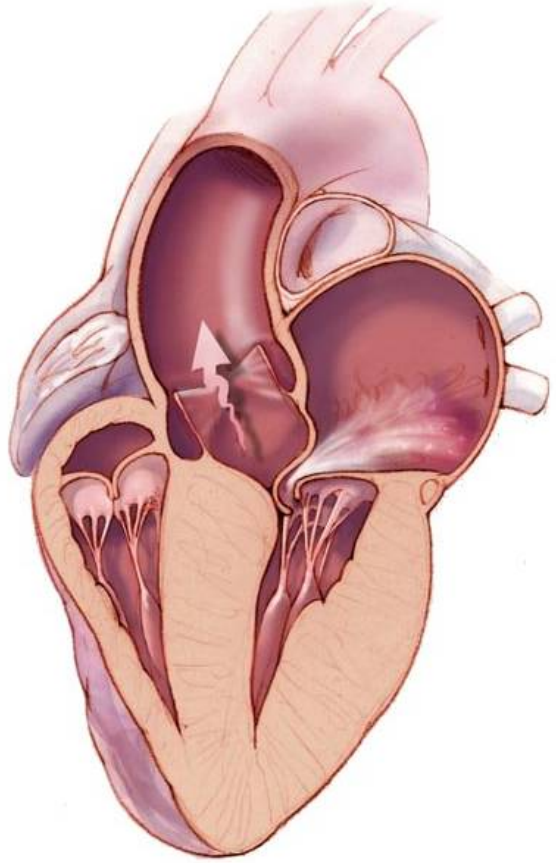
MAYO CLINIC

Hypertrophic Cardiomyopathy: Patient Management in 2018



Mackram F. Eleid, MD

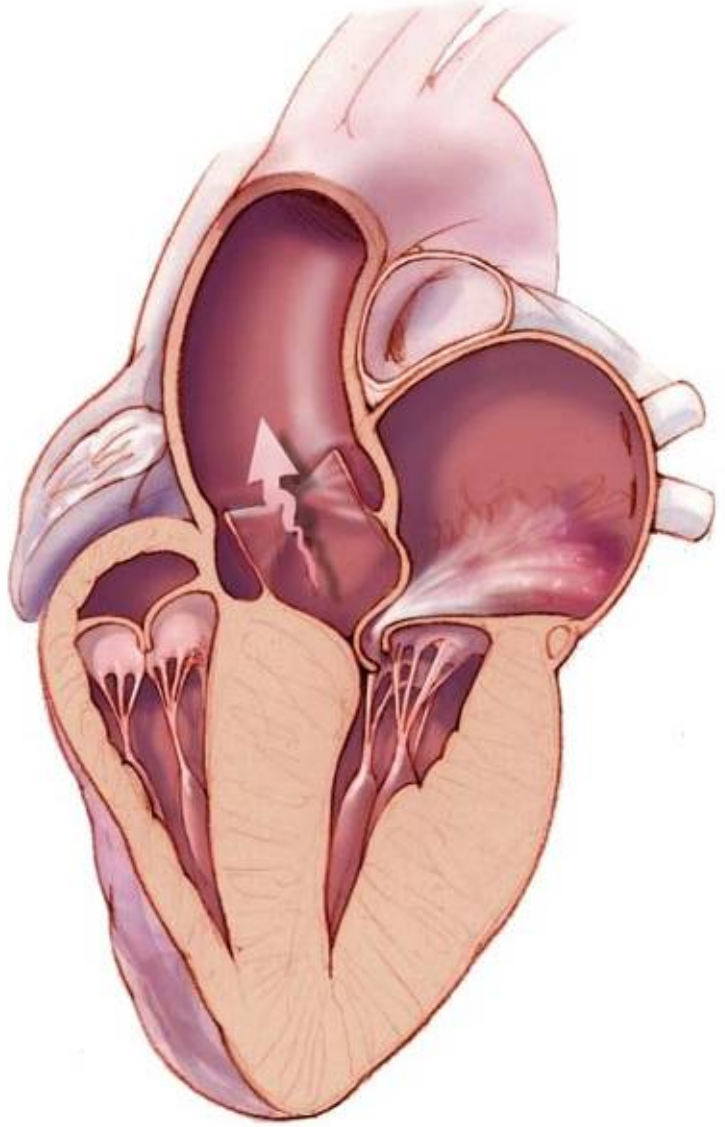
Giornate Cardiologeche Torinesi
October 26, 2018

Disclosures

- No relevant financial relationships to disclose

Outline

- Diagnostic considerations
- Obstruction in HCM
- Clinical outcomes in HCM
- Operative considerations
- Unanswered questions
- Take home points



Question 1: Which of the following statements is true regarding genetic testing in hypertrophic cardiomyopathy (HCM)?

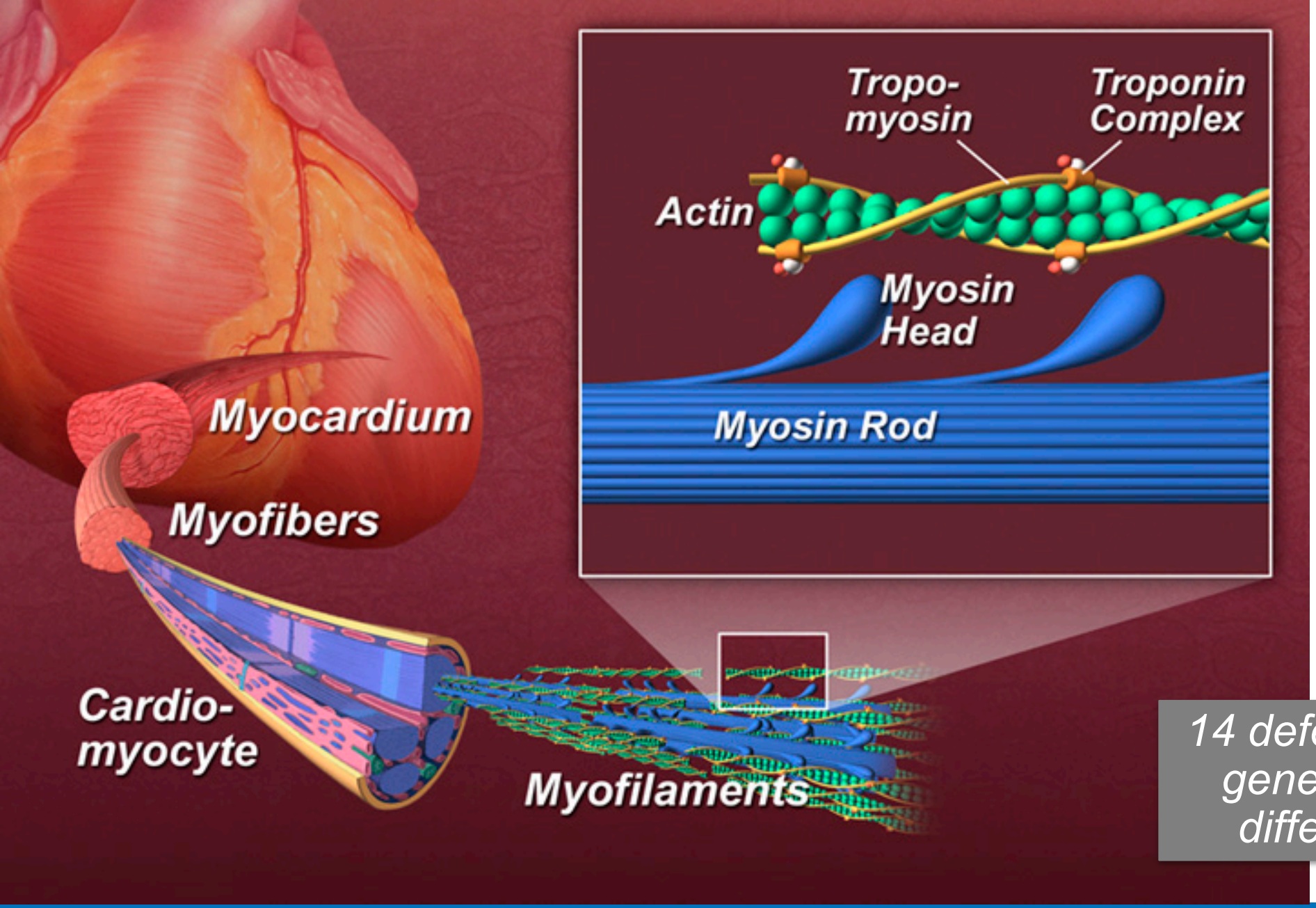
A. Most patients with HCM will have a positive genetic test result

B. The yield of genetic testing is highest in reverse curve morphology subtype

C. Older age at diagnosis is associated with a higher likelihood of a positive genetic test

Question 2: Which of the following statements is true regarding septal reduction therapy for HCM?

A. Septal reduction therapy has been shown to improve survival
B. Alcohol septal ablation is more effective than septal myectomy
C. Survival after septal myectomy and alcohol ablation is similar at 8 years



2 nonsarcomeric genes (PRKAG2 and LAMP2)

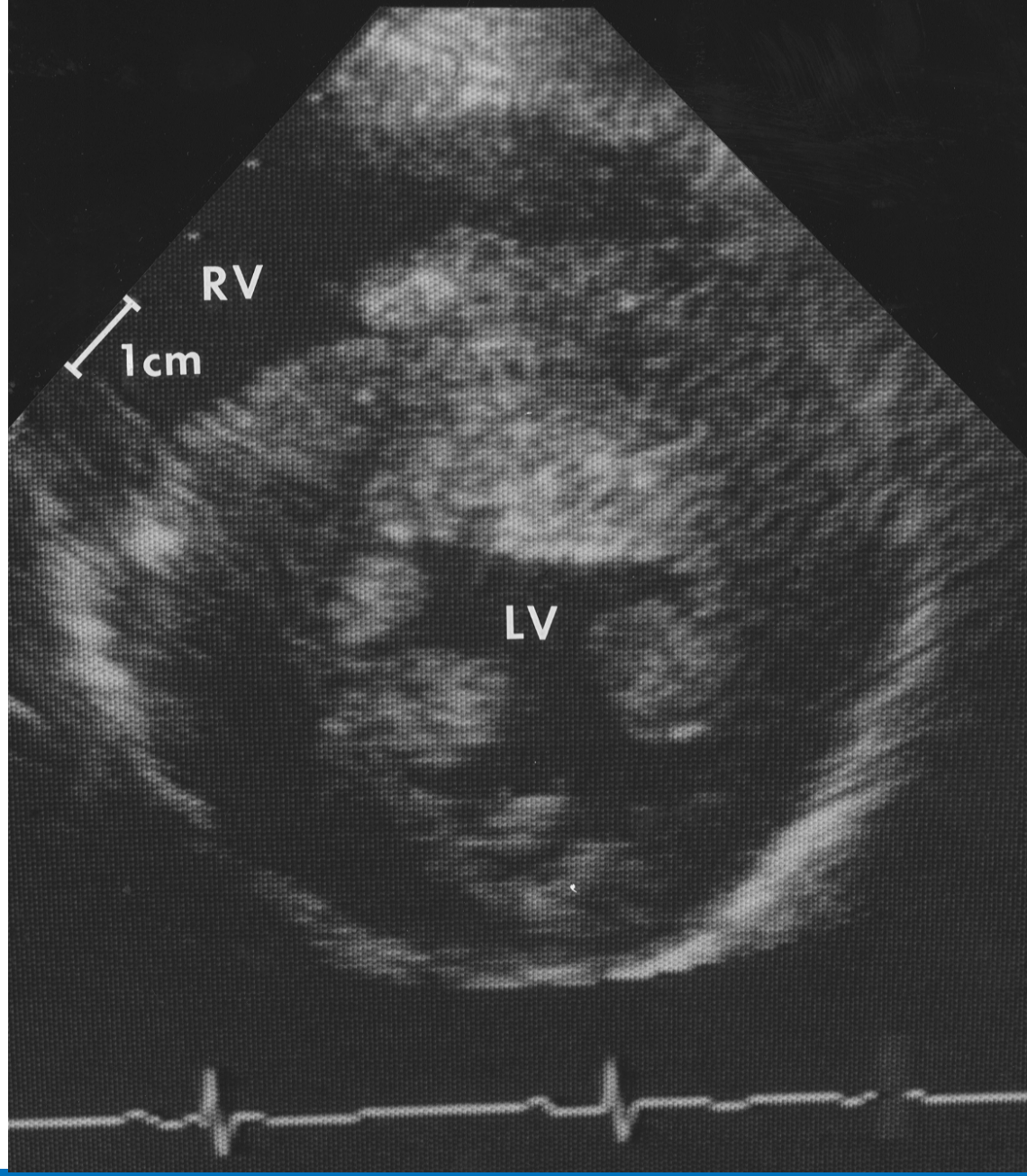
14 defective sarcomeric genes with over 400 different mutations

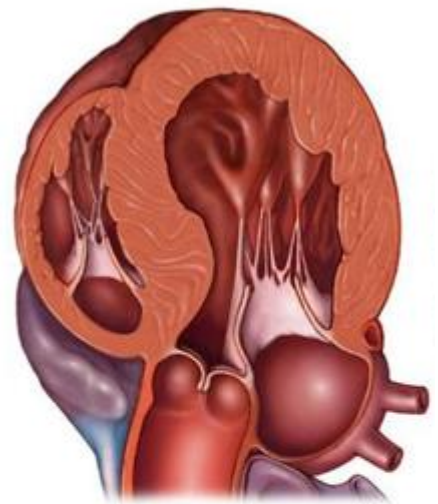
Mutation

Abnormal polypeptide

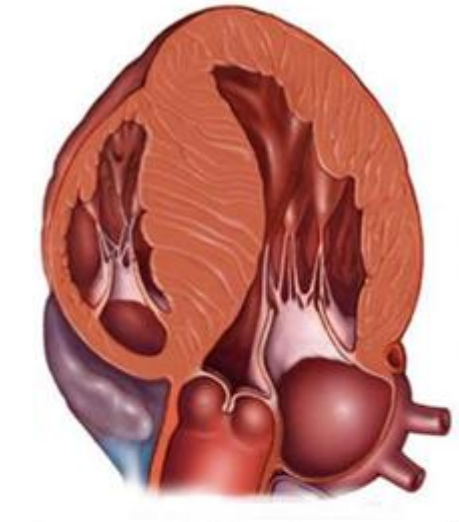
Altered sarcomere structure and function

Compensatory Hypertrophy

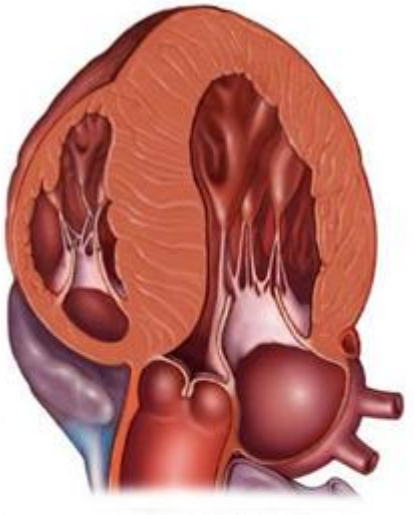




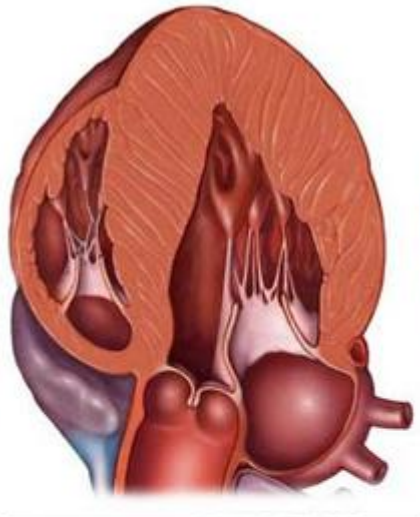
Sigmoidal



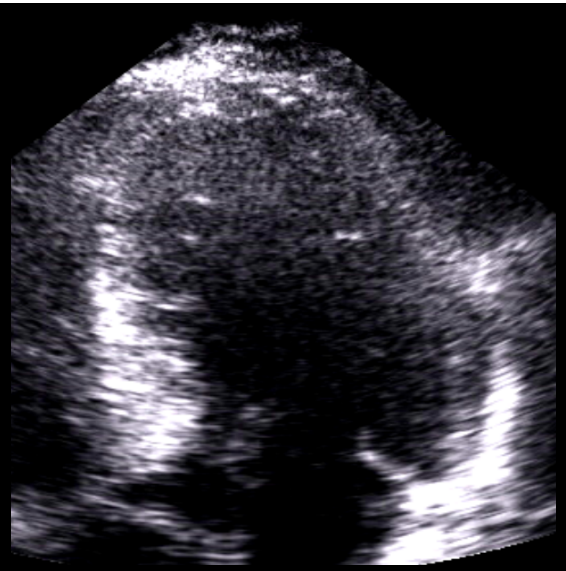
Reverse curve

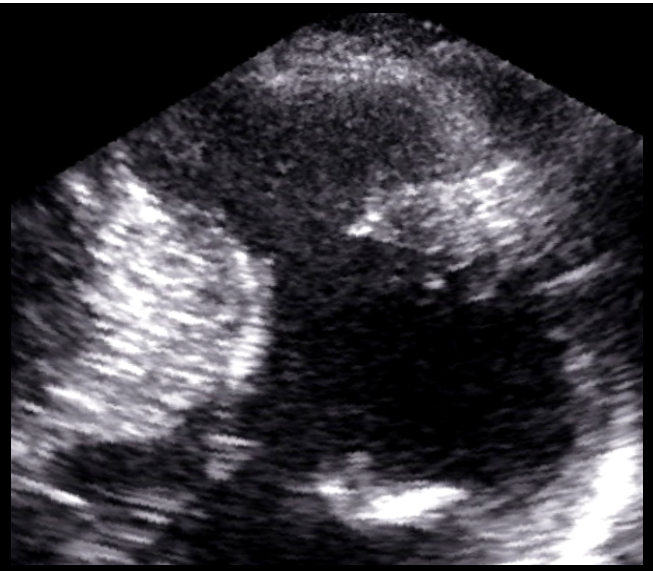


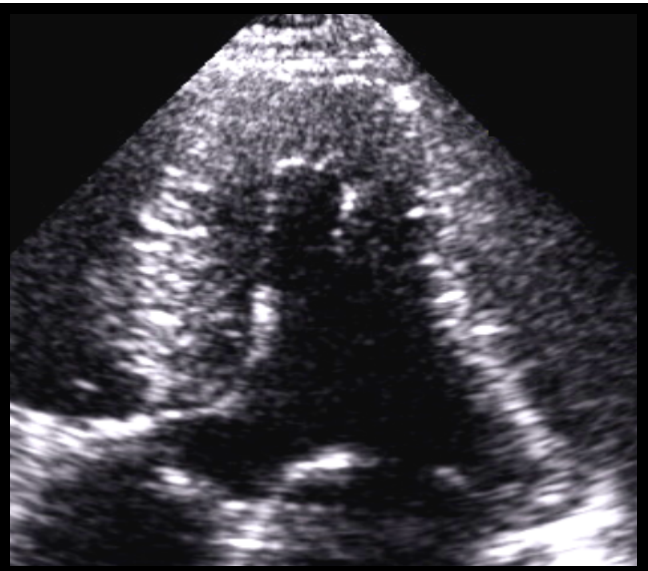
Neutral

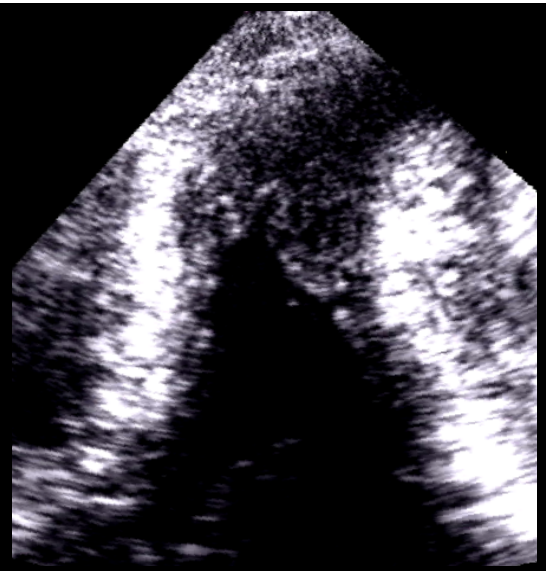


Apical



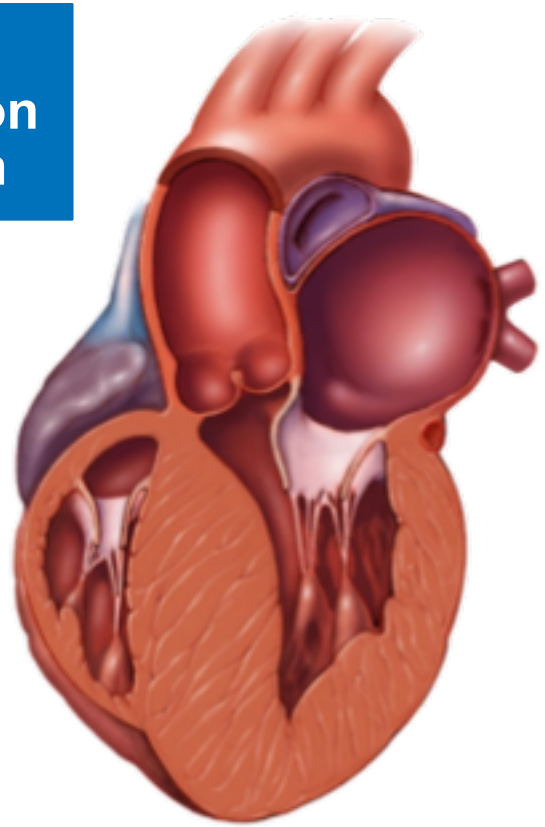






Septal Morphology and Disease Phenotypes

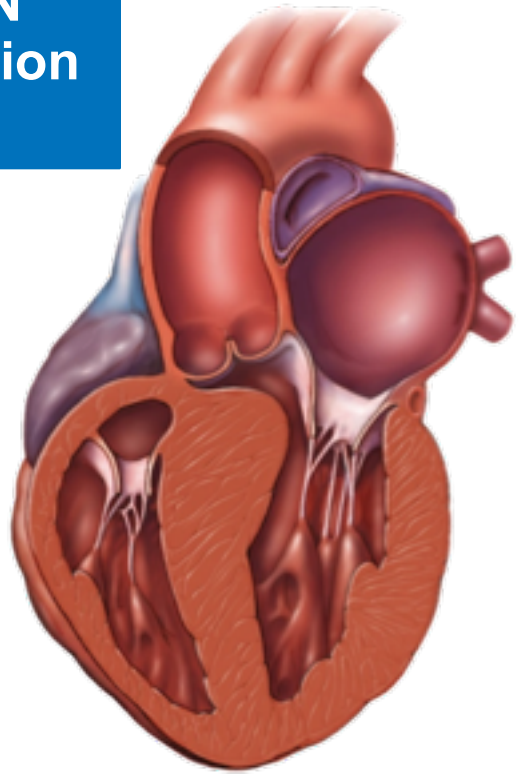
Younger
+ gene mutation
sudden death



104/132 (79%)
Myofilament +

Banana Septum

Older: HTN
- gene mutation
CHF, AF

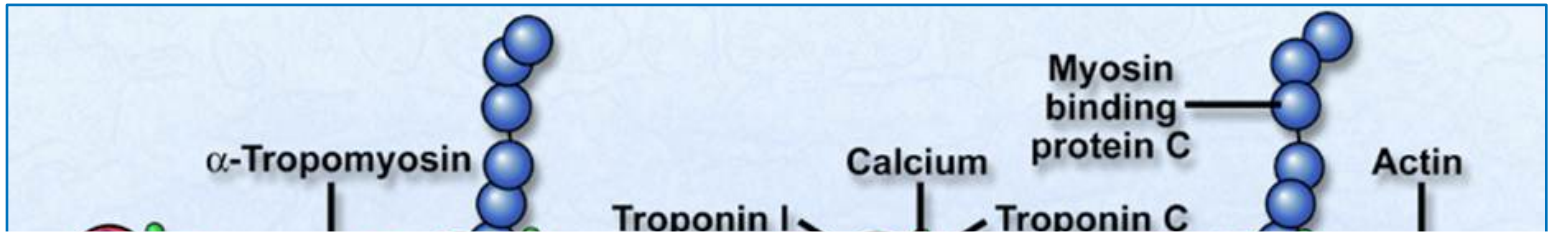


15/181 (8%)
Myofilament +

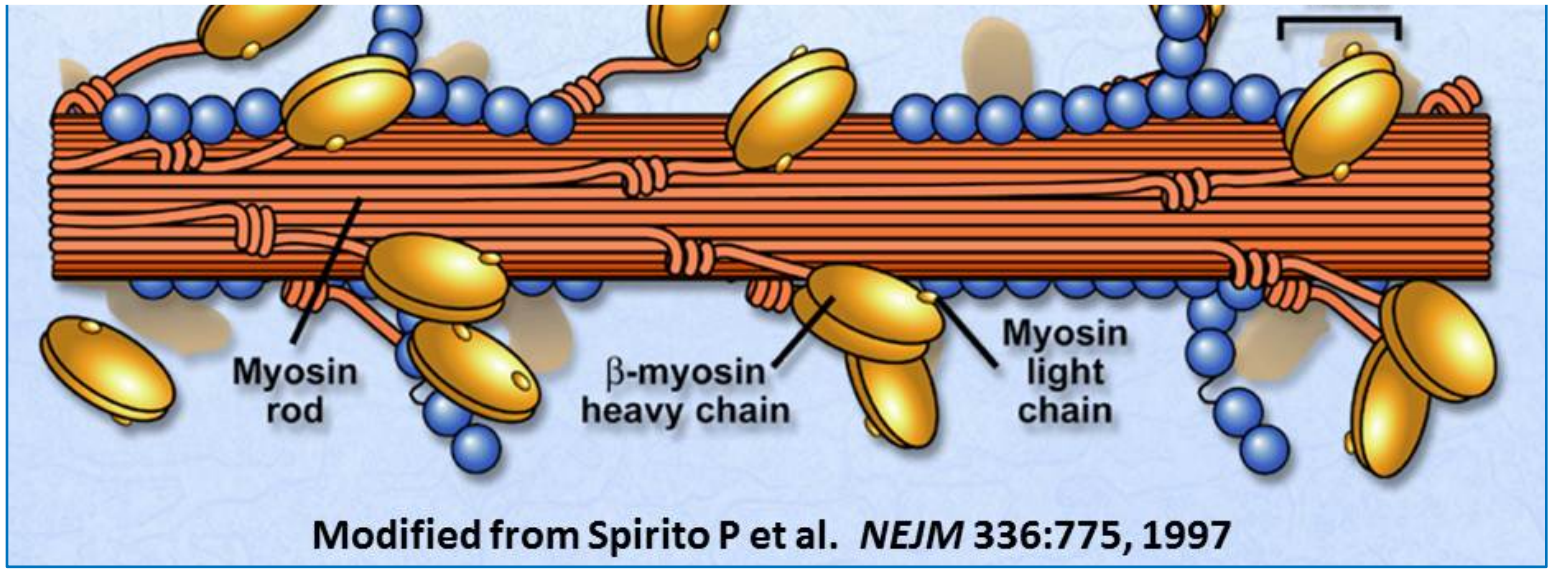
Sigmoid Septum

Bos... Ackerman. Mayo Clin Proc 2014

Mayo Clinic HCM Cohort (>1000 pts)



Yield of genetic testing **34%** with **>80%** of mutations found in myosin binding protein C (MYPBC3) and beta myosin heavy chain (MYH7)

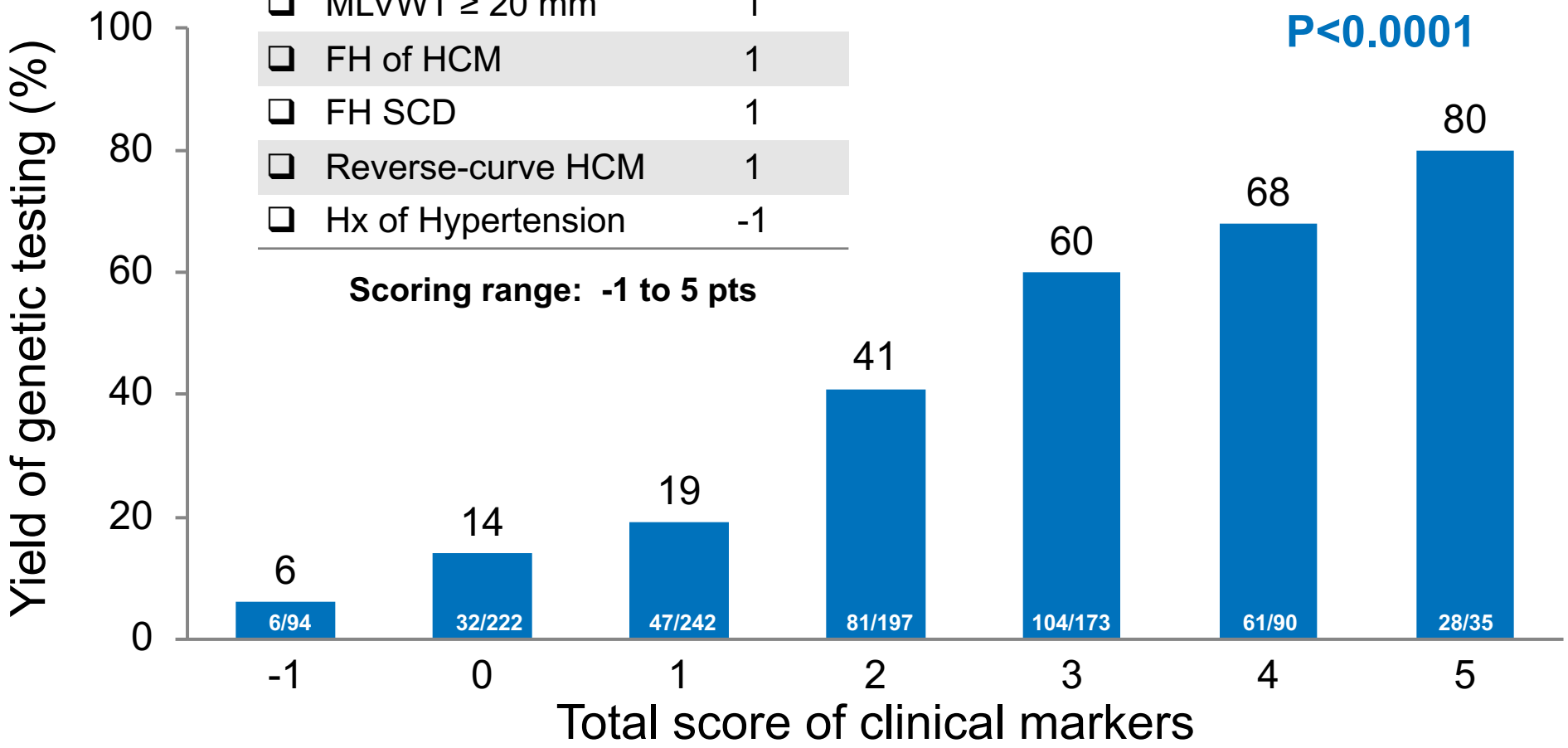


Bos... Ackerman. Mayo Clin Proc 2014

Clinical Markers for Positive Genetic Test

Marker	Patients
❑ Age Dx < 45 yrs	1
❑ MLVWT ≥ 20 mm	1
❑ FH of HCM	1
❑ FH SCD	1
❑ Reverse-curve HCM	1
❑ Hx of Hypertension	-1

Scoring range: -1 to 5 pts

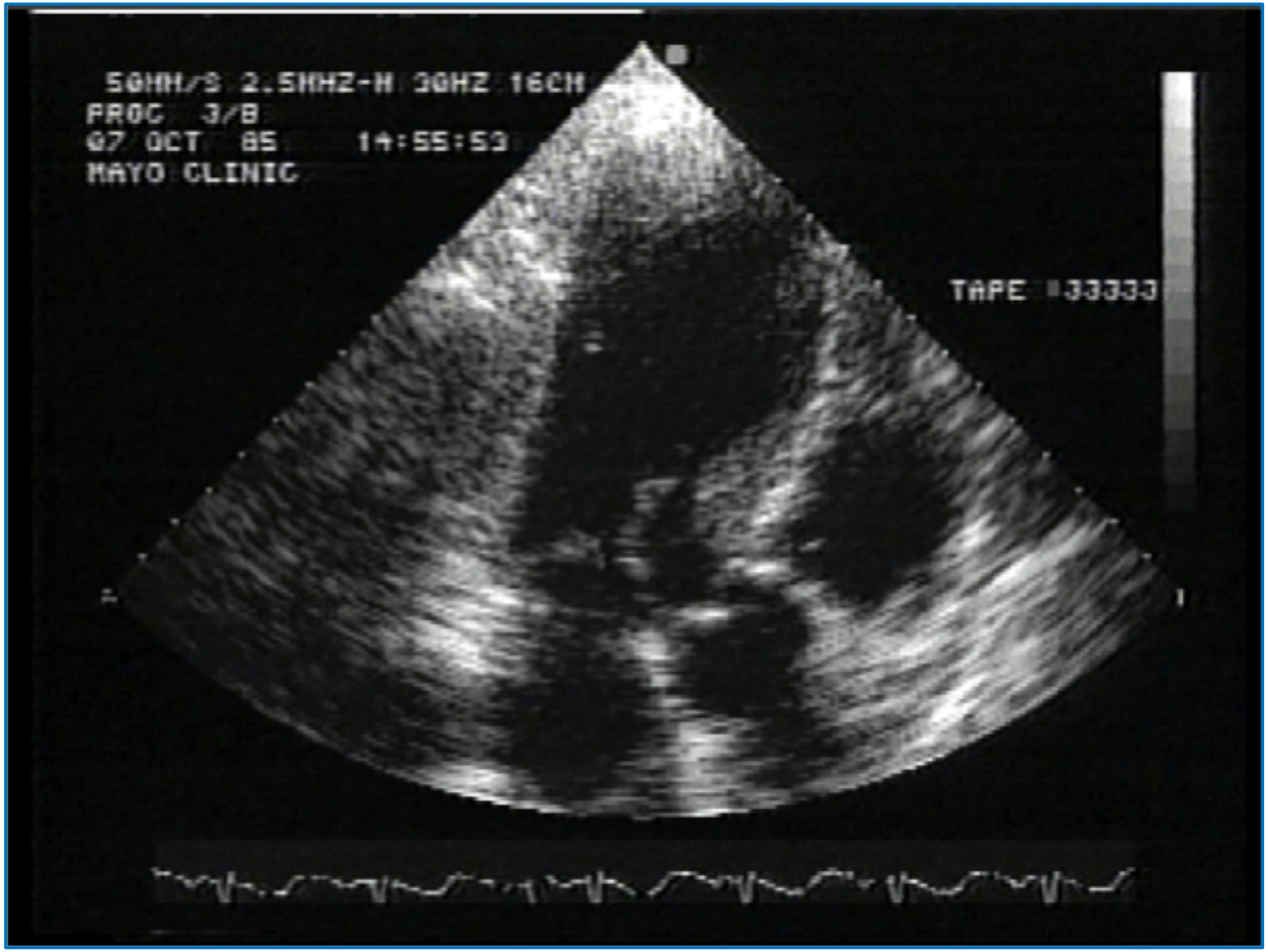


Bos... Ackerman. Mayo Clin Proc 2014

Hypertrophic Cardiomyopathy

Clinical implications – diagnosis

- Hypertrophy anywhere
  - Do not need SAM
  - Do not need ASH
- Rule out other causes


50MM/S 2.5MHZ-H 30HZ 16CM
PROC 3/B
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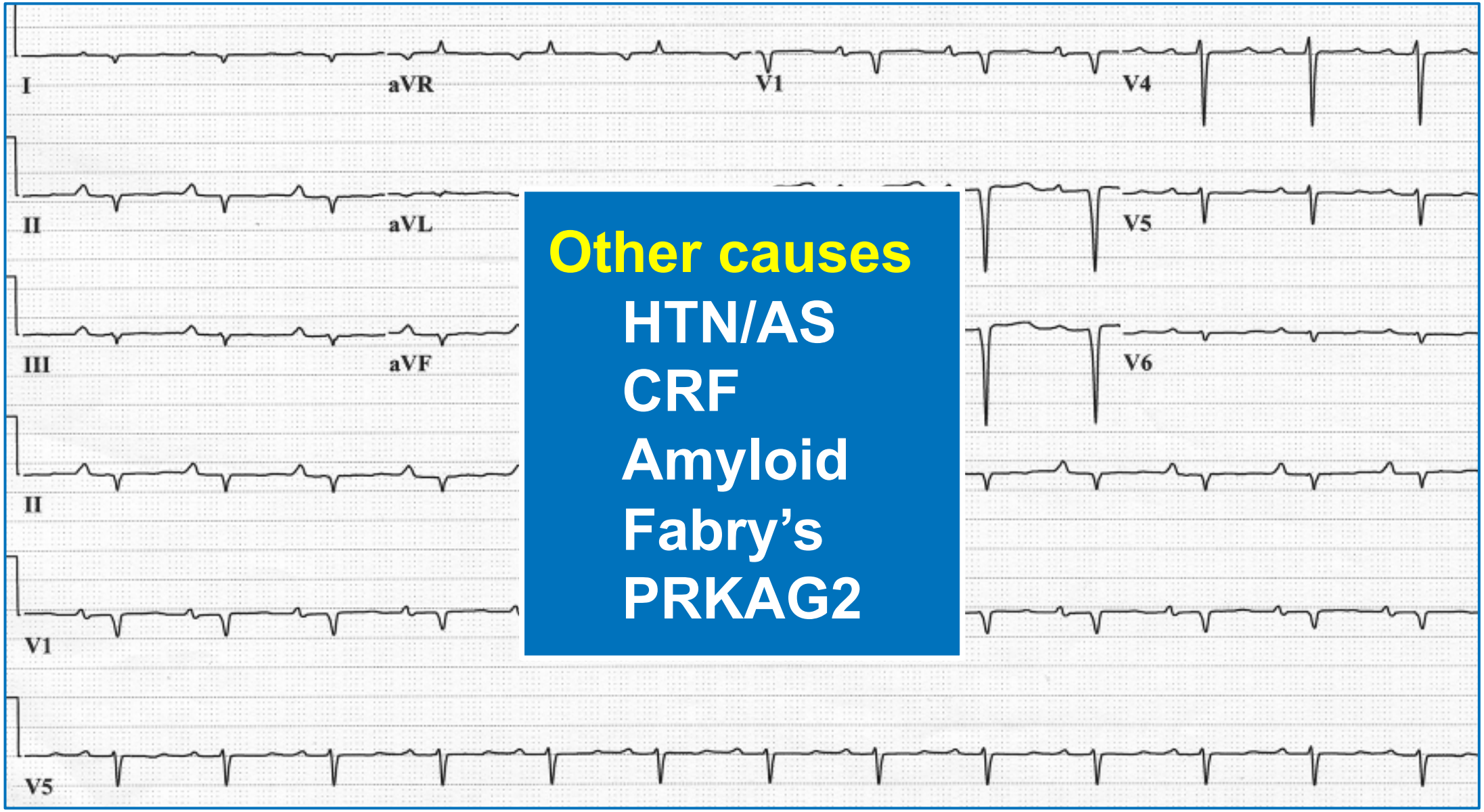
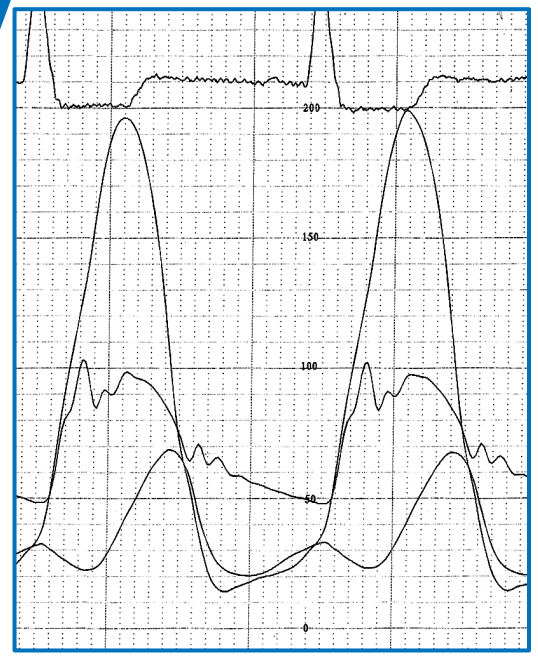

I
aVR
V1
V4
II
aVL
V5
III
aVF
V6
II
V1
V5
Other causes
HTN/AS
CRF
Amyloid
Fabry's
PRKAG2

Complex Pathophysiology

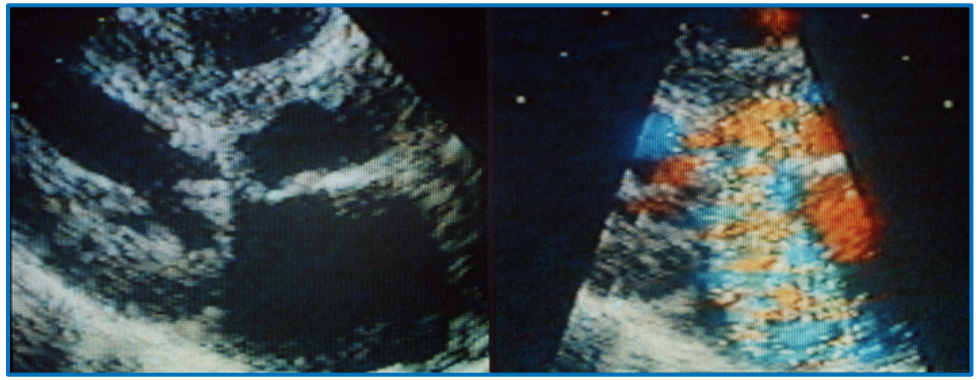
Myocardial Ischemia

Diastolic Dysfunction

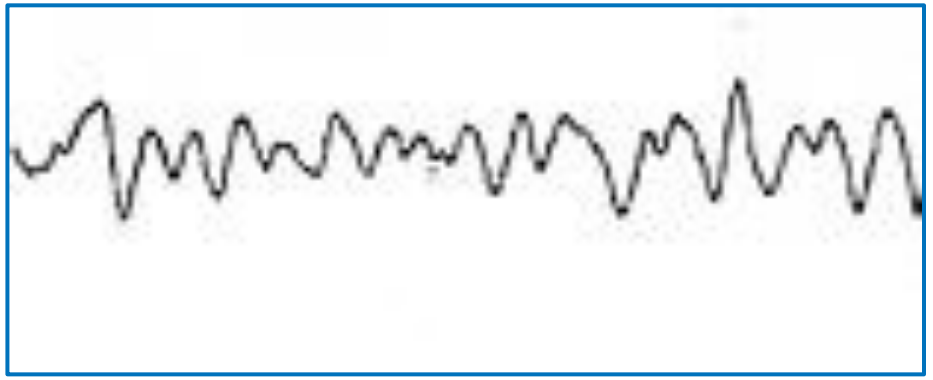


Dynamic LVO Obstruction

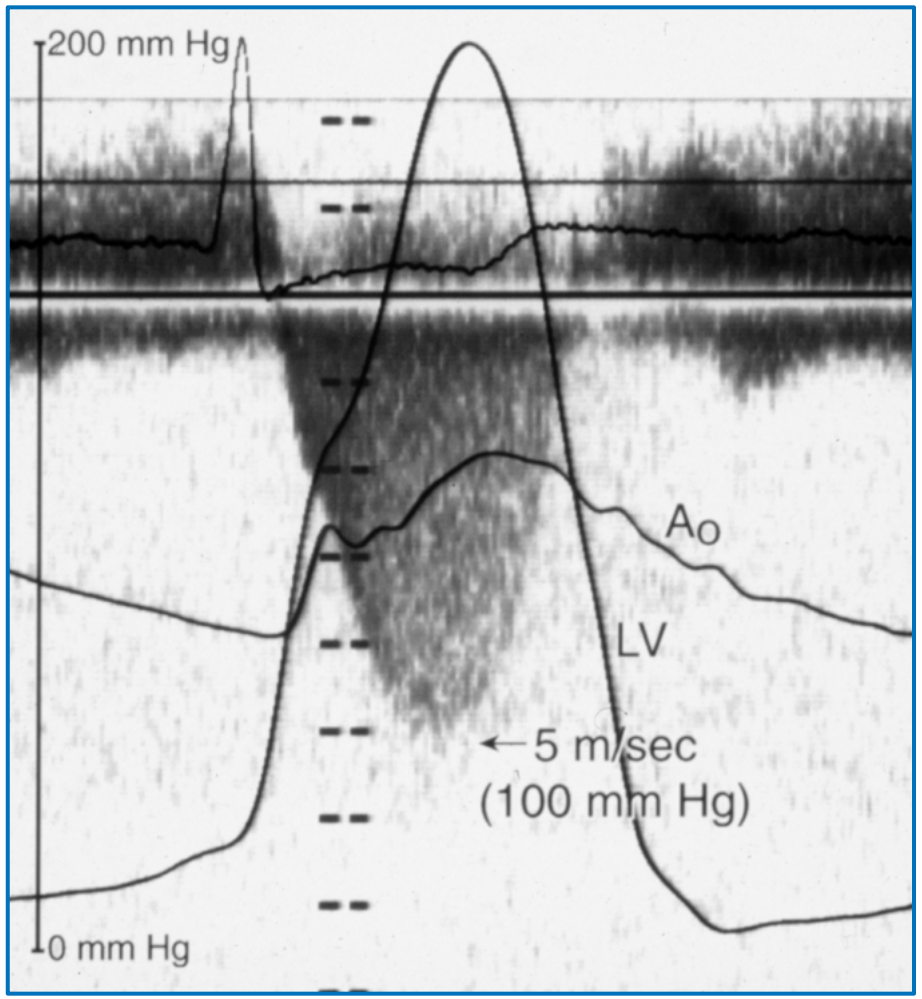
Severe MR

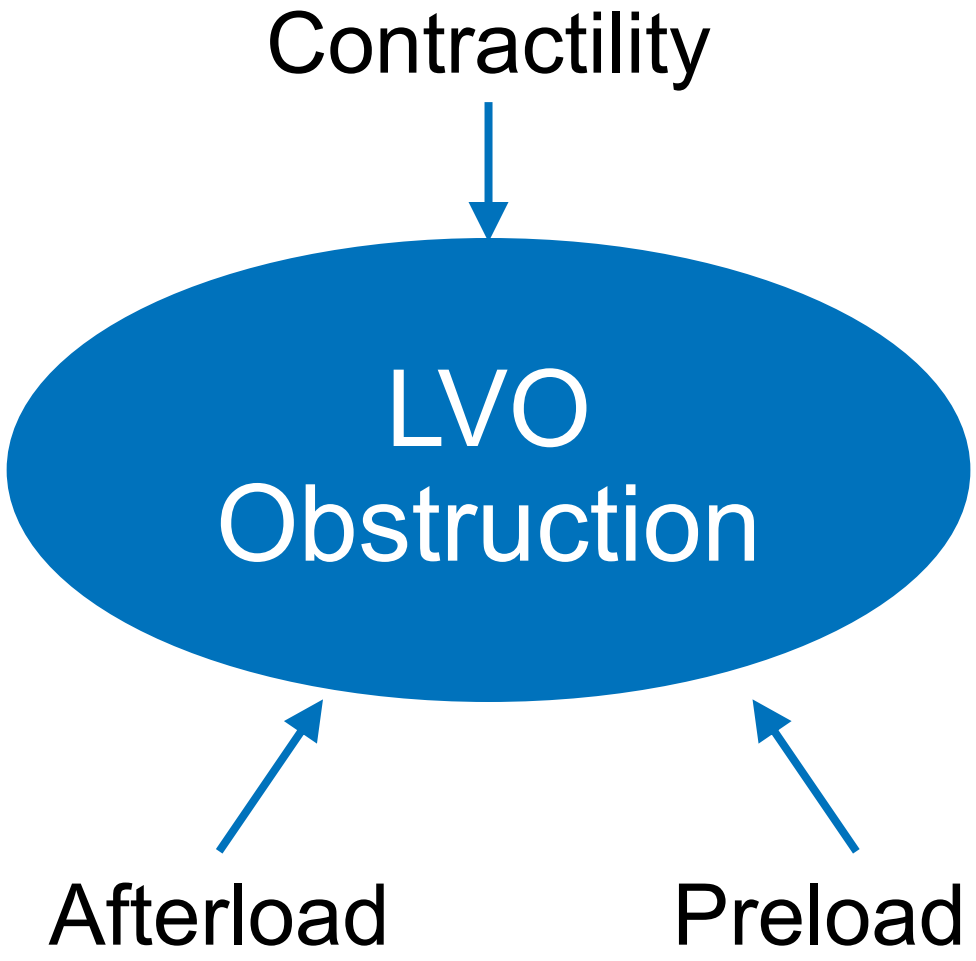


Arrhythmias

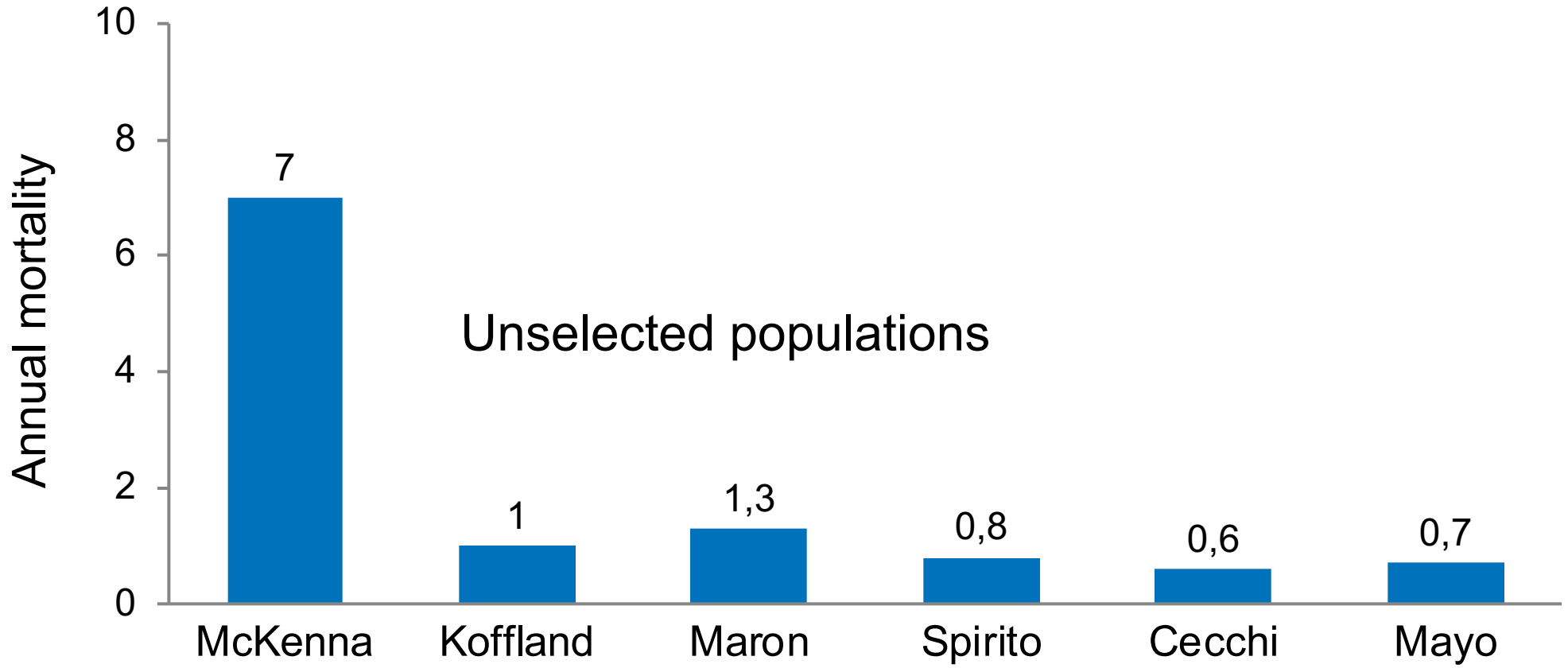


100 mm Hg



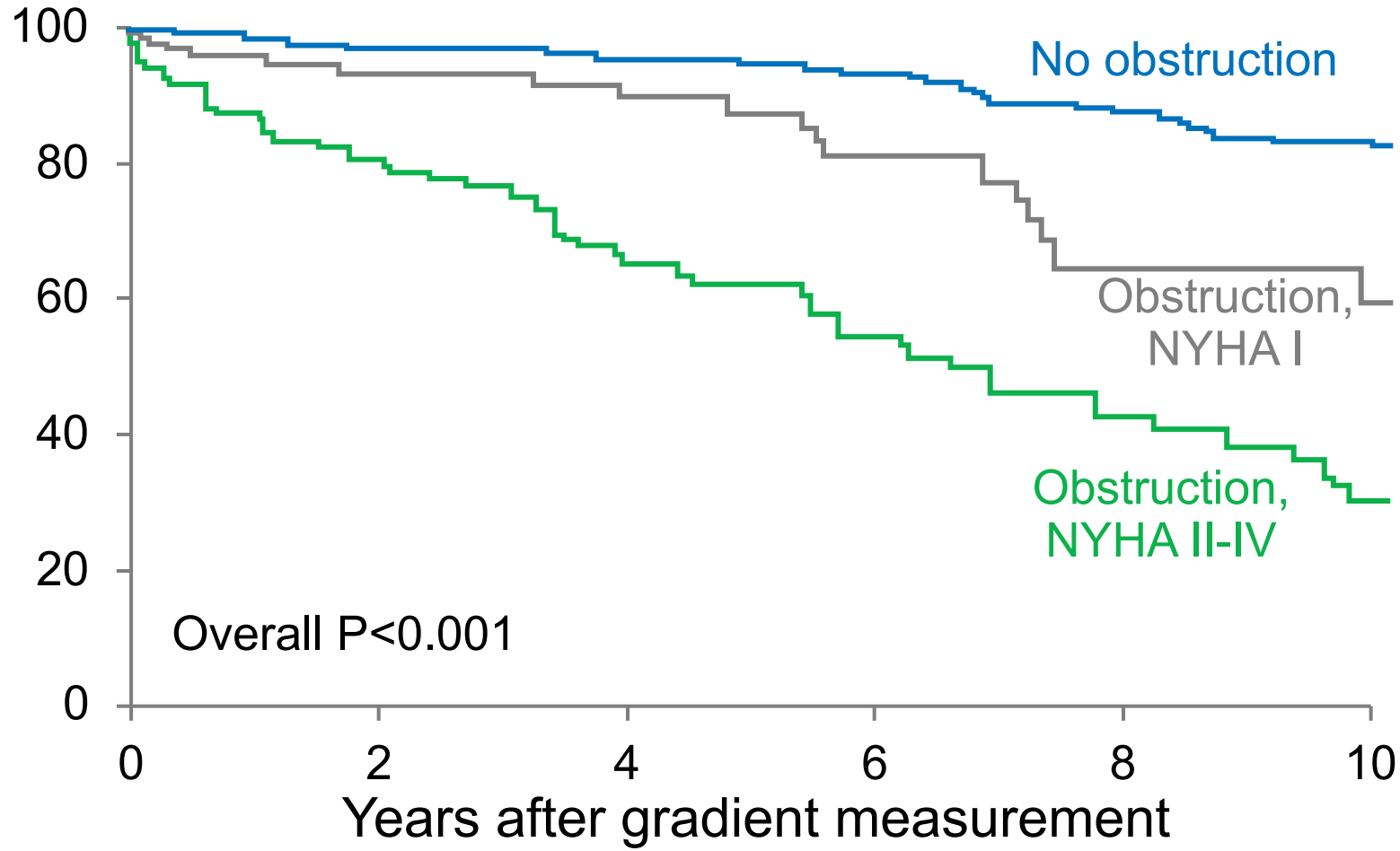


Annual Cardiovascular Mortality



Gradient, Symptoms, & Adverse Events

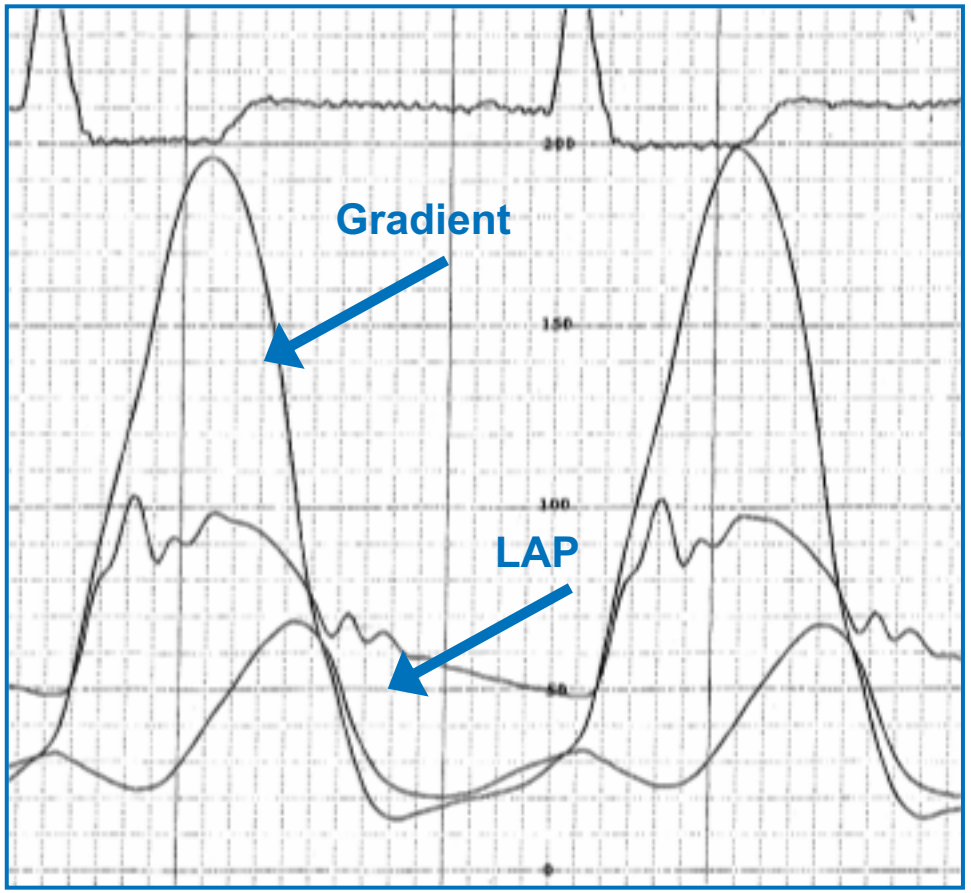
Freedom from progression to NYHA class III or IV and death from heart failure or stroke (%)



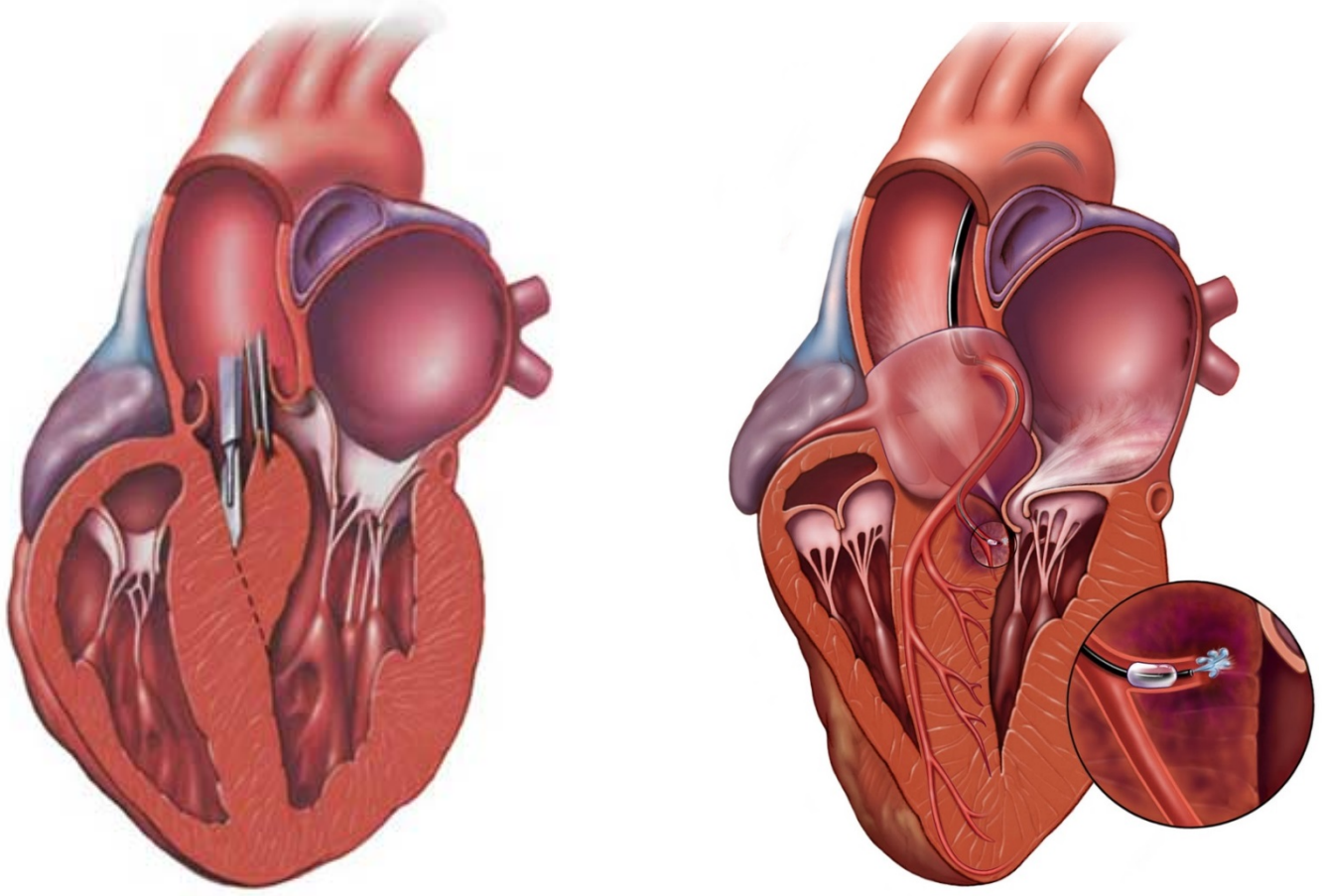
Maron MS et al: NEJM, 2003

Relieve obstruction

- Improve diastolic filling
- Reduce MR
- Improve symptoms



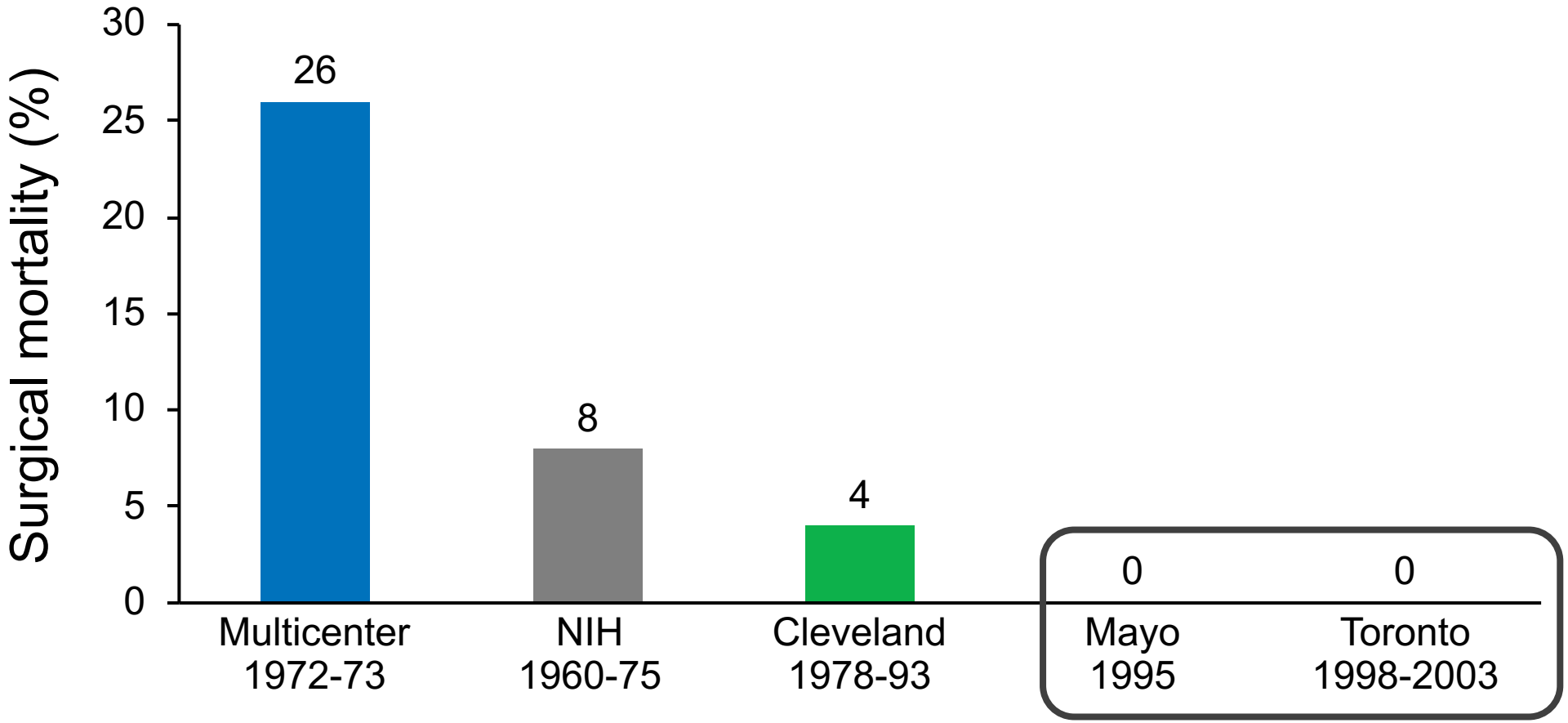
Septal Reduction Therapy



Early Myectomy

- 8-26% operative mortality
- Complications: CHB, AR, VSD
- Frequent mitral valve surgery
- Questions of efficacy
  - A disease of diastole

Minimal Risk Surgery



Shah PM et al: Circ Res, 1974; Maron BJ et al: Circ, 1978
Heric: JTCVS, 1995; McCully RB et al: Circ, 1995; Woo A et al: Circ, 2005

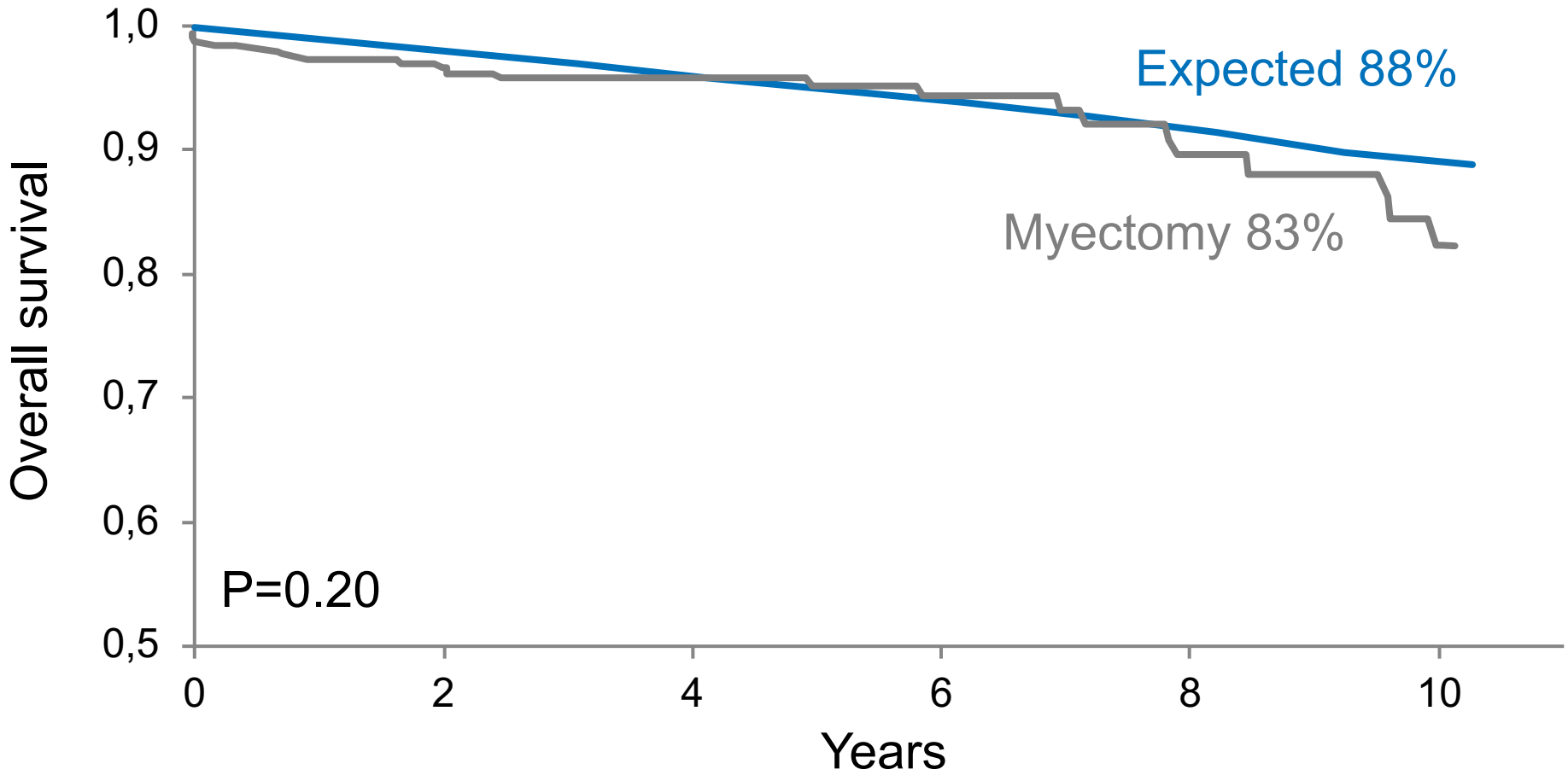
Operative Mortality Associated With Septal Myectomy at North American Hypertrophic Cardiomyopathy Centers

2000–2014

Institution	Myectomies (no.)	Age (yrs)	Male (%)	Operative Deaths*	
				No.	%
Mayo Clinic	1,411	51±14	55	4	0.3
Cleveland Clinic	1,470	55±14	55	6	0.4
Tufts	348	52±15	56	4	1.1
Toronto General	306	49±13	62	2	0.6
Mount Sinai	160	53±14	48	1	0.6
Totals	**3,695**	**54±14**	**55**	**17**	**0.4**

Maron BJ et al: J Am Coll Cardiol 66:1307, 2015

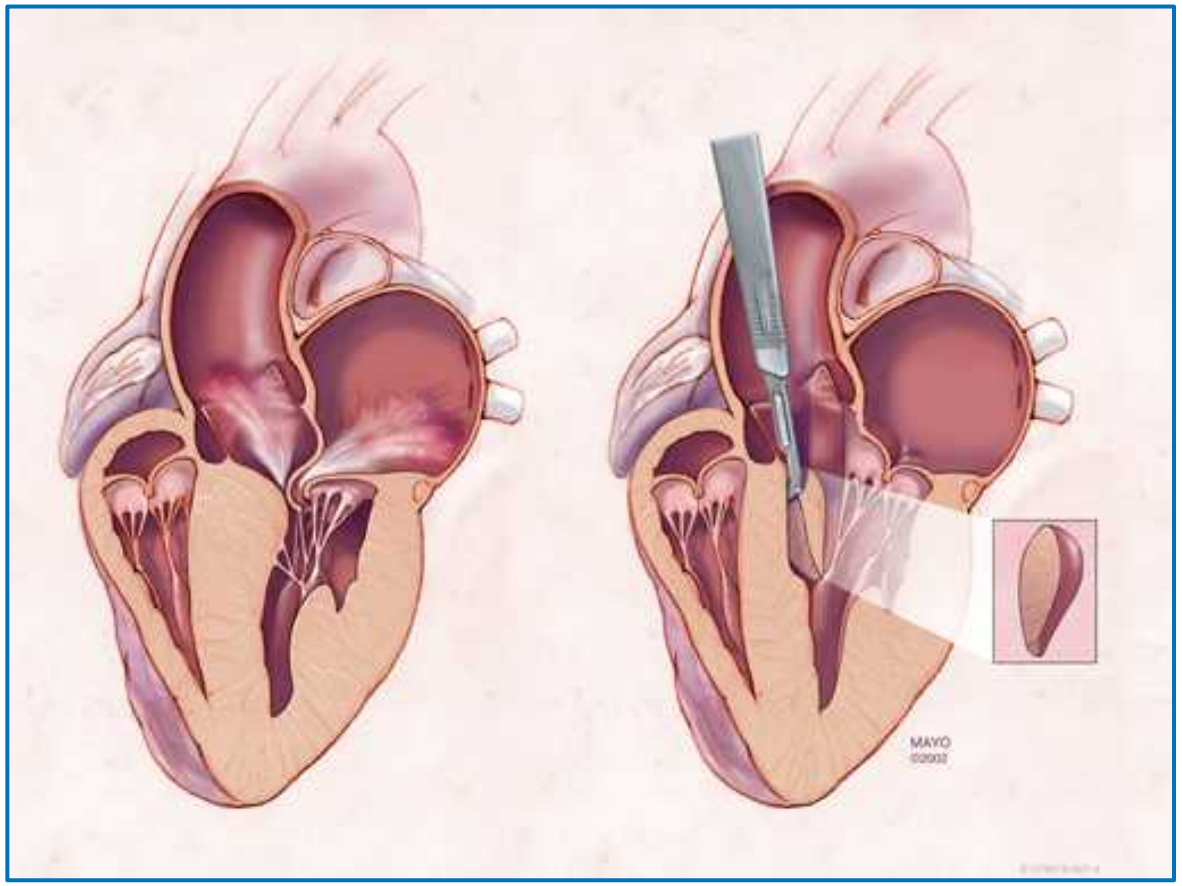
Normal Survival After Myectomy



Ommen et al: JACC 46:470, 2005

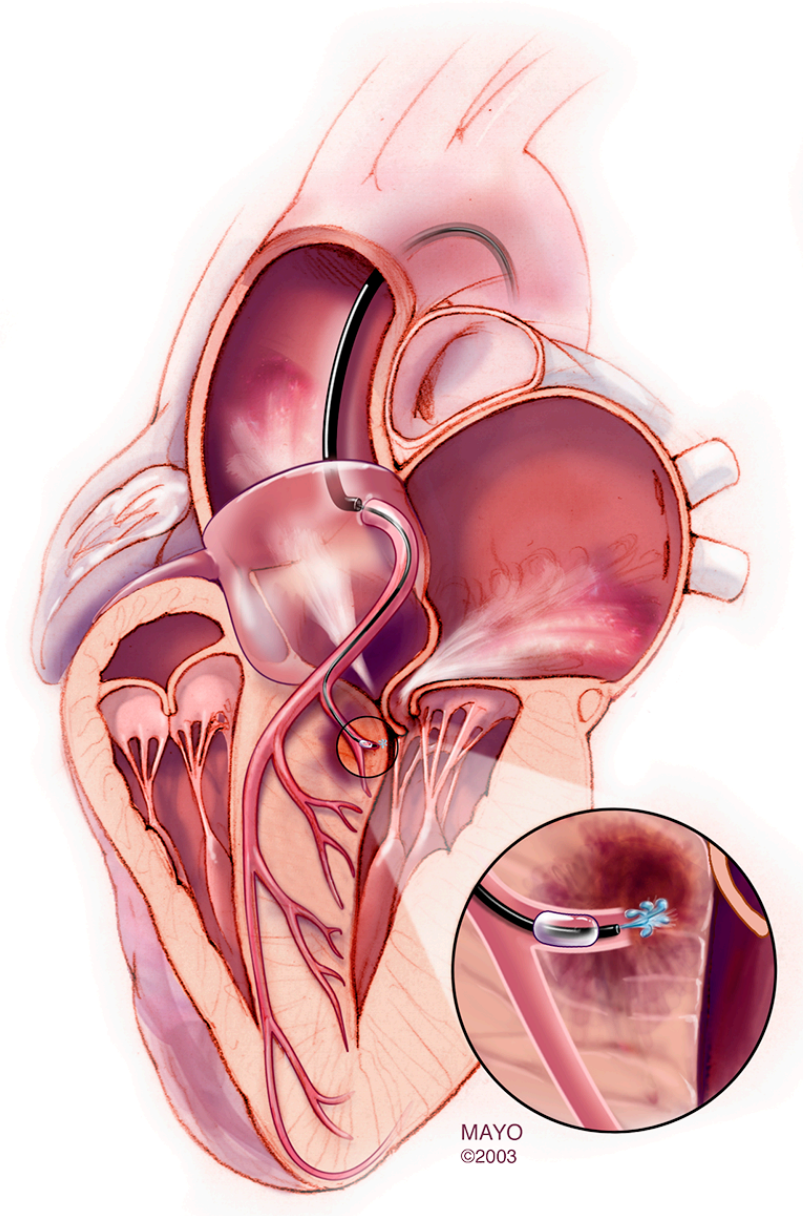
Surgical Myectomy Gold Standard

- Low risk
- >95% sx relief
- Superb survival

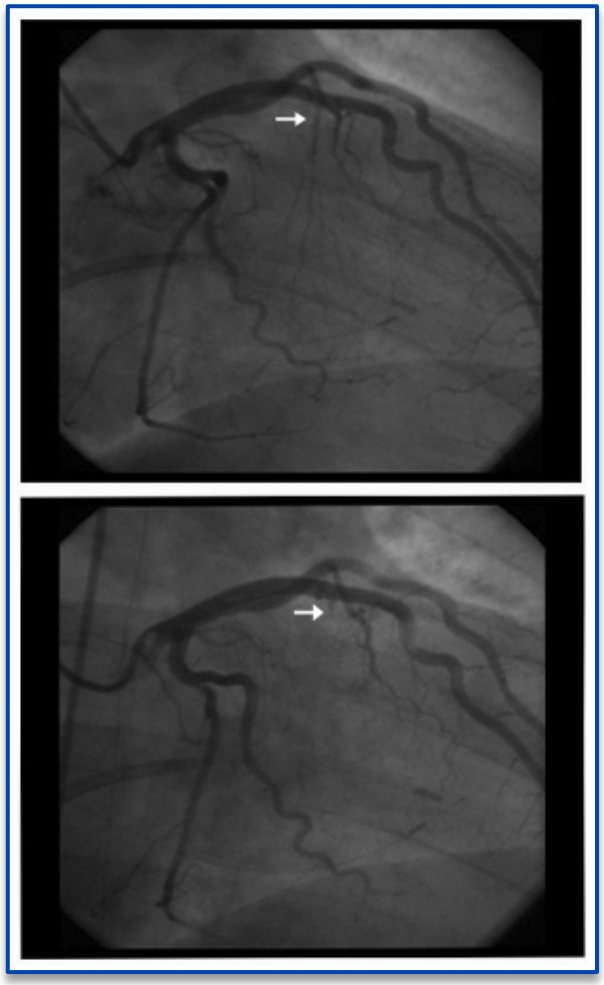


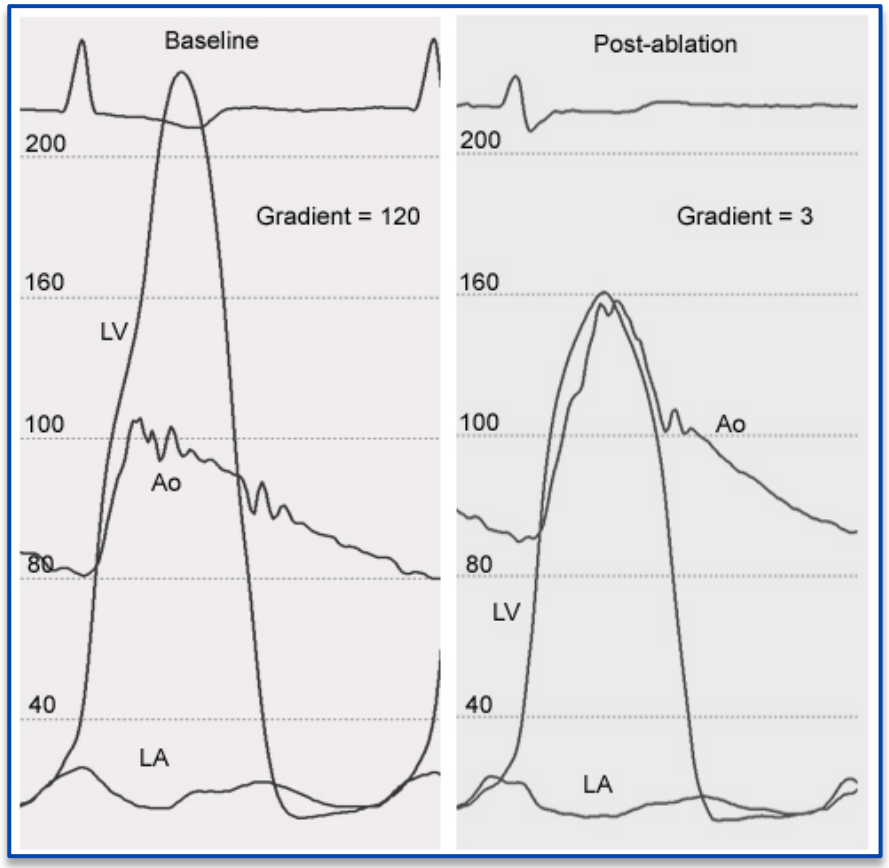
Septal Ablation

- Dr. Ulrich Sigwart
- 1995



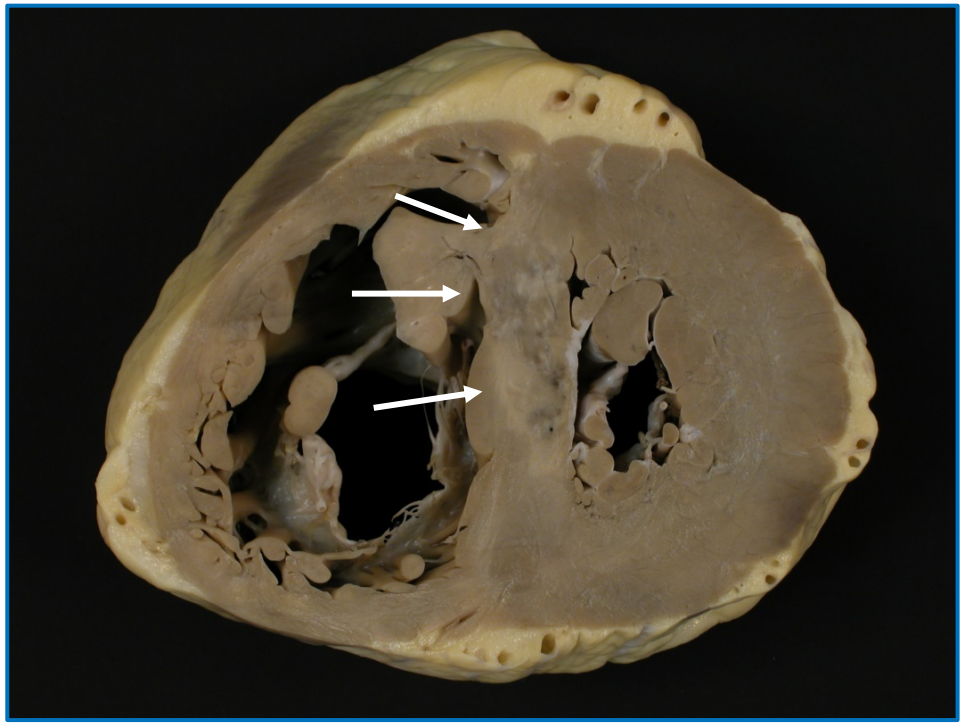
Procedural Success



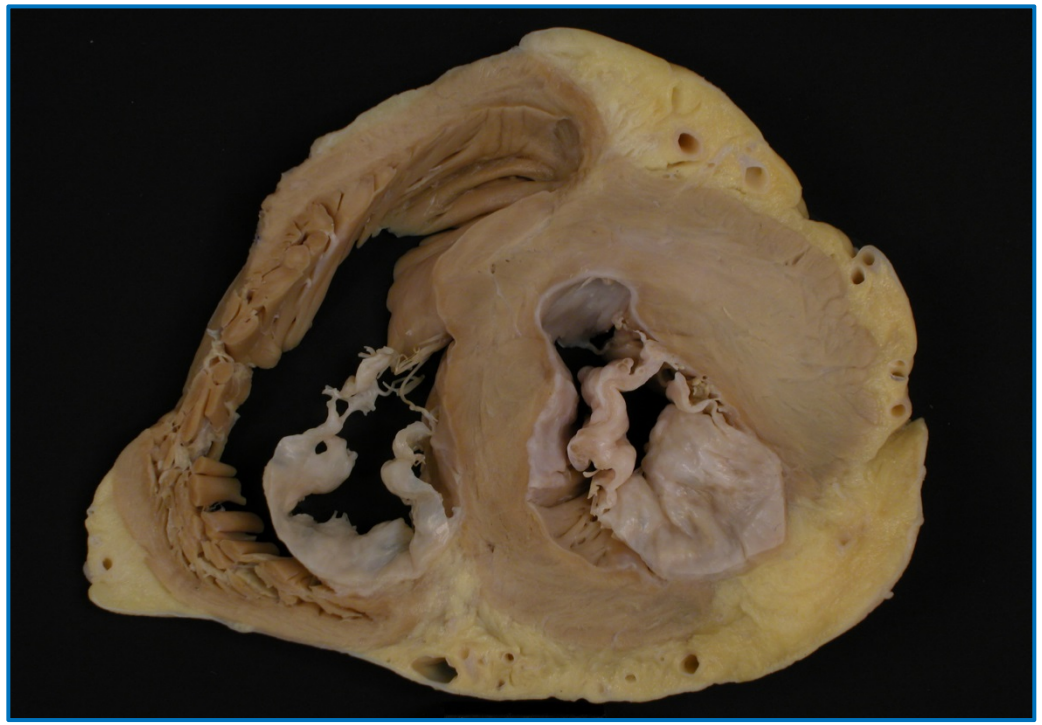


Different Mechanisms

Ablation



Myectomy

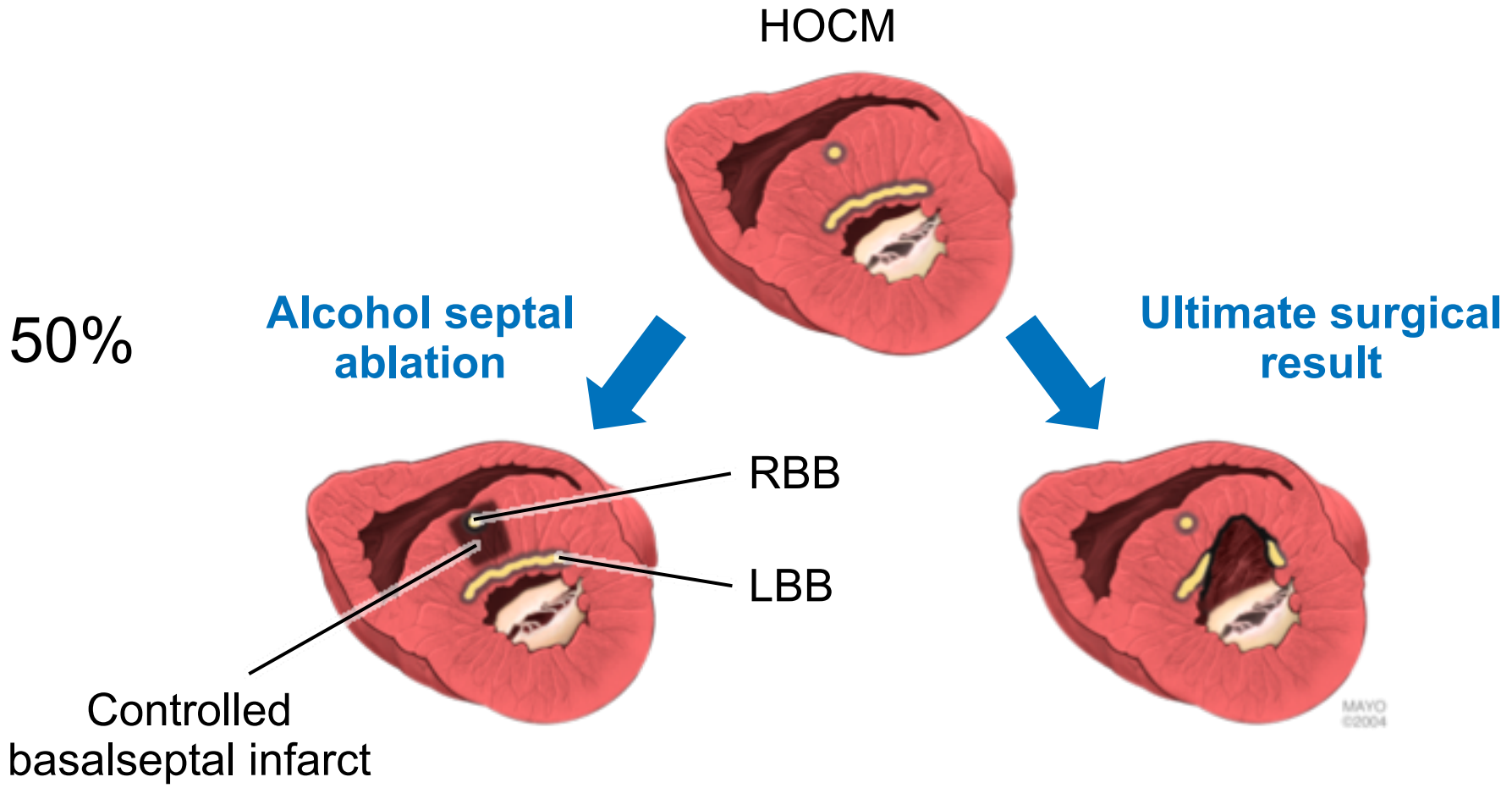


Heart Block

Normal ECG: still ~10%

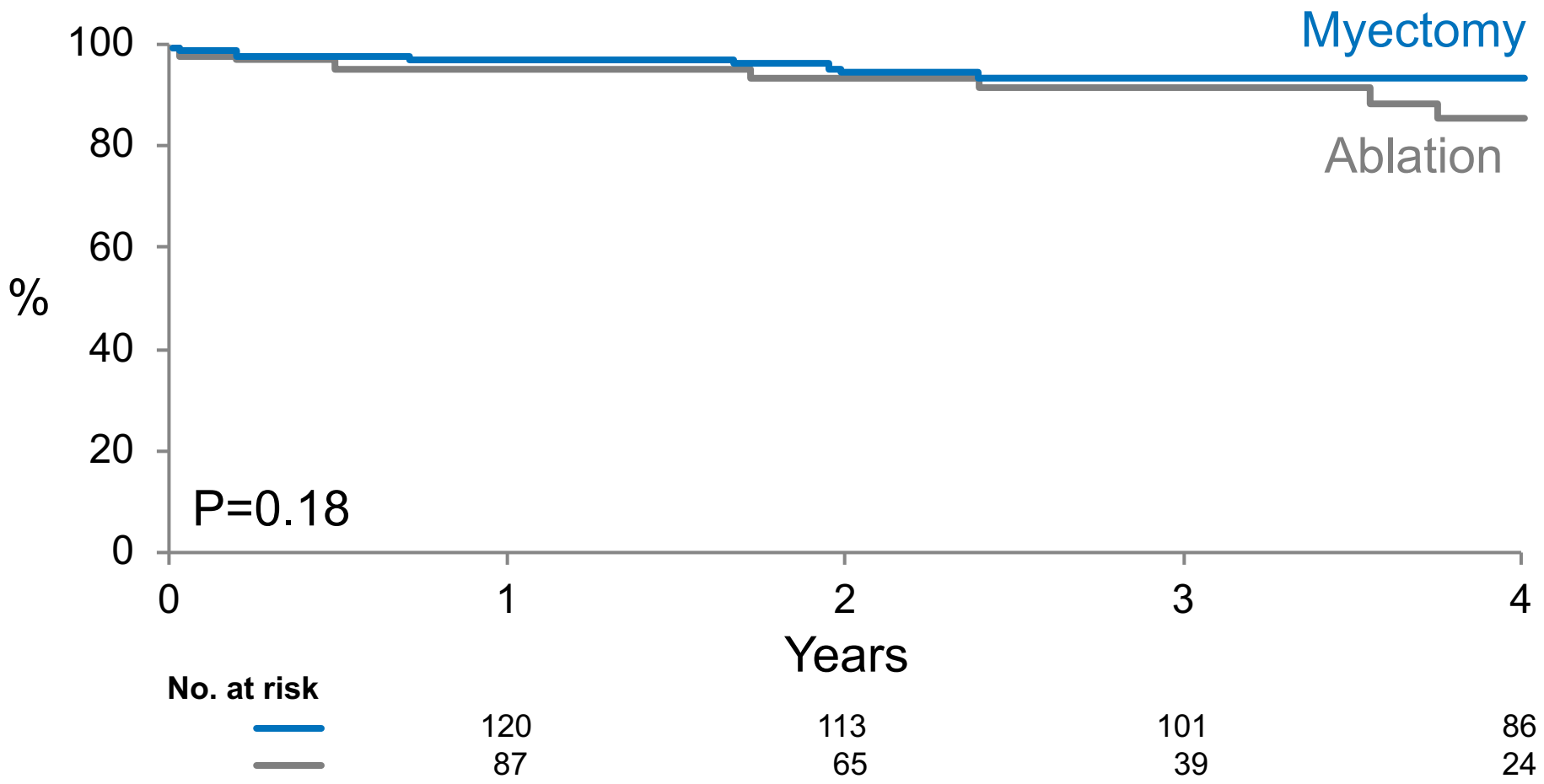
Beware …

- LBBB
- ↑ QRS
- LAD → 50%



Talreja et al: JACC, 2004

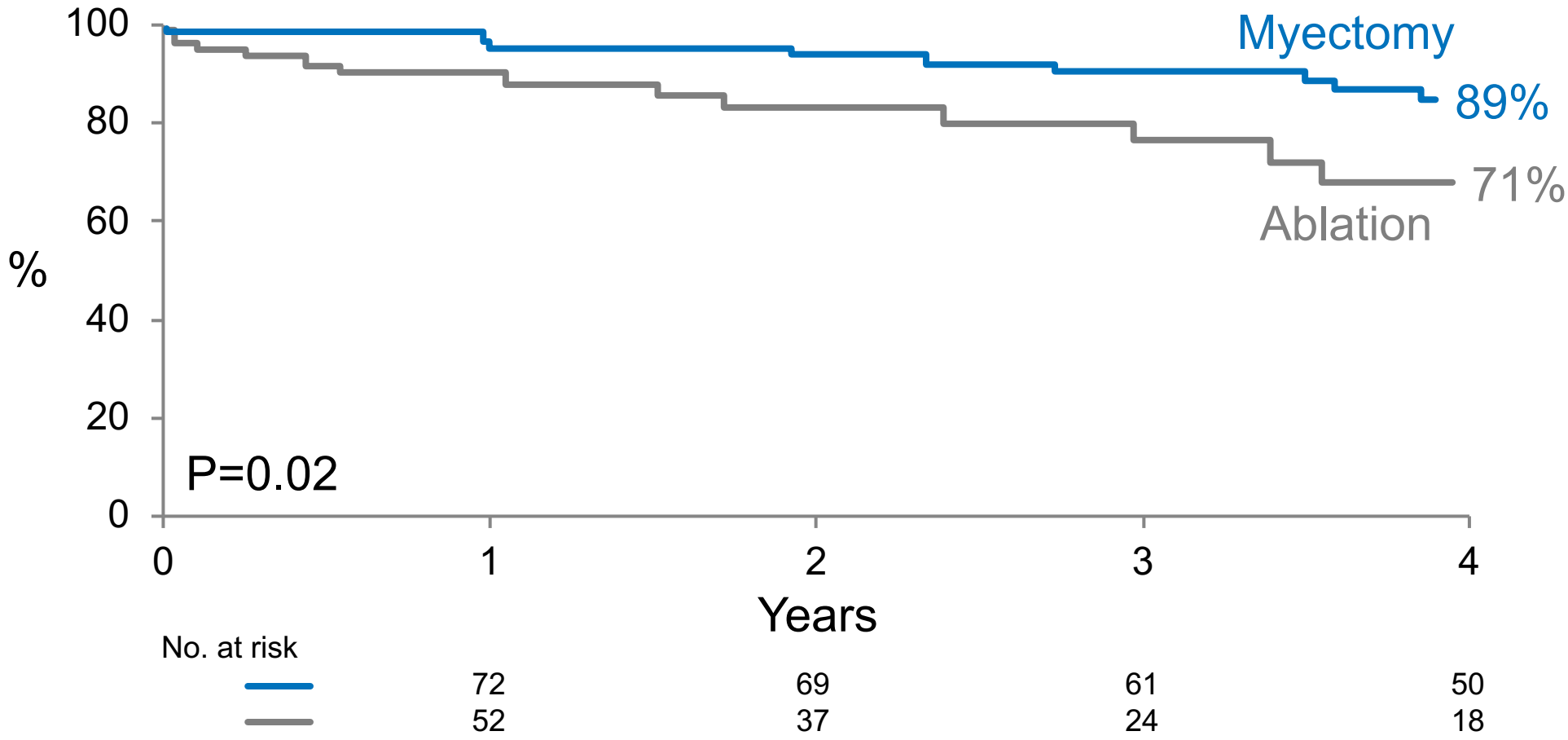
Survival



Sorajja et al: Circ, 2008

Survival Free of Severe Sx

Patients Aged <65 Years



Sorajja et al: Circ, 2008

Long-Term Outcome of Alcohol Septal Ablation in Patients With Obstructive Hypertrophic Cardiomyopathy

A Word of Caution

Folkert J. ten Cate, MD, PhD; Osama I.I. Soliman, MD, PhD; Michelle Michels, MD; Dominic A.M.J. Theuns, PhD; Peter L. de Jong, MD; Marcel L. Geleijnse, MD, PhD; Patrick W. Serruys, MD, PhD

Background—The impact of alcohol septal ablation (ASA)-induced scar is not known. This study sought to examine the long-term outcome of ASA among patients with obstructive hypertrophic cardiomyopathy.

Methods and Results—Ninety-one consecutive patients (aged 54±15 years) with obstructive hypertrophic cardiomyopathy underwent ASA. Primary study end point was a composite of cardiac death and aborted sudden cardiac death including appropriate cardioverter-defibrillator discharges for fast ventricular tachycardia/ventricular fibrillation. Secondary end points were noncardiac death and other nonfatal complications. Outcomes of ASA patients were compared with 40 patients with hypertrophic cardiomyopathy who underwent septal myectomy. During 5.4±2.5 years, primary and/or secondary end points were seen in 35 (38%) ASA patients of whom 19 (21%) patients met the primary end point. The 1-, 5-, and 8-year survival-free from the primary end point was 96%, 86%, and 67%, respectively in ASA patients versus 100%, 96%, and 96%, respectively in myectomy patients during 6.6±2.7 years (log-rank, $P=0.01$). ASA patients had a ≈5-fold increase in the estimated annual primary end point rate (4.4% versus 0.9%) compared with myectomy patients. In a multivariable model including a propensity score, ASA was an independent predictor of the primary end point (unadjusted hazard ratio, 5.2; 95% CI, 1.2 to 22.1; $P=0.02$ and propensity score-adjusted hazard ratio, 6.1; 95% CI, 1.4 to 27.1; $P=0.02$).

Conclusions—This study shows that ASA has potentially unwanted long-term effects. This poses special precaution, given the fact that ASA is practiced worldwide at increasing rate. We recommend myectomy as the preferred intervention in patients with obstructive hypertrophic cardiomyopathy. **(*Circ Heart Fail*. 2010;3:362-369.)**

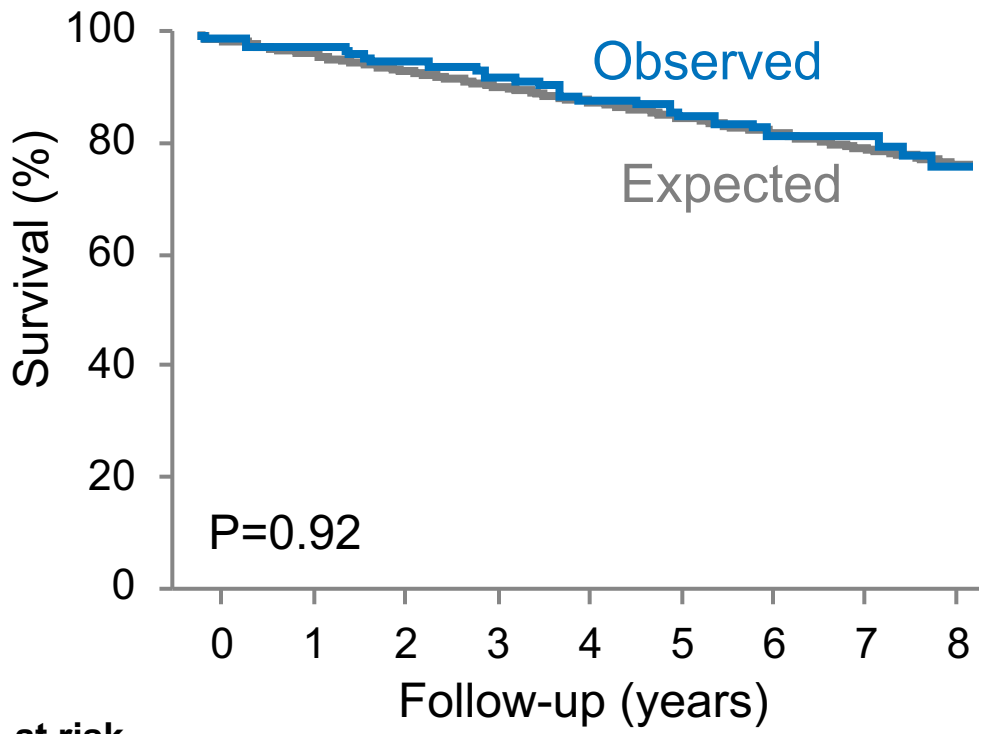
Key Words: hypertrophic cardiomyopathy ■ ablation ■ infarction ■ mortality ■ myectomy ■ defibrillators ■ survival

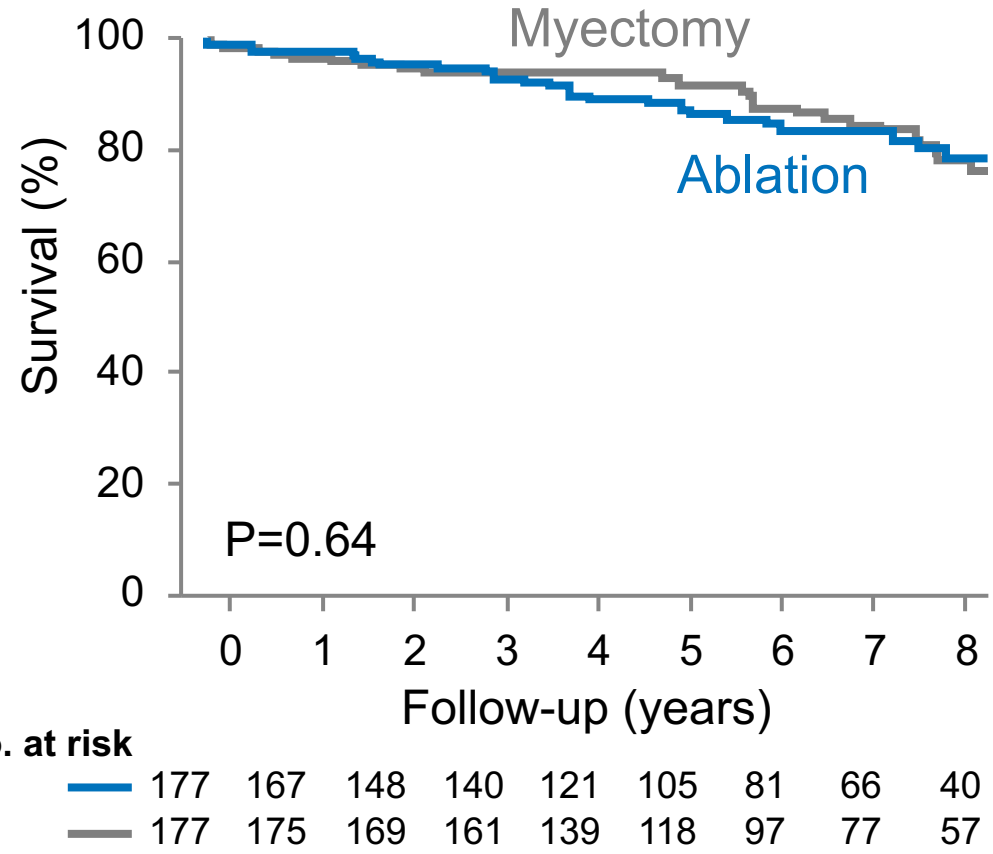
Mean Follow-up = 5.4±2.5 yrs

Arrhythmogenic c/o in **12%** (11 of 91)

Long Term Survival Post ASA at Mayo Clinic

Mean Follow-up = 5.7 yrs
Residual Gradient Predicted Mortality





Sorajja P et al: Circulation, 2012

STRUCTURAL

Long-Term Outcome of Alcohol Septal Ablation for Obstructive Hypertrophic Cardiomyopathy in the Young and the Elderly

Max Liebregts, MD,[a] Robbert C. Steggerda, MD,[b] Pieter A. Vriesendorp, MD,[c] Hannah van Velzen, MD,[c] Arend F.L. Schinkel, MD, PhD,[c] Rik Willems, MD, PhD,[d] Johan van Cleemput, MD, PhD,[d] Maarten P. van den Berg, MD, PhD,[e] Michelle Michels, MD, PhD,[c] Jurriën M. ten Berg, MD, PhD[a]

ABSTRACT

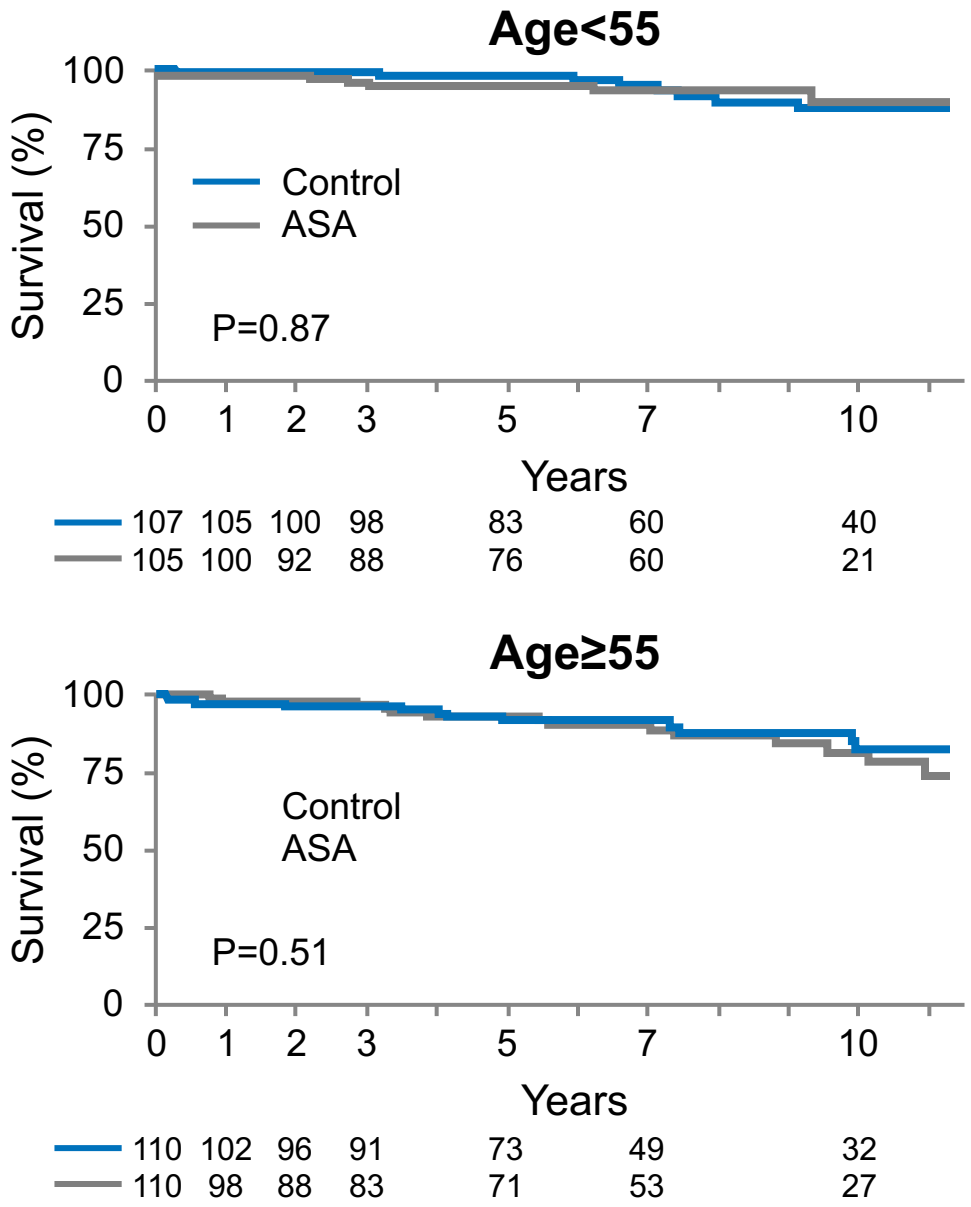
OBJECTIVES The aim of this study was to compare outcomes of alcohol septal ablation (ASA) in young and elderly patients with obstructive hypertrophic cardiomyopathy (HCM).

BACKGROUND The American College of Cardiology Foundation/American Heart Association guidelines reserve ASA for elderly patients and patients with serious comorbidities. Information on long-term age-specific outcomes after ASA is scarce.

METHODS This cohort study included 217 HCM patients (age 54 ± 12 years) who underwent ASA because of symptomatic left ventricular outflow tract obstruction. Patients were divided into young (age ≤55 years) and elderly (age >55 years) groups and matched by age in a 1:1 fashion to nonobstructive HCM patients.

RESULTS Atrioventricular block following ASA was more common in elderly patients (43% vs. 21%; p = 0.001), resulting in pacemaker implantation in 13% and 5%, respectively (p = 0.06). Residual left ventricular outflow tract gradient, post-procedural New York Heart Association functional class, and necessity for additional septal reduction therapy was comparable between age groups. During a follow-up of 7.6 ± 4.6 years, 54 patients died. The 5- and 10-year survival following ASA was 95% and 90% in patients age ≤55 years and 93% and 82% in patients age >55 years, which was comparable to their control groups. The annual adverse arrhythmic event rate following ASA was 0.7%/year in young patients and 1.4%/year in elderly patients, which was comparable to their control groups.

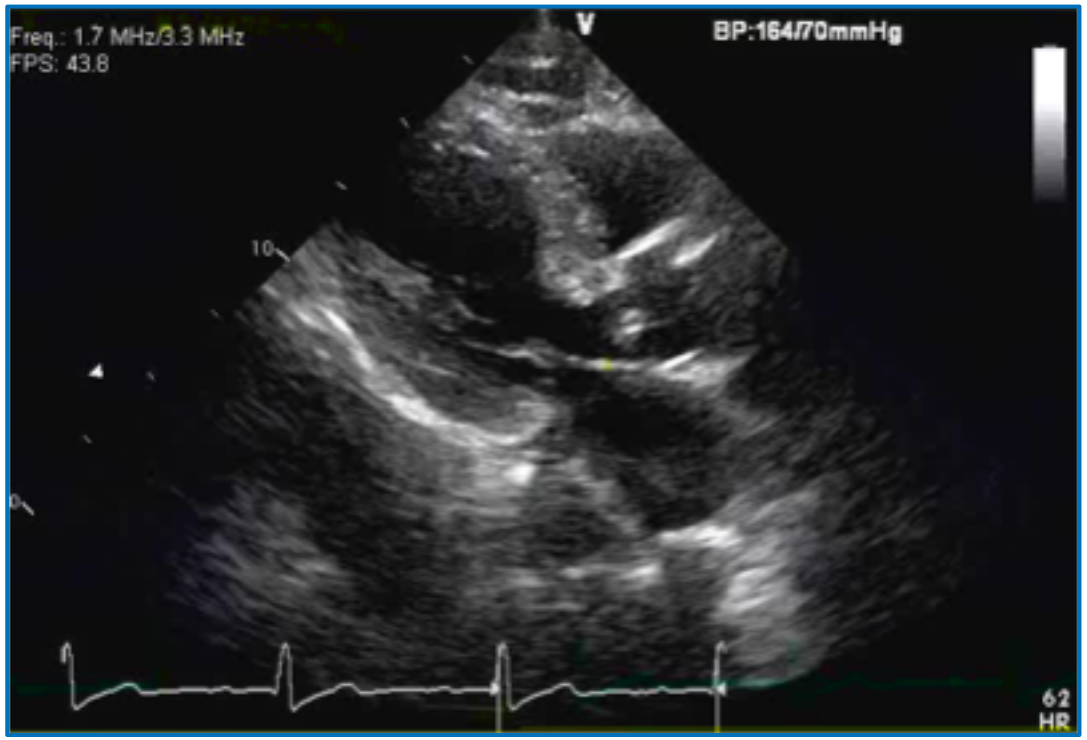
CONCLUSIONS ASA is similarly effective for reduction of symptoms in young and elderly patients; however, younger patients have a lower risk of procedure-related atrioventricular conduction disturbances. The long-term mortality rate and risk of adverse arrhythmic events following ASA are low, both in young and elderly patients, and are comparable to age-matched nonobstructive HCM patients. (J Am Coll Cardiol Intv 2016;9:463–9) © 2016 by the American College of Cardiology Foundation.

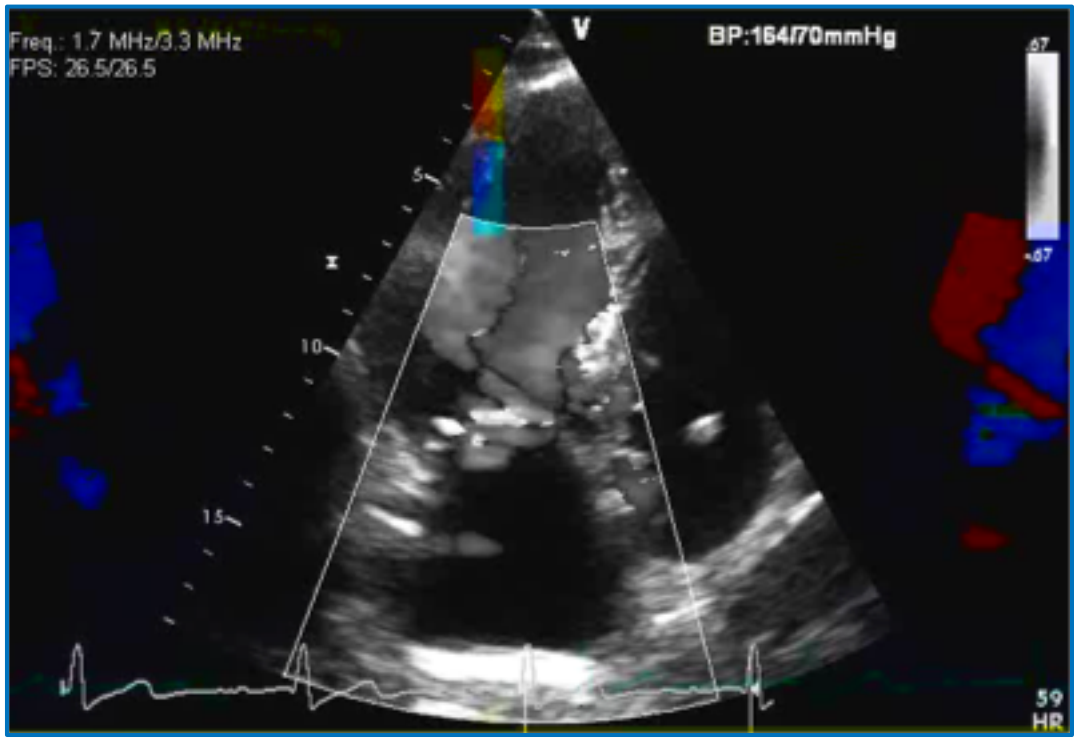


Liebregts et al: JACC Intv, 2016

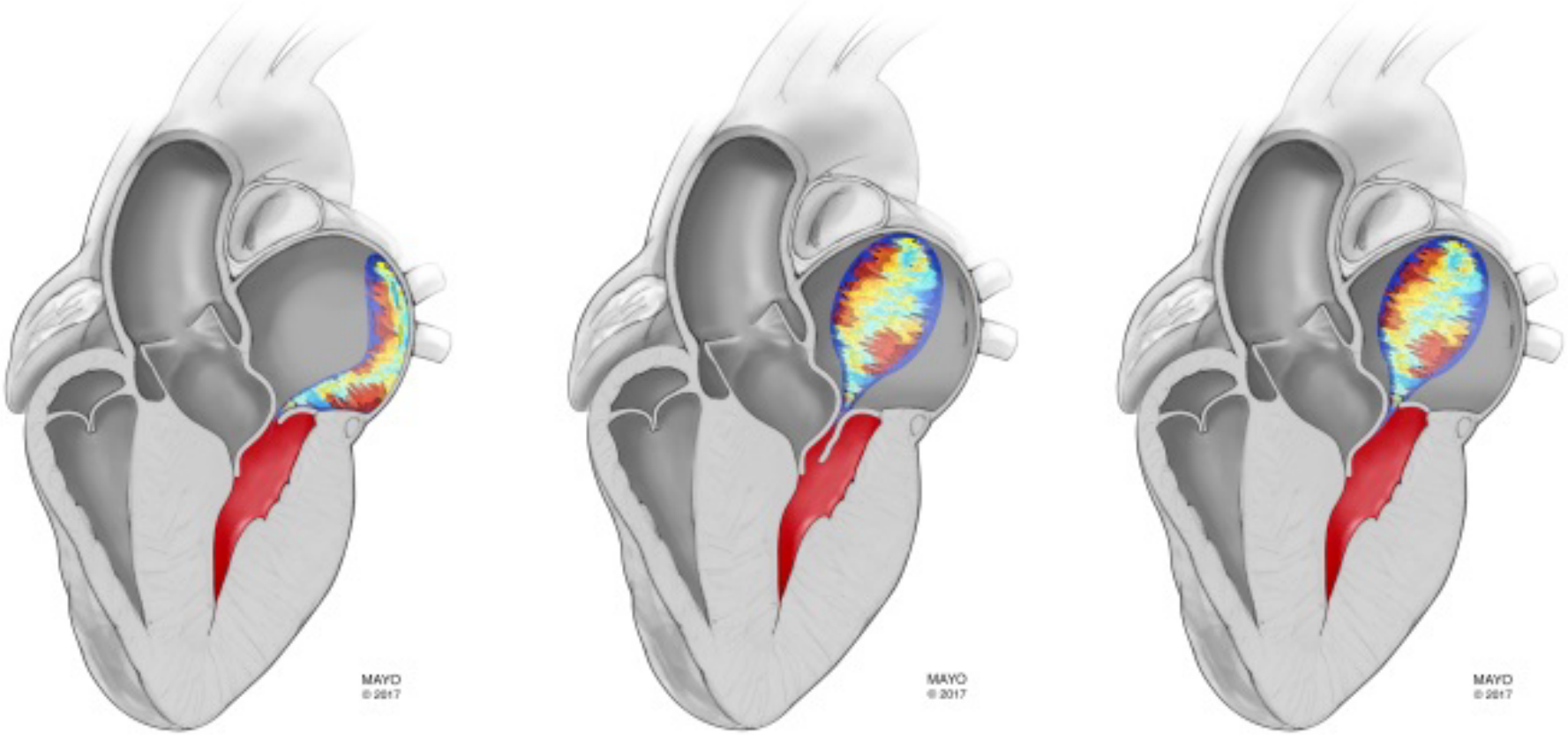
Mitral Valve Considerations

87 year old woman with presyncope: Ablation or Myectomy?

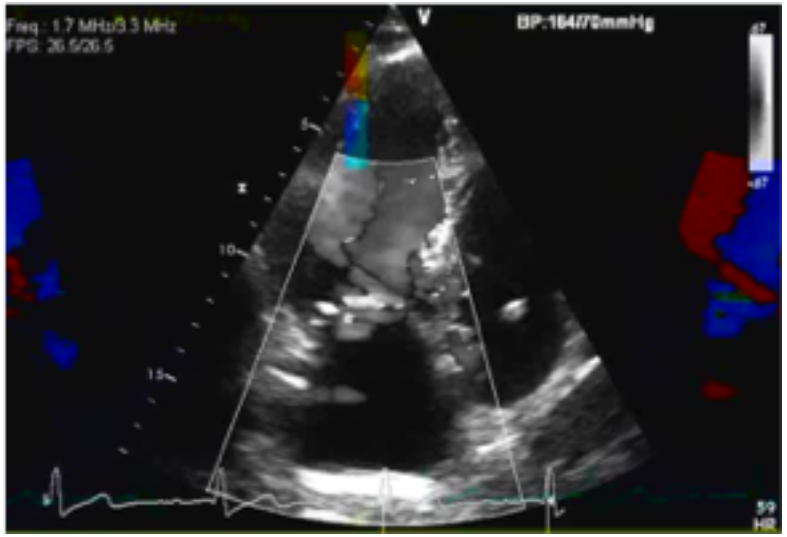




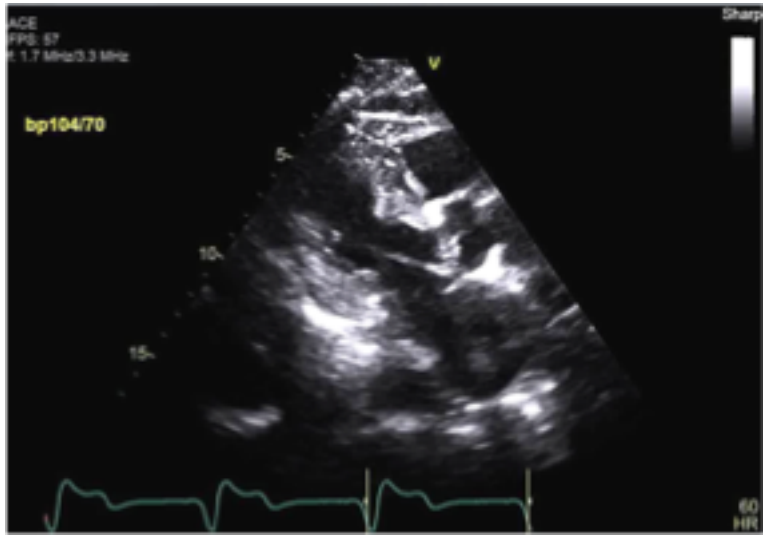
Possible Mechanism by Which Different Posterior Leaflet Lengths can Contribute to a Central Jet by Redirecting the Gap Between Leaflets

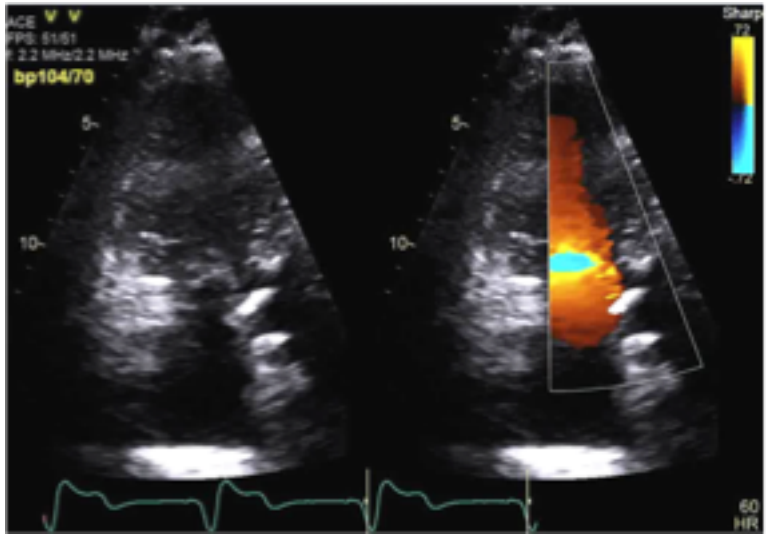


Pre-Ablation



Post-Ablation

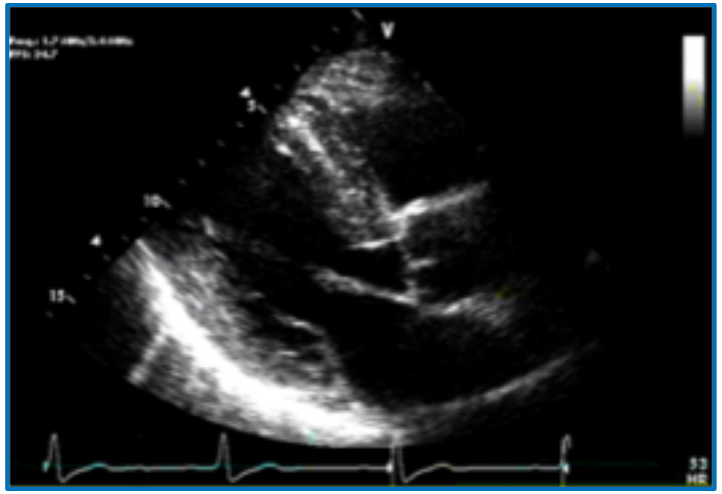


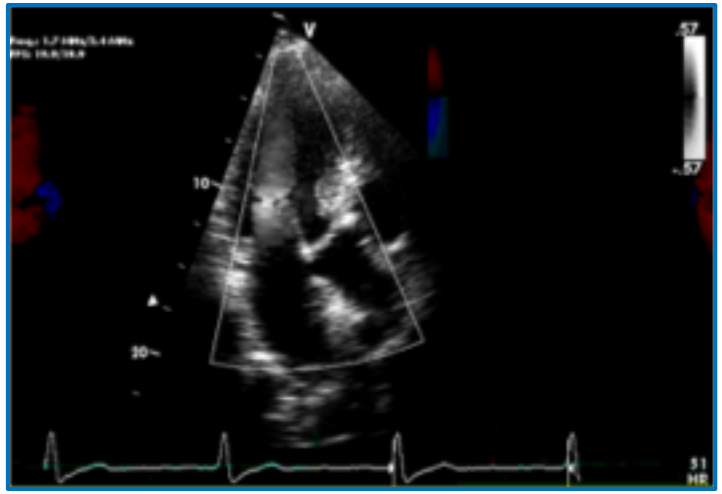


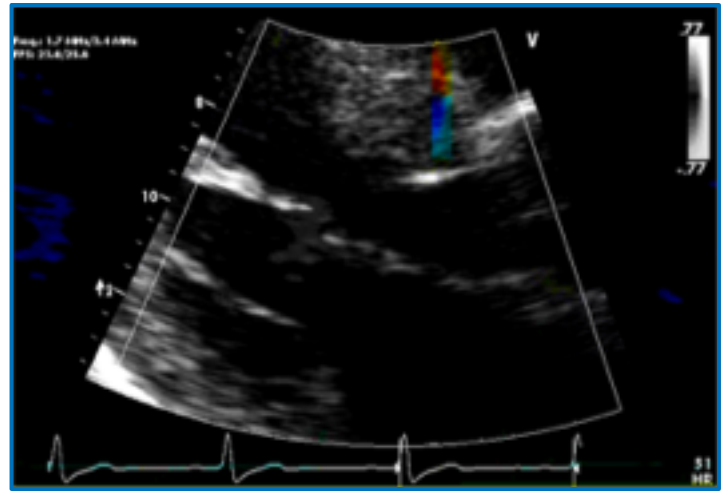
Case #1

A. Ablation

B. Myectomy



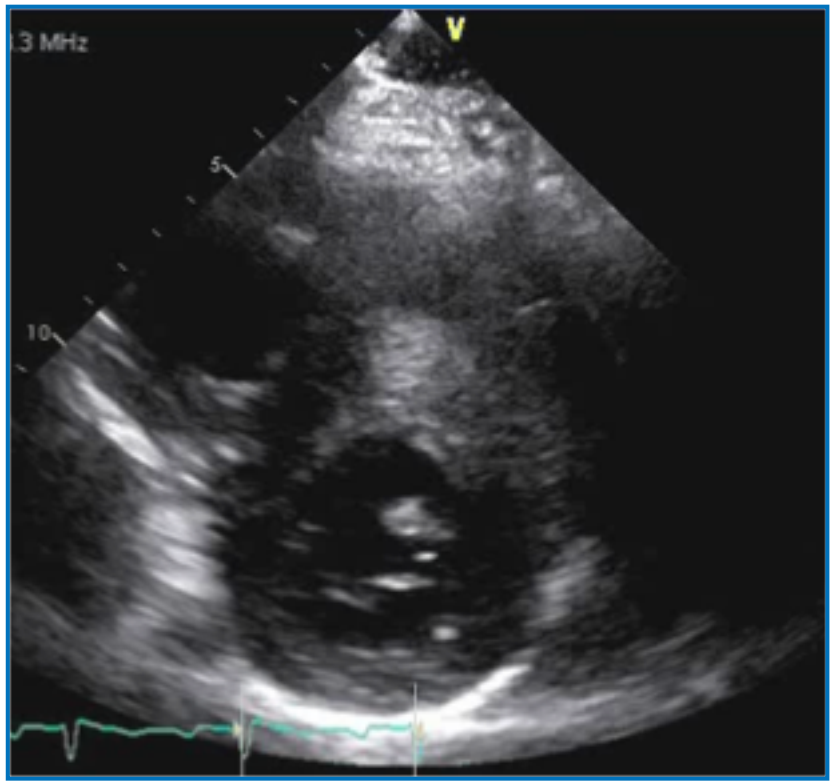


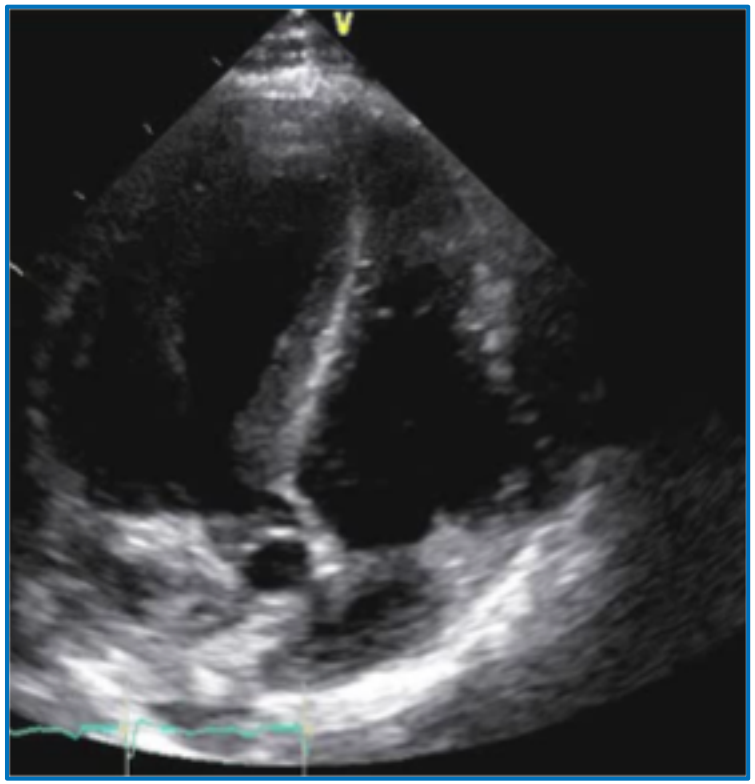


Case #2

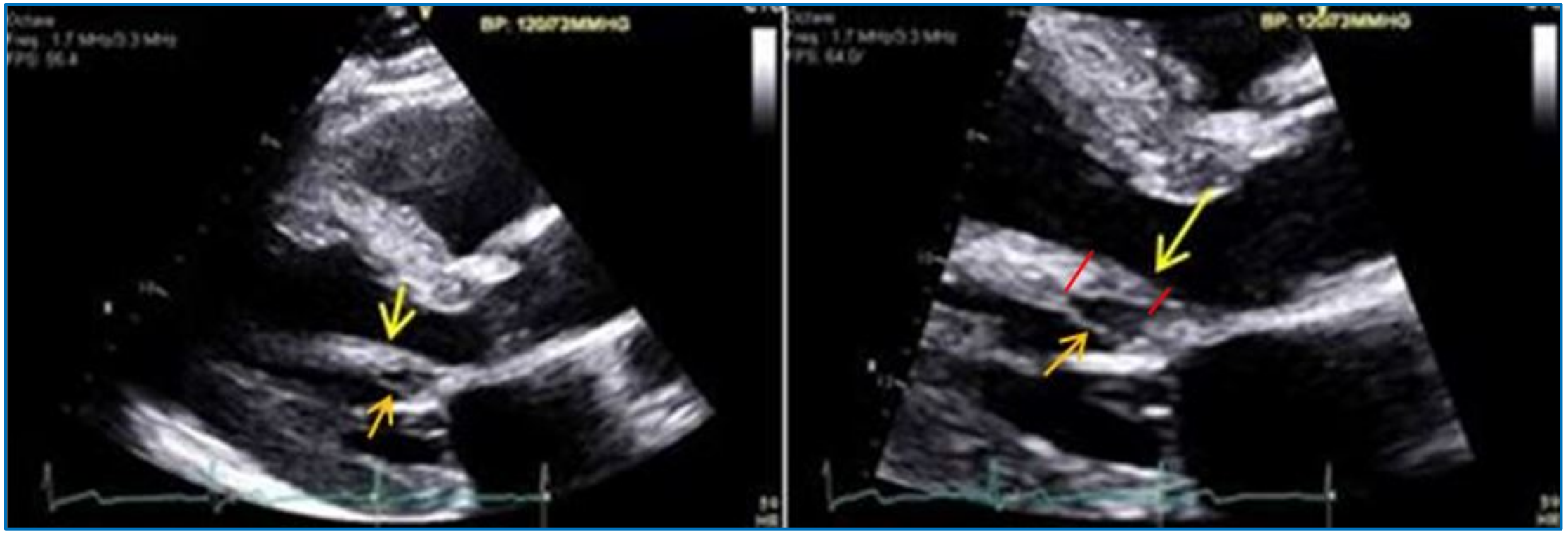
A. Ablation

B. Myectomy



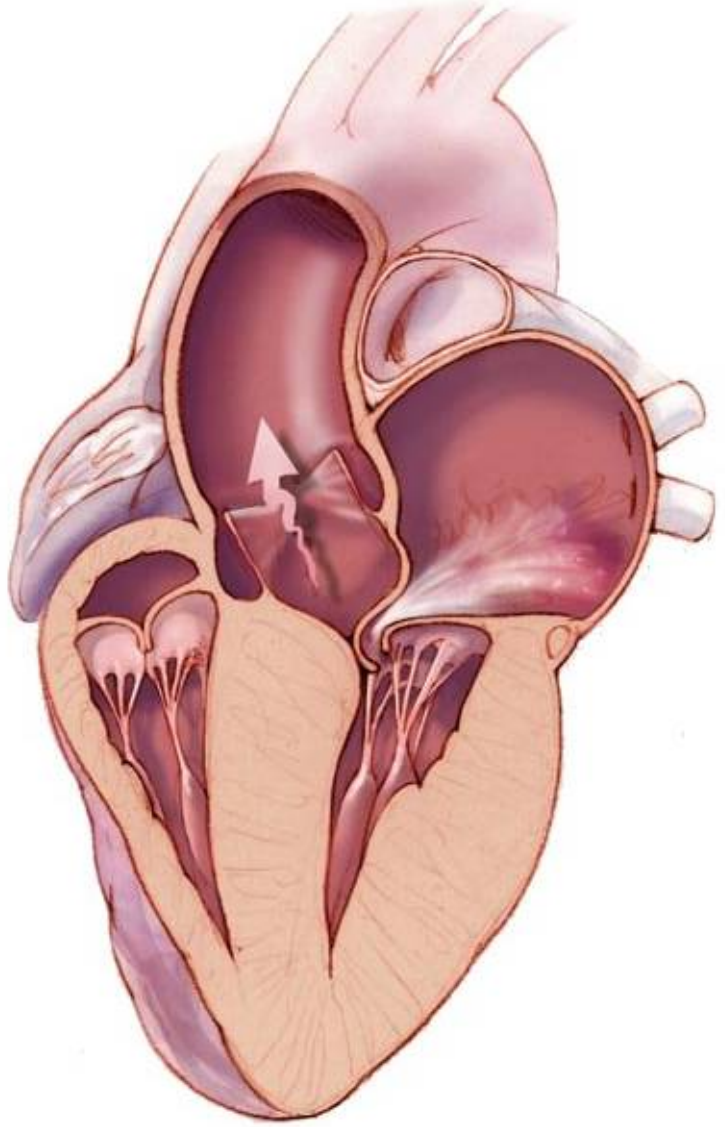


Anomalous Papillary Muscle Insertion



Outline

- Diagnostic considerations
- Obstruction in HCM
- Clinical outcomes in HCM
- Operative considerations
- Unanswered questions
- Take home points

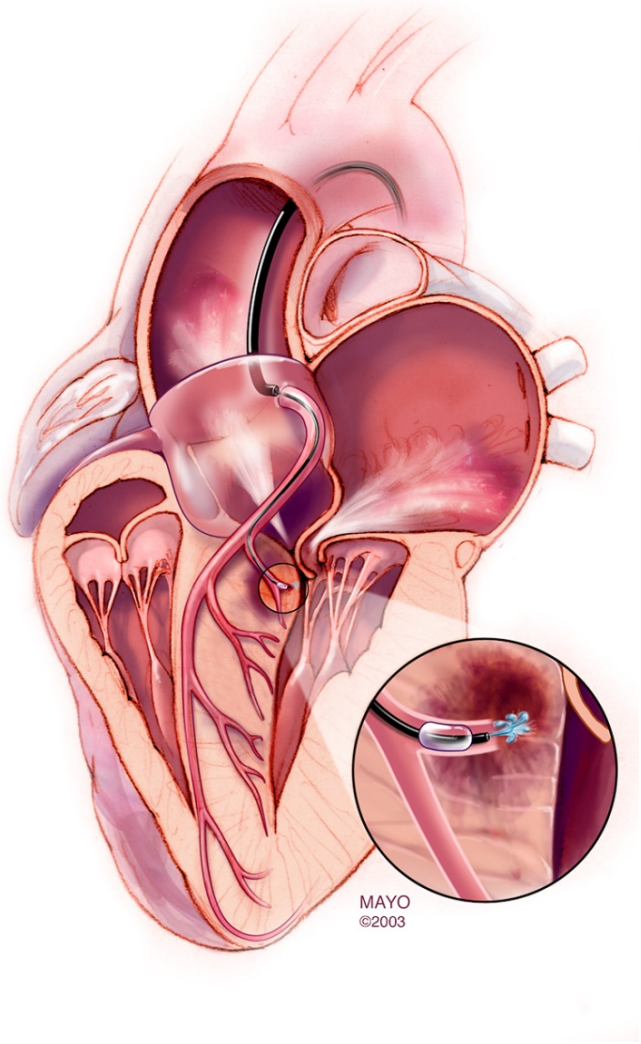


Take Home Points

- HCM is a genetic and heterogeneous disease
- Rule out other causes of increased wall thickness
- Septal morphology predicts yield of genetic testing
- Symptoms result from diastolic dysfunction and dynamic obstruction
- Presence of obstruction is associated with outcome

Septal Reduction Therapy Pearls

- Indications for septal ablation vs myectomy
- Hemodynamic and anatomic assessment is important
- Alcohol ablation is effective minimally invasive procedure
  - Higher pacemaker risk
  - No early survival impairment
- Surgical myectomy is standard of care



Unanswered Questions

- How will genetics shape the management of HCM in the future?
  - Improved/early diagnosis
  - Guide therapy
- What are the long term outcomes of alcohol septal ablation?
- What is the role of newer therapies for septal reduction?
  - Radiofrequency ablation
  - Electroporation

Questions & Discussion

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