Hypertrophic Cardiomyopathy

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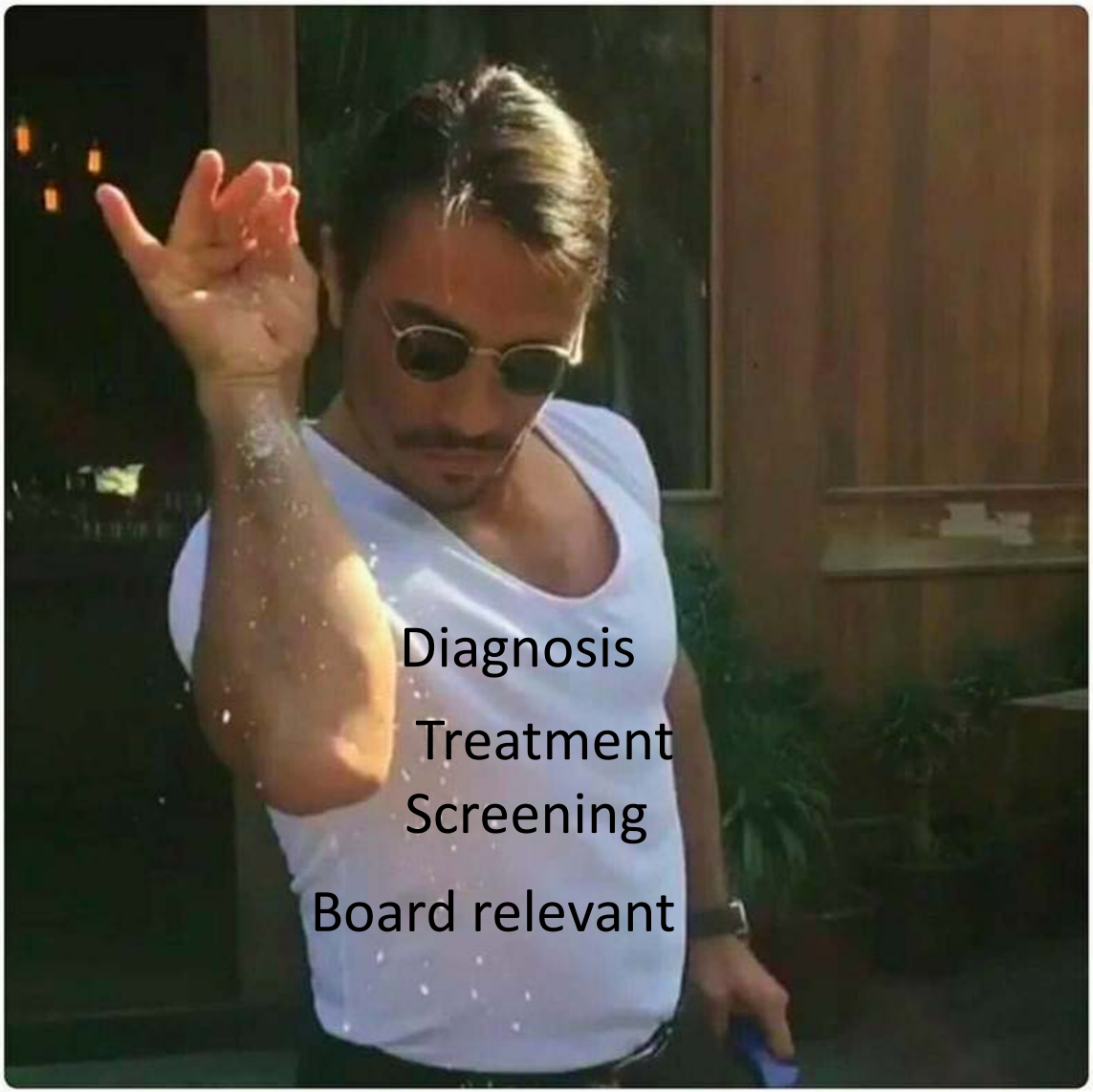
Goals – Sprinkling HCM Knowledge



Definition

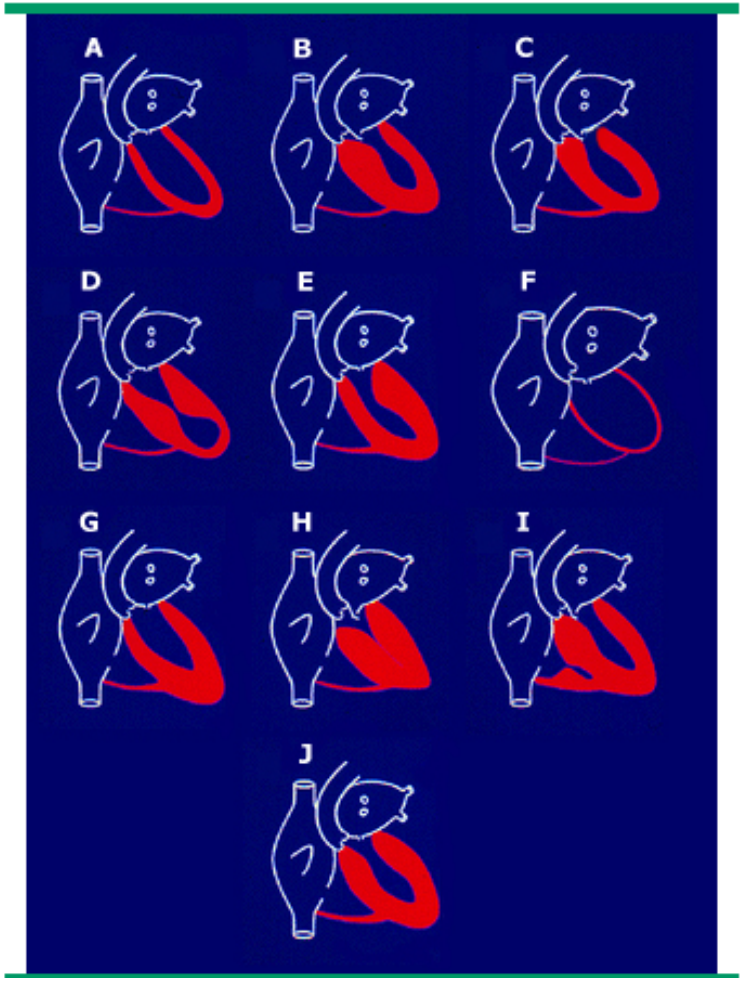
- Hypertrophic cardiomyopathy (HCM) is LV hypertrophy associated with nondilated ventricular chambers in the absence of another cardiac or systemic disease that could produce such hypertrophy.
- Caused by mutations in one of several sarcomere genes which encode components of the contractile apparatus of the heart.

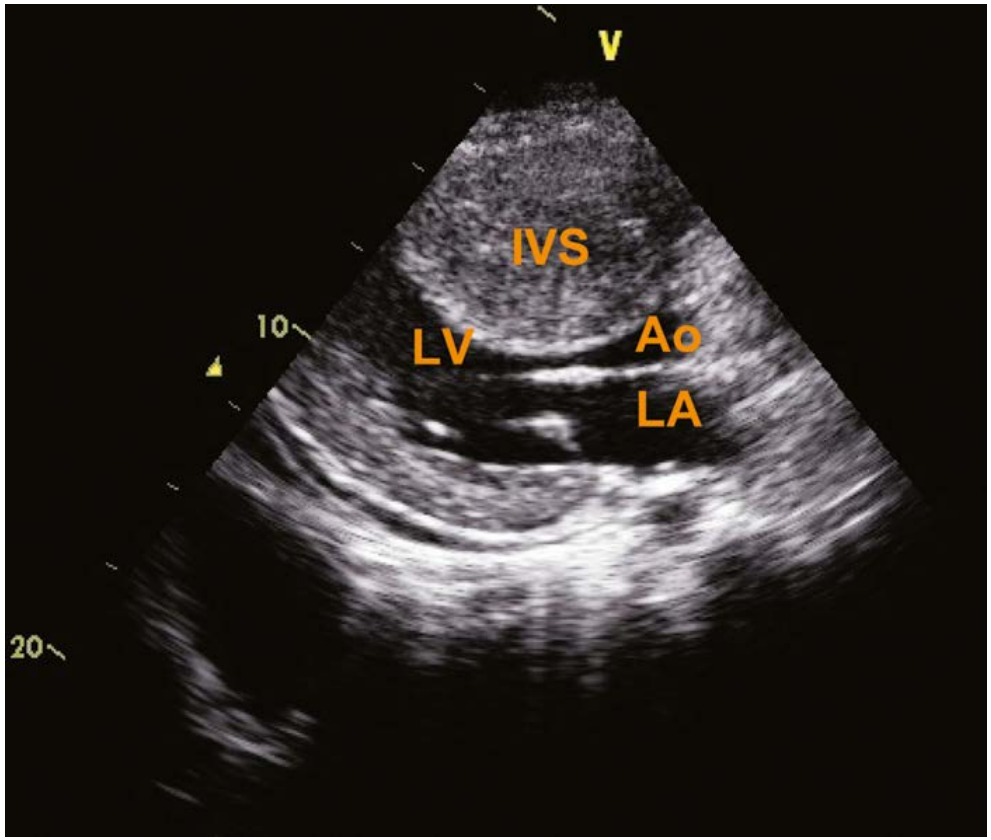
Differential Diagnosis of LV Wall Thickening

- Long-standing hypertension
- Athlete's heart
- Aortic stenosis
- Amyloidosis
- Mitochondrial disease
- Fabry disease
- Friedrich's ataxia
- Danon disease
- Noonan syndrome
- Pompe disease

Morphologic Variants

Morphologic variants of hypertrophic cardiomyopathy



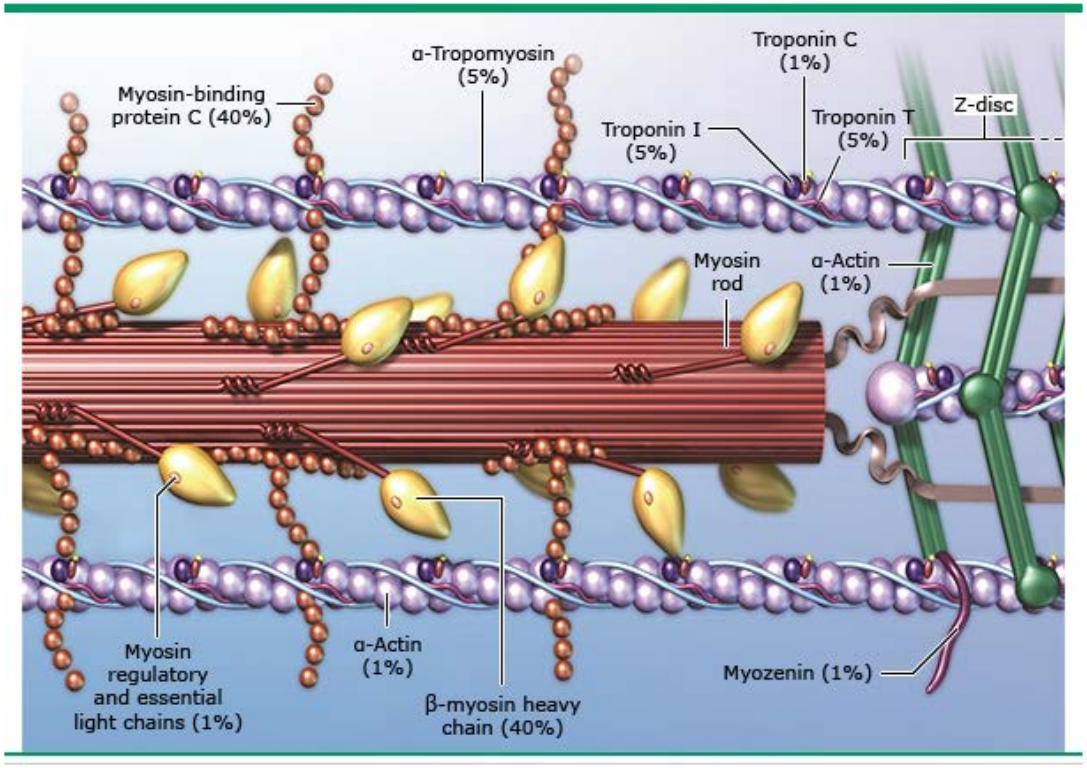


Prevalence

- Approximately 1 in 200-500.
- Leading cause of sudden death among athletes younger than 35.

Genetic Aspects

Sarcomeric gene mutation locations in hypertrophic cardiomyopathy (HCM)

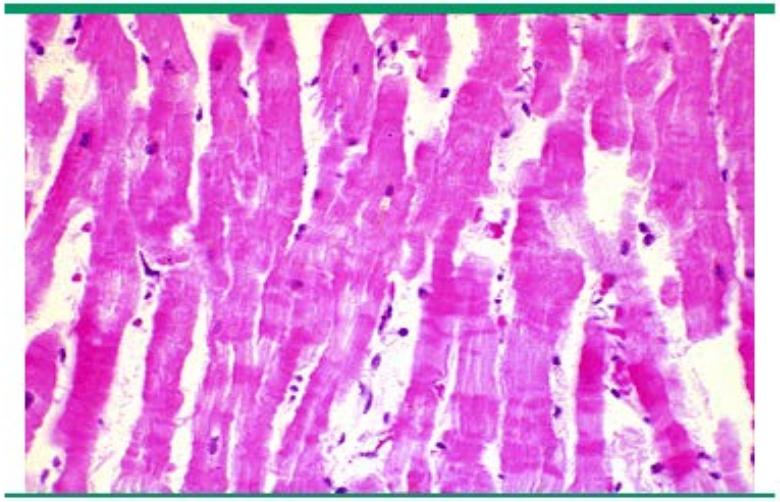


1,400 different mutations
Greater than 27 genes
Autosomal dominant

Pt with identifiable mutation at increased risk of CV death, stroke, and progression to NYHA III-IV HF, compared with no mutation identified.

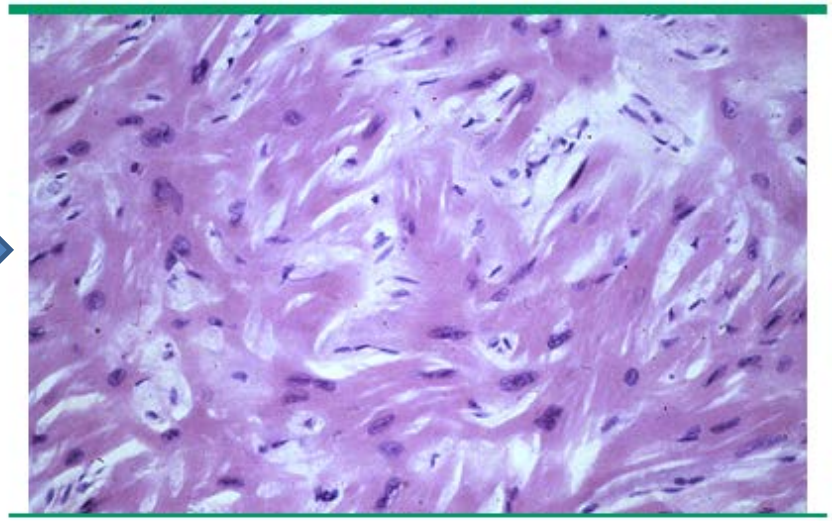
Histologic Features

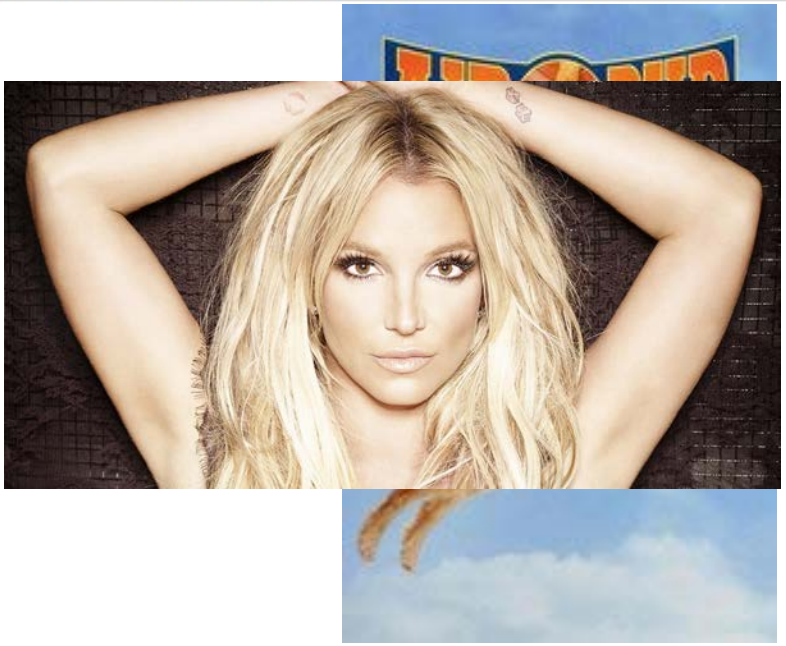
Normal endomyocardial biopsy



Normal endomyocardial biopsy in longitudinal section.

Myocyte disarray in hypertrophic cardiomyopathy





18 y/o man is seen for a pre-participation sports eval. No symptoms. Played varsity basketball and cross country the last 3 years without limitatio hy. He has no fa n death.

PE, BP 11 e normal. (ustained or enlarg ormally split. No has the voice of

Which of manager

A. Echo
B. EKG stress test
C. EKG
D. No further testing

No further testing

- In the absence of suspicious symptoms, exam findings, or FHx in pt undergoing sports physical, additional testing with imaging or EKG to exclude HCM is not indicated.
- The use of EKG, echo, stress testing to exclude HCM in US lacks proven cost-effectiveness, and would require infrastructure that currently does not exist. Additionally may lead to additional testing and false positive results that would lead to unwarranted disqualification from sports.
- These guidelines differ from Europe, where EKG is often incorporated in preparticipation sports exam.

Clinical Manifestations

- Heart Failure
  - Dyspnea, PND, fatigue
  - Caused by diastolic dysfunction and LVOT obstruction
  - Events that accelerate HR, decrease preload, increase LVOT obstruction exacerbate symptoms
  - 5-10% pt progress to severe LV systolic dysfunction
- Myocardial ischemia
  - Mismatch of supply and demand due to thickened vessels and small vessel disease
- Syncope and presyncope
  - Commonly associated with exertion or cardiac arrhythmia
- Sudden death
  - Annual mortality rate for HCM 1%
  - 22% have no symptoms
  - 60% of deaths occur during periods of inactivity
  - Most common among older children and young adults
  - Arrhythmia/ischemia → hypotension, decreased filling time → increased obstruction → death

Physical Exam

- JVP
  - Prominent a wave (lack of RV compliance)
- Palpitation
  - Apical precordial pulse usually laterally displaced and diffuse
  - Carotid pulse is bifid. Rapid upstroke followed by a second peak

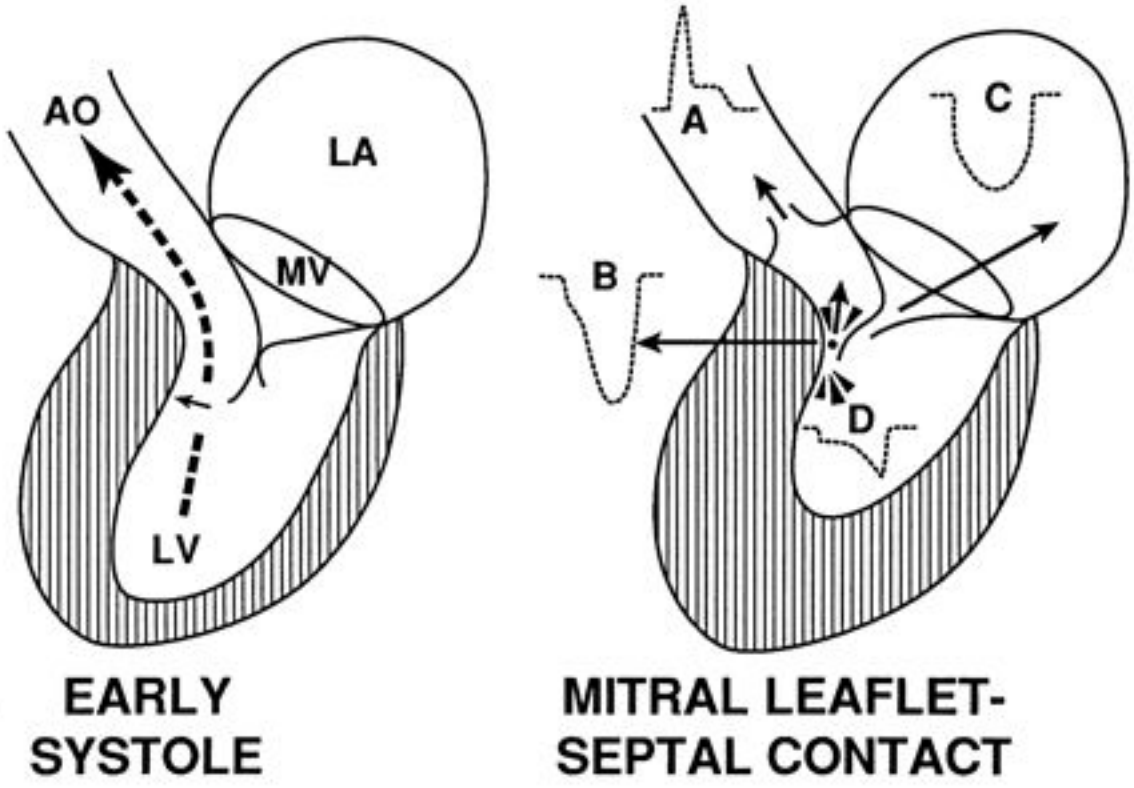
Physical Exam

- Auscultation
  - S1 usually normal and preceded by S4.
  - S2 can be normal or paradoxically split as the result of prolonged ejection time from obstruction.
  - Harsh, crescendo-decrescendo systolic murmur best heard at LSB. Radiates to LLSB but not to neck.
    - Variation in intensity and duration with ventricular loading conditions
    - Concomitant murmur of MR and AI can be found.
    - Maneuvers that affect preload and afterload can be helpful in distinguishing from other SEM.

Effect of maneuvers

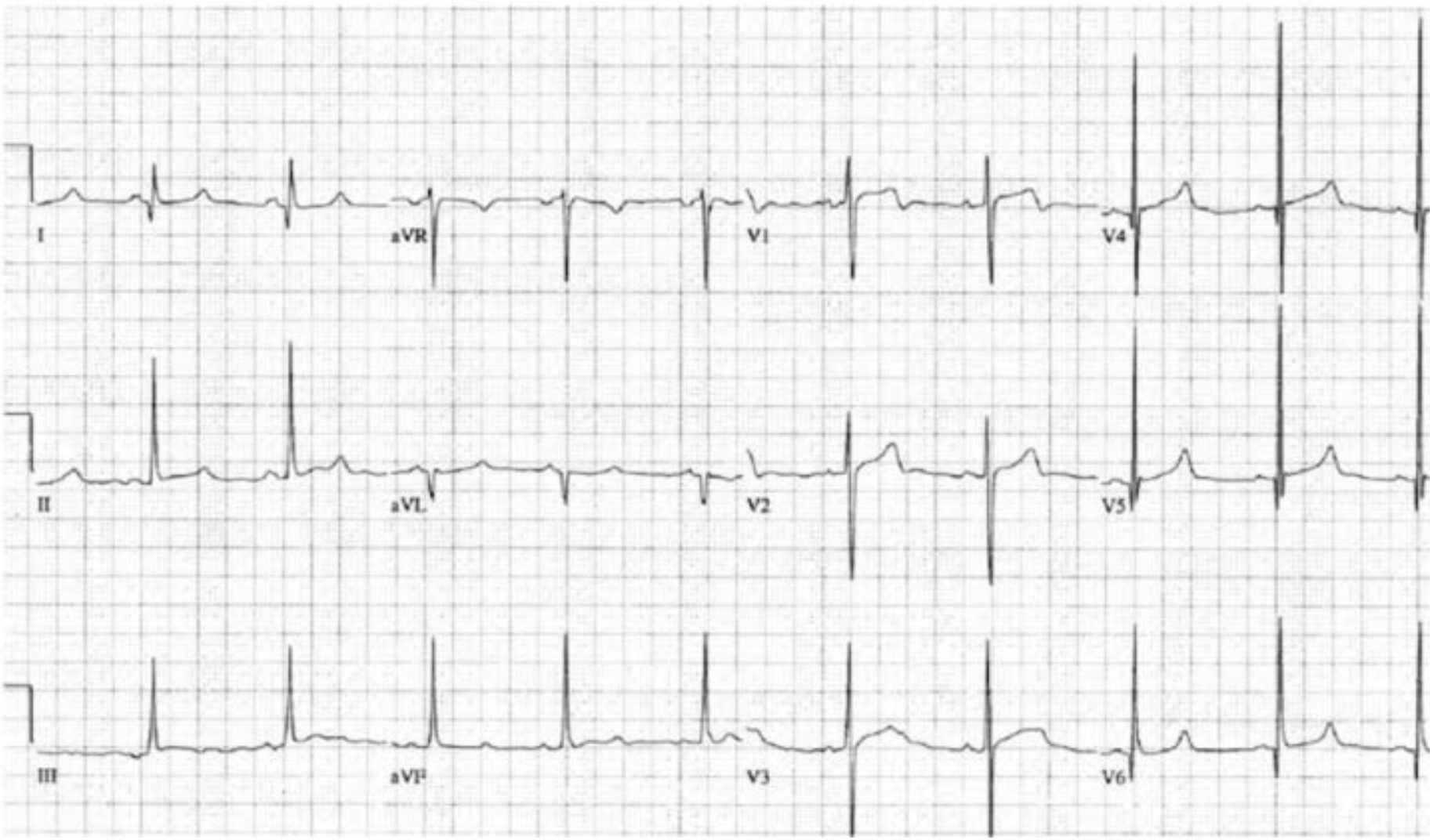
Maneuver	Physiologic Effect	HCM	AS
Valsalva and standing	Decreases VR, SVR, and CO	↑	↓
Squat and handgrip	Increases VR, SVR, and CO	↓	↑
Amyl nitrite	Increases VR Decreases SVR and LV volume	↑	↑
Extrasystole	Decreased LV volume	↑	↓
Post-valsalva release	Increased LV volume	↓	↑

Systolic Anterior Motion MV



Diagnostic testing

- EKG
  - Most pt have EKG evidence of disease but no findings are pathognomonic
  - Right and left atrial enlargement
  - Q waves in inferolateral leads
  - LAD
  - Short PR interval with slurred upstroke
  - LVH
  - Deep inverted T waves (apical HCM)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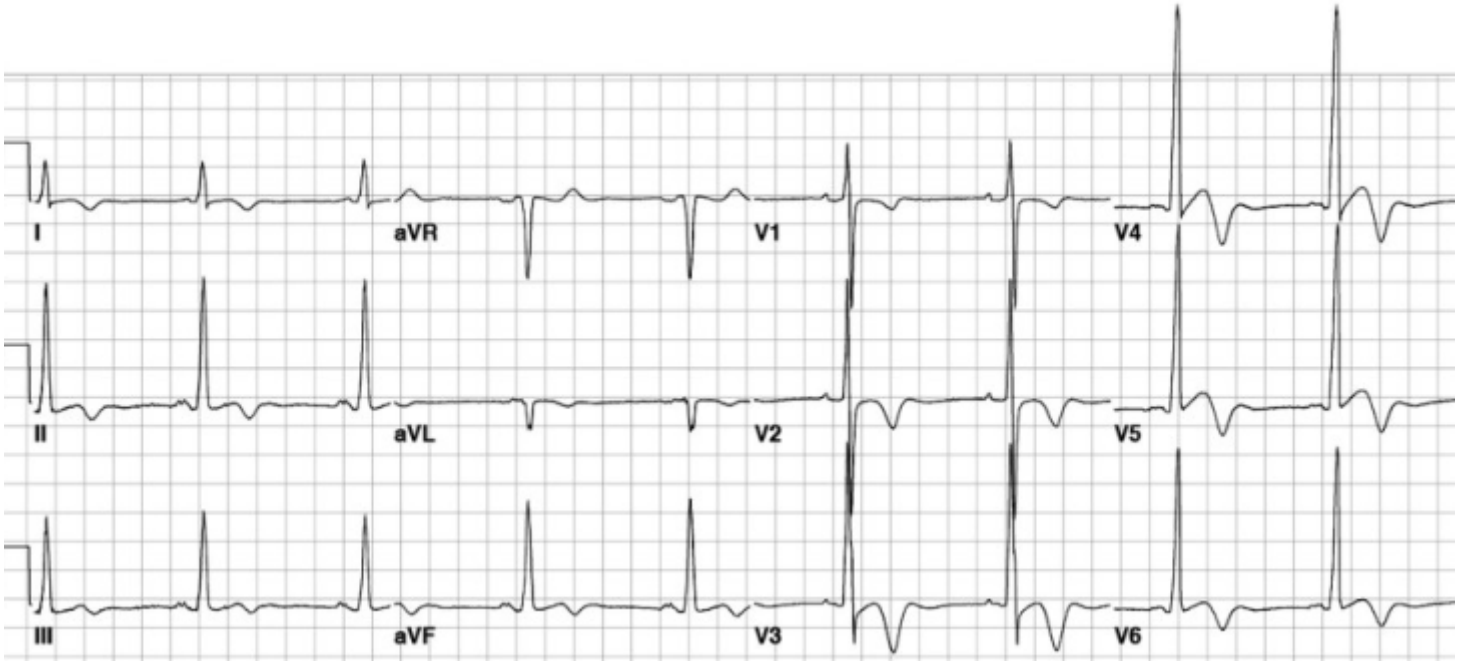
aVR
V1
V4
II
aVL
V2
V5
III
aVF
V3
V6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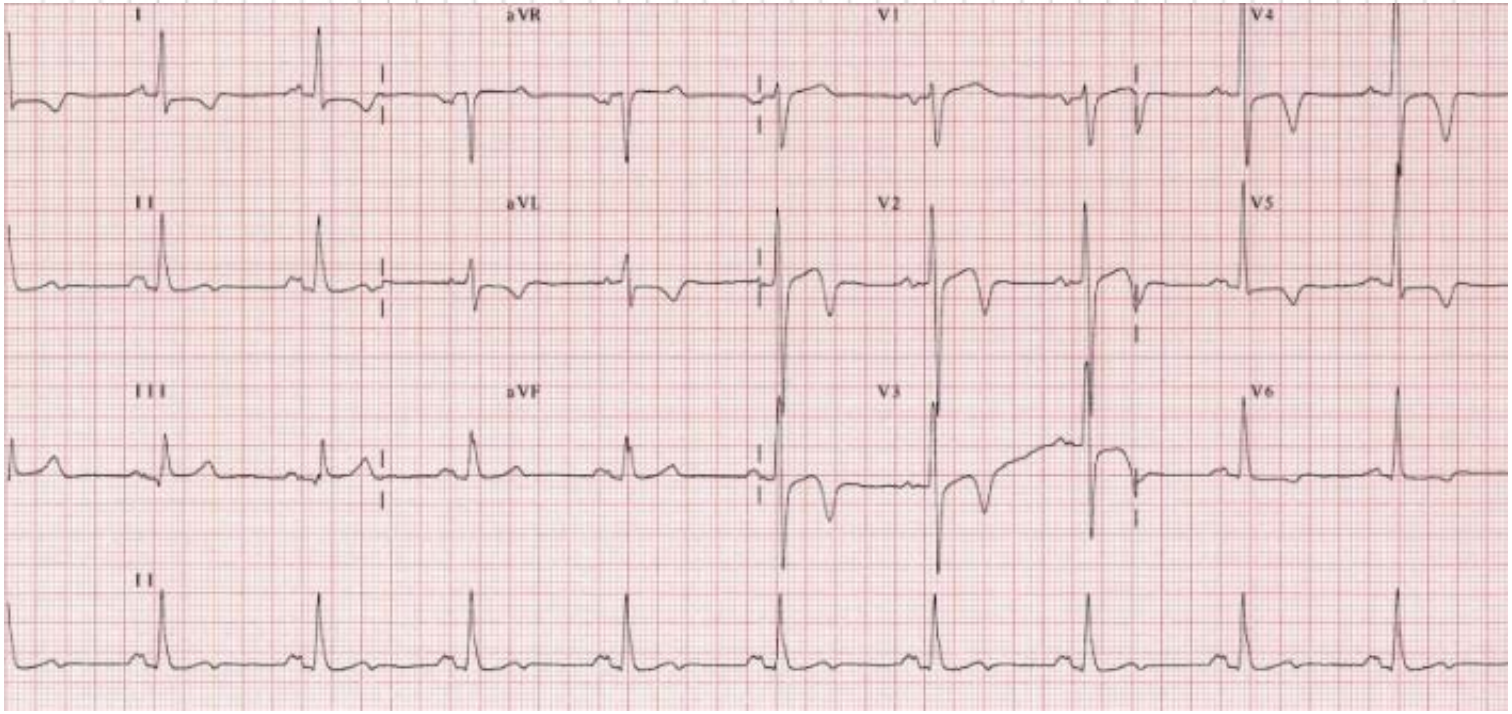
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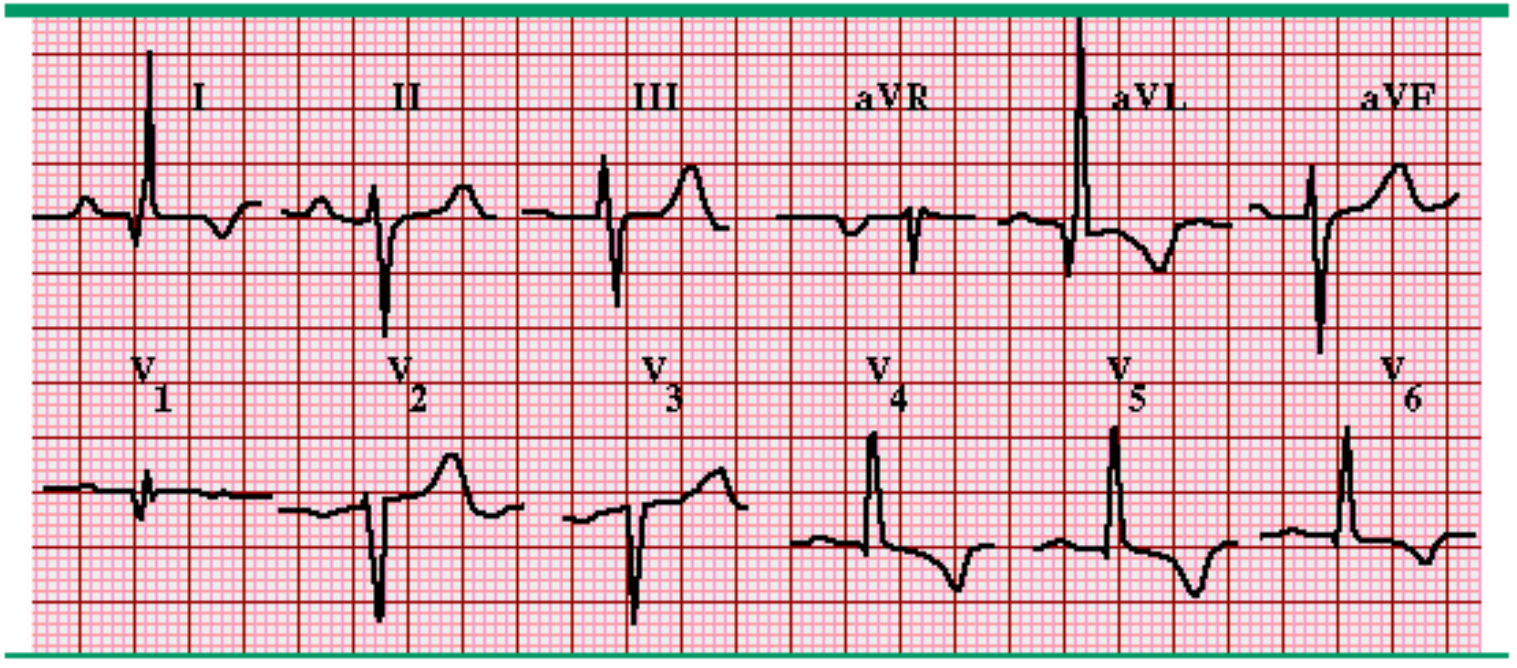
Left ventricular hypertrophy (LVH) with strain pattern



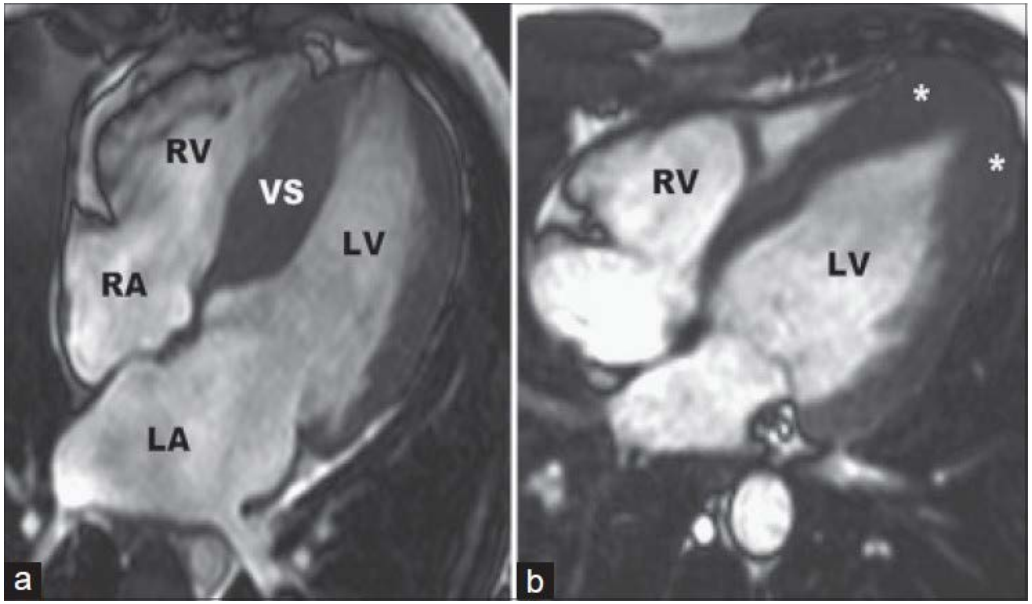
The ST-T wave abnormalities secondary to LVH (often termed "strain") are most often seen in the anterolateral leads (eg, I, aVL, V4-V6). Typical abnormalitites include a horizontal or downsloping ST segment and T wave inversions. In some cases there is concavity to the ST segment which has a final downward turn that blends into an inverted T wave.

Echo

- Preferred diagnostic method
- LV hypertrophy (>=15 mm anywhere in LV wall, 13 mm for those with fam hx)
- Resting gradients > 30 mm Hg
- Provocable gradients > 50 mm Hg
- When there is no mitral valve leaflet abnormality the degree of MR is directly correlated to the severity of obstruction

MRI

- Can assess secondary causes of LVH.
- Helpful if poor images from echo to evaluate LV.
- Able to evaluate myocardial scar.



Exercise Testing

- Indicated in all pt with suspected or known HCM to risk stratify and evaluation for obstruction.
- Echo with symptom limited Bruce protocol preferred method.

Clinically Important Findings

- Development of angina, dyspnea, palpitations or presyncope.
- Increase or development of LVOT obstruction.
- Inappropriate BP response (failure of SBP to rise with increased workload or fall in SBP).
- Clinically significant arrhythmias (a fib, VT).
- Severe ST segment depression may indicate ischemia.
- Increase or development of mitral regurgitation.

A 36 year-old woman is seen in follow-up for dyspnea. Over the past 6 months, she has noticed increasing shortness of breath during her daily run to the spotlight, which she has had to decrease from 2 miles to 1 mile. She is able to complete other aerobic exercises, such as biking and … nced no chest pain … ertension, diagnosed … othiazide.

On PE, BP … examination reveals a … c murmur heard bes … end-expiration

TTE shows … ith a diagnosis

Which of t … treatment?

A. Discontinue HCTZ
B. Dual-chamber pacemaker
C. Initiate lisinopril
D. Surgical myectomy

D/C HCTZ

- HCTZ should be d/c. LVOT obstruction affects 70% of pt with HCM and is exacerbated by decreases in preload (diuretics, squat to stand manuevers) and afterload (expiration or vasodilators) and by increased myocardial contractility (digoxin).
- Initial therapy is medical therapy for pt with symptoms of HCM. Negative inotropic agents BB, CCB, disopyramide are cornerstone of medical therapy.
- Dual-chamber PM implantation has been found to be relatively infective in randomized trials.
- ACEi reduce afterload and exacerbate LVOT obstruction.
- For pt with drug-refractory severely symptomatic HOCM, septal reduction therapy with surgical myectomy or alcohol ablation may be considered.

Medical Therapy

- Beta Blockers
  - First line therapy
  - Improve symptoms and exercise tolerance
- Calcium Channel Blockers
  - Considered second line treatment
  - Limited to verapamil and diltiazem
- Disopyramide
  - May be effective alternative or adjunct to BB or CCB
  - Significant side effect profile so usually not used long term

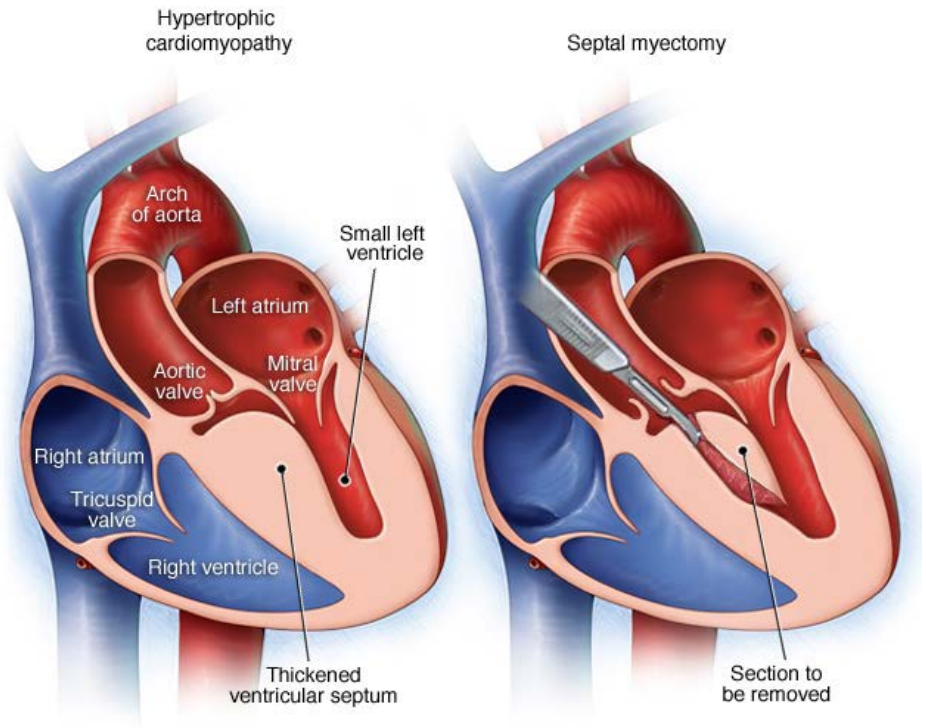
A 41 y/o man comes to the office to discuss management of HCM, which was diagnosed 2 weeks ago after murmur was discovered. HCM

ICD

- ICD is appropriate treatment for pt with HCM who have one or more risk factors for SCD.
  - Massive myocardial hypertrophy (>30 mm)
  - Previous cardiac arrest due to ventricular arrhythmia
  - Blunted BP or hypotension during exercise (< 20 mmHg)
  - Unexplained syncope
  - NSVT on ambulatory EKG (48 hr Holter recommended)
  - Family hx of sudden death due to HCM (< 45 years old)
- Pt who had ICD for secondary prevention (had prior cardiac arrest) appropriate device discharge rate ~ 11% per year. For primary prevention ~4% per year.
- Septal reduction therapy is indicated only for pt with drug-refractory, severe symptoms. Neither ablation nor surgical myectomy is advocated as a means of preventing of SCD.
- B-blocker therapy is reserved principally for patients with symptoms and has not been associated with reduction in risk of SCD.

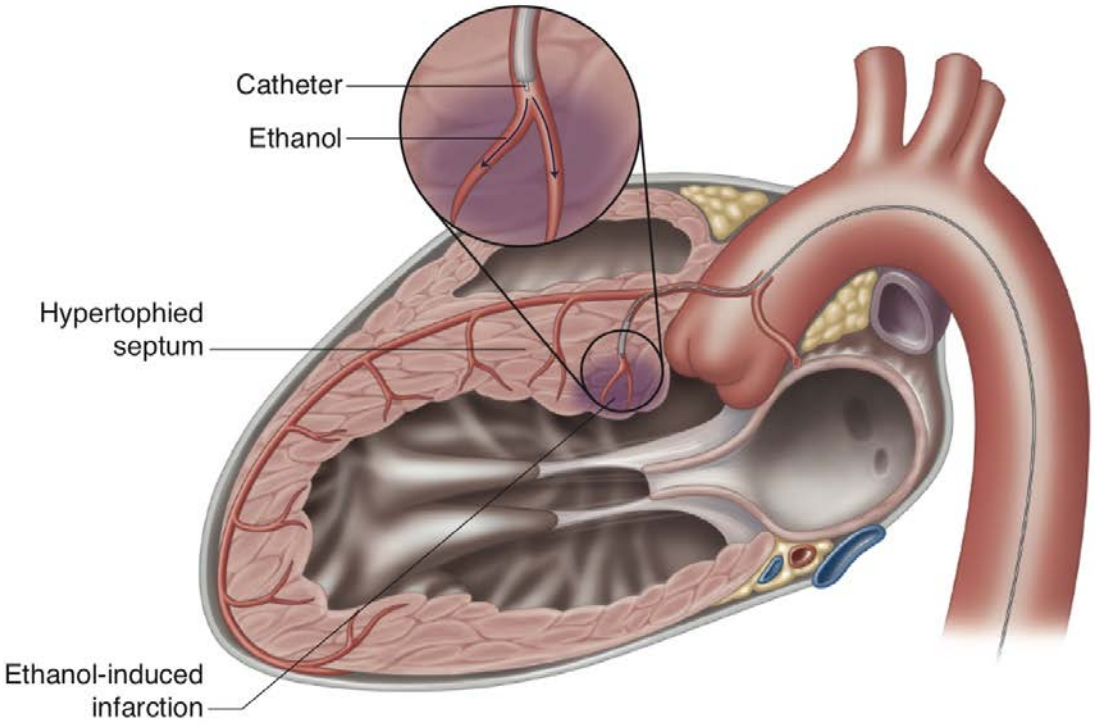
Septal Myectomy

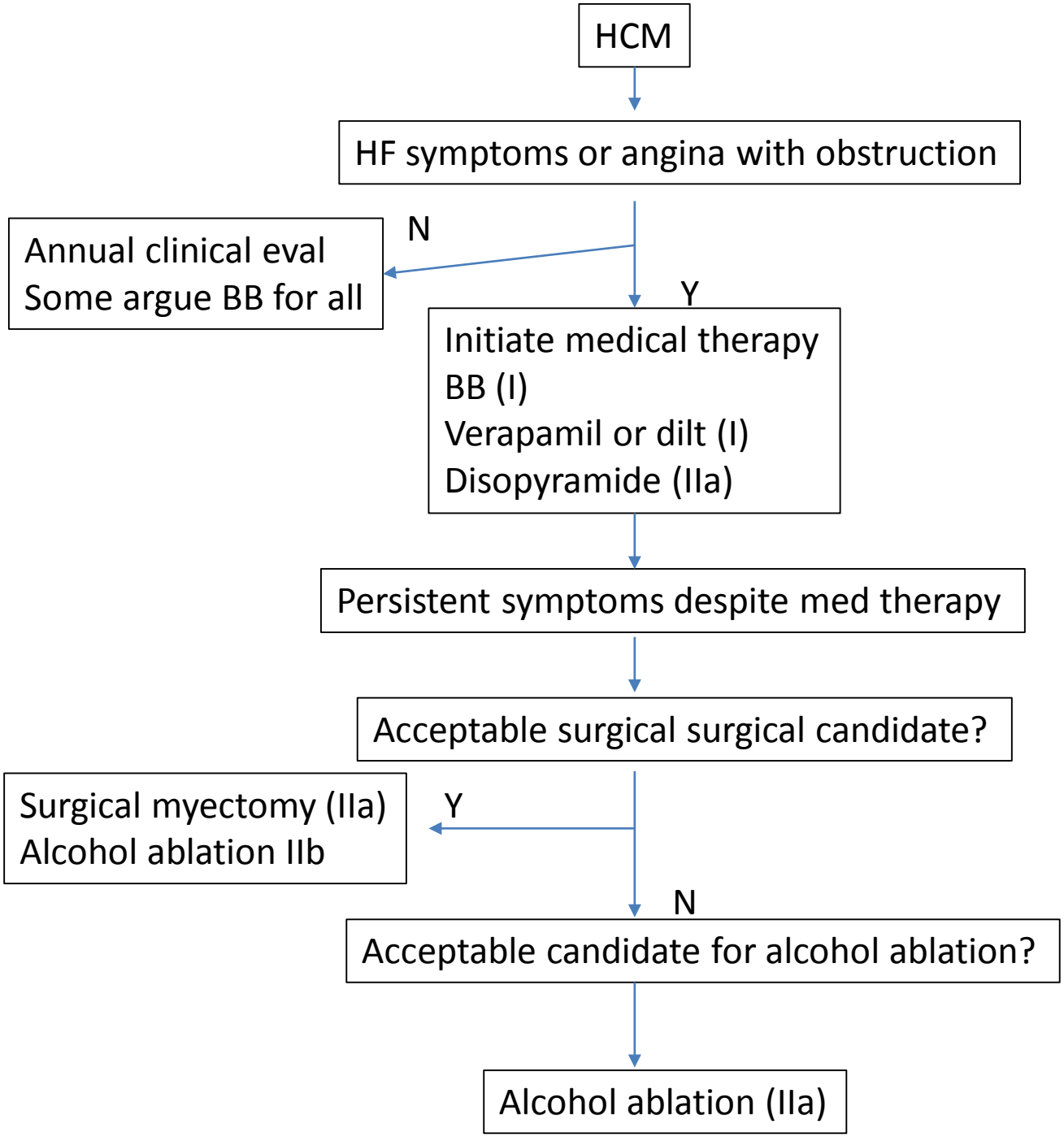
- Procedure of choice for drug refractory functional limitations due to LVOT obstruction



Alcohol Septal Ablation

- Generally used in pt who are not candidates for septal myectomy.




HCM
HF symptoms or angina with obstruction
N
Annual clinical eval
Some argue BB for all
Y
Initiate medical therapy
BB (I)
Verapamil or dilt (I)
Disopyramide (IIa)
Persistent symptoms despite med therapy
Acceptable surgical surgical candidate?
Surgical myectomy (IIa)
Alcohol ablation IIb
Y
N
Acceptable candidate for alcohol ablation?
Alcohol ablation (IIa)

A 56 year old man is being evaluated after his 18-year old son had a syncopal episode during a high school basketball game and was diagnosed with HCM. The patient has no symptoms, including with physical activity such as golfing or playing tennis. He states he is in unremark d that he is the health ne, his health is perfecti story is unremark r other relatives w nias. He takes no m

PE is rema n EKG and echo are n

When sho

A. 6 mo
B. 1-2 ye
C. 5 years
D. No further screening is necessary

5 years

- All first-degree relatives of patients with HCM should undergo screening with PE, EKG, Echo. Because HCM can manifest at any age, lifetime screening in those in whom the disorder has not yet been diagnosed is indicated.

Age Group	Recommendation
<12	Screening optional except 1) presence of symptoms; 2) Fam Hx malignant tachyarrythmias; 3) pt is competitive athlete; 4) clinical suspicion of early LVH.
12 to 18-21	Every 12 to 18 months
>18-21	At symptom onset or at least every 5 years (more frequently in families with malignant tachyarrhythmias)

Genetic Screening

- If definitive pathogenic mutation identified can be used to test other relatives.
- Relatives negative for the family mutation are considered unaffected.
- Relatives testing positive for the same disease-causing mutation with no clinical evidence of LVH, are referred to as being genotype positive/phenotype negative.
- Patient's clinical course cannot be predicted based on the type of mutation.

Activity Restrictions

- Avoidance of competitive sports as well as intense physical activity (sprints, weight lifting, basketball, football, soccer) is recommended.
- Intermediate activities (baseball, jogging) should be assessed on individual basis.
- Low intensity activities (bowling, brisk walking, golf) are ”probably permitted”.

AHA Recommendations

High	Moderate	Low	
Basketball	Baseball	Bowling	5
Full court	Biking	Golf	5
Half court	Modest	Horseback riding[§]	3
Body building[§]	Motorcy	Scuba diving[‖]	0
Ice hockey[§]	Jogging	Skating[#]	5
Racquetball/squash	Sailing[‖]	Snorkeling[‖]	5
Rock climbing[§]	Surfing[‖]	Weights (non–free weights)	4
Running (sprinting)	Swimmi	Brisk walking	5
Skiing (downhill)[§]	Tennis (d		
	Treadmill/stationary bicycle	5	

Take home points

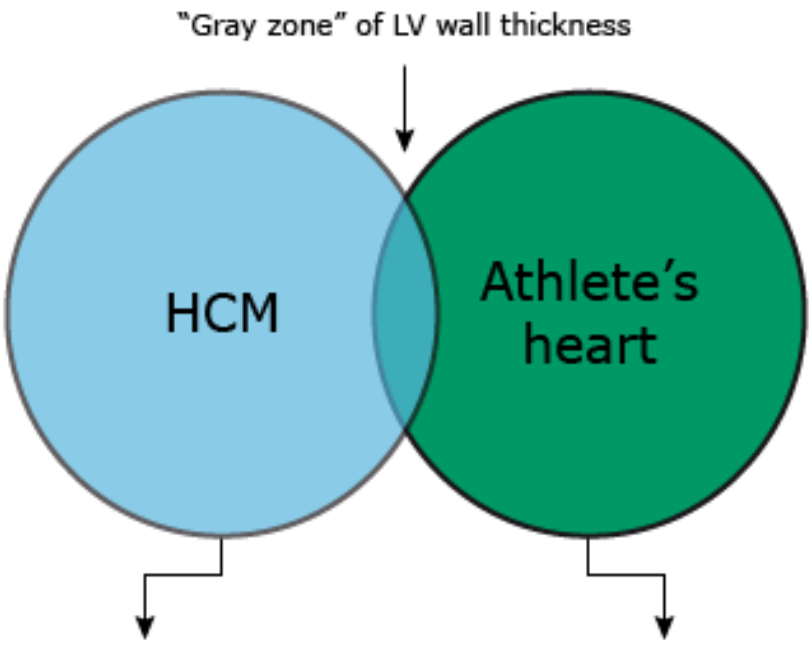
- Clinical manifestations include heart failure, ischemia, syncope/presyncope, SCD.
- Harsh, crescendo-decrescendo systolic murmur best heard at LSB. Radiates to LLSB but not to neck. Changes with ventricular loading conditions.
- EKG findings of LVH, q waves, TWI.
- Echo preferred imaging modality.
- Symptoms start with BB/CCB, if symptoms persist consider myectomy/septal ablation.
- ICD insertion based on risk factors for SCD.
- All first degree relatives should be screened.
- High intensity exercise should be avoided.

Questions?

References

- Hart, Anthony. Gorodeski, Eiran. “Hypertrophic Cardiomyopathy.” *Manual of Cardiovascular Medicine Fourth Edition.* Ed. Brian Griffin. Philadelphia: Lippincott Williams & Wilkins, 2013. 160-175.
- MKSAP 17
- Martin, Marin. “Hypertrophic cardiomyopathy: Clinical manifestations, diagnosis, and evaluation.” UpToDate. Jan 2017.
- www.lifeinthefastlane.com
- Wigle, ED. Et al. Hypertrophic Cardiomyopathy Clinical Spectrum and Treatment. Circulation. 1995;92:1680-1692. October, 1995.

Pathologic LVH vs Physiologic LVH



⊕	Focal LVH pattern	⓪
⊕	LV cavity <45 mm	⓪
⓪	LV cavity >55 mm	⊕
⊕	LA enlargement	⓪
⊕	Bizarre ECG patterns	⊕
⊕	Abnormal LV filling	⓪
⊕	Female gender	⓪
⊕	Family history of HCM	⓪
⊕	Thickness with deconditioning	⓪
⓪	VO_2 ↑ >110 percent	⊕
⊕	Late gadolinium enhancement	⓪
⊕	Pathogenic sarcomere mutation	⓪