVE SMALL VESSELS: ANGINA











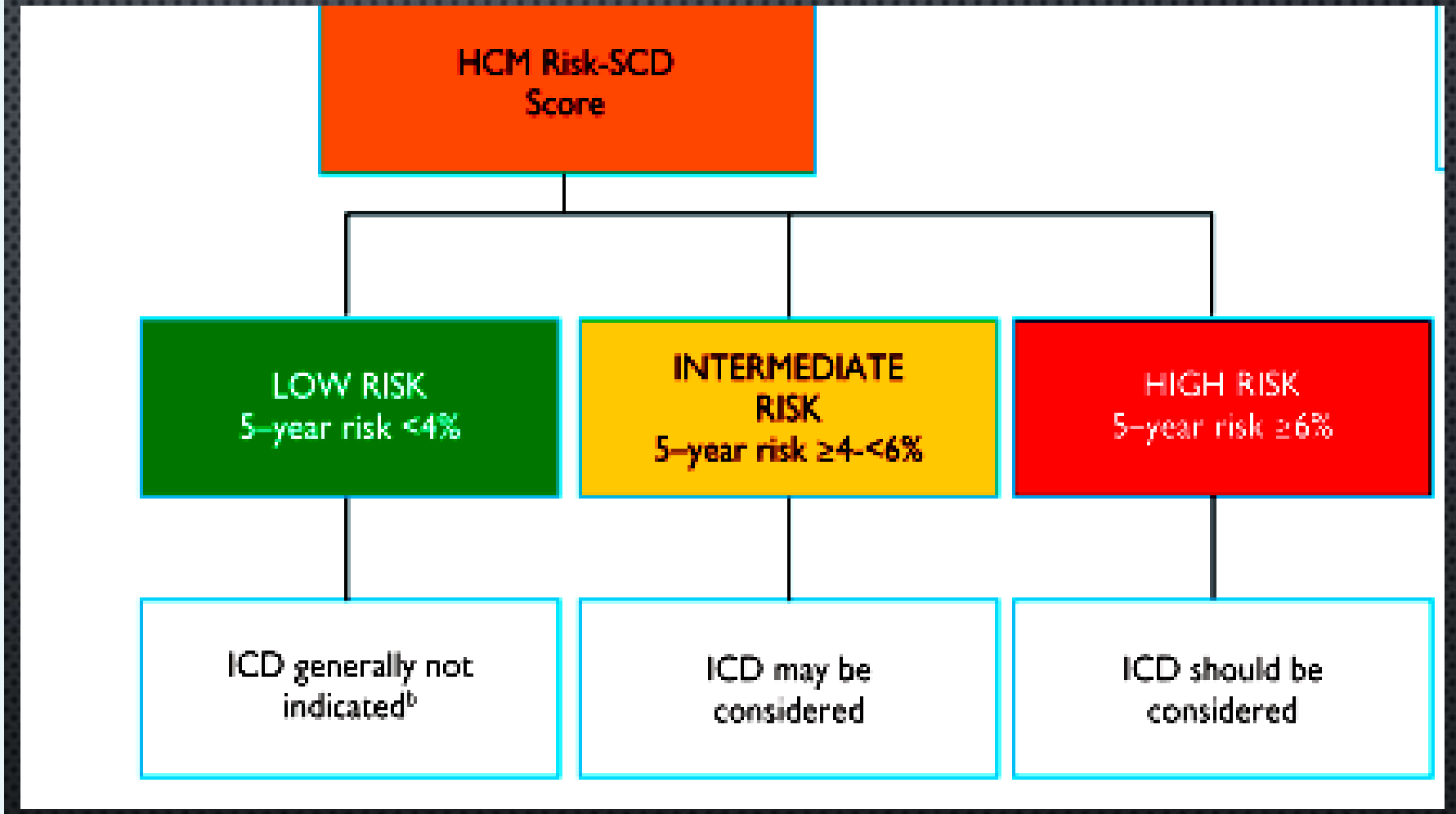
PRIMARY PREVENTION

Recommended assessment:

History
2D/Doppler echocardiogram
48–hour ambulatory ECG

HCM Risk-SCD variables:

- Age
- Family history of sudden cardiac death
- Unexplained syncope
- Left ventricular outflow gradient[a]
- Maximum left ventricular wall thickness[a]
- Left atrial diameter[a]
- NSVT



European Heart Journal (2014) 35, 2010–2020
doi:10.1093/eurheartj/eht439

FASTTRACK CLINICAL RESEARCH
Myocardial disease

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[3], 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[2,3] and Perry M. Elliott[1]*, for the Hypertrophic Cardiomyopathy Outcomes Investigators

European Heart Journal (2014) 35, 2010–2020

Table 4 Summary of the characteristics of patients with sudden cardiac death endpoints and univariable Cox regression models

Predictor variable	SCD group characteristics ($n = 198$)[a,b]	Hazard ratio	95% confidence interval	*P*-value
Age (years)	42.5 ± 15	0.988	0.979, 0.997	0.007
Maximal wall thickness (mm)	21.5 ± 6	1.048	1.025, 1.071	<0.001
Fractional shortening (%)	41.0 ± 10	0.992	0.977, 1.008	0.344
Left atrial diameter (mm)	46.2 ± 9	1.035	1.018, 1.052	<0.001
Left ventricular outflow gradient (mmHg)	18 (6–58)	1.005	1.001, 1.008	0.005
Family history of sudden cardiac death	73 (37%)	1.760	1.318, 2.350	<0.001
Non-sustained ventricular tachycardia	62 (31%)	2.533	1.849, 3.469	<0.001
Unexplained syncope	52 (26%)	2.326	1.693, 3.195	<0.001

Variables are expressed as mean ± standard deviation (SD), median and interquartile range (IQR) or counts and percentages as appropriate.
[a]Range of values (minimum; maximum) in SCD group: age: 16.3; 77.4 years, maximal wall thickness: 9; 37 mm, fractional shortening: 15; 62%, left atrial diameter: 28; 70 mm, maximal left ventricular outflow tract gradient: 2;190 mmHg.
[b]Missing data in SCD group: maximal wall thickness: 3%, fractional shortening: 11%, left atrial diameter: 6%, left ventricular outflow tract gradient: 3%, non-sustained ventricular tachycardia: 19%, unexplained syncope: 2%.

HCM risk prediction.pdf

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 syncope	○ No ○ Yes	*History of unexplained syncope at or prior to evaluation.*

Risk of SCD at 5 years (%):	
ESC recommendation:	

Reset

2014 ESC Guidelines on Diagnosis and Management of Hypertrophic Cardiomyopathy (Eur Heart J 2014 – doi:10.1093/eurheartj/ehu284)

O'Mahony C et al Eur Heart J (2014) 35 (30): 2010-2020

HCM Risk-SCD should not be used in:

- *Paediatric patients (<16 years)*
- *Elite/competitive athletes*
- *HCM associated with metabolic diseases (e.g. Anderson-Fabry disease), and syndromes (e.g. Noonan syndrome).*
- *Patients with a previous history of aborted SCD or sustained ventricular arrhythmia who should be treated with an ICD for secondary prevention.*

Caution should be exercised when assessing the SCD in patients following invasive reduction in left ventricular outflow tract obstruction with myectomy or alcohol septal ablation.

Pending further studies, HCM-RISK should be used cautiously in patients with a maximum left ventricular wall thickness ≥35 mm.

Major clinical features associated with an increased risk of sudden cardiac death in adults

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,[68] severe LVH[375] and unexplained syncope.[99]
Non-sustained ventricular tachycardia	• NSVT (defined as ≥3 consecutive ventricular beats at ≥120 BPM lasting <30 seconds) 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.[68,376]
Maximum left ventricular 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 but there are few data in patients with extreme hypertrophy (≥35 mm).
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.
Syncope **If no other reason**	• Syncope is common in patients with HCM but is challenging to assess as it has multiple causes.[379] • Non-neurocardiogenic syncope for which there is no explanation after investigation is associated with increased risk of SCD. • Episodes within 6 months of evaluation may be more predictive of SCD.[99]
Left atrial diameter	• Two studies have reported a positive association between LA size and SCD.[73,99] 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 (see section 9.4).
Left ventricular outflow tract obstruction	• A number of studies have reported a significant association with LVOTO and SCD.[73,82,83,246,372,380] Several unanswered questions remain, including the prognostic importance of provocable LVOTO and the impact of treatment (medical or invasive) on SCD.
Exercise blood pressure response **<40 drop om ETT Pressure BAD**	• Approximately one third of adult patients with HCM have an abnormal systolic blood pressure response to exercise characterised by progressive hypotension or a failure to augment the systolic blood pressure that is caused by an inappropriate drop in systemic vascular resistance and a low cardiac output reserve.[241,381] • Various definitions for abnormal blood pressure response in patients with HCM have been reported; for the purposes of this guideline an abnormal blood pressure response is defined as a failure to increase systolic pressure by at least 20 mm Hg from rest to peak exercise or a fall of >20 mm Hg from peak pressure.[337] • Abnormal exercise blood pressure response is associated with a higher risk of SCD in patients aged ≤40 years,[337] but its prognostic significance in patients >40 years of age is unknown.

Recommendations on prevention of sudden cardiac death

Recommendations	Class[a]	Level[b]	Ref.[c]
Avoidance of competitive sports[d] is recommended in patients with HCM	I	C	395
ICD implantation is recommended in patients who have survived a cardiac arrest due to VT or VF, or who have spontaneous sustained VT causing syncope or haemodynamic compromise, and have a life expectancy of >1 year.	I	B	327,367, 391–393
HCM Risk-SCD is recommended as a method of estimating risk of sudden death at 5 years in patients aged ≥16 years without a history of resuscitated VT/VF or spontaneous sustained VT causing syncope or haemodynamic compromise.	I	B	73
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	73

Recommendations on prevention of sudden cardiac death

Recommendations	Class[a]	Level[b]	Ref.[c]
ICD implantation is not recommended in patients with an estimated 5-year risk of SCD of <4% and no other clinical features that are of proven prognostic importance.	III	B	73,327, 393,396

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HOCM guidelines euro.pdf

JACC: HEART FAILURE
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Long-Term Outcomes After Medical and Invasive Treatment in Patients With Hypertrophic Cardiomyopathy

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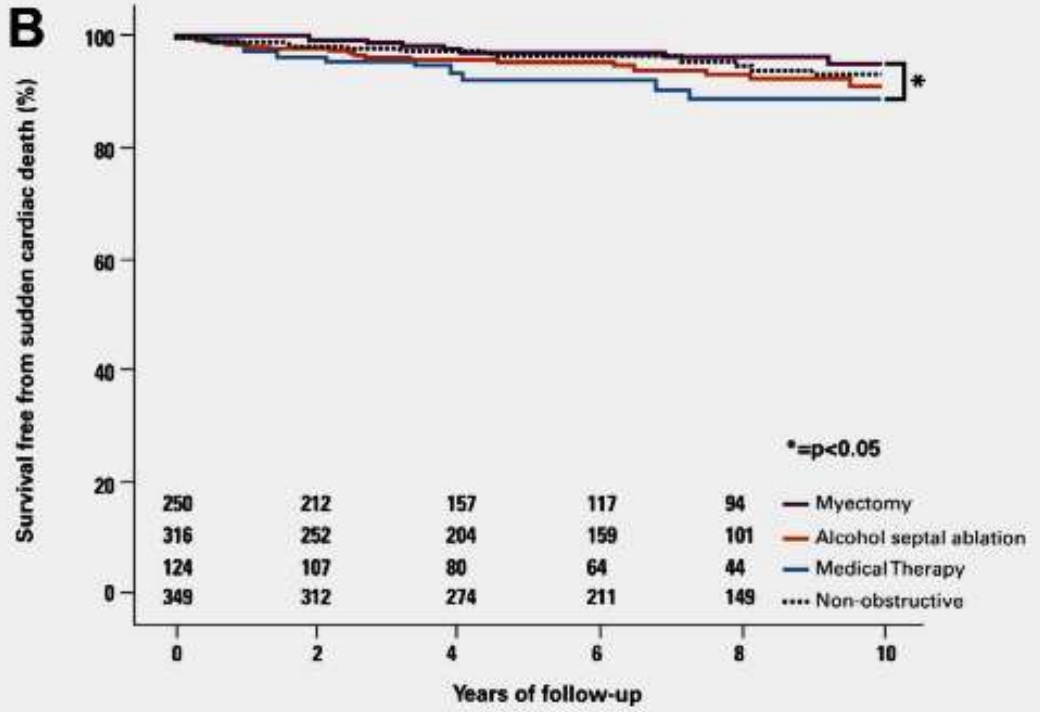


TABLE 3 Mortality and SCD in 1,047 Patients With HCM

Variable	Medical Treatment (n = 124)	ASA (n = 321)	Myectomy (n = 253)	Control (Nonobstructive HCM) (n = 349)
Follow-up (yrs)	7.1 ± 4.8*	6.3 ± 3.6†	7.9 ± 6.1	8.7 ± 5.7
Mortality				
Periprodecural death	–	5 (1.6%)	3 (1.2%)	-
HCM-related death	11 (8.9%)	12 (3.7%)‡	21 (8.4%)	36 (10.3%)
Noncardiac death	8 (6.5%)	23 (7.2%)*	12 (4.8%)	13 (3.7%)
Unknown death	0 (0%)	3 (0.9%)	6 (2.4%)	3 (0.8%)
Total	19 (15.3%)	38 (11.8%)	39 (15.6%)	52 (14.9%)
5-yr survival	89%	91%	92%	95%
10-yr survival	84%	82%	85%	85%

CONCLUSIONS Patients with obstructive HCM who are treated at referral centers for HCM care have good survival and low SCD risk, similar to that of patients with nonobstructive HCM. **The SCD risk of patients after myectomy was lower than after ASA** or in the medical group. (J Am Coll Cardiol HF 2014;2:630–6) © 2014 by the American College of Cardiology Foundation.

Closing summary

Recommended tests in patients with definite or suspected HCM

1. Standard 12-lead electrocardiography.

2. Transthoracic 2-D and Doppler echocardiography (including assessment of left ventricular outflow tract obstruction at rest and during Valsalva manoeuvre in the sitting and semi-supine positions).

3. Upright exercise testing

4. 48 hour ambulatory ECG monitoring.

5. Cardiac magnetic resonance imaging should be considered if local resources and expertise permit.

Management of Atrial tachyarrhythmia

1. Rate control using ß-blockers and non-dihydropyridine calcium channel antagonists, alone or in combination, is recommended in patients with paroxysmal, persistent or permanent AF*. Digoxin and Class IC anti-arrhythmics should be avoided. Amiodarone should be considered for rhythm control and to maintain sinus rhythm after cardioversion.

2. In new onset AF*, elective DC* cardioversion should be considered after a minimum of 3 weeks of effective anticoagulation with a vitamin K antagonist.

3. Use of the CHA2DS2-VASc score to calculate stroke risk is NOT recommended in patients with HCM*.

4. Life long therapy with oral anticoagulants is recommended even when sinus rhythm is restored.

Sudden death prevention

1. Patients with HCM* should be advised not to participate in competitive sports and discouraged from intense physical activity, especially when they have risk factors for sudden cardiac death or left ventricular outflow tract obstruction.

2. ICD* implantation is recommended in patients who have survived a cardiac arrest due to ventricular fibrillation or experienced spontaneous sustained ventricular tachycardia causing haemodynamic compromise.

3. Risk assessment in all other patients should include clinical evaluation, family history, 48 hour ambulatory ECG*, TTE* (or CMR* in the case of poor echo windows) and a symptom limited exercise test. A predefined set of prognostic variables are then used to estimate the 5-year risk of SCD* using the HCM* Risk-SCD* model (see online calculator http://doc2do.com/hcm/webHCM.html) in order to provide advice on prophylactic ICD* therapy.

Routine follow-up

1. A clinical evaluation, including 12-lead ECG* and transthoracic echocardiogram is recommended every 12–24 months in clinically stable patients and whenever there is a change in symptoms.

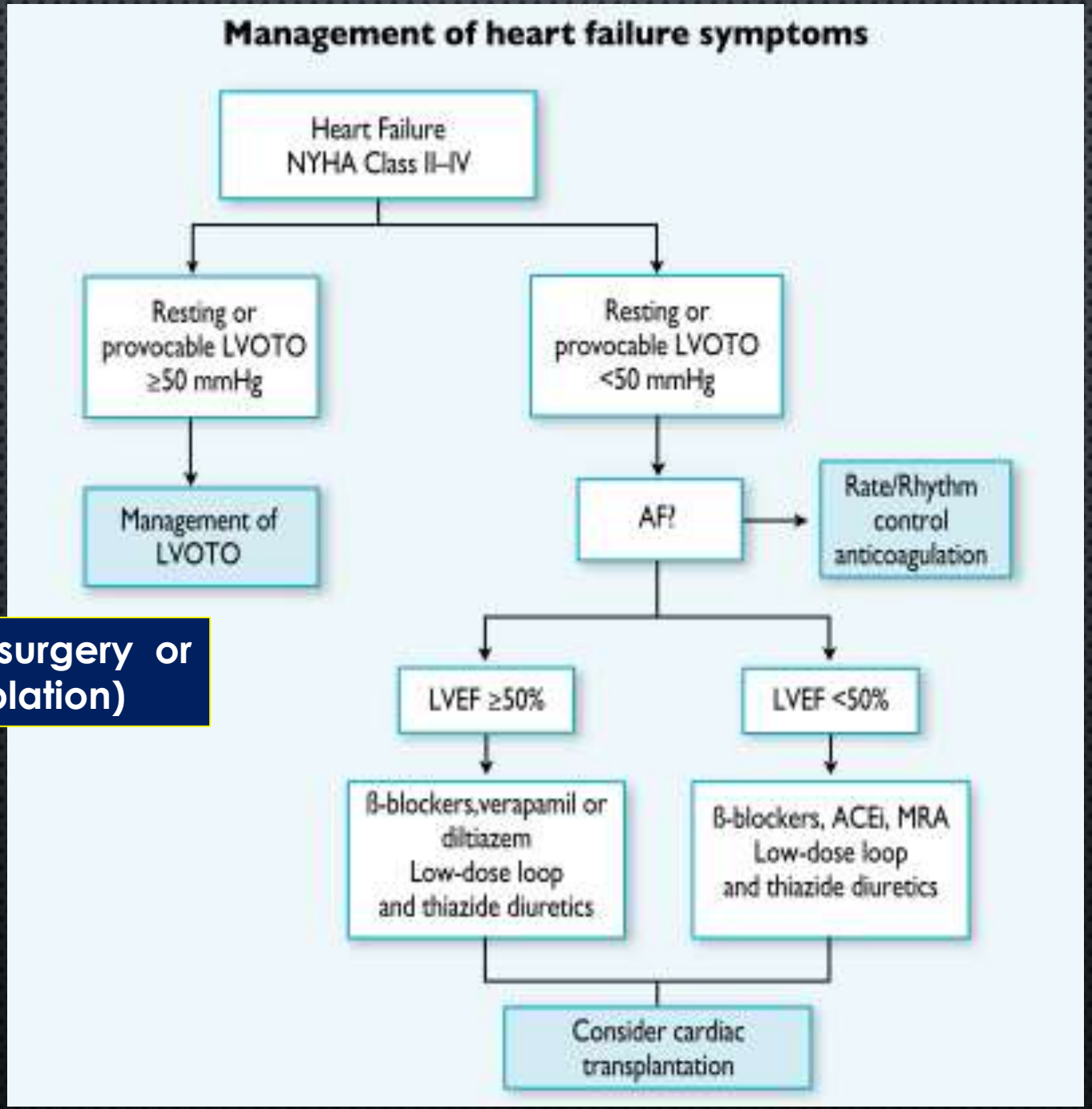
2. 48-hour ambulatory ECG* is recommended every 12–24 months in clinically stable patients, every 6–12 months in patients in sinus rhythm with left atrial dimension ≥45 mm, and whenever patients complain of new palpitations.

Management of left ventricular outflow tract obstruction

1. Patients with left ventricular outflow tract obstruction should avoid dehydration and excess alcohol consumption, and weight loss should be encouraged.

2. Non-vasodilating ß-blockers such as bisoprolol are recommended as first line therapy. If ineffective, additional therapy with disopyramide or alternatives such as verapamil or diltiazem should be considered after specialist evaluation.

3. Invasive treatment (surgery or alcohol septal ablation) to reduce left ventricular outflow tract obstruction should be considered in patients with a left ventricular outflow tract gradient ≥50 mmHg, moderate to severe symptoms (New York Heart Association (NYHA) functional class III-IV) and/or exertional or recurrent syncope resistant to maximum tolerated drug therapy.



Invasive treatment (surgery or alcohol septal ablation)