Alcohol Septal Ablation Versus Surgical Treatment in HCM

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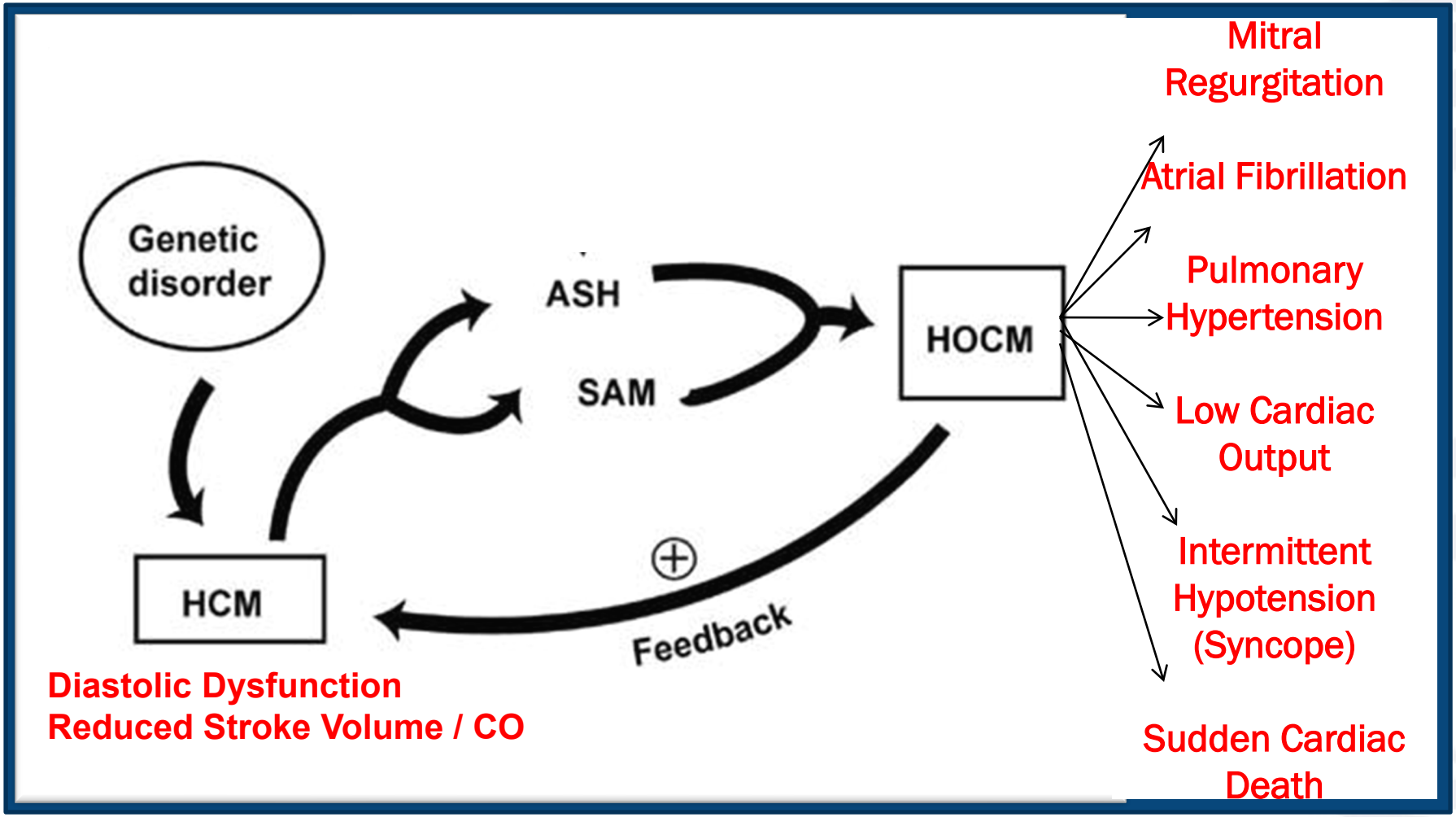
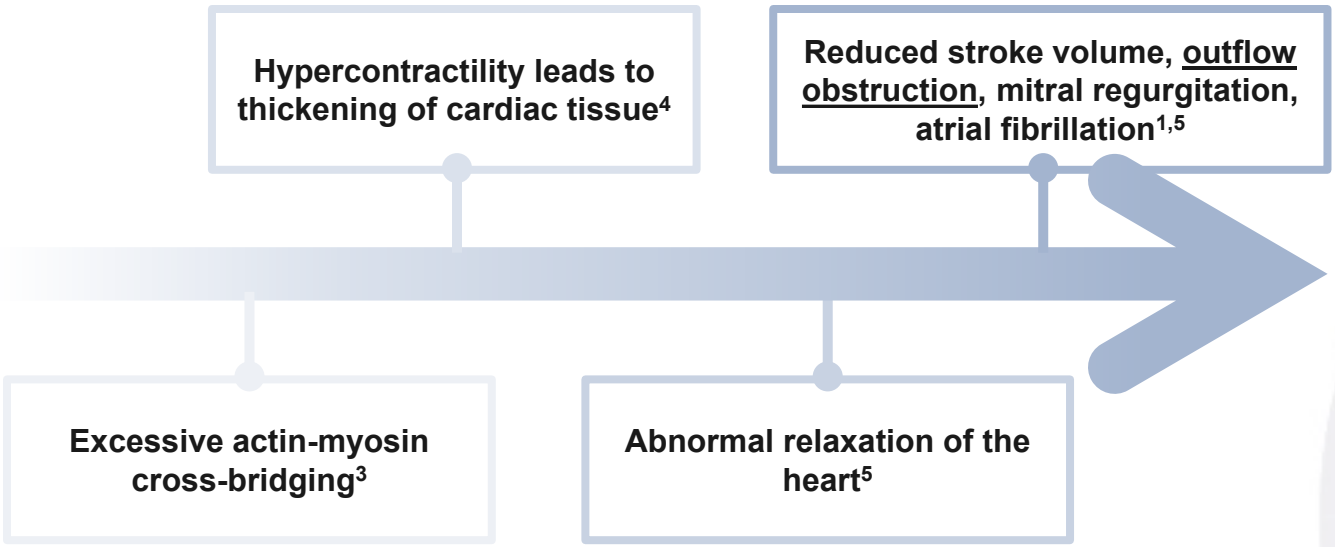
X = @sriharinaidumd

Lifecycle of the HCM Patient (Macroscopic Findings)



Lifecycle of the HCM Patient (Pathophysiologic Findings)



HCM Symptoms

- Dyspnea
- Fatigue
- Chest pain
- Palpitations
- Syncope

HCM Complications

- Heart failure
- Arrythmias
- Stroke
- Sudden cardiac death

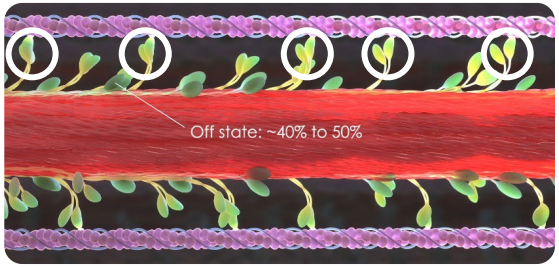
In the early stages of cardiac remodeling or even in the presence of cardiomyopathy, patients with HCM can be asymptomatic or minimally symptomatic

SCA Risk decreases with age, but overall 0.5% per year with relatively normal life expectancy when managed without a center of excellence, but some patients at higher risk

1. Mayo Clinic. https://www.mayoclinic.org/diseases-conditions/hypertrophic-cardiomyopathy/symptoms-causes/syc-20350198. Accessed February 24, 2020. **2.** Maron BJ et al. *Lancet*. 2013;381(9862):242-255. **3.** Nag S et al. *Nat Struct Mol Biol*. 2017;24(6):525-533. **4.** Anderson RL et al. *PNAS*. 2018;115:E8143-E8152. **5.** Gersh BJ et al. *Circulation*. 2011;124:e783-831. **6.** Cleveland Clinic. Hypertrophic Cardiomyopathy. https://my.clevelandclinic.org/health/diseases/17116-hypertrophic-cardiomyopathy. Accessed July 30, 2020. **7.** Elliott PM et al. *Eur Heart J*. 2014;35(39):2733-2779. **8.** Marian AJ et al. *Circ Res*. 2017;121(7):749-770.

Sarcomeric dysfunction : The Fundamental Problem

Normal Sarcomere



Normal contractility

Effective relaxation

Ordered sarcomeres

Dysfunction in sarcomere proteins

HCM Sarcomere
too many myosin–actin cross–bridges

Hypercontractility

Impaired relaxation

Disordered sarcomeres

Cardiac tissue stiffness

Interstitial fibrosis

~ 40-50% off state myosin

~ 15-20% off state myosin

1. Spudich JA et al. *Pflugers Arch* 2019;471:701–717. 2. Trivedi DV et al. *Biophys Rev* 2018;10:27-48. 3. Nag S et al. *Nat Struct Mol Biol* 2017;24:525–533. 4. Alamo L et al. *eLife* 2017;6:e24634.

Guideline recommendations for symptom management w/ traditional meds (class 1)

ACCF/AHA	ESC
• Beta blockers are the primary recommendation for symptomatic HCM • Verapamil recommended if beta blockers do not work or contraindicated • Disopyramide can be used with either beta blockers or verapamil	• Beta blockers are recommended first-line therapy for LVOT obstruction • Verapamil recommended if beta blockers do not work or contraindicated • Disopyramide can be used with either beta blockers or verapamil

The impact of pharmacotherapy on HCM symptoms is unknown due to the limited body of evidence, and all available medications have significant side effects that limit dose escalation and use

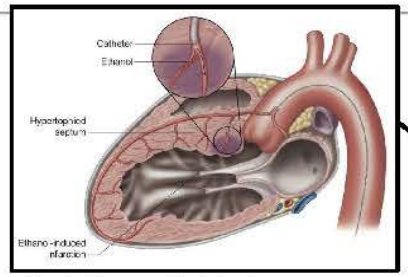
ESC, European Society of Cardiology.

1. Gersh BJ et al. *J Am Coll Cardiol*. 2011;58(2):e212-261. **2.** Elliott P et al. *Eur Heart J*. 2014;35:2733-2779. **3.** Marian AJ et al. *Circ Res*. 2017;121(7):749-770.

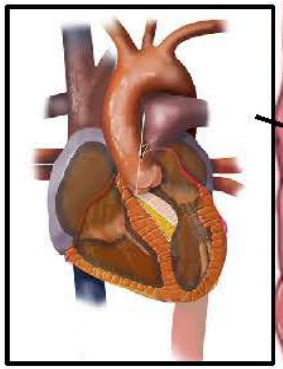
The Challenge with Traditional Meds

- Compliance and BID dosing
- Side effects of medications limit their efficacy
  - ✓ Fatigue, impotence, bronchospasm, bradycardia with BB
  - ✓ Constipation, bradycardia and fatigue with CCB
  - ✓ QTC prolongation and torsades with norpace
  - ✓ Dry mouth, constipation, glaucoma, urinary retention with norpace
- Do not modify the underlying substrate
- Only work while taking the meds, making intercurrent illness and surgeries difficult to manage
  - ✓ An increasing concern as patients get older with obstructive HCM

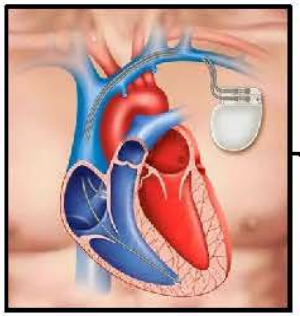
Invasive Therapies for HOCM



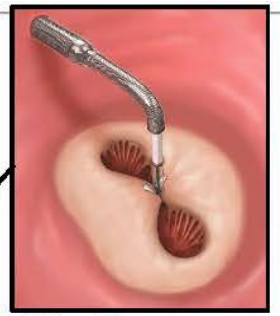
Alcohol Septal Ablation



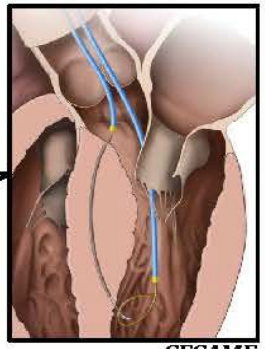
Septal Myectomy



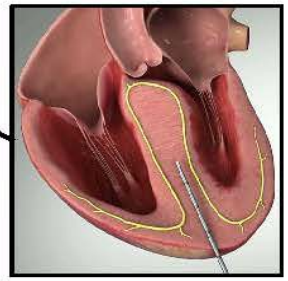
Cardiac Pacing



MitraClip



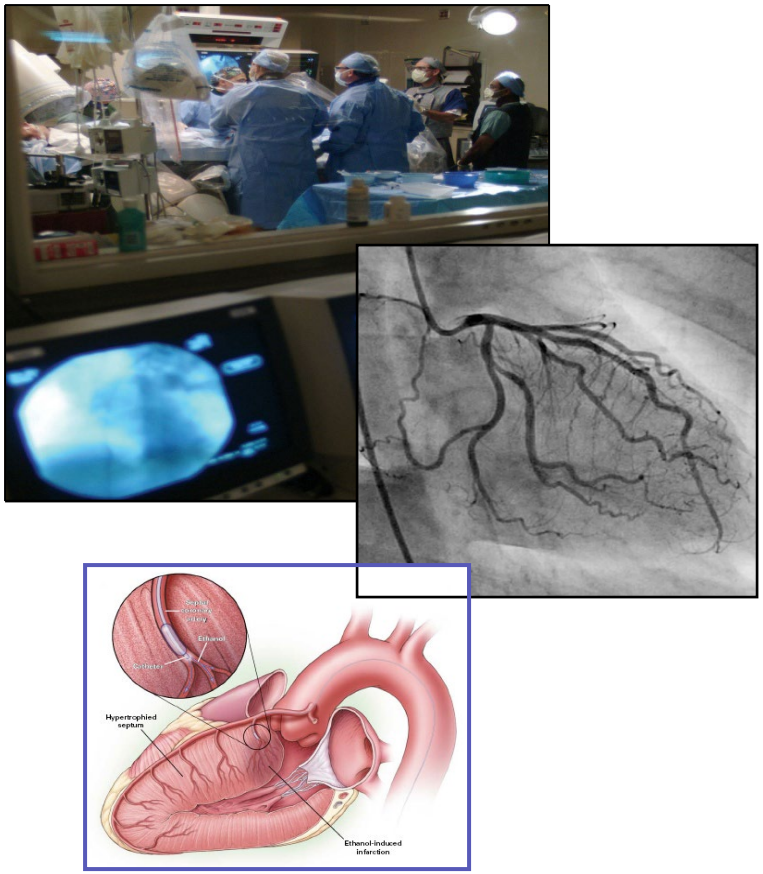
SESAME

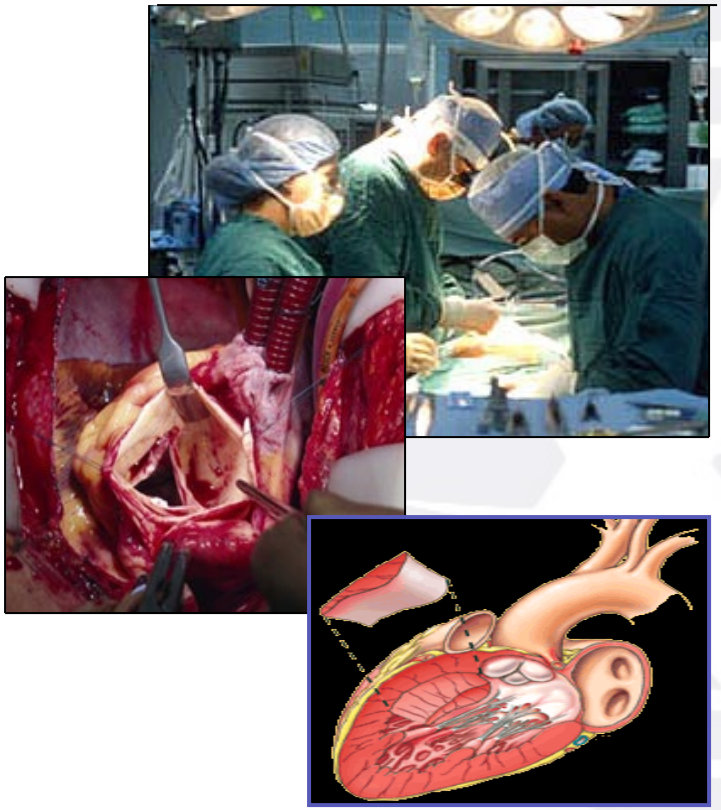


Radiofrequency Septal Ablation

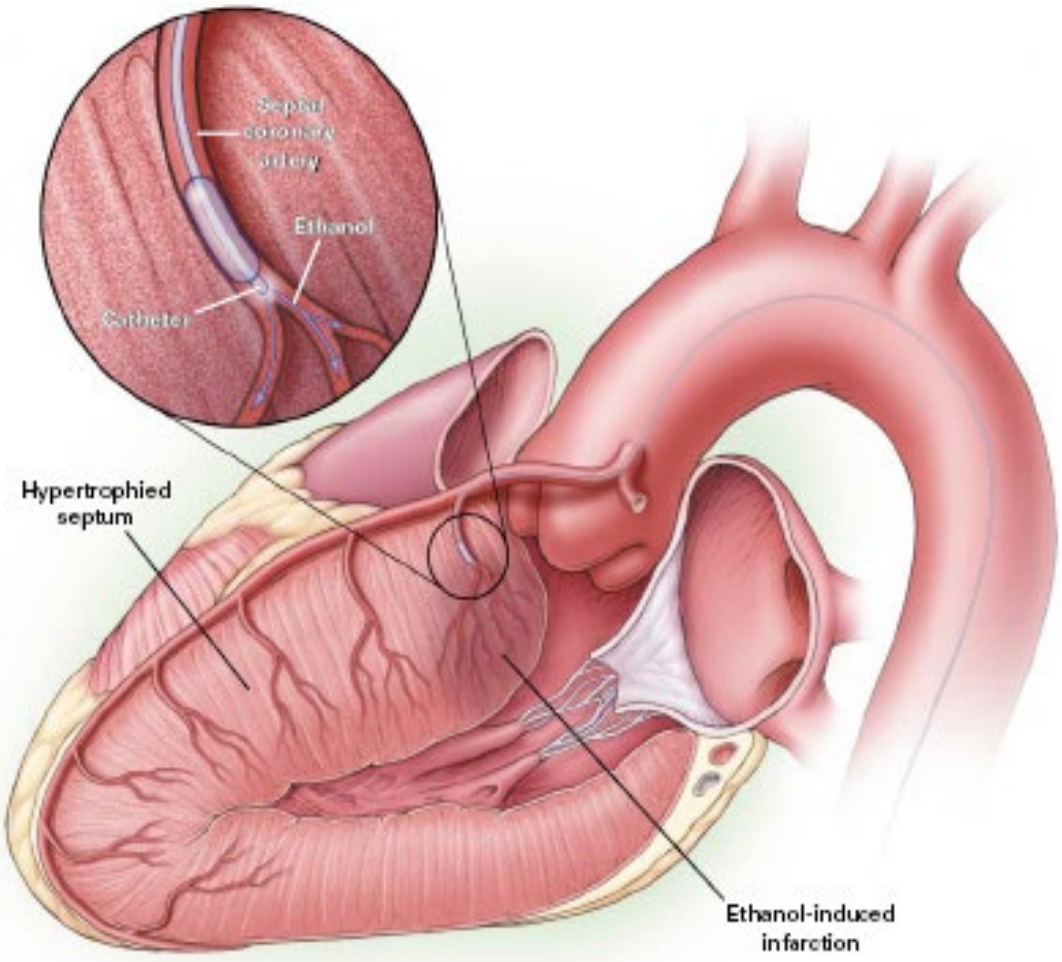
Rao SJ, Iqbal SB, Kanwal AS, Aronow WS, Naidu SS. *Hosp Pract 2023*

Alcohol Septal Ablation vs. Surgical Myectomy



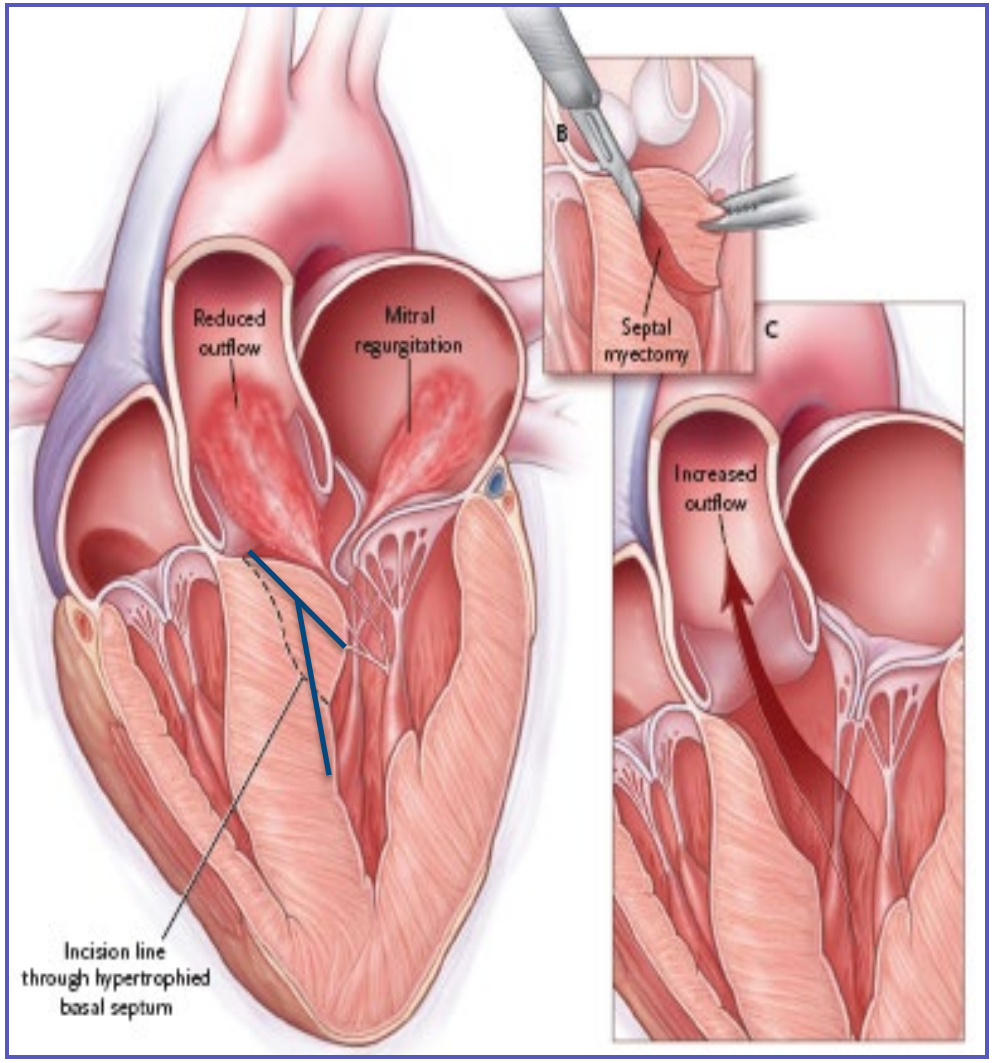


Alcohol Septal Ablation



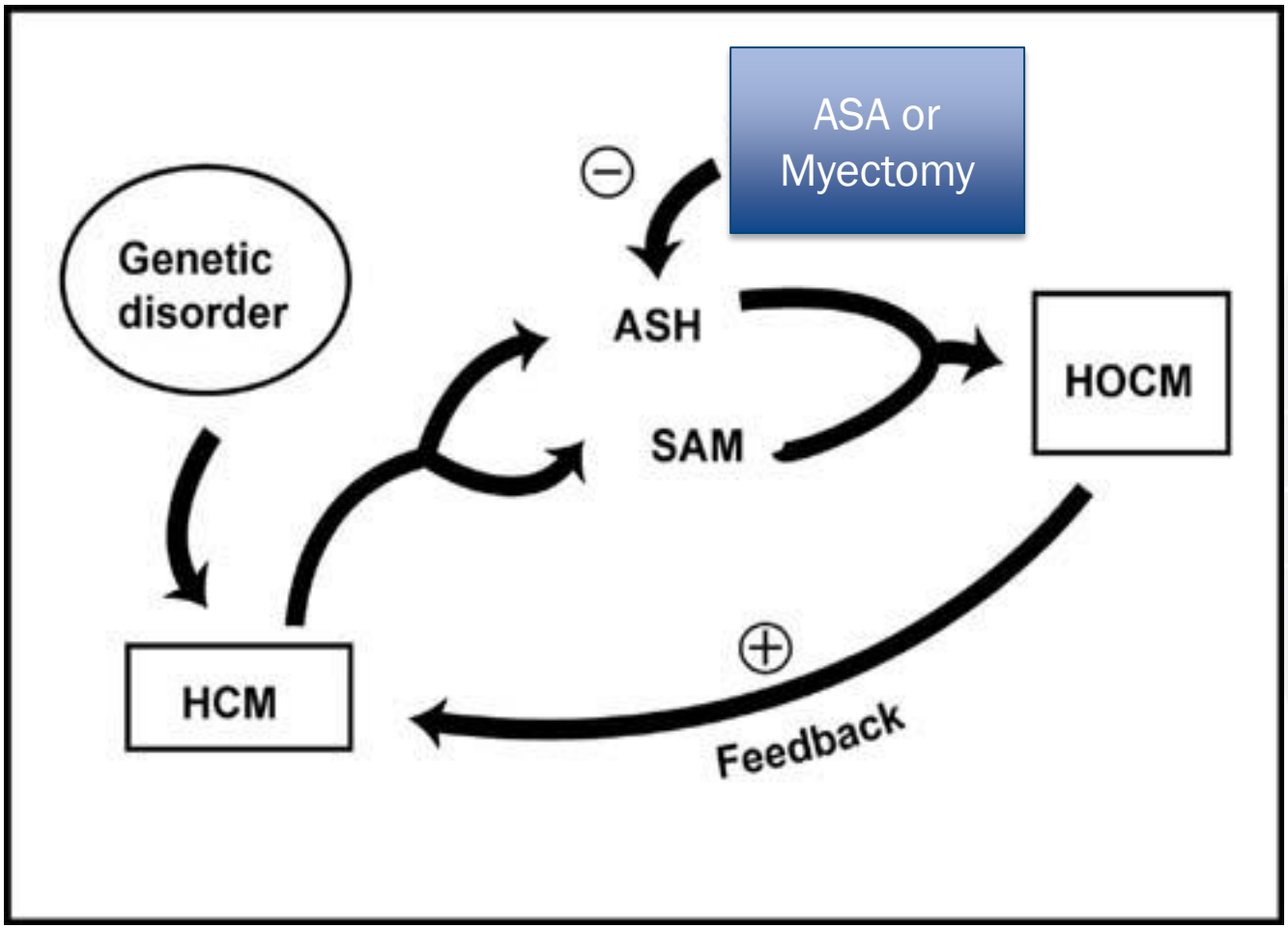
- Performed over 30 years
- Minimally invasive but requires expertise & team approach with echo guidance
- Avoids general anesthesia and intubation, and sternal incision and healing
- Maintains clinical benefits of surgery when done in appropriate patients, but only addresses basal LVOTO
- Reduced cost and LOS
- Higher PPM

Surgical Myectomy



- Performed over 50 years
- Fine-tuned at COEs
  - Significant expertise required
  - Two precise cuts, echo guided
- Excellent symptom improvement and long-term survival
- Can address multiple problems (valve, CAD, AF)
- Requires sternotomy, intubation, and associated morbidity
- Complications from above, riskier in older patients and those with co-morbidities

Mechanism of Action of SRT



- Obstruction
- Symptoms
- LVH
- MR
- PH
- LA Size

Alcohol Septal Ablation for the Treatment of Hypertrophic Obstructive Cardiomyopathy

A Multicenter North American Registry

Sherif F. Nagueh, MD,* Bertron M. Groves, MD,† Leonard Schwartz, MD,‡ Karen M. Smith, MD,§
Andrew Wang, MD,‖ Richard G. Bach, MD,¶ Christopher Nielsen, MD,# Ferdinand Leya, MD,**
John M. Buergler, MD,* Steven K. Rowe, MD,†† Anna Woo, MD,‡
Yolanda Munoz Maldonado, PHD,‡‡ William H. Spencer III, MD#

- 874 patients
- >95% improved to NYHA Class I (72.5%) / II (23%)
- Procedural Mortality 0.7%
- PPM implantation 8.9%
  - ✓ Decreased from 28% to 6.5% over time
  - ✓ Improvements to technique: team approach, reduced ETOH, targeted septals, MCE guidance, and active fixation TVP

Survival After Alcohol Septal Ablation for Obstructive Hypertrophic Cardiomyopathy

Mayo Clinic

Paul Sorajja, MD; Steve R. Ommen, MD; David R. Holmes, Jr, MD; Joseph A. Dearani, MD; Charanjit S. Rihal, MD; Bernard J. Gersh, MB, ChBDPhil; Ryan J. Lennon, MS; Rick A. Nishimura, MD

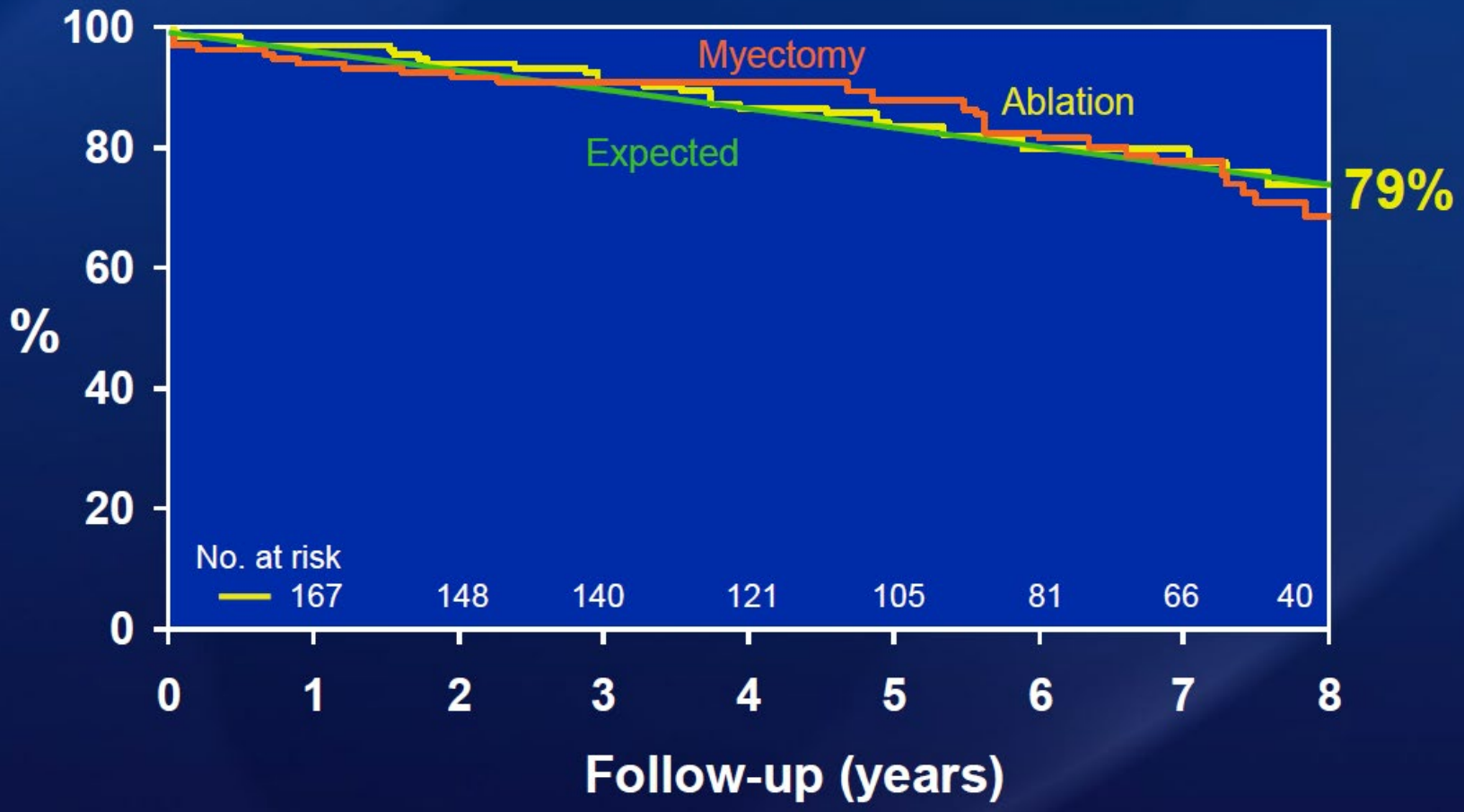
Background—The clinical efficacy of alcohol septal ablation for obstructive hypertrophic cardiomyopathy (HCM) has been demonstrated, but the long-term effects of the procedure remain uncertain. This study examined the survival of patients after septal ablation performed in a tertiary HCM referral center.

Methods and Results—We examined 177 patients (mean age, 64 years; 68% women) who underwent septal ablation at our institution. Over a follow-up of 5.7 years, survival free of all mortality was no different than the expected survival for a comparable general population, and similar to that of age- and sex-matched patients who underwent isolated surgical myectomy (8-year survival estimate, 79% versus 79%; $P=0.64$). For the end point of documented sudden cardiac death or unknown cause of death, the incidence per 100 person-year follow-up was 1.31 (95% confidence interval, 0.60–2.38). Residual left ventricular outflow tract gradient after ablation was an independent predictor of long-term survival free of any death.

Conclusions—In this nonrandomized study of carefully selected patients undergoing septal ablation by experienced operators in a tertiary referral HCM center, long-term survival was favorable and similar to that of an age- and sex-matched general population, and to patients undergoing surgical myectomy, as well, without an increased risk of sudden cardiac death. (*Circulation*. 2012;126:2374-2380.)

Survival After Ablation

Mayo Clinic



MAYO CLINIC

Sorajja et al, Circ. In Press

More Support for Long-Term Equipoise in Survival and SCD

A Systematic Review and Meta-Analysis of Long-Term Outcomes After Septal Reduction Therapy in Patients With Hypertrophic Cardiomyopathy

Max Liebregts, MD,* Pieter A. Vriesendorp, MD,† Bakhtawar K. Mahmoodi, MD, PhD, MPH,*
Arend F.L. Schinkel, MD, PhD,† Michelle Michels, MD, PhD,† Jurriën M. ten Berg, MD, PhD*

(J Am Coll Cardiol HF 2015;3:896–905)

FIGURE 2 Forest Plots and Pooled Estimates of All-Cause Mortality Rates After Alcohol Septal Ablation and Surgical Myectomy

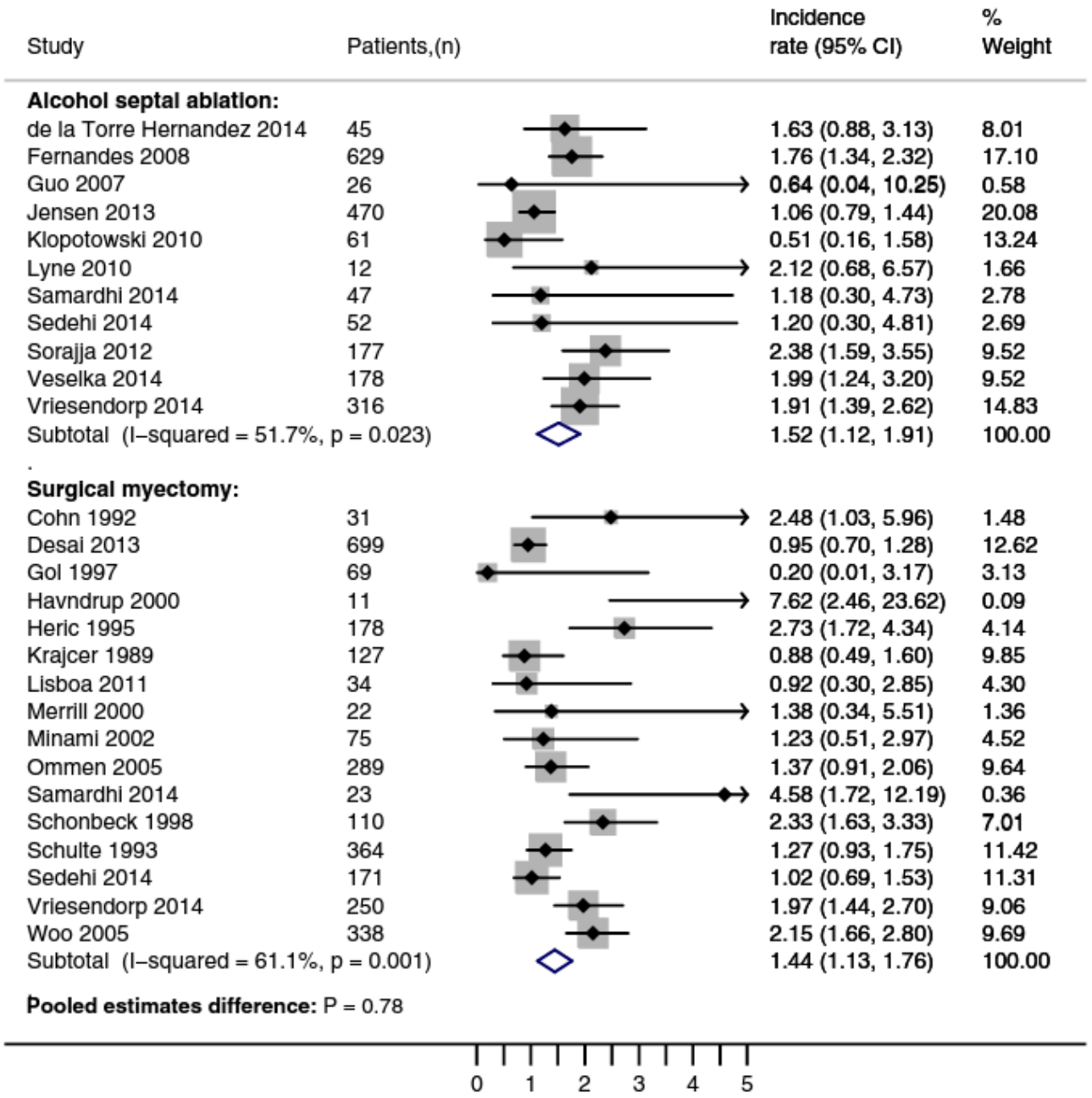


FIGURE 3 Forest Plots and Pooled Estimates of (Aborted) SCD Rates After Alcohol Septal Ablation and Surgical Myectomy, Including ICD Shocks

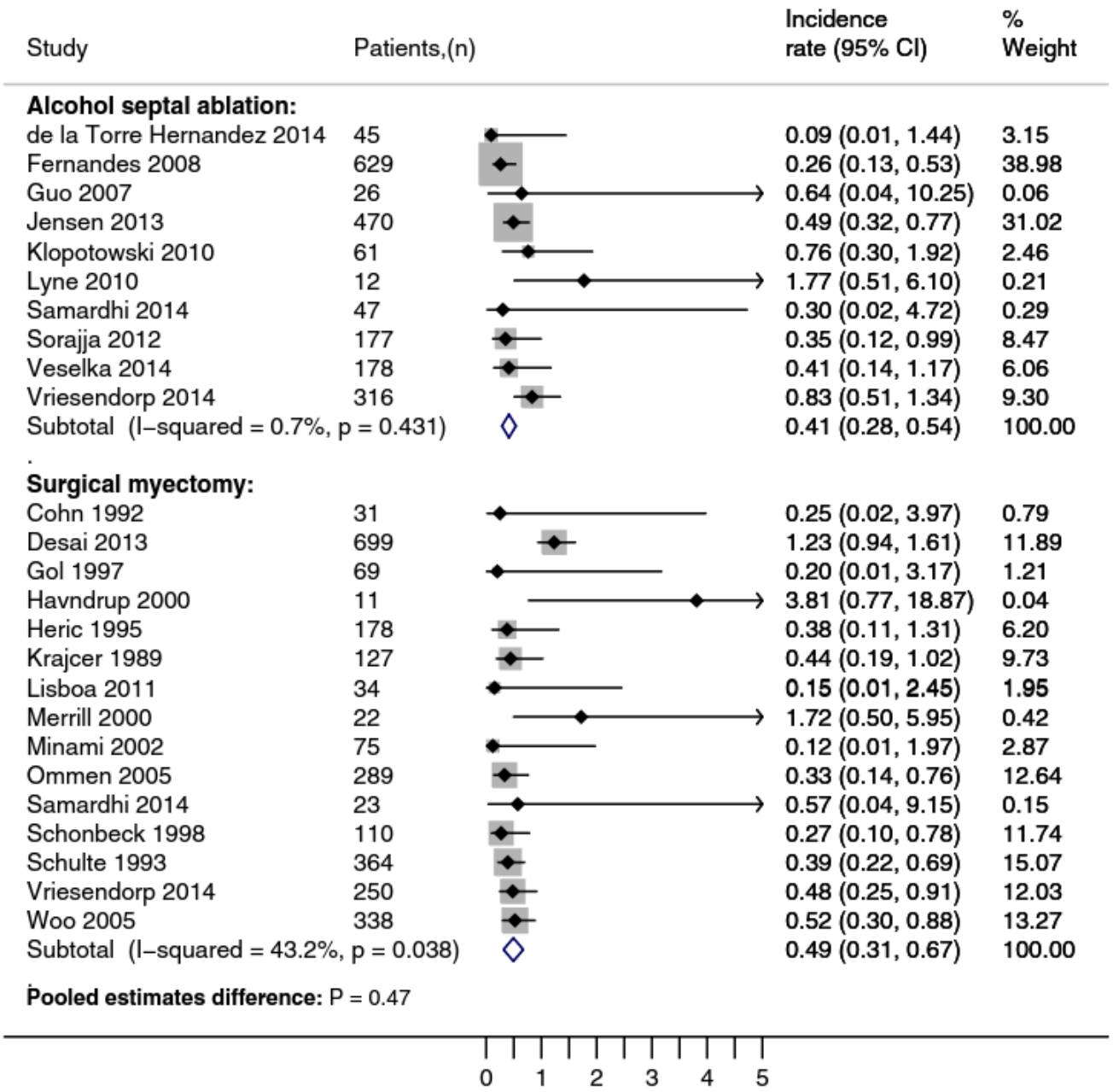


Table. Major Comparative Studies of the Outcomes of PTSMA and Surgical Myectomy

Author	Year		n	Age (years)	Follow-up period (years)	Pacemaker (%)	30-day mortality (%)	Sudden death (%)	Redo (%)
Meta-analysis									
Liebregts et al[49]	2015	Myectomy	2,791	47	7.4	4.4	2.5		1.6
		PTSMA	2,013	56	6.2	10.0	1.3		7.7
Singh et al[50]	2016	Myectomy	1,019	44±12	4.5±4.4		1.6	1.9	1.5
		PTSMA	805	49±14	2.9±2.0		1.0	1.9	9.9
Retrospective cohorts									
Sorajja et al[8]	2012	Myectomy	177	62±12	–	4.3	0.6	1.7	–
		PTSMA	177	63±13	5.7	1.7	1.1	1.7	10.2
Steggerda et al[51]	2014	Myectomy	102	56±16	9.1	9	2.0		1.0
		PTSMA	161	59±14	5.1	11	1.2		6.3
Samardhi et al[52]	2014	Myectomy	23	47	3.8	13	8.7		0
		PTSMA	47	54	3.6	15	0		17.0
Vriesendorp et al[53]	2014	Myectomy	253	52±16	7.1	11.6		2.4	2.3
		PTSMA	321	58±14	6.3	13.0		1.9	9.7

PTSMA, percutaneous transluminal septal myocardial ablation.

Favors Surgery: PPM and Redo rates higher with alc ablation

Favors ASA: 30-d Mortality rate and Cost higher with surgery

These Studies All Compare High Volume ASA COE's to High Volume SM COE's

What About Real-World?

Original Investigation

Hospital Volume Outcomes After Septal Myectomy and Alcohol Septal Ablation for Treatment of Obstructive Hypertrophic Cardiomyopathy

US Nationwide Inpatient Database, 2003-2011

Luke K. Kim, MD; Rajesh V. Swaminathan, MD; Patrick Looser, MD; Robert M. Minutello, MD; S. Chiu Wong, MD; Geoffrey Bergman, MD; Srihari S. Naidu, MD; Christopher L. F. Gade, MD; Konstantinos Charitakis, MD; Harsimran S. Singh, MD; Dmitriy N. Feldman, MD

JAMA Cardiol. 2016;1(3):324-332. doi:10.1001/jamacardio.2016.0252
Published online April 27, 2016. Corrected on January 4, 2017.

Figure 2. Adverse In-Hospital Event Rates After Septal Myectomy and Alcohol Septal Ablation by Tertiles of Hospital Volume

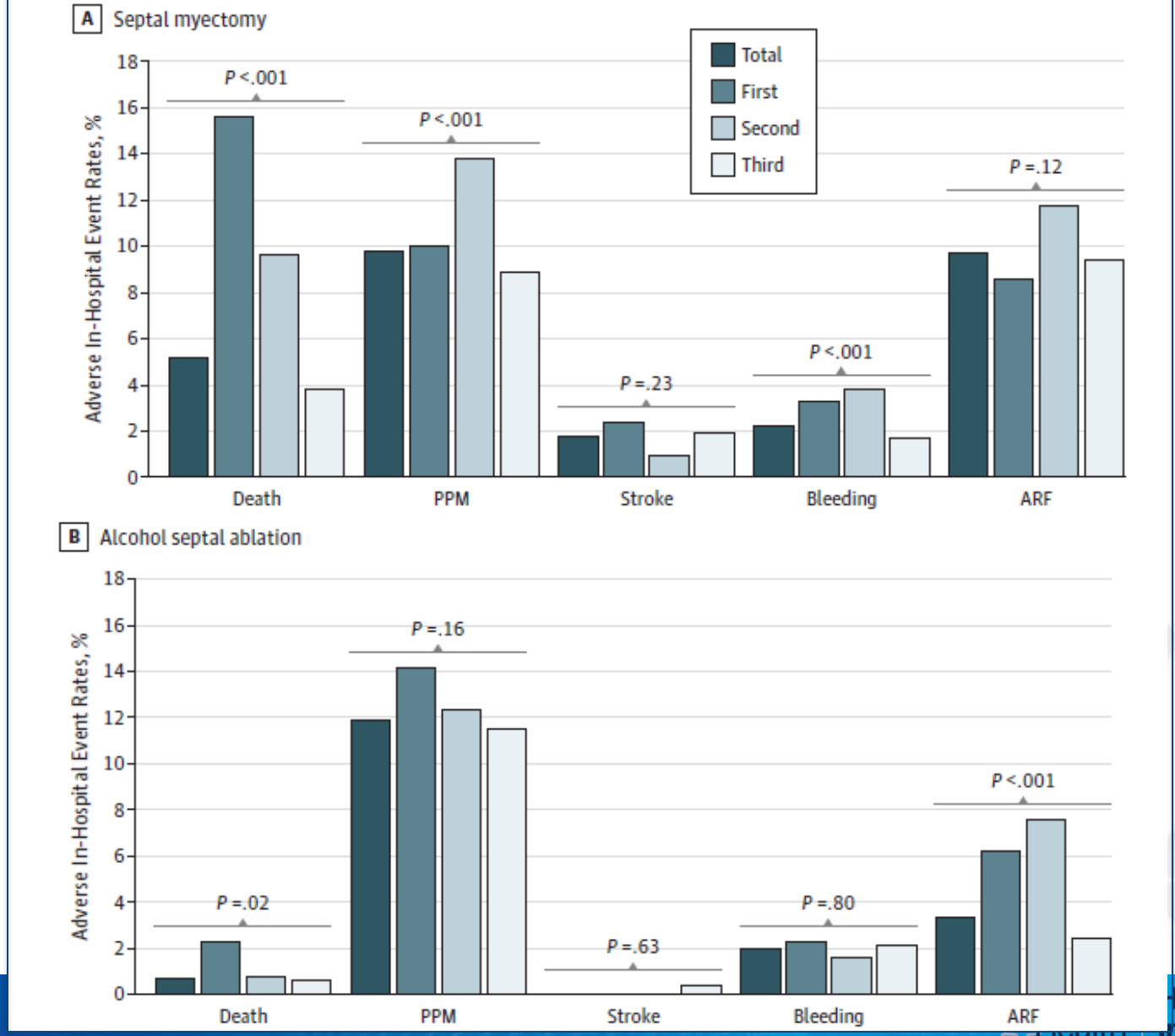
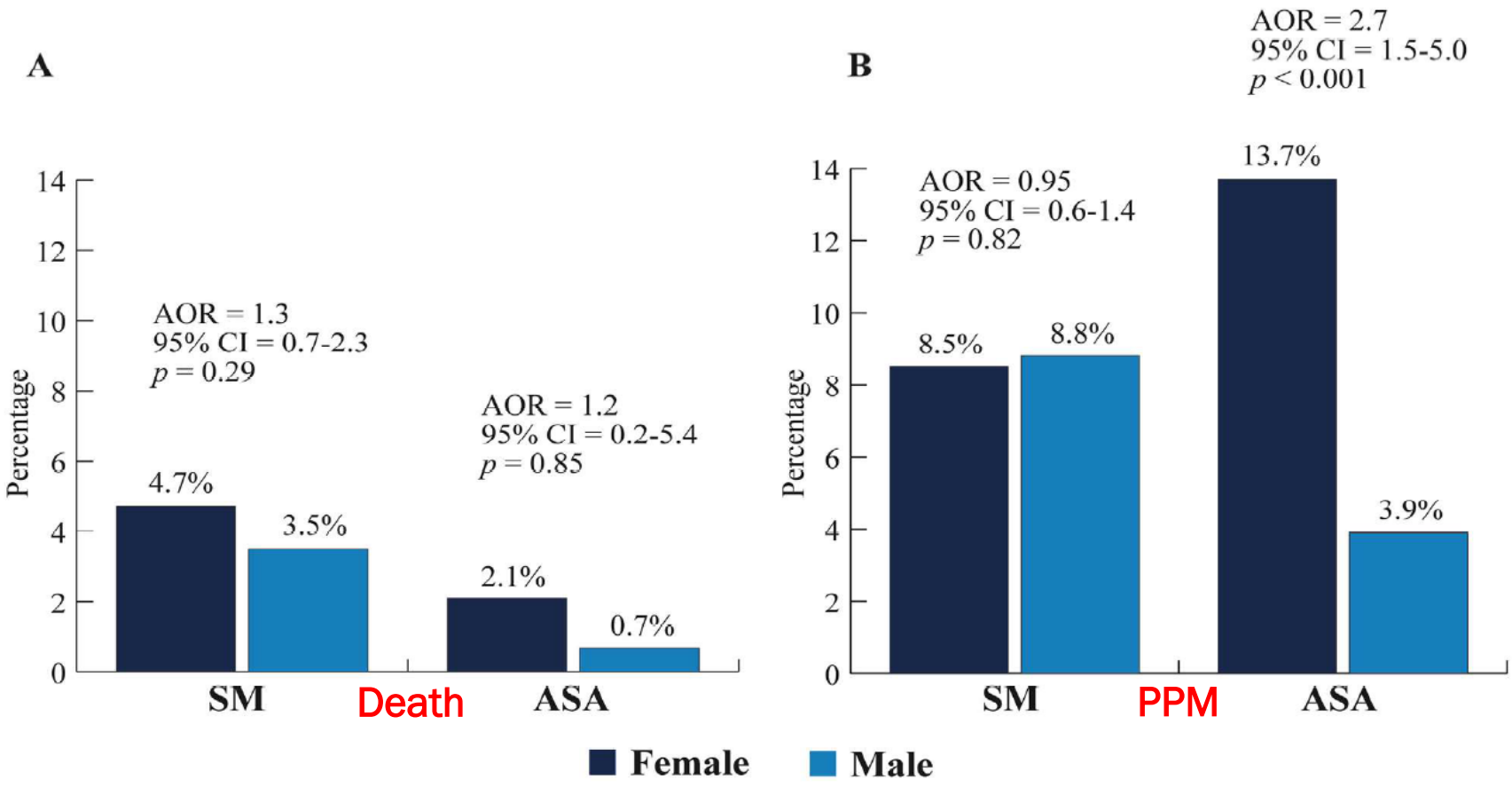


FIGURE 1 Sex Differences in Outcomes Following Septal Reduction Therapy for Obstructive Hypertrophic Cardiomyopathy

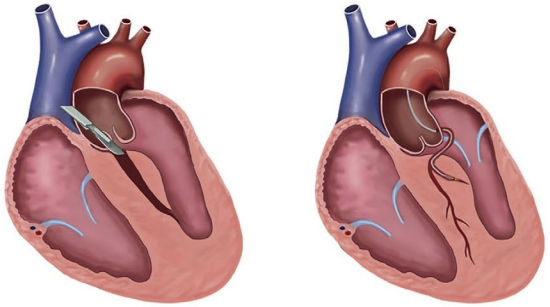


Sex-differences in the **(A)** in-hospital mortality and **(B)** permanent pacemaker implantation rates following septal myectomy (SM) or alcohol septal ablation (ASA) for obstructive hypertrophic cardiomyopathy. Odds ratio was adjusted for age, race, hospital characteristics (urban location, bed size, and teaching status) and Elixhauser comorbidities (myocardial infarction, congestive heart failure, peripheral arterial disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatic disease, peptic ulcer disease, liver diseases, diabetes mellitus with and without complications, hemiplegia or paraplegia, renal disease, malignancy, and human immunodeficiency virus infection). AOR = adjusted odds ratio; CI = confidence interval.

CENTRAL ILLUSTRATION: Summary of Study Findings

A Breakdown of Septal Reduction Therapy Procedures

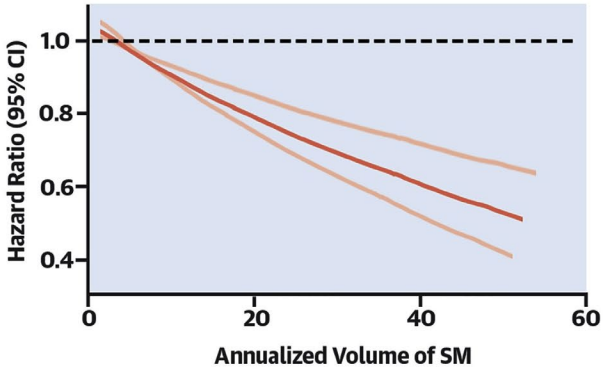
Septal Myectomy (SM) N = 3,680	Alcohol Septal Ablation (ASA) N = 1,999



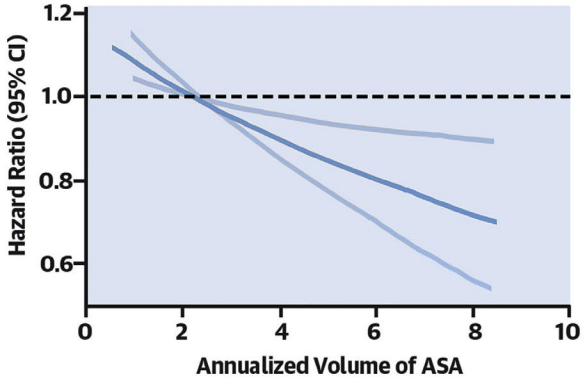
B Primary Findings of the Study

- ↑ Higher complications up to 3 months following SM vs ASA
- ↓ On landmark analysis, SM had better survival after 3 months vs ASA (HR: 0.73, 95% CI: 0.60-0.88, *P < 0.001*)
- ↓ Need for redo SRT after SM vs ASA (HR: 0.10, 95% CI: 0.0607-0.1915, *P < 0.001*)
- ↓ Both SRT reduced HF readmission burden

C Mortality Hazard Ratio as Function of Annualized SM Center Volume



D Mortality Hazard Ratio as Function of Annualized ASA Center Volume



Despite higher volume centers demonstrating better outcomes vs lower-volume centers, 70% of SRT were performed in low-volume centers

Mentias A, et al. J Am Coll Cardiol. 2023;81(2):105-115.

Mortality NS

SM ↑ stroke, Mortality (2X) & ESRD/HD early (procedural)

ASA ↑ mortality Late (25%) (procedural or unmeasured confounders)

SM not as Generalizable

NS early or late in highest volume centers (COEs)

Journal of the American Heart Association

ORIGINAL RESEARCH

Hospital Procedural Volume and Clinical Outcomes Following Septal Reduction Therapy in Obstructive Hypertrophic Cardiomyopathy

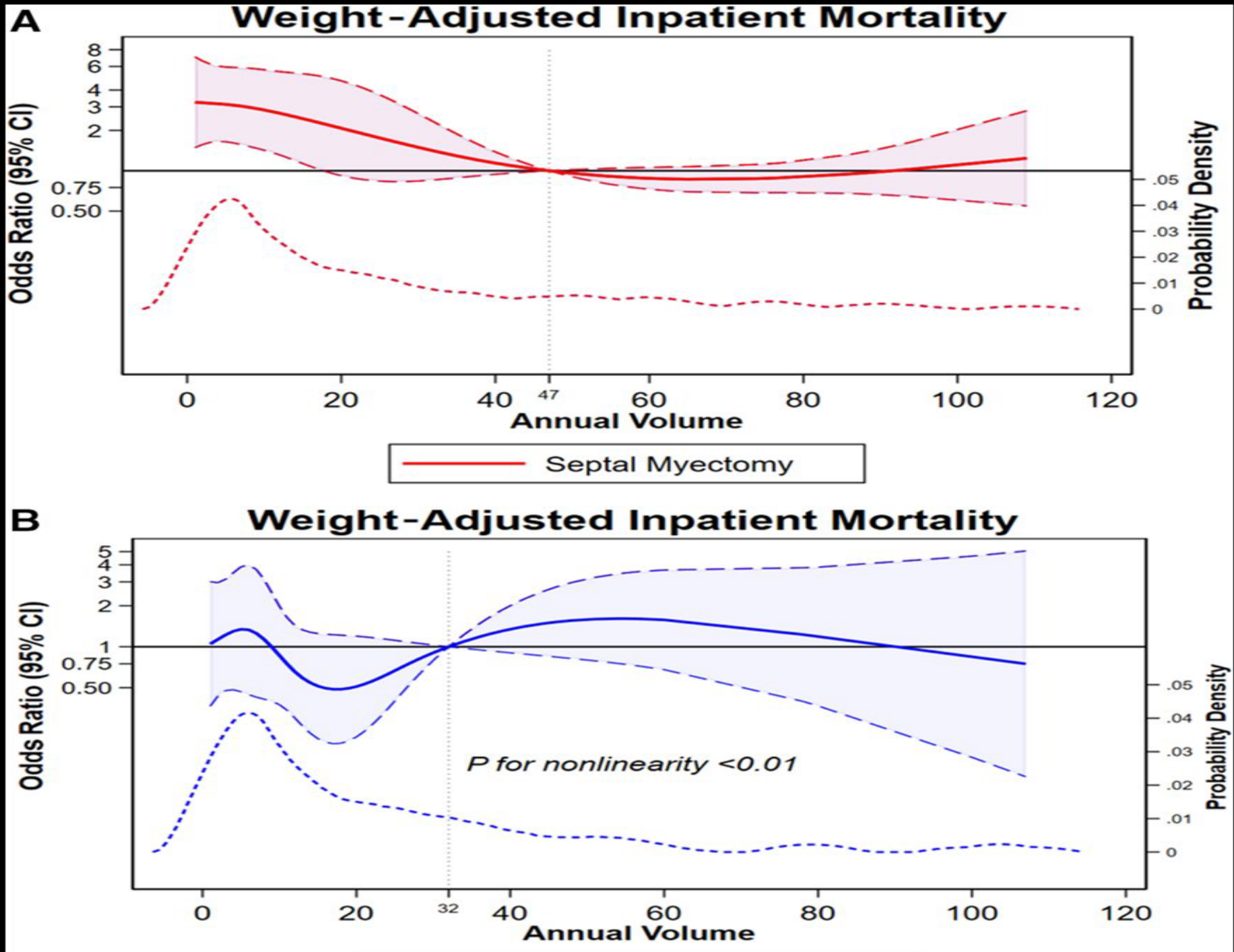
Ahmed M. Altibi, MD, MPH; Fares Ghanem, MD; Yuanzi Zhao, MD, PhD; Miriam Elman, MS MPH; Joaquin Cigarroa, MD; Babak Nazer, MD; Howard K. Song, MD, PhD; Ahmad Masri, MD, MS

BACKGROUND: Prior national data showed a substantial in-hospital mortality in septal myectomy (SM) with an inverse volume–outcomes relationship. This study sought to assess the contemporary outcomes of septal reduction therapy and volume–outcome relationship in obstructive hypertrophic cardiomyopathy.

METHODS AND RESULTS: All septal reduction therapy admissions between 2010 to 2019 in the United States were analyzed using the National Readmission Databases. Hospitals were stratified into tertiles of low-, medium-, and high-volume based on annualized procedural volume of alcohol septal ablation and SM. Of 19007 patients with obstructive hypertrophic cardiomyopathy who underwent septal reduction therapy, 12065 (63%) had SM. Two-thirds of hospitals performed ≤5 SM or alcohol septal ablation annually. In all SM encounters, 482 patients (4.0%) died in-hospital post-SM. In-hospital mortality was <1% in 1505 (88.4%) hospitals, 1% to 10% in 30 (1.8%) hospitals, and ≥10% in 167 (9.8%) hospitals. There were 63 (3.7%) hospitals (averaging 2.2 SM cases/year) with 100% in-hospital mortality. Post-SM (in low-, medium-, and high-volume centers, respectively), in-hospital mortality (5.7% versus 3.9% versus 2.4%, *P*=0.003; adjusted odds ratio [aOR], 2.86 [95% CI, 1.70–4.80], *P*=0.001), adverse in-hospital events (21.30% versus 18.0% versus 12.6%, *P*=0.001; aOR, 1.88 [95% CI, 1.45–2.43], *P*=0.001), and 30-day readmission (17.1% versus 12.9% versus 9.7%, *P*=0.001; adjusted hazard ratio, 1.53 [95% CI, 1.27–1.96], *P*=0.001) were significantly higher in low- versus high-volume hospitals. For alcohol septal ablation, the incidence of in-hospital death and all other outcomes did not differ by hospital volume.

CONCLUSIONS: In-hospital SM mortality was 4% with an inverse volume-mortality relationship. Mortality post-alcohol septal ablation was similar across all volume tertiles. Morbidity associated with SM was substantial across all volume tertiles.

Key Words: alcohol septal ablation ■ hypertrophic cardiomyopathy ■ septal myectomy ■ septal reduction therapy


A
Weight-Adjusted Inpatient Mortality
Odds Ratio (95% CI)
8
6
4
3
2
0.75
0.50
Probability Density
.05
.04
.03
.02
.01
0
0
20
40
47
60
80
100
120
Annual Volume
Septal Myectomy
B
Weight-Adjusted Inpatient Mortality
Odds Ratio (95% CI)
5
4
3
2
1
0.75
0.50
P for nonlinearity <0.01
Probability Density
.05
.04
.03
.02
.01
0
0
20
32
40
60
80
100
120
Annual Volume

Studies Using Peak VO2 as Endpoint

Study	Disease	n	Intervention	Change in peak VO_2 mL/kg/min
Firoozi et al. EHJ 2002	HCM	24	Myectomy	6.7
Firoozi et al. EHJ 2002	HCM	20	ASA	3.1
Malek et al. EJHF 2008	HCM	23	ASA	4
Abozguia et al. Circ 2010	HCM	46	Exercise	1.4
Saberi et al. JAMA 2017	HCM	113	Exercise	1.3
Swank et al. Circ HF 2012	HFrEF	1620	Exercise	0.4
Cazeau et al. NEJM 2001	HFrEF	38	BiV Pacing	1.2

Difference in age b/w ASA and SM ~ 15 years, relative % improvement VO2 same
Overall increased pVO2 by 4-6 c/w exercise and other options

Pharmacological and non-pharmacological treatment of obstructive hypertrophic cardiomyopathy

Luis F. Hidalgo, Srihari S. Naidu and Wilbert S. Aronow

Department of Medicine, Division of Cardiology, Westchester Medical Center, New York Medical College, Valhalla, NY, USA

HCM Heart Team Concept →

Evaluation by multidisciplinary team
Interventional cardiologist, Imaging cardiologist and a Cardiothoracic Surgeon

Naidu, Panza, Spielvogel
Malekan, Mittnacht
Fuisz, Ranjan, Spevack
HF/Tx Attg PRN
Pediatric Cards/CTS PRN
NP/PA/Coordinators

Septal Myectomy:
Usually younger patients
Low surgical risk
To be avoided in patients with right bundle branch block

Factors to be evaluated include:
Age, Comorbidities, risk for surgery, LVOT, mitral and coronary anatomy, Baseline electrocardiogram, pre-existent PPM or ICD, Patient preference, hospital volume, severity of gradient, septal thickness

Alcohol Septal Ablation
Older patients
Higher surgical risk
To be avoided in patients with left bundle branch Block

Figure 1. Treatment of symptomatic obstructive hypertrophic cardiomyopathy.

EXPERT REVIEW OF CARDIOVASCULAR THERAPY, 2018
VOL. 16, NO. 1, 21–26

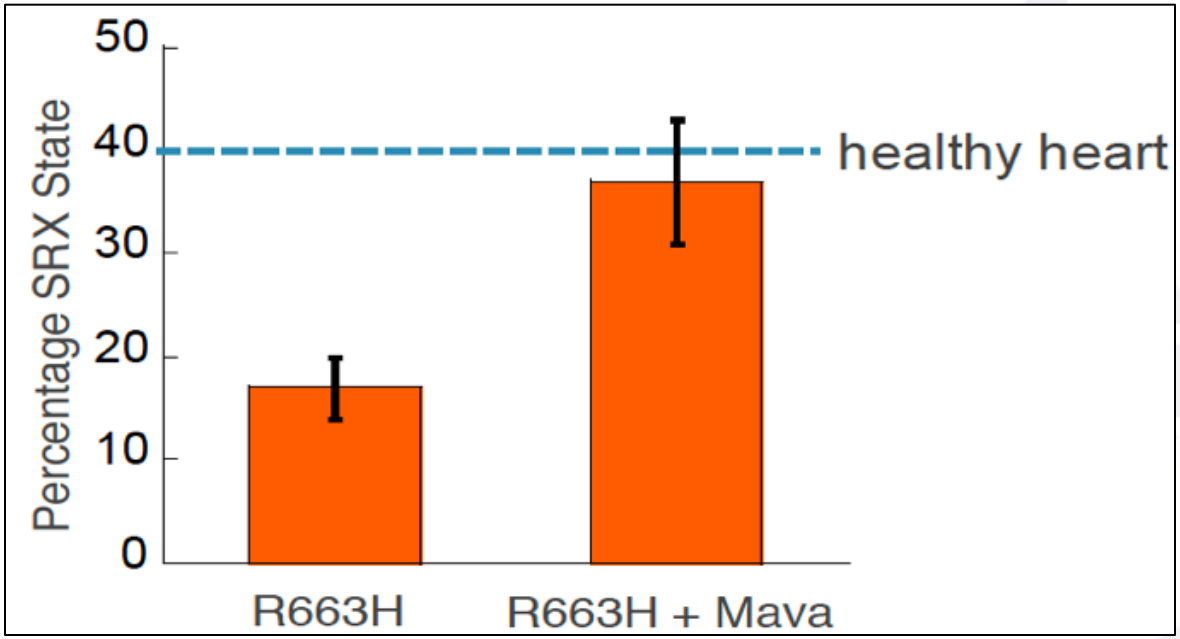
Guidelines 2020

- Both alcohol ablation and surgical myectomy moved to Class 1 recommendations for
  - ✓ Symptomatic
  - ✓ Appropriate anatomy and hemodynamics
  - ✓ Expertise and volume / outcome thresholds
- Developing recommendations for earlier SRT (particularly surgical myectomy, but also alcohol ablation) in patients with lesser symptomatic status if also with PAF, syncope, or PH
- Pendulum was swinging toward earlier SRT

Along come the CMIs (Mava and Afi):
Dealing with the sarcomere

MYK-461 Mavacamten	CK-274 Aficamten

% Myosin
In OFF-STATE
~ Normalizes



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ORIGINAL INVESTIGATIONS

Myosin Inhibition in Patients With Obstructive Hypertrophic Cardiomyopathy Referred for Septal Reduction Therapy

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VALOR-HCM: A Phase 3 Trial for SRT-Eligible Adults With Severely Symptomatic Obstructive HCM[1,2]

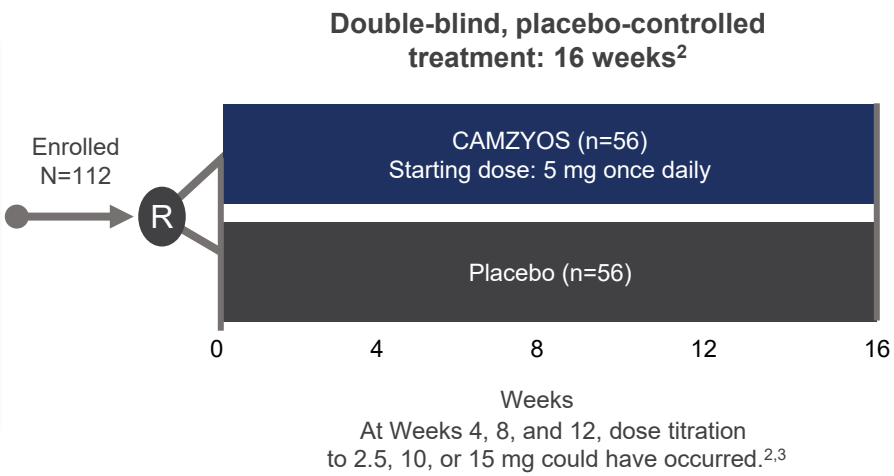
A randomized, double-blind, placebo-controlled trial that evaluated the impact of CAMZYOS on SRT eligibility[1,2]

Select inclusion criteria[1,2]

- Adults who were guideline-eligible for SRT, referred within the past 12 months, and are actively considering the procedure
  - NYHA Class II with exertional syncope or near syncope or NYHA Class III–IV
  - LVOT peak gradient ≥50 mmHg at rest or with provocation
- LVEF ≥60%

Select exclusion criteria[3]

- Known infiltrative or storage disorder that mimics obstructive HCM*
- Planned invasive procedure during the first 32 weeks of the study
- Dose adjustment of medications used to treat HCM <14 days prior to screening or within the first 16 weeks of the study
- Prior treatment with invasive SRT†



95% of patients were on background therapy with a BB, a CCB, or disopyramide, administered as monotherapy or combination therapy[1,2]

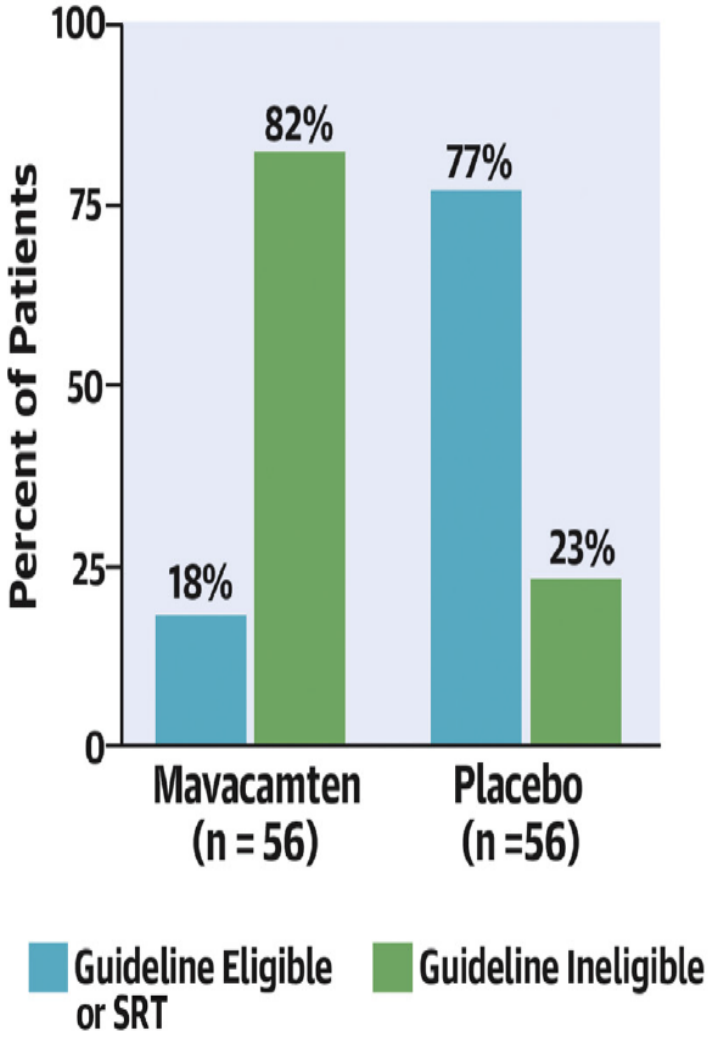
CAMZYOS (n=53/56) | Placebo (n=53/56)

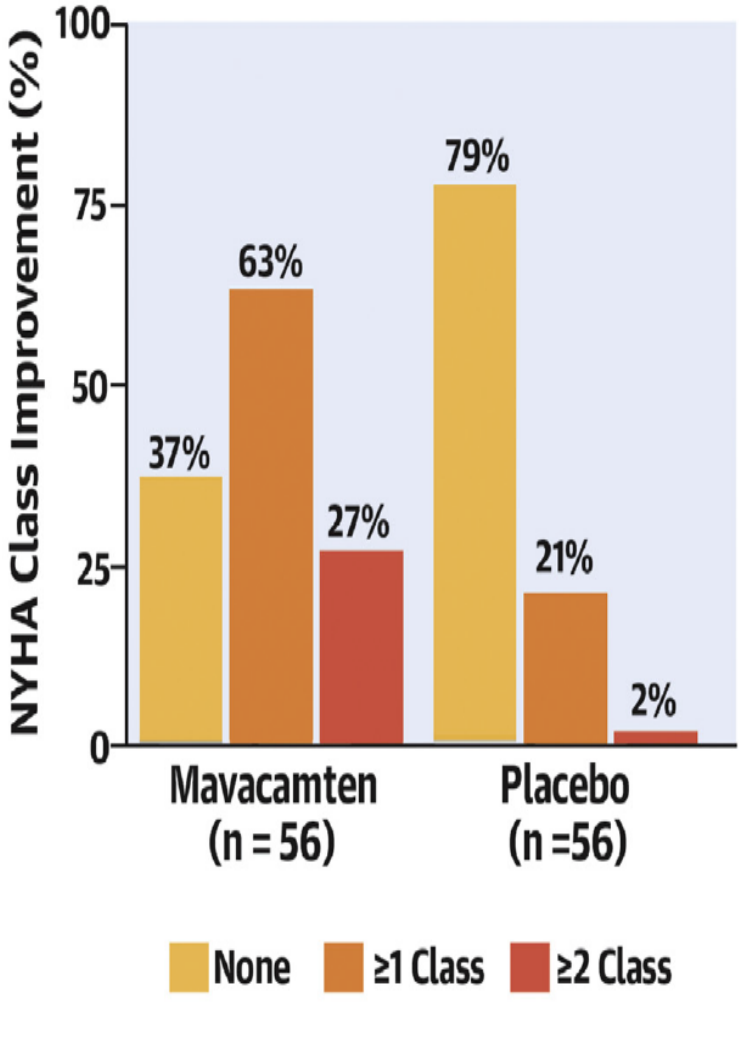
*Includes Fabry disease, amyloidosis, or Noonan syndrome with LVH.[3]

†Patients with suboptimal or failed SRT were considered for enrollment based on study sponsor consultation.[3]

BB=beta blocker; CCB=calcium channel blocker; HCM=hypertrophic cardiomyopathy; LVEF=left ventricular ejection fraction; LVH=left ventricular hypertrophy; LVOT=left ventricular outflow tract; NYHA=New York Heart Association; R=randomized; SRT=septal reduction therapy.

1. CAMZYOS (mavacamten) Product Information (https://rss.medsinfo.com.au/bq/pi.cfm?product=bqpcamzo). **2**. Desai MY, et al. *J Am Coll Cardiol*. 2022;80(2):95-108. **3**. Desai MY, et al. *J Am Coll Cardiol*. 2022;80(2):95-108 [supplementary appendix].





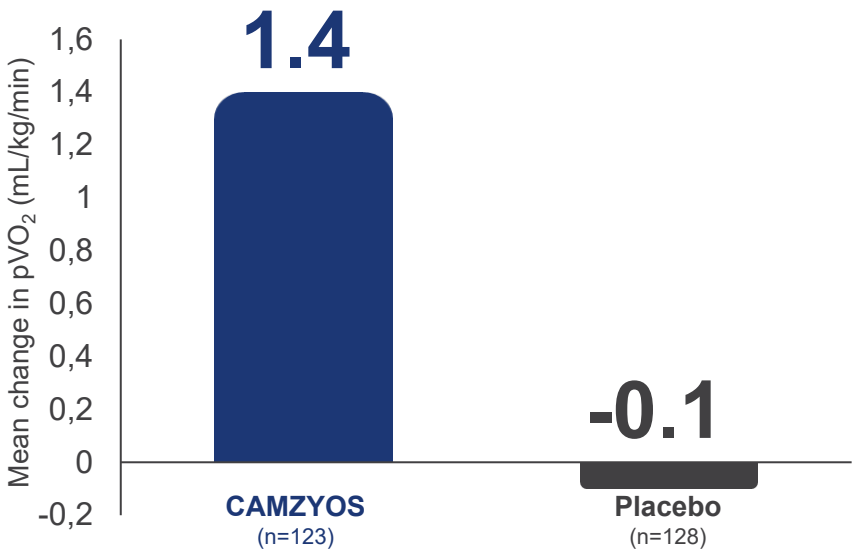
Desai MY, et al. J Am Coll Cardiol. 2022;80(2):95-108.

Secondary endpoint: the effect of mavacamten on pVO_2 vs Placebo[1]

Secondary endpoint: Mean change in pVO_2 from baseline to Week 30*[1,2]

Difference (95% CI): 1.4 (0.6, 2.1)

***P*=0.0006**



- Mean (SD) change in pVO_2 from baseline to Week 30[1]:
  - 1.4 (3.1) mL/kg/min for CAMZYOS
  - -0.1 (3.0) mL/kg/min for placebo

- In other studies, an increase in pVO_2 of ≥1 mL/kg/min has been suggested to represent a clinically relevant threshold of improvement for HCM[3]

Data based on all randomized patients who received ≥1 dose of study treatment.[2]
*pVO_2 measures peak oxygen consumption during CPET.[3]
CI=confidence interval; CPET=cardiopulmonary exercise testing; HCM=hypertrophic cardiomyopathy; NYHA=New York Heart Association; pVO_2=peak oxygen consumption; SD=standard deviation.
1. CAMZYOS (mavacamten) Product Information (https://rss.medsinfo.com.au/bq/pi.cfm?product=bqpcamzo). **2.** Olivotto I, et al. *Lancet.* 2020;396(10253):759-769. **3.** Ho CY, et al. *Circ Heart Fail.* 2020;13(6):e006853.

Mavacamten Patients (n=25)

- Functional Status Improvement
  - ✓ Mean NYHA Class 2.2 → 1.2 at last f/u
- Peak Gradient Improvement
  - ✓ Mean 92.5 mm Hg → 20.2 mm Hg at last f/u

Additional Meds Considerations

- Most people can decrease their other meds once on CMI, and thus side effects may improve
  - ✓ Less fatigue
  - ✓ Less chronotropic incompetence
  - ✓ Less erectile dysfunction
  - ✓ Less norpace side effects and QTc prolongation
- Still a role for disopyramide in:
  - ✓ Elderly with focal ASH
  - ✓ Patients with AF and LVOTO physiology
  - ✓ Those who want to avoid SRT but can't get or take CMI

What are the concerns?

- Patient access
  - ✓ Insurance authorization and cost
  - ✓ Logistics of REMS rollout
- Systolic heart failure from excessive LV dysfunction
  - ✓ Due to inappropriately high or rapid dosing escalation
  - ✓ Due to drug interactions that either compound the effect on LV dysfunction or increase / decrease mava levels
- Interaction with efficacy of other medications
  - ✓ Birth control pills*
- Potential concerns
  - ✓ Pregnancy (fetal toxicity) and Lactation
  - ✓ Atrial fibrillation

Who might be better served with SRT?

- Young patients < 40 who want to have children and/or want to eliminate the need for or side effects of medications
- Willing to accept risks of PPM and invasive Rx (lower in younger to middle aged patients)
- Older patients with focal basal hypertrophy in whom alcohol ablation would have high safety and efficacy (and mava unlikely to be approved) and PPM risk not an issue
- Patients with recurrent PAF or borderline EF
- Intrinsic valve disease or significant CAD
- Those who simply would rather an invasive approach over long term medications, monitoring and testing
- Pre-TAVR or TMVR

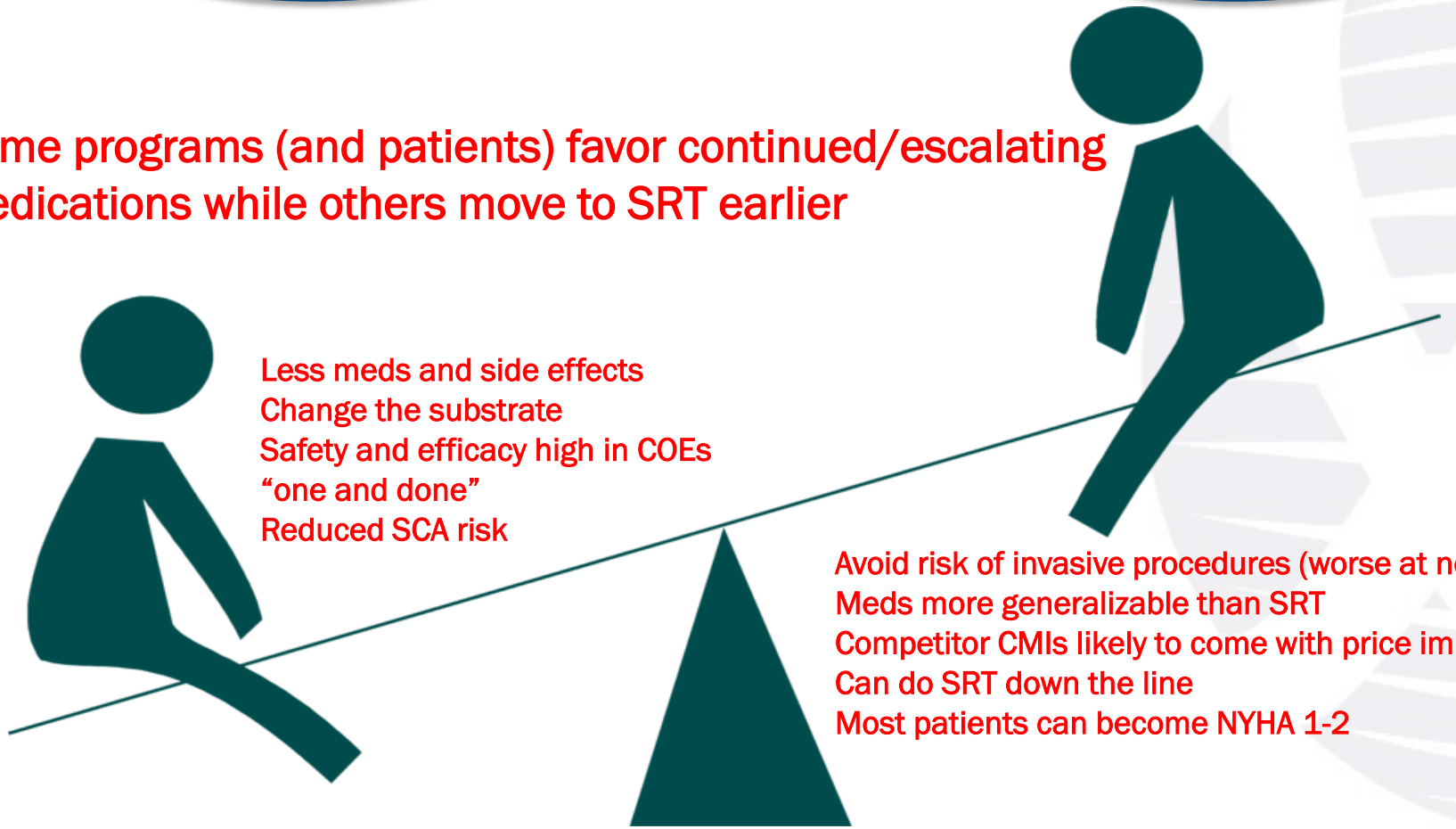
Septal Reduction

Alcohol Ablation,
Myectomy

Medications

CMIs
(BB, CCB,
Disopyramide)

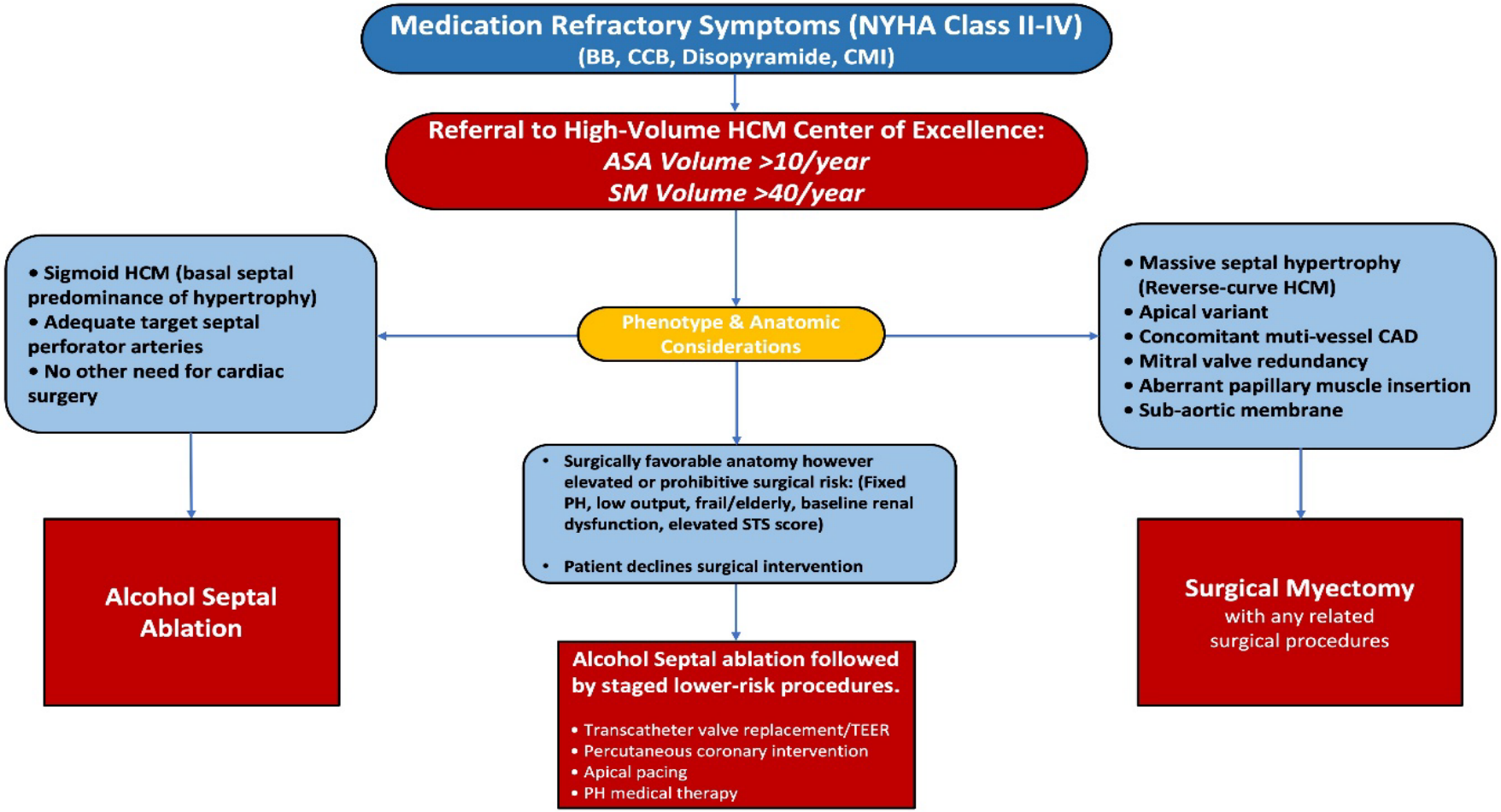
Some programs (and patients) favor continued/escalating medications while others move to SRT earlier



Less meds and side effects
Change the substrate
Safety and efficacy high in COEs
"one and done"
Reduced SCA risk

Avoid risk of invasive procedures (worse at non COEs)
Meds more generalizable than SRT
Competitor CMIs likely to come with price improvement
Can do SRT down the line
Most patients can become NYHA 1-2

Central Illustration: Septal Reduction Therapy Algorithm for Obstructive HCM



Abbreviations:
NYHA – New York Heart Association
HCM – hypertrophic cardiomyopathy, ASA – alcohol septal ablation, SM – surgical myectomy, BB – beta blockers, CCB – calcium channel blockers, CMI – cardiac myosin inhibitor, CAD – coronary artery disease, CKD - Chronic kidney disease, PH – pulmonary hypertension, TEER – transcatheter edge-edge repair

Bali AD, Malik A, Naidu SS

Central Illustration: Proposed algorithm for septal reduction therapy in patients with symptoms refractory to medical therapy, integrating hospital and operator volumes for both ASA and SM.

Summary: Mava or SRT?

- **Novel Meds**
  - ✓ Avoid invasive procedure and risks (PPM, VSD, Bleeds, Stroke)
  - ✓ Can defer SRT for a later time if needed
  - ✓ May target diastolic dysfunction and fibrosis in addition to obstruction
  - ✓ REMS program, at risk populations, and significant drops in EF may limit use (esp in AF)
  - ✓ Marginal improvement in pVO2 c/w SRT (so far)
  - ✓ Robust data and long term data will take time
- **Invasive Therapies (SM and ASA)**
  - ✓ May double the VO2 increase, although no head-to-head comparisons
  - ✓ More significant and durable improvement in NYHA class (70% I, 20% II)
  - ✓ Large clinical data on outcomes, including survival (out to 10-15 years now)
  - ✓ Many patients can eliminate medications and associated side effects
  - ✓ Reduction in SCA risk and mortality appearing in long-term data
  - ✓ Procedural risks have come down significantly with volume
  - ✓ Significant regional variability in use and outcomes (not generalizable to wider community)
  - ✓ PPM and open surgical complications inherent to invasive procedures

HCM Center of Excellence

Clinical Trials and Observational Research
VALOR
SEQUOIA
ACACIA
ODYSSEY
Pacing in HCM

Academic Contributions
AHA Registry
Textbook
Guidelines
Publications
Grand Rounds

Basic Imaging Echo and TEE

Advanced Imaging MRI / CT

Pediatrics

Pulm HTN

Genetic Testing / Screening

Amyloid, Sarcoid

Heart Failure and Transplant

EP Devices and Ablations

Cath, TMVR, TAVR and Alc Abl

Surgical Myectomy and Valves CABG

HCM Offices & Outreach

Innovation and New Therapy Rollout
ASA Course
CMI Clinic

Marketing and Media Presence / Community Outreach
Library Events
Maria Fareri
Heart Month

1345 Unique Patient Initial Visits & 6398 Follow Up Visits
~75% from outside WMC Health Network

The WMC Hypertrophic Cardiomyopathy Program Outcomes 2017-2023

165

Number of percutaneous alcohol septal ablations performed at WMC

- 1 surgical myectomy/MVR
- 1 VSD repaired

96

Number of surgical septal myectomies performed at WMC

- 2 returns for ASA
- 1 VSD (clinically nonsignificant)
- 1 mortality

0.38%

Mortality of patients undergoing septal reduction therapy (n=1)

Mortality Goal < 1% (0.38%)
Crossover Rate 1.5%

Department of Cardiology
Quality Program

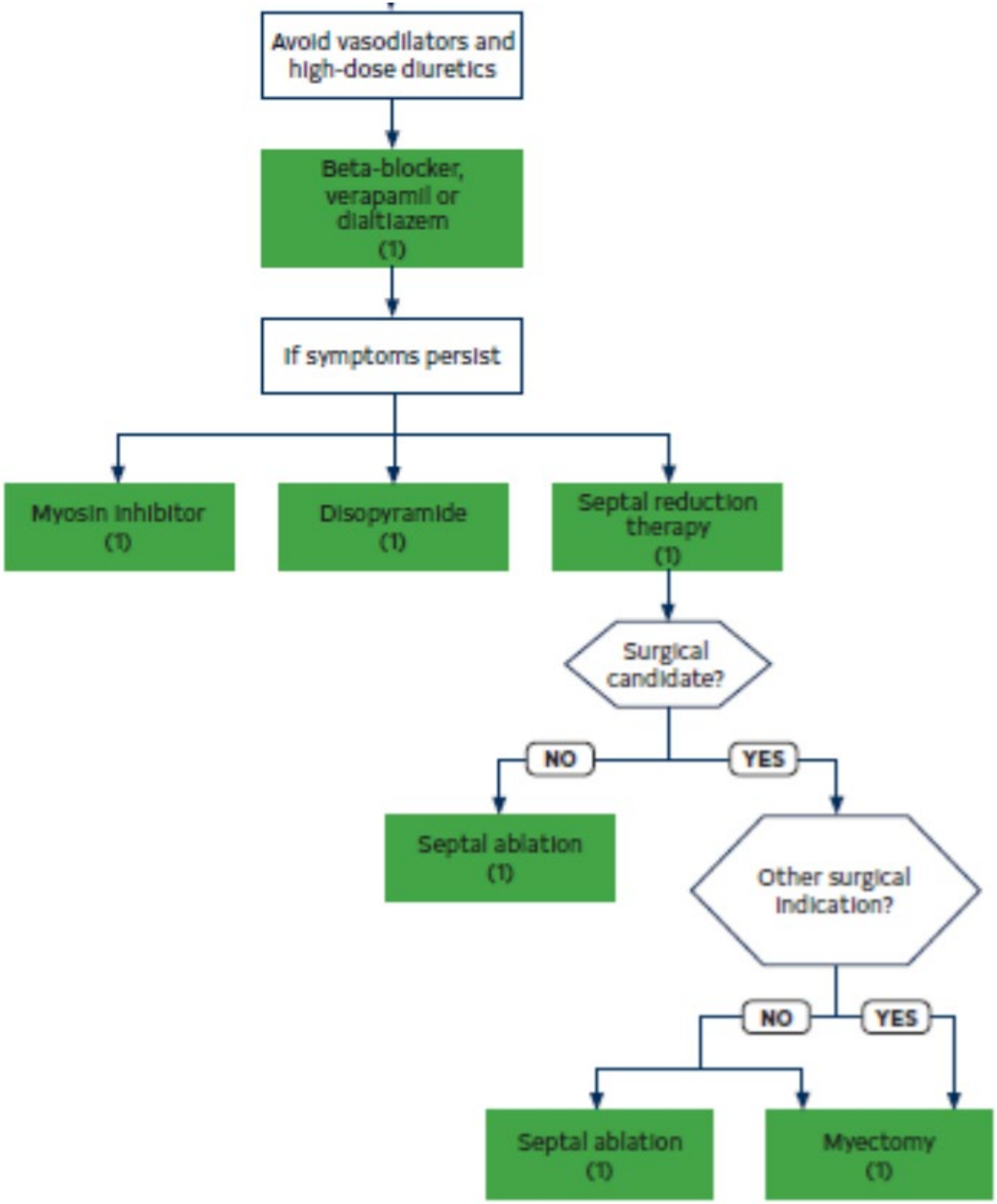
WMC Health | Heart & Vascular Institute
Westchester Medical Center Health Network

2024 Guidelines

Symptomatic oHCM

- BB first
- Can move to CMI or SRT or diso
- SRT indications largely unchanged but essentially moved up

More options



Individualized Patient Care Within the Context of a Well Balanced, Safe and Effective COE

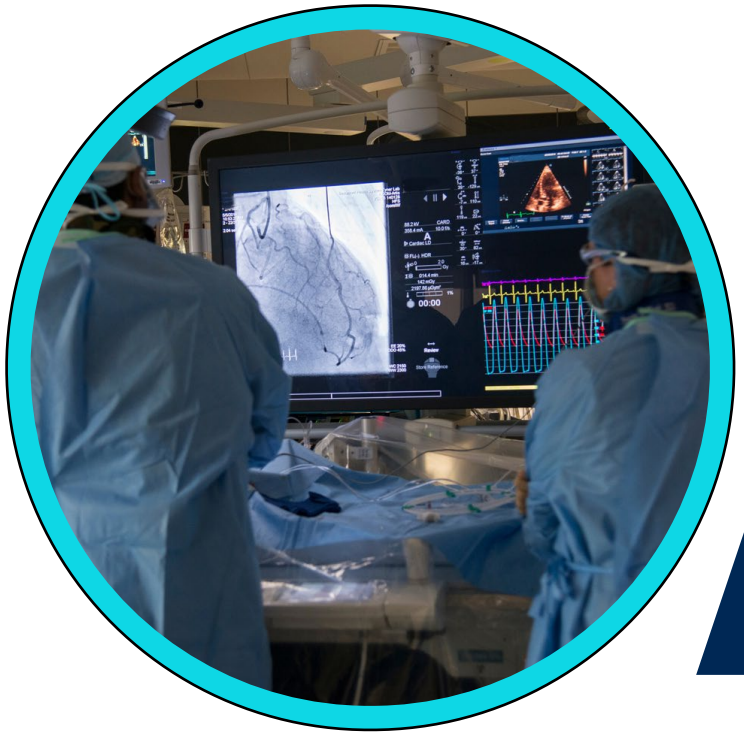
Logistical, tactical, data, volume,
Survival & mortality is the prime directive

Prioritize loved ones, side effects, stroke,
recovery, career, pain, next 5 years

Alcohol Ablation

LIVE PROCTORING COURSE

ADDITIONAL DETAILS



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APRIL 21-23, 2024

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Thank You!