PERSONALIZED RISK ASSESSMENT IN HCM: LIFETIME SUDDEN DEATH AND HEART FAILURE RISK

A Collaborative Approach to Hypertrophic Cardiomyopathy

October 5, 2019

Adam Helms, MD, MS
University of Michigan
1. Case Presentations
2. Familial versus Non-Familial HCM
3. Impact of Genetic Testing on Lifetime Risk
4. SCD Risk Prediction
5. Heart Failure Risk Prediction
CASE 1: EARLY ONSET HCM DUE TO A SARCOMERE GENE MUTATION

- Age 23: HCM Diagnosed, hypertrophy throughout septum (reverse curve)
- Age 24: ICD implanted
- Age 25: LVOT obstruction treated with myectomy
- Age 28: Appropriate shock
- Age 34: Diuretic-requiring heart failure
- Age 36: Atrial fibrillation, further complicating heart failure

Echo at Age 26
CASE 2: LATE AGE PRESENTATION HCM WITH NEGATIVE GENETIC TESTING

HCM Diagnosed, hypertrophy primarily at basilar septum
LVOT obstruction treated with myectomy
Atrial fibrillation, managed medically
Doing well
HCM: LIKELIHOOD OF + GENETIC TEST IS DETERMINED BY CLINICAL PROFILE

- Earlier age of diagnosis
- Family history of HCM
- Lack of hypertension
- Morphology of hypertrophy

Binder, Ommen, et al., Mayo Clinic Proc 2006
Gruner, et al., Circ Cardiovasc Genet 2013
Ko, et al., Genetics in Medicine 2017
High Familial Risk: Standard Screening

Genetic Testing and 3-Generation Family History

Genetic Test +, Family History +

Genetic Test +, Family History -

Genetic Test Negative

AND

Family History Negative

Clinical Profile

Autosomal Dominant, Familial HCM

Multifactorial, Non-Familial HCM

Low Familial Risk: One-time screening for adult family members

Michigan Experience: Yield of familial screening with negative genetic testing and negative family history is very low. Ko, et al. 2017, Genetics in Medicine
Familial (Sarcomere Gene Positive) HCM → More Adverse Events at Younger Age

Familial / Sarcomere Mutation HCM: Significantly greater risk of heart failure and SCD by age 50

Ho, et al., Circ 2018
FAMILIAL VS. NON-FAMILIAL HCM KEY POINTS

- HCM can be generally divided into Familial HCM and Non-Familial HCM
- Familial HCM is identified by a combination of
  - Clinical features: earlier onset, LVH morphology, lack of HTN
  - Family history (but a negative FamHx does NOT rule out familial HCM)
  - Genetic testing
- Screening efforts should be focused on family members of individuals with higher likelihood of Familial HCM
SUDDEN DEATH RISK ASSESSMENT IN HCM

• Traditional Risk Factors
  • Max wall >30 mm, NSVT (> 3 beats, > 120 bpm), family hx of early (<40 yo) sudden death, syncope, abnormal blood pressure response to exercise

• European Society of Cardiology (ESC) HCM Risk Estimate
  • Adds age-weighting for greater risk at younger age
  • Adds left atrial size
  • Adds max wall thickness as a continuous variable
  • Adds LVOT gradient
  • Removes blood pressure response
  • Does not include genetics or MRI

ESC Risk Calculator: Google:“ESC HCM risk”

O’Mahony, et al., EHJ 2014
SUDDEN DEATH RISK ASSESSMENT IN HCM: CASE 1

70 yo with HCM, sigmoidal septal hypertrophy, LVOT obstruction with 60 mm Hg gradient, max thickness 19 mm, LA 46 mm

- 5-year risk = 1.7%
- If NSVT = 3.9%

Strategy: Yearly follow-up, minimal rhythm monitoring, MRI only if septal reduction planned

Google: “HCM ESC risk”  
O’Mahony, et al., EHJ 2014
20 yo with HCM, reverse curve septal hypertrophy, no obstruction, max thickness 19 mm

- 5-year risk = 2.9%
- Risk by age 40 = 11.6%
- If NSVT = 6.4%

Strategy: Yearly follow-up, extended event monitoring yearly, MRI, advice on warning symptoms

Google: “HCM ESC risk”
SCD ASSESSMENT: ADDITIONAL CONSIDERATIONS

- ESC risk calculator does not include genetic testing
  - Positive genetic test → MRI, longer rhythm monitoring
- ESC risk calculator does not include MRI LGE
  - MRI if intermediate risk and/or young sarcomere + patients with LVH >15 mm
  - Substantial marked LGE → likely high risk
- ESC risk calculator gives blanket recommendations for ICD based on 5-yr estimate
  - Young patients → higher lifetime burden of risk
- ESC risk calculator does not include HCM with apical aneurysm → high risk regardless of other variables

40 yo with MYBPC3 mutation, nonobstructive HCM, max LVT 20 mm, LA 50 mm, ESC risk: 2.7%
MRI: Dense LGE in septum
UM Risk Estimate: High
HETEROGENEITY OF HEART FAILURE TYPES IN HCM

Diastolic Dysfunction

LVOT Obstruction

Advanced Fibrosis / Systolic Dysfunction

Heart Failure
NON-OBSTRUCTED HCM WITH DIASTOLIC HEART FAILURE

• Driven by hypertrophy burden and diastolic dysfunction
• Also occurs with restrictive HCM (especially: thin filament gene mutations)
• Risk factors:
  • Sarcomere mutation, max wall thickness, left atrial enlargement, age of presentation
• Can be precursor to systolic dysfunction and/or
• Progress to refractory diastolic/restrictive
“END-STAGE” WITH COMBINED SYSTOLIC / DIASTOLIC HEART FAILURE

• Driven by hypertrophy burden, diastolic dysfunction, microvascular ischemia, and fibrotic remodeling

• Advanced fibrosis leads to relative chamber dilation, systolic dysfunction

• Risk markers: sarcomere mutation, “double” sarcomere mutations, LV dilation, EF ≤55%

• Systolic dysfunction often “mild”

• Prognosis is poor

• If suspected: refer to HF/Transplant Specialist

Funada, et al., Heart Vessels 2014
CONCLUSIONS

• For both individual and family risk assessment, HCM should be viewed as 2 separate conditions:
  Genetic/Familial HCM or Non-Familial HCM
• Most familial/genetic cases due to sarcomere gene mutations
  Caveat: small proportion of early onset HCM with negative genetic testing
• Risk of SCD most accurately assessed by combination of ESC risk estimation + MRI + genetics
• Sarcomere mutation HCM is associated with earlier diagnosis and greater cumulative lifetime risk
WHEN TO REFER TO AN HCM CENTER?

- Young HCM patients (age <40)
- Risk factors for heart failure and/or SCD
- LVOT obstruction refractory to medical management
- Cardiac genetic counseling
- Single consults or long-term co-management
- Also evaluate familial DCM, ARVC, inherited arrhythmias