Hypertrophic Cardiomyopathy is a Genetic Disorder

- Autosomal dominant
- Many sarcomeric gene mutations have been identified
  - β-myosin heavy chain
  - α-tropomyosin
  - Cardiac troponin T & I
  - Myosin-binding protein C
  - Myosin-light chain

Hypertrophic Cardiomyopathy Echocardiography

- Diagnosis
- Morphologic variants
- Identifying and quantitating obstruction
- Strain imaging
- Risk stratifying for sudden cardiac death
- Family screening
- Intraoperative/intra-procedure monitoring
- Post-operative/post-procedure assessment

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

Maron BJ and McKenna WJ, et al. JACC 2003; 42: 1687

Hypertrophic Cardiomyopathy

- Not Mandatory for Diagnosis of HCM
  - Asymmetric Septal Hypertrophy (ASH)
  - Systolic Anterior Motion (SAM)
  - Dynamic LVOT obstruction
Hypertrophic Cardiomyopathy
Morphologic Variants

Left Ventricular Morphology in HCM

- Sigmoid Septum: 181 (47%) Gene + 8%
- Reverse Septum: 132 (35%) Gene + 79%
- Neutral Septum: 32 (8%) Gene + 41%
- Apical Variant: 37 (10%) Gene + 32%


Typical Hypertrophic Cardiomyopathy

- Septal Thickness = 24 mm

The 74 year old man with this ECG most likely has what type of HCM?

1. Basal septal
2. Concentric
3. Apical
4. Full septal
5. Mid ventricular
52 Year Old Man with Suspected Hypertrophic Cardiomyopathy
Apical Variant

Apical And Mid Ventricular Variants Of HCM
• 10-20% with ApHCM may develop apical aneurysm/diverticulum
• Frequently have normal epicardial coronary arteries
• Stress nuclear testing often demonstrates apical ischemia
• Increased risk of systemic emboli
• Increased incidence of sustained ventricular arrhythmias

51 Year Old Woman
Apical HCM with Pouch

Echo Contrast

54 Year Old Man With Hypertrophic Cardiomyopathy
Mid Ventricular Variant
54 Year Old Man With Hypertrophic Cardiomyopathy

Hypertrophic Cardiomyopathy
Outflow Tract Obstruction

Typical Septal HCM
Obstruction present
Resting
Latent
Provoked with maneuvers, exercise and/or drugs
Obstruction absent

Dynamic LVOT Obstruction
Classic Explanation
• Septal hypertrophy narrows LVOT
• Vigorous contraction
• Venturi effect created in LVOT

Newer Explanation for Mitral SAM
• Hypertrophy remodels LV chamber
• Papillary muscles displaced
• Direction of ejection flow redirected
• The flow creates drag on MV leaflets
• Leaflets are \textit{pushed} into LVOT

Mechanism of SAM
Hypertrophic Cardiomyopathy
LV Outflow Obstruction

Increased by
\[ \downarrow \text{preload} \]
\[ \downarrow \text{afterload} \]
\[ \uparrow \text{contractility} \]

Decreased by
\[ \uparrow \text{preload} \]
\[ \uparrow \text{afterload} \]
\[ \downarrow \text{contractility} \]

Provoke gradient with Valsalva, amyl or exercise

Hypertrophic Cardiomyopathy
Provocative Maneuvers for Obstruction in the Echo Lab

• Post PVC
• Valsalva maneuver
• Amyl nitrite inhalation
• Exercise
  • Supine or upright bike
  • Treadmill

Hypertrophic Cardiomyopathy
Imaging During Provocative Maneuver

At rest and during provocation

- Apical long axis view with zoom to include LVOT, AV, MV and all of LA
- CW Doppler through LVOT
- 2D image to check degree of mitral SAM
- Color flow imaging to check turbulence in LVOT and degree of MR

58 Year Old Man with HCM
Amyl Nitrite

Zoom on LVOT, AV, MV and Entire LA

CW Doppler LVOT

REST

AMYL NITRITE
58 Year Old Man with HCM

Amyl Nitrite

Calculate LVOT Gradient

Using MR Velocity

\[ a) \text{LV - LA = (4) x (MR velocity)}^2 \]
\[ = (4) x (8.0)^2 \]
\[ = (4) x (64) = 256 \text{ mmHg} \]

\[ b) \text{LV = (256 mmHg)} + (\text{LA}) \]
Assume LA = 15 mmHg

\[ \text{LV = (256 mmHg)} + (15 \text{ mmHg}) \]
\[ = 271 \text{ mmHg} \]

54 Year Old Man With Hypertrophic Cardiomyopathy

Mid Ventricular Obstruction

Hypertrophic Cardiomyopathy

Using Mitral Regurgitation to Calculate Maximum LVOT Gradient

MR velocity 8 m/sec

Calculate LVOT Gradient

Using MR Velocity (cont)

c) Systolic blood pressure = 98 mmHg

d) LVOT Gradient = (LV) - (Ao)
\[ = (271 \text{ mmHg)} - (98 \text{ mmHg}) \]
\[ = 173 \text{ mmHg} \]

*Gradient was 164 mmHg using LVOT velocity

Hypertrophic Cardiomyopathy

Diastolic Dysfunction
For patients with HCM, markedly delayed relaxation can mask the usual effects of increased preload on MV and PV Doppler patterns. The delayed relaxation PW patterns do not always indicate low or normal filling pressure for HCM patients.

Hypertrophic Cardiomyopathy

Measurement of the mitral annular early diastolic velocity (e´) and calculation of the mitral E/e´ ratio is useful for estimating LV filling pressure.

Hypertrophic Cardiomyopathy

63 Year Old Man With Hypertrophic Cardiomyopathy

Echo

E = 0.8 m/sec
E/A = 1.0
DT = 225 msec

E = 0.8 m/sec
E/A = 1.0
DT = 225 msec

Hypertrophic Cardiomyopathy

Strain Imaging

Typical Septal Hypertrophic Cardiomyopathy
Apical HCM

43 Year Old Woman With Hypertrophic Cardiomyopathy

Maximum Instantaneous Gradient LVOT = 92 mmHg

52 Year Old Man with Hypertrophic Cardiomyopathy, Apical Variant

GLPSS = 19%

52 Year Old Man with Hypertrophic Cardiomyopathy, Apical Variant
52 Year Old Man with Hypertrophic Cardiomyopathy, Apical Variant

52 Year Old Man with Hypertrophic Cardiomyopathy, Apical Variant

GLPSS -17%

54 Year Old Man With Hypertrophic Cardiomyopathy
Mid Ventricular Variant

54 Year Old Man With Hypertrophic Cardiomyopathy
Mid Ventricular Variant
Hypertrophic Cardiomyopathy
Risk Stratification For Sudden Cardiac Death (SCD)

Primary Risk Factors
- Family Hx of $\geq 1$ HCM related SCD
- Unexplained syncope ($\geq 1$ episode)
- Nonsustained VT on Holter
- Exercise BP response $\downarrow$ or $\uparrow$
- Massive LVH ($\geq 30$ mm thickness)

Secondary Risk Factors
- Intramyocardial Fibrosis:
  - Delayed gadolinium enhancement on MRI
- Apical LV aneurysm (Apical variant of HCM)
- Prior alcohol septal ablation
- Burned out phase of HCM (1-5% incidence)
- LVOT obstruction $>30$ mmHg at rest
  ($\leq 10\%$ Positive Predictive Value)
Intramycocardial Fibrosis in HCM

**Predictors of DGE**

- Reversed septal morphology
- Septal thickness > 20 mm
- LV Mass > 150 gm
- LVEF < 50%

Rubinshtein R; Circ Heart Fail 2010 (3): 51

**Intramycocardial Fibrosis in HCM**

*Detection by Echocardiography?*

- Abnormal global and/or regional LV systolic function
- Normal global and regional LV systolic function

- Fibrosis likely where LV is dysfunctional
- Speckle Tracking Strain Imaging

Rubinshtein R; Circ Heart Fail 2010 (3): 51

**“Burned Out” Late Stage HCM**

- Marked LVH
- Myocardial ischemia → micro-infarction → fibrosis
- LV dilatation and wall thinning
- LV remodeling → systolic dysfunction

Maron BJ and Spirito P. Am J Cardiol 1998; 81: 1339

**Sudden Cardiac Death (SCD) in HCM**

**Uncertain Risk Factors**

- Gene mutation (>1,000 mutations; 11 genes)
- Atrial fibrillation
- Coronary artery bridging
- Diastolic dysfunction

**Modifiable Risk Factors**

- Highly competitive sports
- Coronary artery disease

Maron BJ. Circulation 2010; 121: 445
Hypertrophic Cardiomyopathy

Family Screening

53 Year Old Woman with Family Hx of HCM

- No cardiovascular medications
- Rides bicycle and takes brisk walks
- No angina, dyspnea on exertion or near syncope/syncope
- No palpitations

53 Year Old Woman with Family Hx HCM LVOT Zoom

- Basal Septal Thickness 13 mm

Systolic (S') and Early Diastolic (e') Annular Velocities for

- Normal subjects
- Mutation but no hypertrophy (M+ LVH-)
- Mutation and hypertrophy (M+ LVH+)

53 Year Old Woman

Family History

- Maternal GM had a "very large heart" and CHF
- Mother diagnosed with HCM in her 60s; died at age 70 yr
- Brother and sister have HCM
- Nephews, in their 20s and 30s, both diagnosed with HCM
- Two children in 20s are both asymptomatic; have not undergone screening
53 Year Old Woman with Family Hx HCM

LV Longitudinal Peak Systolic Strain

Normal Global strain (~ 20%)
Abnormal Regional strain
basal septal and basal anterior

53 Year Old Woman with Family Hx HCM

CW Doppler LVOT 1.5 m/sec

53 Year Old Woman with Family Hx HCM

LVOT with Valsalva

53 Year Old Woman with Family Hx HCM

CW Doppler LVOT 1.5 m/sec

53 Year Old Woman with Family Hx HCM

Amyl Nitrite Inhalation
53 Year Old Woman with Family Hx HCM
LVOT CW Doppler During Amyl Nitrite Inhalation

LVOT Max Gradient 81 mmHg
4.5 m/sec

53 Year Old Woman with HCM and Latent Obstruction
Genetic Testing
- Genetic mutation in gene MYBPC3
- Frameshift mutation
- Strongly expected to predispose to HCM
- Family members wishing to be screened can undergo site specific genetic testing

53 Year Old Woman with HCM and Latent Obstruction
Recommendations
- No need for beta blocker (she is asymptomatic)
- Do not train for marathon (as previously planned)
- Brisk running and cycling OK; slow down if cannot carry on conversation during exercise
- No risk factors to warrant defibrillator
- Reassess in 18 months

Hypertrophic Cardiomyopathy Apical Variant
There is about 30% chance of identifying causative genetic mutation for patients with apical variant

Hypertrophic Cardiomyopathy Apical Variant
Recommendations for Screening of Relatives ECG and Echo
- Every 5 years for first and second degree relatives not participating in athletics (annually if participating in athletics)
- Annually for adolescent first degree relatives
- Every 2-3 years for children; annually after onset of puberty
- Screen nieces, nephews and grandchildren before starting competitive athletics
Hypertrophic Cardiomyopathy

Treatment for Obstruction

- Medications
- Dual chamber pacing
- Surgical myectomy
- Catheter septal ablation
- Cardiac transplantation

Hypertrophic Cardiomyopathy with Obstruction

Surgical Myectomy


1,337 consecutive patients with HCM 1983 to 2001

- Surgical myectomy (289 patients)
- LVOT obstruction without operation (228 patients)
- Non-obstructive HCM (820 patients)

Hypertrophic Cardiomyopathy

LVOT Gradient is Dynamic

Increases with
- Vasodilators
- Diuretics
- Positive inotropes

Decreases with
- Negative inotropes
  - β-blockers
  - Verapamil
  - Diisopyramide

Hypertrophic Cardiomyopathy

Septal Myectomy

- Procedural mortality 0.8% (289 patients)
- Long-term survival similar to that of the general population
- Long-term survival was superior to survival for patients with obstructive HCM and no myectomy

Ommen SR; JACC 46(3); August 2005
Hypertrophic Cardiomyopathy
Septal Myectomy

There is a surgical procedure that benefits appropriately selected patients with apical variant hypertrophic cardiomyopathy.

Schaff H; Journal Thor and CV Surgery 139 March 2010

63 Year Old Man With Hypertrophic Cardiomyopathy
Coronary Angio (Outside)

• Mild to moderate disease
• 30% lesions LAD, Cx and RCA

Echocardiography After Septal Myectomy
Check For
• Residual LVOT obstruction
• Residual mitral regurgitation
• Aortic regurgitation
• VSD

63 Year Old Man With Hypertrophic Cardiomyopathy
• CVA seven years ago
• Diagnosed with hypertrophic cardiomyopathy, apical variant
• ICD placement two years ago
• Tolerated metoprolol ER 100 mg daily, but not larger doses
• Dyspnea with 2 flights of stairs at time of Dx
• Positional lightheadedness

63 Year Old Man With Hypertrophic Cardiomyopathy
ECG
63 Year Old Man With Hypertrophic Cardiomyopathy

Echo

63 Year Old Man With Hypertrophic Cardiomyopathy

Echo

Apical Short Axis Views

E = 0.8 m/sec
E/A = 1.0
DT = 225 msec

e' medial: 0.05 m/sec
E/e' = 16

e' lateral: 0.05 m/sec
E/e' = 16

63 Year Old Man With Hypertrophic Cardiomyopathy

Echo With Intravenous Contrast

63 Year Old Man With Hypertrophic Cardiomyopathy

Echo
63 Year Old Man With Hypertrophic Cardiomyopathy

Echo

GLPSS -8%

Role of Dual Chamber Pacing

Hypertrophic Cardiomyopathy

NSR
PACE

63 Year Old Man With Hypertrophic Cardiomyopathy
• Uncomplicated post-op course
• Beta blocker and warfarin restarted
• Dismissed from hospital day 5

Hypertrophic Cardiomyopathy

Role of Dual Chamber Pacing

NSR
PACE

63 Year Old Man With Hypertrophic Cardiomyopathy

Surgery
• Transapical mid ventricular myectomy
• Excised apical aneurysm/pouch
• Repaired LV apex with two felt strips and mattress sutures
• No thrombus within the pouch
• Pre myectomy resting mid MIG 50 mmHg; 80 mmHg post PVC
• After myectomy there was no gradient at rest or with PVC

Nonsurgical Septal Ablation

LVOT gradient complete reduction in ~ 80%
Gradient reduced by > 1/2 in 90% with echo and 70% without echo

Hypertrophic Cardiomyopathy

Anteriorly-Directed MR Jet

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