Hypertrophic Cardiomyopathy

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2/7/2017
Goals – Sprinkling HCM Knowledge

- Diagnosis
- Treatment
- Screening
- Board relevant
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 of Hypertrophic Cardiomyopathy

Morphologic variants of hypertrophic cardiomyopathy

A
B
C
D
E
F
G
H
I
J

LV
Ao
LA
IVS
Prevalence

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

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

Myocyte disarray in hypertrophic cardiomyopathy

Normal endomyocardial biopsy in longitudinal section.
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 limitation. Father has htn; two younger siblings are both healthy. He has no family history of cardiomyopathy or unexplained sudden death.

PE, BP 112/62 mmHg, HR 52. Lungs CTAB. JVP , carotid upstroke normal. CV exam shows prominent apical impulse that is not sustained or enlarged. The intensity of S1 is slightly increased and S2 is normally split. No m/r/g. His attitude is slightly abrasive and rude but he has the voice of an angel and rock hard abs.

Which of the following is the most appropriate next step in management?

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

<table>
<thead>
<tr>
<th>Maneuver</th>
<th>Physiologic Effect</th>
<th>HCM</th>
<th>AS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valsalva and standing</td>
<td>Decreases VR, SVR, and CO</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Squat and handgrip</td>
<td>Increases VR, SVR, and CO</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Amyl nitrite</td>
<td>Increases VR</td>
<td>↑</td>
<td>↑</td>
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<tr>
<td></td>
<td>Decreases SVR and LV volume</td>
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<tr>
<td>Extrasystole</td>
<td>Decreased LV volume</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Post-valsalva release</td>
<td>Increased LV volume</td>
<td>↓</td>
<td>↑</td>
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</table>
Systolic Anterior Motion MV

EARLY SYSTOLE

MITRAL LEAFLET-SEPTAL CONTACT
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)
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 abnormalities 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 tennis, with minimal limitation. She has experienced no chest pain or syncope. Medical history is significant for hypertension, diagnosed 10 years ago. Her only medication is hydrochlorothiazide.

On PE, BP 122/70 mmHg, HR 66/min. Lungs CTAB. Cardiac examination reveals a rapid carotid upstroke and a grade 3/6 holosystolic murmur heard best at the LLSB. The murmur increases during both end-expiration and squat-to-stand maneuvers.

TTE shows LVH and dynamic LVOT obstruction consistent with a diagnosis of HOCM.

Which of the following is the most appropriate next step in 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 maneuvers) 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 has since been diagnosed in his father and brother during family screening. There is no family history of sudden cardiac death. He has upset stomach from eating candy, candy canes, candy corns and syrup from stress of his recent diagnosis. ROS is otherwise negative. On PE a soft holosystolic murmur is heard, which decreases during both handgrip and stand to squat maneuver.

TTE shows myocardial hypertrophy (max septal wall thickness, 32 mm) and mild LVOT obstruction at rest (gradient, 31 mmHg). On a 24 hour ambulatory EKG, a 4 beat run of NSVT is present.

Which of the following is the most appropriate next step in treatment?

A. Alcohol septal ablation
B. B-blocker therapy
C. ICD
D. Surgical myectomy
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

Annual clinical eval
Some argue BB for all

Y

Initiate medical therapy
BB (I)
Verapamil or dilt (I)
Disopyramide (IIa)

N

Persistent symptoms despite med therapy

Acceptable surgical surgical candidate?

Surgical myectomy (IIa)
Alcohol ablation IIb

Y

Acceptable candidate for alcohol ablation?

N

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 unremarkable health and that he is the healthiest individual to hold his current job. Medical history is unremarkable, and a review of family history is negative for other relatives with HCM, sudden cardiac death or tachyarrhythmias. He takes no medications.

PE is remarkable for large hands but otherwise normal. An EKG and echo are normal with no evidence of HCM.

When should this patient next be screened for HCM?

A. 6 months
B. 1-2 years
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.

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Recommendation</th>
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<tbody>
<tr>
<td>&lt;12</td>
<td>Screening optional except 1) presence of symptoms; 2) Fam Hx malignant tachyarrhythmias; 3) pt is competitive athlete; 4) clinical suspicion of early LVH.</td>
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<tr>
<td>12 to 18-21</td>
<td>Every 12 to 18 months</td>
</tr>
<tr>
<td>&gt;18-21</td>
<td>At symptom onset or at least every 5 years (more frequently in families with malignant tachyarrhythmias)</td>
</tr>
</tbody>
</table>
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".
| High                                    | Moderate          | Low                             |
|----------------------------------------|-------------------|---------------------------------
| Basketball                             | Baseball          | Bowling                         |
| Full court                             | Biking            | Golf                            |
| Half court                             | Modest            | Horseback riding$               |
| Body building$                         | Motorcy           | Scuba diving$                   |
| Ice hockey$                            | Jogging           | Skating#                        |
| Racquetball/squash                     | Sailing$          | Snorkeling$                     |
| Rock climbing$                         | Surfing$          | Weights (non–free weights)      |
| Running (sprinting)                    | Swimming$         | Brisk walking                   |
| Skiing (downhill)$                     | Tennis (c)        | Treadmill/stationary bicycle    |
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


• MKSAP 17


• www.lifeinthefastlane.com

Pathologic LVH vs Physiologic LVH

"Gray zone" of LV wall thickness

HCM

Athlete's heart

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Pathologic LVH</th>
<th>Physiologic LVH</th>
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</thead>
<tbody>
<tr>
<td>Focal LVH pattern</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>LV cavity &lt;45 mm</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>LV cavity &gt;55 mm</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>LA enlargement</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>Bizarre ECG patterns</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>Abnormal LV filling</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Female gender</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Family history of HCM</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Thickness with deconditioning</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>VO₂ t &gt;110 percent</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Late gadolinium enhancement</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>Pathogenic sarcomere mutation</td>
<td>0</td>
<td>+</td>
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