Hypertrophic Cardiomyopathy
" HCM "– Latest Management

Cardiology Structured Training Course
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HK College of Cardiology / HKPHCA Ltd
July, 2019

Conflicts of Interest

- I have ***NOTHING*** to disclose concerning this presentation

Outlines

- Epidemiology
- Diagnosis of HCM
- Differentiating from Athlete's Heart
- Overview of Treatment Options - Medical vs Surgical
- Role of Genetic Testing
- Sudden Cardiac Death
    - Assessing Risk
    - Assess ICD use

Recent Guidelines :

HCM – European Heart J, 2014;35, 2733-2779
JACC 2015;66;2362-2371
JACC Heart Failure; 11,Apr,2018

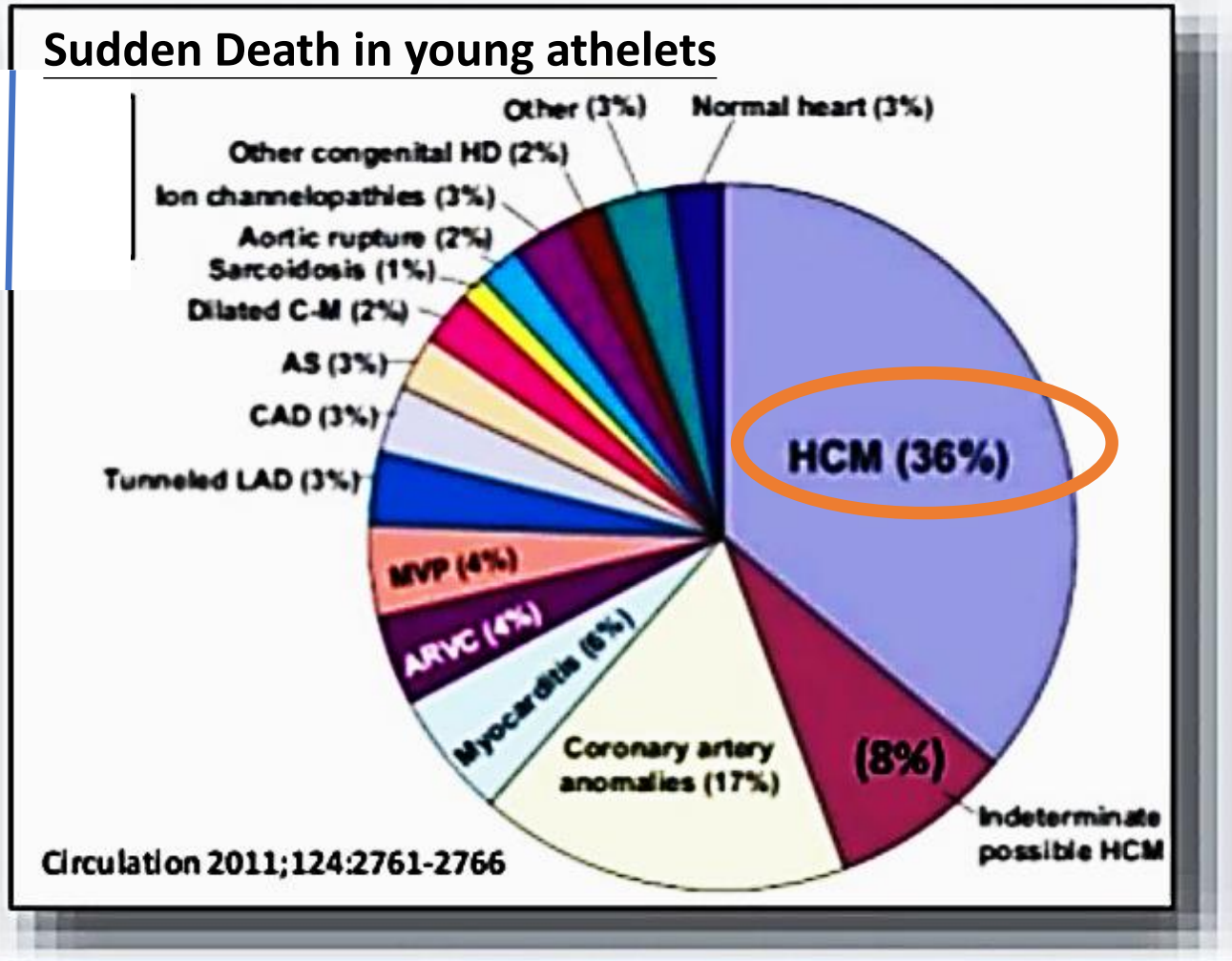
Sudden Death - EHJ 2015;36;2793-2867
Circulation 2015;133;1006-1026
Heart Rhythm, 15;10,oct,18

EPIDEMIOLOGY

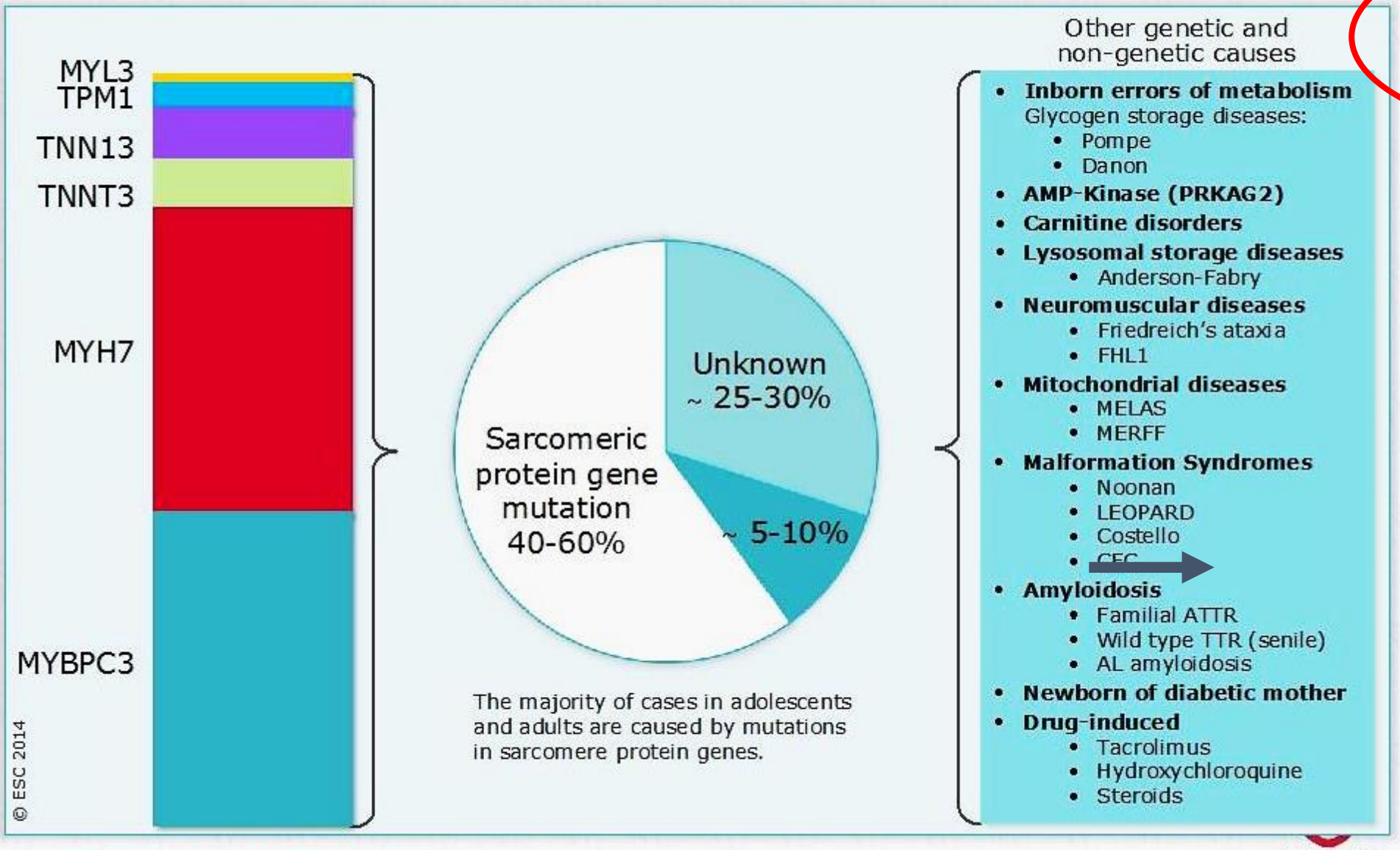
- Estimated that 700,000 to 1 million Americans have HCM
- Estimates pre-ICD era that HCM and SD mortality rates about 1.5% per year

* Now SCD around 1%/ year

From US National Registry of Sudden Death in Athletes. Recent update (no real change)
Am J Medicine 2016;129:1170



Diverse aetiology of hypertrophic cardiomyopathy



www.escardio.org/guidelines European Heart Journal (2014);35:2733-2779 - doi:10.1093/eurheartj/ehu284

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-**Autosomal Dominant Variable Penetrance and expressability**

-Caused by mutation in 1 of 11 cardiac sarcomere genes or adjacent Z disc genes

-1500 individual mutations known

-90% missense

Mutant genes - %

Beta-myosin Heavy chain -30-40%

Myosin binding protein C -30-40%

Troponin T - 10%

HCM - Diagnosis

HCM – Diagnosis

- LV wall thickness ≥ 15mm by Echocardiogram; CMR or CT in **Absence of Secondary causes**

- LVH typically manifests as **Asymmetrical Septal Hypertrophy**
- Other patterns : Apical; Concentric; Lateral wall or RT ventricular can occur
- **FIRST degree relatives** of PATIENTS with unequivocal diseases; Unexplained wall thickness >/= 13 mm -> Sufficient for diagnosis

Clinical Diagnosis of HCM

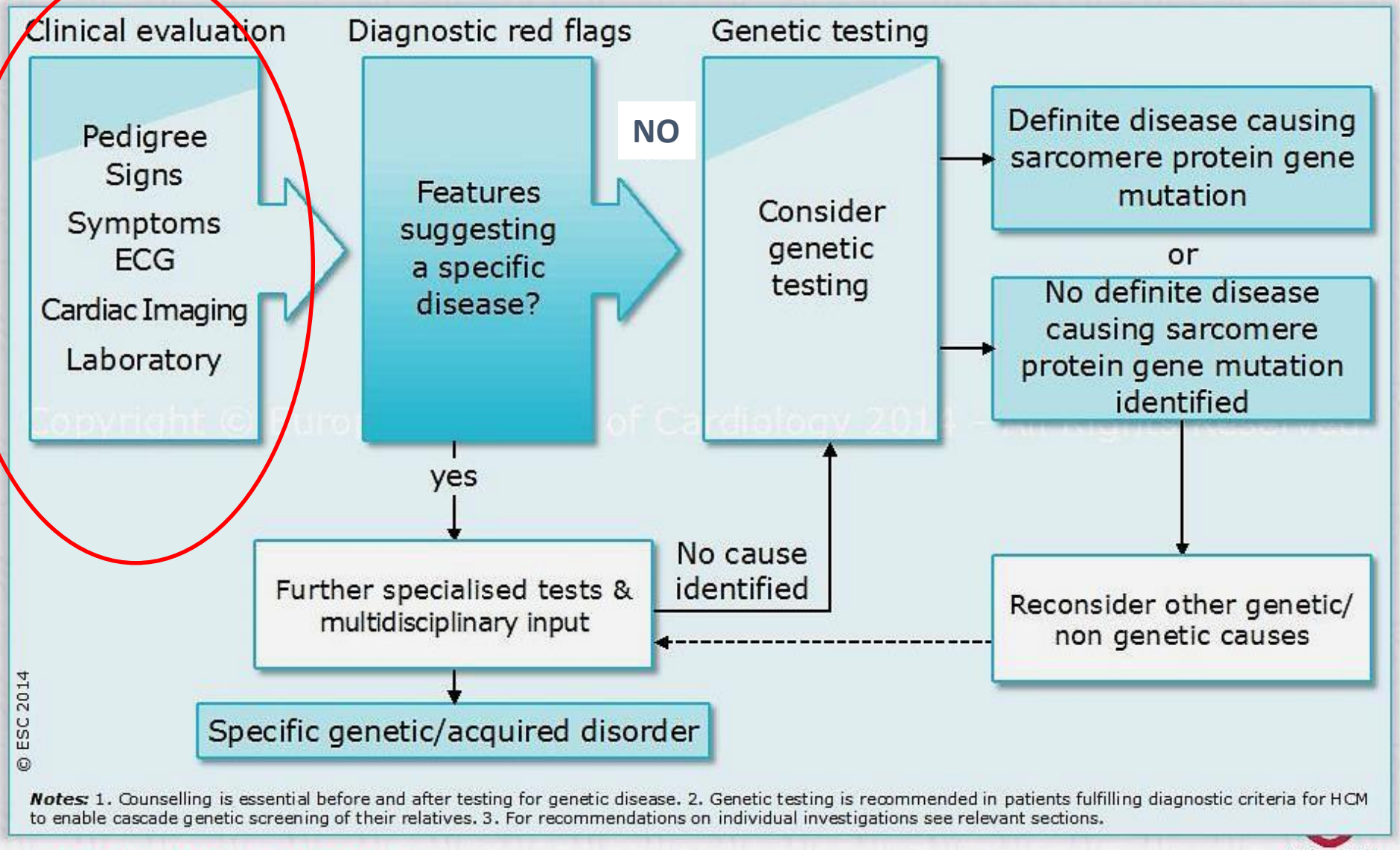
- ***In Adults:*** **One or more LV myocardial segments 15 mm or more in thickness**
- ***In Children:*** **Wall thickness > 2 standard deviations above mean**
- ***In Relatives:*** **One or more LV myocardial segments 13 mm or more**

- ***Dynamic LVOT obstruction definition:*** **>30 mmHg**

If LVOTO > 50 mmHg – Cause hemodynamic consequences

- **Common Challenges:**
  - LVH in athlete's heart caused by training
  - LVH due to hypertension or aortic stenosis
  - Isolated basal septal hypertrophy in the elderly (Sigmoid septum)
  - Severe LVH due to infiltrative diseases
  - LV noncompaction
  - Late stage wall thinning

Schematic summarising the general approach to the diagnosis of hypertrophic cardiomyopathy



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

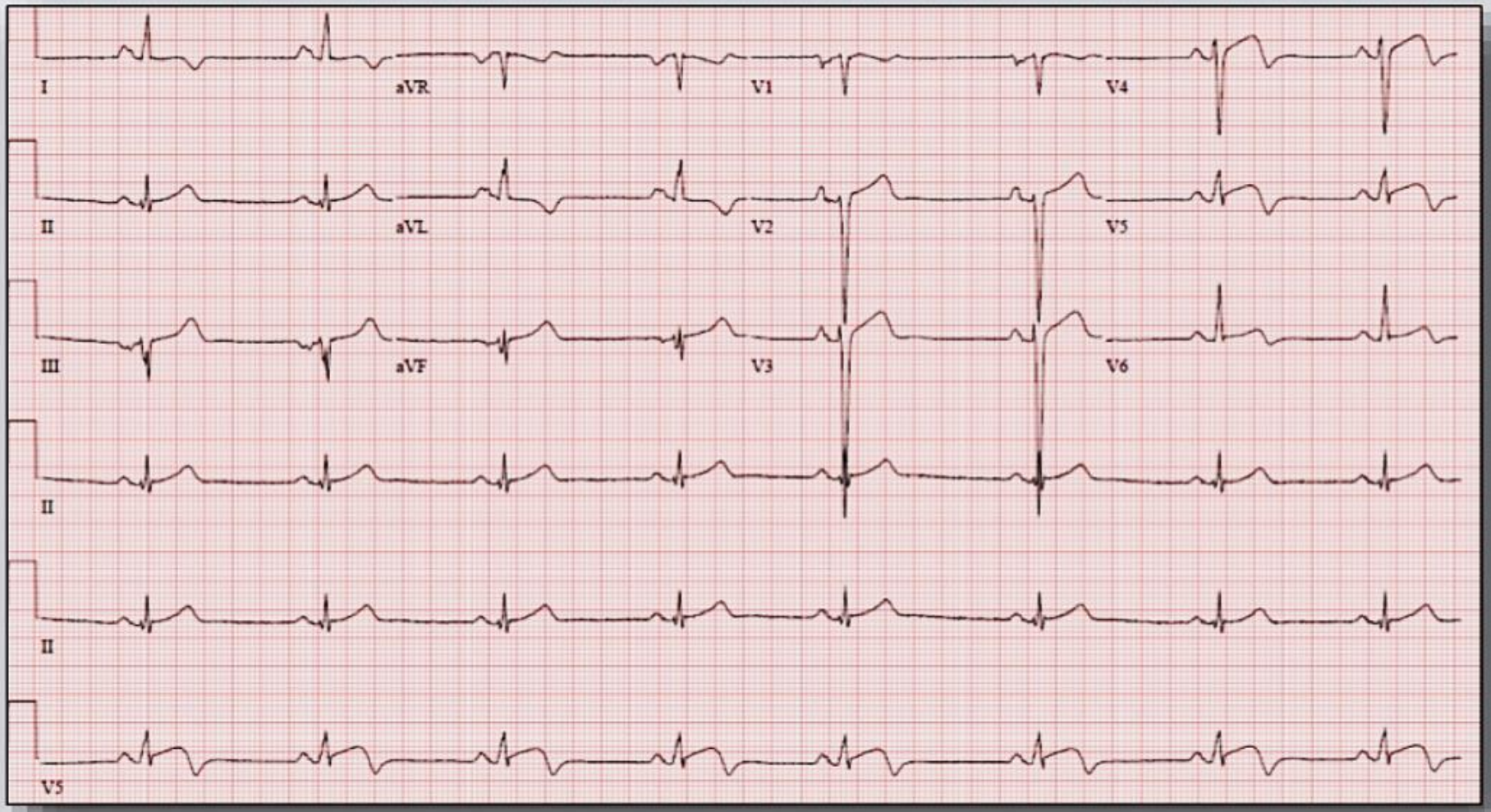
www.escardio.org/guidelines European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

Electrocardiography

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

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

ECG in Apical HCM



Transthoracic echocardiography evaluation in hypertrophic cardiomyopathy

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

STRESS ECHO

www.escardio.org/guidelines European Heart Journal (2014);35:2733–2779 - doi:10.1093/eurheartj/ehu284

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Hypertrophic Cardiomyopathy

Echocardiographic Diagnosis

Left Ventricular Hypertrophy ≥ 15 mm
(Asymmetric >> Symmetric)

In the absence of another cardiovascular or systemic disease associated with LVH or myocardial wall thickening

Gersh, BJ, et al. JACC 2011; 58: e212 ACC/AHA Guidelines

Hypertrophic Cardiomyopathy

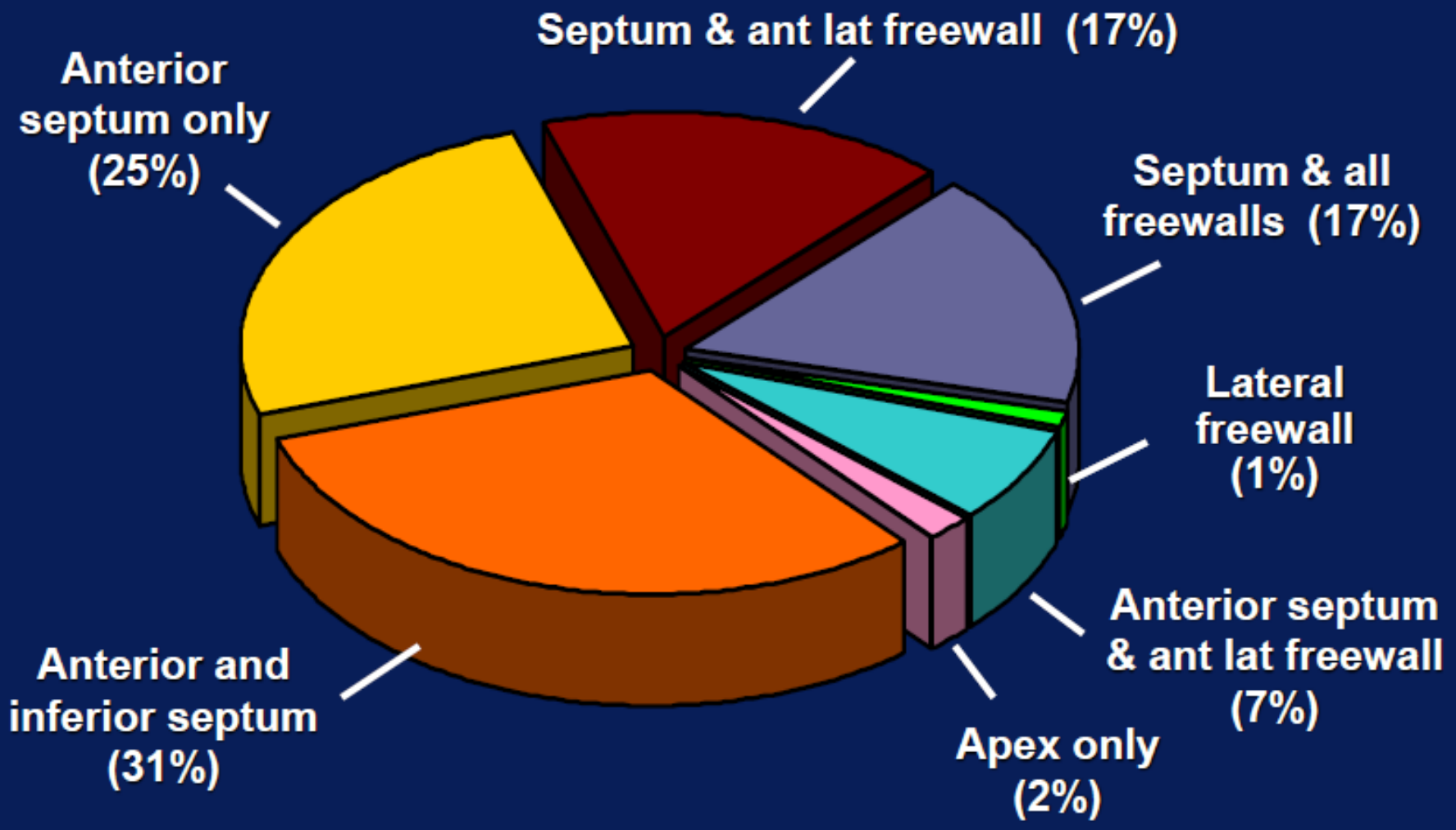
Echocardiographic Diagnosis

Not Mandatory for Diagnosis of HCM

- Asymmetric Septal Hypertrophy (ASH)
- Systolic Anterior Motion (SAM)
- Dynamic LVOT obstruction

Hypertrophic Cardiomyopathy

Distribution of LVH (600 Patients)

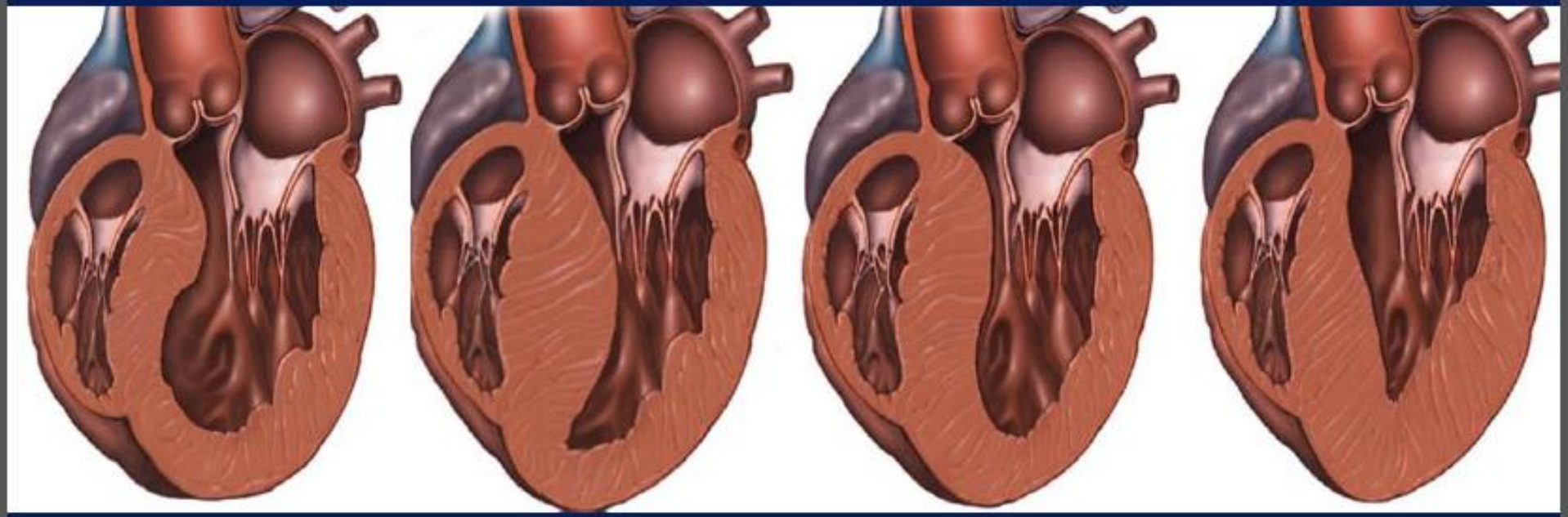


MAYO CLINIC

Klues HG, JACC 1995; 26: 1699

Left Ventricular Morphology in HCM

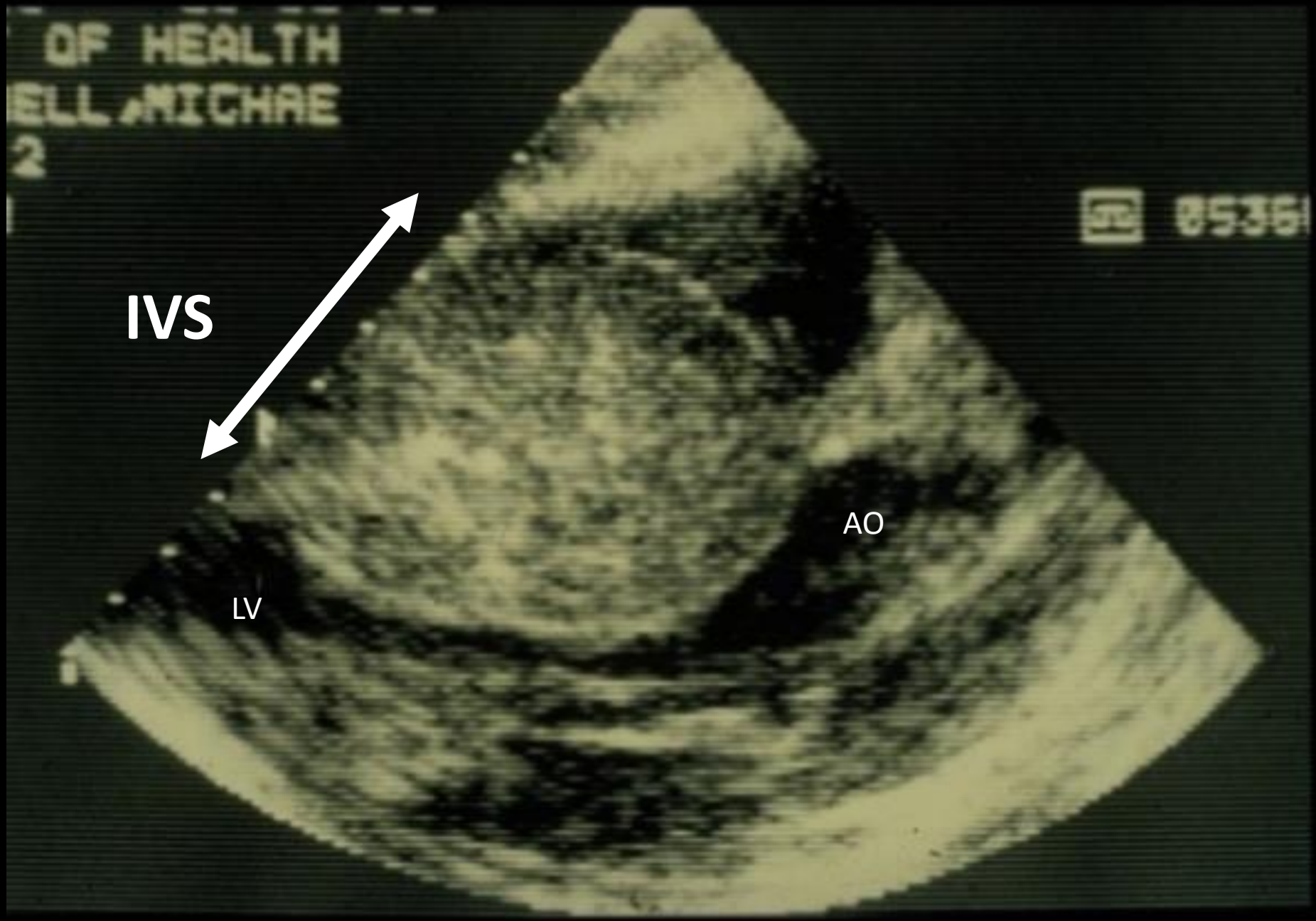
Sigmoid Septum	Reverse Septum	Neutral Septum	Apical Variant



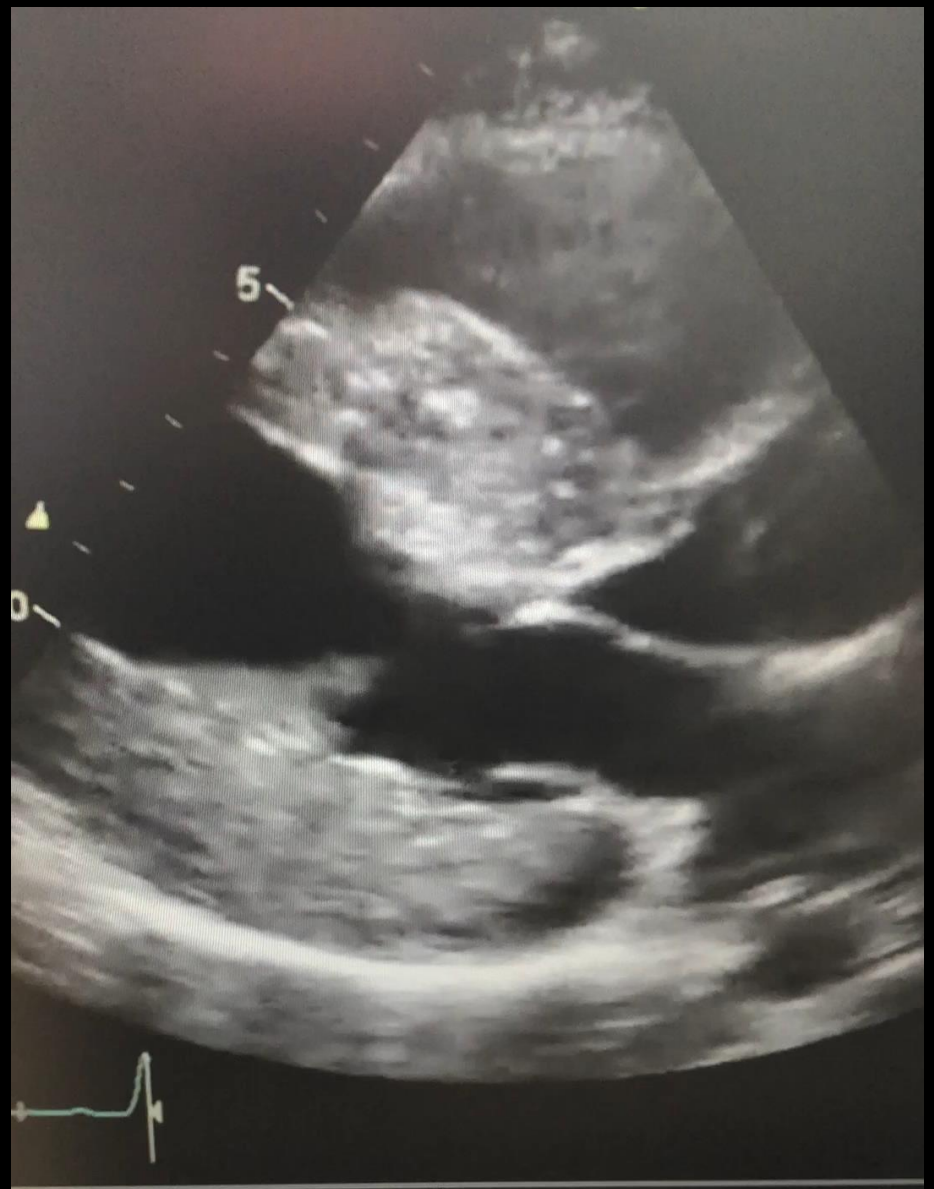
181(47%)	132(35%)	32(8%)	37(10%)
Gene + (8%)	Gene + (79%)	Gene + (41%)	Gene + (32%)

MAYO CLINIC

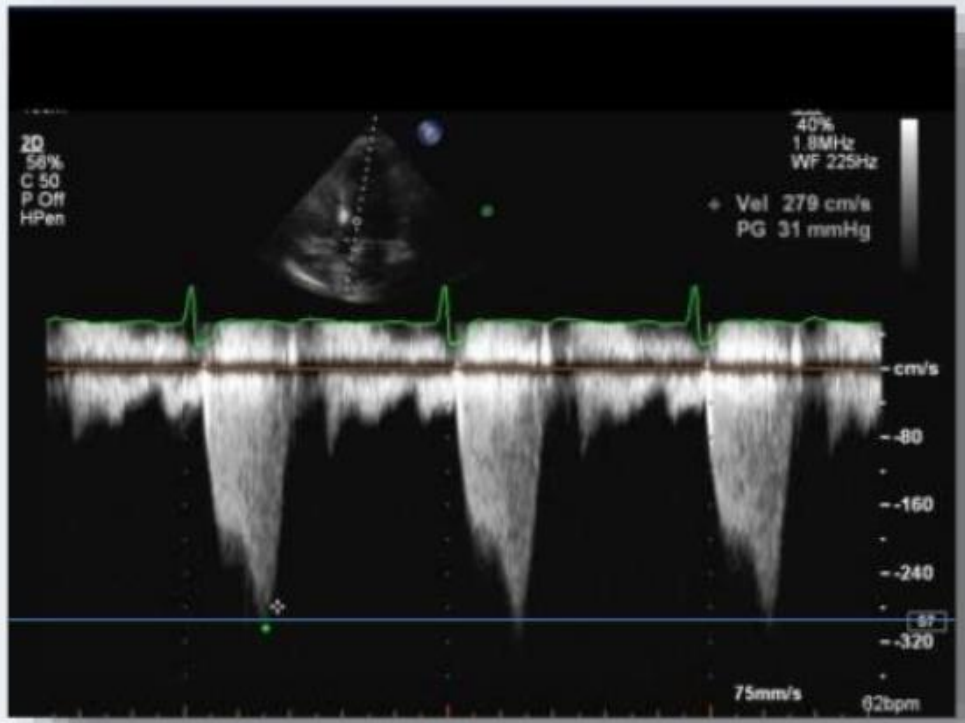
Binder J, et al. Mayo Clin Proc 2006; 81: 459.

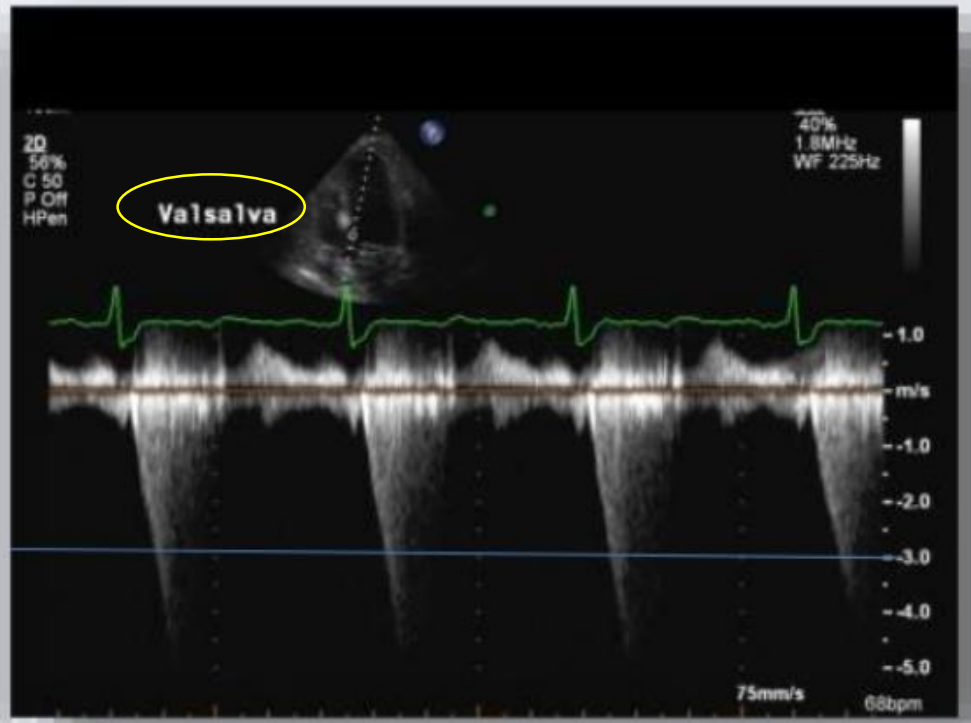

OF HEALTH
ELL MICHAE
2
IVS
AO
LV

ECHOCARDIOGRAM in HCM



Outflow Gradient at Rest and with Valsalva When LV Outflow Tract Obstruction Present





Resting Intraventricular Gradient= 31 mmHg → Gradient with Valsalva=60 mmHg

Cardiac -MRI in HCM

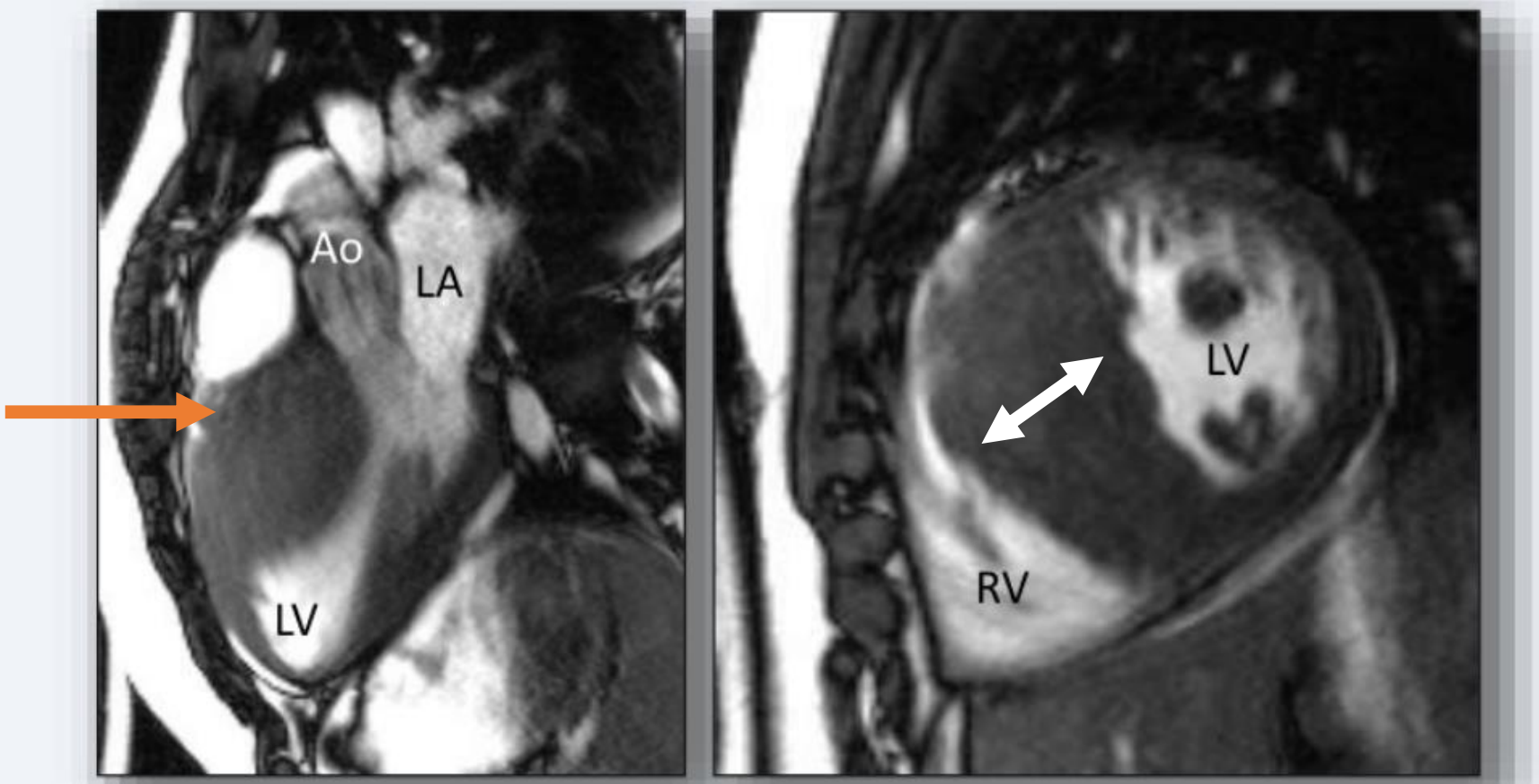
- **Advantages :**

- Superior spatial resolution
- Accurate volumetric assessment of **ALL chambers** ; LV mass calculation
- **NO** Limited echo windows – in Lung diseases; chest wall AbN
- Better define apical aneurysm, thrombus etc
- **LGE for fibrosis**

Drawbacks :

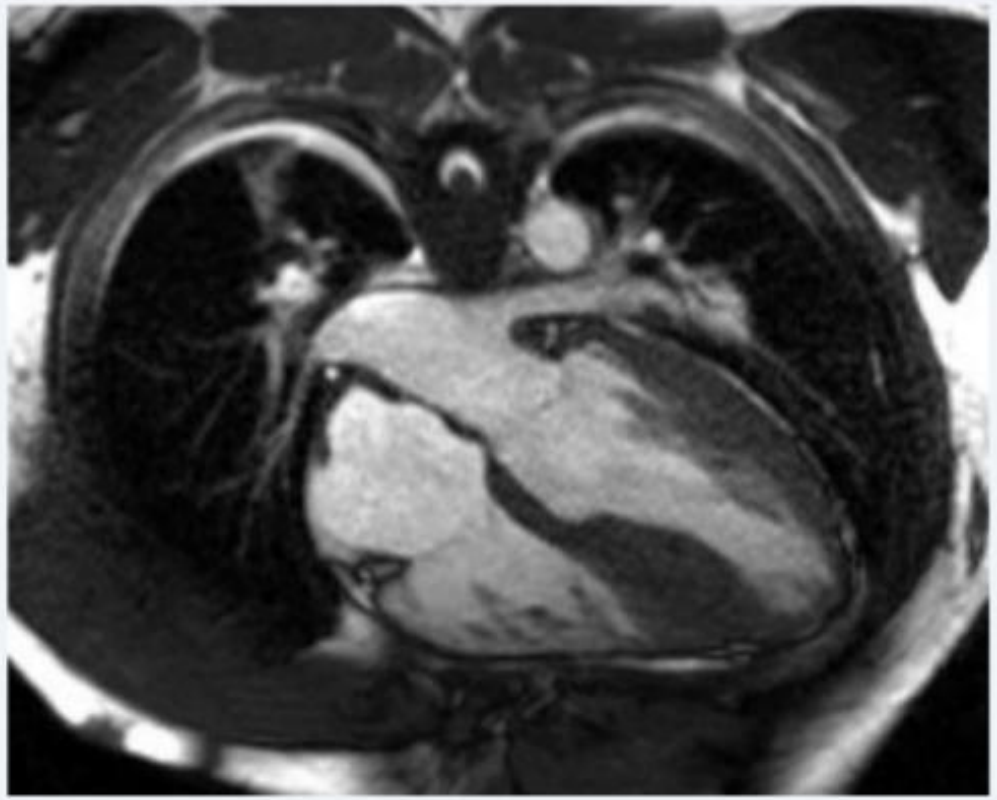
- Costs
- Inaccessible
- CRF- C/I for gadolinium
- Prolonged breath holding

MRI Findings of Hypertrophic Segmental Location

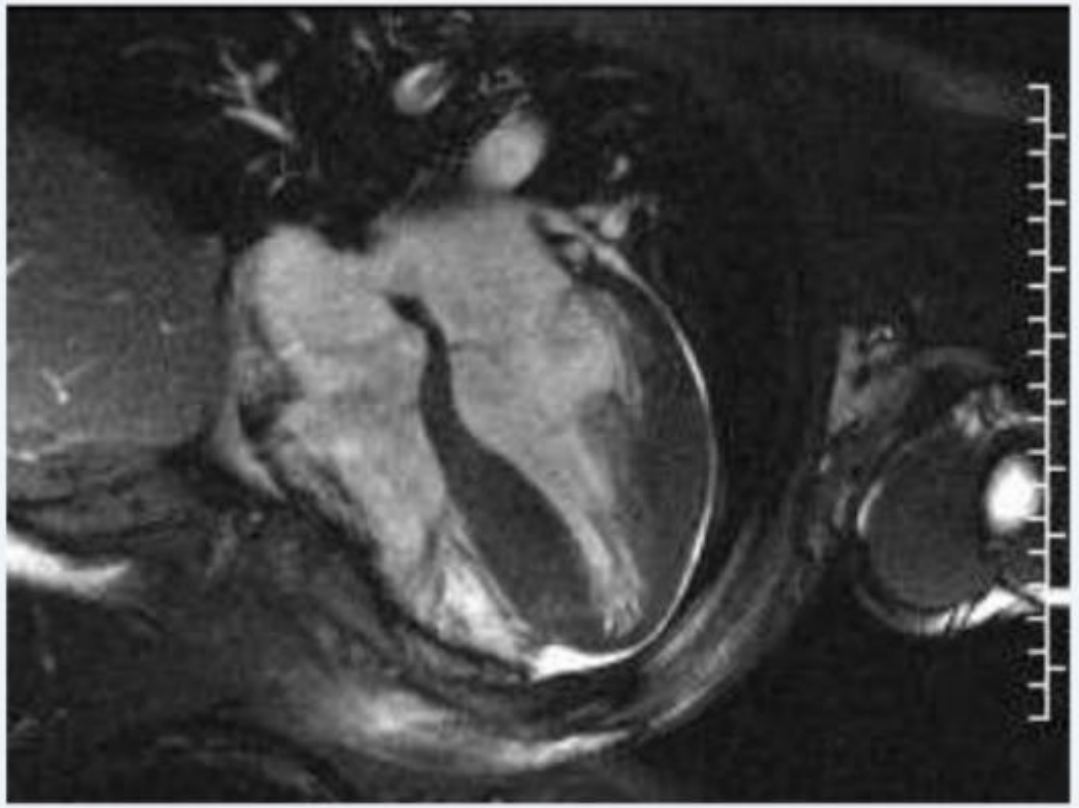


Marked Septal Hypertrophy

MRI Finding of Hypertrophic Location

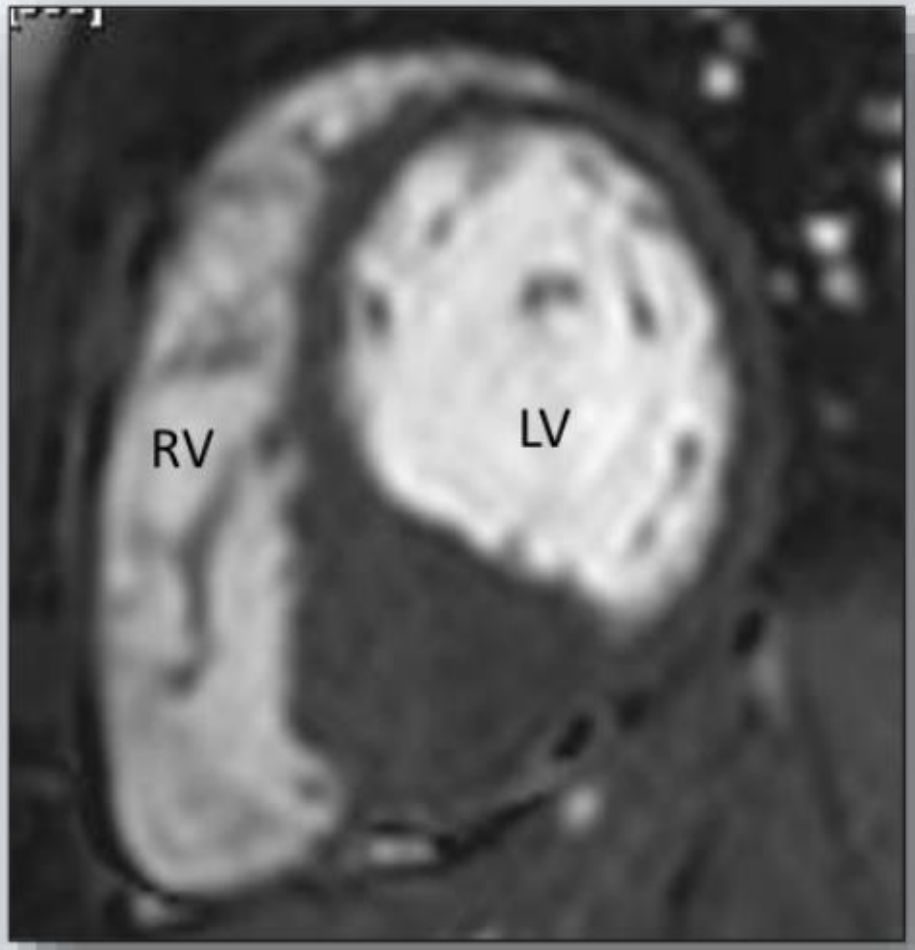


Mid-ventricular HCM

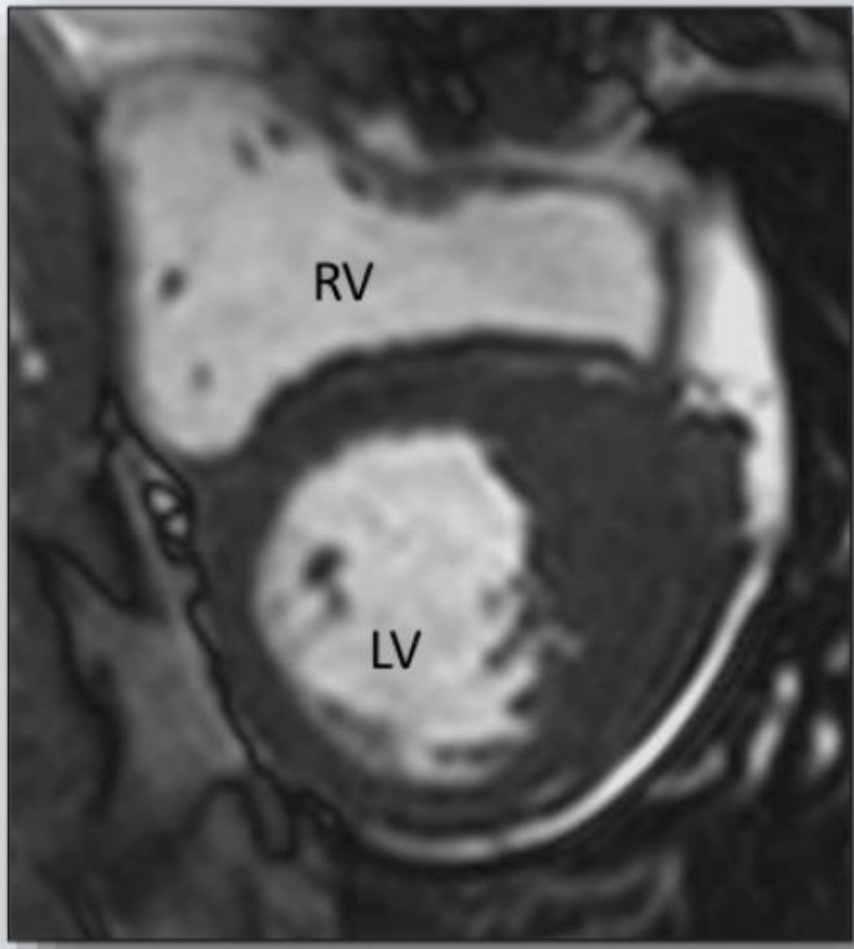


Apical HCM

MRI Finding of Hypertrophic Location

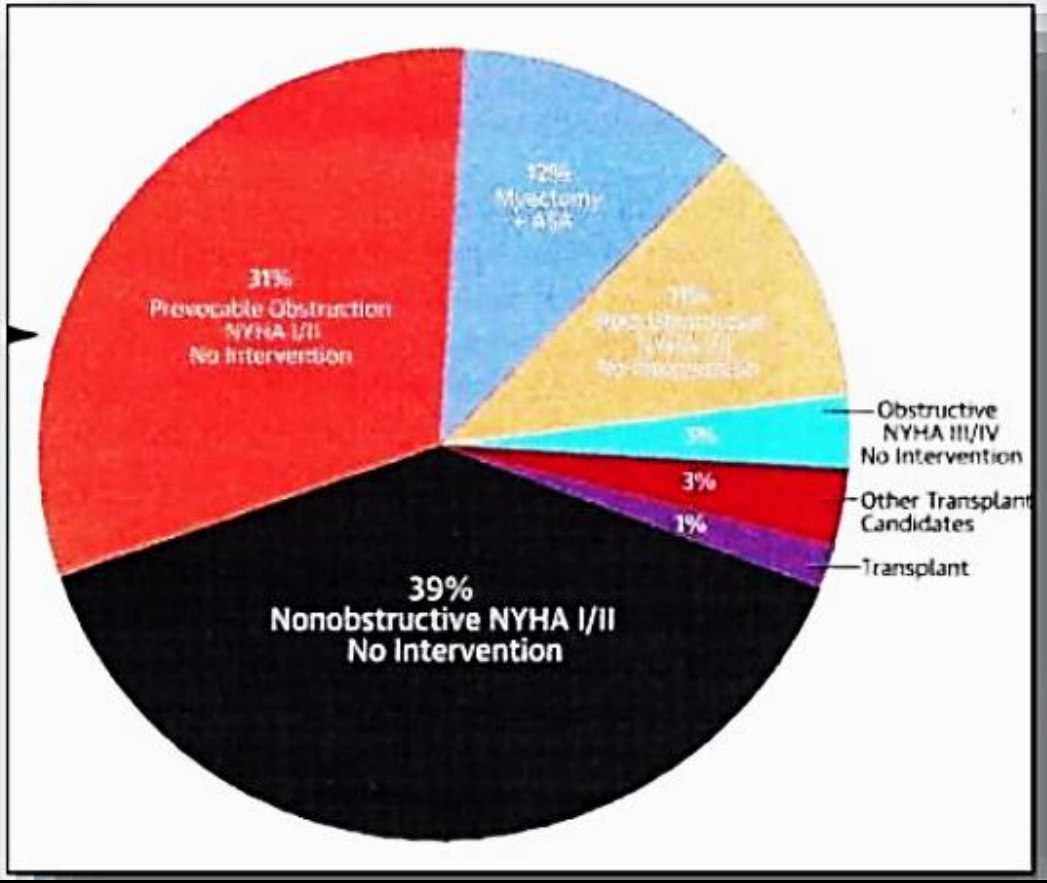


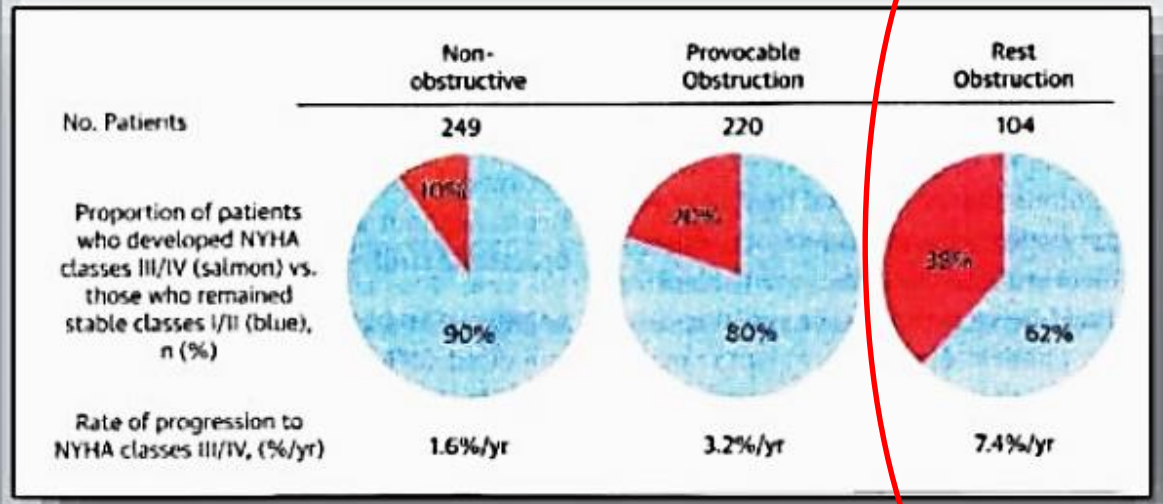
Basal Septum Only



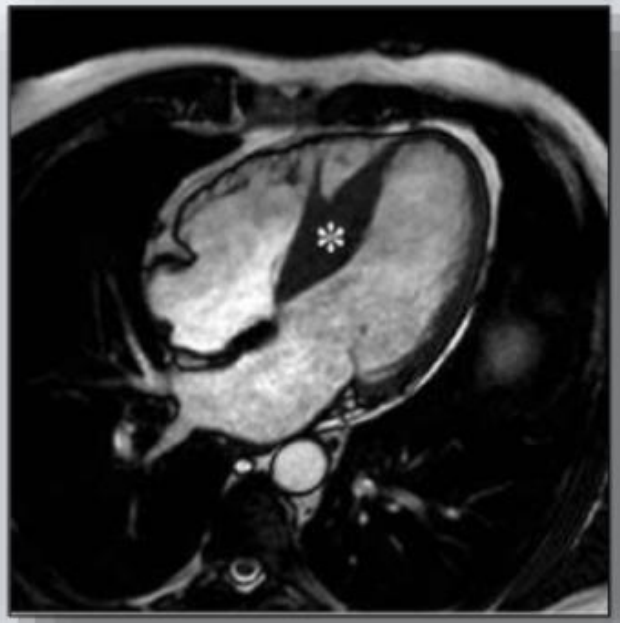
Anterolateral Free Wall

Location, Location, Location
A Better Prognosis if Nonobstructive

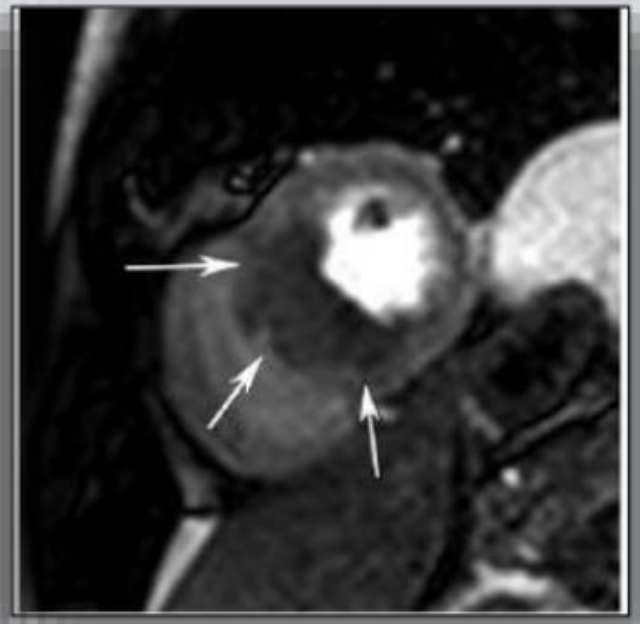




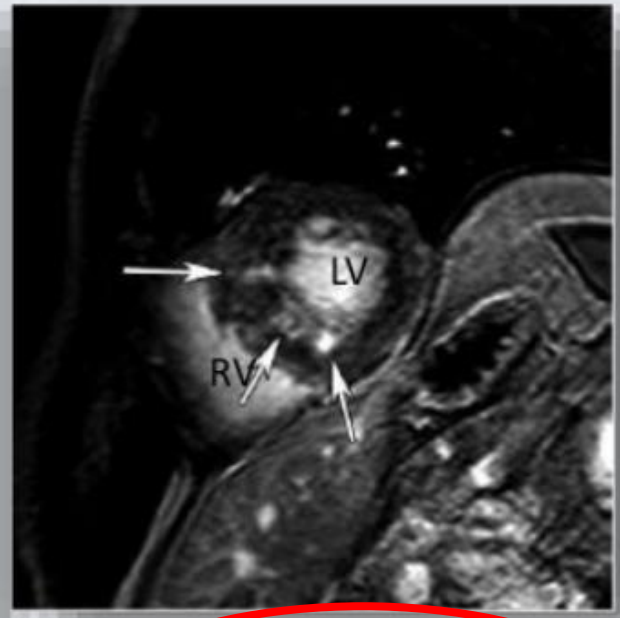
MRI Assessment



Anatomy

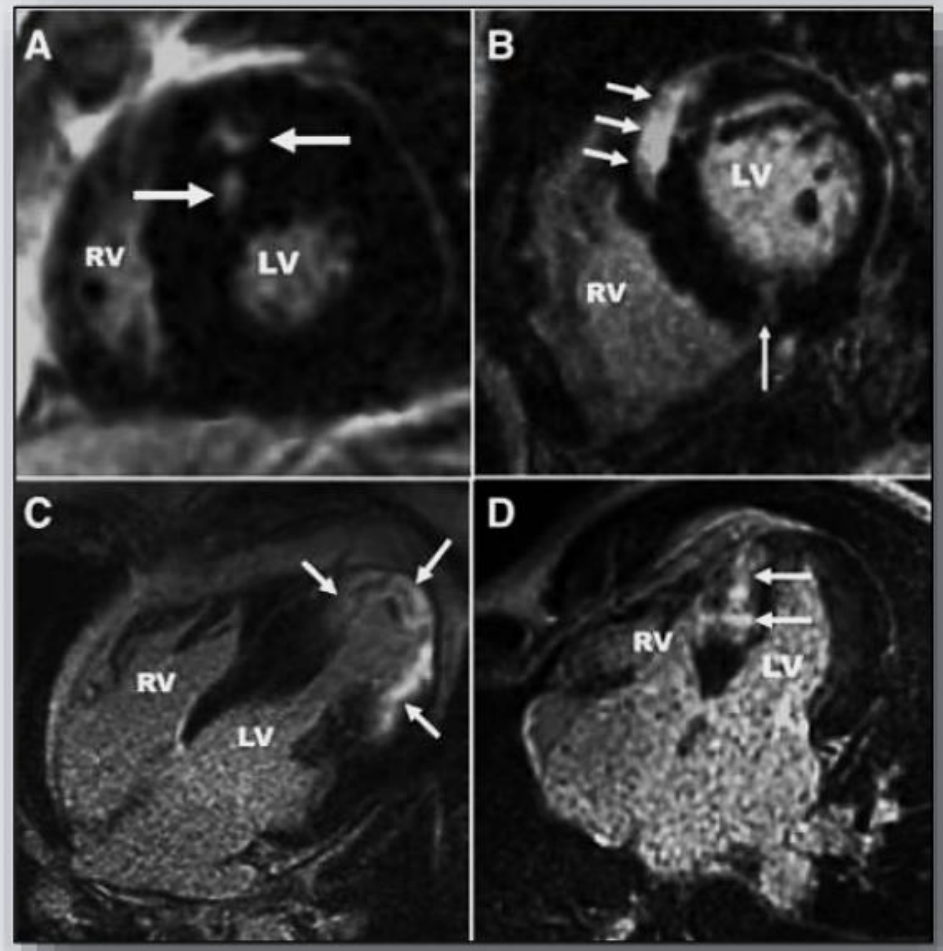


Myocardial Perfusion Abnormaliities

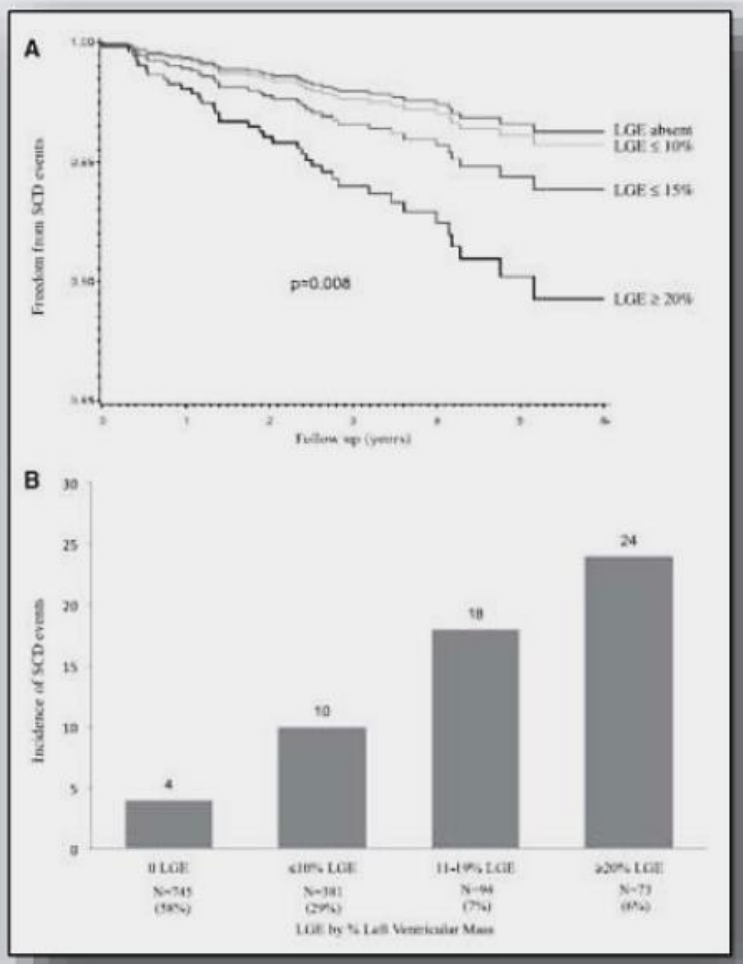


Late Gadolinium Enhancement (Scar)
RV Attachment and Midventricular

Degree of MRI Hyper-enhancement and Sudden Death Risk



Varying degrees of hyperenhancement



Endomyocardial biopsy

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

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

- **Differential Diagnosis - DDX**

Hypertrophic Cardiomyopathy

Differential Diagnosis of Thickened LV Walls

Cardiovascular

Acquired

Hypertension
Aortic stenosis
Athlete's heart

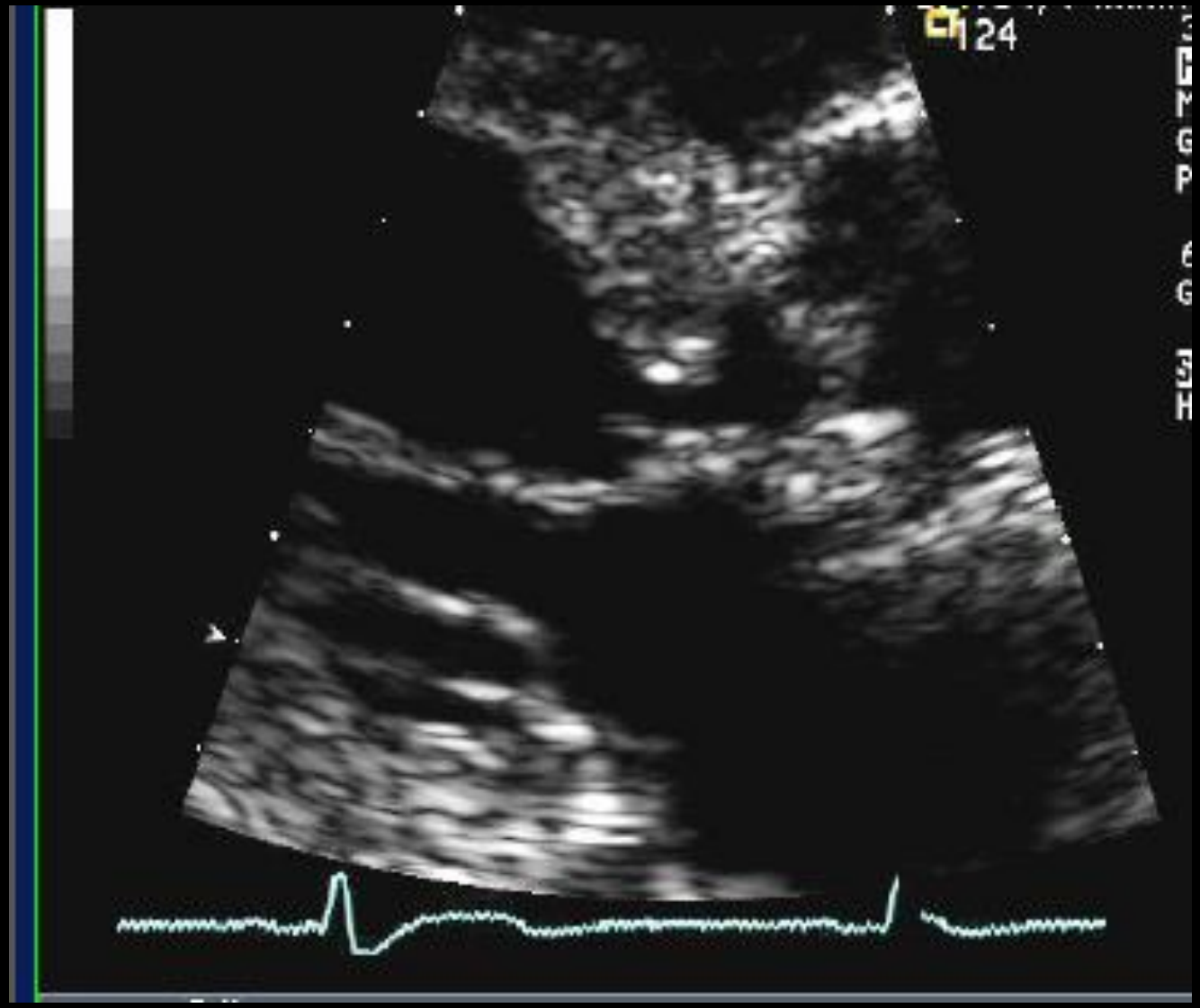
Congenital

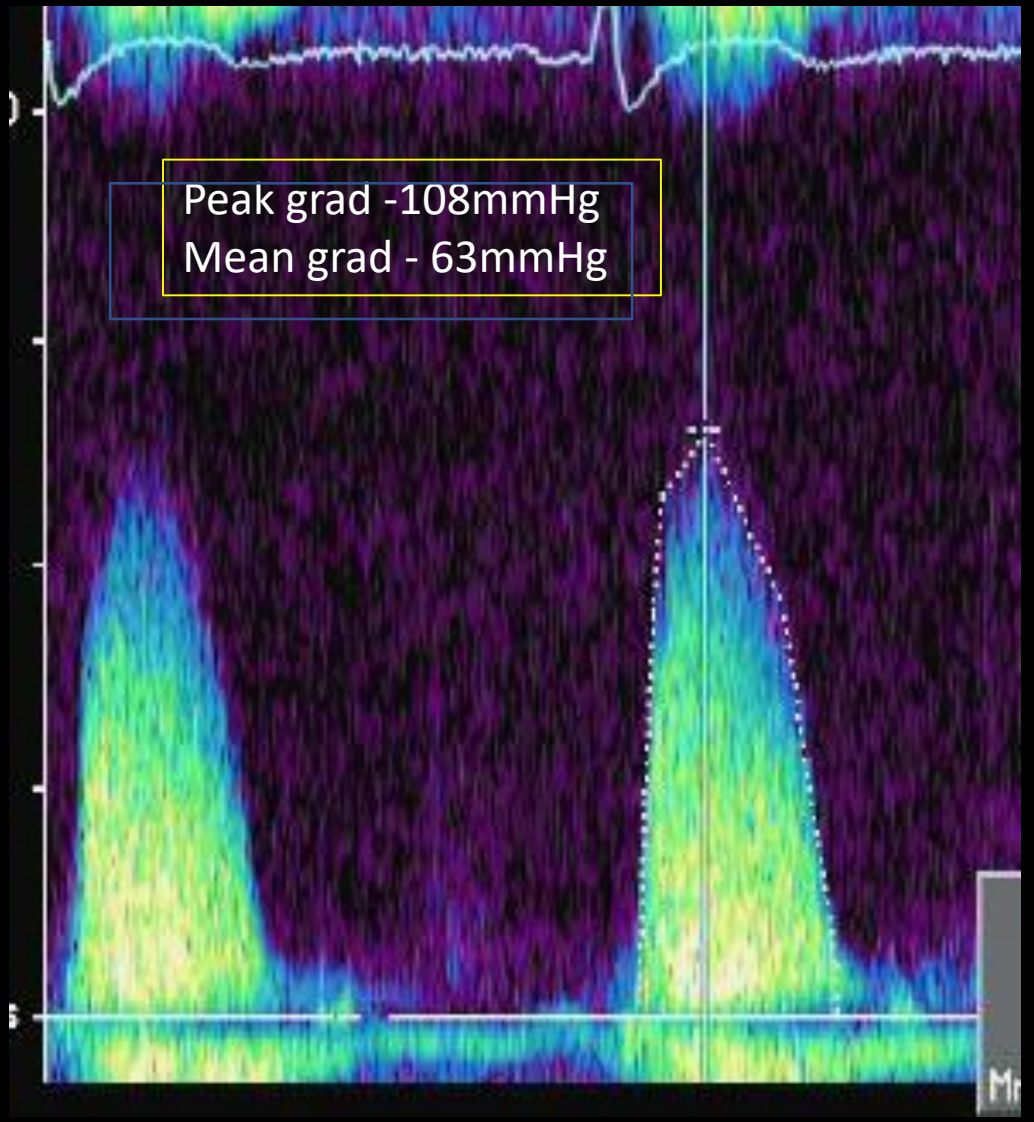
Subaortic stenosis
LV noncompaction

Systemic Disease

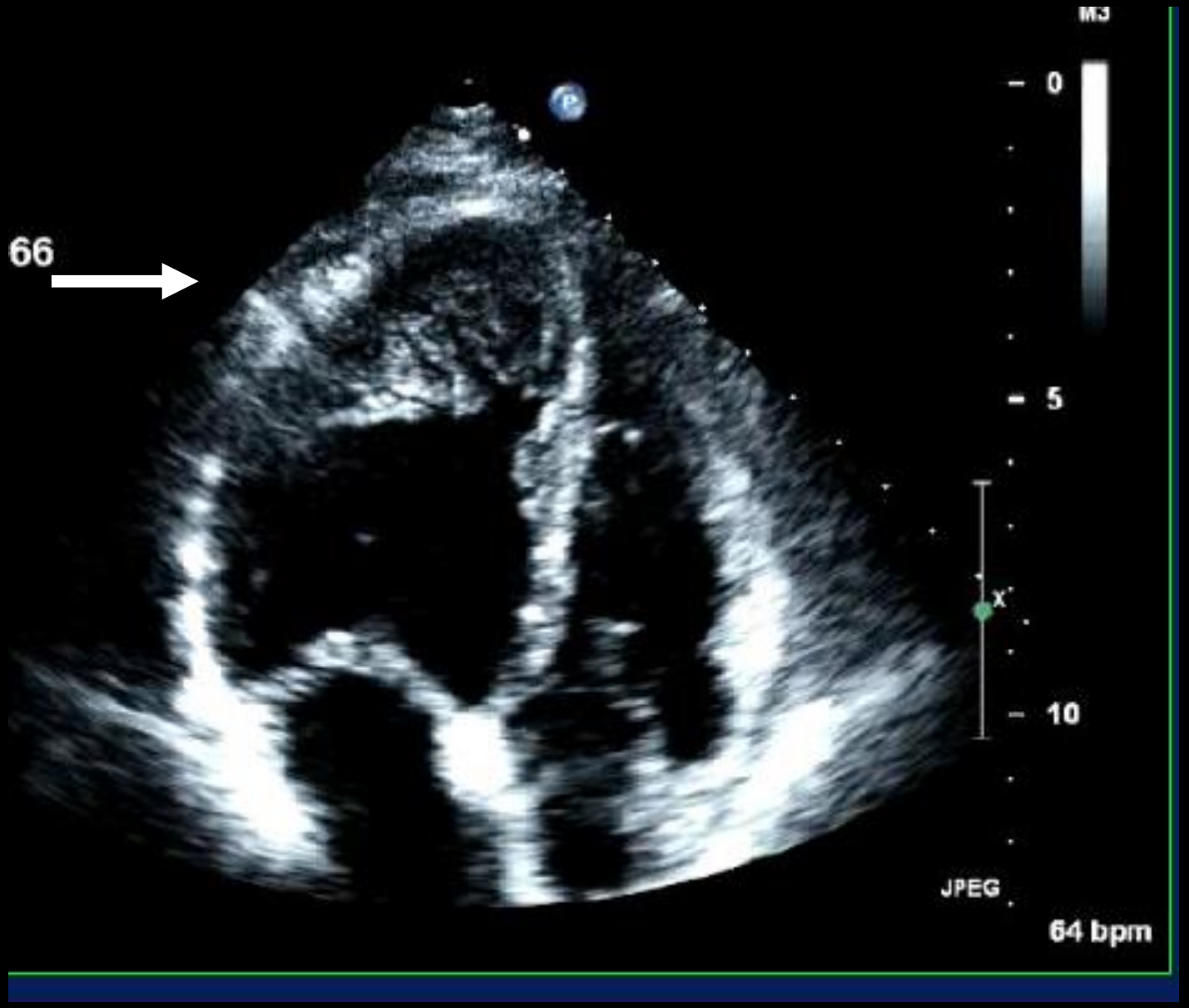
Fabry disease
Cardiac amyloidosis
Hypereosinophilic syndrome

Congenital Subaortic Stenosis – Fibromuscular membrane

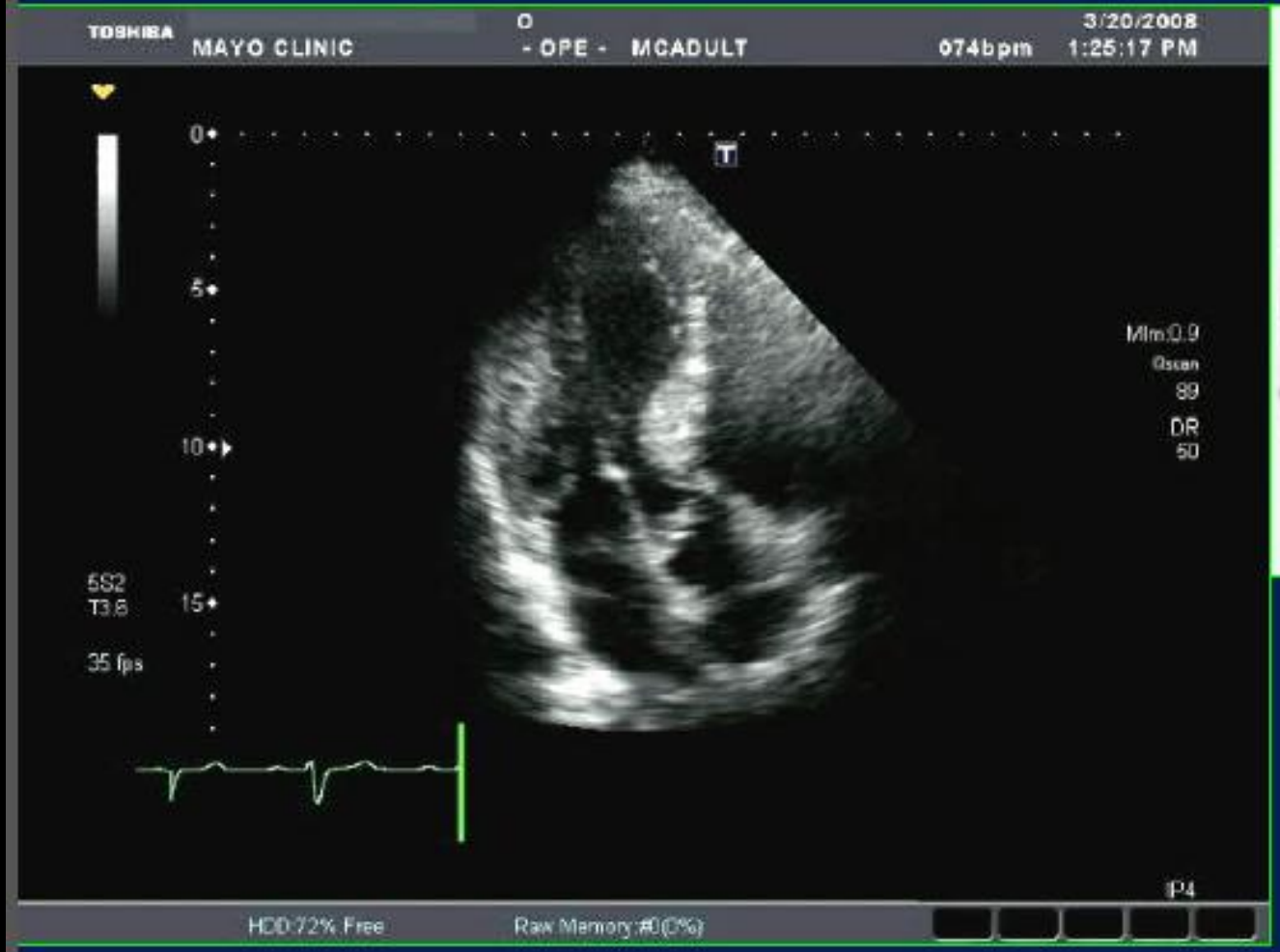


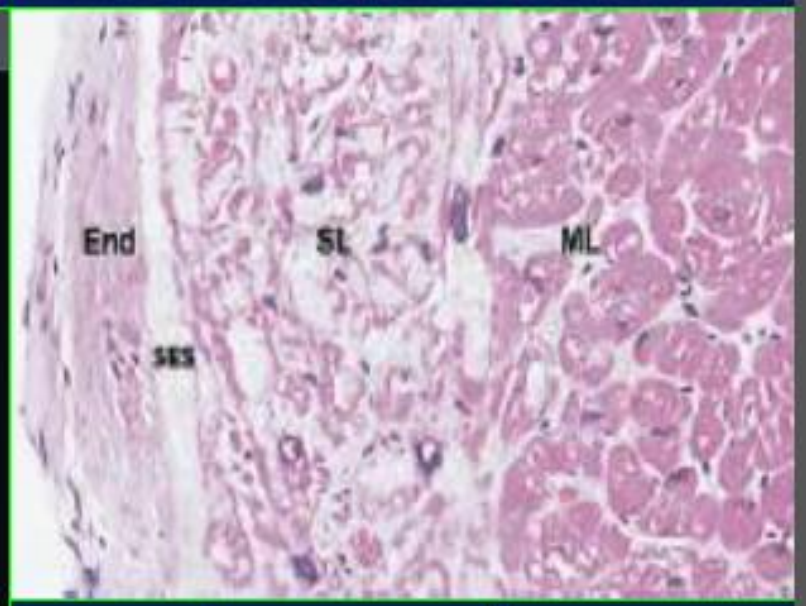


Left Ventricular NON-Compaction Syndrome



Fabry Disease (Alpha-Galactosidase A Deficiency)





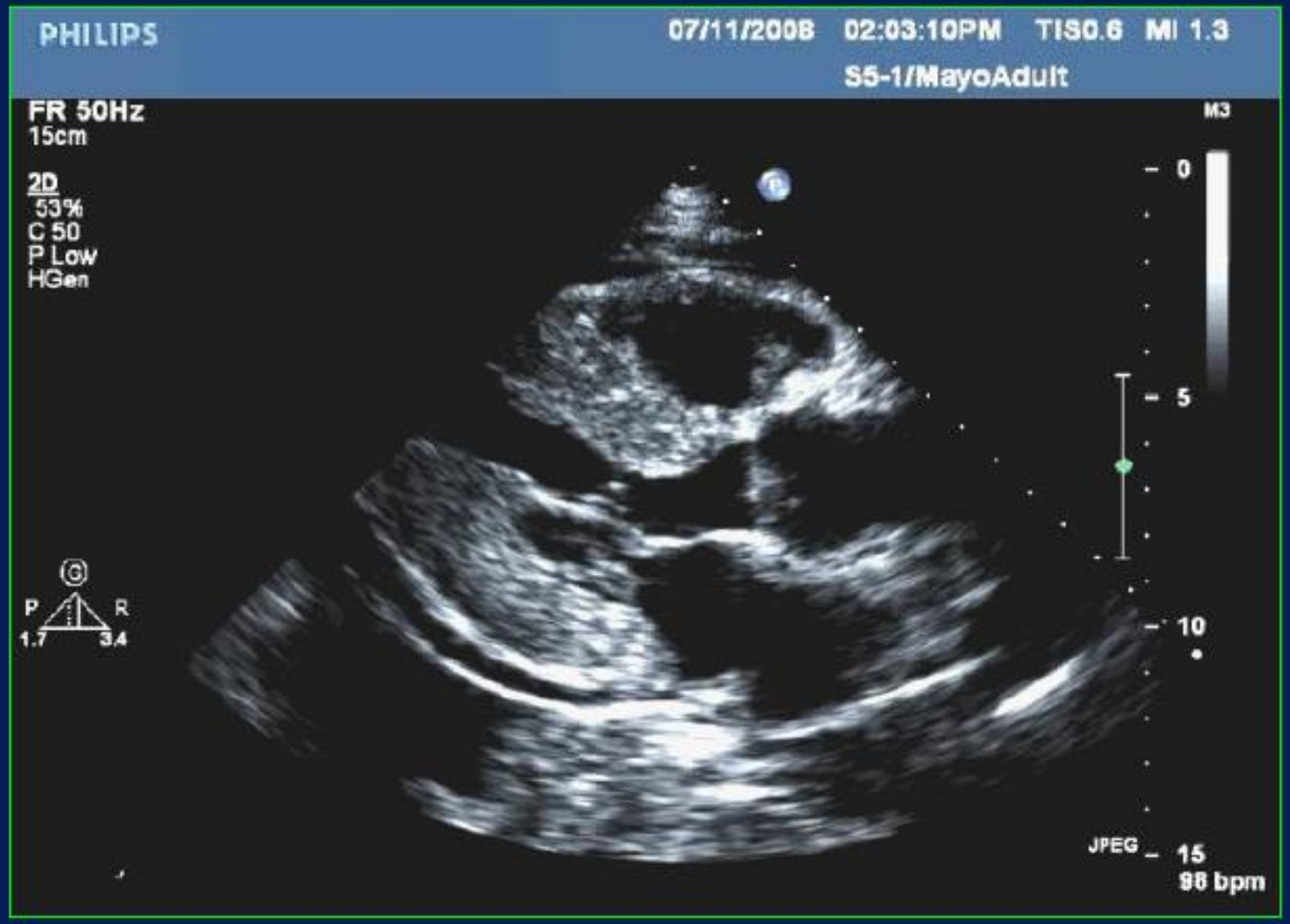
Glycosphingolipid Accumulation

Hyper-refractile subendocardial border:
94% Sensitive
100% Specific

MAYO CLINIC

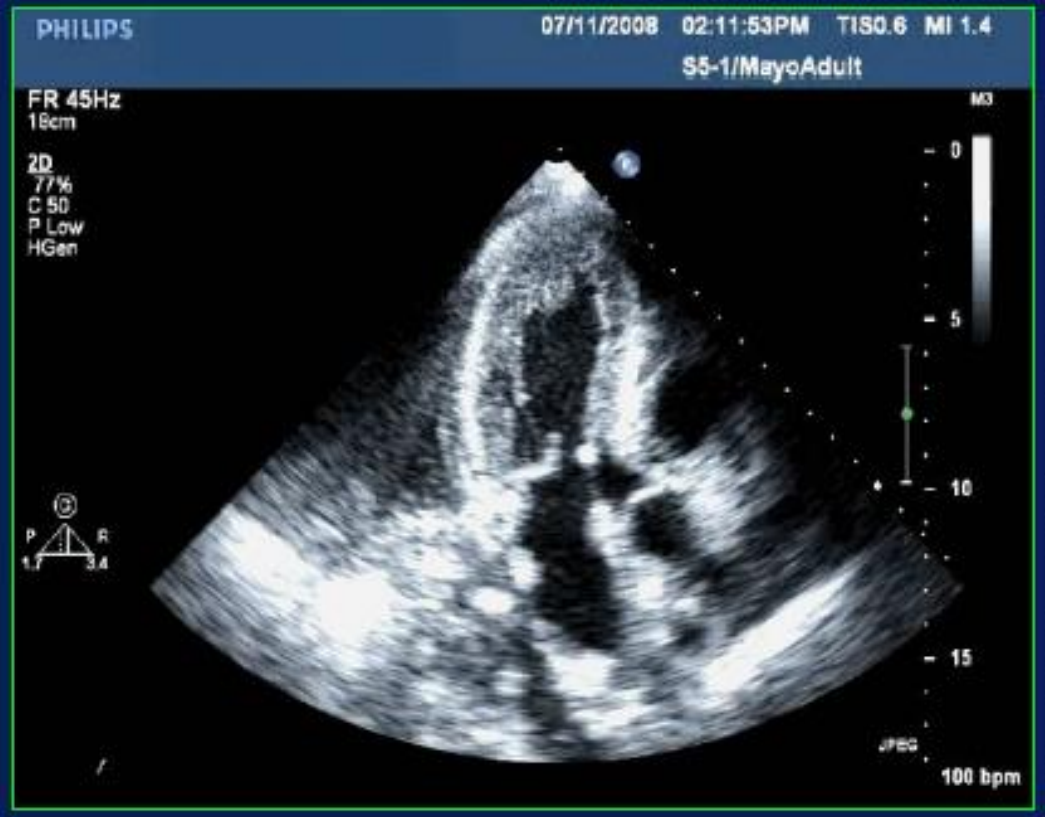
Pieroni M, et al. JACC 2006; 47: 1663

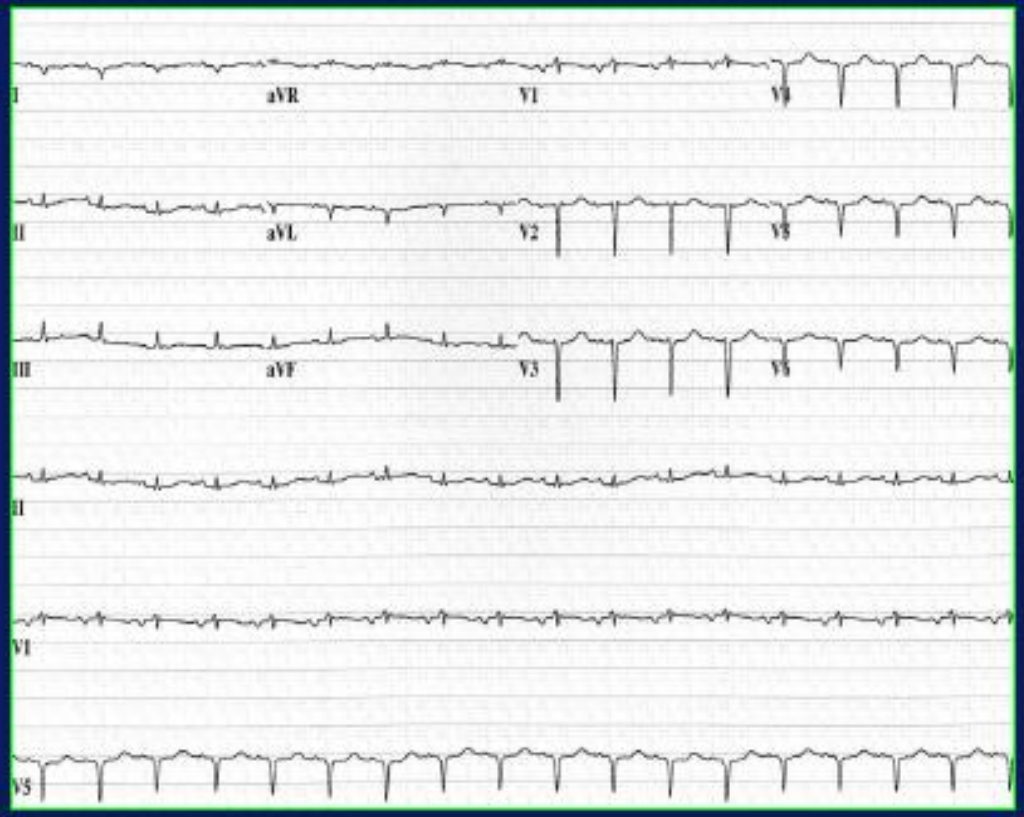
Amyloid Infiltrative Cardiomyopathy



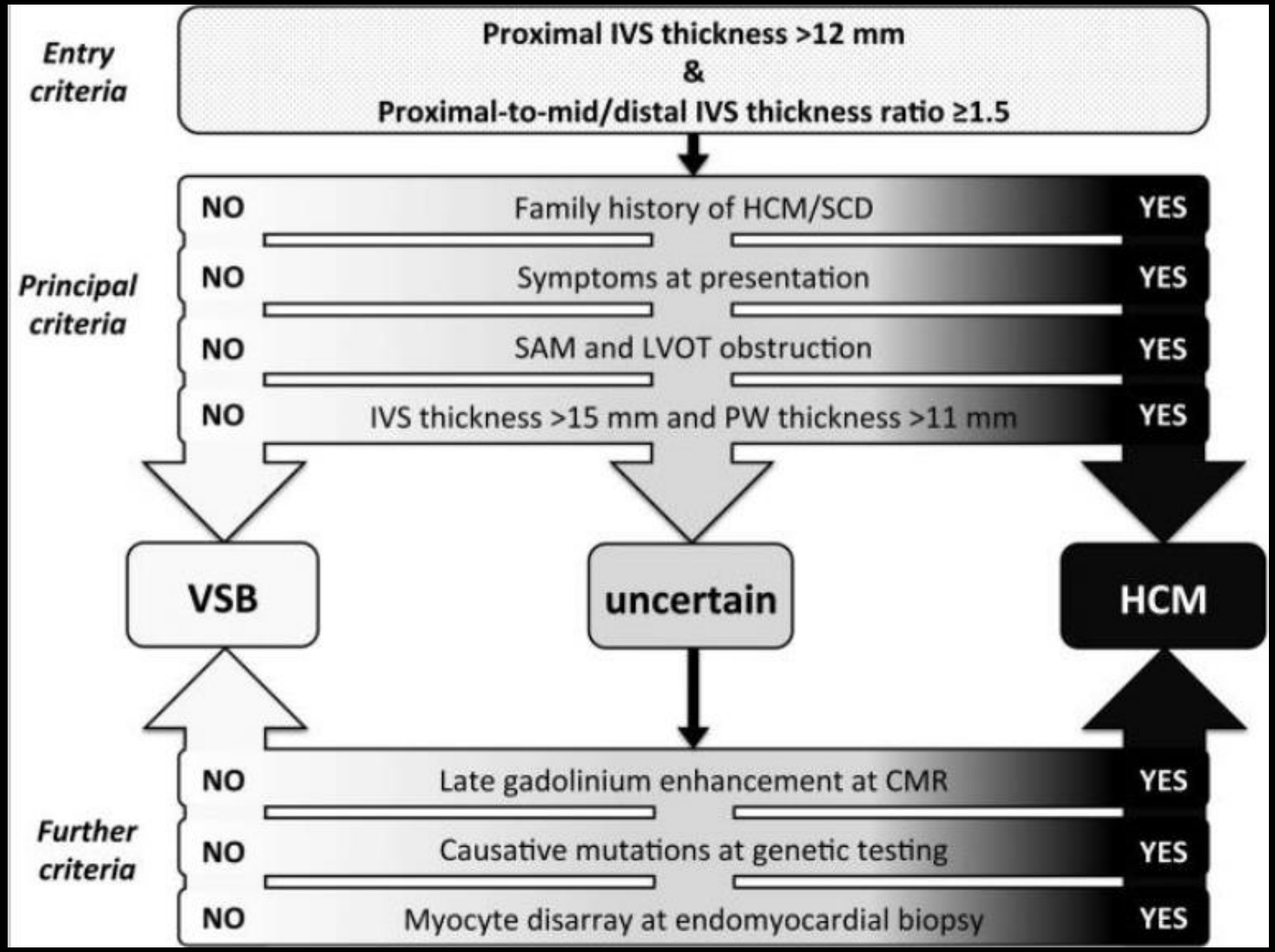
Amyloid Infiltrative Cardiomyopathy

- Low voltage QRS
- Anteroseptal Pseudoinfarction Pattern

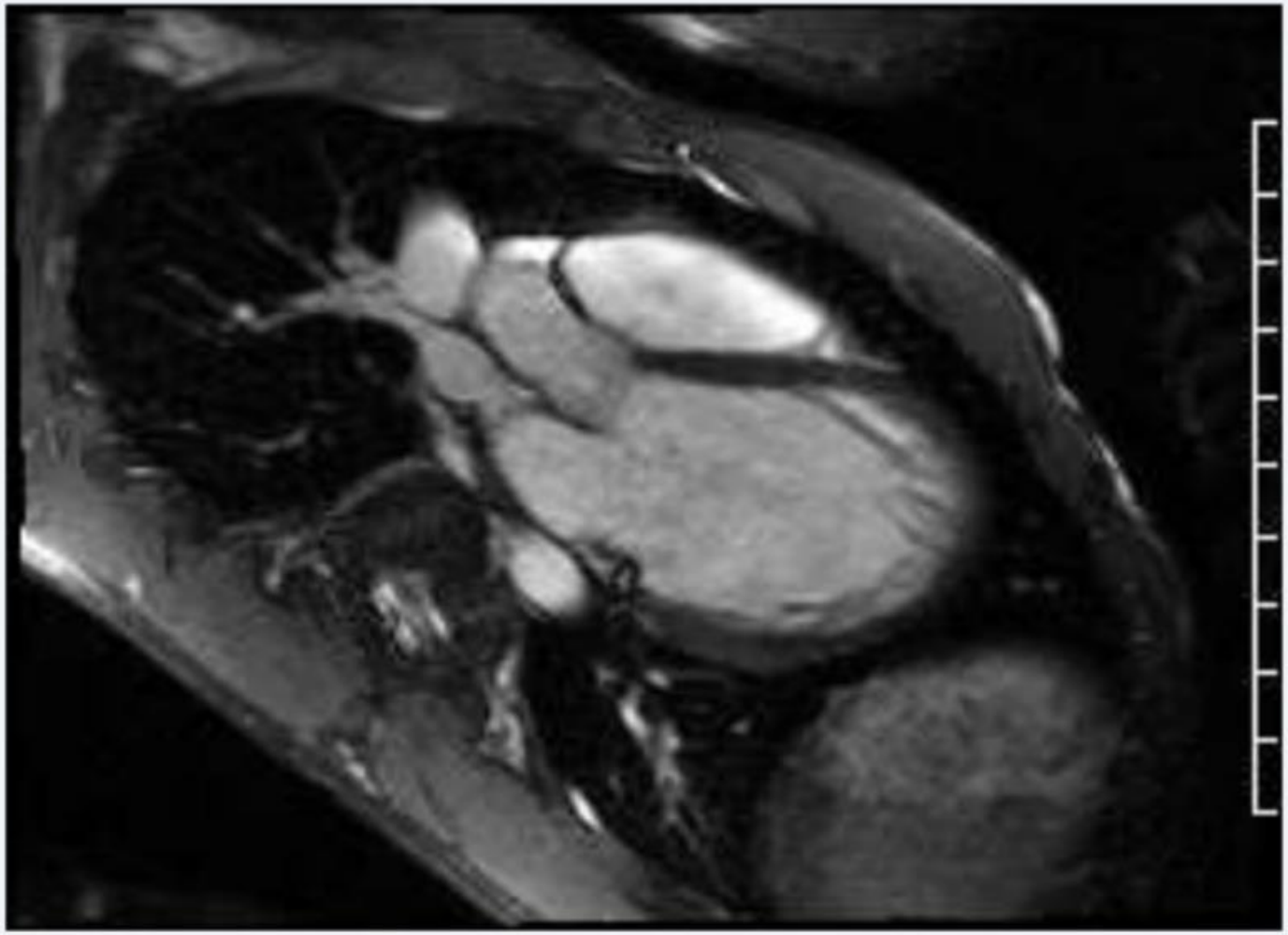




HCM vs Ventricular Septal Bulge (Sigmoid Septum)



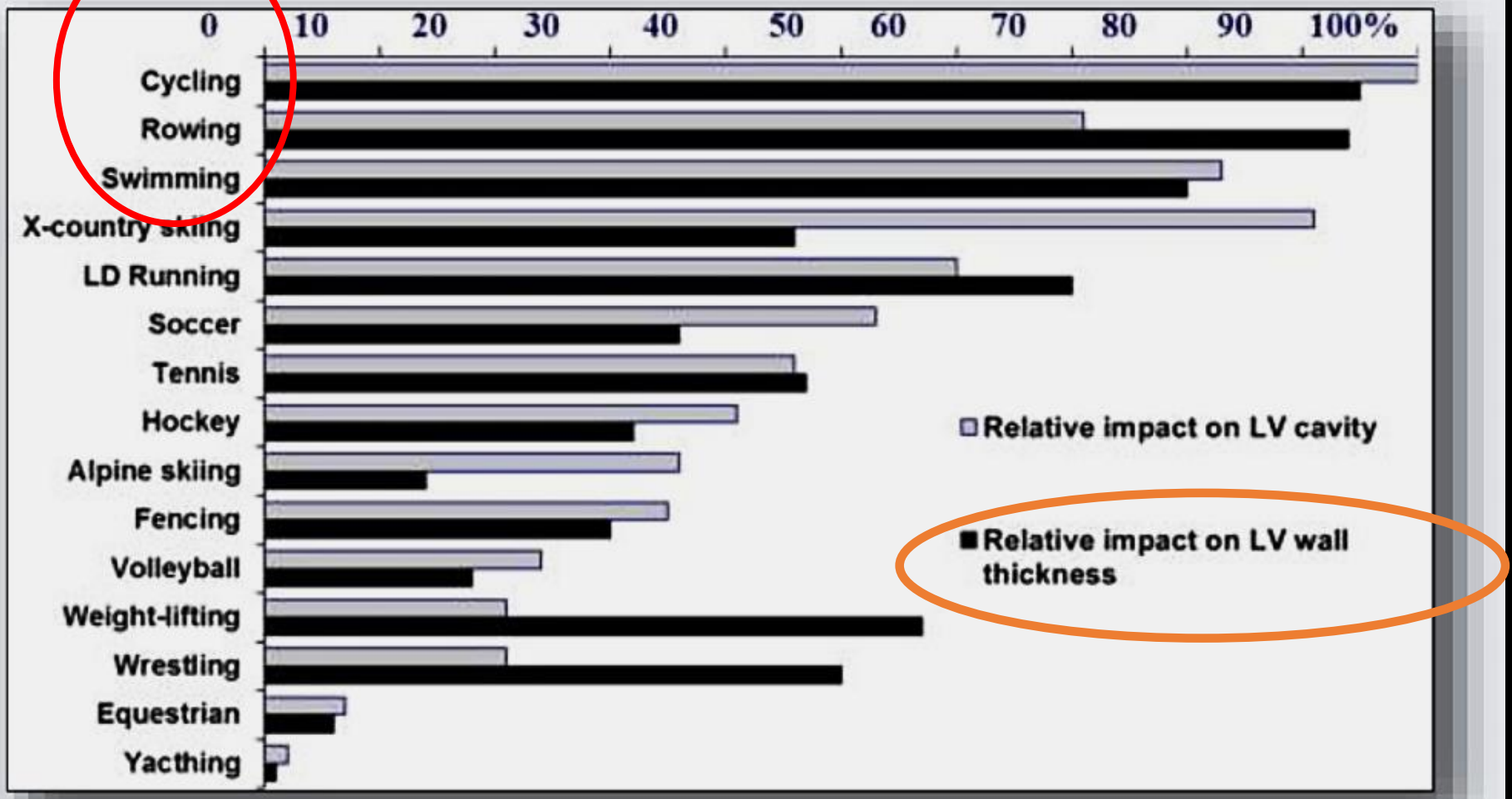
Differentiating Athlete's Heart from HCM



Marc-Vivien Foé

HOCM – Sudden Death During Competitive Sports

Specific Sports Training Effects on Heart Size and Wall Thickness

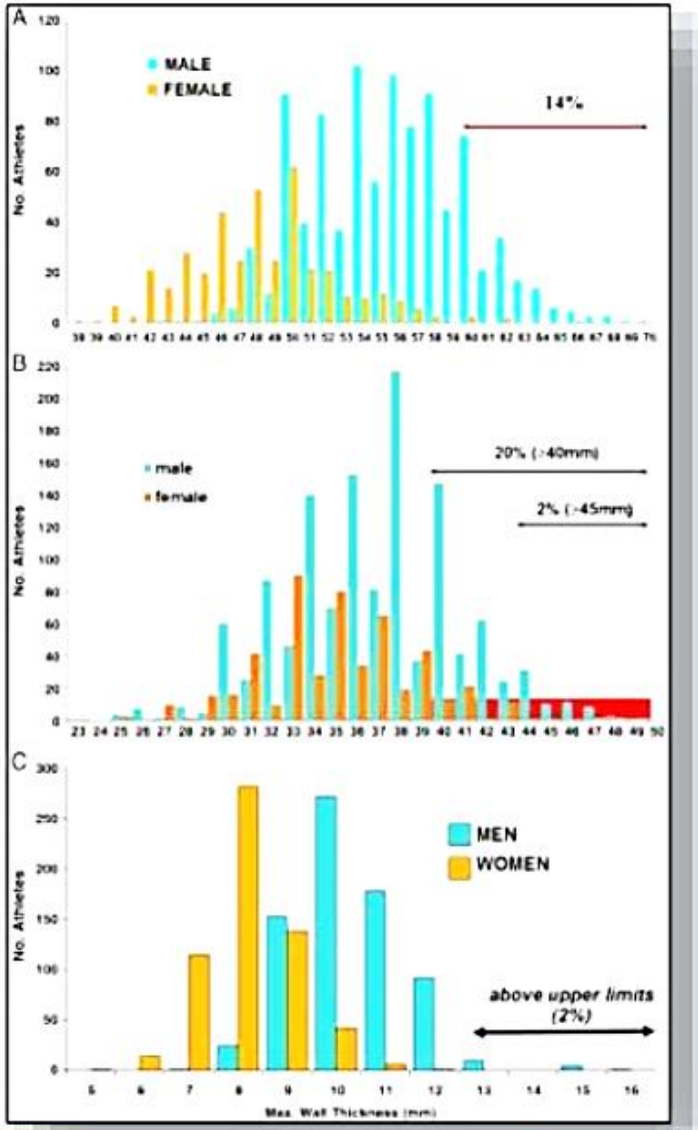


Normal Athlete Heart Sizes

LV End-diastolic Dimensions

LA Sizes

Max. Wall Thickness



14% have an LVEDD over 60 mm

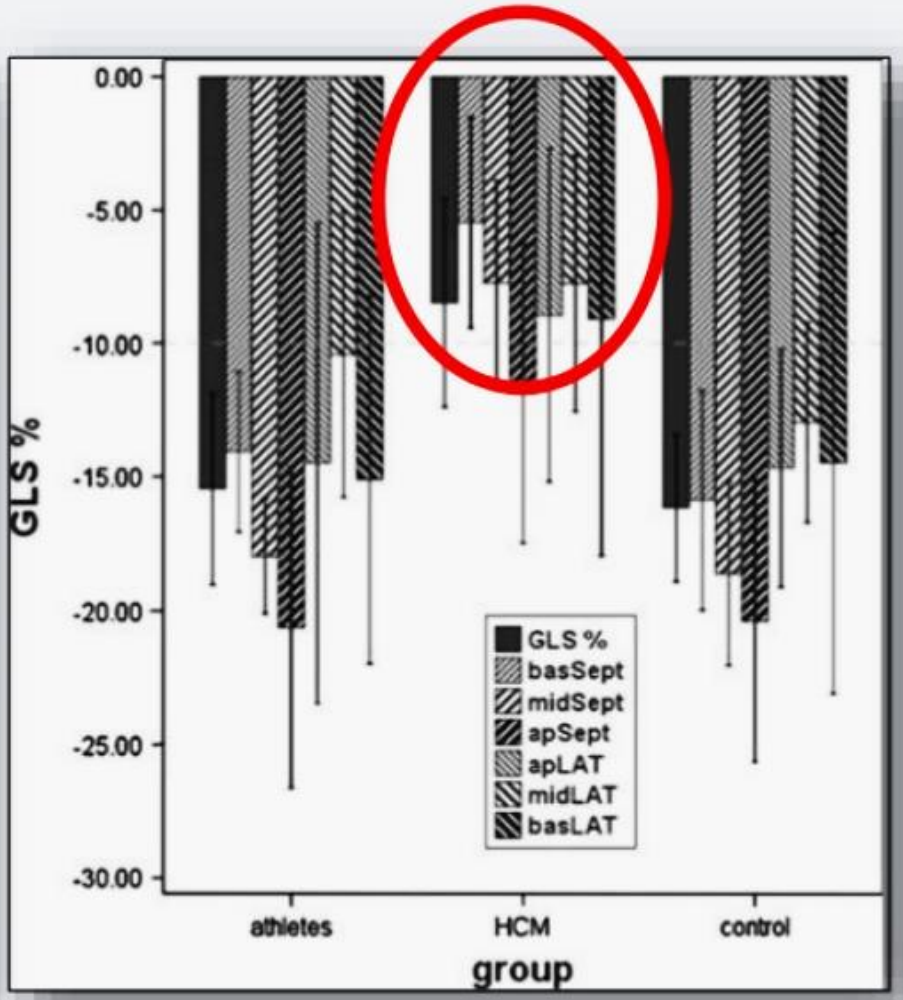
20% have an enlarged LA

2% exceed 13 mm

Echo Tissue Doppler and Strain Analysis in HCM vs Athletes

Table 2 Tissue Doppler imaging (TDI) variables in athletes and in HCM

TDI	Athletes	HCM	*P* value
S′ septal (cm/s)	9.6 ± 1.5	4.6 ± 1.7	<0.001
S′ lateral (cm/s)	11.0 ± 2.0	6.1 ± 2.6	<0.001
S′ averaged (cm/s)	10.0 ± 1.9	4.3 ± 2.1	<0.001
E′ septal (cm/s)	13.6 ± 2.2	4.7 ± 2.2	<0.001
E′ lateral (cm/s)	17.2 ± 4.1	8.4 ± 4.0	<0.001
E′ averaged (cm/s)	15.0 ± 3.3	6.1 ± 3.0	<0.001
E/E′ ratio (septal)	6.1 ± 1.4	20.4 ± 12.	<0.001
E/E′ ratio (lateral)	4.9 ± 0.8	10.4 ± 3.7	<0.001
E/E′ averaged (cm/s)	5.4 ± 1.0	14.4 ± 8.5	<0.001
GFI septal	0.66 ± 0.21	6.54 ± 7.45	<0.01
GFI lateral	0.46 ± 0.13	2.12 ± 1.26	<0.001
GFI averaged	0.55 ± 0.13	4.50 ± 4.25	<0.001



Abnormal Diastolic Parameters from Tissue Doppler

Reduced Global Longitudinal Strain

Athlete's Heart versus HCM

	HCM	vs	Athlete's Heart
LV wall thickness Morphology	≥ 15 mm Asymmetric		< 15 mm (usually < 13 mm) Symmetric
LVEDD	<45mm		>55mm
Diastolic filling	Abnormal		Normal
LA volume	Increased		Normal
Response to deconditioning	None		Regression of LVH
Strain Imaging*	Abnormal		Normal

Maron BJ. Heart 2005; 91: 1380

* Butz T, et al. Int J Cardiovasc Imaging 2011; 27:101

Competitive Sports Recommendations

- ***Class III (LOE C)*** **Those identified with the HCM phenotype should not participate in competitive sports** (exception: those with low intensity). This is independent of all other findings, history or procedures that might have been performed.
- ***Class IIa (LOE C):*** Asymptomatic, genotype positive HCM with no LVH and no FH of SCD may participate in competitive sports.
- ***Class III:*** Pharmacologic agents *(LOE C)* or prophylactic ICDs *(LOE B)* should not be used for the sole purpose of allowing athletes to participate in competitive sports.

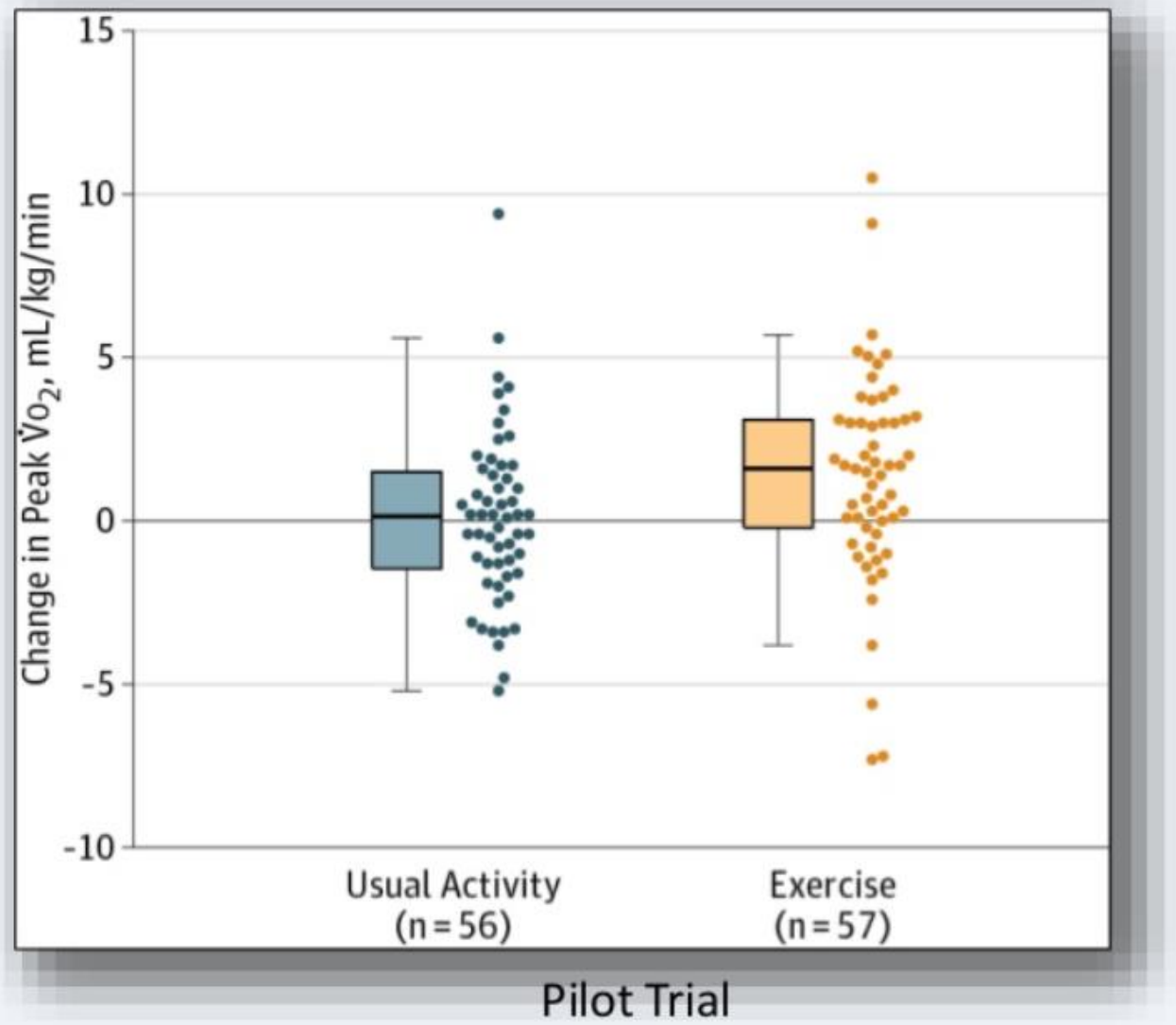
Recommendations for Noncompetitive Sports Participation for HCM Patients

- **High Intensity**
  - *Not advised:* Basketball,body building, ice hockey, racquetball, rock climbing, sprinting, soccer, singles tennis, football, windsurfing
  - *Intermediate:* Gymnastics, skiing
- **Moderate Intensity**
  - *Intermediate:* Weightlifting, hiking, motorcycling, jogging, surfing, baseball, sailing
  - *Permitted:* Biking, modest hiking, swimming laps, doubles tennis, treadmill or stationary bike
- **Low Intensity**
  - *Not advised:* Scuba diving
  - *Intermediate:* Horseback riding
  - *Permitted:* Bowling, brisk walking, golf, skating, snorkeling, nonfree weights

Exercise in HCM

RESET-HCM (Randomized Exploratory Study of Exercise Training in HCM)

Moderate-intensity, unsupervised aerobic training after consultation with an exercise physiologist vs usual activity in 136 adults with hypertrophic cardiomyopathy over a 4-month follow-up period.



Treatment

- Life Styles Measures
- Symptomatic treatment

  (**MEDICAL vs. SURGICAL**)
- Prevention of Sudden Cardiac Death

General LIFE Styles Measures

General lifestyle considerations for patients with hypertrophic cardiomyopathy

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

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

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

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

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

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

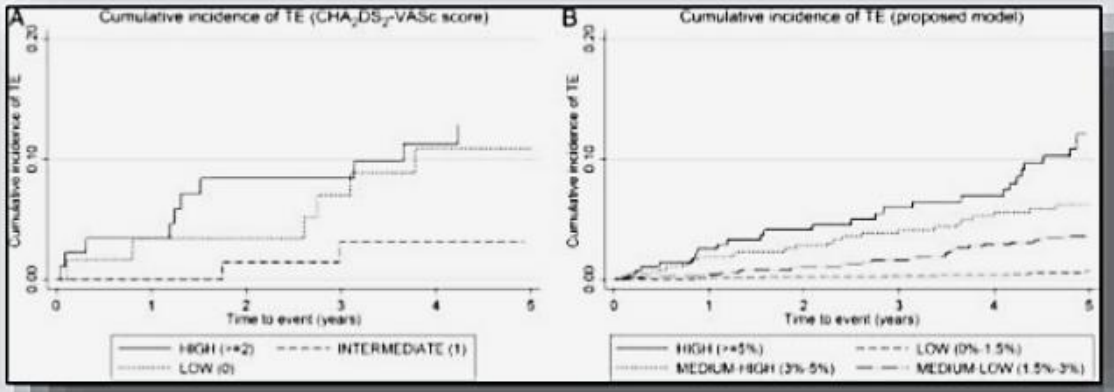
Topic	General guidance
Driving	• Most patients should be eligible for an ordinary driving licence and can continue driving unless they experience distracting or disabling symptoms. • Advice on driving licences for heavy goods or passenger-carrying vehicles should be in line with local legislation. •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

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

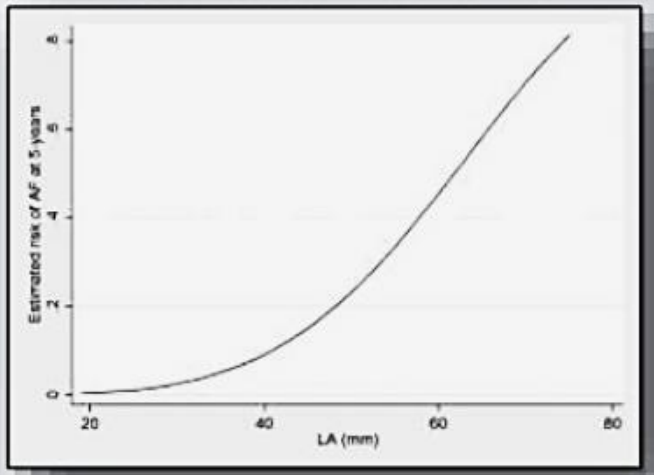
Symptom Treatment

Therapeutic Options in HCM

- **Atrial Fibrillation/Flutter- up to 25%. NOT associated with increased risk of SCD.**
  - Amiodarone first choice. Sotalol second.
  - Anticoagulants. Either warfarin or NOAC
  - Ablation- either catheter or surgical if drug intolerant or failure
  - **CHA_2DS_2-VaSc Score NOT validated**



LA Size Risk of Afib in HCM



HCM AF Anticoagulant Scoring System: Complex formula with age, NYHA CHF class, prior events, LA size, maximal wall thickness, vascular disease

Eur Heart J 2015;17:837

Symptom Treatment

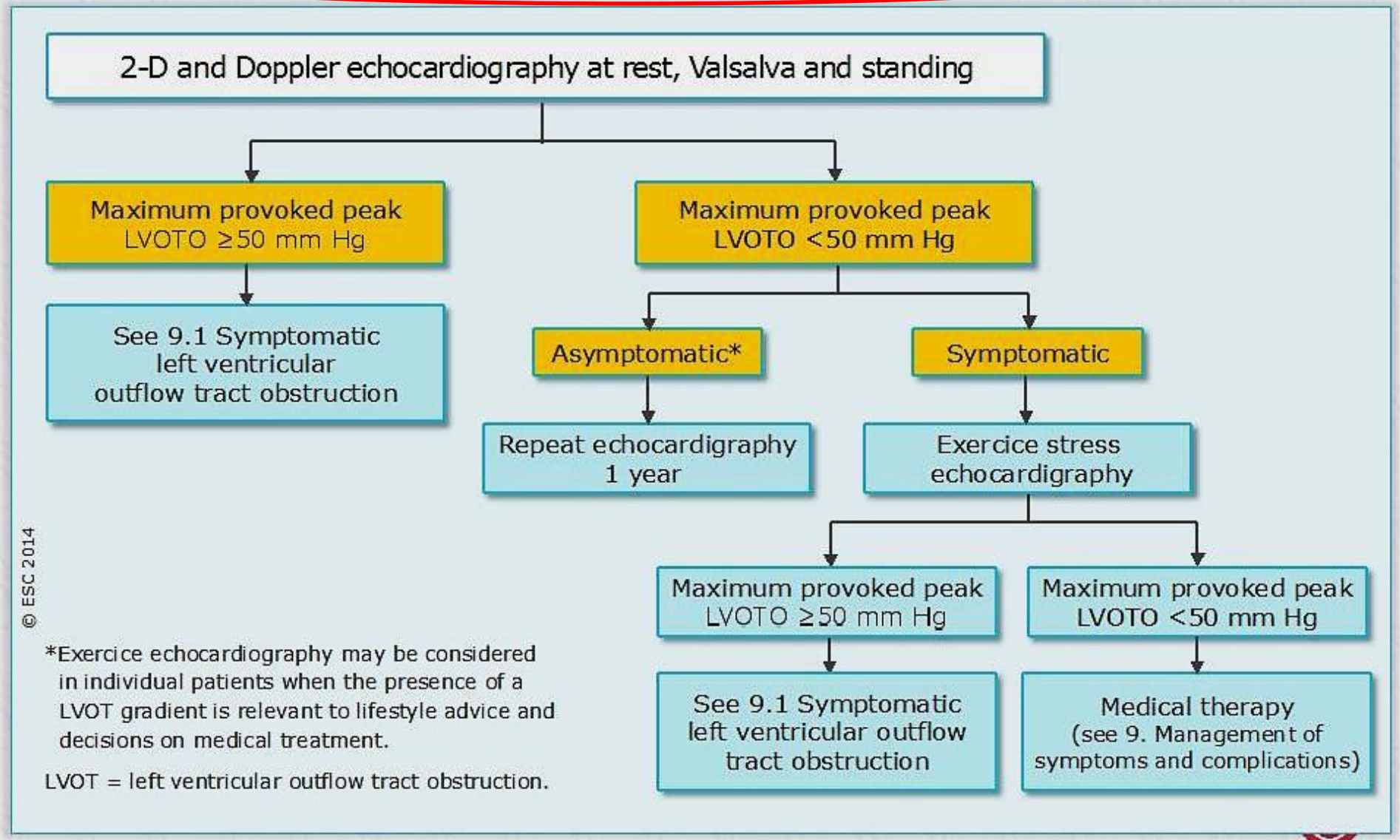
Therapeutic Options in HCM

- **Chest pain**
  - Verapamil, diltiazem
- **Heart Failure with Obstructive HOCM**
  - Beta blockers or verapamil. (Do not use verapamil if severe obstruction), disopyramide (Norpace®)
  - Septal reduction therapy (if >50 mm Hg gradient at rest or exercise)

    Surgical Myectomy preferred over alcohol ablation in younger pts due to:

    Need for repeat procedures, 10% incidence of CHB and pacer, and question of increased risk of ventricular tachyarrhythmias
  - Little enthusiasm remains for dual chamber pacing
- **Heart Failure without Obstruction- diastolic dysfunction**
  - Beta blockers, verapamil, ?disopyramide
  - Diuretics with caution. ACE or ARB use is controversial with no evidence supporting benefit

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



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

Treatment of left ventricular outflow tract obstruction: General measures

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

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

Medical treatment of left ventricular outflow tract obstruction

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

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

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

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

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

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

Septal reduction therapy

Recommendations	Class	Level
It is recommended that septal reduction therapies be performed by experienced operators, working as part of a multidisciplinary team expert in the management of HCM.	I	C
Septal reduction therapy to improve symptoms is recommended in patients with a resting or maximum provoked LVOT gradient of ≥50 mm Hg, who are in NYHA functional Class III–IV despite maximum tolerated medical therapy.	I	B
Septal reduction therapy should be considered in patients with recurrent exertional syncope caused by a resting or maximum provoked LVOTO gradient ≥50 mm Hg despite optimal medical therapy.	IIa	C
Septal myectomy, rather than SAA, is recommended in patients with an indication for septal reduction therapy and other lesions requiring surgical intervention (e.g. mitral valve repair/replacement, papillary muscle intervention).	I	C
Mitral valve repair or replacement should be considered in symptomatic patients with a resting or maximum provoked LVOTO gradient ≥50 mm Hg and moderate-to-severe mitral regurgitation not caused by SAM of the mitral valve alone.	IIa	C
Mitral valve repair or replacement may be considered in patients with a resting or maximum provoked LVOTO gradient ≥50 mm Hg and a maximum septal thickness ≤16 mm at the point of the mitral leaflet–septal contact or when there is moderate-to-severe mitral regurgitation following isolated myectomy.	IIb	C

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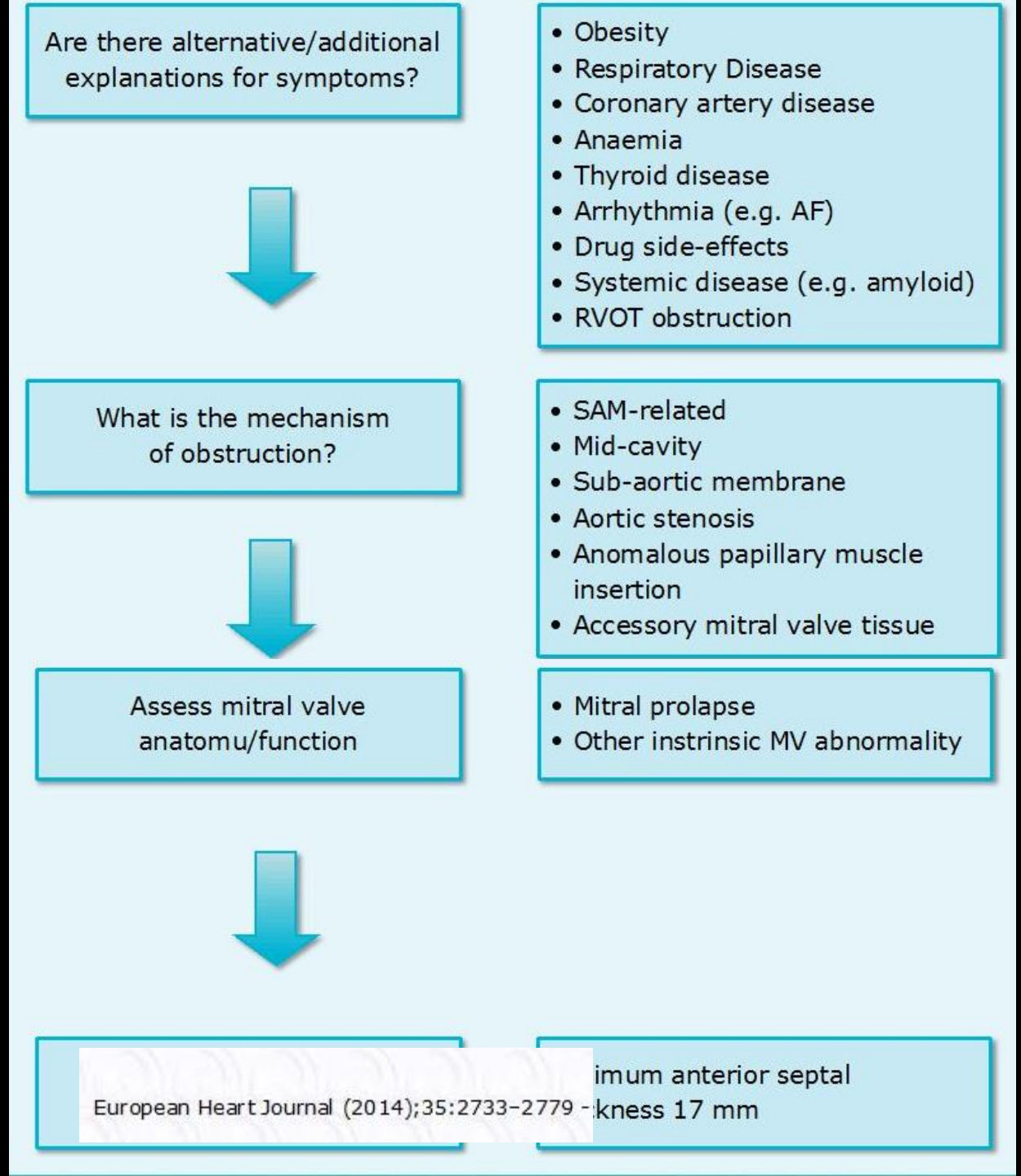
Pre-assessment Checklist for INVASIVE Septal Reduction therapies



EHJ 2014;35:2733-2779

Indications for cardiac pacing in patients with obstruction

Recommendations	Class	Level
Sequential AV pacing, with optimal AV interval to reduce the LV outflow tract gradient or to facilitate medical treatment with ß-blockers and/or verapamil, may be considered in selected patients with resting or provocable LVOTO ≥50 mm Hg, sinus rhythm and drug-refractory symptoms, who have contra-indications for septal alcohol ablation or septal myectomy or are at high-risk of developing heart block following septal alcohol ablation or septal myectomy.	IIb	C
In patients with resting or provocable LVOTO ≥50 mm Hg, sinus rhythm and drug-refractory symptoms, in whom there is an indication for an ICD, a dual-chamber ICD (instead of a single-lead device) may be considered, to reduce the LV outflow tract gradient or to facilitate medical treatment with ß-blockers and/or verapamil.	IIb	C

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

- **Predication / Prevention of Sudden Cardiac Death**

Clinical Features That May Be Associated with Increased Risk of Sudden Cardiac Death

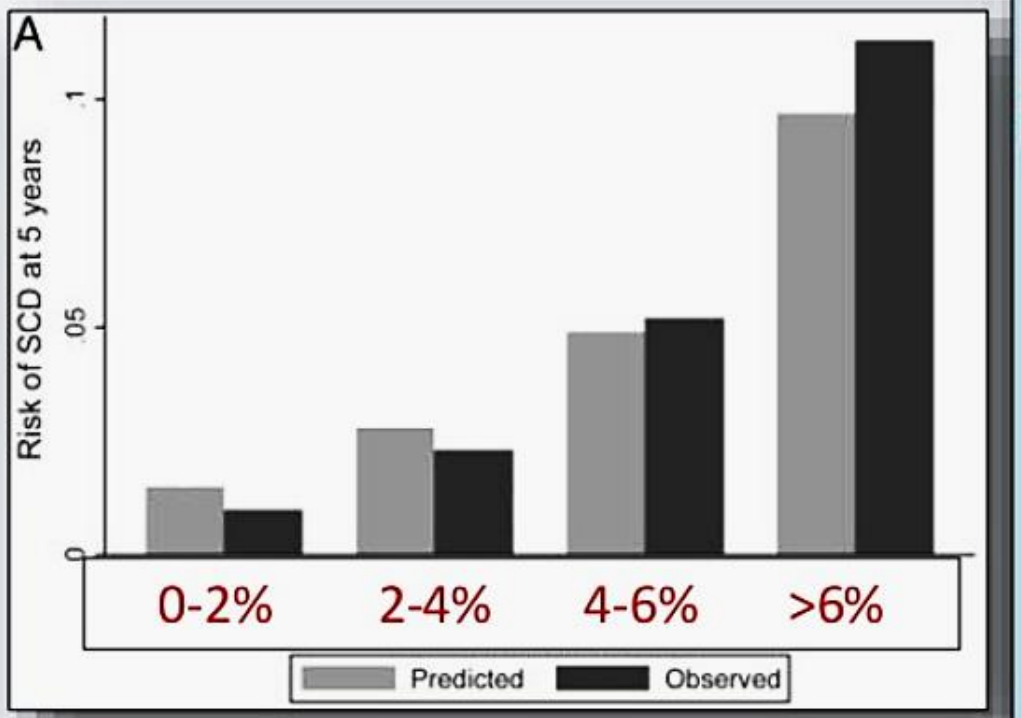
- **Age:** Increased risk in younger patients
- **NSVT:** (>3 beats at >120 pm lasting <30 sec). *No evidence frequency, duration or rate of NSVT influences risk of SCD*
- **Maximal LV wall thickness**: Greatest risk when >30 mm
- **FH of SCD** at young age (<40) or when SCD has occurred in first degree relative with HCM
- **Syncope:** Only when no other explanation
- **Left atrial diameter**: Larger diameters at higher risk
- **LV outflow track obstruction:** High gradients increase risk, though importance of provocable gradient and impact of treatment unclear
- **Exercise blood pressure response:** Failure of systolic blood pressure to rise >20 mmHg or its fall is abnormal exercise response. Greatest significance is in patients <40 years of age
- **More extensive fibrosis:** demonstrated by MRI LGE

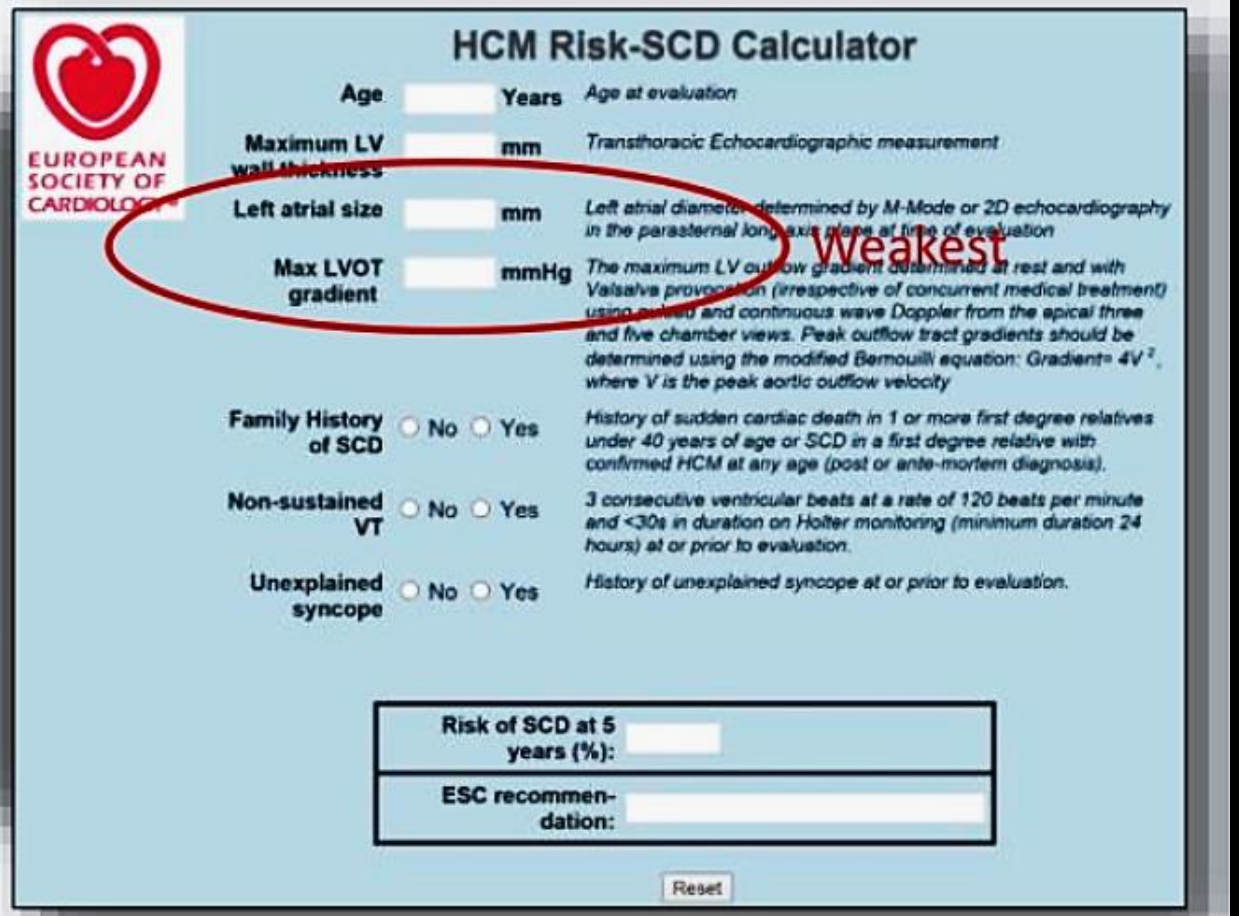
SCD Risk Prediction Models

ESC 2014

- **HCM Risk-SCD Prediction Model:**
  - Probability of SCD at 5 years= 1- $0.998^{(\text{Prognostic Index})}$
  - Prognostic Index includes:
    - Maximal wall thickness
    - LA diameter
    - LVOT gradient
    - FH of sudden death
    - Unexplained syncope
    - Age
- **Did not include stress BP or MRI results when developed**
- **Controversial**

ESC Prediction Model for Sudden Death





http://www.doc2do.com/hcm/webHCM.html

ESC Recommendations for prevention of SCD in HCM

Class I

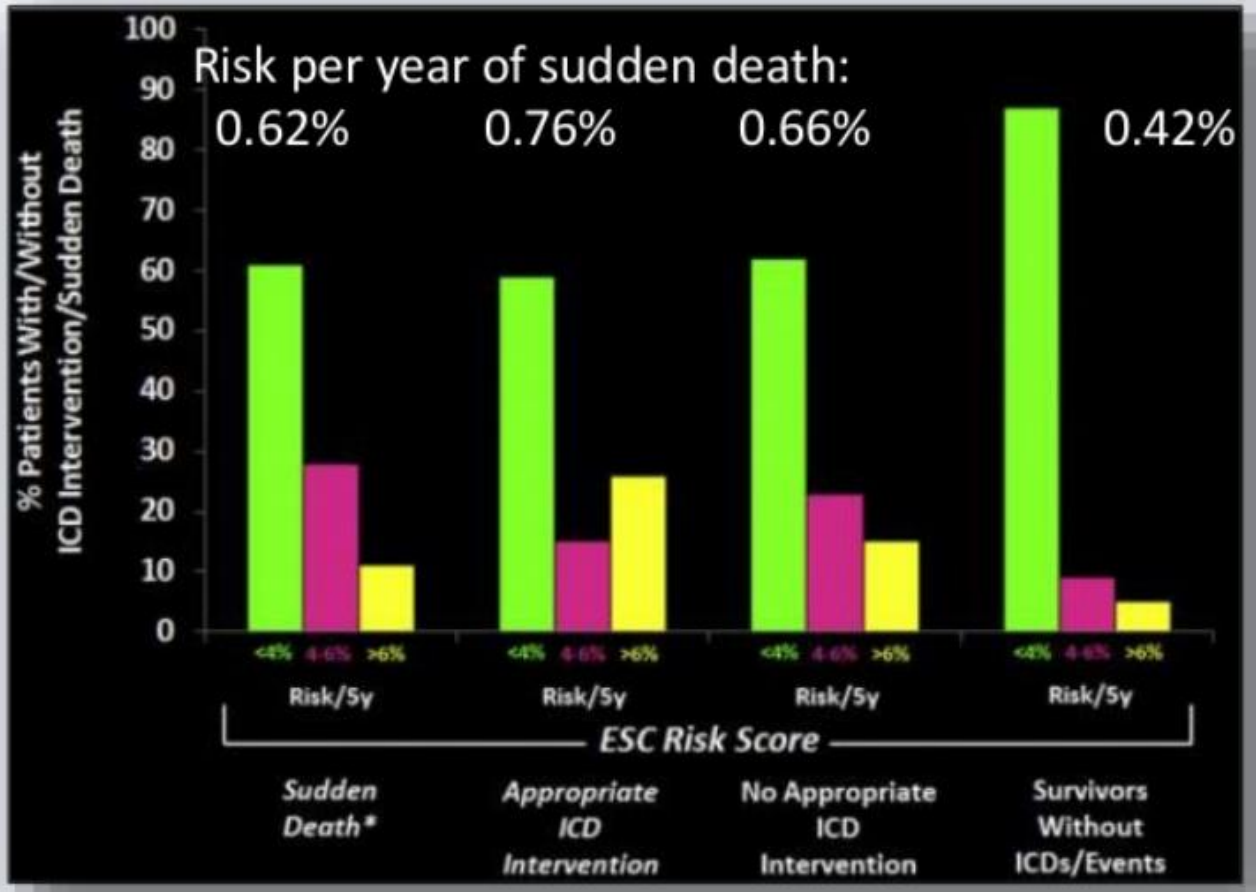
1. Avoidance of competitive sports (LOE C)
2. ICD if hx cardiac arrest or sustained VT with sx (LOE B)
3. Estimate risk using risk score every 1-2 years (LOE C)

Class II (LOE B)

1. Class IIa: definite ICD if 5 year risk of SCD >=6%.
2. Class IIb: maybe ICD if 5 year risk of SCD 4-6%
3. Class IIb: no ICD if 5 year risk <4% unless there are clinical features of proven prognostic importance

Critique of ESC Risk Calculator

- 1629 pts >16 years of age in HOCM Center of Minneapolis Heart Institute and Tufts (1992-2014). 35 had incurred SCD. 460 had ICDs implanted.



SCD group (n=35): only 4 (11%) had high risk score. Most would not have gotten ICD.

High risk with appropriate ICD for VF/VT (n=46): 59% had low risk scores and only 26% high risk

High risk ICD with no shocks (n=414): 62% had low risk score.

Survivors with no ICD (n=944): 87% low risk; 8.7% medium and 4.5% high risk.

Electrophysiologic testing

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

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

2017 AHA/ACC/HRS Guideline for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death

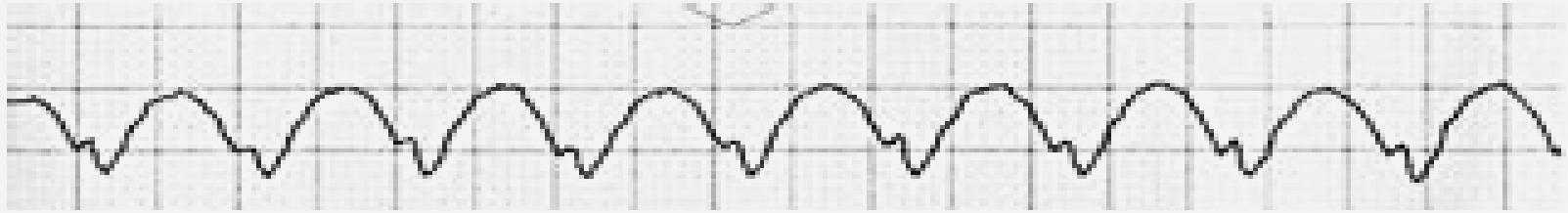
October 30, 2017—The 2017 AHA/ACC/HRS Guideline for Management of Patients with Ventricular Arrhythmias and the Prevention of Sudden Cardiac Death, accompanied by the Executive Summary and the Systematic Review, is intended to guide management of adults who have ventricular arrhythmias or who are at risk for sudden cardiac death (SCD), including diseases and syndromes associated with a risk of SCD from ventricular arrhythmias.

Table 5 Table of Definitions of Commonly Used Terms in this Document

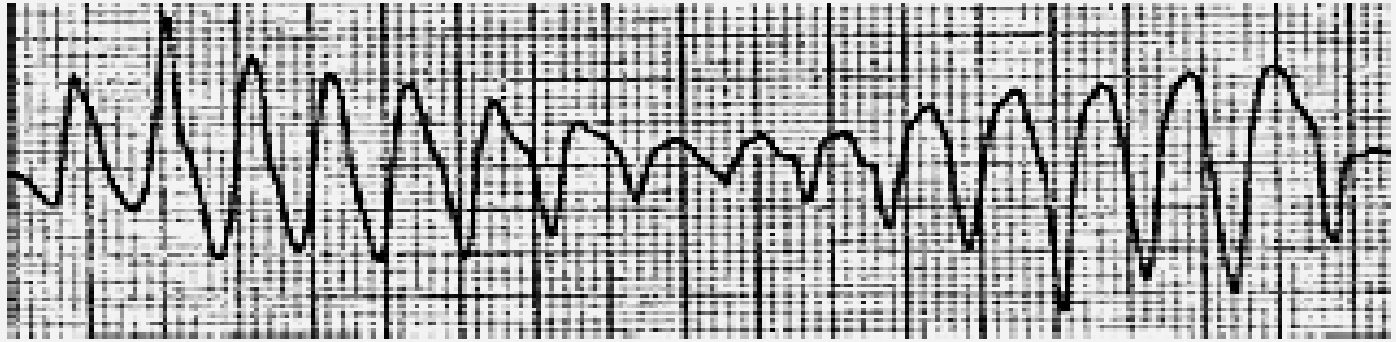
Term	Definition or Description
Ventricular tachycardia (S2.2.2-2)	Cardiac arrhythmia of ≥3 consecutive complexes originating in the ventricles at a rate >100 bpm (cycle length: <600 ms). ■ Sustained: VT >30 s or requiring termination due to hemodynamic compromise in <30 s. ■ Nonsustained/unsustained: ≥3 beats, ter ntaneously. ■ Monomorphic: Stable single QRS morphology from beat to beat. ■ Polymorphic: Changing or multiform QRS morphology from beat to beat. ■ Bidirectional: VT with a beat-to-beat alternation in the QRS frontal plane axis, often seen in the setting of digitalis toxicity or catecholaminergic polymorphic VT

Types of VT :

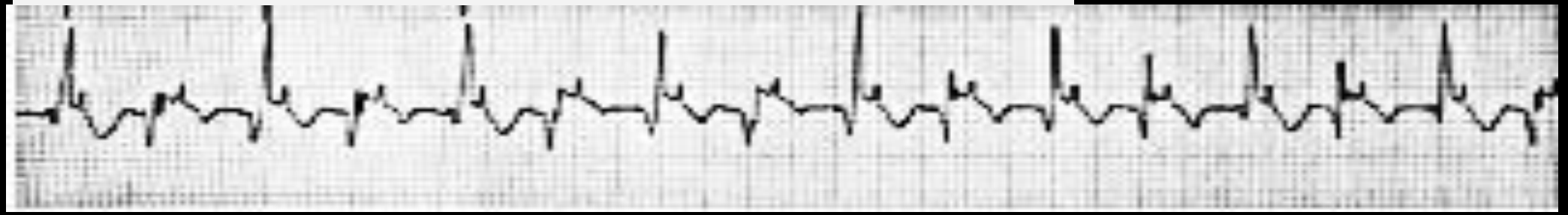
2017 ACC/ AHA/HRS Guidelines



Monomorphic VT



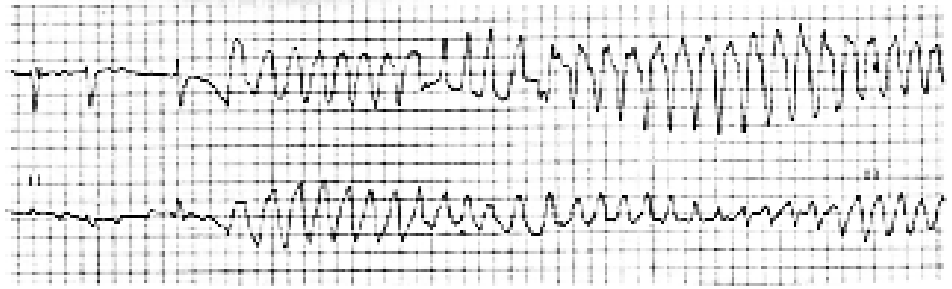
Polymorphic VT



Bidirectional VT

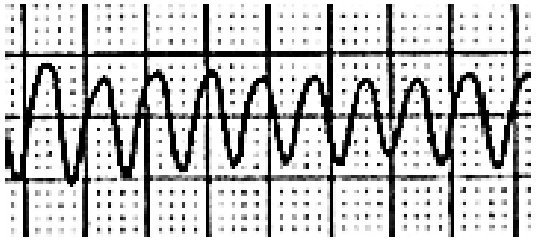
Torsades de pointes (S2.2.2-2)

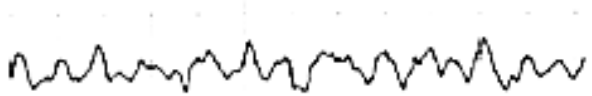
Torsades de pointes is polymorphic VT that occurs in the setting of a long QT interval and is characterized by a waxing and waning QRS amplitude. It often has a long-short initiating sequence with a long coupling interval to the first VT beat and may present with salvos of NSVT. The twisting of the points, although characteristic, may not always be seen, especially if the episode is nonsustained or if only a limited number of leads are available. Torsades de pointes can result from bradycardia including high-grade AV block that leads to a long-short sequence initiating torsades de pointes.



Ventricular flutter (S2.2.2-2)

A regular VA ≈ 300 bpm (cycle length: 200 ms) with a sinusoidal, monomorphic appearance; no isoelectric interval between successive QRS complexes.



Term	Definition or Description
Ventricular fibrillation (S2.2.2-2)	Rapid, grossly irregular electrical activity with marked variability in electrocardiographic waveform, ventricular rate usually >300 bpm (cycle length: <200 ms). 
Sudden cardiac arrest (S2.2.2-2)	SCA is the sudden cessation of cardiac activity such that the victim becomes unresponsive, with either persisting gasping respirations or absence of any respiratory movements, and no signs of circulation as manifest by the absence of a perceptible pulse. An arrest is presumed to be of cardiac etiology unless it is known or likely to have been caused by trauma, drowning, respiratory failure or asphyxia, electrocution, drug overdose, or any other noncardiac cause.
Sudden cardiac death (S2.2.2-2)	Sudden and unexpected death occurring within an hour of the onset of symptoms, or occurring in patients found dead within 24 h of being asymptomatic and presumably due to a cardiac arrhythmia or hemodynamic catastrophe.
VT/VF storm (S2.2.2-3)	VT/VF storm (electrical storm or arrhythmic storm) refers to a state of cardiac electrical instability that is defined by ≥3 episodes of sustained VT, VF, or appropriate shocks from an ICD within 24 h.
Primary prevention ICD (S2.2.2-2)	ICD placement with the intention of preventing SCD in a patient who has not had sustained VT or SCA but who is at an increased risk for these events.
Secondary prevention ICD (S2.2.2-2)	ICD placement in a patient with prior SCA, sustained VT, or syncope caused by VA.
Structural heart disease*	This term encompasses IHD, all types of cardiomyopathy, valvular heart disease, and adult congenital heart disease.
Cardiac channelopathy (S2.2.2-4)	Arrhythmogenic disease due to a genetic abnormality that results in dysfunction of a cardiac ion channel (e.g., long QT syndrome, catecholaminergic polymorphic VT).

AV = atrioventricular; ICD = implantable cardioverter-defibrillator; IHD = ischemic heart disease; NSVT = nonsustained ventricular tachycardia; SCA = sudden cardiac arrest; SCD = sudden cardiac death; VA = ventricular arrhythmia; VF = ventricular fibrillation; VT = ventricular tachycardia.

*The definition of this term may differ across publications. Refer to the entry for the definition used in this document.

2017ACC/AHA/HRS Guidelines

Table 8 Major Clinical Features Associated With Increased Risk of SCD in Patients With HCM

Established risk factors*

- Survival from a cardiac arrest due to VT or VF (S7.4-1,S7.4-5,S7.4-6)
- Spontaneous sustained VT causing syncope or hemodynamic compromise (S7.4-1,S7.4-5,S7.4-6)
- Family history of SCD associated with HCM (S7.4-25,S7.4-26)
- LV wall thickness ≥30 mm (S7.4-2,S7.4-3,S7.4-23,S7.4-24)
- Unexplained syncope within 6 mo (S7.4-8,S7.4-26)
- NSVT ≥3 beats (S7.4-2,S7.4-26,S7.4-27)
- Abnormal blood pressure response during exercise† (S7.4-5,S7.4-28,S7.4-29)

Potential risk modifiers‡

- <30 y (S7.4-5,S7.4-26)
- Delayed hyperenhancement on cardiac MRI (S7.4-37—S7.4-39,S7.4-54)
- LVOT obstruction (S7.4-2,S7.4-4)
- Syncope ≥5 y ago (S7.4-8,S7.4-26)

High-risk subsets§

- LV aneurysm (S7.4-40,S7.4-55,S7.4-56)
- LVEF <50% (S7.4-52)

HCM = hypertrophic cardiomyopathy; ICD = implantable cardioverter-defibrillator; LV = left ventricular; LVEF = left ventricular ejection fraction; LVOT = left ventricular outflow tract; NSVT = nonsustained ventricular tachycardia; SCD = sudden cardiac death; VT = ventricular tachycardia; VF = ventricular fibrillation.

*There is general agreement in the literature that these factors independently convey an increased risk for SCD in patients with HCM.

†Decrease in blood pressure of 20 mm Hg or failure to increase systolic blood pressure >20 mm Hg during exertion.

‡There is a lack of agreement in the literature that these modifiers independently convey an increased risk of SCD in patients with HCM; however, a risk modifier when combined with a risk factor often identifies a patient with HCM at increased risk for SCD beyond the risk conveyed by the risk factor alone.

§A small subset of patients with an LVEF <50% (end-stage disease) or an LV aneurysm warrant consideration for ICD implantation (S7.4-52).

2017 ACC/ AHA/ HRS Guidelines

Recommendations for HCM
References that support the recommendations are summarized in Online Data Supplement 31.

COR	LOE	Recommendations
I	B-NR	1. In patients with HCM, SCD risk stratification should be performed at the time of initial evaluation and periodically thereafter (S7.4-1—S7.4-8).
I	B-NR	2. In patients with HCM who have survived an SCA due to VT or VF, or have spontaneous sustained VT causing syncope or hemodynamic compromise, an ICD is recommended if meaningful survival greater than 1 year is expected (S7.4-1,S7.4-6,S7.4-9,S7.4-10).
I	B-NR	3. In first-degree relatives of patients with HCM, an ECG and echocardiogram should be performed (S7.4-11—S7.4-17).
I	B-NR	4. In first-degree relatives of patients with HCM due to a known causative mutation, genetic counseling and mutation-specific genetic testing are recommended (S7.4-13—S7.4-15,S7.4-18,S7.4-19).
IIa	B-NR	5. In patients with clinically suspected or diagnosed HCM, genetic counseling and genetic testing are reasonable (S7.4-13—S7.4-15,S7.4-18—S7.4-22).
IIa	B-NR	6. In patients with HCM and 1 or more of the following risk factors, an ICD is reasonable if meaningful survival of greater than 1 year is expected:
	C-LD	a. Maximum LV wall thickness ≥30 mm (LOE: B-NR) (S7.4-2,S7.4-3,S7.4-23,S7.4-24).
	C-LD	b. SCD in 1 or more first-degree relatives presumably caused by HCM (LOE: C-LD) (S7.4-25,S7.4-26).
		c. 1 or more episodes of unexplained syncope within the preceding 6 months (LOE: C-LD) (S7.4-8, S7.4-26).

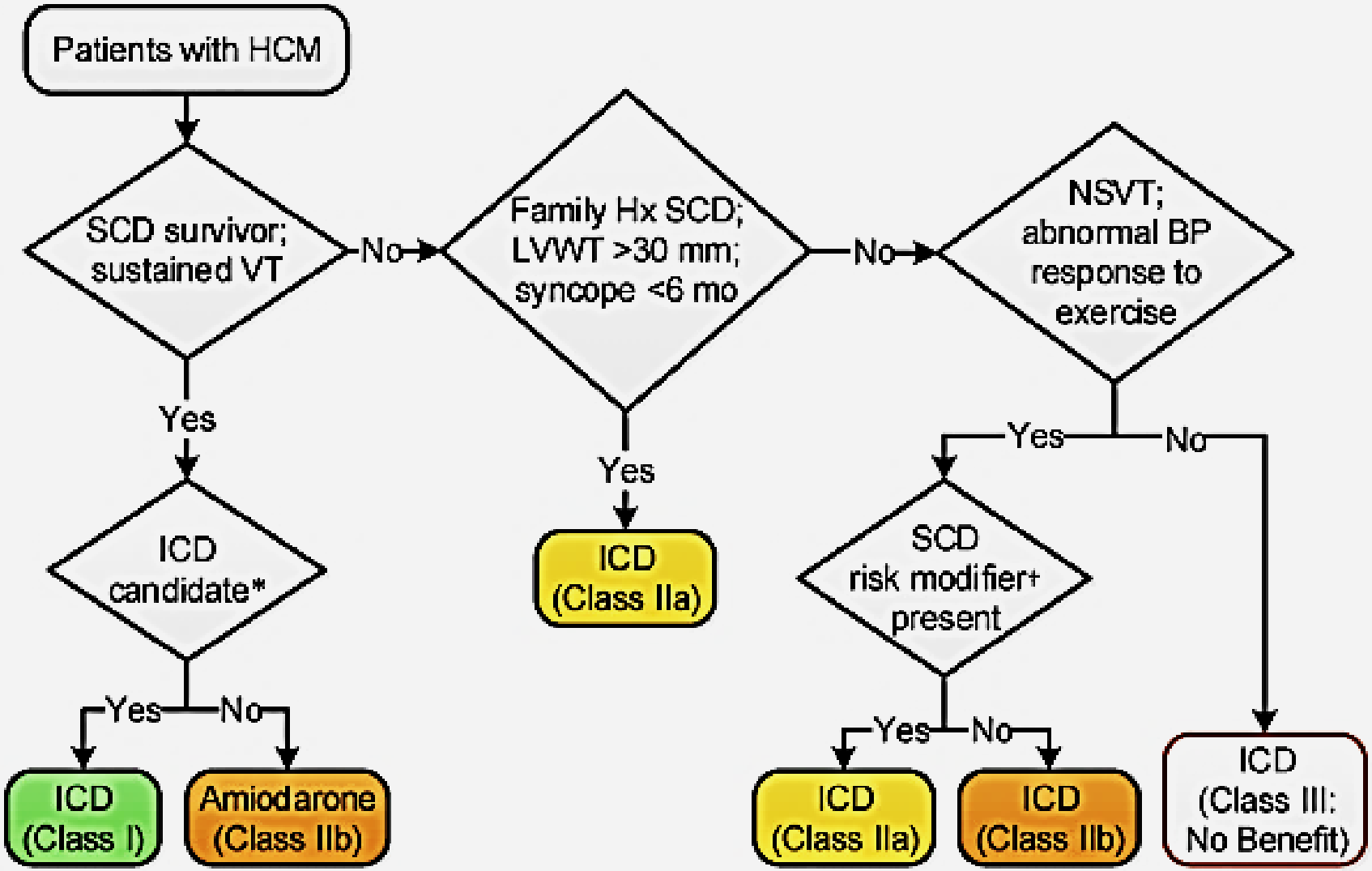
(Continued)

2017 ACC/ AHA/ HRS Guidelines

(Continued)

COR	LOE	Recommendations
IIa	B-NR C-LD	7. In patients with HCM who have spontaneous NSVT (LOE: C-LD) (S7.4-2,S7.4-26,S7.4-27) or an abnormal blood pressure response with exercise (LOE: B-NR) (S7.4-5,S7.4-28,S7.4-29), who also have additional SCD risk modifiers or high-risk features, an ICD is reasonable if meaningful survival greater than 1 year is expected.
IIb	B-NR B-NR	8. In patients with HCM who have NSVT (LOE: B-NR) (S7.4-2,S7.4-26,S7.4-27) or an abnormal blood pressure response with exercise (LOE: B-NR) (S7.4-5,S7.4-28,S7.4-29) but do not have any other SCD risk modifiers, an ICD may be considered, but its benefit is uncertain.
IIb	C-LD	9. In patients with HCM and a history of sustained VT or VF, amiodarone may be considered when an ICD is not feasible or not preferred by the patient (S7.4-30,S7.4-31).
III: No Benefit	B-NR	10. In patients with HCM, an invasive electrophysiological study with programmed ventricular stimulation should not be performed for risk stratification (S7.4-32,S7.4-33).
III: No Benefit	B-NR	11. In patients with an identified HCM genotype in the absence of SCD risk factors, an ICD should not be implanted (S7.4-7,S7.4-34,S7.4-35).

Prevention of SCD in HCM Patients



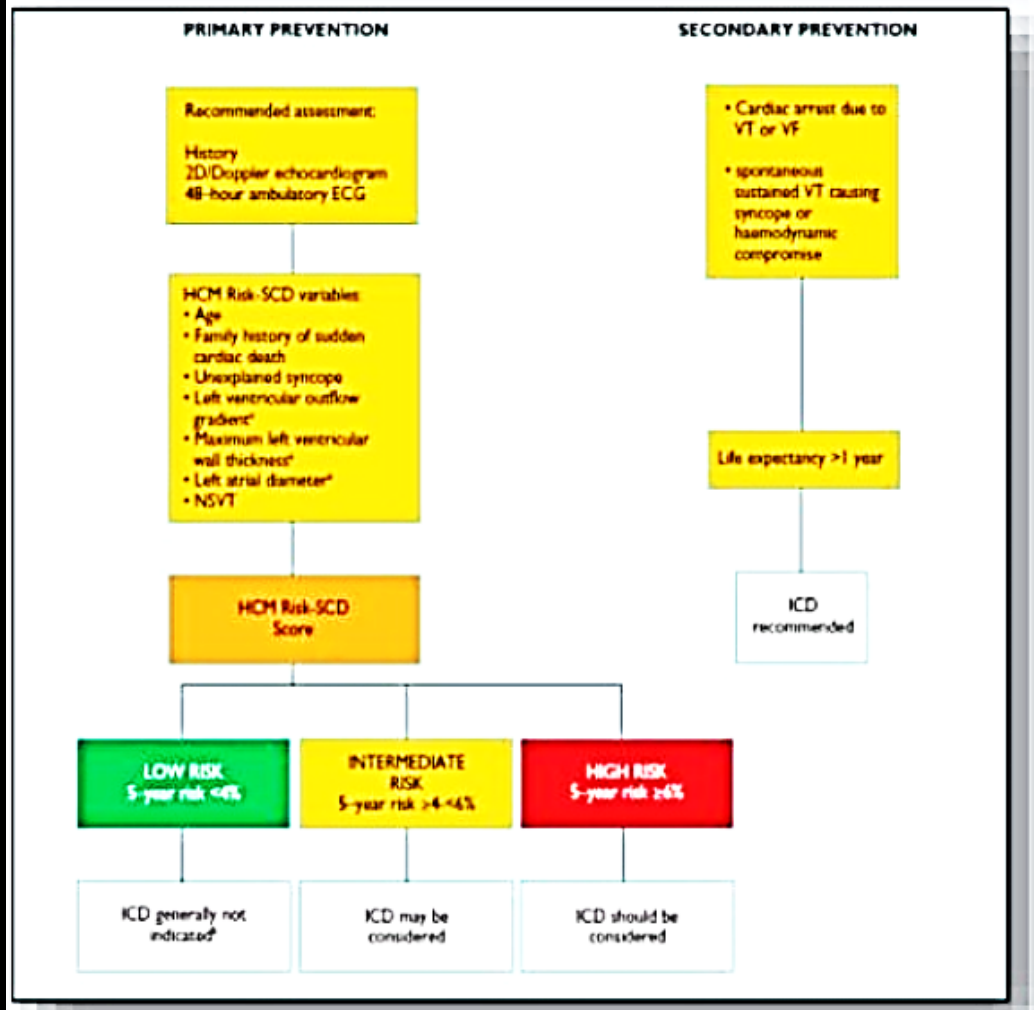
Recommendations for ICD Use in HCM-
ESC Risk Scoring System and AHA/ACC Algorithm

ESC

Vs

ACC/ AHA

Guidelines



Eur Heart J 2014; 35:2739

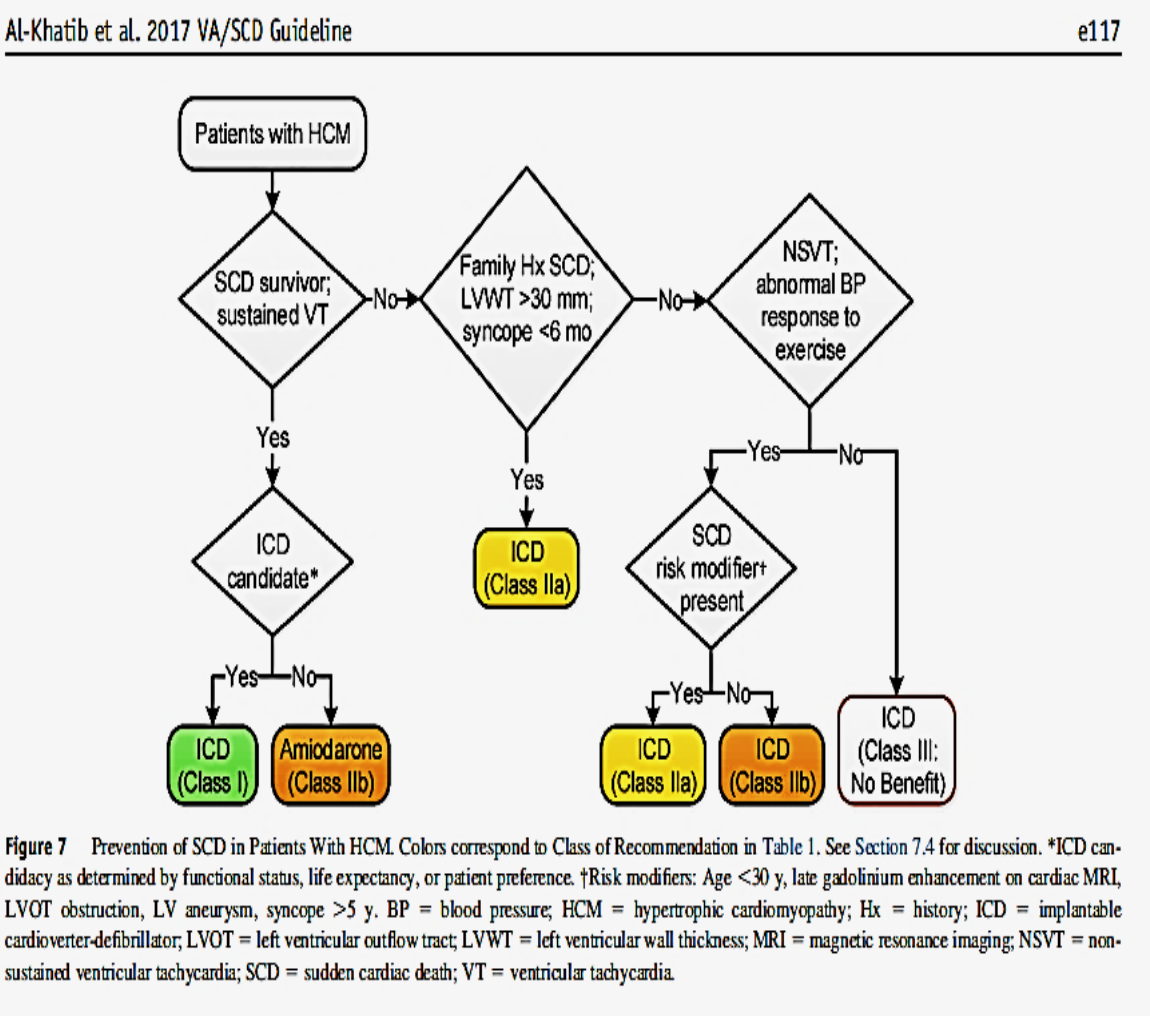


Figure 7 Prevention of SCD in Patients With HCM. Colors correspond to Class of Recommendation in Table 1. See Section 7.4 for discussion. *ICD candidacy as determined by functional status, life expectancy, or patient preference. †Risk modifiers: Age <30 y, late gadolinium enhancement on cardiac MRI, LVOT obstruction, LV aneurysm, syncope >5 y. BP = blood pressure; HCM = hypertrophic cardiomyopathy; Hx = history; ICD = implantable cardioverter-defibrillator; LVOT = left ventricular outflow tract; LVWT = left ventricular wall thickness; MRI = magnetic resonance imaging; NSVT = non-sustained ventricular tachycardia; SCD = sudden cardiac death; VT = ventricular tachycardia.

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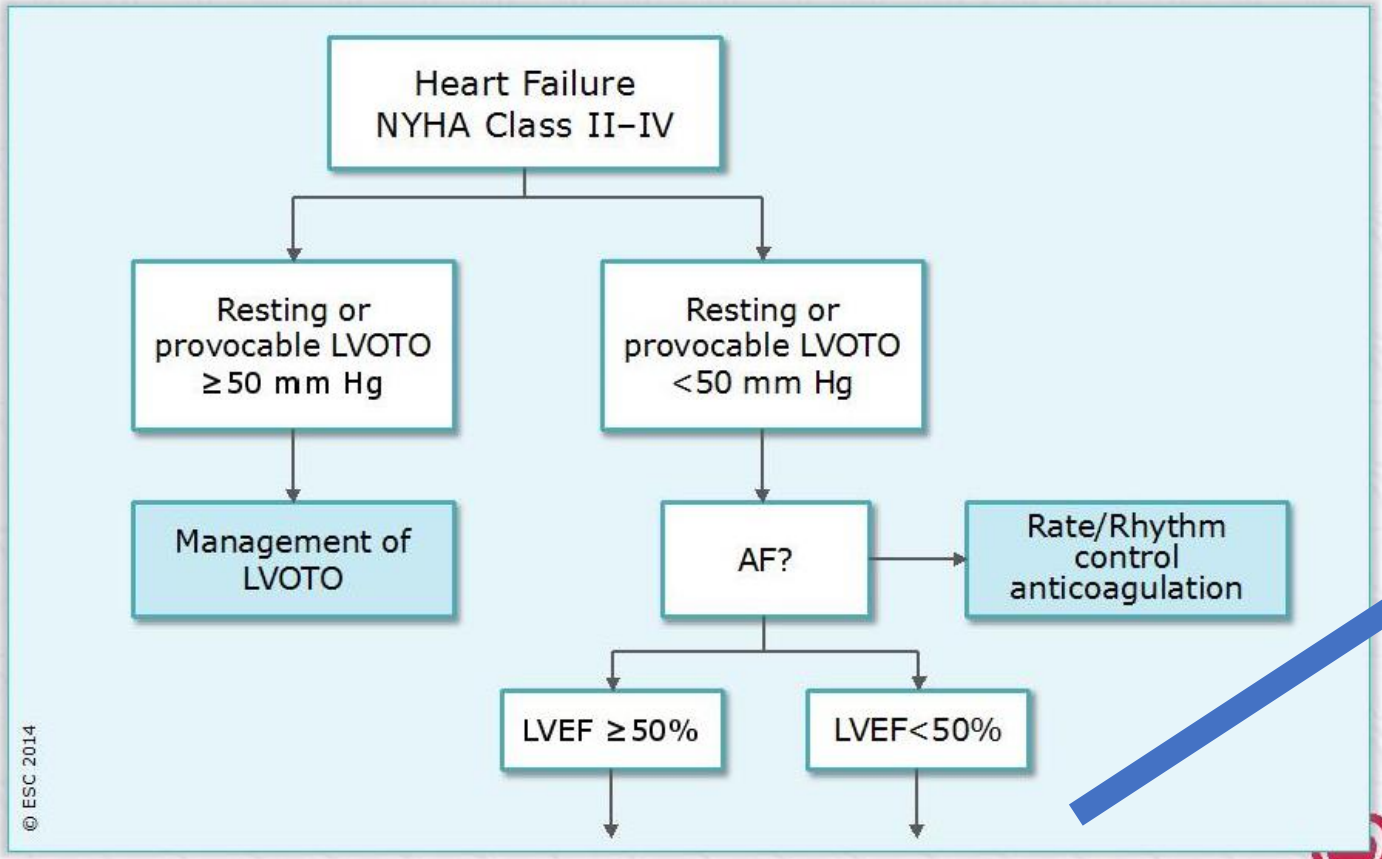
Heart Failure Treatment in HCM

Algorithm for the treatment of heart failure in hypertrophic cardiomyopathy



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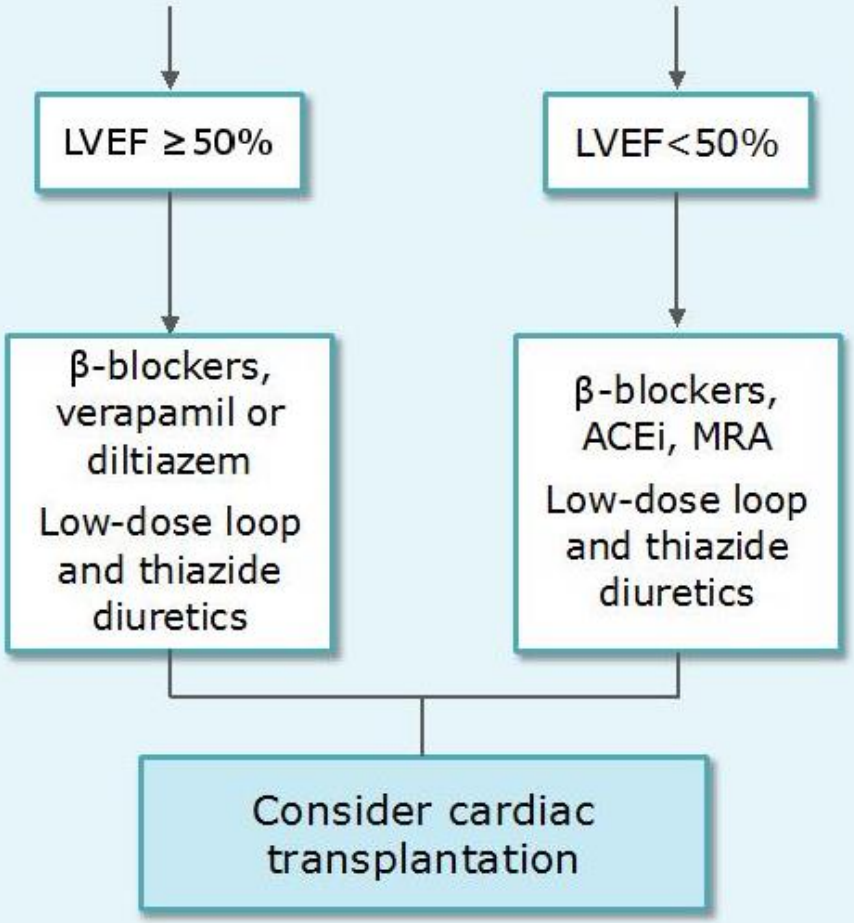

Patients with heart failure and preserved LV ejection fraction (≥50%)

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

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

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

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

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STATE-OF-THE-ART PAPER

Clinical Spectrum and Management of Heart Failure in Hypertrophic Cardiomyopathy

Barry J. Maron, MD, Ethan J. Rowin, MD, James E. Udelson, MD, Martin S. Maron, MD

ABSTRACT

Heart failure (HF), characterized by excessive exertional dyspnea, is a common complication within the broad clinical spectrum of hypertrophic cardiomyopathy (HCM). HF has become an increasingly prominent management issue with the reduction in sudden deaths due to use of implantable defibrillators in this disease. Exertional dyspnea ranges in severity from mild to severe (New York Heart Association functional classes II to IV) and not uncommonly becomes refractory to medical management, leading to progressive disability, but largely in the absence of pulmonary congestion and volume overload requiring hospitalization. HCM-related HF is most commonly due to dynamic mechanical impedance to left ventricular outflow produced by mitral valve systolic anterior motion, leading to high intracavity pressures. Surgical septal myectomy with low operative mortality (<1%) produces HF reversal and symptom relief in 90% to 95% of patients, while also conveying a survival benefit. Exercise echocardiography has assumed an important role in the evaluation of patients with HCM, i.e., by identifying candidates for septal reduction therapy with refractory HF when outflow gradients are present only with physiological exercise, distinguishing highly symptomatic nonobstructive patients as heart transplant candidates, and predicting future development of progressive HF. Notably, mortality directly attributable to HF has become exceedingly uncommon in HCM (<0.5%/year) in contrast with HF in non-HCM diseases (by 20-fold). In conclusion, HF in HCM is associated with diverse and complex pathophysiology, but a substantially more favorable prognosis than conventional non-HCM HF, and highly amenable to effective treatment options in the vast majority of patients. (J Am Coll Cardiol HF 2017;■:■-■) © 2017 by the American College of Cardiology Foundation.

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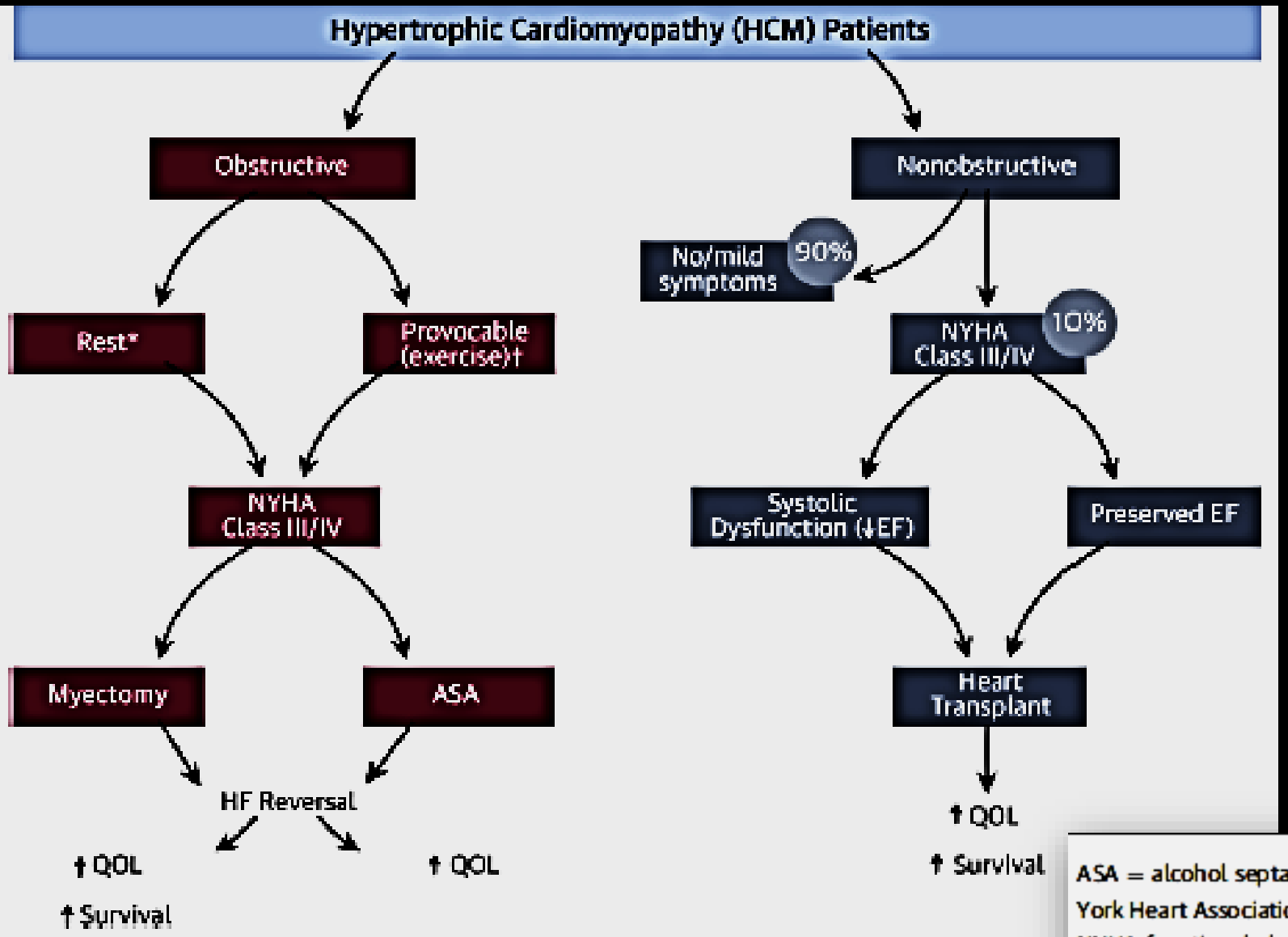
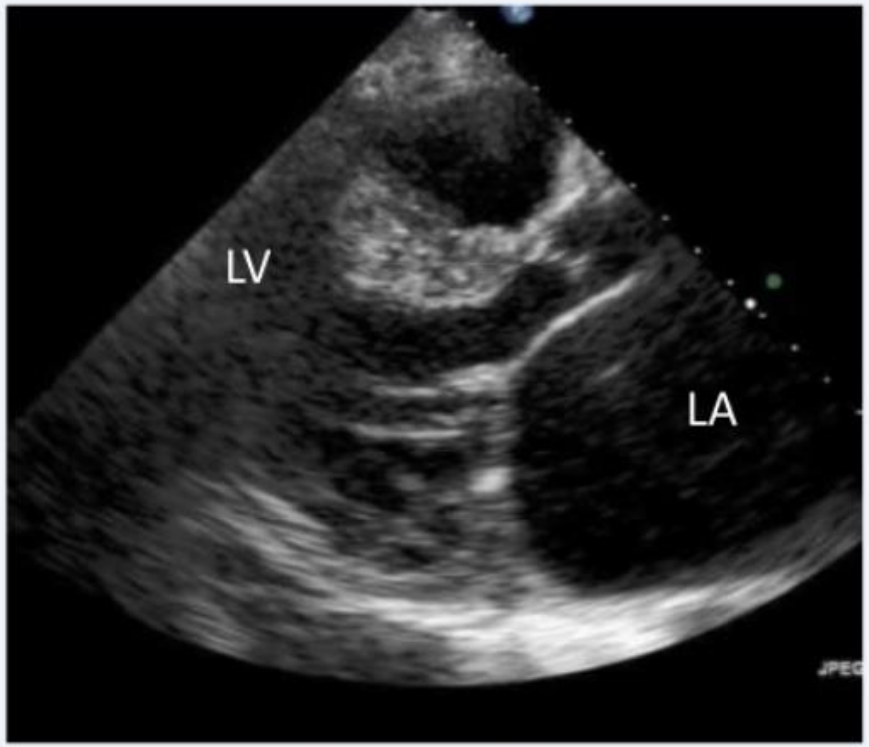
Clinical Course in HCM associated with HF Symptoms and Functional Impairment



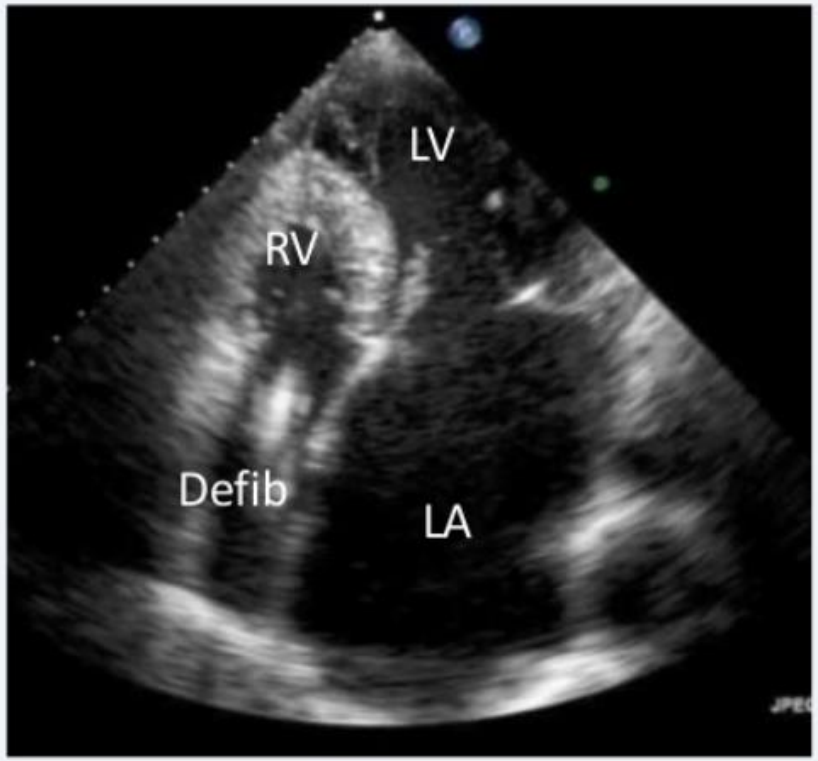
ASA = alcohol septal ablation; EF = ejection fraction; HF = heart failure; NYHA = New York Heart Association; QOL = quality of life. *A 7.4% per year rate of HF progression to NYHA functional class III/IV. †A 3.2% per year rate of HF progression to class NYHA functional class III/IV. ‡A 1.6% per year rate of HF progression to NYHA functional class III/IV.

Maron, B.J. et al. J Am Coll Cardiol HF. 2017;■(■):■-■.

End-stage "Burnt out" HCM



Long Axis



4 Chamber

End-stage Cardiomyopathy in HCM

- **About 5% develop "burned out" phase**
- **EF <50%**
- **Predictors:**
  - Family history of end-stage HCM
  - Extensive gadolinium enhancement (fibrosis)
- **Treatment**
  - Similar to end-stage cardiomyopathy
  - Afterload reducing agents, beta blockers, diuretics, ICD, biventricular pacing, advanced heart failure therapies
  - Cardiac transplantation

- **Role of GENETIC Testing**

Genetic counselling

Recommendations	Class	Level
Genetic counselling is recommended for all patients with HCM when their disease cannot be explained solely by a non-genetic cause, whether or not clinical or genetic testing will be used to screen family members.	I	B
Genetic counselling should be performed by professionals trained for this specific task working within a multidisciplinary specialist team.	IIa	C

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

Genetic testing in probands

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

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

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Genetic and clinical testing of adult relatives

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

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

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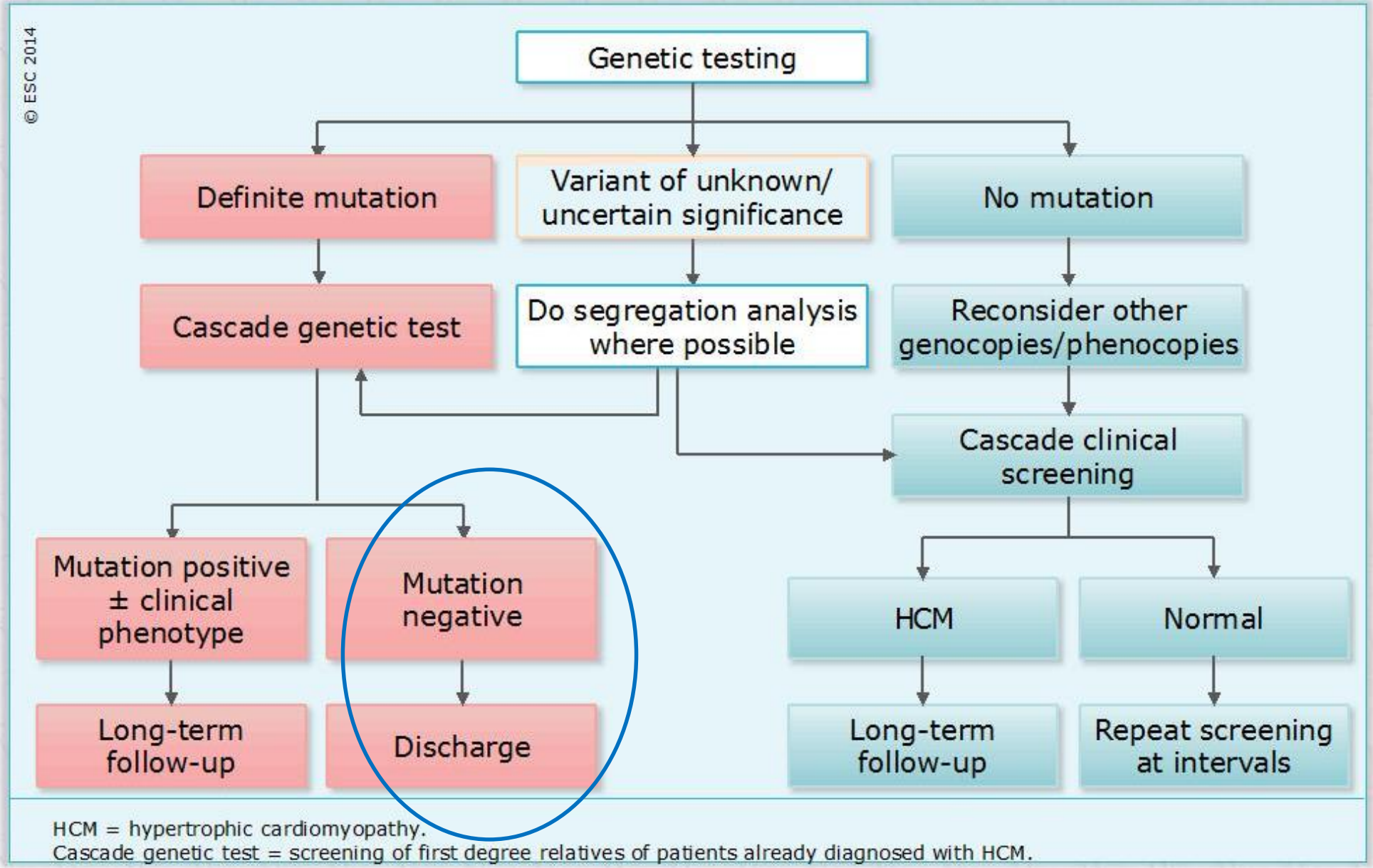
Flow chart for the genetic and clinical screening of probands and relatives



SUMMARY

- **Most HCM has a genetic basis**
- **Genetic testing recommended to assess the HCM patient's family and first degree relatives**
- **Wall thickness important, LV outflow obstruction not required for Dx**
- **Differentiating HCM from HBP, Athlete's Heart or other causes of LVH.**
  - Major key: HCM generally affects diastolic functional measures
- **Symptomatic treatment may vary dependent on presence or absence of LV outflow obstruction and degree of diastolic dysfunction**
- **Risk factor assessment for sudden cardiac death is still undergoing refinement**
- **ICD requirement based anatomic features, FH and sx**

SUMMARY

Class 1 Recommendations for Evaluation and Following Patients with HCM

- ECG in all
- 48 hr Holter in all: first visit and anytime syncope or palpitations
- Echo/Doppler with Valsalva in all
- In symptomatic patients with LVOT gradient <50 mmHg, echo/Doppler upright or with exercise
- Cardiac MRI if echo unclear or to confirm dx
- Genetic counselling regardless of genetic testing
- Genetic testing when it enables screening of relatives
- TEE if considering surgical myectomy
- Intracoronary contrast echo if considering ablation
- Coronary angiography in pts who have had cardiac arrest, VT or angina
- EP study if ablation possible for atrial arrhythmias or WPW

- **Thank you very much**

- Questions and Answers

Genetic and clinical screening in children

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

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Differentiating Athlete's Heart from HCM

LV wall thickness >15 mm

LV wall thickness <13 mm

Unusual patterns of LVH
LV cavity <45 mm
Marked LA enlargement
Bizarre ECG patterns
Abnormal LV diastolic filling
Female sex
Family history of HCM

Favors HCM

LV cavity >55 mm
Normal diastolic filling
Normal LA size
Male sex
Thickness decreases with deconditioning
No Family history of HCM
Max VO_2 > 45 ml/kg/min or >110% predicted

Favors Athlete's Heart