Alcohol Septal Ablation for HOCM: Case selection

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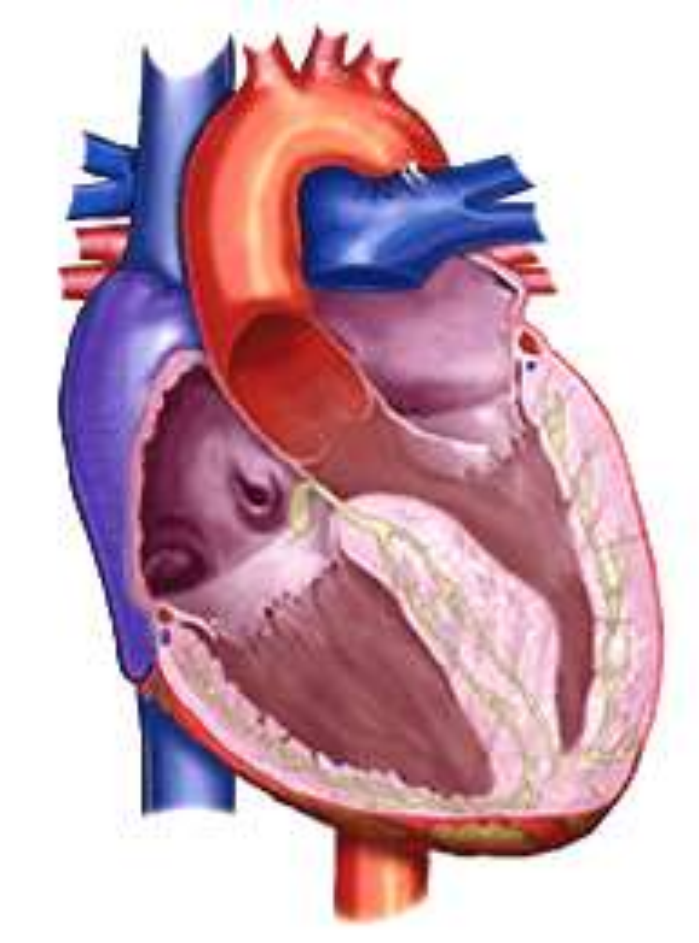
Background

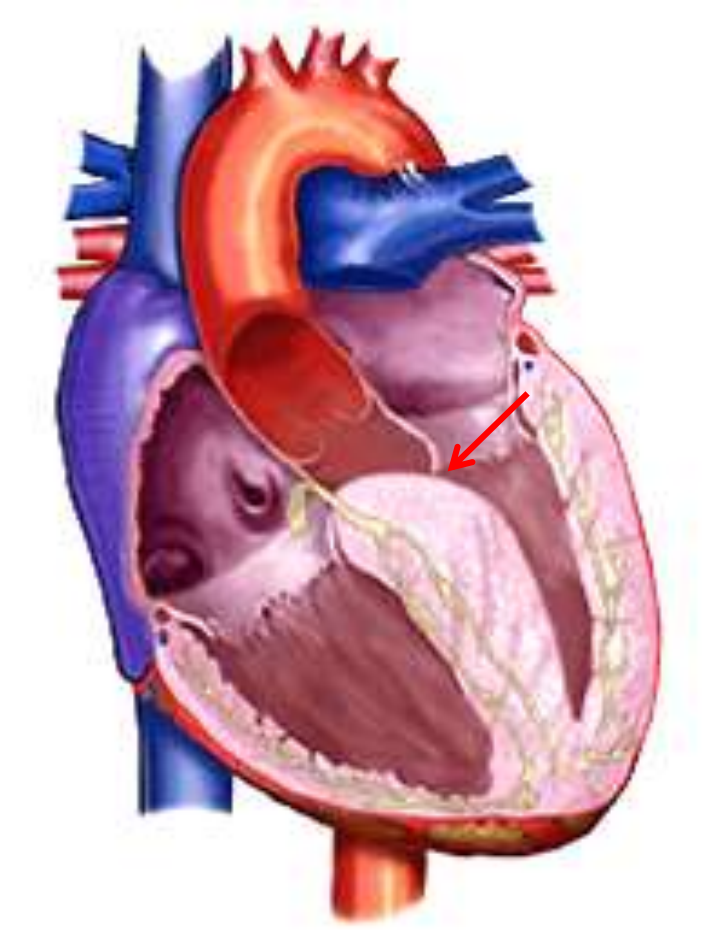
- Hypertrophic (obstructive) cardiomyopathy (HOCM/HCM) is characterized by: - hypertrophy of IVS (>12 mm)
  - narrowed LV outflow tract
  - systolic anterior motion of MV resulting in dynamic LV outflow obstruction (≈1/3rd)
- Is the most common genetic CV disease transmitted as autosomal dominant trait
- Occurs in 1 in 500 (≈0.2%) of general population
- In the USA there are currently 300,000 people with HOCM
- Most patients are identified in their 30's and 40's
- <1% of patients are referred for echocardiography
- Probably #1 cause of sudden cardiac death in young athlete
- More common in men; women likely to be severely disabled

Background

HOCM/HCM



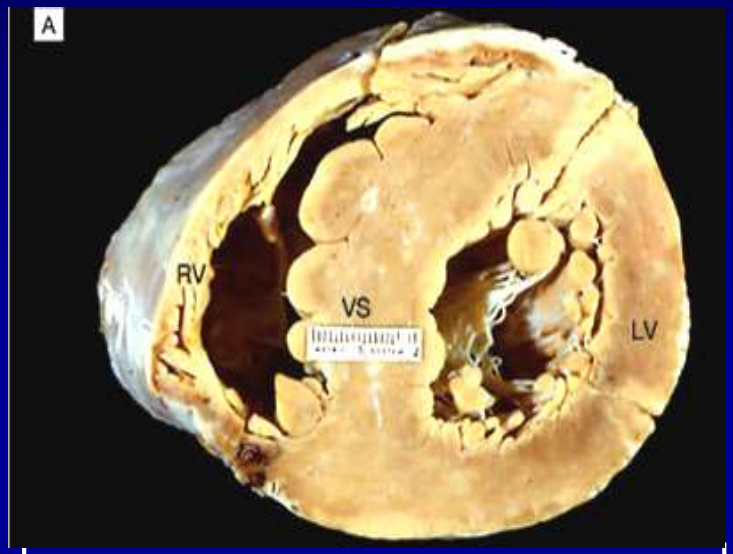
Asymmetric septal hypertrophic (ASH) without obstruction (≈ 70%)



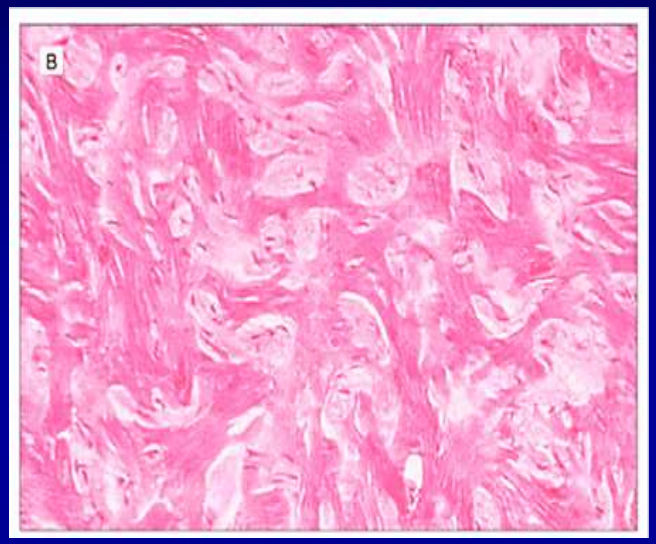
Asymmetric septal hypertrophic (ASH) with obstruction (≈ 30%)

Myocardial Changes in HOCM

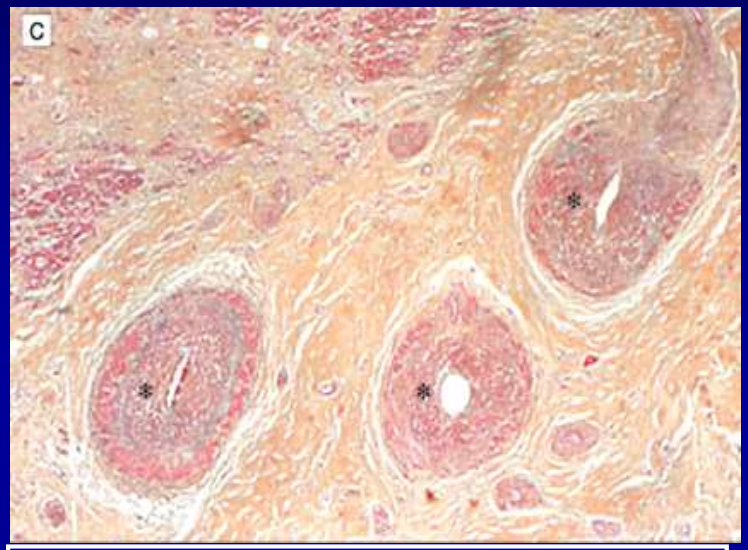
Morphologic Features for Sudden Death



Disproportionate thickening of the ventricular septum (VS) with respect to left ventricular (LV) free wall; gross heart specimen from a 13-yr old.



Marked disarray of cardiac muscle cells in the disproportionately thickened VS forming typical disorganized architecture of HOCM



LV myocardium showing several abnormal intramural coronary arteries with markedly thickened walls and narrowed lumen, dispersed

Maron et al. JAMA 2002;287:1308

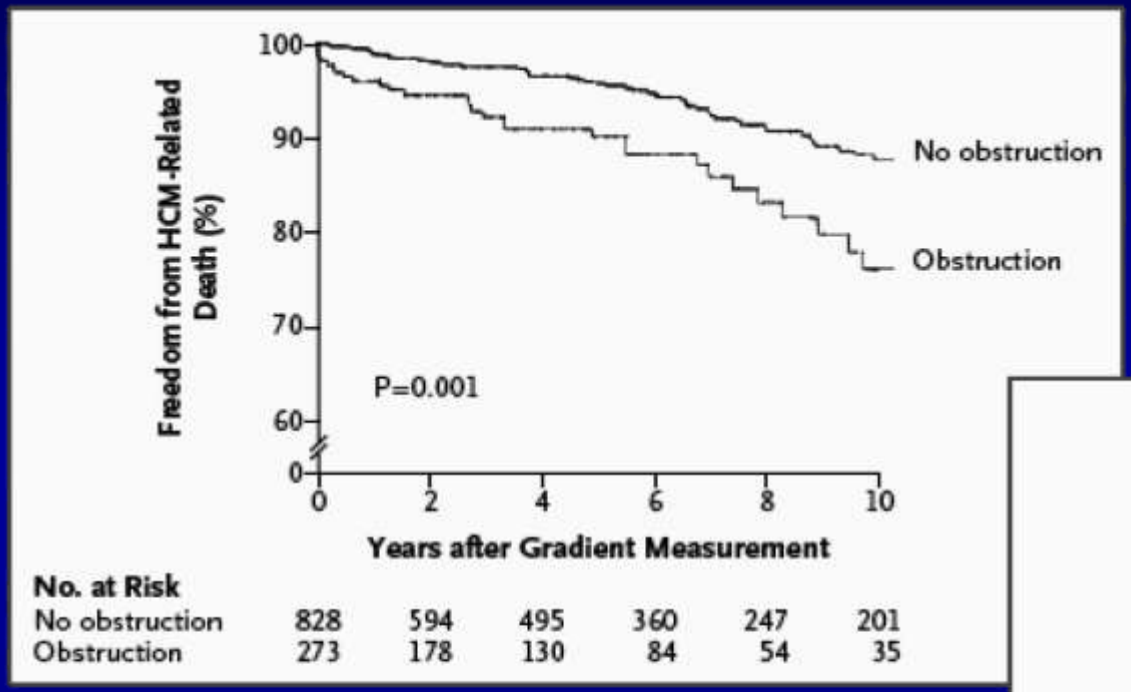
Clinical Manifestations

HOCM

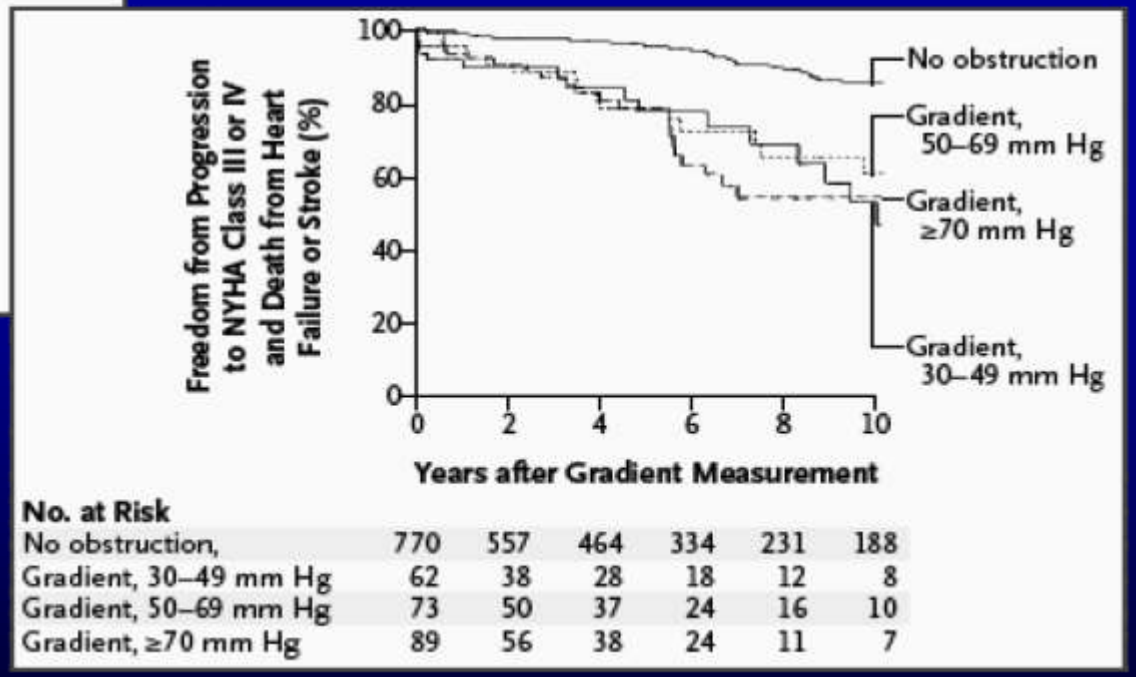
Majority of patients are asymptomatic or only mildly symptomatic;

- **Shortness of breath occurs in 90% of symptomatic patients due to increased LVEDP**
- **Fatigue, presyncope, syncope**
- **Chest pain on exertion in 75% of patients, due to demand-supply imbalance, epicardial coronaries are usually normal**
- **Rarely sudden death.**

Implications of LV Outflow Tract Obstruction in HOCM



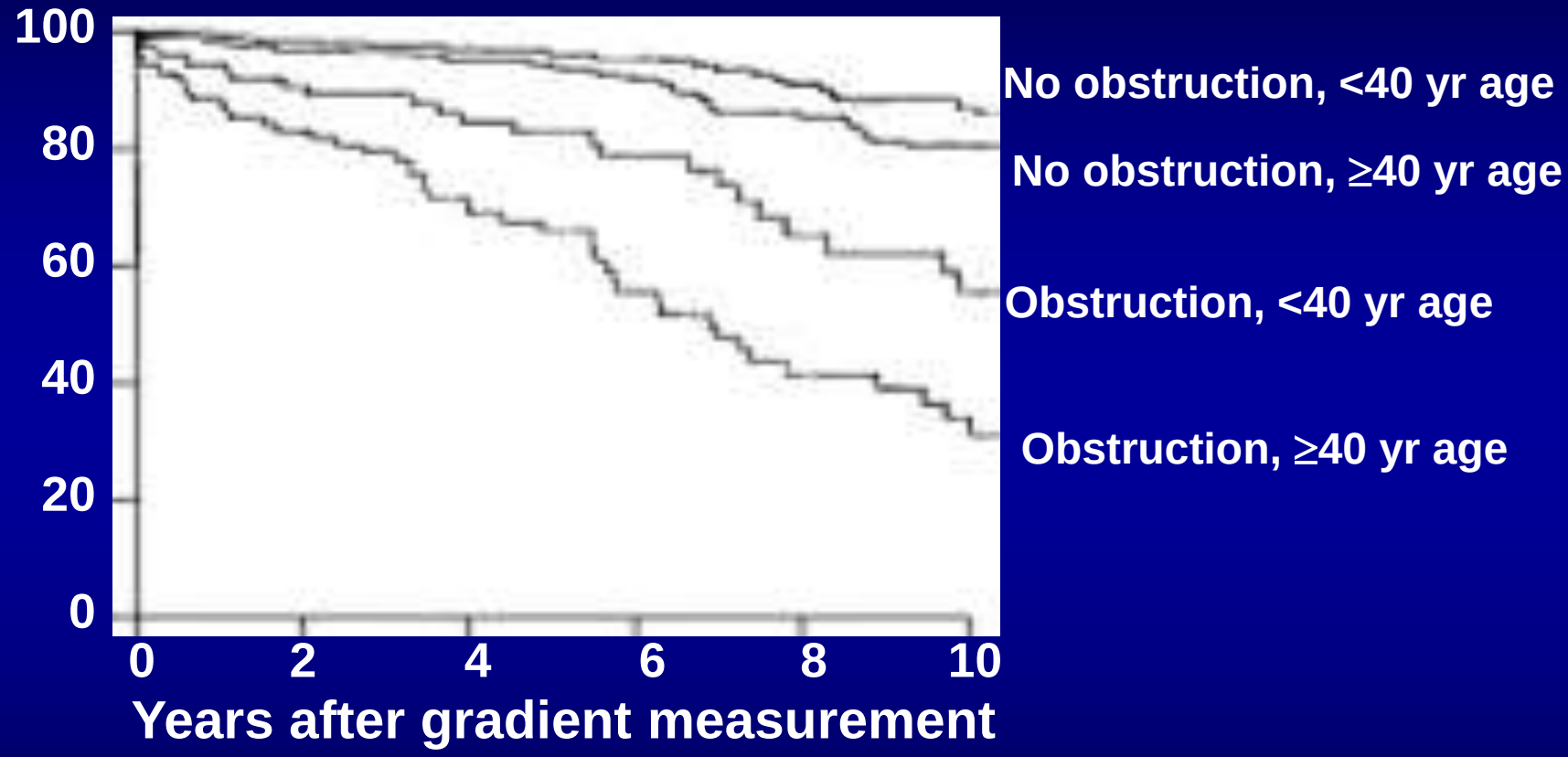
Variable	Death from Any Cause	
	Relative Risk (95% CI)	P Value
Left ventricular outflow obstruction (≥30 mm Hg)	1.6 (1.1–2.2)	0.02
NYHA class II, III, or IV at entry	1.5 (1.1–2.1)	0.02
Paroxysmal or chronic atrial fibrillation	1.4 (1.0–1.9)	0.04
Maximal left ventricular thickness ≥30 mm	1.6 (1.1–2.4)	0.01



1,101 consecutive patients with HCM (outflow gradient ≥30 mmHg

Maron et al., N Engl J Med 2003;348:298

Effect of LV Outflow Tract Obstruction and Age on Clinical Outcome in HOCM



No. at Risk

No obstruction, <40 yr of age	349	251	206	146	103	80
No obstruction, ≥40 yr of age	421	306	258	188	128	108
Obstruction, <40 yr of age	106	70	52	37	21	15
Obstruction, ≥40 yr of age	118	74	51	29	18	10

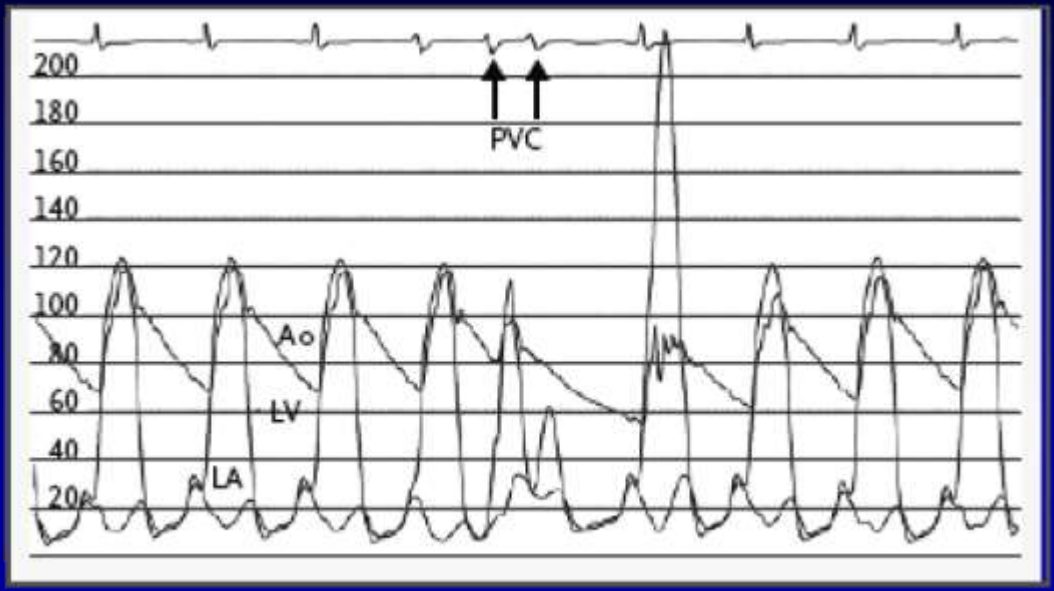
Maron et al., NEJM 2003;348:295

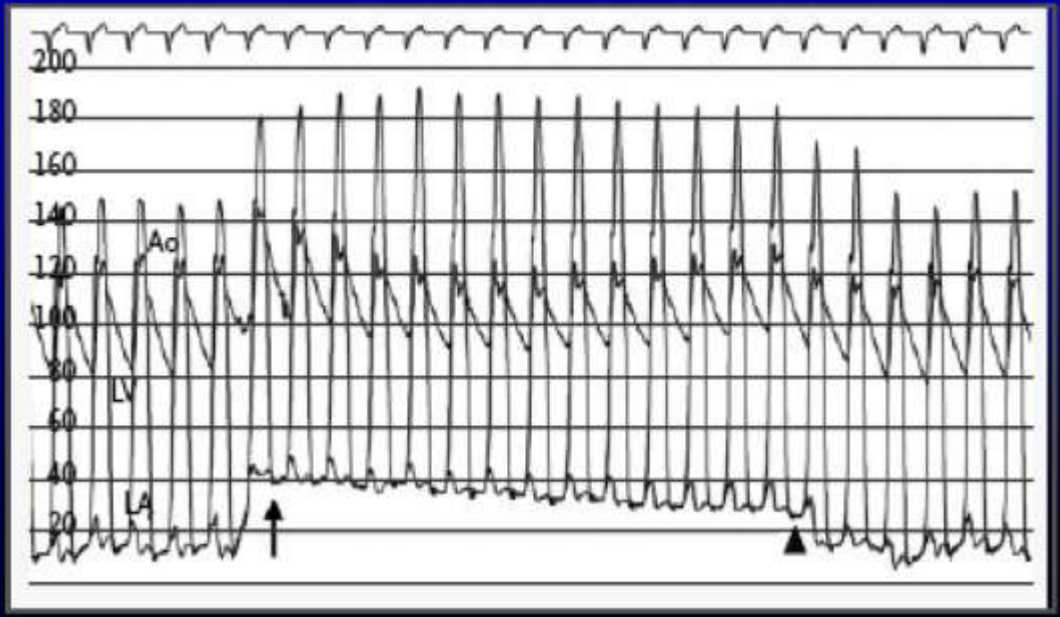
Evaluation of LVOT Obstruction

Brockenbrough-Braunwald phenomenon – reliable sign of dynamic obstruction

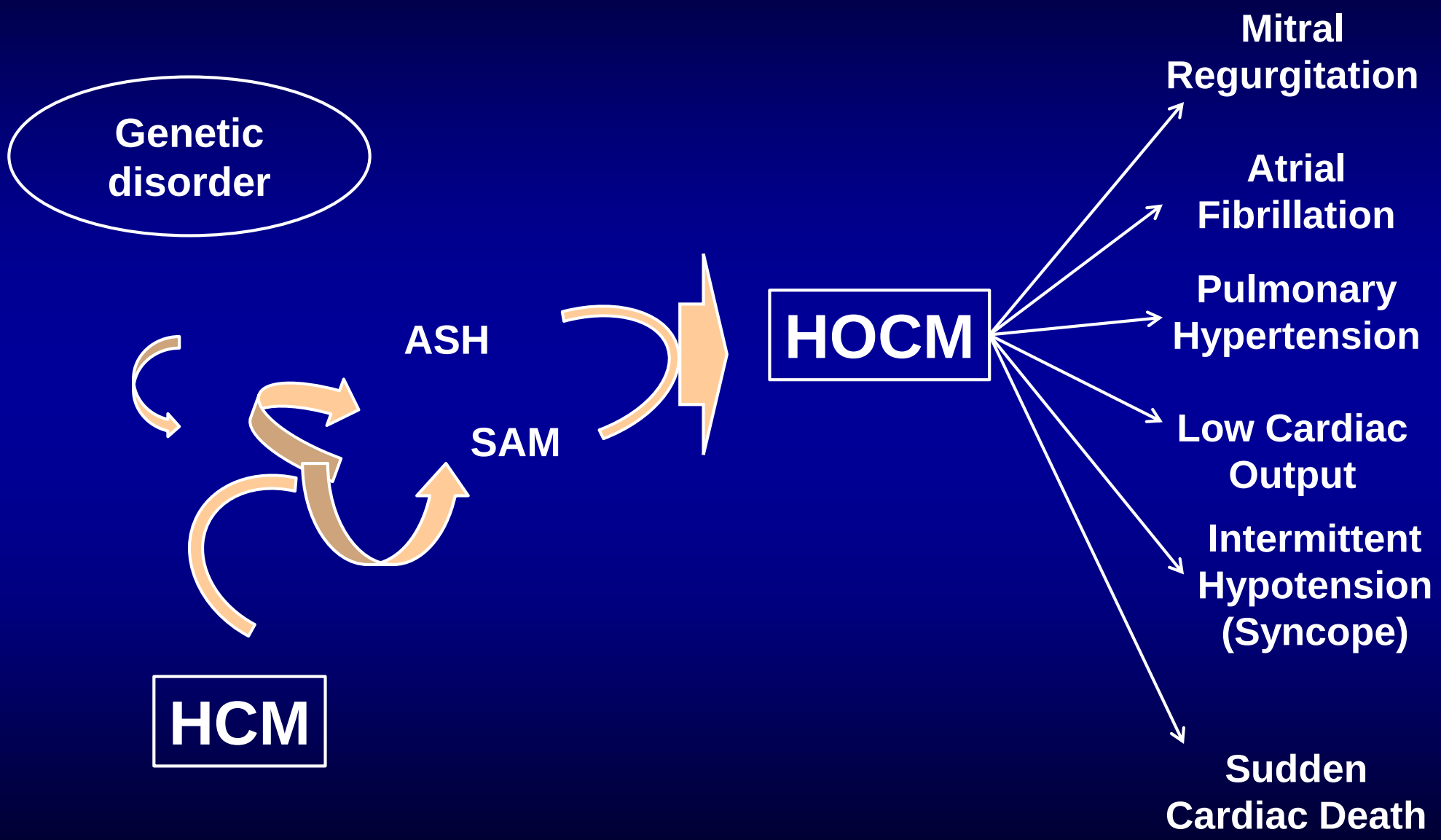
<u>Mechanism</u>: increased ventricular filling overwhelming by increase in contractility; arterial pulse pressure fails to increase as expected (or decreases)

Dynamic obstruction during the strain phase of a Valsalva maneuver

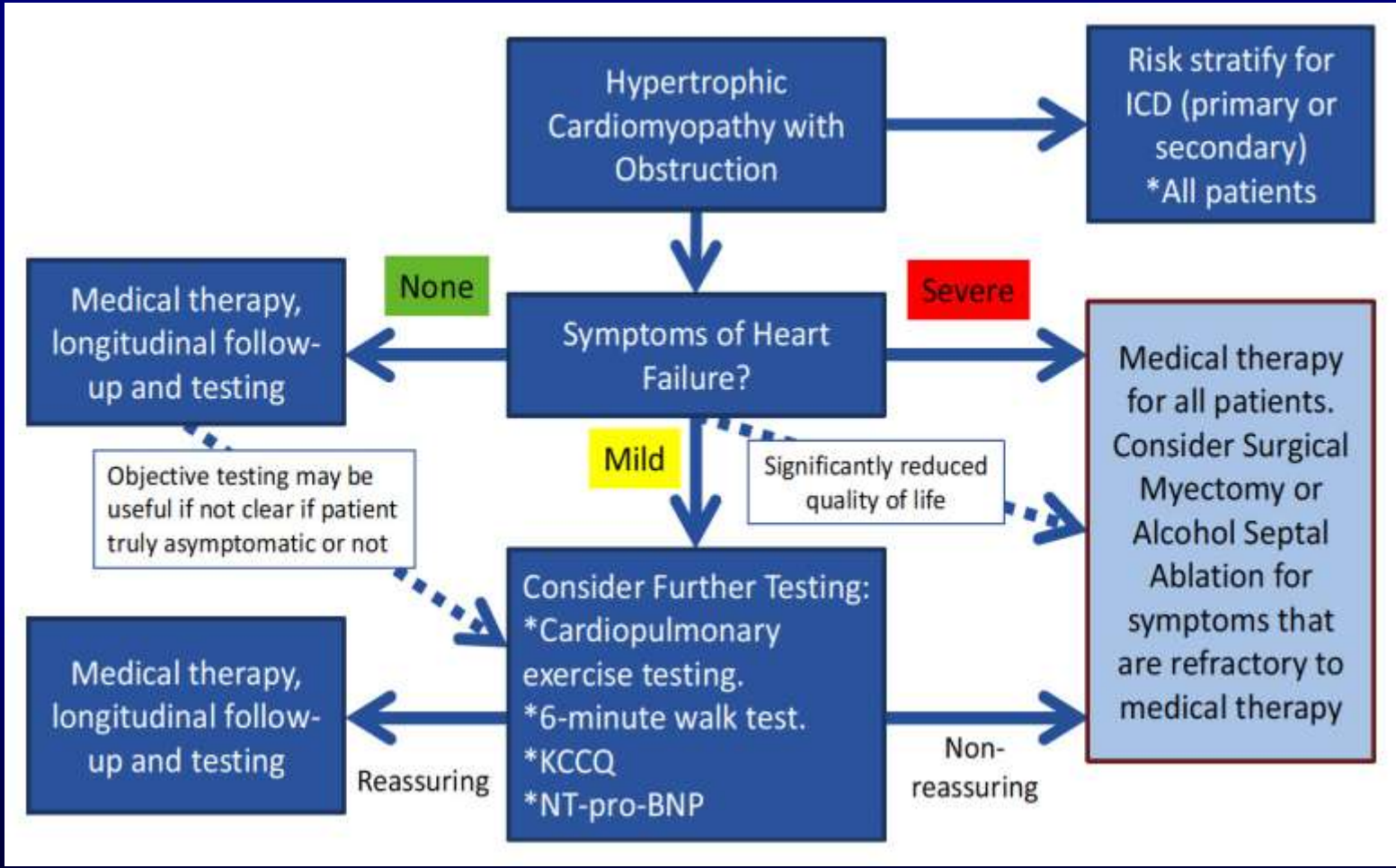




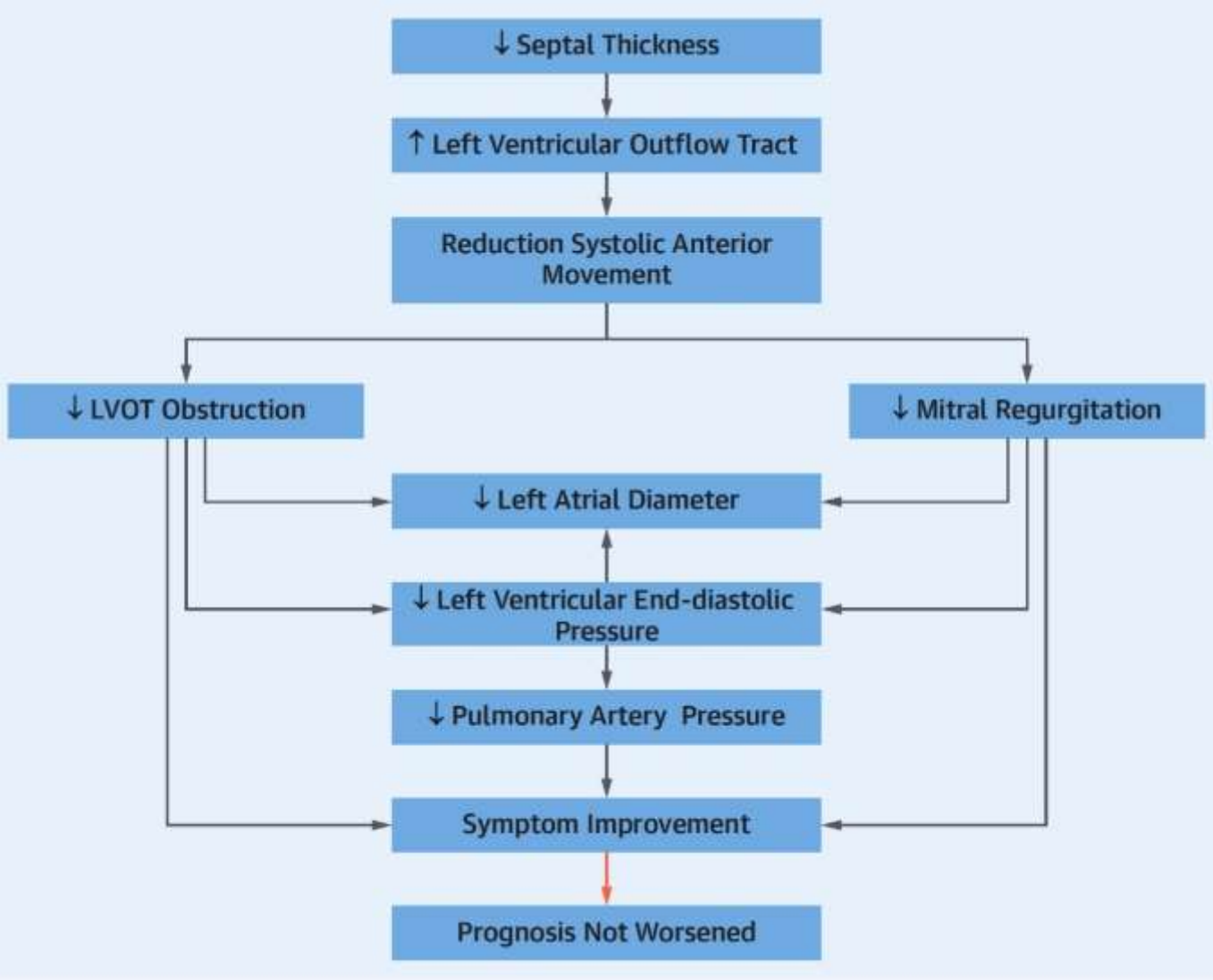
LVOT Obstruction and Symptoms



Algorithm for Evaluating Patients with HCM with Significant Obstruction Based on the Severity of Symptoms



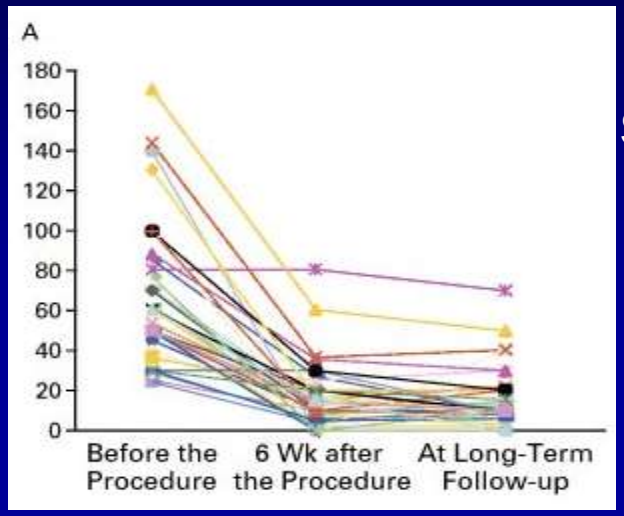
Clinical, Hemodynamic, and Morphologic Changes After ASA in HOCM



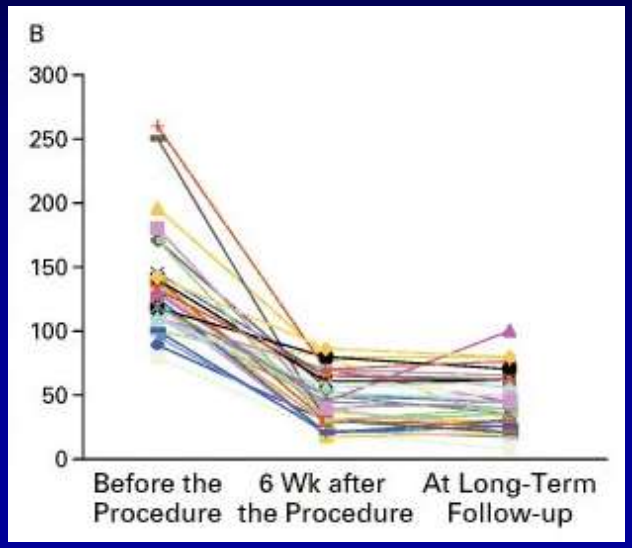
Alcohol Septal Ablation in HOCM

Results at Follow-up 3.0±1.3 Years

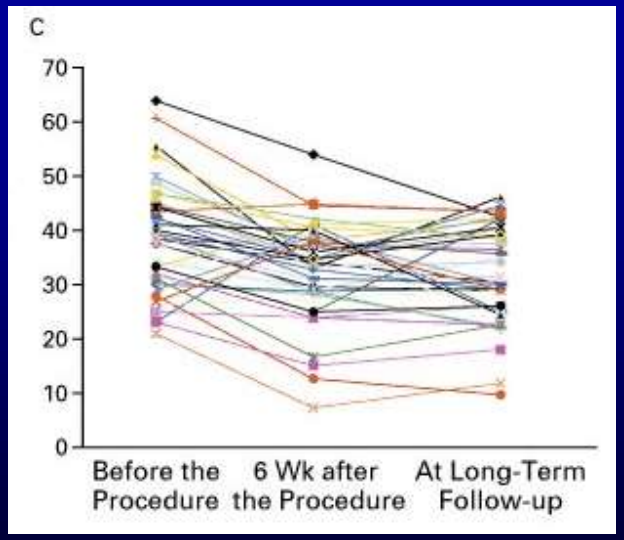
Resting LVOT (mm Hg)



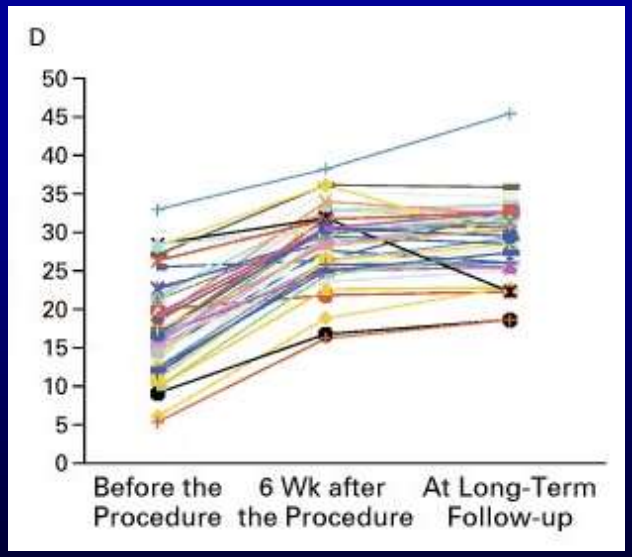
Stress-induced LVOT (mm Hg)



LVEF %



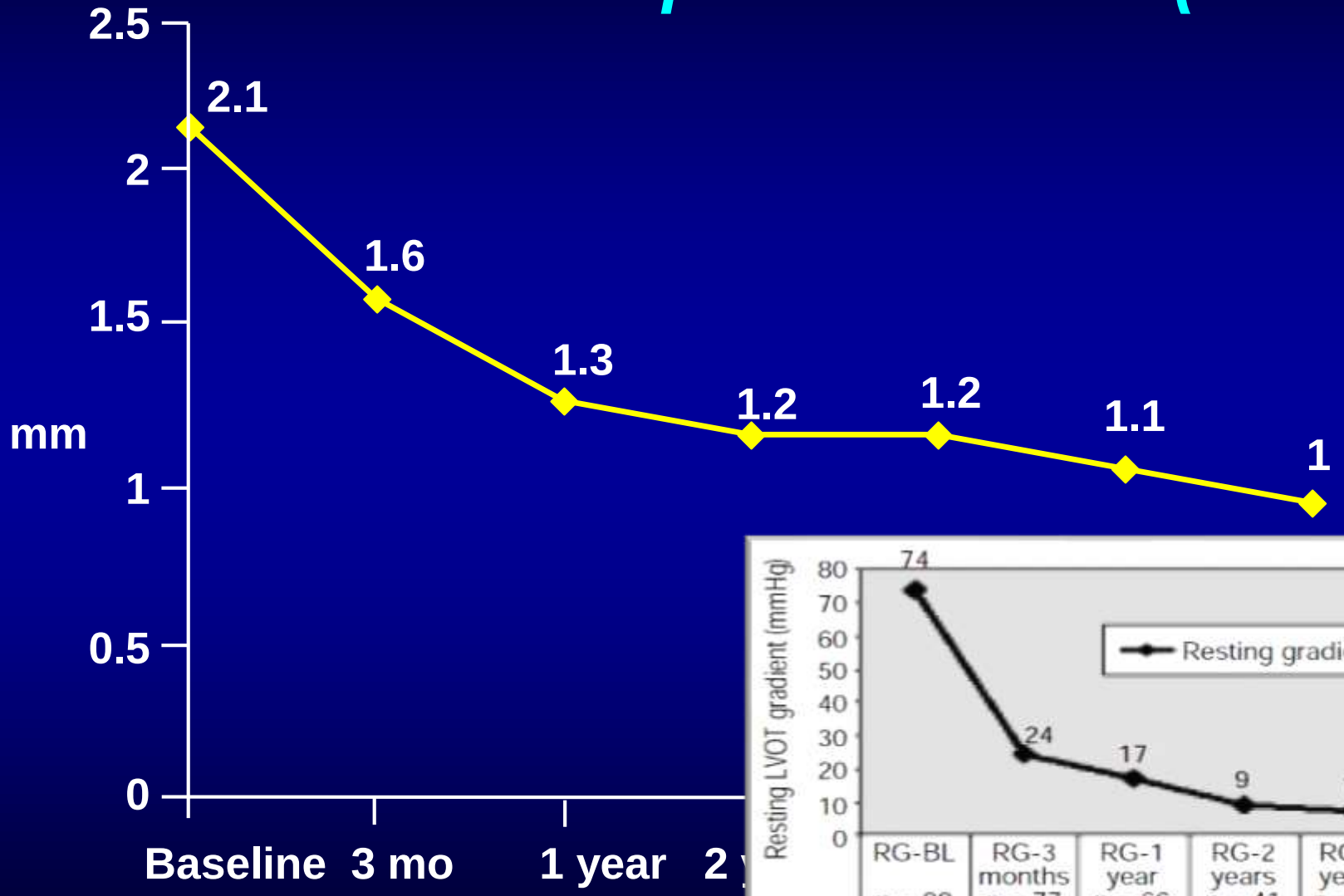
Peak Oxygen Consumption (ml/kg/min)

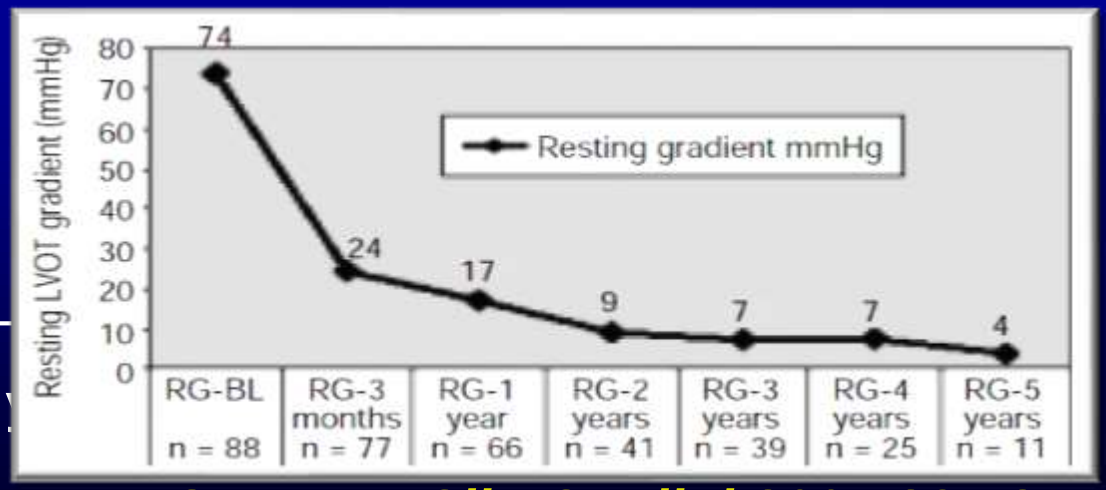


Shamim et al. N Engl J Med 2002;347:1326

Alcohol Septal Ablation in HOCM

Reduction in Septal Thickness (N=63)





Spencer, Clin Cardiol 2005;28:124

Alcohol Septal Ablation in HOCM

Method

- One or more septal perforators
- 1-5cc absolute (desiccated) alcohol
- Temporary pacemaker via RIJ
- Co-axial guide catheter to avoid trauma to LMCA
- Small short balloons (Maverick 1.5-2.5/9mm)
- Runthrough or BMW or any hydrophilic floppy wires
- Contrast echocardiography
- Liberal use of Versed and Morphine
- 1cc/min slow continuous alcohol infusion, guided by echo
- Measure gradient – catheter and echo
- In CCU for 2 days with TPM and then d/c once CKMB <60U

Zena and Michael A. Wiener
Cardiovascular Institute

Marie-Josée and Henry R. Kravis
Center for Cardiovascular Health

STEPS for Alcohol Septal Ablation (ASA) for HOCM

Indications:

1.) Severe drug (β blockers/Ca^{++} blockers/disopyramide) resistant symptoms of CHF (NHYA Class III-IV) or intolerance to drugs.
2.) Drug resistant angina (III-IV).
3.) Syncope
4.) Resting LVOT gradient >30 mmHg.
5.) Provoked LVOT gradient >50 mmHg if resting gradient <30 mmHg.

Procedure:

1.) If no PPM, a temporary pacemaker via right internal jugular vein.
2.) Two arterial sheaths, 6 Fr and 5 Fr
3.) Two transducers to measure simultaneous LV and peripheral pressures
4.) 95% absolute alcohol (3-5 cc) available as 1 cc/ampule
5.) Echo team for pre-procedure and intra-procedure myocardial contrast echo.
6.) Filder/Wispher 190 cm wire.
7.) 1.5/2.0/2.5-9 mm Maverick OTW balloon

Steps for Operator:

1.) 5 Fr MP catheter in the LV and 6 Fr appropriate guide catheter for septal ablation. Measure the resting and post PVC gradients.
2.) Baseline bloods including CPK/MB, troponin, chemistry and CBC.
3.) IV Heparin bolus of 5000 unit and keep ACT = 275-300 sec.
4.) Coronary angiography to define septal artery in RAO caudal and AP cranial views.
5.) Wire the major septal and inflate the balloon and inject the echo contrast (Affinity) material to delineate the hypertrophied septum. Change the balloon position in the same septal or different septal artery until the correct septal artery is identified.
6.) Document the balloon position in the septal artery without LAD comprise during balloon inflation by short cine of the left coronary artery.
7.) Inject absolute alcohol through the lumen of inflated balloon no more than 1cc/min.
8.) Total balloon inflation time of at least 5 minutes.
9.) Repeat echo and measure the LVOT gradient while the balloon is inflated and remove any residual alcohol from the lumen by additional saline flush.
10.) If resting gradient < 20 mmHg and post PVC gradient of <40 mmHg, deflate the balloon and finish the procedure after confirming LAD patency.

Watch for following complications during procedure :

1.) Chest pain during alcohol injection (Rx with liberal use of IV morphine and Versed).
2.) Brady arrhythmia/complete heart block (prophylactic temporary pacemaker).
3.) Ventricular tachycardia/VF (keep the defib paddles charged).

Post Procedure:

1.) Needs post intervention orders and admission to CCU; continue reduced dosage of pre-ASA negative inotropic meds and start aspirin 81 mg PO daily for one year.
2.) Temporary pacemaker needs to be left in place for minimum of 48 hours and then can be removed if no paced rhythm. If still paced after 48 hours, then PPM should be implanted. PPM for unresolved CHB is required in 8-10% of cases.
3.) Monitor CPK/MB Q 8 hrly x 24 hours and later if still rising; discharge when CKMB falls below <10x normal (<60 unit) .
4.) Transthoracic echo next day to evaluate resting gradient, LV function, and MR.

To be expected:

1.) No. of arteries to be injected = 1.7
2.) Mean volume of alcohol injection = 3 cc
3.) Peak CPK release around 800 unit. Mean time to peak CPK rise 12 hours
4.) Peak CPK rise correlated with the volume of ethanol injected
5.) 10-20% of patients develop new conduction abnormalities (RBBB, LAFB, LBBB)
6.) 30% may develop transient CHB especially if patients have baseline (RBBB or LBBB)
7.) 8-10% of patients may require PPM after ASA for persistent complete heart block
8.) Resting gradient should decrease to < 10-20 mmHg
9.) There will be additional 30% reduction in septal thickness over next 4- 6 weeks on follow-up echo

ASA: Safety and Complications

- In-hospital Mortality
  - 0.7% in North American Registry (n=874)
  - 0.7% in European Multi-center Registry (n=421)
  - 0.3% in Scandinavian Registry (n=313)

Data are similar to Surgical Myectomy mortality as shown in Mayo Clinic, Cleveland Clinic and Toronto General Hospital (i.e. <1%)

Complete Heart Block after ASA

- 261 consecutive pts
- 37 had PPM/AICD before ASA
- 14% (31/224) developed CHB and required PPM post-ASA
- 30 pts developed CHB in-hospital, 1 pt came back with CHB in 1 week

Multivariate Predictors of PPM Placement after ASA

	Odds Ratio	95% CI	p Value
LBBB	39	3.6–416	0.002
>2 septals injected	4.6	1.3–16	0.016
Bolus injection of ethanol	51	3.5–735	0.004
First-degree AV block	14	3–69	0.001
Female gender	4.3	1.3–15	0.02

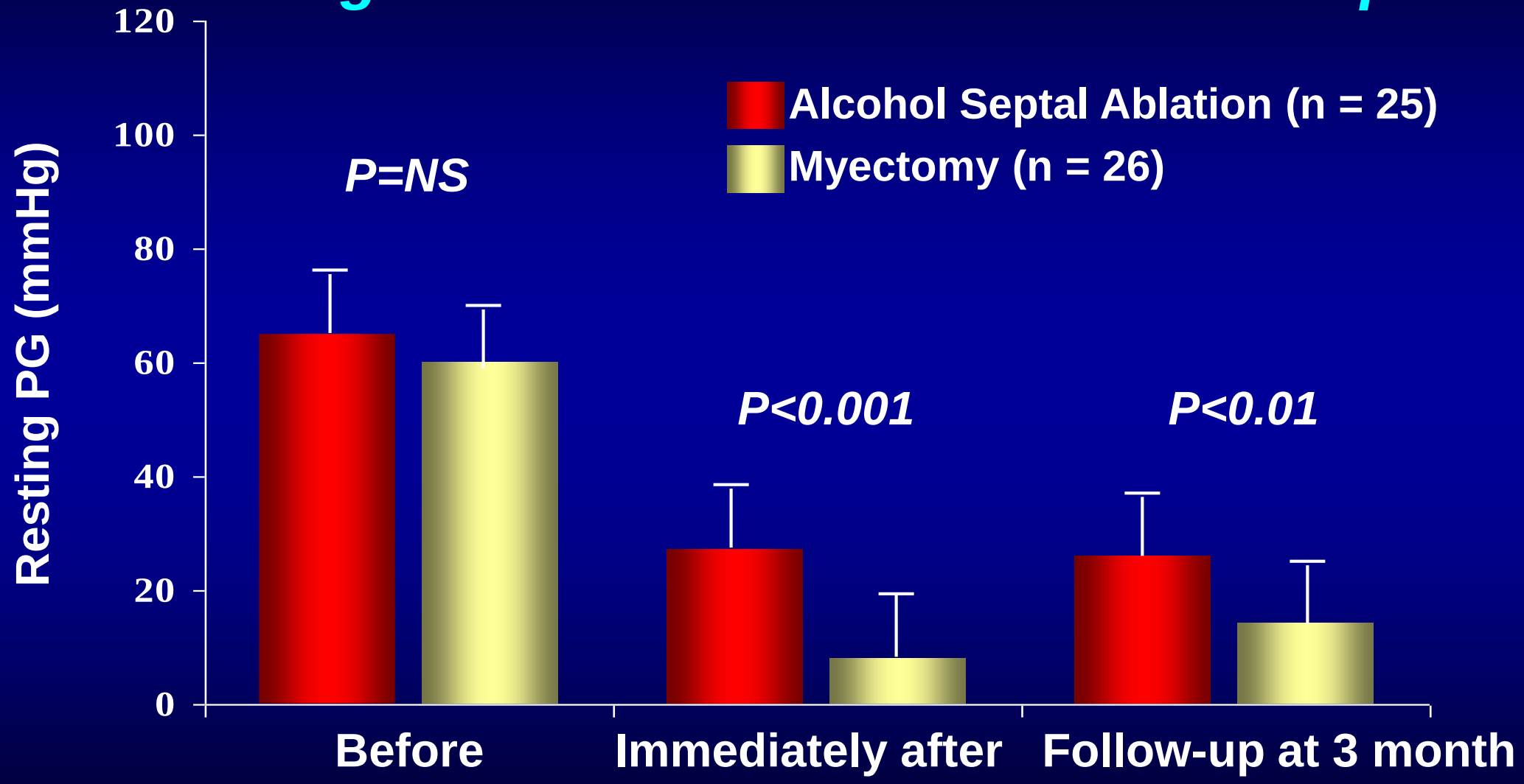
Clinical and Echocardiographic Outcome of Pts Who Require vs Who did Not Require PPM

	PPM n = 31	No PPM n = 193	p Value
NYHA class improvement	1.76 ± 0.63	1.47 ± 0.74	0.09
IVS reduction	0.82 ± 0.67	0.56 ± 0.54	0.063
% IVS reduction	37 ± 20	27 ± 26	0.003
Rest LVOTG reduction	56 ± 42	40 ± 37	0.07
Increase in exercise duration(s)	68 ± 149	102 ± 138	0.35

Chang et al., J Am Coll Cardiol 2003;42:296

Alcohol Septal Ablation Vs. Myectomy in HOCM

Average Pressure Gradients at Follow-up



Qin et al., JACC 2001;38:1994

Alcohol Septal Ablation vs Myectomy

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- No difference in short or long term survival
- No difference in functional status improvement
- No difference in NYHA heart failure class improvement
- No difference in arrhythmias
- No difference in rates of repeat procedures
- No difference in improvement of mitral regurgitation

- Higher need for pacemaker
- Higher residual gradients after ablation

"The choice of treatment strategy should be made after a thorough discussion of the procedures with the individual patient"

LVOTG. The choice of treatment strategy should be made after a thorough discussion of the procedures with the individual patient. (J Am Coll Cardiol 2010;55:823–34) © 2010 by the American College of Cardiology Foundation

Mount Sinai Heart

Arrhythmia/Electrophysiology

Survival After Alcohol Septal Ablation for Obstructive Hypertrophic Cardiomyopathy

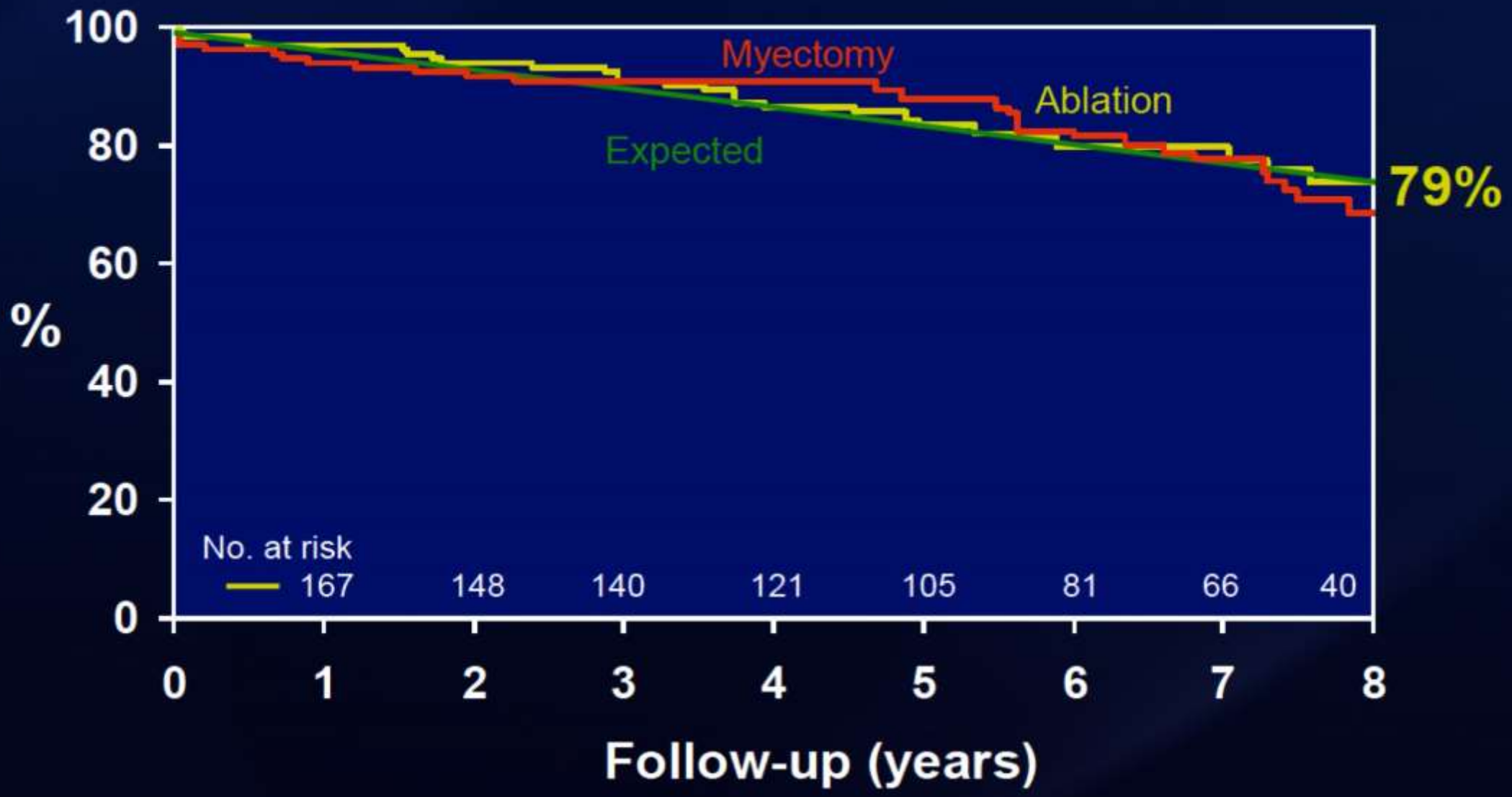
Paul Sorajja, MD; Steve R. Ommen, MD; David R. Holmes, Jr, MD; Joseph A. Dearani, MD; Charanjit S. Rihal, MD; Bernard J. Gersh, MB, ChBDPhil; Ryan J. Lennon, MS; Rick A. Nishimura, MD

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 Alcohol Septal Ablation



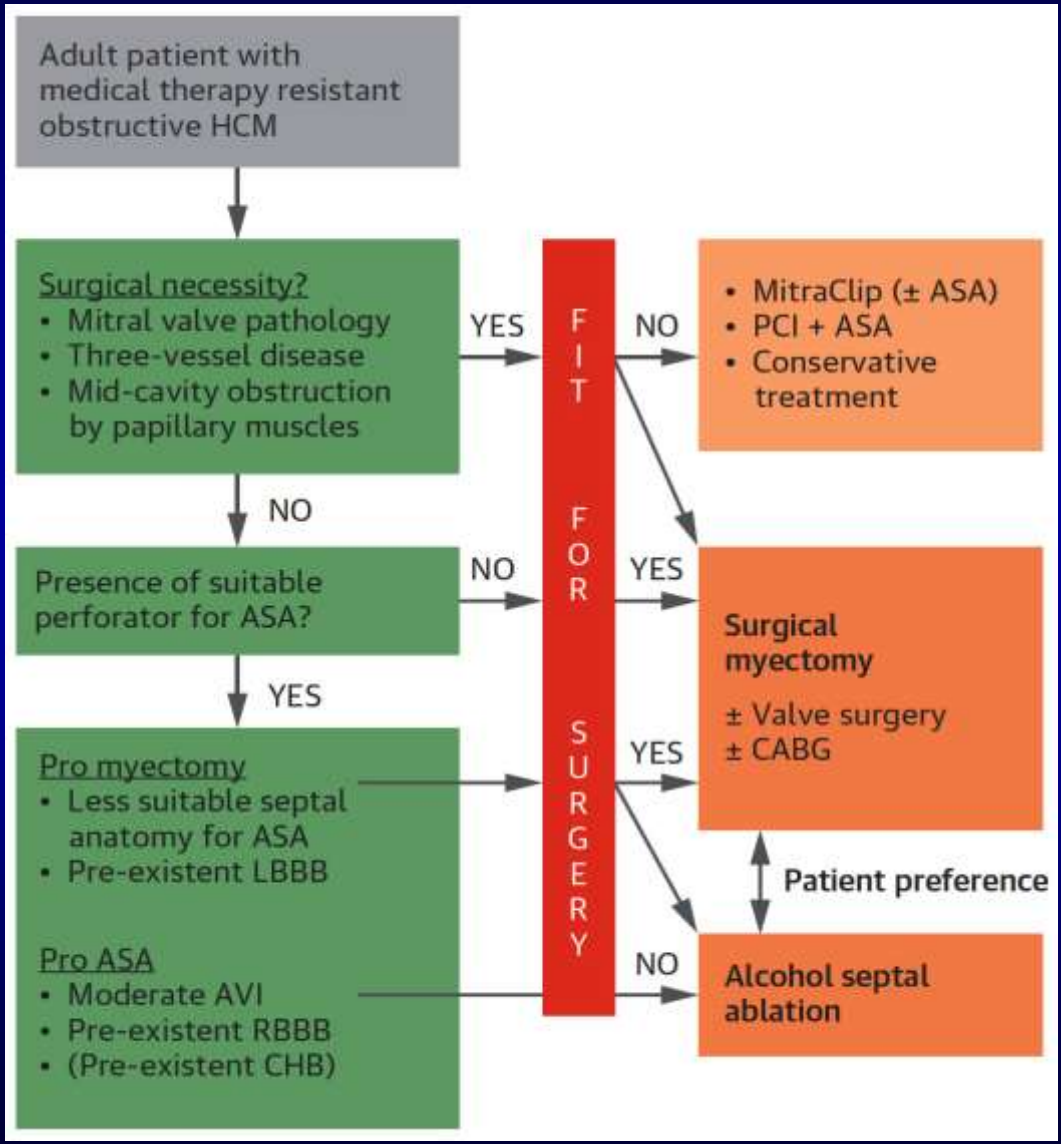
Sorajja et al., Circulation 2012;126:2374

Outcomes of All Studies Comparing ASA with SM with a Mean F/U Duration of at Least 3 Yrs and Results of Meta-Analyses Comparing ASA with Myectomy

First Author, Year	Country	Period	n	Mean Follow-Up, yrs	Mean Age, yrs	Peri Mortality, %	Peri (A)SCD, %	Pacemaker, %	Mean LVOTG, mm Hg	REDO, %	All-Cause Mortality (Annual), %	(A)SCD (Annual), %
Agarwal, 2010	6 countries	1986-2006	380/326	–	55/49	NS	NS	OR: 2.6 (favors SM)	SMD 0.45 (favors SM)	NS	–	–
ten Cate, 2010	the Netherlands	1999-2007	91/40	5.4/6.6	54/49	2.2/0	5.5/0	4/3	8/-	11/5	1.8/0.8	–
Sorajja, 2012	United States, Rochester	1983-2010	177/177	5.7/5.7	63/62	1.1/0.6	1.7/0.6	22/4	13/-	9/1	2.5/2.4	1.3/1.1
Steggerda, 2014	the Netherlands	1981-2010	161/102	5.1/9.1	59/56	1.2/2.0	2.5/0	7/9	19/10	6/1	1.5/2.2	–
Vriesendorp, 2014	Belgium and the Netherlands	1990-2012	316/250	6.3/7.9	58/52	1.6/1.2	3.1/0.4	–	10/9	10/2	1.9/2.0	1.0/0.8
Samardhi, 2014	Australia	1981-2012	47/23	3.6/3.8	57/47	0/8.7	4.3/0	15/13	27/13	17/0	1.2/4.6	0/0
Sedehi, 2015	United States, Stanford	1972-2006	52/171	3.2/13.7	57/48	0/2.9	–	8/6	36/34	–	1.2/1.0	–
Liebregts, 2015	16 countries	1963-2013	2,013/2,791	6.2/7.4	56/47	1.3/1.1	2.2/0.6	10/4	–	8/2	1.5/1.4	0.4/0.5
Yang, 2015	China	2001-2014	22/37	3.0/3.0	46/45	0/0	4.5/2.7	0/0	–	5/0	1.5/0.9	0/0.9

Liebregts et al., J Am Coll Cardiol 2017;70:481

Decision Tree for Patients with Obstructive HCM and Complicating Patient Factors



JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 72, NO. 24, 2018

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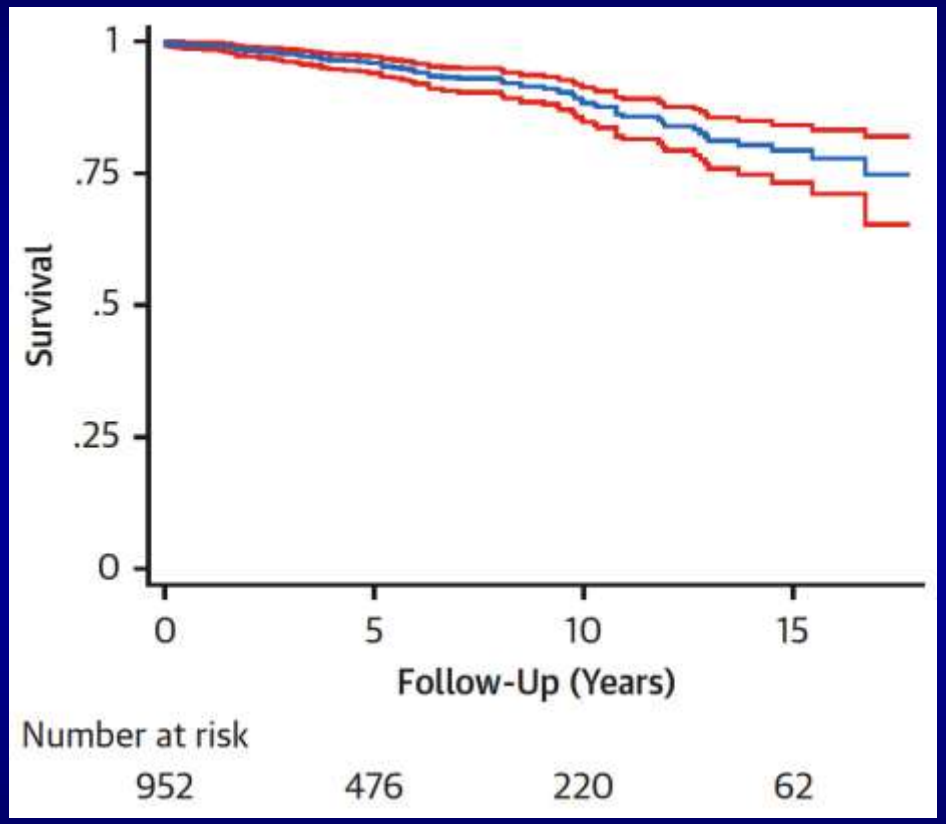
ORIGINAL INVESTIGATIONS

Survival After Alcohol Septal Ablation in Patients With Hypertrophic Obstructive Cardiomyopathy

Angelika Batzner, MD,[a,b] Barbara Pfeiffer, MD,[b] Anna Neugebauer, MD,[b] Diaa Aicha, MD,[b] Christoph Blank, MD,[b] Hubert Seggewiss, MD[a,b]

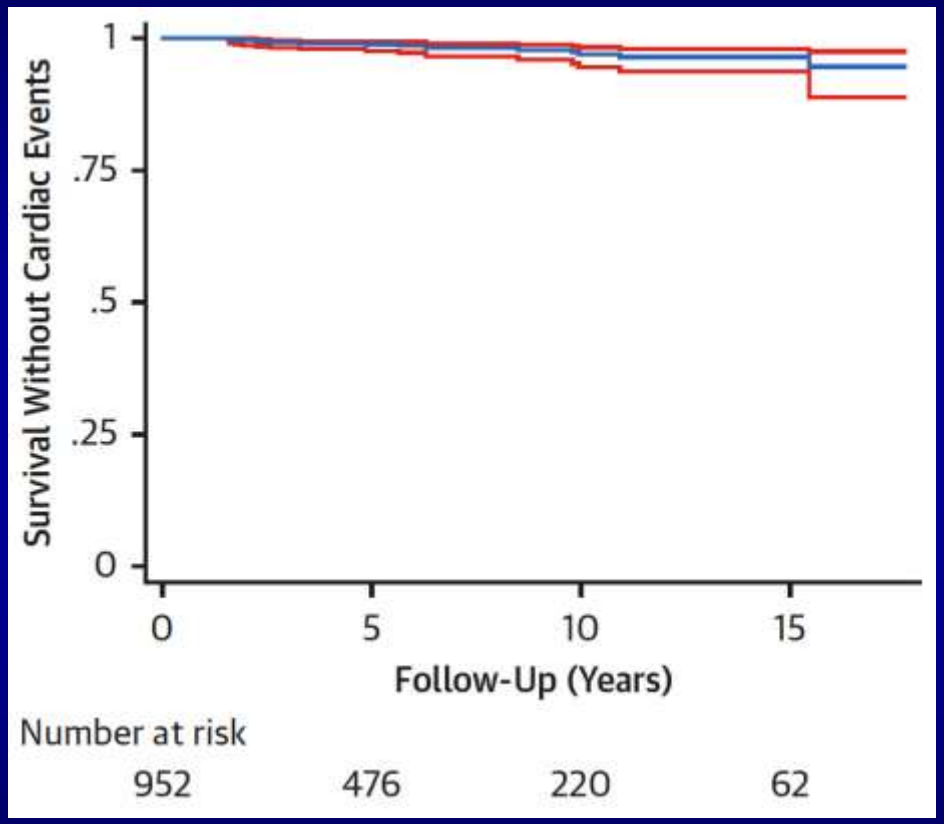
Kaplan-Meier Survival Analysis

Overall Survival with 95% CI After PTSMA in 952 Patients



Analysis after PTSMA estimated:
5-yr survival of 95.8%
10-yr survival of 88.3%
15-yr survival of 79.7%

Estimated Survival Free of Cardiac Events with 95% CI After PTSMA in 952 Patients



Analysis after PTSMA estimated:
5-yr survival free of cardiac events - 98.9%
10-yr survival free of cardiac events - 88.3%
15-yr survival free of cardiac events - 79.7%

Batzner et al., J Am Coll Cardiol 2018;72:3087

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ORIGINAL INVESTIGATIONS

Survival After Alcohol Septal Ablation in Patients With Hypertrophic Obstructive Cardiomyopathy

CONCLUSIONS In this study, PTSMA could be proofed as a safe procedure with ongoing symptomatic improvement and excellent long-term survival. Therefore, PTSMA is a reasonable alternative to surgical myectomy in HOCM.
(J Am Coll Cardiol 2018;72:3087-94)

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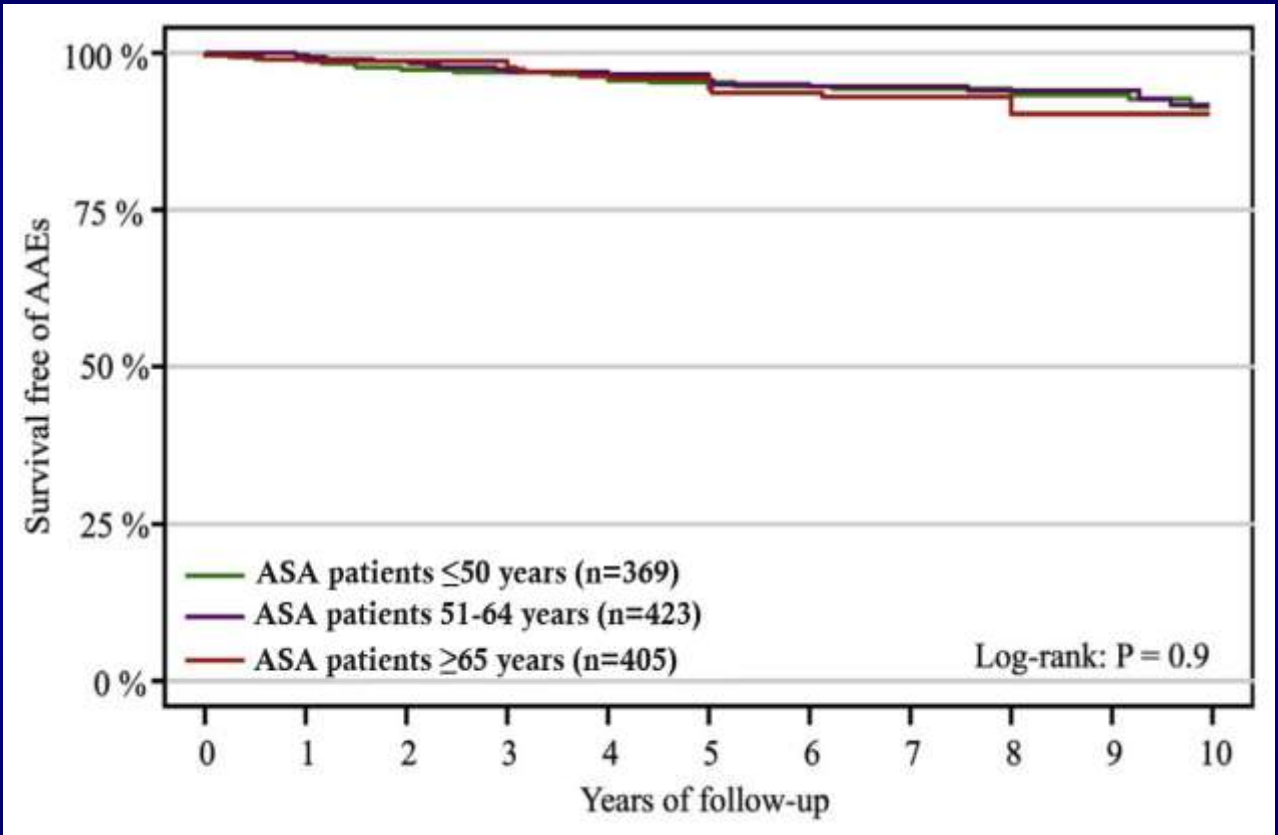
STRUCTURAL

Outcomes of Alcohol Septal Ablation in Younger Patients With Obstructive Hypertrophic Cardiomyopathy

Max Liebregts, MD,[a] Lothar Faber, MD,[b] Morten K. Jensen, MD,[c] Pieter A. Vriesendorp, MD, PhD,[d] Jaroslav Januska, MD,[e] Jan Krejci, MD, PhD,[f] Peter R. Hansen, MD, DMSc, PhD,[g] Hubert Seggewiss, MD,[b,h] Dieter Horstkotte, MD,[b] Radka Adlova, MD,[i] Henning Bundgaard, MD, DMSc,[c] Jurriën M. ten Berg, MD, PhD,[a] Josef Veselka, MD, PhD[i]

Survival Free of Adverse Arrhythmic Events Following ASA (n=1,197)



Long-term (>30 days) AAE Rates following ASA:
Young (≤50 yrs) = 0.8%
Middle-Age (51-64 yrs) = 0.8%
Older (≥65 yrs) = 1.0%

Approximately 2/3 of AAEs were fatal in both young and older patients

No independent predictors of AAEs in young and middle-age patients

Older patients, ≥2 conventional risk factors for SCD predicted AAEs during long-term f/u

ICD implantation following ASA was more common in young compared to older patients (6% vs 3%, p=0.04)

Liebregts et al., J Am Coll Cariol Intv 2017;10:1134

How to Choose Between Alcohol Septal Ablation and Surgical Myectomy?

Alcohol Septal Ablation	Surgical Myectomy
Adults and elderlies	Children and adolescents
Septal bulge	Mitral valve intervention
Right bundle branch clock	Left bundle branch block
Previous cardiac surgery	Low operative risk
Expert interventional team	Expert surgical team

Pelliccia et al., EuroIntervention 2019 Mar 12 [Epub ahead of print]

Alcohol Septal Ablation Vs. Myectomy in HOCM

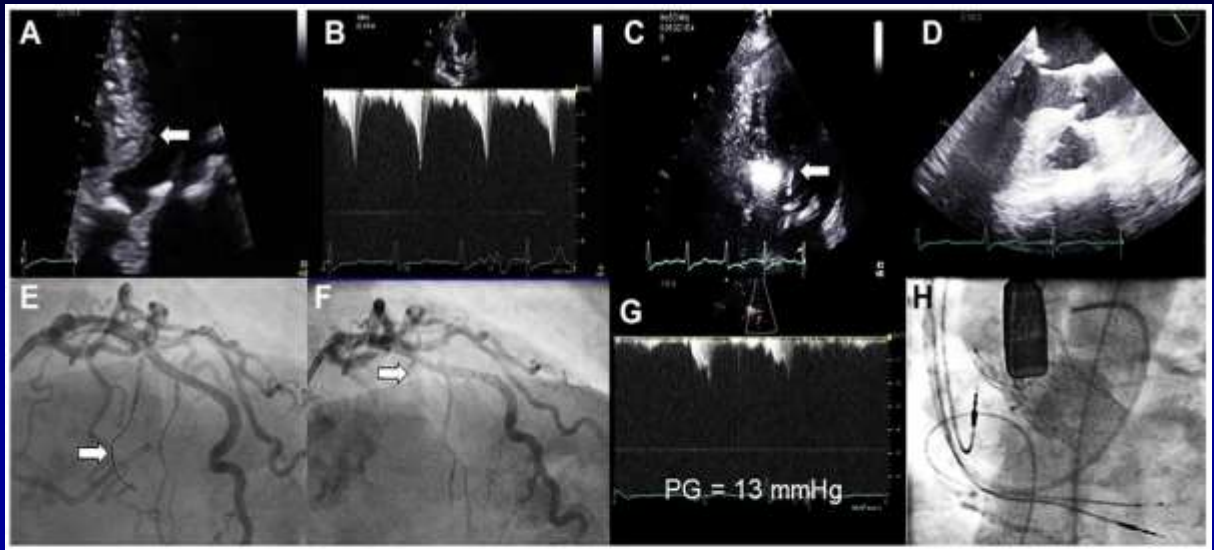
Procedural Data and Choice at MSH

	Alcohol Septal Ablation (ASA)	Surgical Myectomy (SM)
Length of stay (days)	4 ± 2	8 ± 3
PPM	Higher (12%)	Lower (4%)
Procedure mortality	<1%	<1%
Available F/U (yrs)	>8	>30
Septal thickness (mm)	14-28	>25
Treatment of choice	Elderly with co-morbidities and no significant MR	Young with no comorbidities and other valve disease/CAD

Newer Techniques of Septal Ablation in HOCM

1. Coil embolization
2. Radiofrequency ablation
3. Cryoablation
4. Covered stent in LAD over septal
5. MitraClip in patients with only modest septal hypertrophy

Management of ASH to Facilitate TAVR



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Patient	IVS Thickness (cm)	Peak LV Gradient (mmHg)	ASA Procedural Success	Need for Pacemaker	IVS Thickness post ASA (cm)	Valve Type	TAVR Procedural Success	Paravalvular Leak
1	1.6	None	Unsuccessful	Yes, post TAVR	1.6	Balloon expandable	Yes	Trivial
2	2.4	None	Successful	Yes	1.3	Balloon expandable	Yes	Mild
3	2.3	60	Successful	No	1.5	Self-expanding valve-in valve	Yes	None
4	1.6	33	Successful	No	1.4	Self-expanding	Yes	None
5	1.6	None	Successful	No	1.4	Self-expanding	Yes	None
6	1.7	41	Successful	No	1.2	Self-expanding	Yes	None
7	1.6	69	Successful	No	1.0	Balloon expandable	Yes	None
8	1.7	20	Successful	Yes, post TAVR	1.2	Self-expanding	Yes	None
9	2.0	None	Successful	No	1.0	Self-expanding	Yes	None
10	1.6	30	Successful	Yes	1.2	Self-expanding	Yes	None

A – ASH present on TEE
B – LVOT gradient
C – Upper septal contrast enhancement following contrast injection in septal artery
D – TEE image of reduced upper septum post-ASA (4 weeks post ablation)
E – Fluoroscopic image of coronary wire in a large septal branch with over-the-wire balloon during ASA
F – Successful occlusion of the septal artery
G – Reduced LVOT gradient post-ASA
H – Fluoroscopic view of CoreValve post-implantation
I – Experience and Outcomes with this Management Strategy

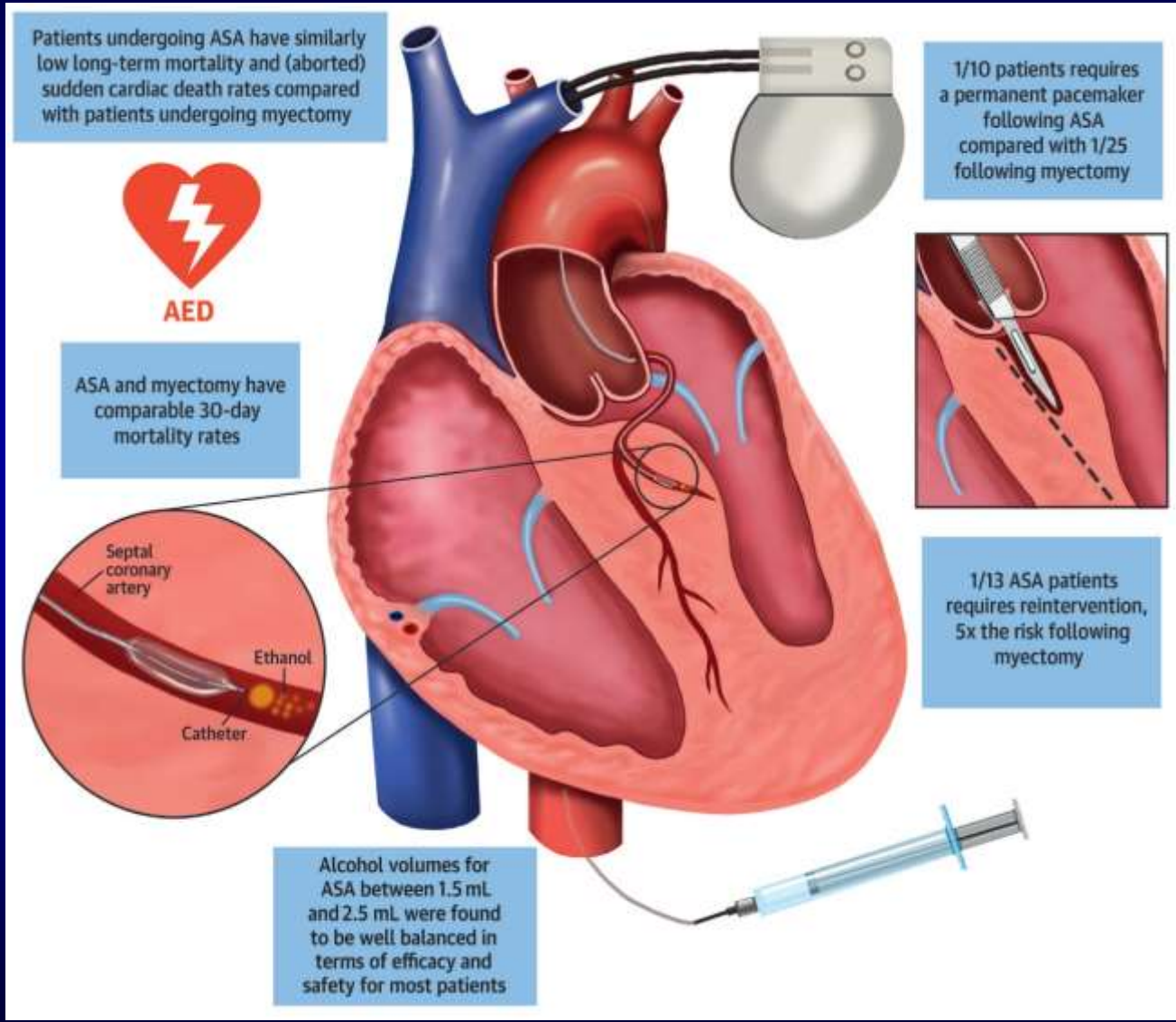
Khan, Tang, Dangas,Sharma, Kini et al., J Am Coll Cardiol Intv 2019 (Article in Press)

Alcohol Septal Ablation in HOCM

Mount Sinai Hospital Experience (9/2001-6/2019)

	N = 254
Mean age (years)/ Female gender (%)	55 ± 12/ 72
Baseline resting gradient mean (mm Hg)	42 ± 15
Baseline post-PVC gradient (mm Hg)	90 ± 22
Post ASA resting gradient (mm Hg)	10 ± 6
Post ASA post-PVC gradient (mm Hg)	28 ± 16
Alcohol dose (cc)	2.5 (1-5)
Peak CPK/ peak MB (U/L)	1600 ± 520 /162± 42
Need for permanent pacemaker	10
In-hospital death	1 pt (ref VT)
Average LOS (days)	3 ± 1
5Yr need for re-ASA (%)	4.5% (1 SM)

Alcohol Septal Ablation for Obstructive Hypertrophic Cardiomyopathy: Key Messages



Liebregts et al., J Am Coll Cardiol 2017;70:481