# Diagnostic challenges with symptomatic obstructive hypertrophic cardiomyopathy

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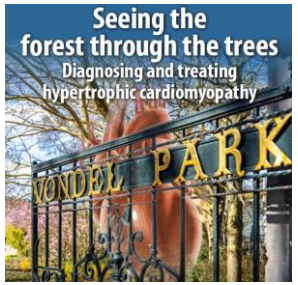
**Seeing the forest through the trees - Diagnosing and treating hypertrophic cardiomyopathy**

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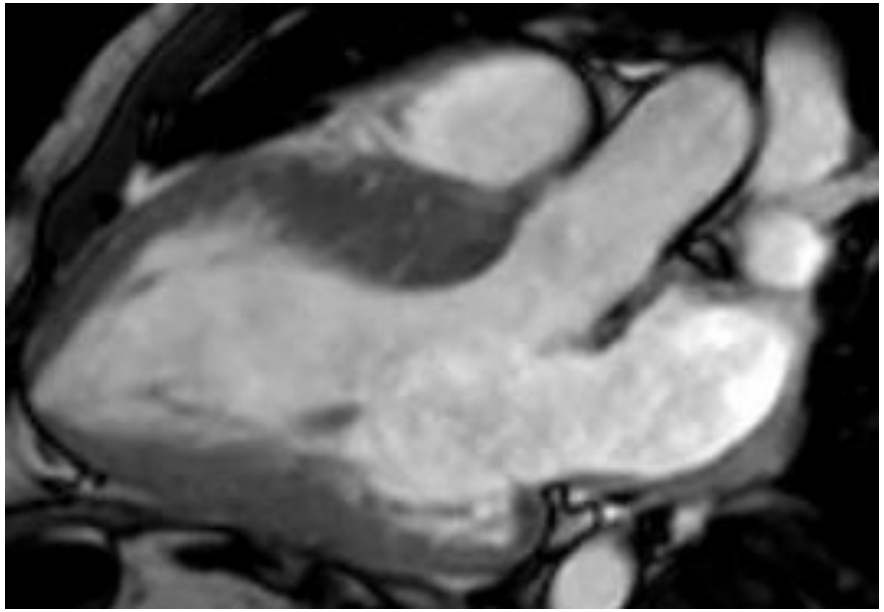
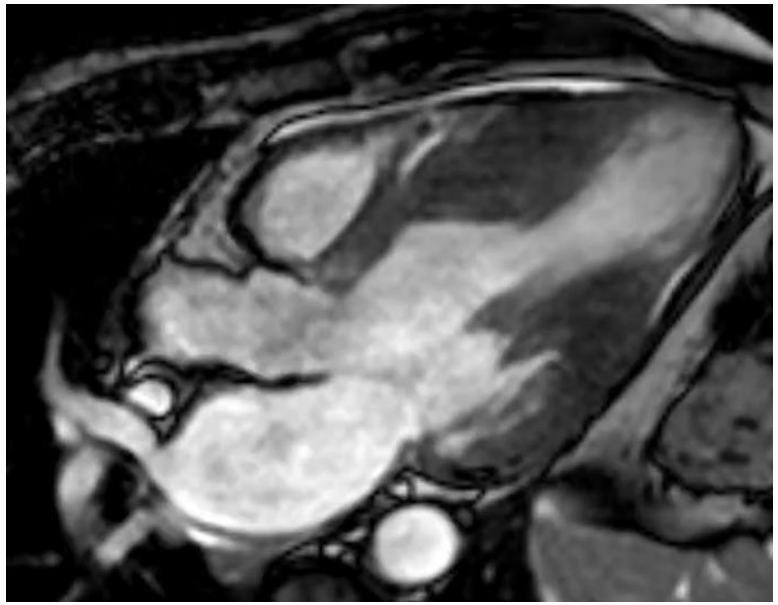
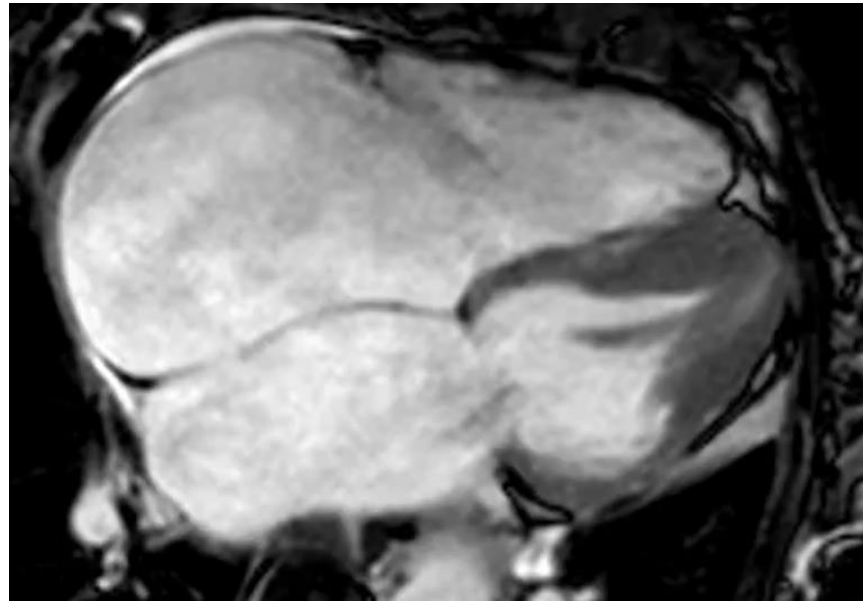
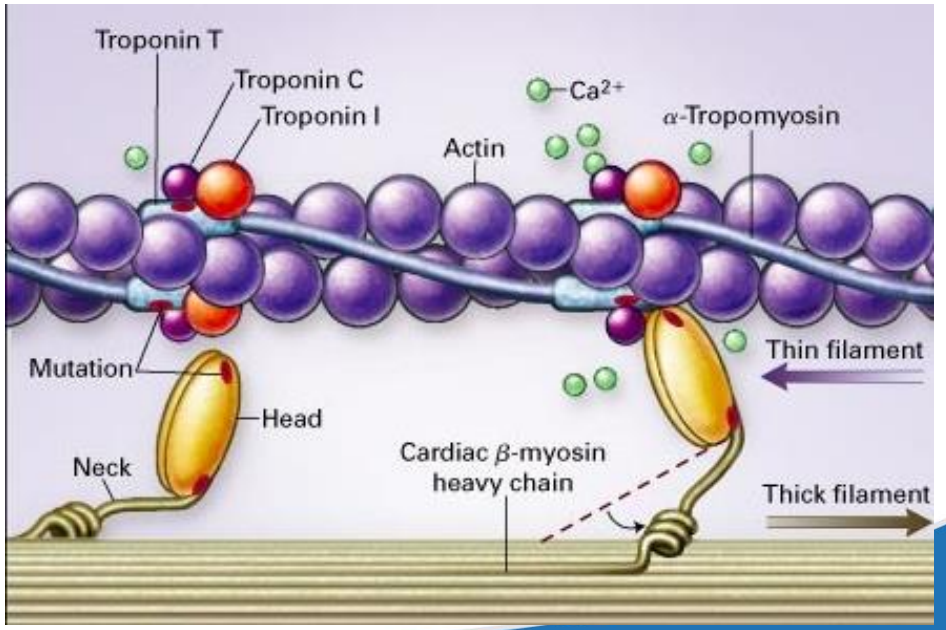
# Disclosures

- Consulting fees from Lexeo, Rocket Pharmaceuticals, Cytokinetics and BMS.
- Speaker for BMS.
- Clinical Trial support from Cytokinetics and BMS.

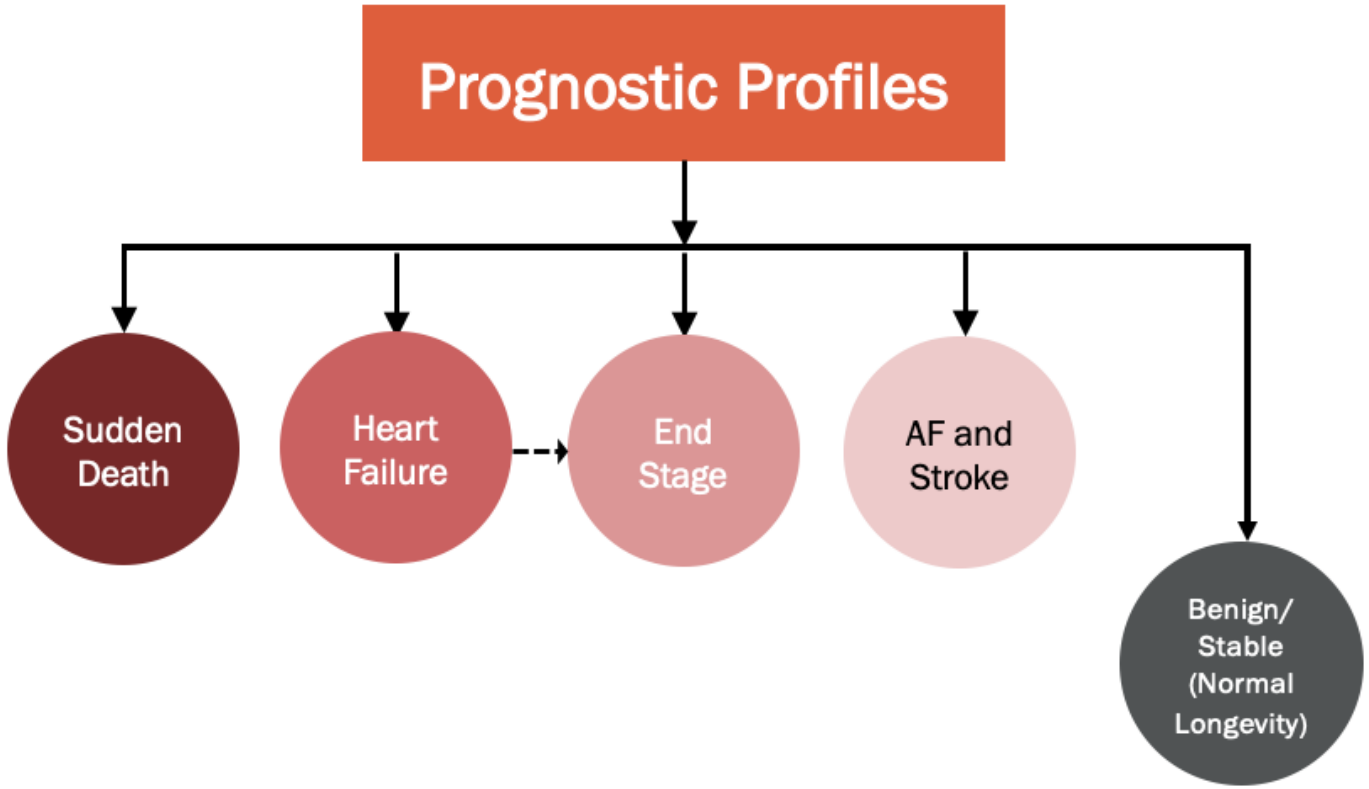
## HCM Pathophysiology

**Hypertrophy & Increased Fibrosis**
**Hypercontractility**
**Impaired relaxation**
**Altered myocardial energetics**




N Engl J Med 2000; 343:1688-1696

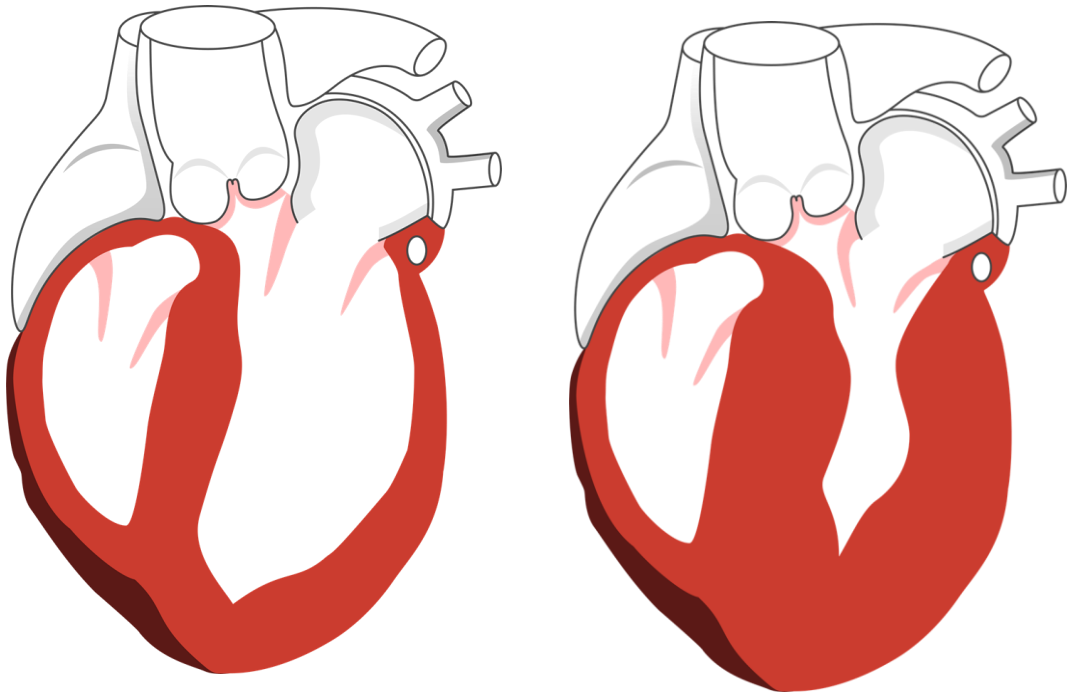
# HCM Clinical Course



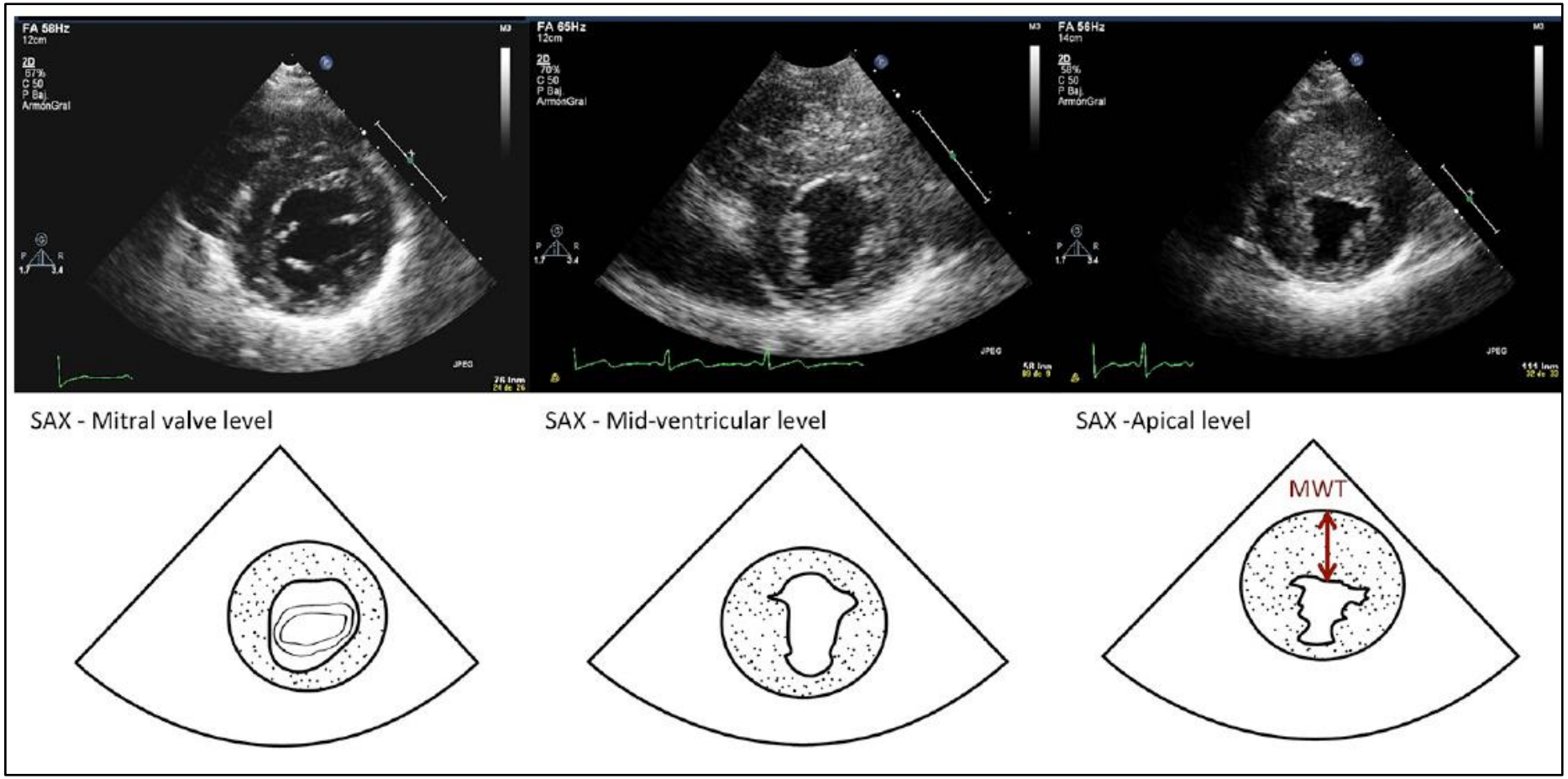

*Gersh et al. Circulation* 2011;124:2761-96

# HCM is characterized by left ventricular hypertrophy (LVH)

- Defining characteristic
  - "LVH in the absence of another cardiac, systemic, or metabolic disease capable of producing the magnitude of hypertrophy"
- Clinical diagnostic criteria
  - ADULTS: maximal end-diastolic wall thickness of ≥15 mm anywhere in the left ventricle
    - 13–14 mm can be diagnostic in family members of a patient with HCM / a positive genetic test
  - CHILDREN: adjusted z-score of ≥2 standard deviations above the mean

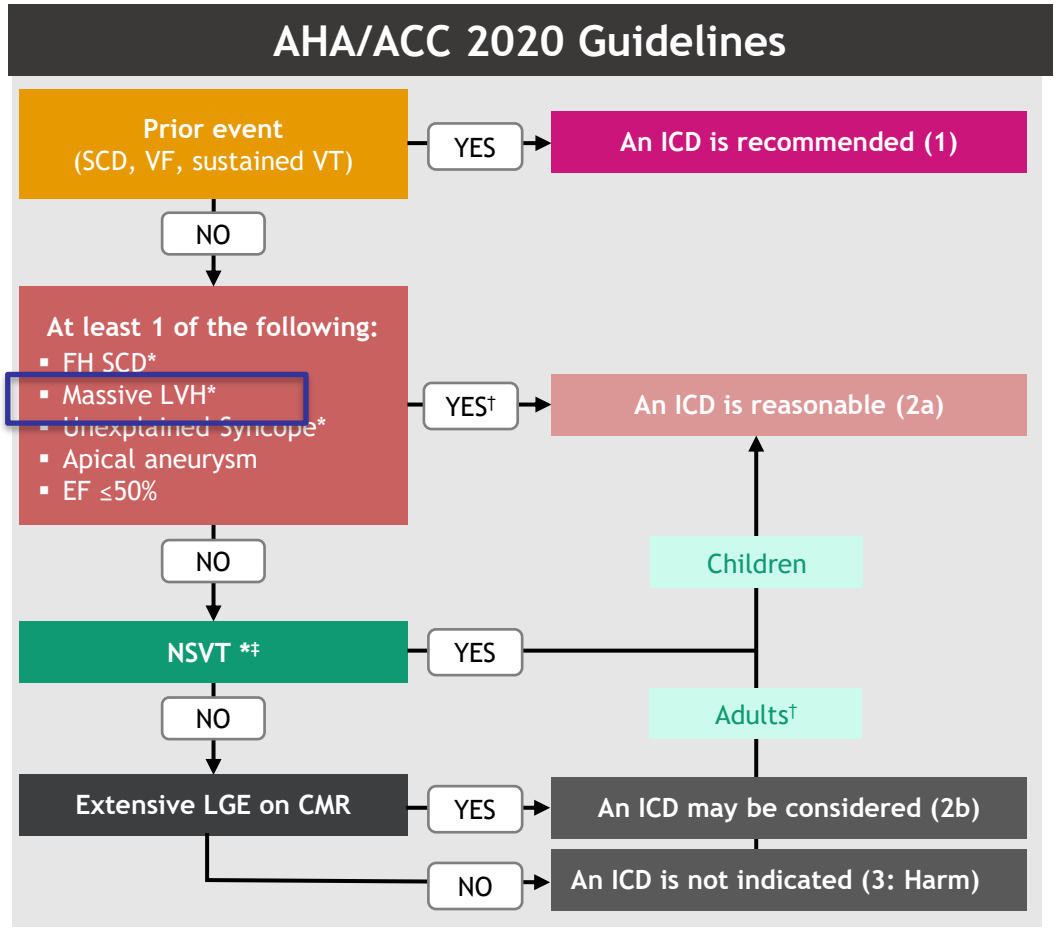


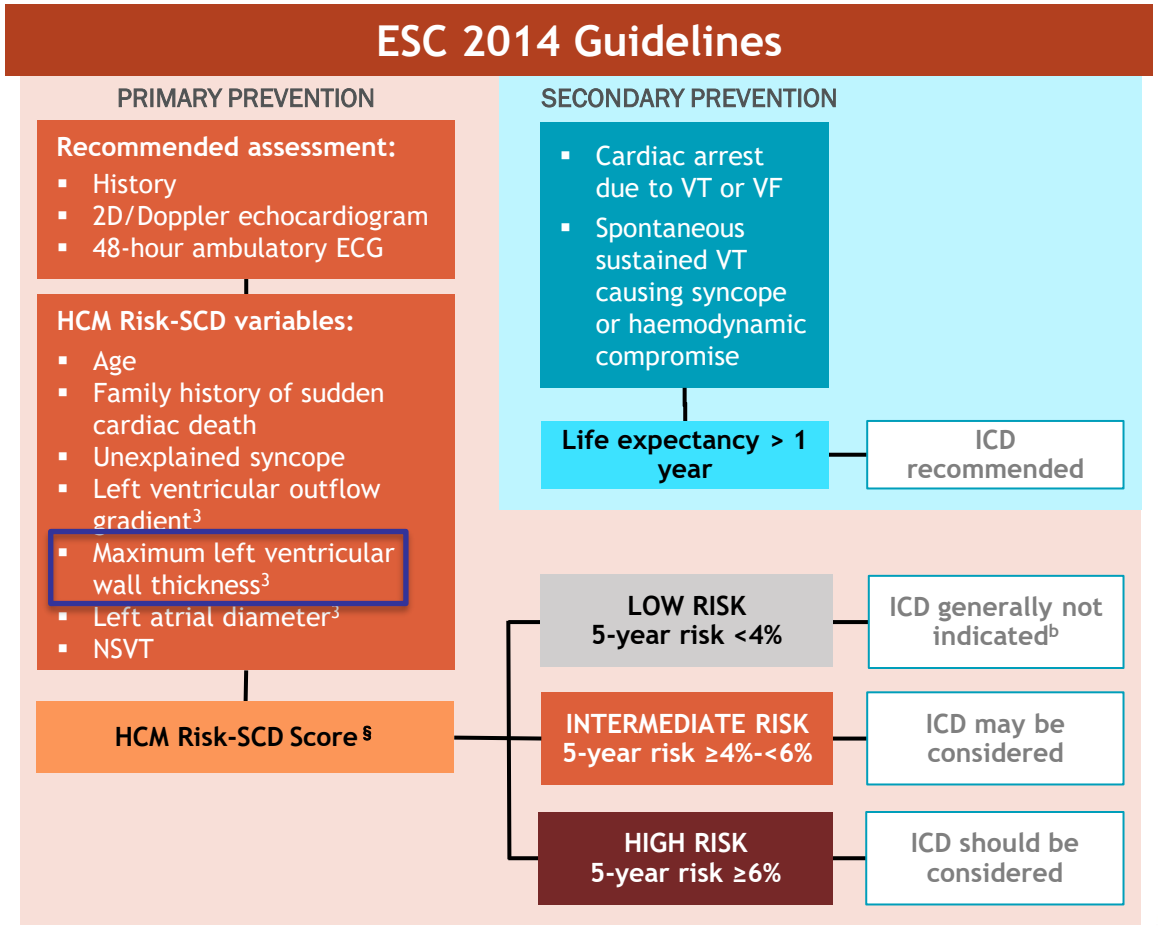
# LVH measurement




Dominguez, Garcia-Pavia et al. Heart 2018

# SCD prevention



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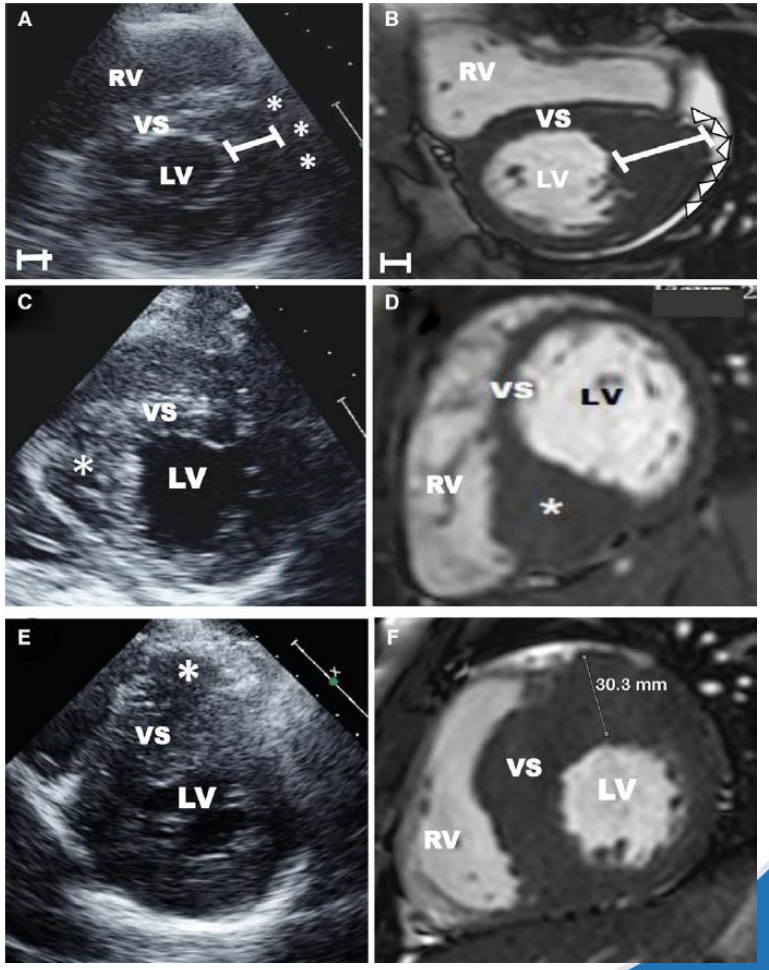
# Cardiac MRI

- Echocardiography is the primary imaging modality, but CMR may be warranted
- CMR provides 3D assessment of cardiac anatomy for measurement of myocardial wall thickness, imaging of SAM, and quantification of LGE/scar burden
- CMR imaging has a class 1 (strong) recommendation in Guidelines when:
  - HCM is suspected but the ECHO is inconclusive
  - LVH is suspected to be due to other causes
  - The anatomic cause of the obstruction is unclear

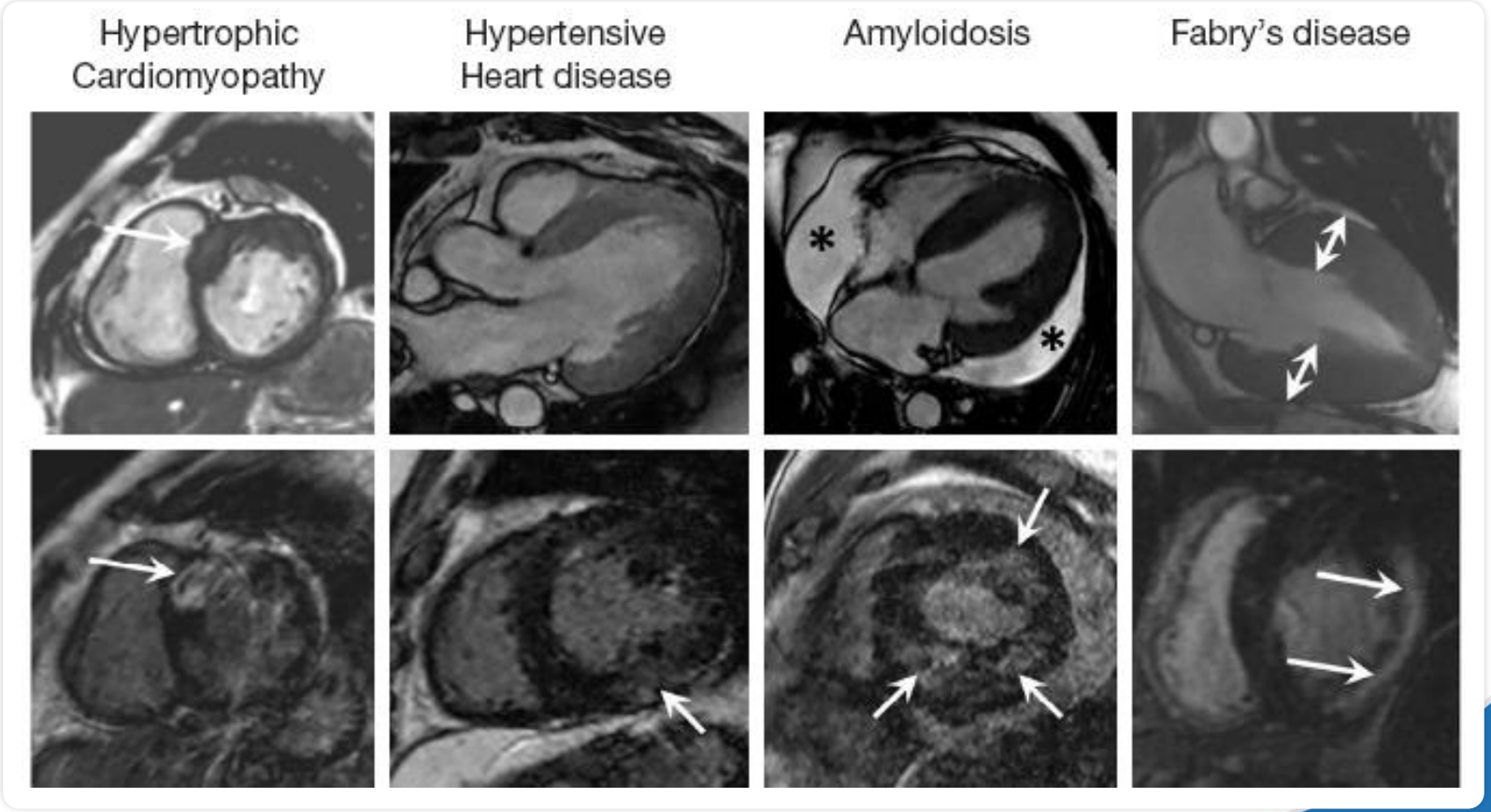
## Advantage of CMR compared with 2-dimensional ECHO



# HCM phenocopies, differential diagnoses of LVH

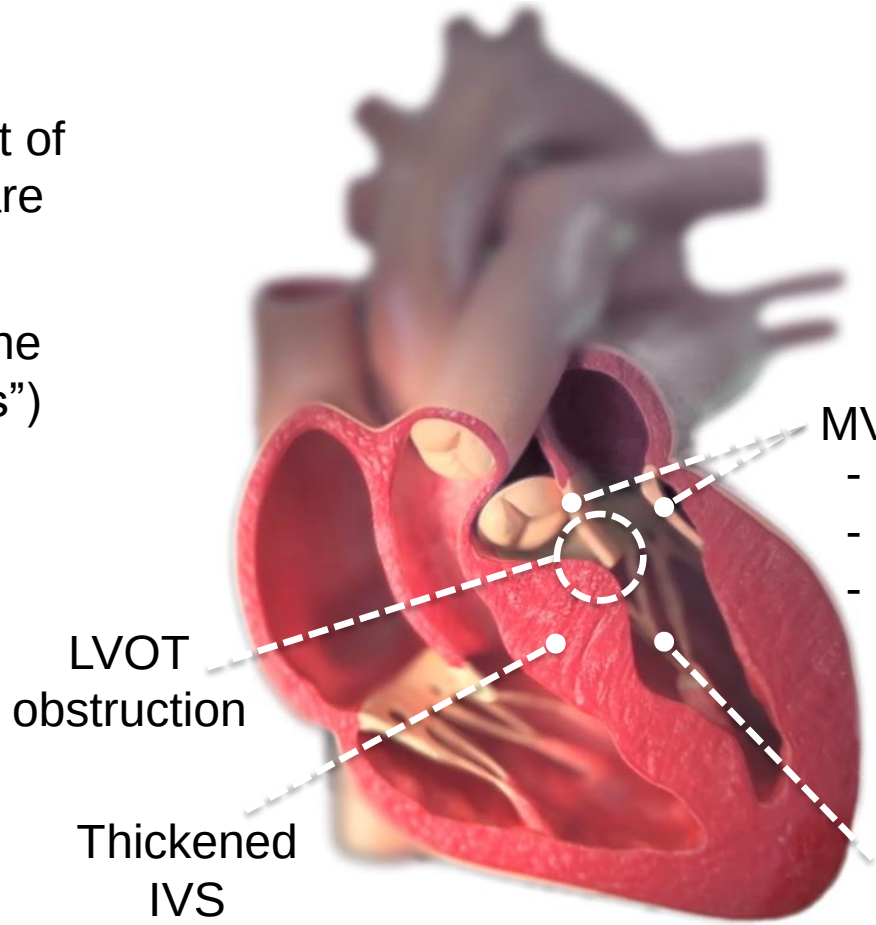
- Anderson-Fabry disease
- Amyloidosis
- Hypertension
- Renal failure
- Aortic stenosis
- Danon disease
- Pompe Disease
- Mucopolysaccharidoses

## CMR for LVH Differential Diagnosis



# HCM pathology expands beyond LVH to affect the mitral valve, coronary arteries, and more

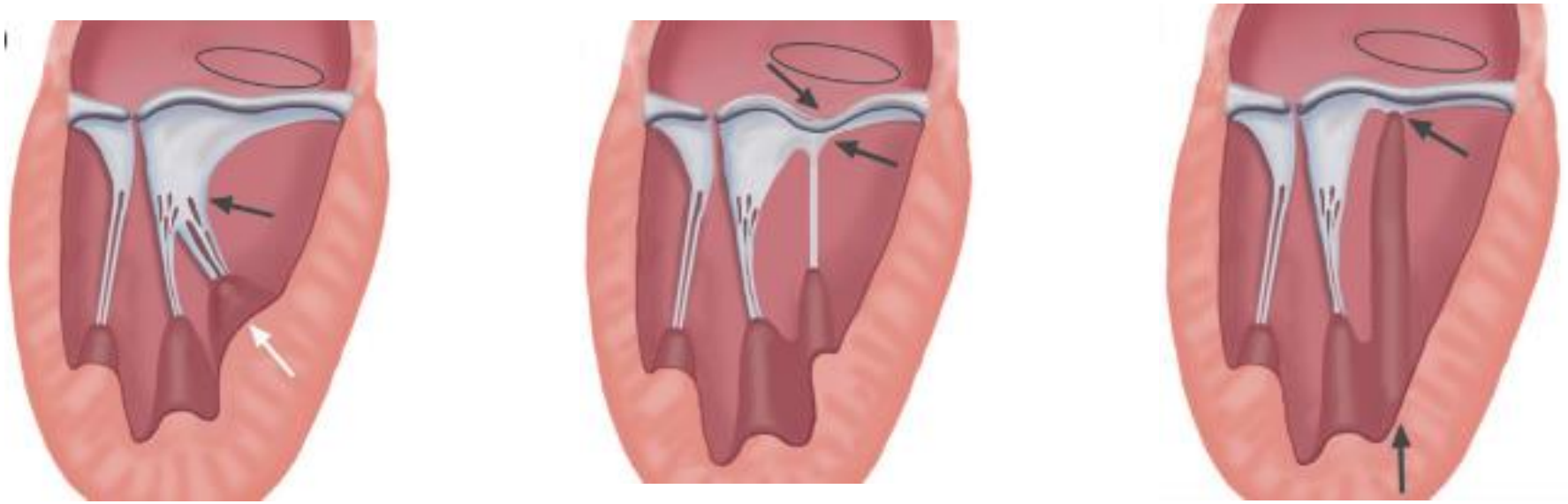
- While myocardial hypertrophy is an essential part of the HCM phenotype, mitral valve abnormalities are another important pathologic feature
- Patients with HCM may also have narrowing of the intramural small coronary arteries (“small vessels”) caused by intimal and medial hypertrophy of the smooth muscle cells in their walls
  - This can contribute to ischemia, even in the absence of atherosclerotic narrowing of the epicardial coronary arteries




HCM, hypertrophic cardiomyopathy; IVS, interventricular septum; LVOT, left ventricular outflow tract; MV, mitral valve; SAM, systolic anterior motion.

Argulian E et al. *Am J Med* 2016;129(2):148-152.

# Papillary muscles abnormalities



Sherrid MV et al. *J Am Coll Cardiol 2016*

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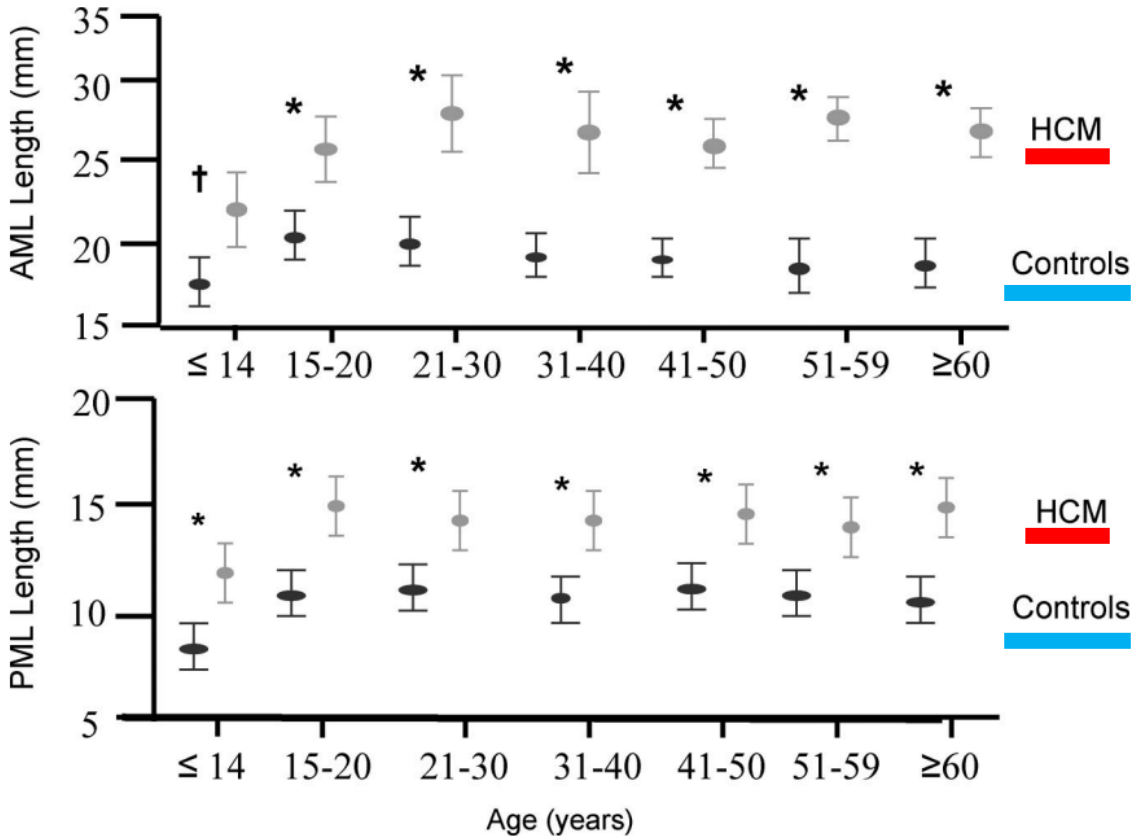
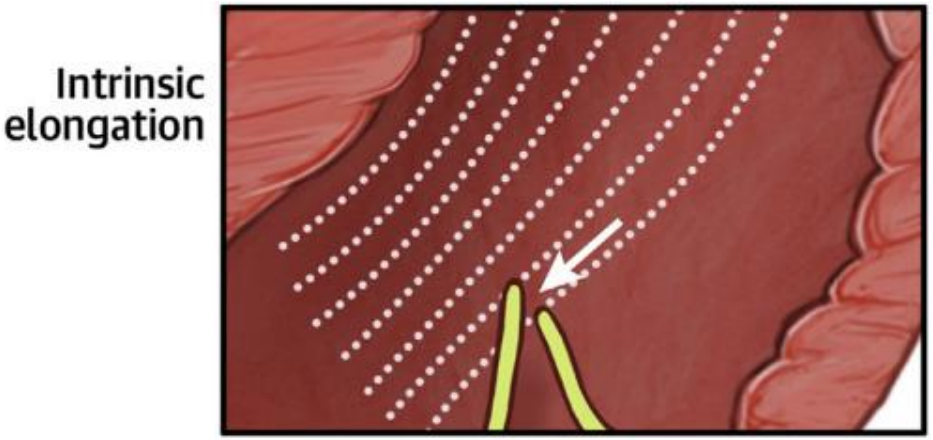
# Mitral Valve Abnormalities Identified by Cardiovascular Magnetic Resonance Represent a Primary Phenotypic Expression of Hypertrophic Cardiomyopathy

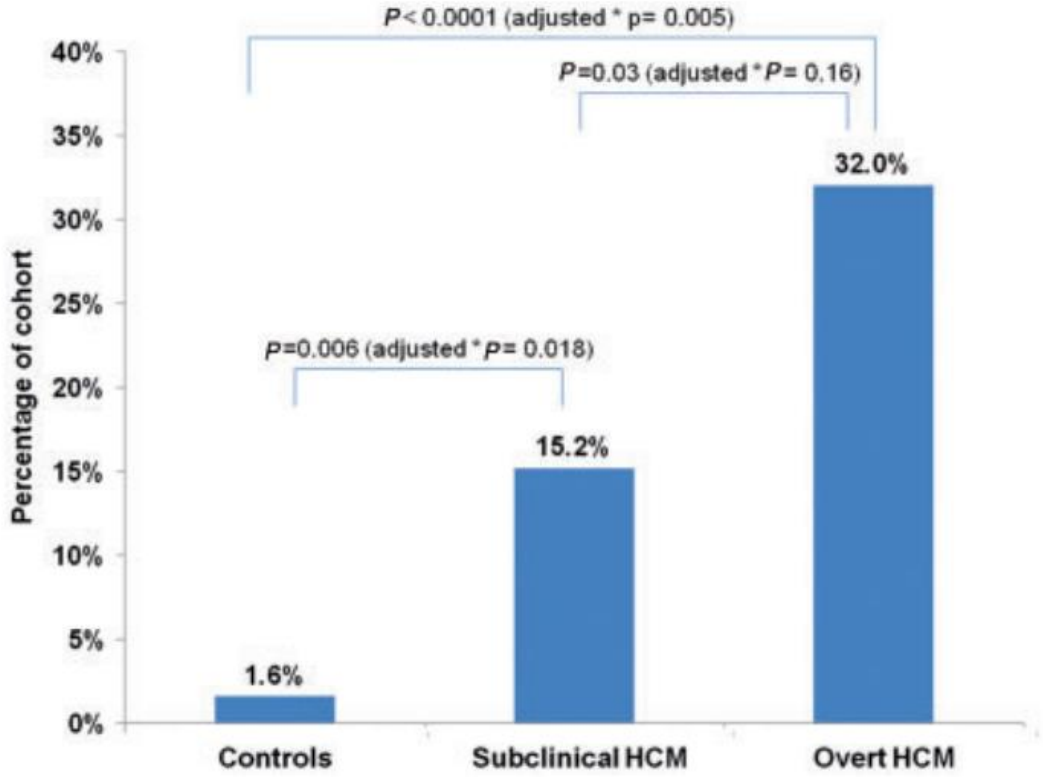



Maron MS et al. Circulation. 2011
Troy AL et al. JACC Advances 2023

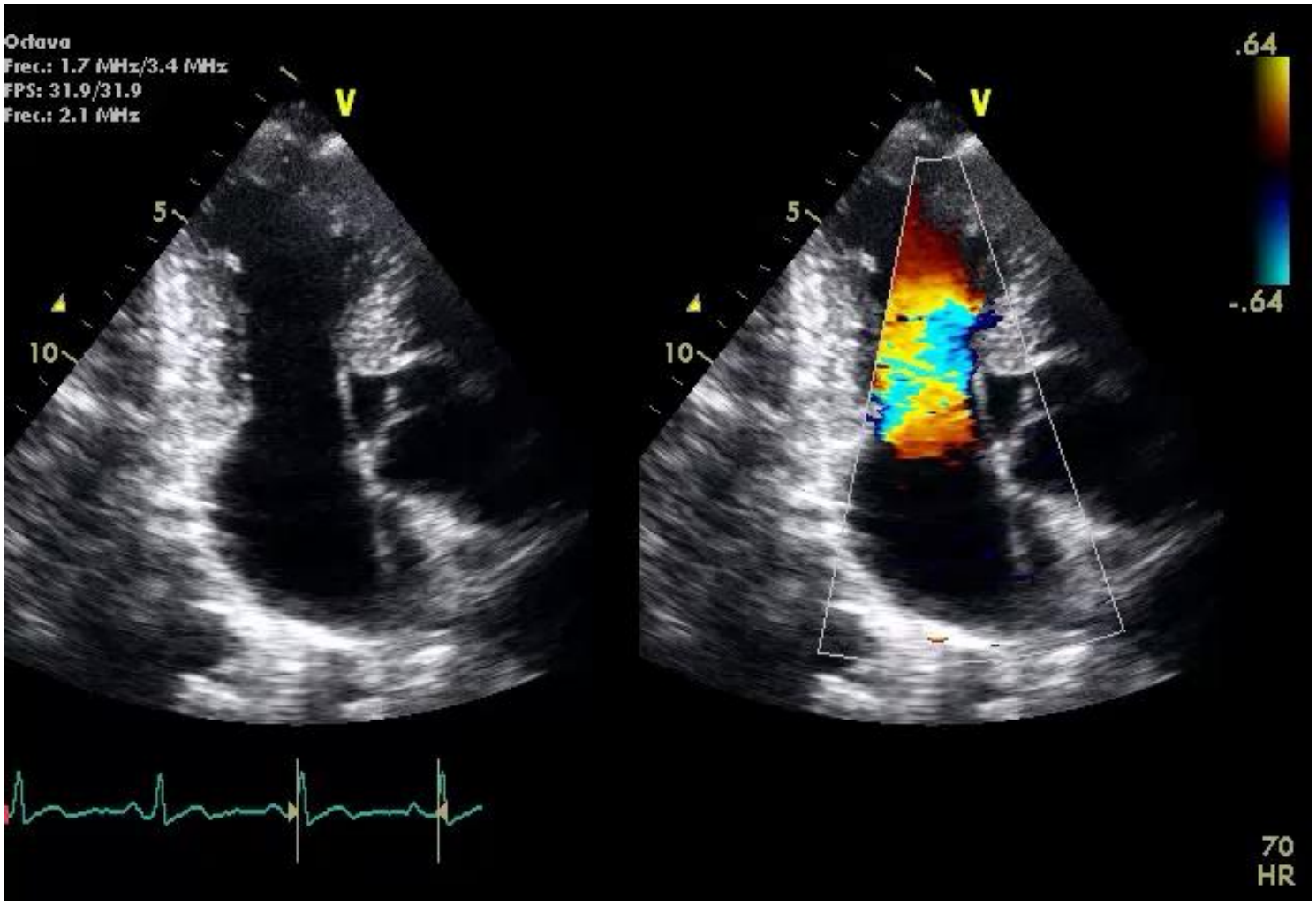
# Intrinsic mitral valve alterations in hypertrophic cardiomyopathy sarcomere mutation carriers

John D. Groarke[1], Patrycja Z. Galazka[1], Allison L. Cirino[1], Neal K. Lakdawala[1], Jens J. Thune[2], Henning Bundgaard[3], E. John Orav[4], Robert A. Levine[5], and Carolyn Y. Ho[1]*

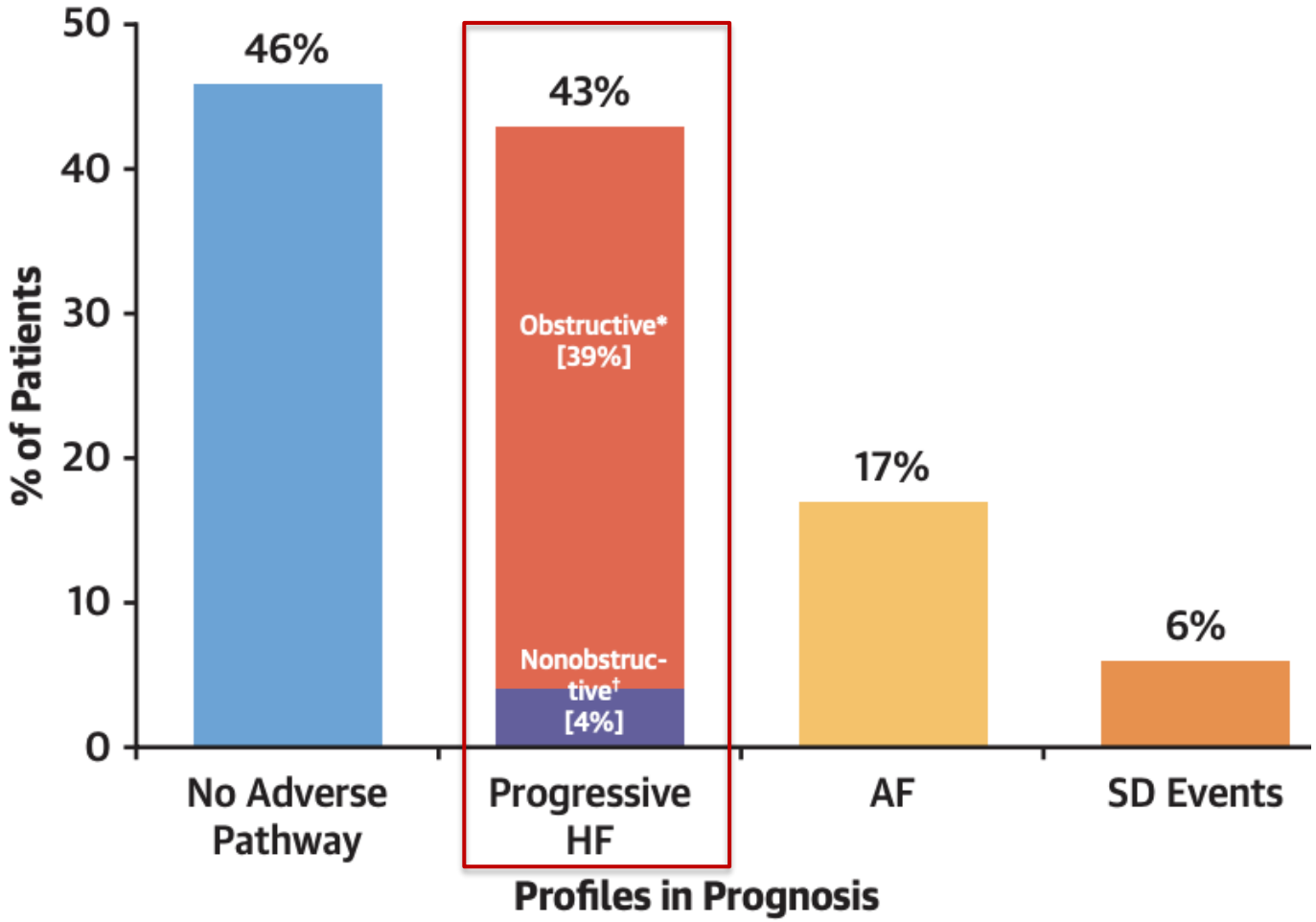



Goarke JD et al. Eur Heart J CV Imaging 2018

# LVH, mitral valve and papillary muscles abnormalities contribute to LVOT Obstruction

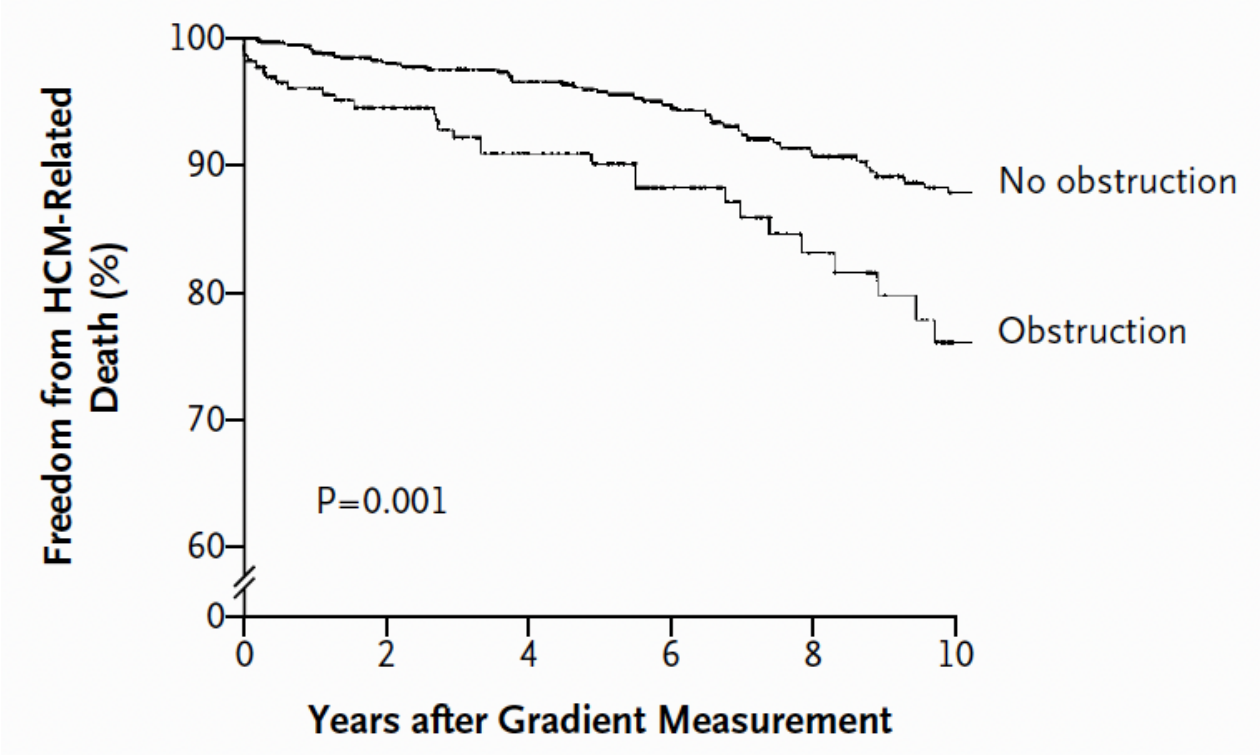


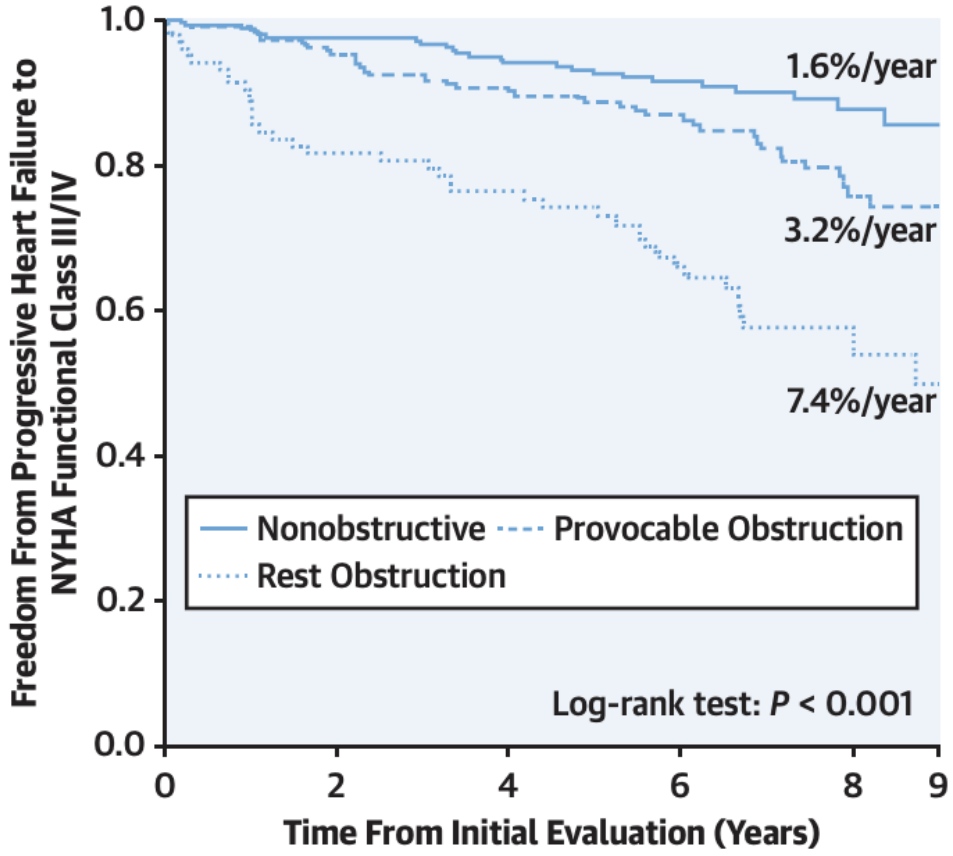

Courtesy Dr Ana Garcia-Alvarez




Maron BJ et al. JACC 2022: 372-389

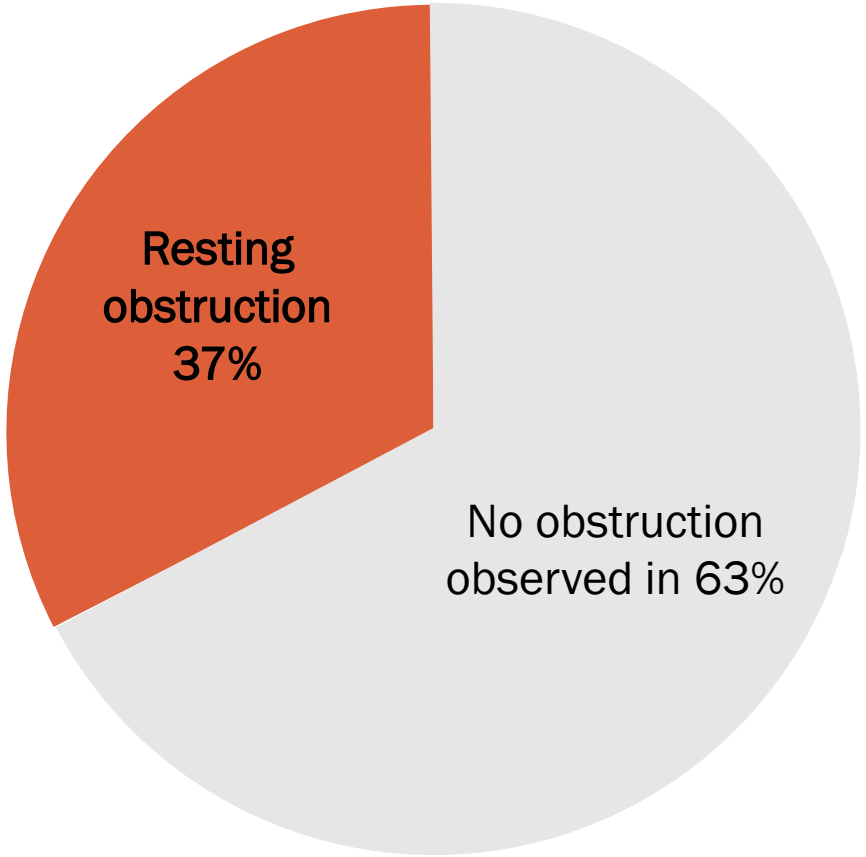
# Obstruction is associated with worse prognosis



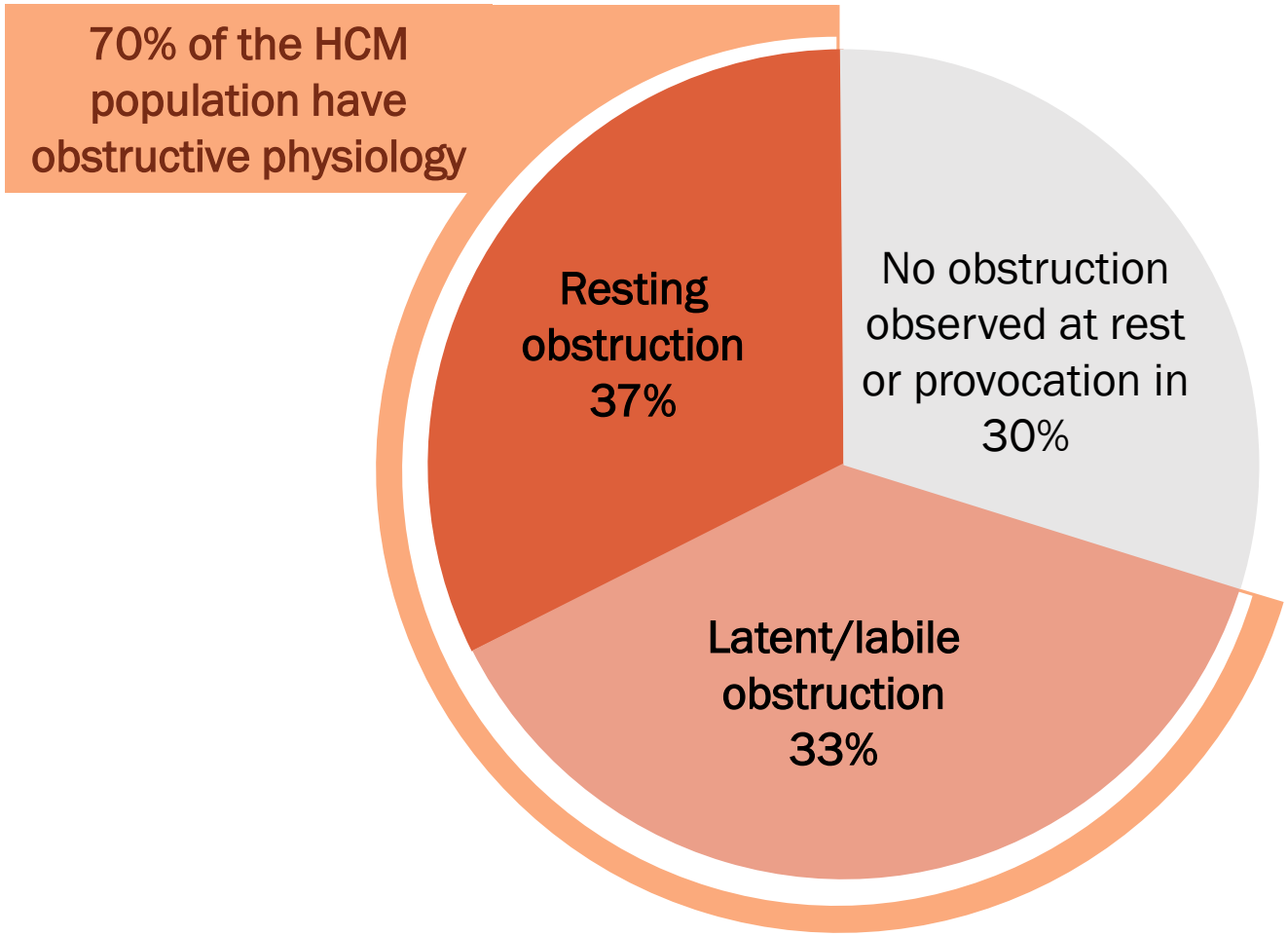

Maron BJ et al. JACC 2022: 372-389
Maron MS et al. N Engl J Med 2003;348:295-303.

# LVOT obstruction observed at rest

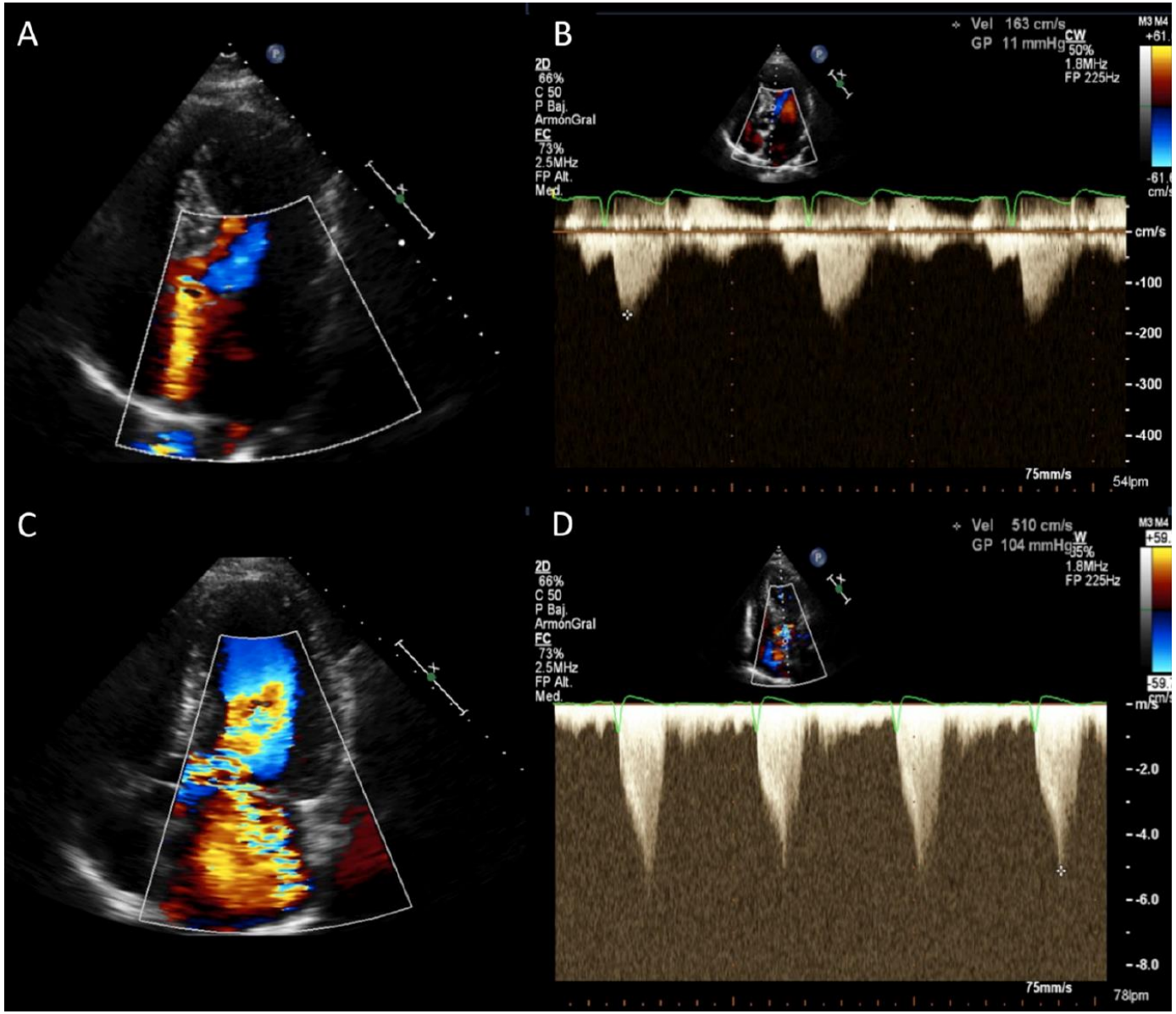



Maron MS et al. Circulation. 2006;114:2232

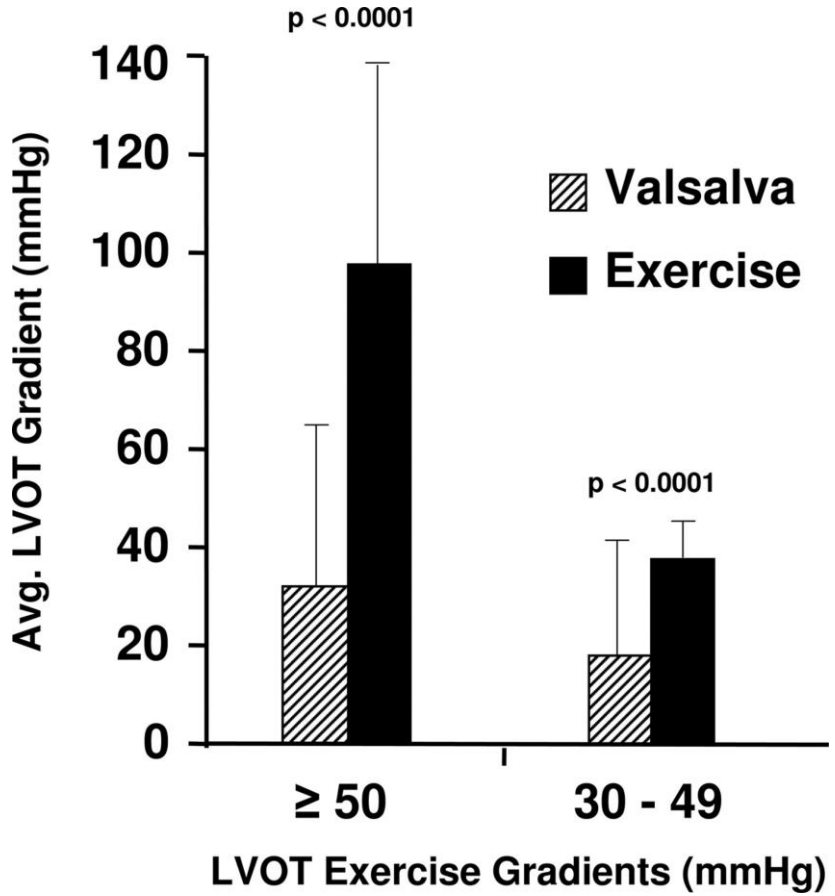
# LVOT obstruction observed at resting and on provocation

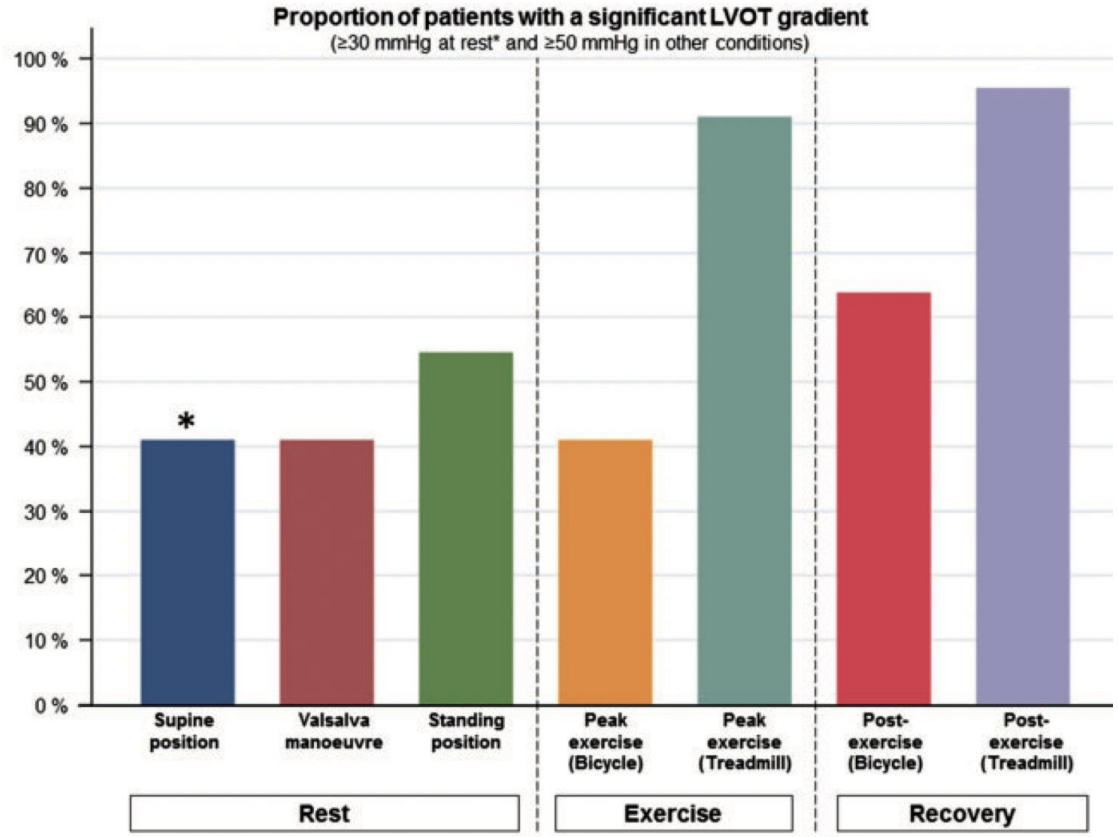



Maron MS et al. Circulation. 2006;114:2232

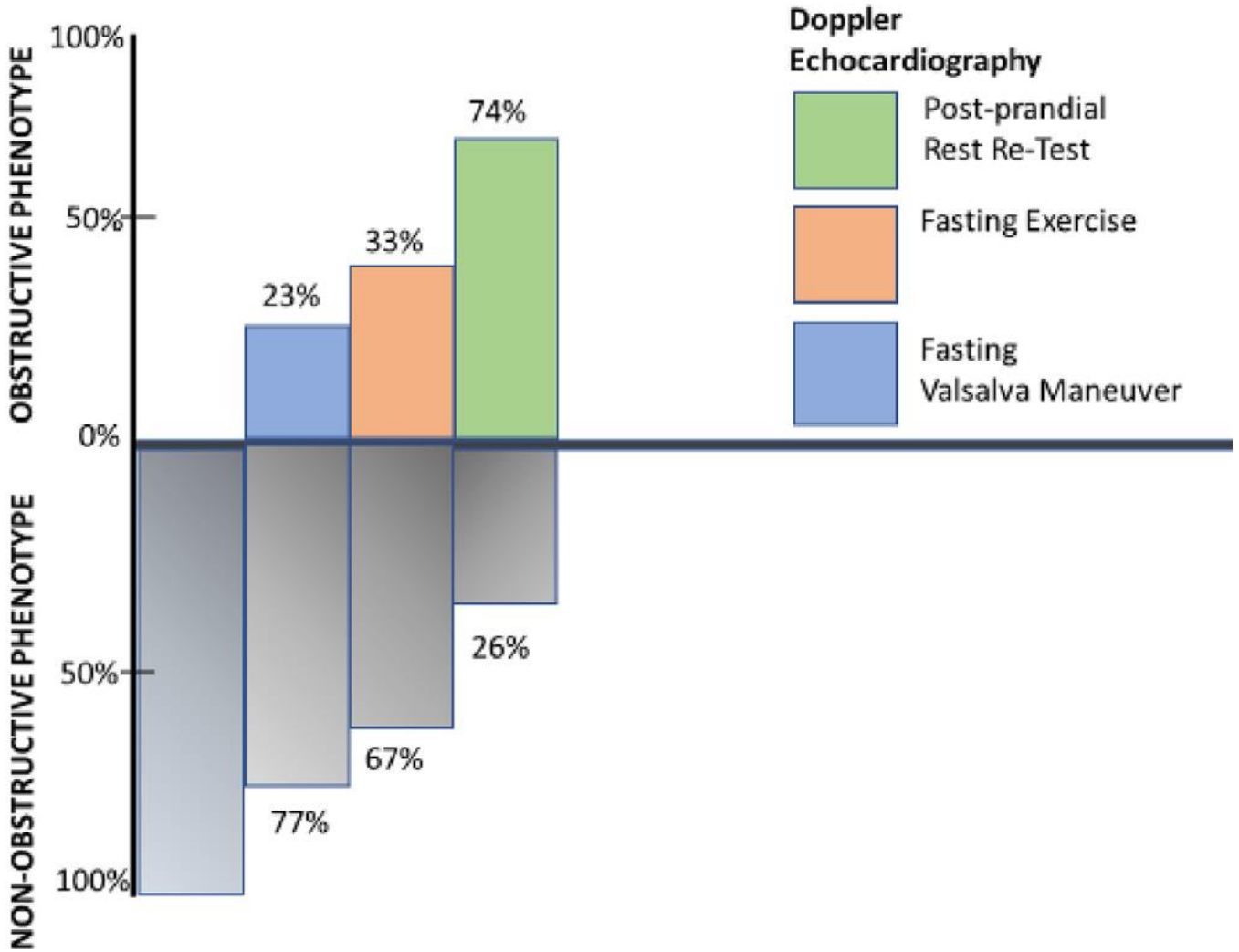



Dominguez, Garcia-Pavia et al. Heart 2018

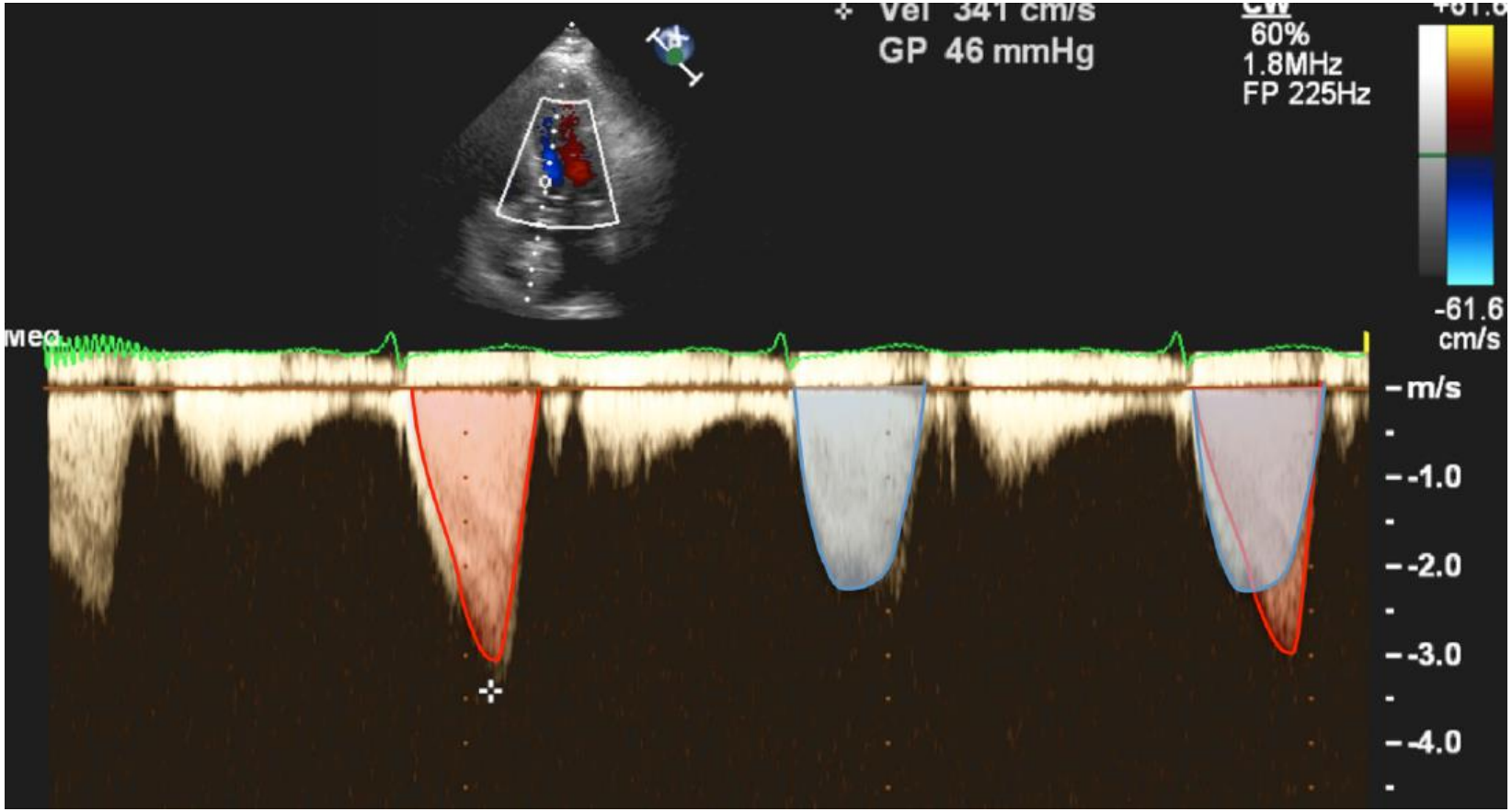



Maron MS et al. Circulation 2006
Reant et al . Eur J Cardiovasc Imaging 2018




La Canna et al. Am J Cardiol 2020




Dominguez, Garcia-Pavia et al. Heart 2018

# CONCLUSIONS

- HCM is a heterogeneous disease with heterogeneous clinical course.
- LVH characterizes HCM and it should be correctly assessed.
- HCM pathology expands beyond LVH of LV walls and involves also papillary muscles and mitral valve apparatus. These structures play a pivotal role in LVOTO.
- LVOTO is present in up to 2/3 of patients.
- Appropriate evaluation of LVOTO with provocation techniques is required in symptomatic patients.

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