HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY

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Morning Report 7/21/04
HOCM

- Nondilated cardiac hypertrophy, in the absence of another disease
- Dynamic LV outflow obstruction gradient (between LV outflow tract and aorta) which may or may not be present at rest, but can become apparent with changes in hemodynamics
- 75% of patients do NOT have a resting gradient and this may develop at any age
Autosomal dominant missense mutation of gene encoding cardiac sarcomere

Clinically apparent in approximately 1 in 350-625 people

10 genes identified thus far which contribute e.g. β-myosin heavy chain, cardiac troponin T and myosin-binding protein C (70-80% of cases)

- Certain mutations of β-myosin heavy chain and troponin T associated with higher rates of premature death
Sarcomere. Gene with mutations associated with HCM in red.
Cannon Ro. NEJM 2003; 349:1016.
Pathology

- Mutations lead to impaired contractility which in turn causes upregulation of growth factors leading to hypertrophy and fibrosis="sarcomere disarray"

- Microvascular disease from abnormal coronary arteries with increased intimal and medial collagen and disproportion between heart muscle and vasculature
Symptoms

*Phenotypic Diversity*

- Asymptomatic
- Dyspnea (most common)
- Chest pain
- Palpitations
- Pre / syncope (15-25%)
- Orthopnea / PND
Complications

- Mitral valve disease--mechanical dysfunction from hypertrophy, papillary muscle insertion abnormality
- Congestive heart failure (5X more likely than general population)
- Atrial fibrillation (decompensation easier) and higher risk of thromboembolism
- Endocarditis (esp. mitral valve)--need to give antibiotics prophylactically
- Sudden cardiac death via ventricular arrhythmias
Clinical Exam Findings

- Harsh crescendo-decrescendo systolic ejection murmur best heard at apex and LLSB
- Increases with changing from squatting to standing position, Valsalva, NTG,
- Decreases with changing from standing to sitting, handgrip, leg elevation
- Radiates to axilla/base (less likely to radiate to neck), +/- S4 and LV lift
- Carotid pulse brisk upstroke
Diagnostic Tools

- **EKG**--LVH, inf/lat Q waves, LAD, LAE/RAE
- **2D TTE**--asymmetric hypertrophy, septum usually thicker than free wall
- **Continuous wave Doppler Echo**--resting high velocity, late peaking jet across LV outflow tract (25% of pts)
- **Exercise with Echo**--may identify obstruction that is not apparent at rest
- **Cardiac Catheterization**--measure gradient and provoke with Valsalva, amyl nitrate inhalation or infusion of isoproterenol
- **Holter monitor/Loop monitor**--not diagnostic but can help document ventricular tachyarrhythmias
TTE showing LV outflow obstruction in systole.

Nishimura and Holmes. NEJM 2004; 350: 1320.
Definitions based on TTE

- OBSTRUCTIVE = 30 mmHG peak outflow gradient at rest or >50 with provocation

- HYPERTROPHY = LV wall thickness > 13mm and severe if >30mm

\[ G = 4v \]

(modified Bernoulli equation)

\[ G = \text{LV outflow tract gradient} \]

\[ V = \text{LV outflow tract velocity} \]
Evaluation of Relatives

- Should screen all 1st degree family members with history / physical, EKG, Echo
  - If between ages 12-18, needs annual assessment
  - If over age 18, need reevaluation every 5 years

Genetic mutation analysis is possible
Overall Population With Hypertrophic Cardiomyopathy (HCM)

- Genotype-Positive Phenotype-Negative
  - Longitudinal Follow-up

- None or Mild Symptoms
  - No Treatment or Drug Therapy

- Progressive Heart Failure Symptoms
  - Drug Therapy

High Risk of Sudden Death
- Implantable Cardioverter-Defibrillator

Atrial Fibrillation
- Pharmacological Rate Control
- Cardioversion
- Anticoagulation

Drug-Refractory Heart Failure Symptoms

Alternatives to Surgery
- Alcohol Septal Ablation
- Chronic Dual-Chamber Pacing

Obstructive HCM (Rest or Provocation)
- Ventricular Septal Myotomy-Myectomy

Nonobstructive HCM (Rest and Provocation)
- Heart Transplantation (for End-Stage Systolic Dysfunction)

Maron. JAMA 287.
**BEST INITIAL APPROACH TO MANAGE SYMPTOMS**

**Goal**—block catecholamines and slow heart rate to increase filling

- Beta Blocker: 60-80% response rate
- Verapamil: Used if contraindication or intolerance to BB, however patients with severe symptoms, pHTN, severe outflow obstruction, there has been an association with verapamil and sudden death
- Disopyramide: add to BB if BB alone is not controlling symptoms
- Amiodarone has not been studied to see if can reduce SCD
Other Things to Watch For:

- Avoid dehydration
- Correct anemia
- Avoid drugs that alter decrease preload or afterload
  - eg. ACE-I, nitroglycerin, diuretics
What if medical management fails?

Other options:

- Surgical Septal Myectomy
- Septal Ablation
- Dual Chamber Pacemaker

NONE HAVE SHOWN TO DECREASE MORTALITY
Myectomy “Morrow procedure”

- Gold standard for symptomatic HOCM
- Resects basal septum, can combine with mitral valve surgery
- 90% who undergo procedure are subsequently symptom free--associated with increase peak oxygen consumption and decrease in NYHA classification
- Peri-operative mortality 1-2%
- Follow up studies 30 years out suggest patients still have improved symptoms and no recurrence of obstruction
Myectomy Procedure

Nishimura and Holmes. NEJM 2004; 350: 1320.
Septal Ablation

- Infusion of 100% alcohol into septal artery which supplies the myocardium along the outflow tract, thereby causing a myocardial infarction in this area which leads to thinning and decreasing obstruction.
- Complicated by complete heart block (also vfib, VSD, large MI, perforation).
- Can be used with contrast echocardiogram to localize area perfused by septal branch prior to alcohol administration.
- Consider if CHF NYHA III-IV, outflow gradient >50, septal wall >18mm.
Alcohol-induced Septal Ablation

Braunwald. NEJM 2002; 347: 1306.
Dual Chamber Pacemaker

- Unclear mechanism of causing symptomatic relief, may alter contraction of basal septum with less outflow obstruction
- Large placebo effect--still have large residual gradient after pacing (30-50mmHg)
- Follow up in 5 years--<40% still reported improvement in symptoms
- May be useful in pt cannot undergo surgery or needs pacer because of bradycardia with medical therapy
Summary of non-pharmacological therapies.
Nishimura and Holmes. NEJM 2004; 350:1320.
Sudden Death and LVH

- 480 patients with HCM, placed into categories based on LV wall thickness:
  - <15mm, 16-19mm, 20-24mm, 25-29mm, 30mm+
    - Follow up of 6.5 years
    - 65/480 died = 14% (23 died suddenly)
    - When LV thickness accounted for, risk of SCD increased with thickness
Implanted Cardiac Defibrillator

- If there is a risk for sudden death; unfortunately, no specific guidelines exist for who is a candidate.
- Currently driven by clinical history.
- No need to do EP study because inducing VT/Vfib during the study does not predict outcome of sudden death.

Features of Hypertrophic Cardiomyopathy That Increase the Risk of Cardiovascular Events.

| Genetic                  | Family history of sudden death |
|                         | Specific mutations in sarcomeric proteins |
| Clinical                | Resuscitation after cardiac arrest |
|                         | Recurrent syncope |
|                         | Ventricular tachycardia on monitoring |
| Morphologic             | Extreme left ventricular hypertrophy (>3 cm) |
| Hemodynamic             | Left ventricular outflow pressure gradient (>30 mm Hg) |
|                         | Fall in blood pressure during exercise |
|                         | Limited myocardial flow reserve |

NEJM.
ACC/AHA Guidelines

- CLASS II B recommendation by ACA/AHA/NASPE 2002 guidelines regarding ICD placement

(Class II B = Usefulness/efficacy less well established by evidence/opinion.)

"Familial or inherited conditions with a high risk for life threatening ventricular tachyarrhythmias eg. long QT or hypertrophy cardiomyopathy"
ICD / Sudden Death / HCM

- Retrospective study of 128 patients to evaluate efficacy of ICD to prevent SCD, follow up 3.1 years
- Total of 29/128 patients had appropriate firing (23%), 21 of those stored data that showed VT/VF instigator for discharge
- 43 placed for secondary prophylaxis (eg. survived cardiac arrest or had sustained VT); 19/43 had appropriate discharge of ICD (44%)
- 85 placed for primary prophylaxis for syncope, family hx of SCD, NSVT, LV wall thickness > 30mm; 10/85 had appropriate discharge of ICD (12%)
- Total of inappropriate firings 25%
- Complications in 18/128--lead malfunction, infection, hemorrhage requiring thoractomy, subclavian thrombus, hematoma

Maron NEJM 2000.
The Future

- Losartan decreases fibrosis and down regulates growth factor β in mice trials
- Simvastatin decreases fibrosis and hypertrophy in rabbits by 50%
- Routine Screening-not feasible currently
  - DNA microarrays, mass spectrometry

NEED FOR HUMAN TRIALS
References:


Marian AJ and Roberts R. To screen or not is not the question—it is when and how to screen. Circulation 2003; 107: 2171-2174.


References:


