Calling Primary Care Partners to Action in Hypertrophic Cardiomyopathy

Shortening the Time to Diagnosis for Improved Patient Outcomes

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Please feel free to ask questions at the end of the presentation.

Our Goals for Today

- Share how to recognize symptoms and aspects of family history that may indicate risk for HCM and how to perform further evaluation using tools such as ECG and echocardiography
- Provide insights on managing the comorbidities commonly associated with HCM in a shared-care model with specialty providers
- Increase your confidence in participating in follow-up care and monitoring of patients diagnosed with HCM, including checking for drug–drug interactions

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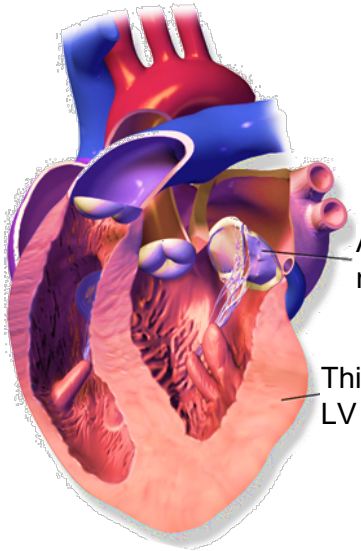
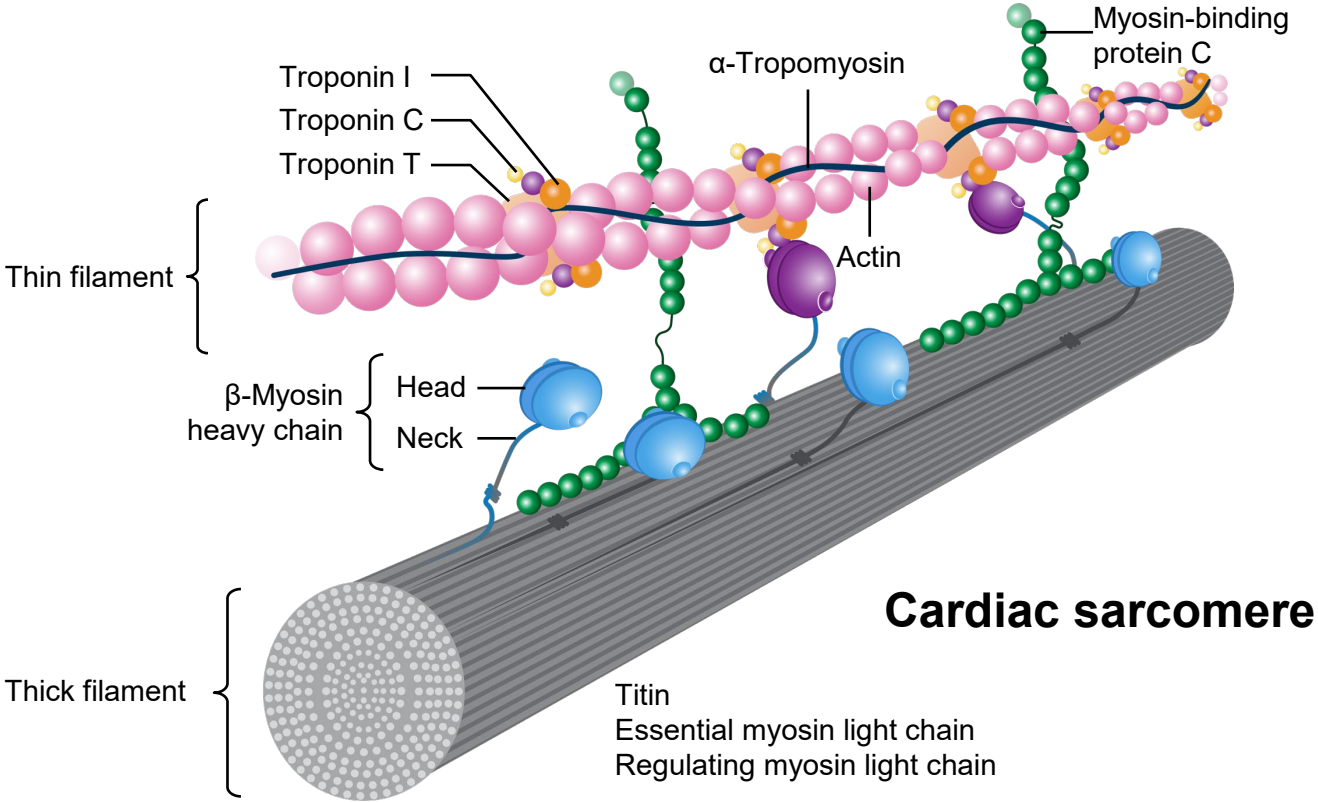
Sarcomeric HCM Is the Most Common Genetic Cause of LVH[1-3]

Key Anatomical Characteristics of HCM

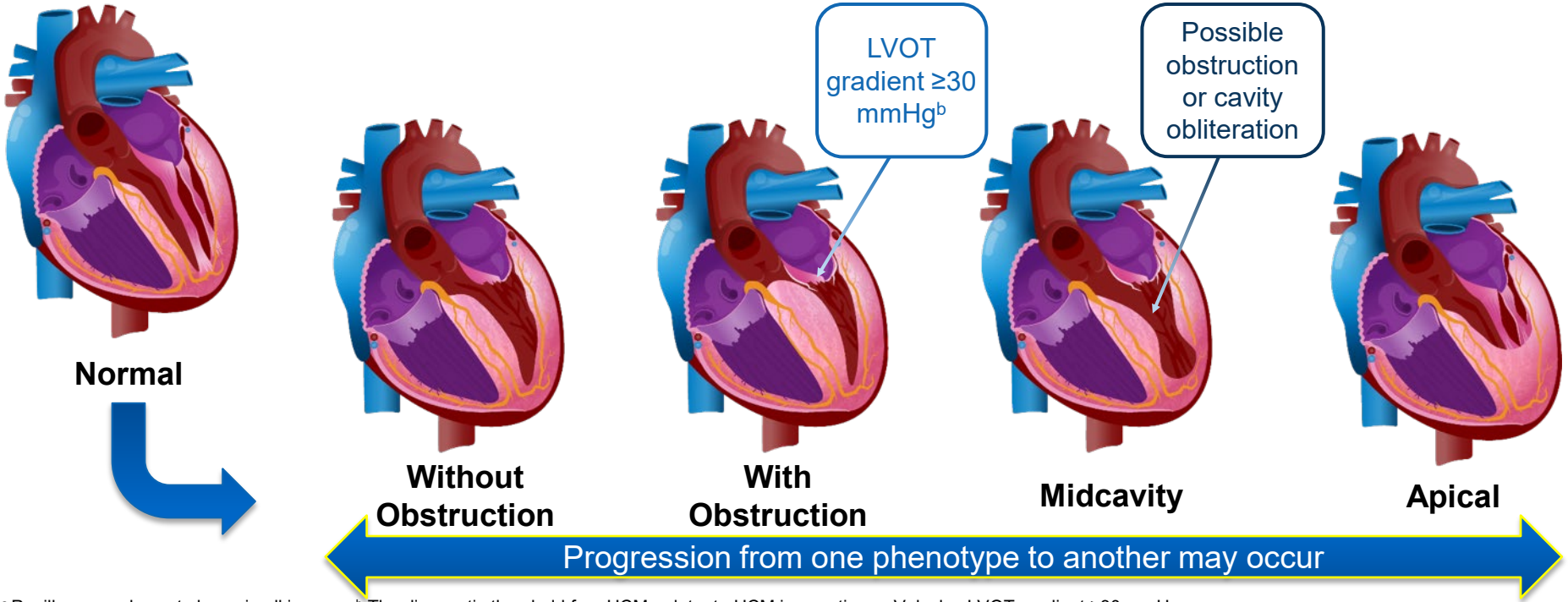




1. Maron BJ et al. *J Am Coll Cardiol*. 2022;79:372-389. 2. https://www.cdc.gov/genomics/disease/hcm.htm#ref9.
3. Semsarian C et al. *J Am Coll Cardiol*. 2015;65:1249-1254.

oHCM vs nHCM: Anatomy[1,2,a]

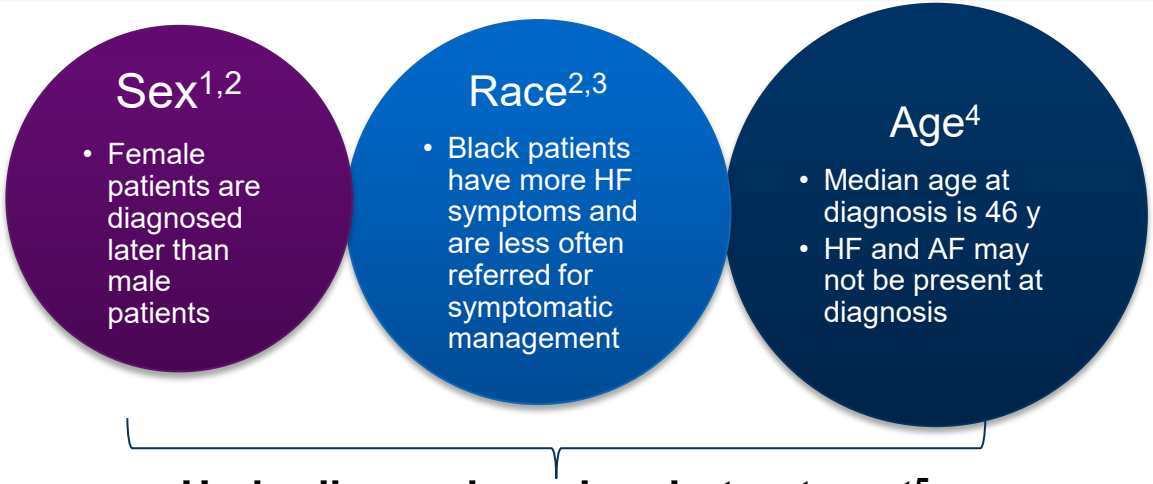
An LV wall thickness of ≥15 mm or ≥13 mm in individuals with a family history of HCM or in conjunction with a positive genetic test is diagnostic for HCM



[a] Papillary muscles not shown in all images. [b] The diagnostic threshold for oHCM or latent oHCM is a resting or Valsalva LVOT gradient ≥30 mmHg.

1. https://4hcm.org/. 2. Ommen SR et al. *Circulation*. 2020;142:e558-e631.

HCM Affects All Sexes, All Races, and All Ages in All Places



Disparities in treatment and in-hospital mortality have been documented by sex, race, insurance status, rural location, region of the country, hospital size, and hospital nonprofit status[2,6]

- Estimated prevalence of HCM is 1:500 (based on disease phenotype by imaging)
- HCM is not rare but clinically underdiagnosed by a factor of almost 3x
- Potentially affects ~700,000 Americans

1. Rowin EJ et al. *J Am Heart Assoc*. 2019;8:e012041. 2. Maron BJ et al. *J Am Coll Cardiol*. 2022;79:372-389. 3. Ntusi NAB, Sliwa K. *J Am Coll Cardiol*. 2021;78:2573-2579. 4. Ho CY et al. *Circulation*. 2018;138:1387-1398. 5. Massera D et al. *Int J Cardiol*. 2023;382:64-67. 6. Johnson DY et al. *J Am Heart Assoc*. 2023;12:e029930.

What Role Does Primary Care Have in the Diagnosis of HCM?[1]

Insights from the HCMA Voice of the Patient Survey

33%
of symptomatic patients initially sought care from a PCP

13%
pursued care due to a family member's diagnosis with HCM or sudden cardiac arrent

10%
listed family history of heart disease as their reason for seeking care

3%
took part in cascade or family screening

14%
received genetic testing

1. https://4hcm.org/wp-content/uploads/2021/06/Voice-of-the-HCM-patient-Report-final-January-9-2021.pdf.

Delays and Errors in HCM Diagnosis Are Common[1]

3,888 adults with oHCM → 1,573 (40.5%) without misdiagnoses

→ **2,315 (59.5%) with at least 1 misdiagnosis**

Events during diagnostic journey

78.4% saw a cardiologist

n = 4.7 cardiologist office visits (mean)

n = 4.0 misdiagnoses (mean)

32.1% had an ED visit

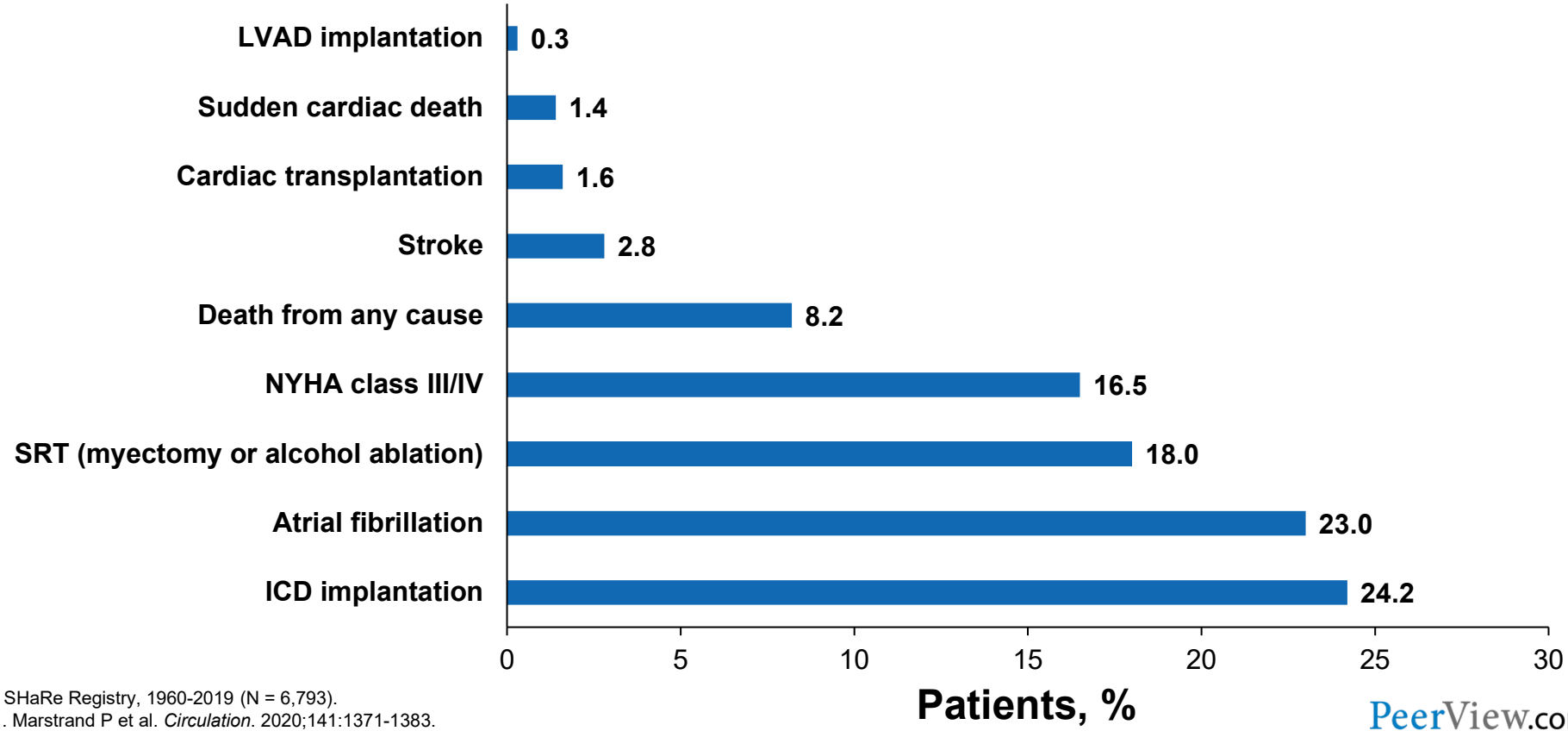
26.8% had an inpatient stay

15.7% may have had inappropriate treatment

Definitive oHCM diagnosis within 2 years

1. Naidu SS et al. *J Med Econ.* 2023;26:682-690.

Natural History of HCM: Lifetime Events Reported to the SHaRe Registry (1960-2019)[1,a]



[a] SHaRe Registry, 1960-2019 (N = 6,793).

1. Marstrand P et al. *Circulation*. 2020;141:1371-1383.

Introducing Our Patients

Corbin

- Male patient aged 17 years
- Football team physician thought he heard a murmur during a preseason sports physical

Delia

- Female patient aged 67 years
- New patient
- Dissatisfied with the care she received from another doctor

Edward

- Male patient aged 37 years
- New patient
- Gets winded more easily while running his usual route

Patient Case #1: Corbin

Corbin

Patient Info

- Male patient aged 17 years
- No previous medical hx
- Football team physician thought he heard a murmur during a preseason sports physical

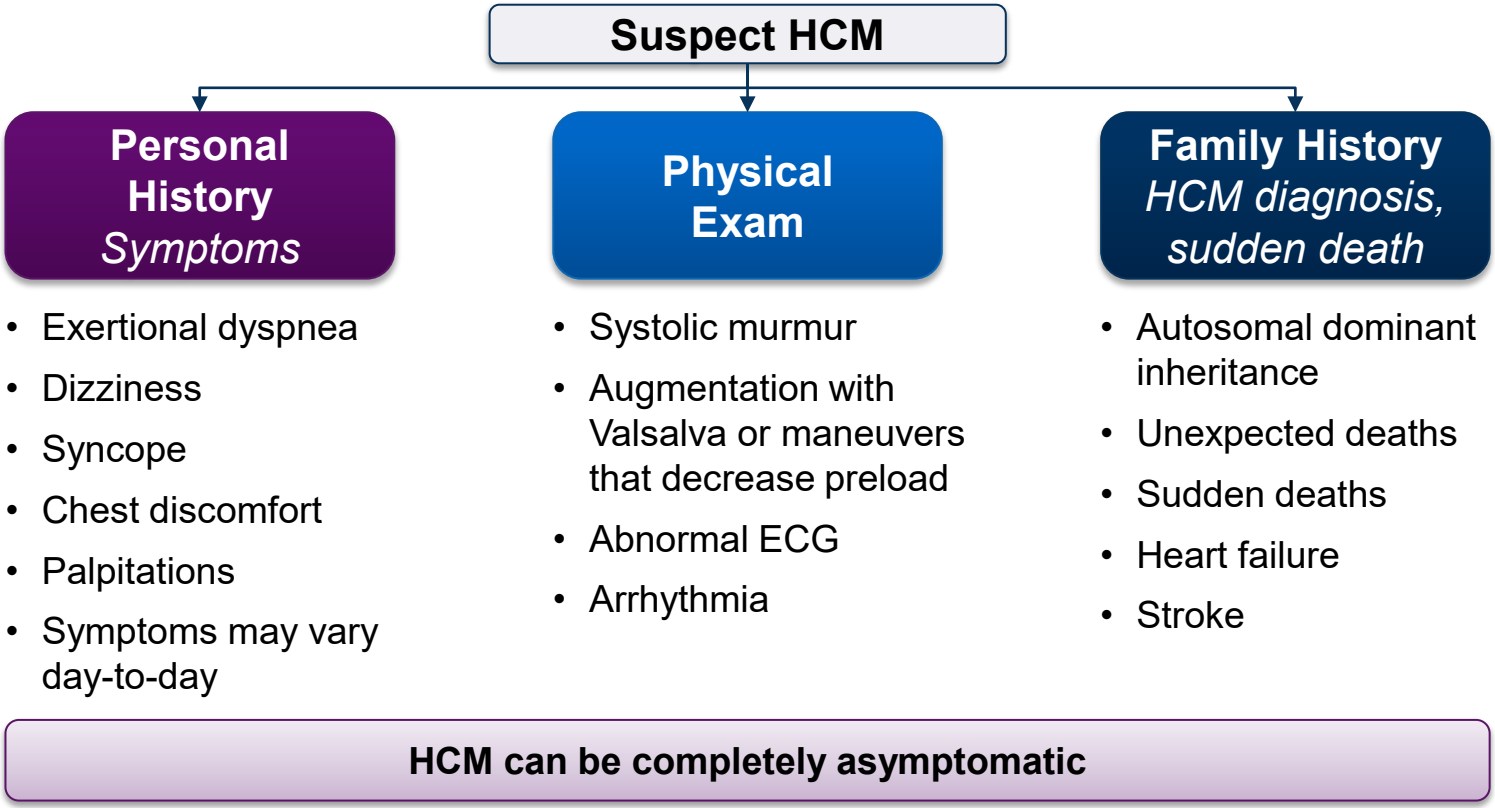
Family History

- Father died aged 51 years from a cardiac condition
- Uncle died aged 47 years from unknown causes
- Mother, older sister, and older brother are healthy

Physical Exam

- HR 59, pulse regular
- BP 102/64 mmHg
- BMI 24 kg/m^2
- Lungs clear, no wheezing, no rales
- Murmur that is especially noticeable when standing from a squat

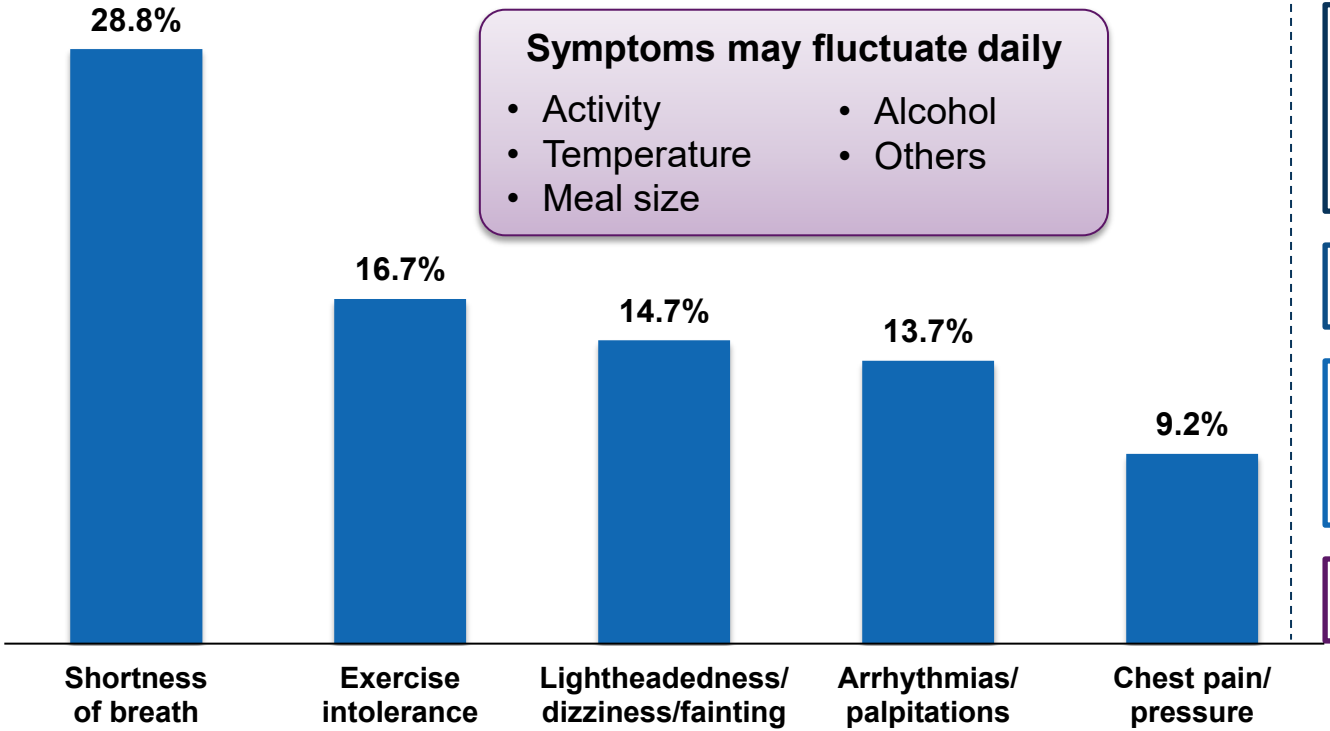
When Should I Suspect HCM?[1-6]



1. Maron BJ et al. *J Am Coll Cardiol*. 2022;79:372-389. 2. Ommen SR et al. *Circulation*. 2020;142:e558-e631. 3. Geske JB et al. *J Am Coll Cardiol HF*. 2018;6:364-375.
4. Lawler PR et al. *Circulation*. 2014;129:1703-1711. 5. Cavalcante JL et al. *Prog Cardiovasc Dis*. 2012;54:517-522. 6. Arbelo E et al. *Eur Heart J*. 2023;44:3503-3626.

Most Frequently Reported Symptoms of HCM[1,2]

HCMA Voice of the Patient Survey



Symptoms may fluctuate daily

- Activity
- Temperature
- Meal size
- Alcohol
- Others

Questions to Ask Your Patient (Last 24 h)

SoB Domain

- Any SoB?
- SoB with light activity?
- SoB with moderate activity?
- How often SoB?

Tiredness Domain

- Any tiredness?

CV Symptoms Domain

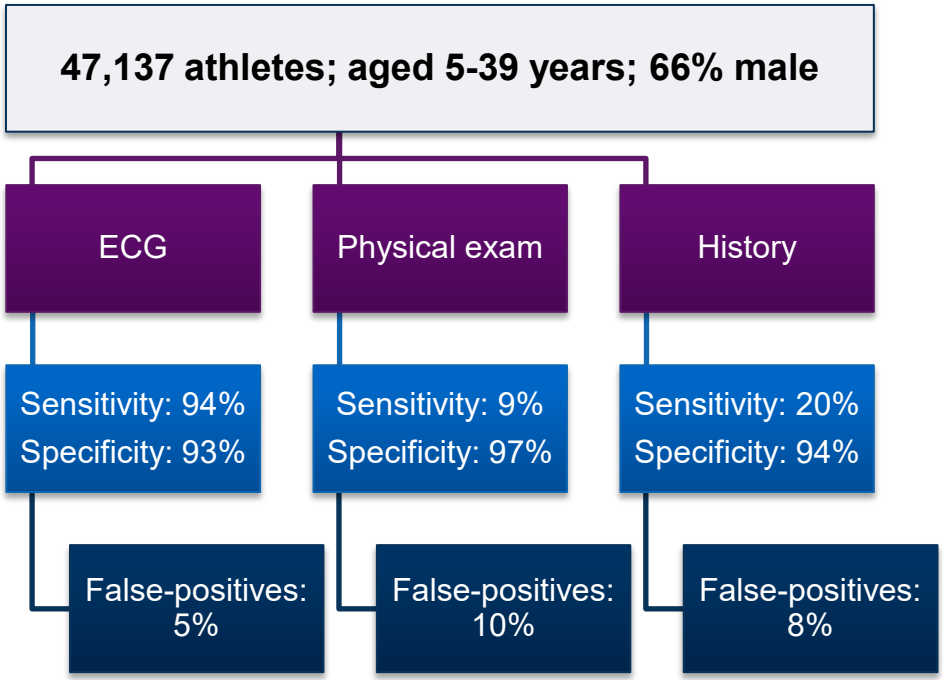
- Rapid heartbeat or flutter?
- Chest pain?
- Dizziness/lightheadedness?

Syncope Domain

- Faint/lose consciousness?

1. https://4hcm.org/wp-content/uploads/2021/06/Voice-of-the-HCM-patient-Report-final-January-9-2021.pdf. 2. Reaney M et al. *Pharmacoecon Open*. 2022;6:563-574.

Optimal Screening Methods to Detect Cardiac Disorders in Athletes: Results of a Meta-Analysis[1]



- **A total of 160 potentially lethal CV conditions were detected**
  - 0.3% (1 in 294 athletes)
- Diagnoses
  - 42% WPW syndrome
  - 11% Long QT syndrome
  - **11% HCM**
  - 7% dilated cardiomyopathy
  - 6% CAD or MI
  - 3% arrhythmogenic RV cardiomyopathy

A 12-lead ECG is the most effective screening strategy

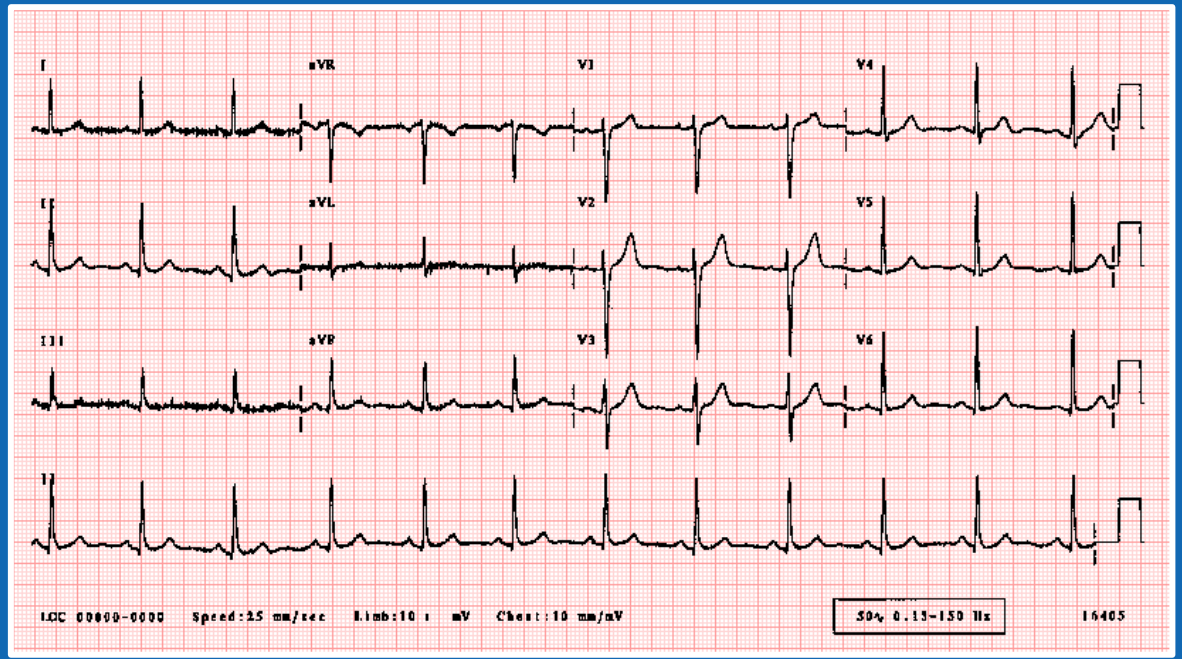
1. Winkelmann ZK, Crossway AK. *J Athl Train*. 2017;52:1168-1170.

Patient Case #1 Revisited: Corbin's ECG[a]

Corbin

Patient Info

- Male patient aged 17 years
- No previous medical hx
- Football team physician thought he heard a murmur during a preseason sports physical

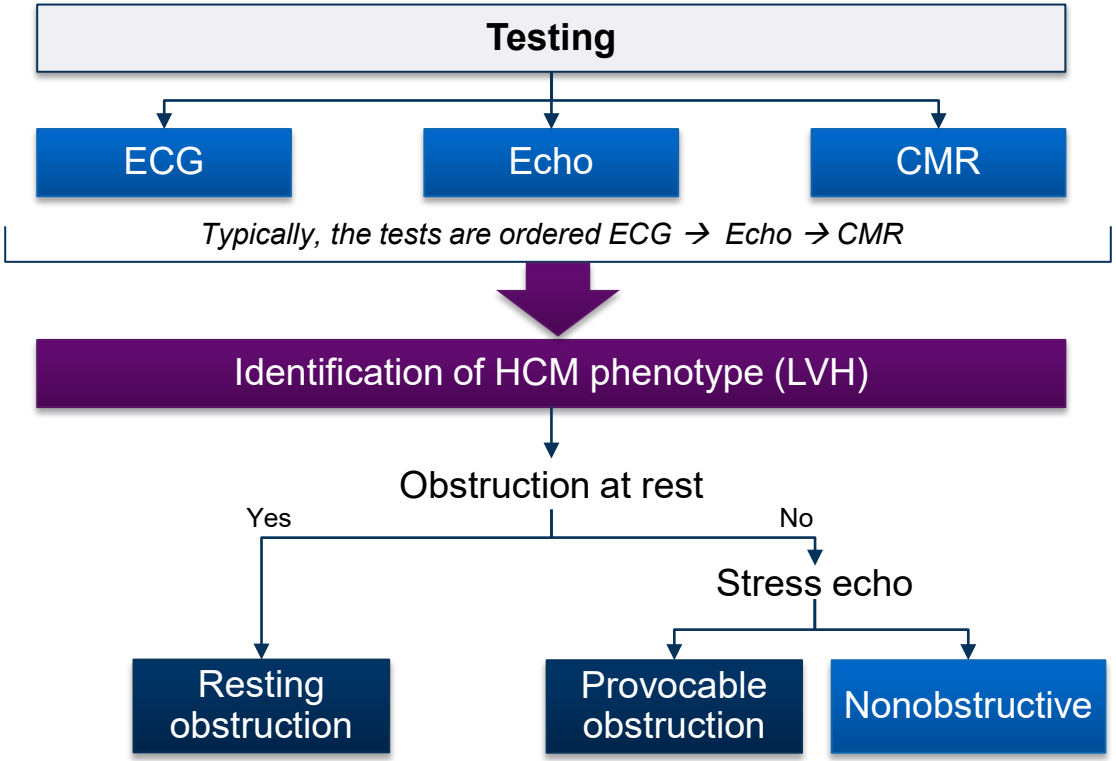


[a] Image source ECG Library.

Clinical Evaluation and Testing Algorithm for Patients With or Suspected of Having HCM[1,2]

A Normal ECG Does Not Rule Out HCM!

18% of the Johns Hopkins HCM Clinic Cohort (N = 395) had a normal ECG



1. Maron BJ et al. *J Am Coll Cardiol.* 2022;79:372-389. 2. Sorensen LL et al. *Am J Cardiol.* 2016;117:1815-1820.

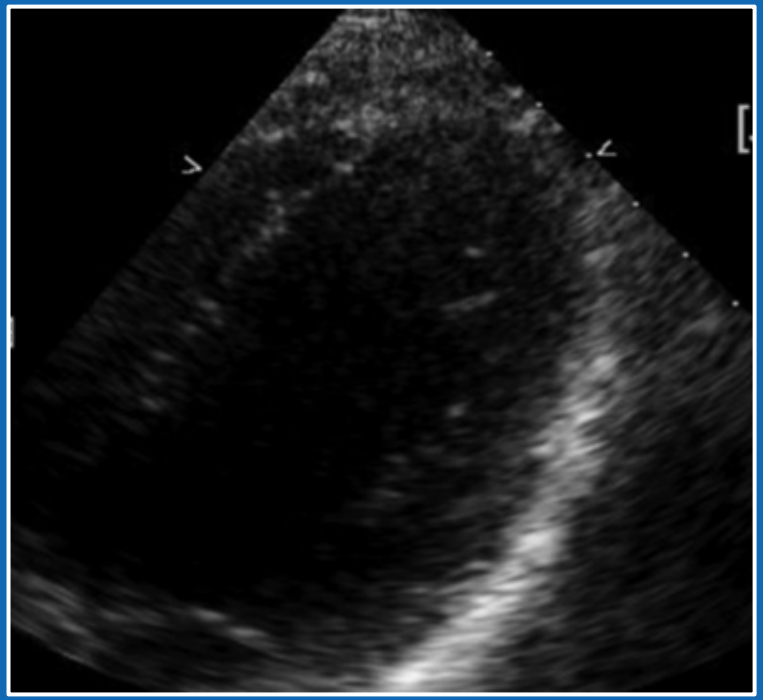
Patient Case #1 Revisited: Corbin's Imaging[1]

Corbin

Patient Info

- Male patient aged 17 years
- No previous medical hx
- Football team physician thought he heard a murmur during a preseason sports physical

- Echocardiography was ordered
- Apical endocardial border poorly defined
- Patient was referred for CMR

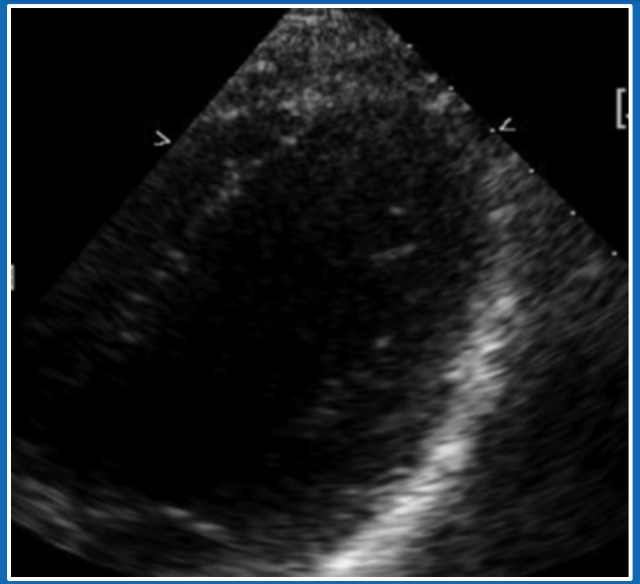


1. Chun EJ et al. *Radiographics*. 2010;30:1309-1328.

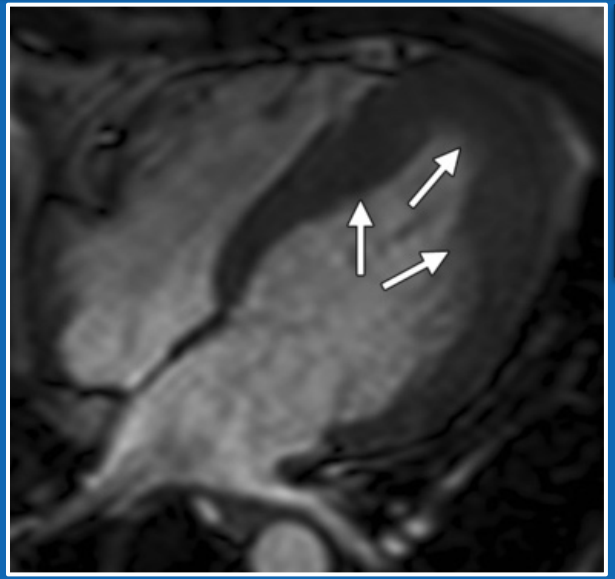
Patient Case #1 Revisited: Corbin's Imaging[1]

Corbin

Echocardiography
Apical endocardial border poorly defined



Cardiac MRI
Apical endocardial border denoted by arrows



Athlete's heart does not cause this degree of hypertrophy

1. Chun EJ et al. *Radiographics*. 2010;30:1309-1328.

Should We Perform Genetic Testing?[1-4]

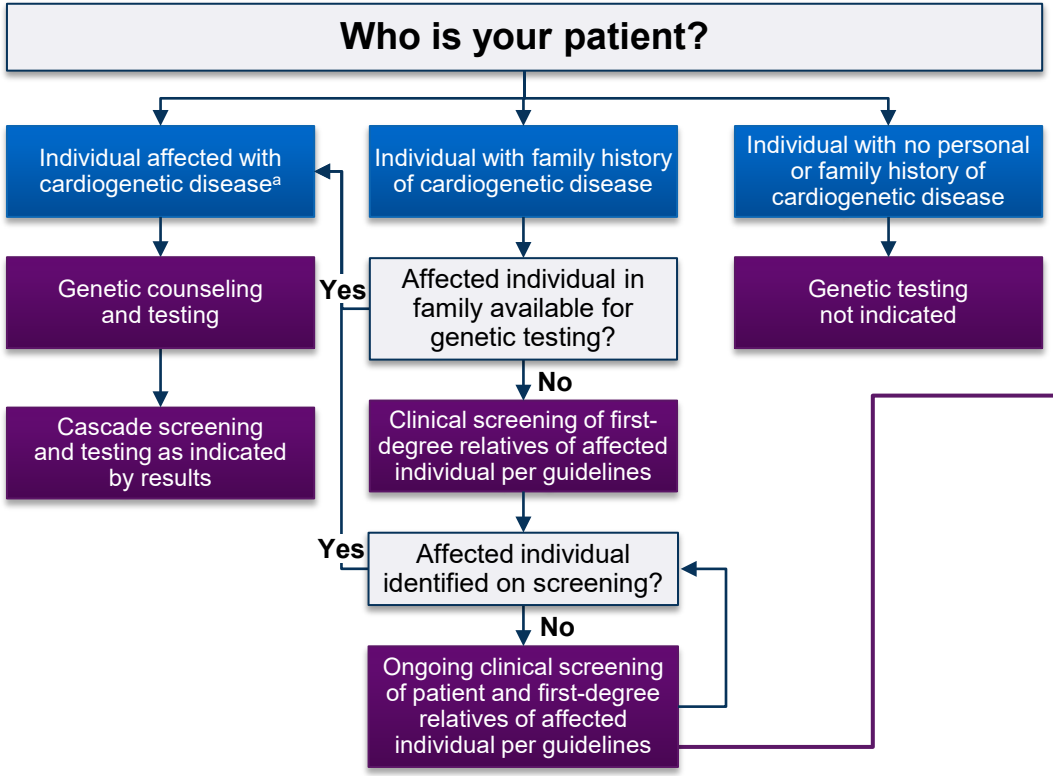
Individual affected with cardiogenetic disease

Genetic counseling and testing

The **Mayo Clinic HCM Genotype Prediction Score** estimates the likelihood of identifying a pathogenic sarcomere variant from age and echo findings[2]

1. Chowns J et al. *Med Clin North Am*. 2022;106:313-324. 2. Ommen SR et al. *Circulation*. 2020;142:e558-e631. 3. Bos JM et al. *Mayo Clin Proc*. 2014;89:727-737.
4. Towe EC et al. *Congenit Heart Dis*. 2015;10:E139-E145.

Who Else Needs Genetic Testing?[1,2]



Age of First-Degree Relative	Initiation of Screening	Surveillance Interval
Children and adolescents from genotype-positive family and/or family with early onset HCM	At the time of diagnosis in another family member	Every 1-2 y
All other children and adolescents	At any time after the diagnosis in the family but no later than puberty	Every 2-3 y
Adults	At the time of diagnosis in another family member	Every 3-5 y

[a] If there are multiple affected individuals in the family, testing should ideally start with the individual who is most severely affected and/or had the youngest age of onset.

1. Chowns J et al. *Med Clin North Am*. 2022;106:313-324. 2. Ommen SR et al. *Circulation*. 2020;142:e558-e631.

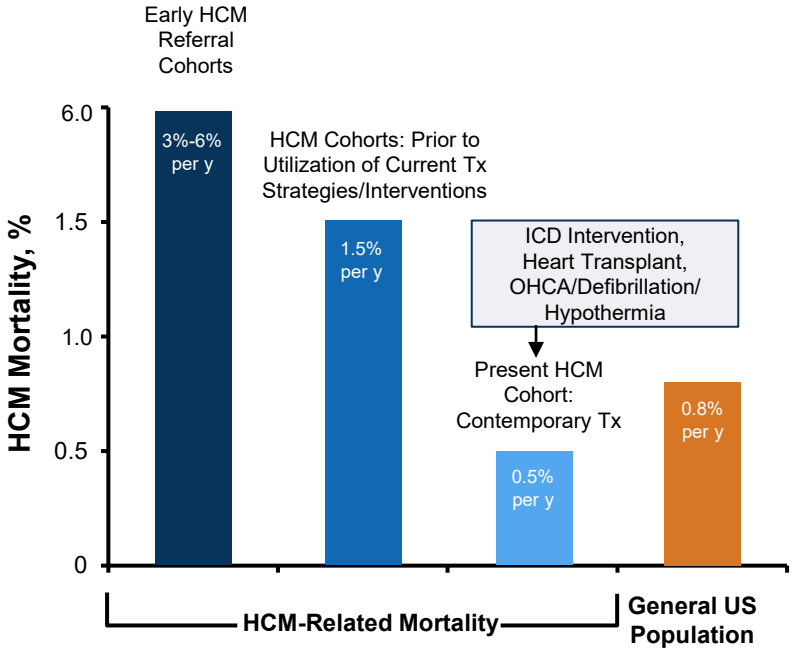
Reassure Patients That the Outlook for HCM Has Improved With Contemporary Treatment[1]

Describe HCM

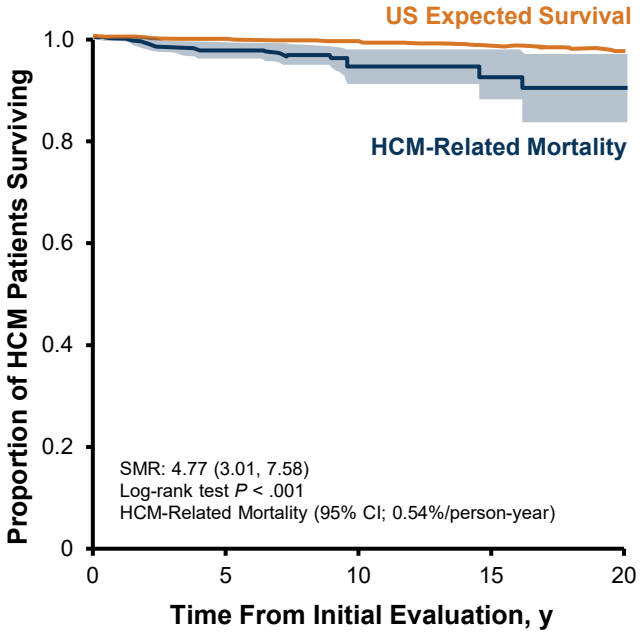
- Treatable condition
- Compatible with normal life expectancy

Age at Diagnosis and HCM-Related Mortality

Adult



Child or Young Adult



1. Maron BJ et al. *J Am Coll Cardiol*. 2015;65:1915-1928.

Can We Do Something to Slow the Progression of HCM in Genotype-Positive Individuals? Maybe!

Valsartan may slow the progression of HCM in early-stage disease: VANISH phase 2 study[1,2]

Study Design

- 178 adults and children with early-stage sarcomeric HCM
  - 43% were aged ≤18 years
  - ~17 mm mean LV thickness (maximum ≤25 mm)
- Double-blind RCT, 1:1 randomization, 2-year follow-up
  - Valsartan 320 mg/d, adults; 80-160 mg/d, children
- Primary outcome was a composite z-score of echocardiography structural and functional measurements and biomarkers of cardiac damage (LV thickness, LV mass, LV and LA volume, E', S', NT-proBNP, and troponin T)

Study Results

- Valsartan improved cardiac structure and function and was well-tolerated
  - Increased LV end diastolic volume
  - Increased E' velocity
  - Reduced NT-proBNP
- Better results were seen with *MYH7* variant than with *MYPBC3* variant
- Prespecified exploratory cohort of patients with subclinical HCM was underpowered to identify potential beneficial effects

Further study is needed

1. Ho CY et al. *Nat Med*. 2021;27:1818-1824. 2. Vissing CR et al. *JAMA Cardiol*. 2023;8:1083-1088.

Patient Case #2: Delia

Delia

Patient Info

- Female patient aged 67 years
- New patient
- Hx of obesity and GERD
- Dissatisfied with the care she received from another doctor
- Previous diagnosis of anxiety (age 22) and exercise-induced asthma (age 50) that did not respond to 1L or 2L asthma medications

Recent Medical History

- 2 ED visits in the last 12 months for palpitations and chest pain
- Cardiac catheterization at community hospital

Physical Exam

- HR 70, pulse regular
- BP 142/91 mmHg
- BMI 31 kg/m^2
- Lungs clear, no wheezing, no rales

Current Medications

- Omeprazole
- Cimetidine

Current Lab Results

- Elevated high-sensitivity troponin
- Coronary arteries normal

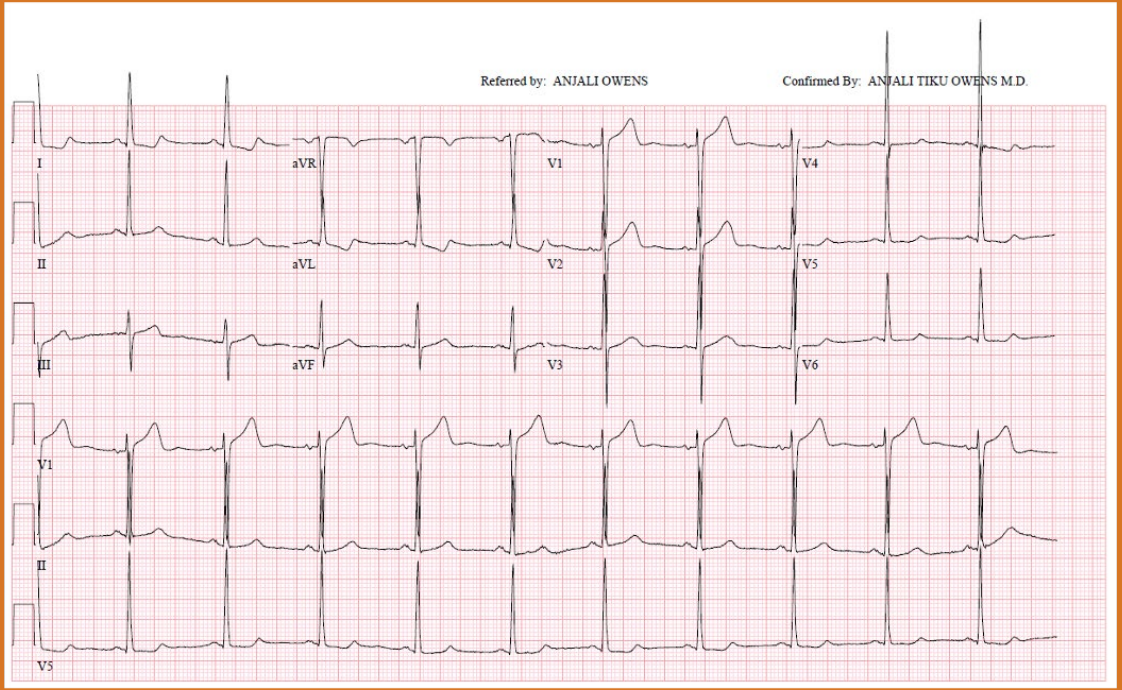
Diagnostic Pitfalls: Potential Misdiagnoses and Overlap With Symptoms of HCM[1-3]

Exercise-induced asthma	Shortness of breath in HCM can mimic asthma
Mitral valve prolapse	Heart murmur in HCM may be diagnosed as a mitral valve prolapse, which also causes a heart murmur
Innocent heart murmur	If the HCM murmur is intermittent, it might be diagnosed as an innocent heart murmur and nothing to worry about
Panic attack/anxiety	Palpitations, lightheadedness, and sense of unease can overlap with anxiety symptoms; persistent, troubling symptoms may be repeatedly dismissed by HCPs, including cardiologists
Syncope	Incorrectly attributed to vasovagal event

1. https://4hcm.org/pathways-of-hypertrophic-cardiomyopathy/. 2. Subasic K. *J Nurs Scholarsh*. 2013;45:371-379. 3. Zytnick D et al. *Heart Lung*. 2021;50:788-793.

Patient Case #2: ECG Results for Delia

Delia



Typical ECG Features in HCM[1,2]

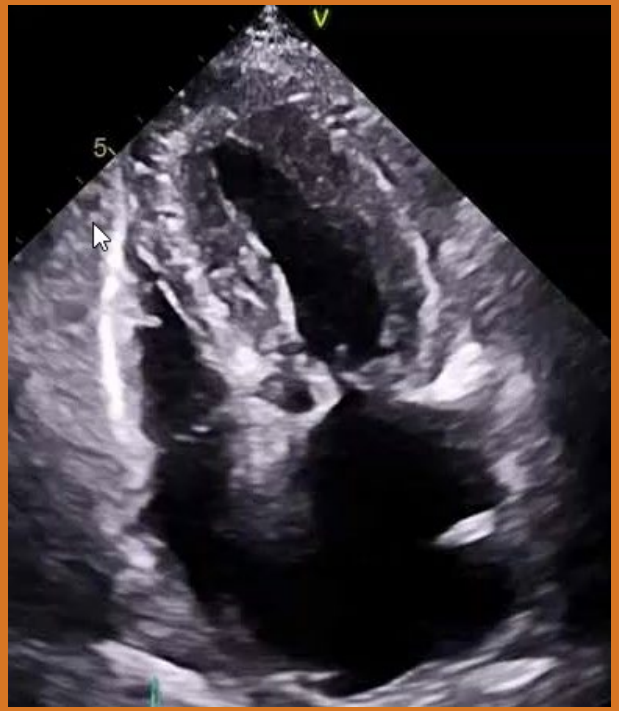
- Repolarization abnormalities
- T-wave inversion
- Left atrial abnormalities
- LVH (Cornell or Sokolow-Lyon)
- ST depression
- Q waves

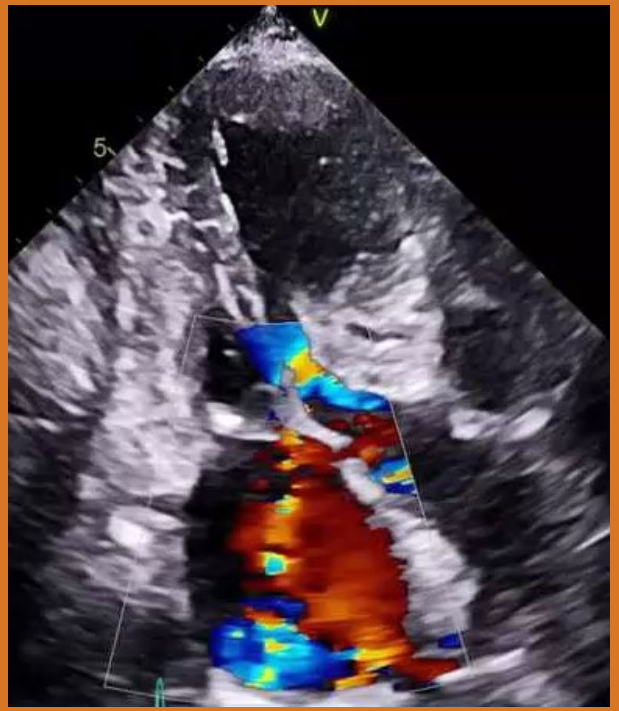
Case provided by Anjali Owens, MD.

1. Ommen SR et al. *Circulation*. 2020;142:e558-e631. 2. Sorensen LL et al. *Am J Cardiol*. 2016;117:1815-1820.

Patient Case #2: Echocardiogram Results for Delia

Delia



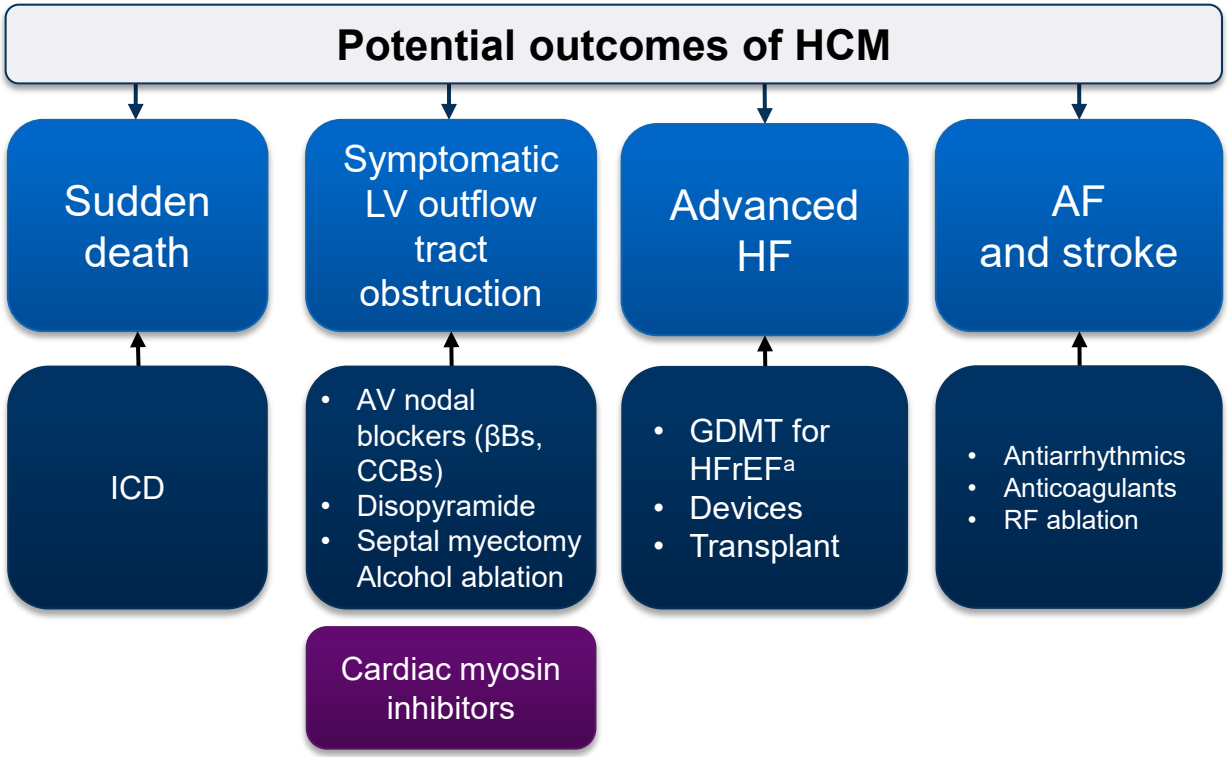


- NYHA class III
- LVEF 75%
- E/e' = 31
- LVOT gradient >80 mmHg
- Severe SAM, mitral regurgitation
- LAVI 55 mL/m^2

Diagnosis: oHCM

Case provided by Anjali Owens, MD.

Treatments for HCM[1-2]



How do cardiac myosin inhibitors differ from previous treatments?[3]

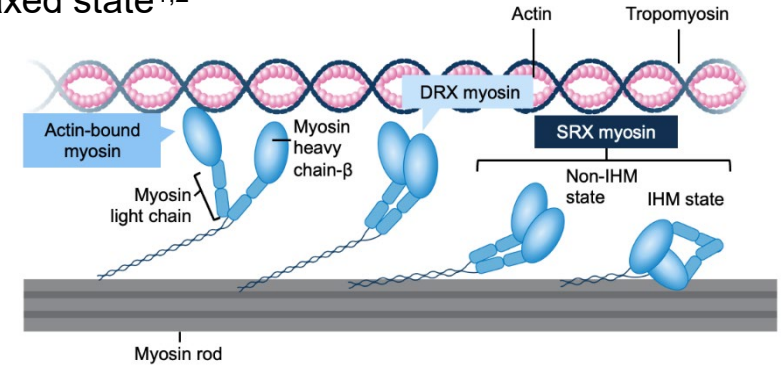
- Designed as potentially disease-modifying treatments specifically for HCM
- Administered as oral pills
- Can be used in combination with conventional treatments

[a] GDMT for HFrEF includes: ACEis/ARBs or ARNI, beta blockers, SGLT2is, MRA, and diuretics as needed.[4]

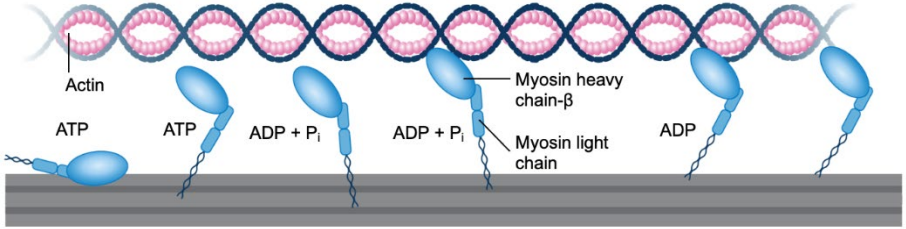
1. Adapted from Maron BJ et al. *JAMA Cardiol*. 2016;1:98-105. 2. Ommen SR et al. *Circulation*. 2020;142:e558-e631.
3. Alsulami K, Marston S. *Int J Molec Sci*. 2020;21:9599. 4. Heidenreich PA et al. *J Am Coll Cardiol*. 2022;79:e263-e421.

Small-Molecule Cardiac Myosin Inhibitors Are Being Evaluated in Clinical Trials for HCM

Mavacamten: reduces myosin head availability; stabilizes the myosin super-relaxed state[1,2]



Aficamten: slows phosphate release from myosin; stabilizes weak actin-binding myosin conformation[1,2]



How do cardiac myosin inhibitors differ from previous treatments?[3]

- Designed as potentially disease-modifying treatments specifically for HCM

How are cardiac myosin inhibitors used?

- Administered as daily oral pills
- Can be used in combination with conventional treatments

1. Tiku Owens A. ACC 2022. Oral presentation: 683-610. 2. Lehman SJ et al. *Nat Rev Cardiol*. 2022;19:353-363.
3. Alsulami K, Marston S. *Int J Molec Sci*. 2020;21:9599.

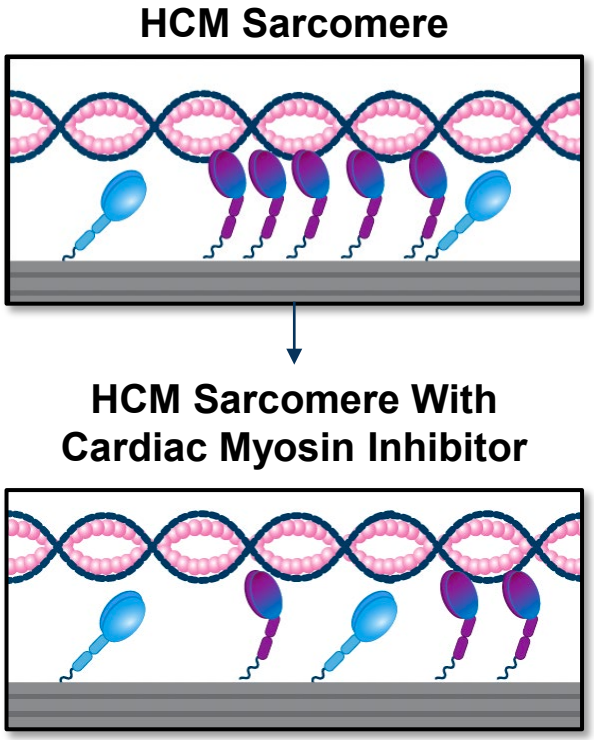
What You Need to Know About Cardiac Myosin Inhibitors[1-8]

Mavacamten: FDA-approved for symptomatic oHCM[2-4]

- **Works to stabilize the relaxed state**
- ↓ obstruction and symptoms
- ↑ exercise tolerance
- ↓ need for invasive procedures (septal myectomy, alcohol ablation)
- ↑ QoL

Aficamten: still in clinical trials[5-7]

- **Works to slow phosphate release from myosin**
- Completed phase 3 for oHCM
- Positive topline results

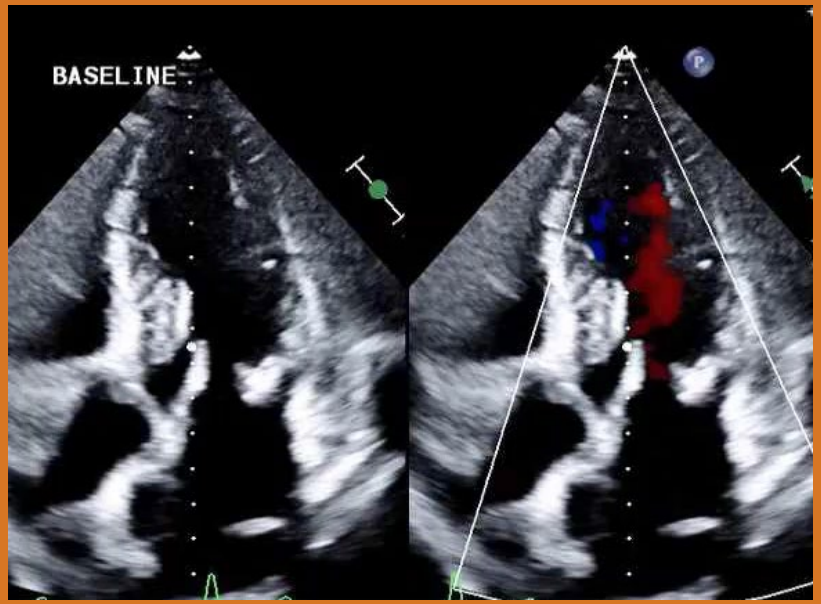


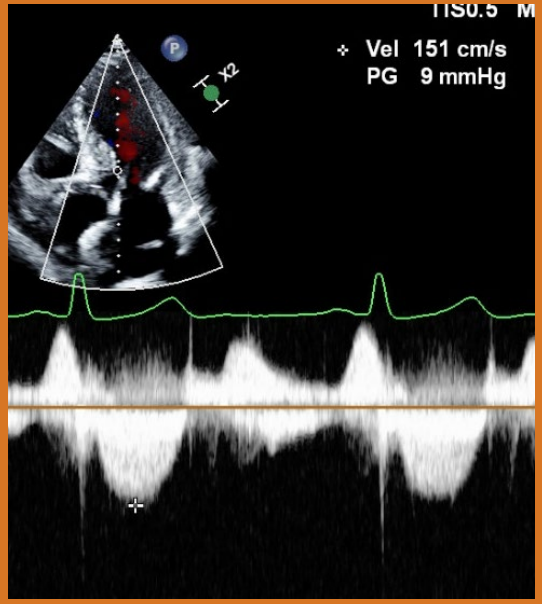
1. Alsulami K, Marston S. *Int J Molec Sci*. 2020;21:9599. 2. Garcia-Pavia P et al. ESC 2023. https://esc365.escardio.org/presentation/267191.
3. Desai MY et al. *Circulation*. 2023;147:850-863. 4. Desai MY et al. *JAMA Cardiol*. 2023;8:968-977. 5. Owens AT et al. *J Card Fail*. 2023;29:1576-1582.
6. Maron MS et al. *J Am Coll Cardiol*. 2023;81:34-45. 7. Coats CJ et al. *JACC Heart Fail*. 2023 Nov 18 [Epub ahead of print]. 8.
https://www.statnews.com/2023/12/27/cytokinetics-aficamten-obstructive-hypertrophic-cardiomyopathy-hcm-study/.

Patient Case #2: Repeat Echo Results for Delia

Delia

After 9 months on a cardiac myosin inhibitor …





- NYHA class II
- LVEF 65%
- E/e' = 31 → 19
- LVOT gradient = 9 mmHg
- Mild MR, mild SAM
- LAVI 41 mL/m^2

Treatment: metoprolol succinate 50 mg/d, mavacamten 5 mg/d

Case provided by Anjali Owens, MD.

Avoiding DDIs[1]

- **Mavacamten is contraindicated for use with some CYP450 inhibitors and inducers**
  - moderate to strong CYP2C19 inhibitors or inducers
  - strong CYP3A4 inhibitors or moderate to strong CYP3A4 inducers
- **Some of the more prominent DDIs include**
  - nirmatrelvir with ritonavir (contraindicated)
  - omeprazole (use pantoprazole instead)
  - cimetidine
  - fluconazole and other antifungals
  - amiodarone (dose adjustment needed)
- **Additionally, clinical experience suggests that there are probably interactions with alcohol and marijuana (get a thorough social history)**

1. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/214998s001lbl.pdf.

What Do I Need to Know About the Mavacamten REMS?[1]

Reduced LVEF may occur

Mavacamten reversibly reduces hypercontractility

- LVEF monitoring is needed
- Don't initiate if LVEF <55%
- Interrupt use if LVEF <50%

DDIs can increase the risk of HF

Some CYP450 inhibitors or inducers
- Weak CYP2C19 inhibitors
- Moderate CYP3A4 inhibitors

- Check medication list at every visit
- No new prescription or nonprescription meds should be initiated without checking DDIs first

Everyone needs to be on the same page

REMS includes a brief training program for all key stakeholders

- Physicians, pharmacists, pharmacies, and patients all require training

1. https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/214998s000lbl.pdf.

Mavacamten Requires Ongoing Echocardiography to Monitor Cardiac Structure and Function

Prior to initiating therapy

4 weeks after initiating therapy

8 weeks after initiating therapy

12 weeks after initiating therapy

4 weeks after every dose increase

Every 3 months once a stable dose is achieved

- Mavacamten is associated with substantial net health benefits for patients with symptomatic obstructive HCM, including improved symptoms and QoL[1]
- However, the imaging burden should be discussed with patients before initiating therapy[2]

1. Desai N et al. *Clin Ther*. 2022;44:52-66. 2. Altibi A et al. *Curr Cardiol Rep*. 2023;25:583-595.

Common Comorbidities of HCM Require Treatment to Prevent Worsening of HCM Symptoms[1-4]

Comorbidity	Prevalence and Consequences
Hypertension	• Highly prevalent in the general population; may also be present in patients with unequivocal HCM • May increase LV mass but rarely increases LV thickness >16 mm • HCM is accompanied by mitral valve abnormalities not found in hypertensive cardiomyopathy
Sleep apnea	• Reported in up to 70% of patients with HCM • Worsens hemodynamics of HCM, increases symptom burden
Obesity	• More common in HCM than in general population • oHCM observed in >50% of patients with HCM and BMI >30 • Increases LV mass, more rapid clinical progression, worsens HF symptoms, increases risk of AF (especially in middle-aged adults)
CAD	• Myocardial ischemia is often observed in patients with HCM • Major prognostic indicator, associated with increased overall mortality, SCD, and cardiac events
Atrial fibrillation	• Common in HCM; more likely with *MYH7* sarcomere variants • Higher BMI, LA volume, and moderate to severe MR increase risk of AF events

1. Finocchiaro G et al. *J Am Heart Assoc*. 2017;6:e007161. 2. Kramer CM et al. *J Am Coll Cardiol EP*. 2021;7:1376-1386.
3. Lee SP et al. *Circ Heart Fail*. 2018;11:e005191. 4. Marstrand P et al. *Circulation*. 2020;141:1371-1383.

Patient Case #3: Edward

Edward

Patient Info

- Male patient aged 37 years
- New patient
- Gets winded more easily while running his usual route

Physical Exam

- NYHA class II
- HR 67
- BP 129/77 mmHg
- BMI 28 kg/m^2
- Lungs clear, no wheezing, no rales
- Auscultation findings: regular rate and rhythm, no murmur, no gallop

Current Medications

- Fluconazole (for athlete's foot)

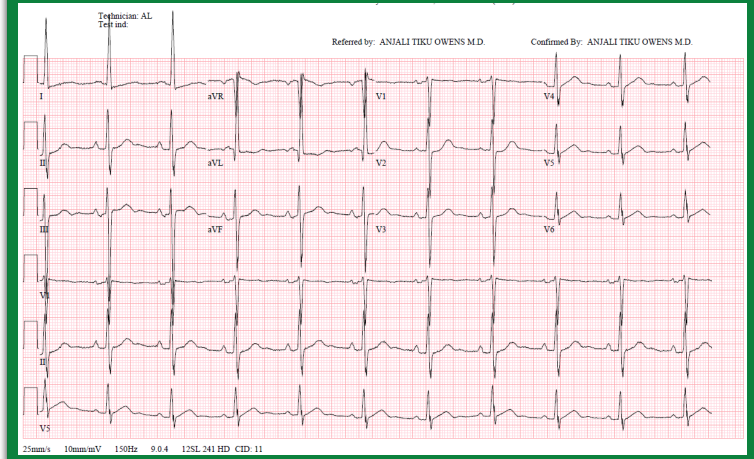
Selected Lab Findings

- LDL-C 107 mg/dL
- Hct 47%
- Hb 16.1 g/dL

Patient Case #3: ECG and Imaging Studies for Edward

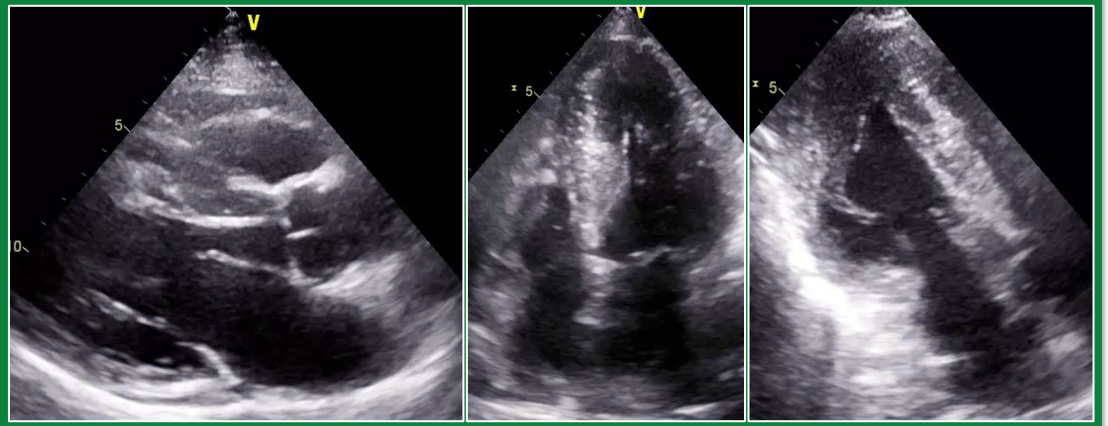
Edward

ECG



- High voltage consistent with LVH

Echocardiography

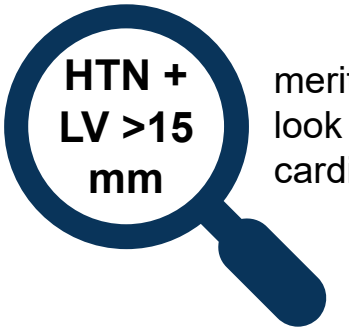


- Maximal septal wall thickness 2.6 cm
- Valsalva gradient: 5 mmHg
- Additional laboratory testing: NT-proBNP 1,351

How Can I Differentiate nHCM From Other Causes of HFpEF?

Could it be HCM?[1]

- "Unexplained" wall thickness ≥15 mm in any myocardial segment (or ≥13 mm with positive family history)
- High normal LVEF (eg, 60%-70%)
- CMR needed to differentiate from other causes of hypertrophy



merits a closer look from a cardiologist

How much hypertrophy is too much?

- HCM more likely with asymmetric, septal-predominant thickening
- Hypertensive hypertrophy is usually concentric, 12-14 mm

Any wall thickness >20 mm is a red flag!

Which laboratory tests are helpful in differentiating HCM from other cardiomyopathies?[2]

- CK
- Troponin
- NT-proBNP
- Proteinuria
- Renal function
- LFT

1. Baron T et al. *Eur Heart J Cardiovasc Imag*. 2023;24:1343-1351. 2. Arbelo E et al. *Eur Heart J*. 2023;44:3503-3626.

Phenocopies (Mimics) of HCM[1,2]

Disease	Gene	Cardiac	Extracardiac
Fabry disease	*GLA*	• ECG: short PR interval, conduction disease • CMR: fibrosis in basal inferolateral wall; low native T1	Angiokeratoma, cornea verticillata, neuropathic pain, CVA, tinnitus, hearing impairment, renal failure and proteinuria, GI symptoms
***PRKAG2* cardiomyopathy**	*PRKAG2*	• ECG: short PR interval, pre-excitation, conduction disease, SVT	Skeletal myopathy
Amyloidosis	*TTR*	• ECG: pseudo-infarct pattern, low-voltage, conduction disease • CMR: global subendocardial or transmural late enhancement, suboptimal myocardial nulling	Neuropathy, autonomic dysfunction, carpal tunnel syndrome, renal failure and proteinuria
Danon disease	*LAMP2*	• ECG: pre-excitation pattern, short PR interval	Skeletal myopathy, intellectual disability
Noonan syndrome	*PTPN11* *RAF1*	• ECHO: pulmonary stenosis	Typical facies, short stature, webbed neck, pectus deformity, developmental delay, bleeding disorders

Commercially available testing panels for cardiomyopathy include all these genes

1. Hoss S et al. *Circ Genom Precis Med*. 2020;13:e002748.
2. https://www.ncbi.nlm.nih.gov/gtr/all/tests/?term=cardiomyopathy,%20hypertrophic&filter=testtype:clinical;testpurpose:diagnosis,screening.

Treatments for HFpEF Differ by Cause[1]

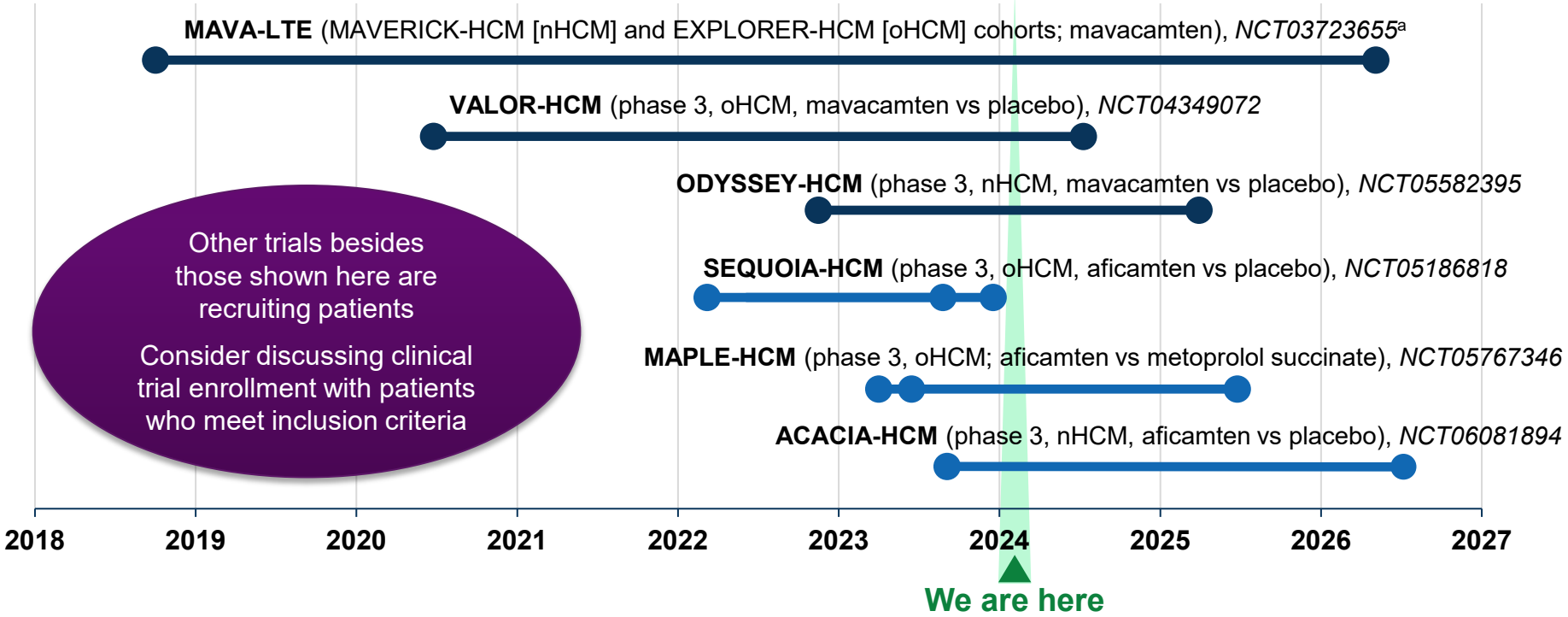
Umbrella Concept	Final Diagnosis Informed by Imaging	Main Current Therapeutic Options
 • HFpEF symptoms/ signs of HF • EF ≥50% • Structural/ functional abnormality	"Classic" HFpEF	Risk factor modification, aldosterone antagonists, SGLT2 inhibitors
	CAD/coronary microvascular dysfunction	Anti-ischemic drugs, statins, revascularization
	HCM	β-receptor blockers, calcium antagonists, mavacamten, aficamten[a], SRT, ICD
	Cardiac amyloidosis	Chemotherapy in AL amyloidosis, tafamidis in ATTR amyloidosis
	Fabry-Anderson	Enzyme replacement therapy, chaperone therapy
	Cardiac hemochromatosis	Iron chelation therapy
	Cardiac sarcoidosis	Immunosuppressive therapy, ICD
	Constrictive pericarditis	Pericardiectomy
	Right-sided heart disease	Medical or interventional/surgical therapy

[a] Investigational agent.

1. Baron T et al. *Eur Heart J Cardiovasc Imag*. 2023;24:1343-1351.

What's Next for Cardiac Myosin Inhibitors?[1]

Phase 3 Clinical Trial Milestone Dates



[a] MAVA-LTE is not placebo controlled. The parent trials (MAVERICK-HCM and EXPLORER-HCM) were placebo controlled.

1. https://clinicaltrials.gov.

How Can I, as a Primary Care Clinician, Care for Patients With HCM?

Proposed Management of Modifiable Risk Factors in Patients With HCM[1]

Lifestyle/Clinical Variable	Possible Effects
LDL <100 mg/dL[a]	↓ risk of CAD ↓ risk of MI
BP <130/80 mmHg[a]	↓ risk of secondary LVH caused by increased afterload
Moderate exercise	↑ diastolic function ↑ exercise capacity ↓ risk of obesity
Weight management	↓ risk of obesity ↓ risk of development of a more marked LVH caused by increased afterload

[a] The standards for control of modifiable CV risk factors should arguably recapitulate those used for secondary prevention in patients with CAD, in all genetic cardiomyopathies, based on the principle that superimposed ASCVD seems to have synergistic rather than additive effects.

1. Finocchiaro G et al. *J Am Heart Assoc.* 2017;6:e007161.

Can People With HCM Exercise?

- **Most people with HCM can exercise safely[1]**
  - Include exercises for endurance, muscle strengthening, and flexibility
  - Precede with a warm-up and follow with a cool-down
  - Gradually increase intensity based on patient's adaptation to exercise, training experience, age, and clinical characteristics
- **Competitive athletes and HCM[2-4]**
  - In a case series of NCAA athletes, HCM caused 13% of sudden deaths
  - Detailed, individualized evaluation is needed
  - Refer to a comprehensive HCM center for determinations of eligibility

1. Cavigli L et al. *Eur J Prev Cardiol.* 2021;28:1093-1099. 2. Petek BJ et al. *Circulation*. 2023 Nov 13 [Epub ahead of print].
3. Maron MS et al. *J Am Coll Cardiol*. 2023;82:828-832. 4. Martinez KA et al. *J Am Coll Cardiol*. 2023;82:661-670.

Patient Case #3 Revisited: Edward

Edward

Patient Info

- Male patient aged 37 years
- New patient **diagnosed with nHCM**
- Gets winded more easily while running his usual route

Physical Exam

- NYHA class II
- HR 67
- BP 129/77 mmHg
- BMI 28 kg/m^2
- Lungs clear, no wheezing, no rales
- Auscultation findings: regular rate and rhythm, no murmur, no gallop

Current Medications

- Fluconazole (for athlete's foot)
- **Metoprolol**

Selected Lab Findings

- LDL-C 107 mg/dL
- Hct 47%
- Hb 16.1 g/dL

HCM Management Is a Team Sport[1]

Care Teams
- HCM team
- Advanced HF team
- CV surgical & structural team
- **Primary care team**
- Research team

Specialized HCPs
- HCM cardiologist
- Primary cardiologist
- Electrophysiologist
- Genetic counselors

Wellness Factors
- Lifestyle
- Nutrition
- Wellbeing

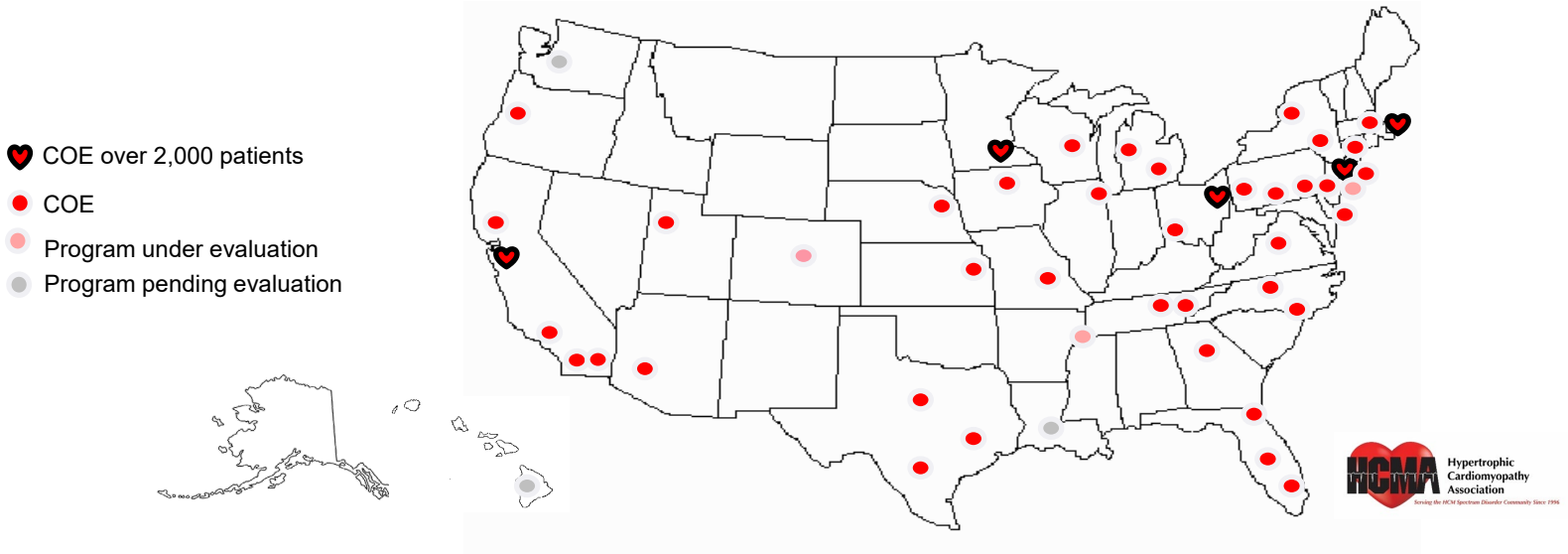
Testing
- Genetic testing
- Advanced cardiac imaging

- Multidisciplinary management and shared decision-making are musts, not nice-to-haves[1-3]
- Patients have a very reasonable expectation that all of their HCPs are working collaboratively and talk to one another[4]

1. https://www.acc.org/Latest-in-Cardiology/Articles/2021/03/17/13/21/Hypertrophic-Cardiomyopathy-2020. 2. Ommen SR et al. *Circulation*. 2020;142:e558-e631.
3. Arbelo E et al. *Eur Heart J*. 2023;44:3503-3626. 4. Zytnick D et al. *Heart Lung*. 2021;50:788-793.

Comprehensive Centers Play an Indispensable Role in Managing HCM

HCMA Centers of Excellence, October 2021[1]



High-volume centers have significantly better mortality outcomes for surgical treatments for HCM than low-volume centers or community hospitals[2,3]

1. www.4hcm.org. 2. Mentias A et al. *J Am Coll Cardiol.* 2023;81:105-115. 3. Ashraf M et al. *Am J Cardiol*. 2023;191:51-58.

Collaboration Pathways With Comprehensive HCM Centers[1]

HCM Centers
- **May be the primary source of care for patients with HCM**
- Visit 1-2 times/year
- Monitoring, blood tests, ECGs, echocardiogram, review/adjust medications
- Interventional HCM treatments
- Often consulted for second opinions on treatment

Cardiologist
- **May coordinate HCM care**
- Visit 1-2 times/year
- Monitoring, blood tests, ECGs, echocardiogram
- Review/adjust medications

Behavioral Health Specialist
- Assist with psychological effects of living with HCM

Electrophysiologist
- If ICD is placed
  - Visit 1-2 times/year
  - Remote monitoring also performed

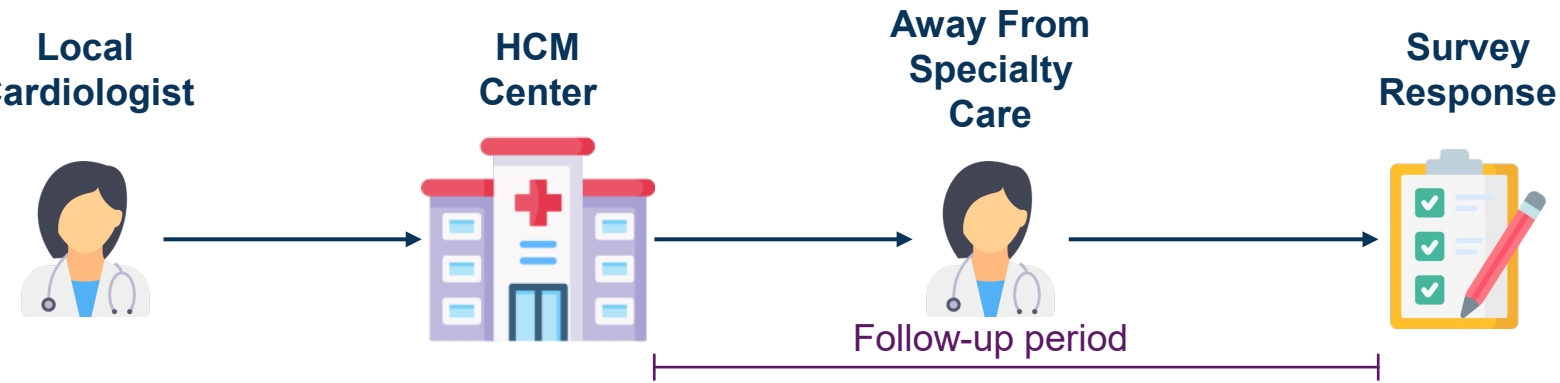
Primary Care
- **May coordinate HCM care or may delegate HCM care to specialists**
- Manage other chronic conditions (eg, DM, hypothyroidism)
- Preventive healthcare

Interdisciplinary/Interprofessional Communication Issues Reported by Patients
- Limited or dysfunctional communication among team members
- Anger/possessiveness when care is sought from other professionals

1. Zytnick D et al. *Heart Lung*. 2021;50:788-793.

What Happens to Patients With HCM Between Visits to a HCM Specialty Center? Mayo Clinic Experience[1]

Study Design to Characterize Clinical Course of Patients With HCM Away From Specialty Care



HCM patients leaving specialty care represent a high-risk cohort with a high rate of morbidities

High-Risk Cohort
~1 ventricular arrhythmic event per 100 y

20% ≥1 cardiac hospitalization

25% ≥1 cardiac procedure

Exertional symptoms and female sex associated with ↑ morbidities

1. Garmany R et al. *ESC Heart Fail.* 2023;10:1919-1927.

Key Takeaways

- HCM is the most common genetic cause of cardiomyopathy but is frequently misdiagnosed
- Cardiac imaging to measure wall thickness is needed to diagnose HCM
- First-degree family members need clinical screening to look for signs of HCM
- Medical and surgical treatments are available and more are in development
- Primary care clinicians can help with screening, care coordination, diagnosis, and with treating comorbidities of HCM that have the potential to worsen symptoms (eg, hypertension, dyslipidemia, OSA)

Audience Q&A

Thank you, and have a good day.

PeerView Live

Abbreviations

1L: first line
2L: second line
ACC: American College of Cardiology
ACEi: angiotensin-converting enzyme inhibitor
ADP: adenosine-diphosphate
AF: atrial fibrillation
AL: amyloid light chain
ARB: angiotensin receptor blockers
ATP: adenosine triphosphate
ATTR: transthyretin-related amyloidosis
AV: atrioventricular
βB: beta blocker
BMI: body mass index
BP: blood pressure
CAD: coronary artery disease
CCB: calcium channel blocker
CHA2DS2-VASc:
CK: creatine kinase
CMR: cardiovascular magnetic resonance
COE: center of excellence
CV: cardiovascular
CVA: cerebrovascular accident
DDI: drug–drug interaction
DM: diabetes mellitus
DOAC: direct oral anticoagulants
DRX: disordered relaxed state
ECG: electrocardiogram
ECHO: echocardiogram
ED: emergency department
EF: ejection fraction
GDMT: guideline-directed management and therapy
GERD: gastroesophageal reflux disease
GI: gastrointestinal
GLS: global longitudinal strain

Abbreviations

Hb: hemoglobin
HCM-AF: hypertrophic cardiomyopathy–atrial fibrillation
HCM-SD: hypertrophic cardiomyopathy–sudden death
HCM: hypertrophic cardiomyopathy
HCMA: Hypertrophic Cardiomyopathy Association
Hct: hematocrit
HF: heart failure
HFpEF: heart failure with preserved ejection fraction
HFrEF: heart failure with reduced ejection fraction
HR: heart rate
HTN: hypertension
ICD: implantable cardioverter defibrillator
IHM: interacting-heads motif
LA: left atrium
LAVI: left atrial volume index
LDL: low-density lipoprotein
LFT: liver function test
LGE: late gadolinium enhancement
LV: left ventricle
LVEF: left ventricular ejection fraction
LVH: left ventricular hypertrophy
LVOT: left ventricular outflow tract
MI: myocardial infarction
MR: mitral regurgitation
MRA: mineralocorticoid receptor antagonist
MRI: magnetic resonance imaging
NCAA: National Collegiate Athletic Association
nHCM: nonobstructive hypertrophic cardiomyopathy
NSCT: non-sustained ventricular tachycardia
NT-proBNP: amino-terminal pro-B-type natriuretic peptide
NYHA: New York Heart Association
OHCA: out-of-hospital cardiac arrest
oHCM: obstructive hypertrophic cardiomyopathy
OSA: obstructive sleep apnea

Abbreviations

QoL: quality of life
RCT: randomized controlled trials
REMS: Risk Evaluation and Mitigation Strategy
RF: radiofrequency
RV: right ventricle
SAM: systolic anterior motion
SCD: sudden cardiac death
SD: sudden death
SGLT2i: sodium-glucose cotransporter 2 inhibitor
SHaRe: Sarcomeric Human Cardiomyopathy Registry
SMR: standardized mortality ratio
SoB: shortness of breath
SRT: septal reduction therapy
SRX: super-relaxed state
SVT: supraventricular tachycardia
WPW: Wolff-Parkinson-White