Alcohol Septal Ablation - What is the Current Experience and Indication?

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Hadassah University Hospital
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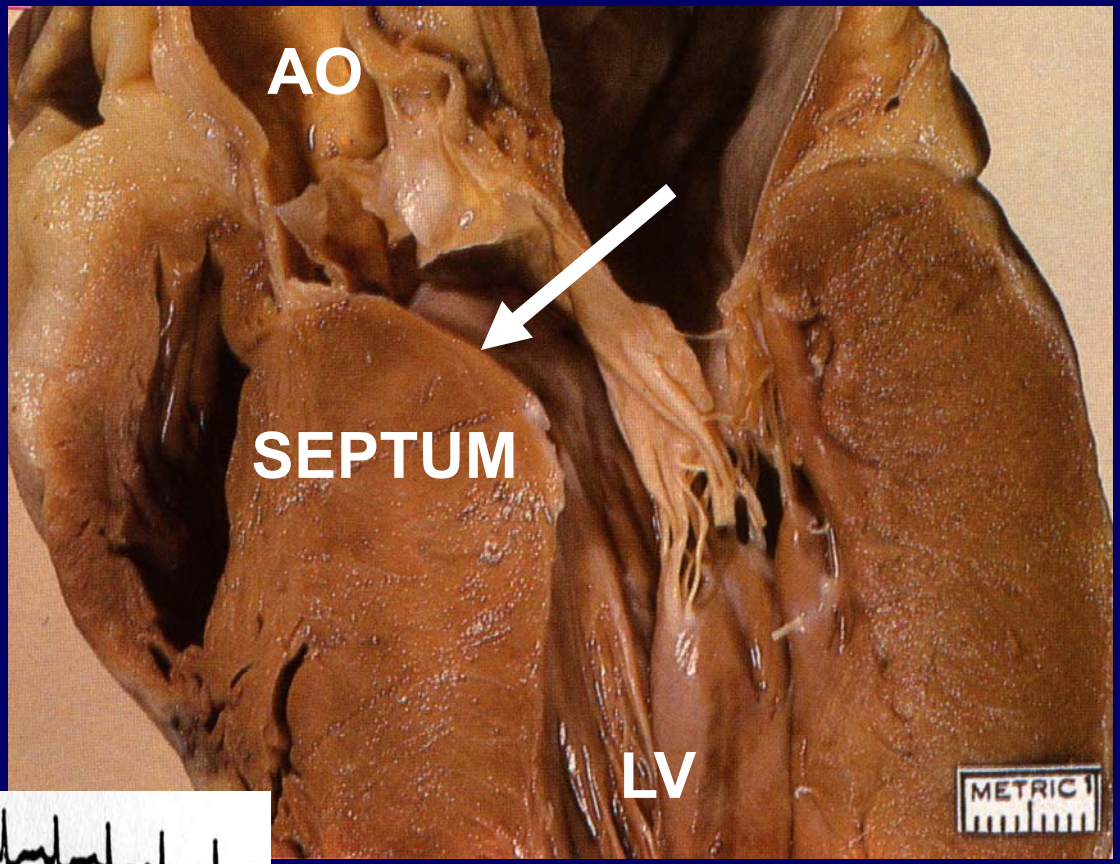
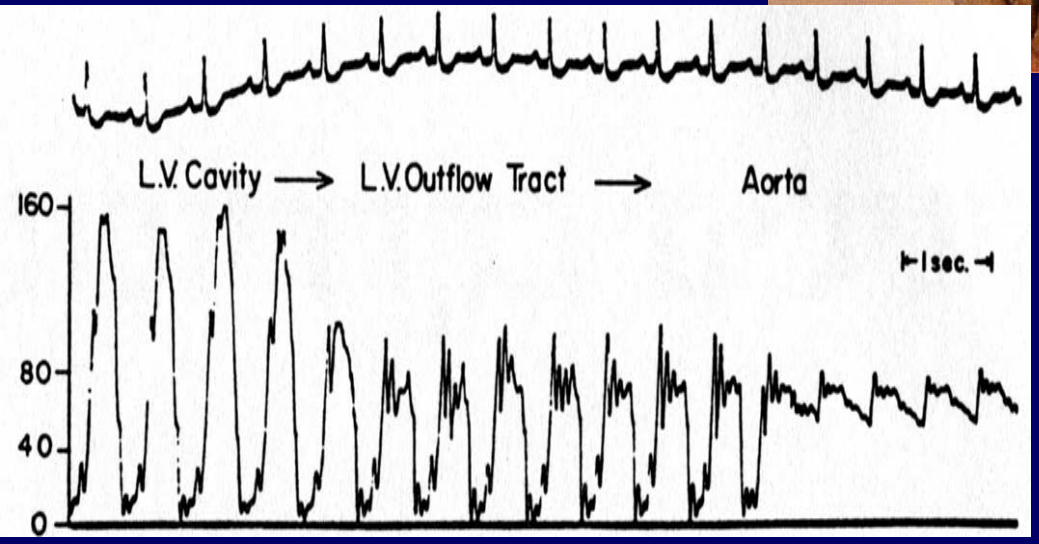
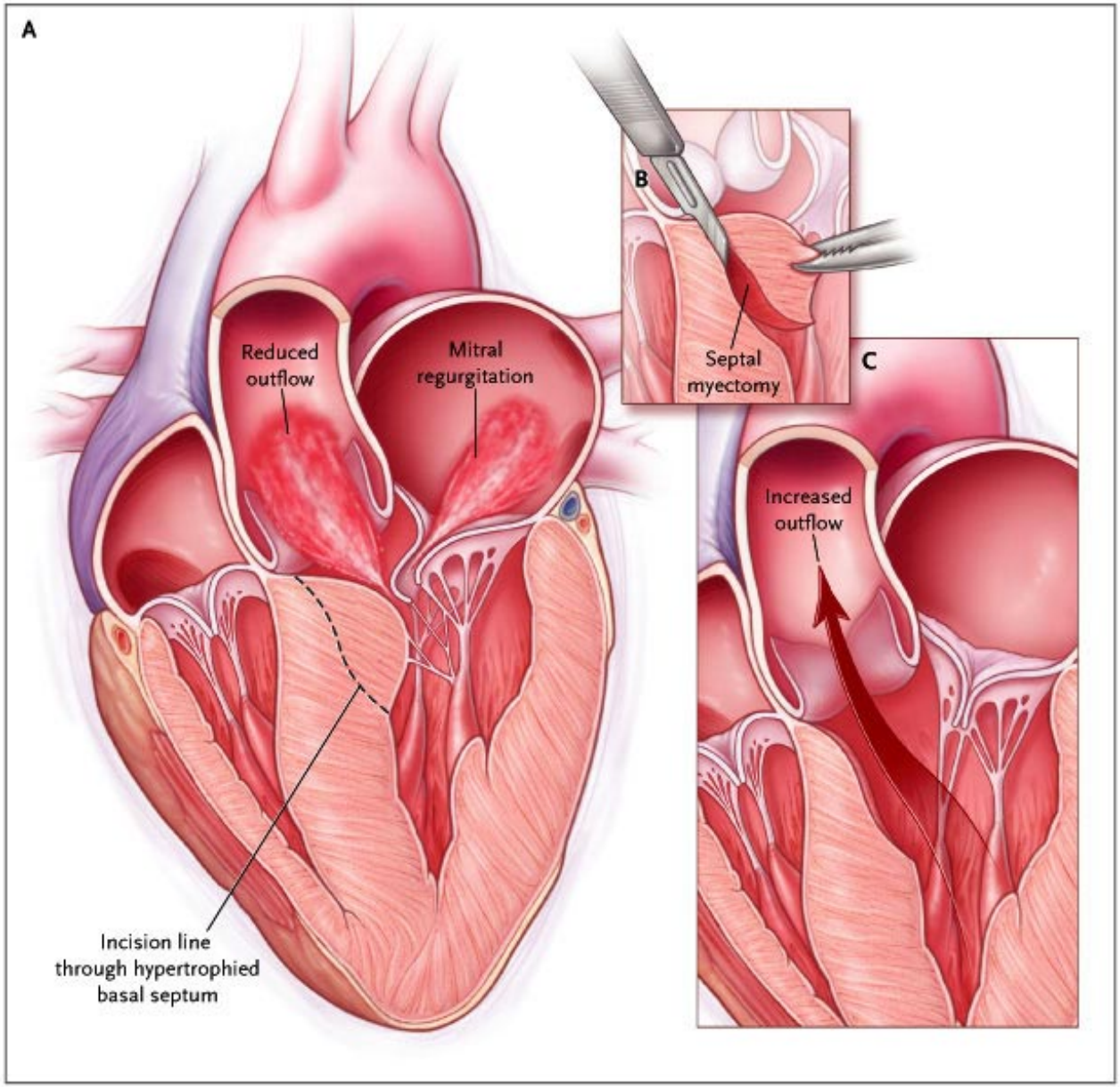
Israel Heart Society Meeting,
Jerusalem, 23.4.2013

HOCM

(Hypertrophic **obstructive** CM)

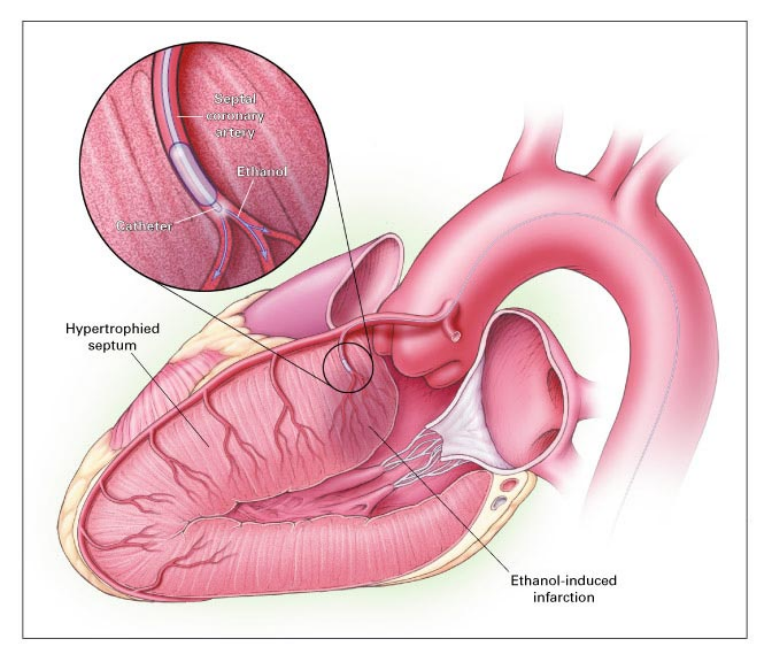




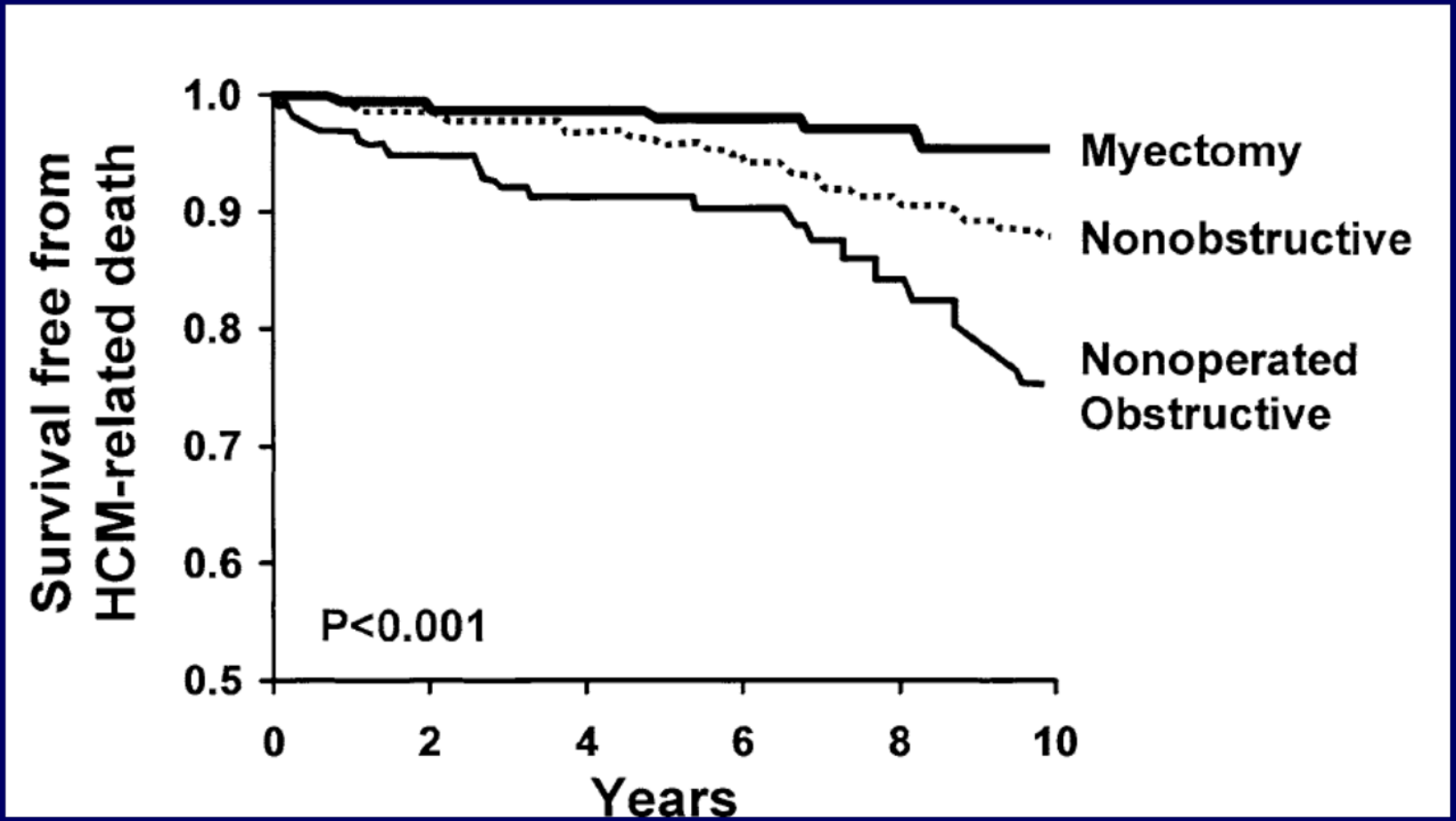


Nishimura RA. NEJM 2004;350:1320-7

HYPERTROPHIC OBSTRUCTIVE CARDIOMYOPATHY

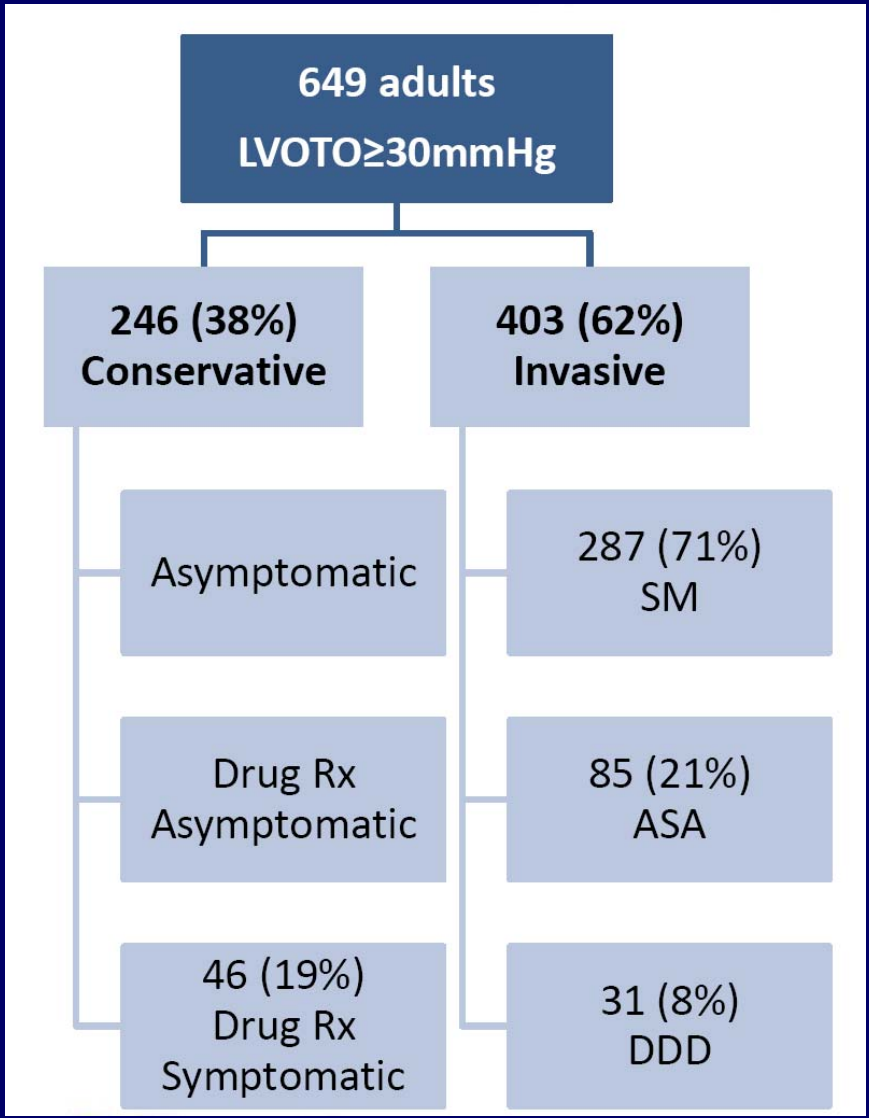


DA, 17 yo, 4..2.2007



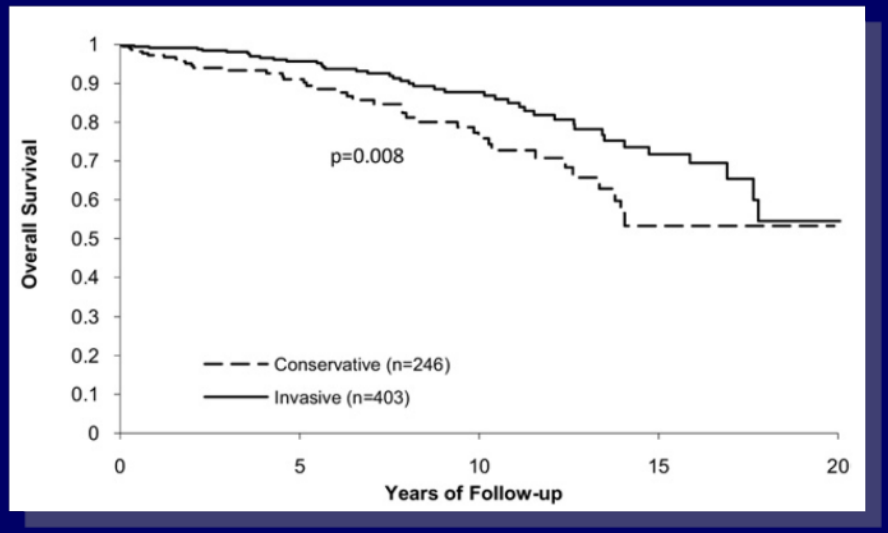
Ommen SR. J Am Coll Cardiol 2005;46:470-476

Long Term Survival in 649 Patients with Resting Obstructive Hypertrophic Cardiomyopathy



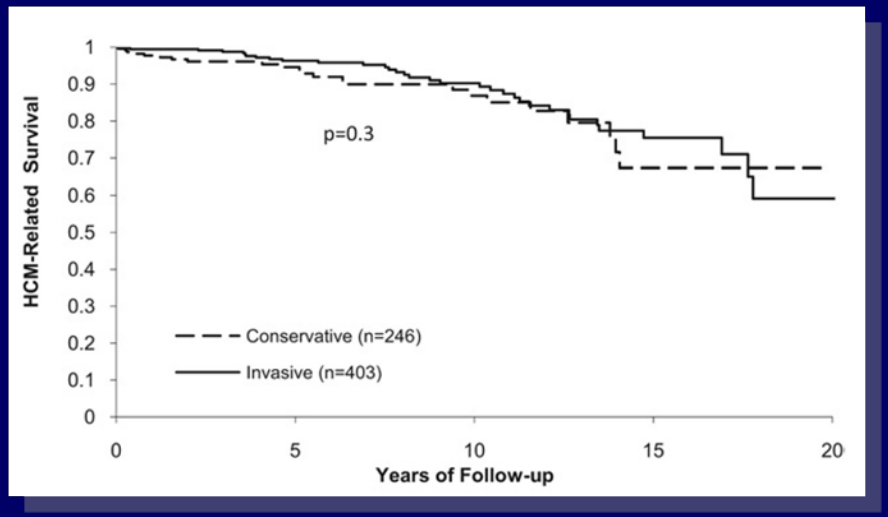
Ball W, J Am Coll Cardiol 2011;58:2313-2321

Long Term Survival in 649 Patients with Resting Obstructive Hypertrophic Cardiomyopathy



Overall Survival

No difference in 5 years survival between SM and ASA



HCM Related Survival

Ball W, J Am Coll Cardiol 2011;58:2313-2321

Major Points to be Discussed

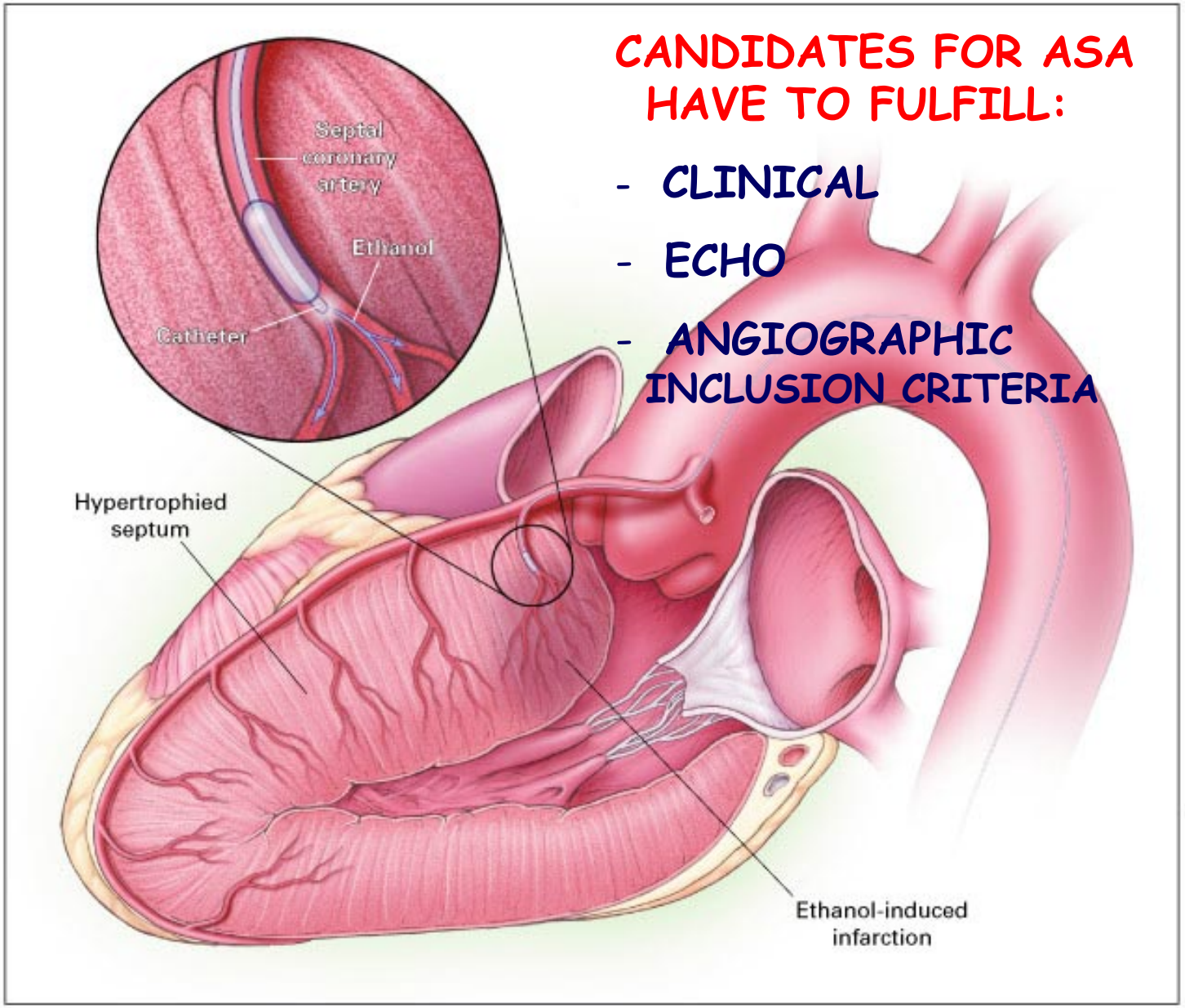
- Indications and Main Results of ASA
- Does ASA induce an Arrythmogenic Scar?
- How do the results of ASA compare with SM?

Indications for Septal Ablation and Myectomy in HOCM

- Severely symptomatic pts unresponsive to medical therapy (class III / IV)
- LVOTO >50 mmHg rest or >100 mmHg provocable
- Class II pts with limitations and/or with syncope related to LVOTO

CANDIDATES FOR ASA HAVE TO FULFILL:

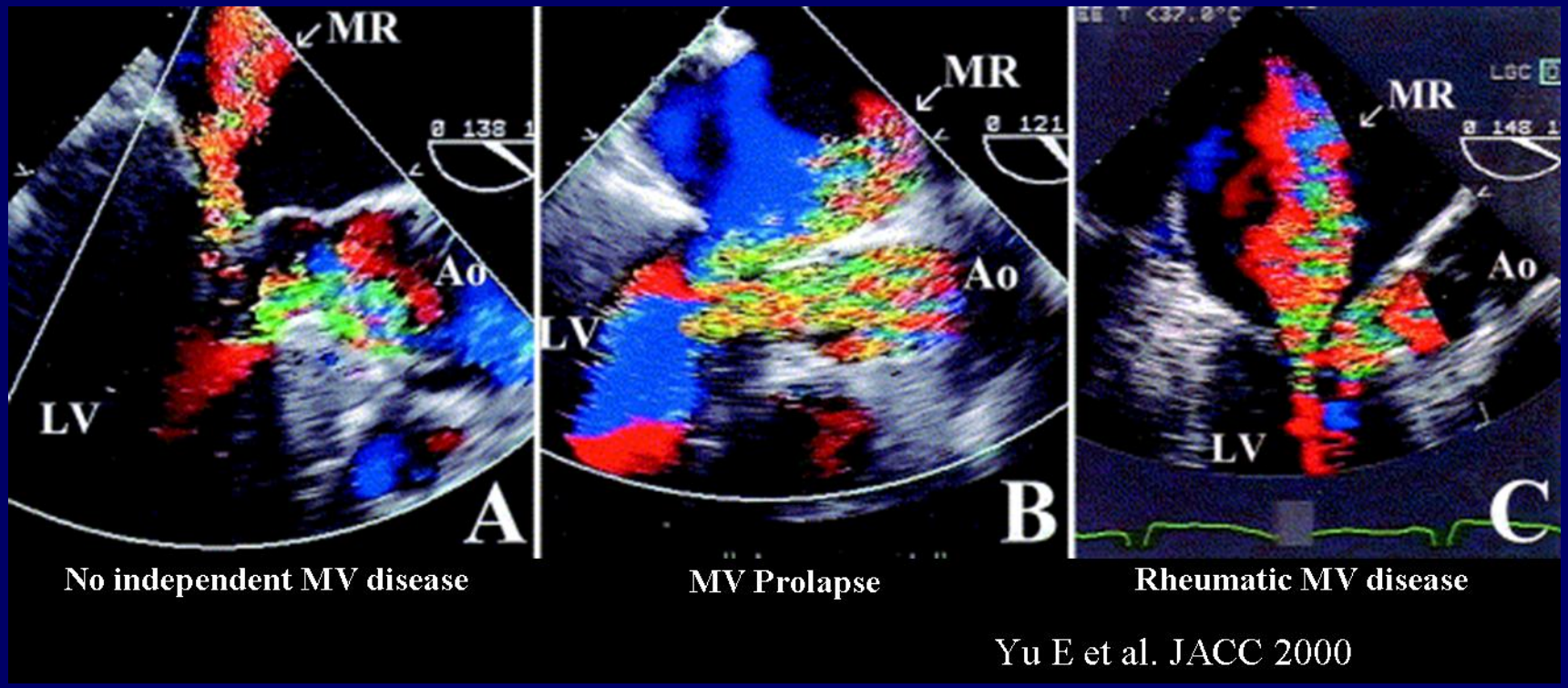
- CLINICAL
- ECHO
- ANGIOGRAPHIC INCLUSION CRITERIA



NEJM 347:1307,2002

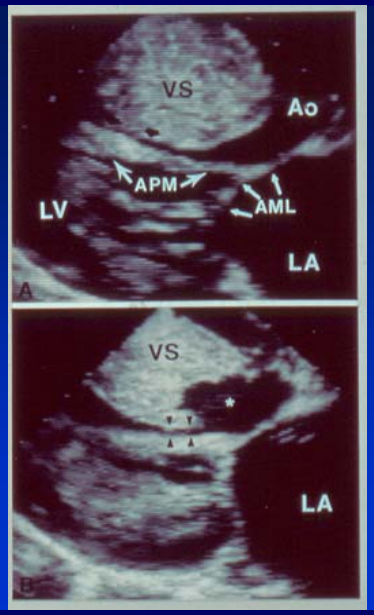
Echocardiographic Inclusion Criteria

- IVS thickness of ≥ 1.7 cm
- SAM & NO ORGANIC MV DISEASE

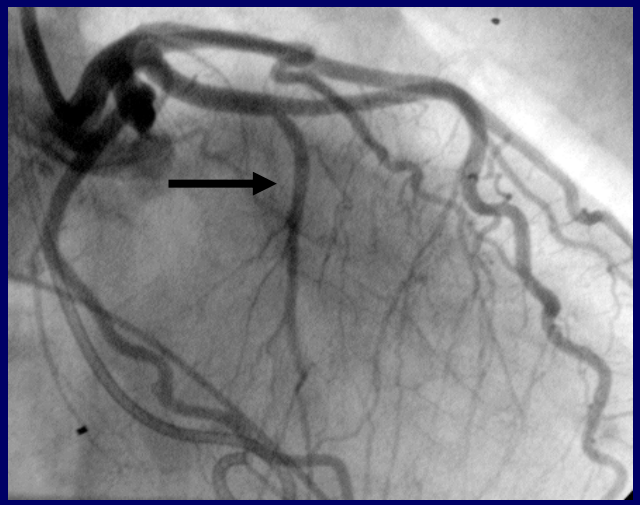


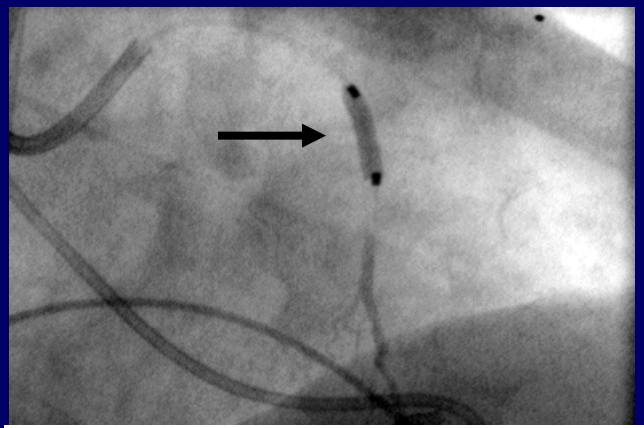
Independent MV Pathology in ~10%

Klues HG, MaronBJ Circulation 1992

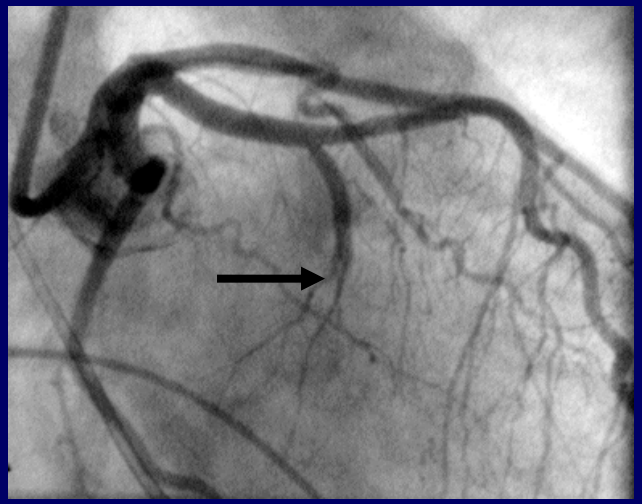


ANGIOGRAFIC INCLUSION CRITERIA





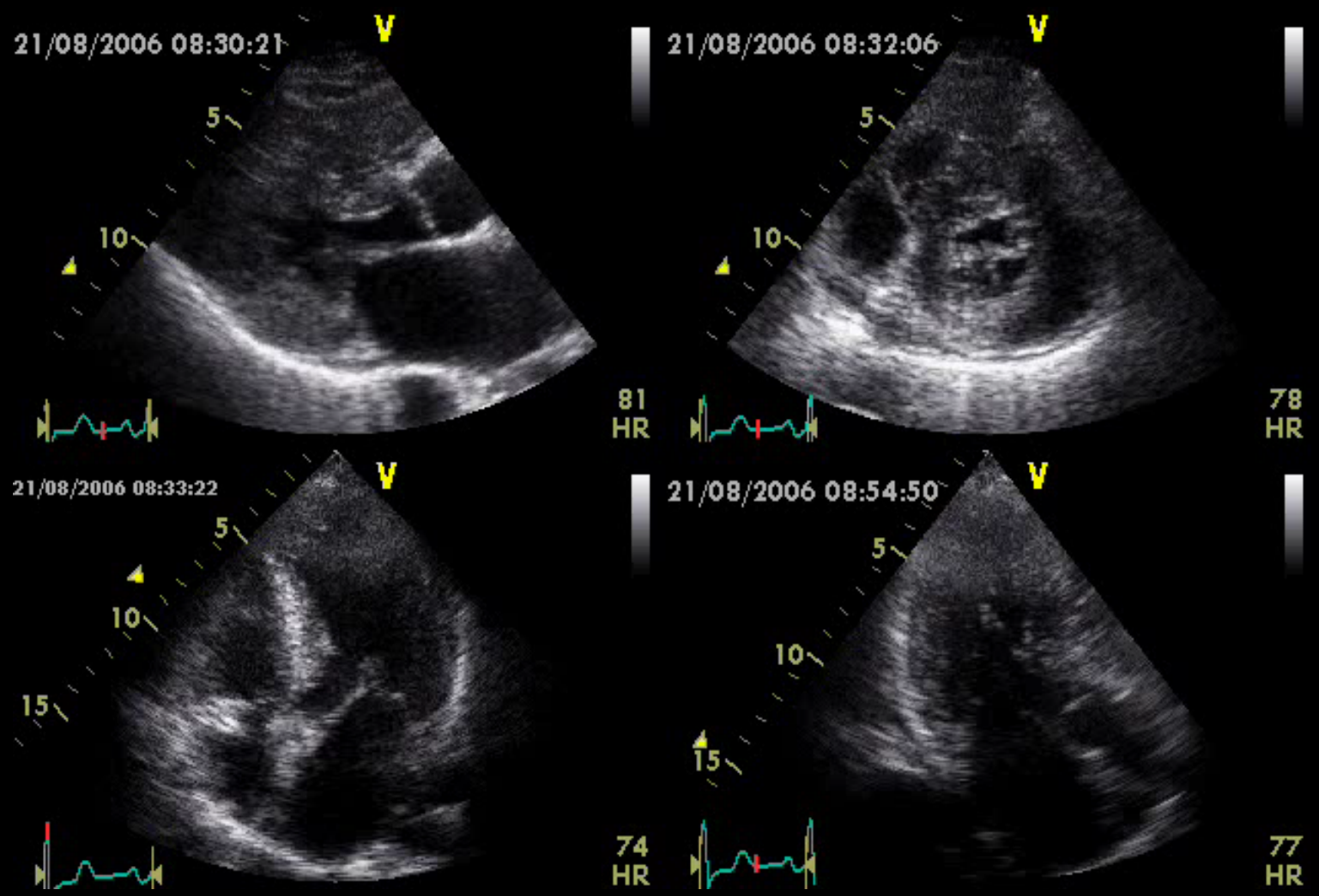
Exclude LAD leakage



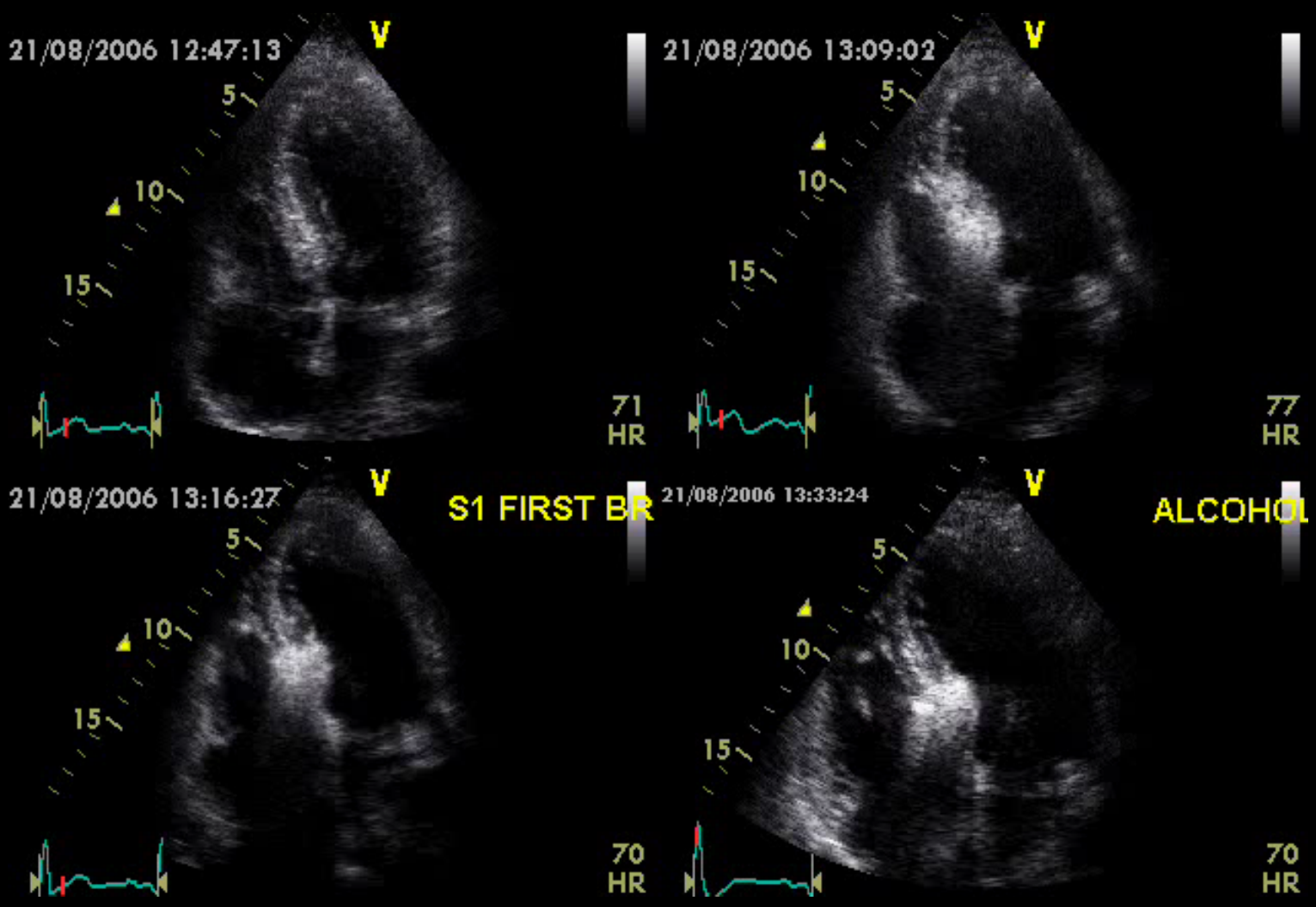
Courtesy of Seggewiss H

Myocardial Echo Contrast (MEC) – for target branch selection

In the cath lab: Multiple views, Target area

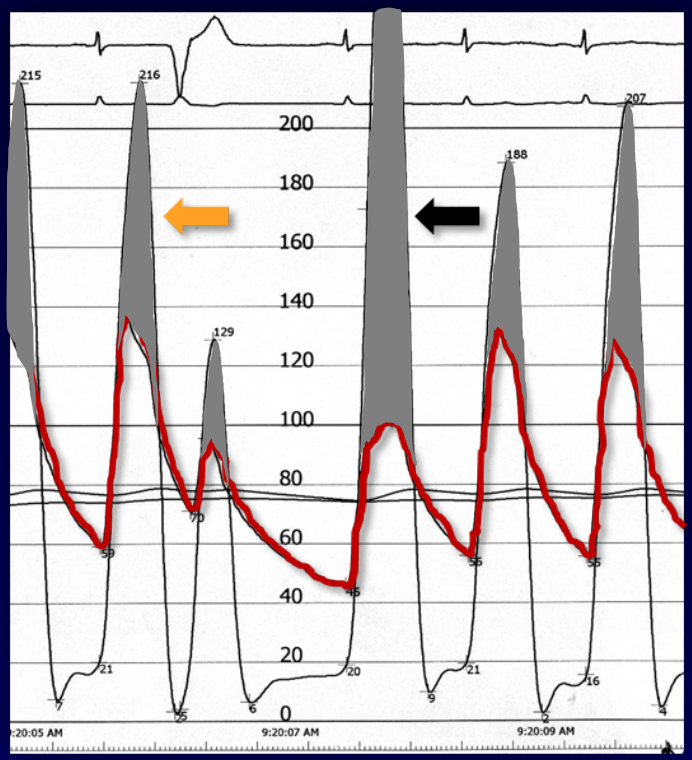


S1 2nd sub branch

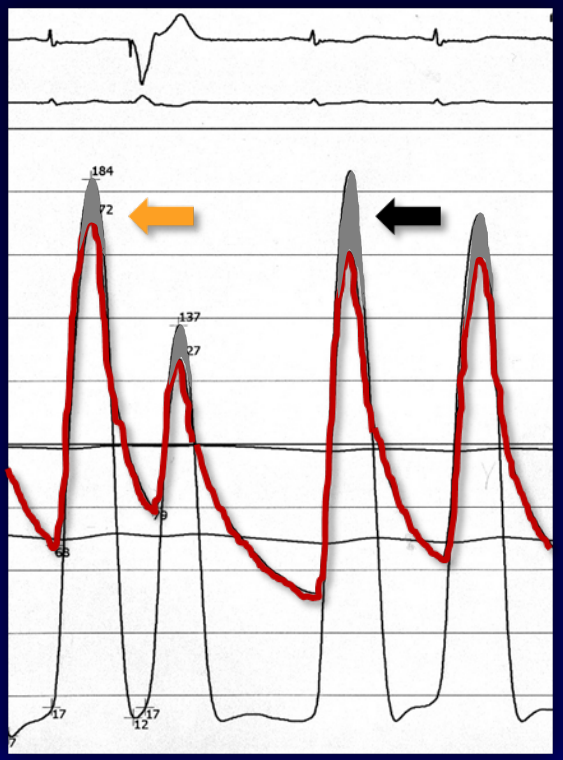


LVOT Gradient

Pre ASA



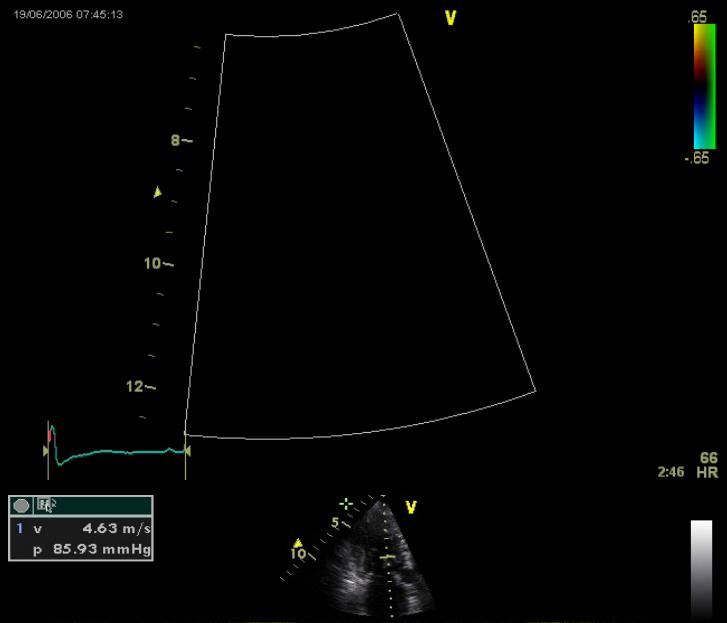
End of ASA

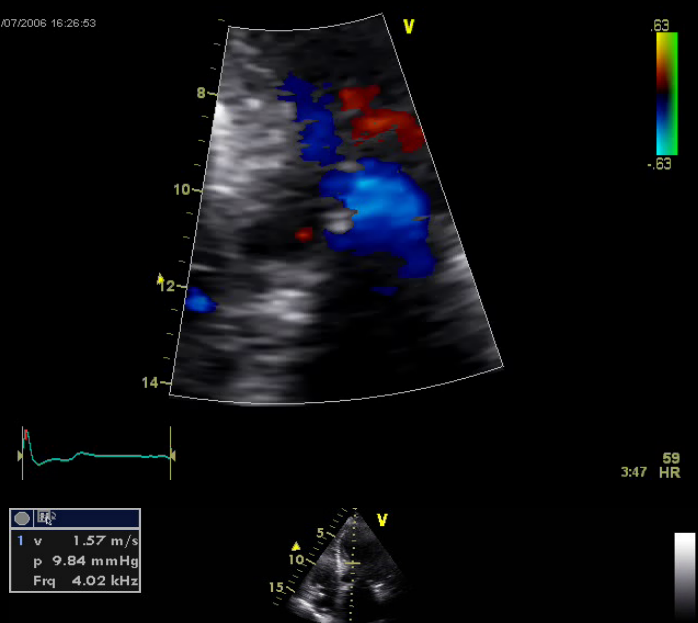


Baseline

Discharge

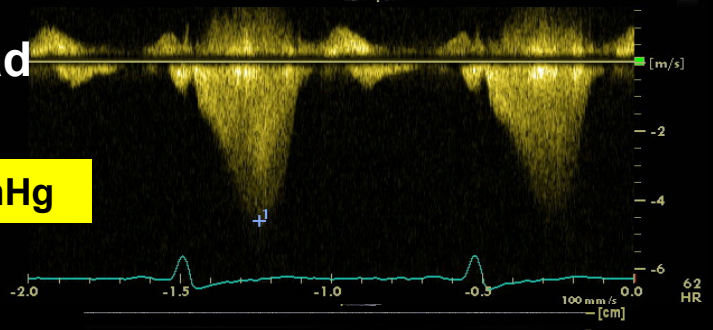
MR



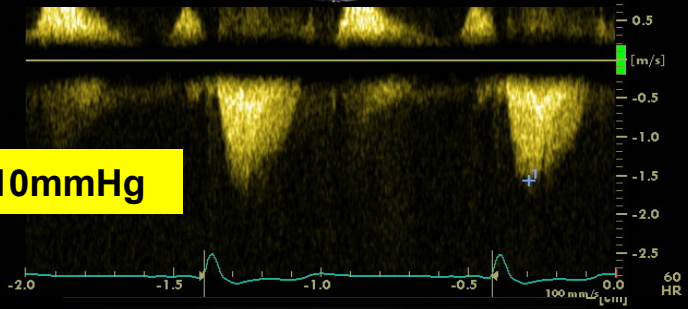


LVOT Grad

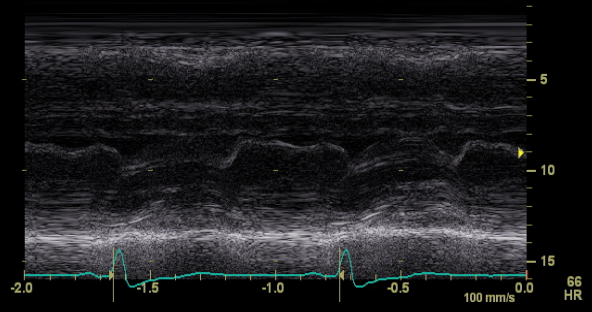
86mmHg

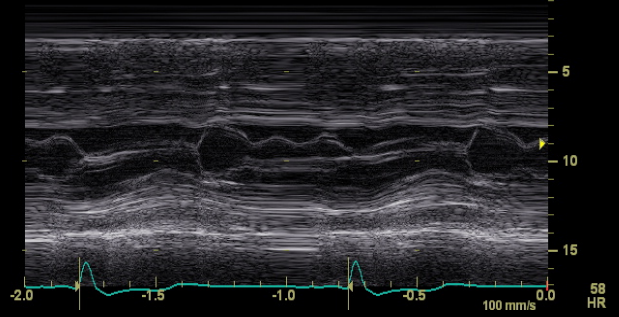


10mmHg



SAM





Biphasic Behavior of the LVOT Gradient Post ASA

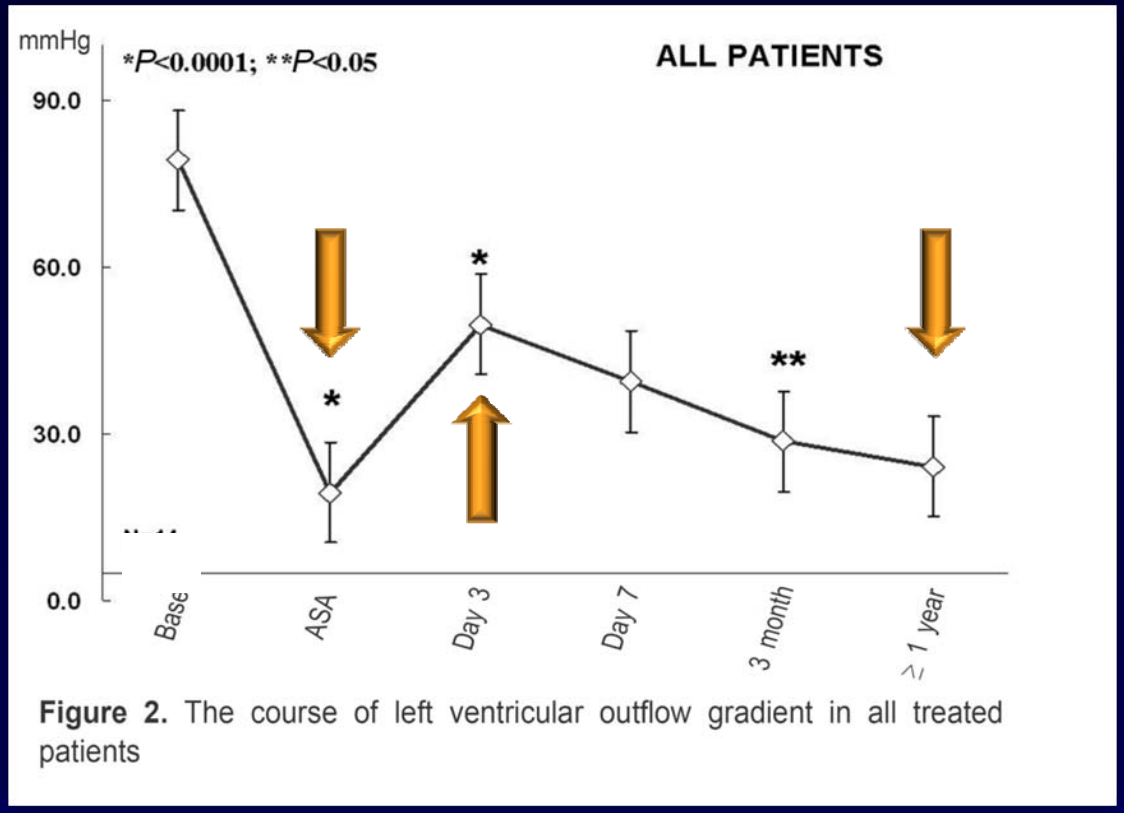


Figure 2. The course of left ventricular outflow gradient in all treated patients

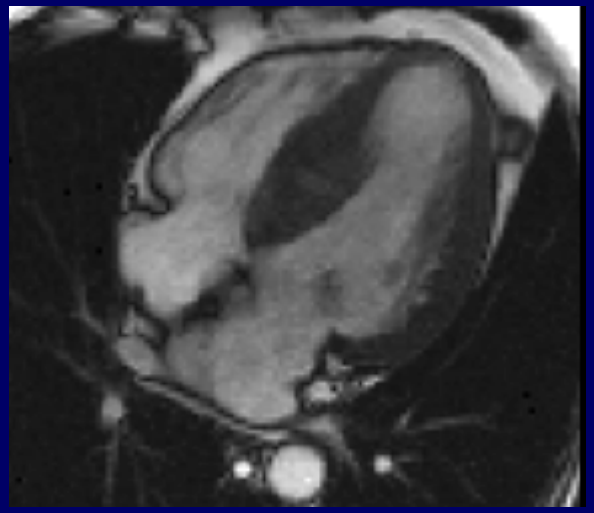
Keren A et al. IMAJ 2007;9:239-42

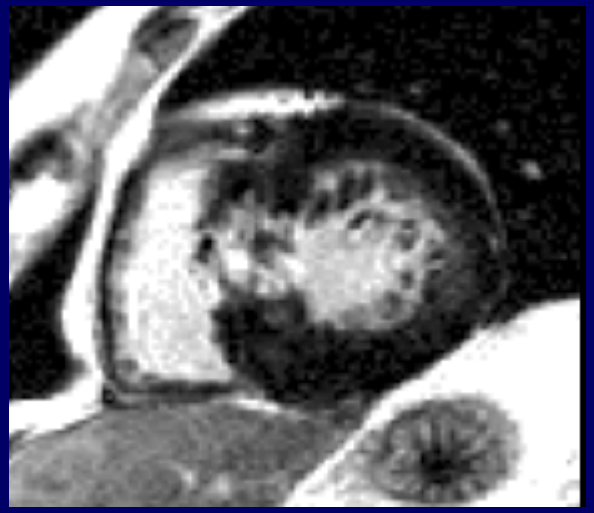
Table 1. Major clinical and hemodynamic parameters before and after alcohol septal ablation.

		LVOT gradient (mmHg)					Exercise test	
	NYHA class	Base	Valsalva	Exercise test	IVS (mm)	MR Severity	Duration (min)	BP Score
Pre-ASA	3.4±0.4	80±30	111±38	98±50	19±2.0	3.8±1.5	2.6±1.4	1.5±0.6
Follow-up	1.9±0.7	24±20	28±35	27±17	17±2.8	1.1±0.3	6.5±2.9	0.6±0.6
P	<0.00002	<0.003	<0.0004	<0.002	<0.008	<0.0007	<0.0004	<0.005

ASA = alcohol septal ablation, BP = blood pressure, IVS = interventricular septum, LVOT = left ventricular outflow tract, MR = mitral regurgitation, NYHA = New York Heart Association. For mitral regurgitation severity and blood pressure response scoring see text.

Keren A et al. IMAJ 2007;9:239-42





Keren A, 2006

8 days post procedure

Septal Damage Size Decreases Over Time

Quantitative Sestamibi SPECT

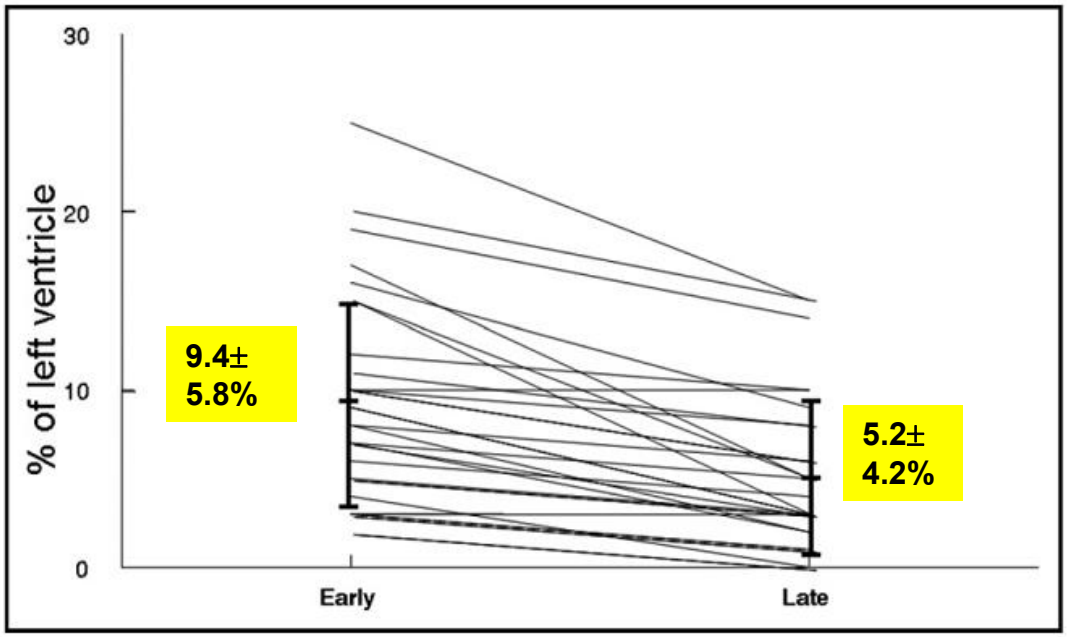
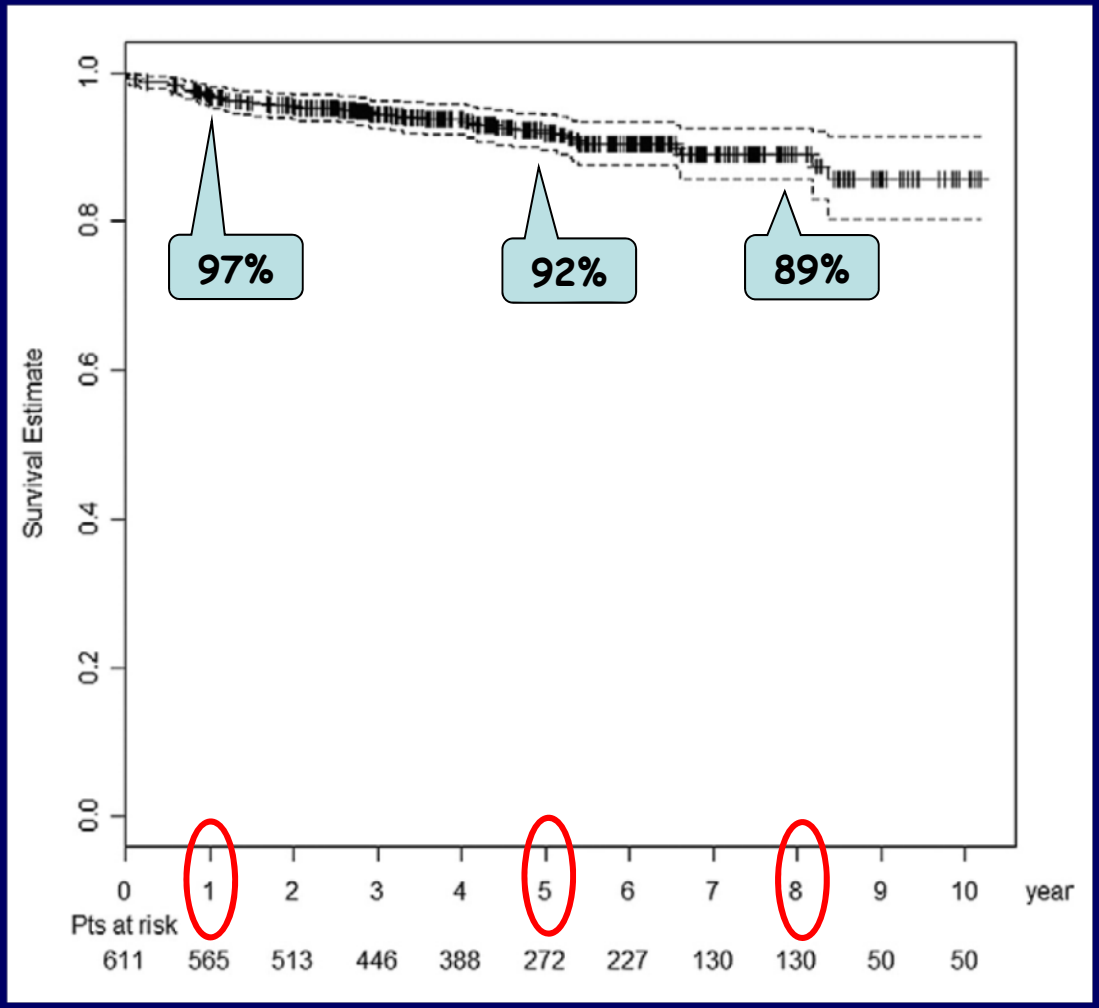


Figure 3. Septal defect size as a percent of the left ventricle assessed by automated polar maps early and late after alcohol septal ablation in 30 patients. A septal defect in perfusion imaging is detected early after alcohol septal ablation but tends to decrease in size when assessed late after ablation. Data represented as mean ± SD *(bold)*.

Aqel AR et al, Am J Cardiol 101:1328, 2008

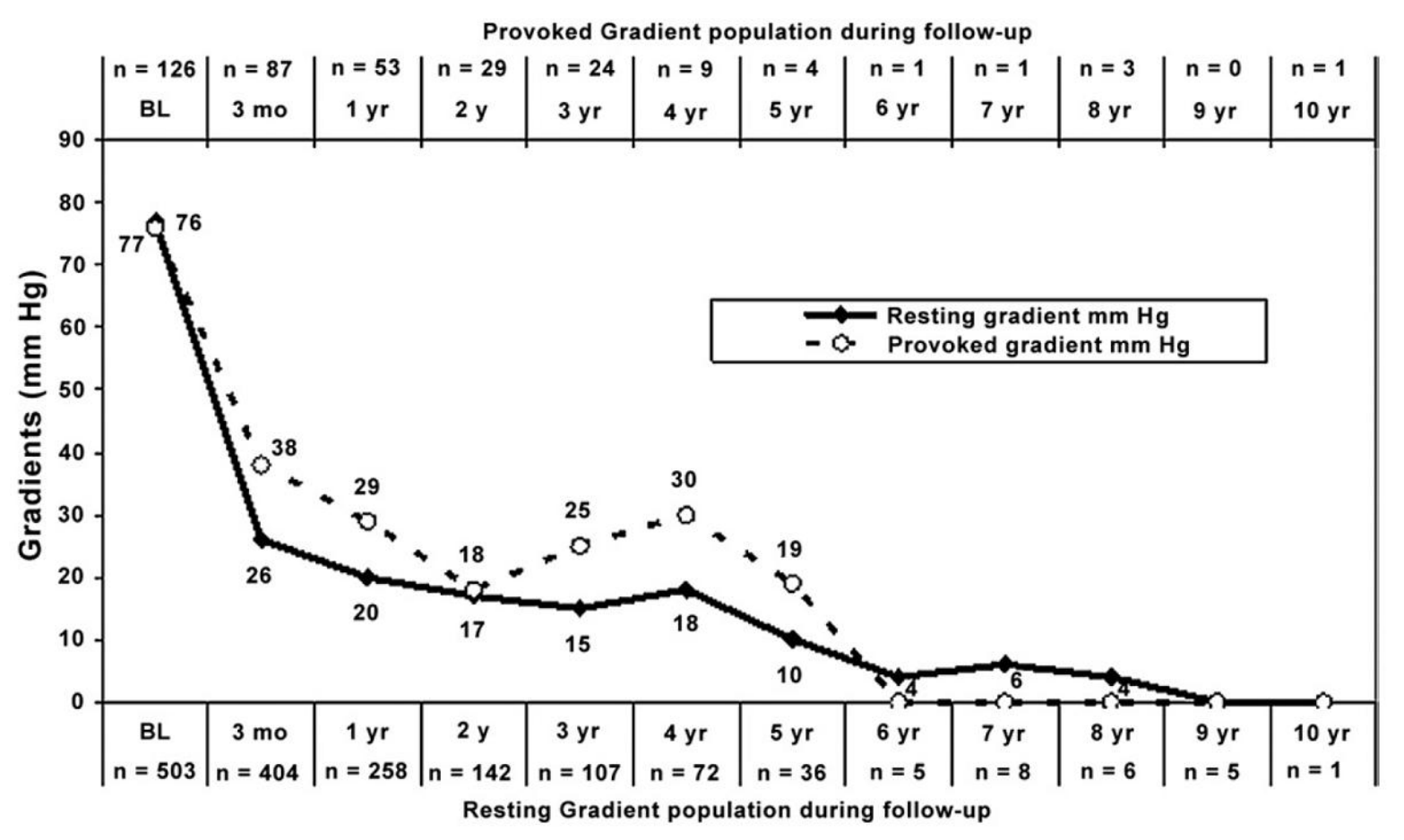
ASA: The Baylor and Medical University of South Carolina Experience 1996 – 2007

619 pts, Follow up of 4.6±2.5 years

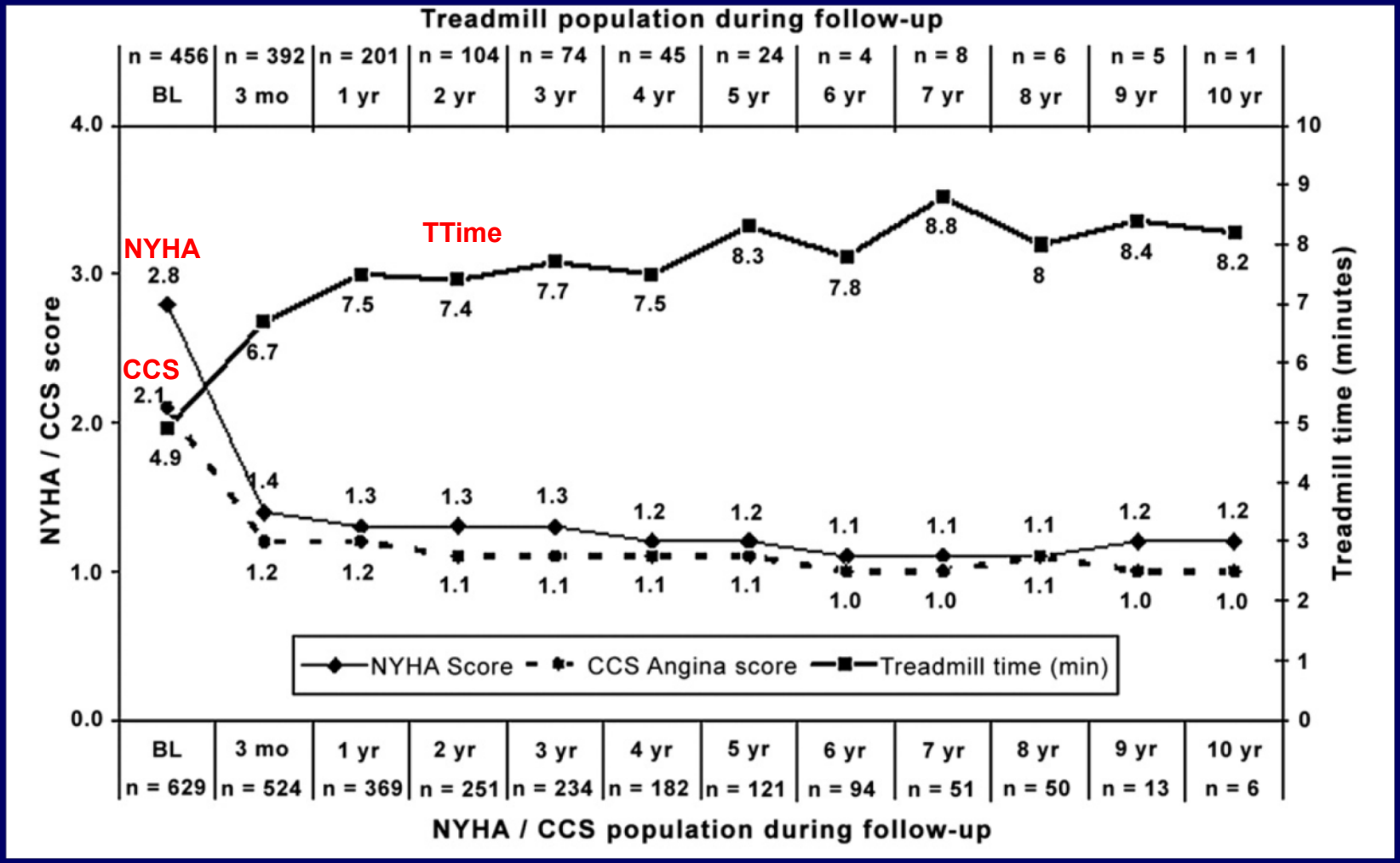


Fernandes VL et al. JACC:Cvasc interventions 2008;1:561-570

Decrease in LVOT Gradient



Fernandes VL et al. JACC:Cvasc interventions 2008;1:561-570



Fernandes VL et al. JACC:Cvasc interventions 2008;1:561-570

Results of ASA

Table 1 Clinical parameters at baseline and following alcohol septal ablation

	Alam M [a] [22] n = 2959	Faber L [b] [33] n = 312	Seggewiss H [b] [34] n = 100
Age, years	53.3 ± 0.1	54 ± 15	52 ± 15
Males (%)	53	59	50
Follow-up (months)	12.7 ± 0.3	12	58 ± 14
Prior pacemakers (%)	10	6	5
Prior myectomy (%)	3.5	3	2
Prior ICD (%)	2.7	1	NA
Beta-blockers (%)	51	36	36
Calcium channel blockers (%)	53	59	62
Other drugs (%)	30	25	NA
NYHA prior to ASA	2.9 ± 0.01	2.9 ± 0.4	2.5 ± 0.6
post ASA	1.2 ± 0.01	1.5 ± 0.7	1.6 ± 0.7
CCS prior to ASA	1.9 ± 0.01	1.7 ± 1.3	1.9 ± 1.3
post ASA	0.4 ± 0.02	0.9 ± 0.9	NA
Syncope and presyncope (%) (prior to/post ASA)	32/NA	34/NA	31/1
Exercise capacity (seconds)			
prior to ASA	325 ± 2	NA	366 ± 198
post ASA	437 ± 4	NA	564 ± 174
Exercise capacity (watts)			
prior to ASA	86 ± 0.4	94 ± 51	90 ± 99
post ASA	123 ± 1.6	119 ± 40	121 ± 45
Clinical improvement post ASA (%)	89	91	96
Repeat ASA (%)	7	5	0
Myectomy post ASA (%)	2	1	0
Pacemakers post ASA (%)	11	7	10
Death: periprocedural (%)	1.5	1.3	1
late, cardiovascular (%)	0.4	0.7	2

[a] Values given as mean ± SEM; [b] values given as mean ± SD

Alam M et al.
J Interv Card;19:319-324,2006.

Faber L, Welke D, et al
Clin Res Cardiol, 96:864-73.2007 .

Seggewiss H, Rigopoulos A, et al

Clin Res Cardiol, 96:856-63.2007

Pauschinger M, Keren A. . Editorial.

Clin Res Cardiol, 96:851-5, 2007

Main Results of ASA

- Highly effective (85-90%) in improving:
  - the hemodynamic parameters (gradient, MR)
  - symptoms
  - exercise capacity (VO2 max)
  - BP response to exercise and syncopes
- Periop mortality 1-2%, Pacemakers 10-20%, re-do procedures 5-10%

Major Points to be Discussed

- Indications and Main Results of ASA
- **Does ASA induce an Arrythmogenic Scar?**
- How do the results of ASA compare with SM?
- Are ASA and SE just competitive or complementary procedures?

Increase in Sudden Death Rate Due to the Arrhythmogenic Scar After ASA?

Maron BJ, Spirito P, Shen WK, et al. JAMA 2007;298:405-412

506 pts with HCM and ICD, were followed for 3.7 years

Intervention rate: Primary prevention ***3.6%/year***

Secondary prevention ***10.6%/year***

ICD discharges of *10.4%/year in ASA* (4/17pts) c/w *2.6%/year* in SM (6/50pts)

"The results suggest that ASA may increase the risk of sudden death in some patients with HCM"

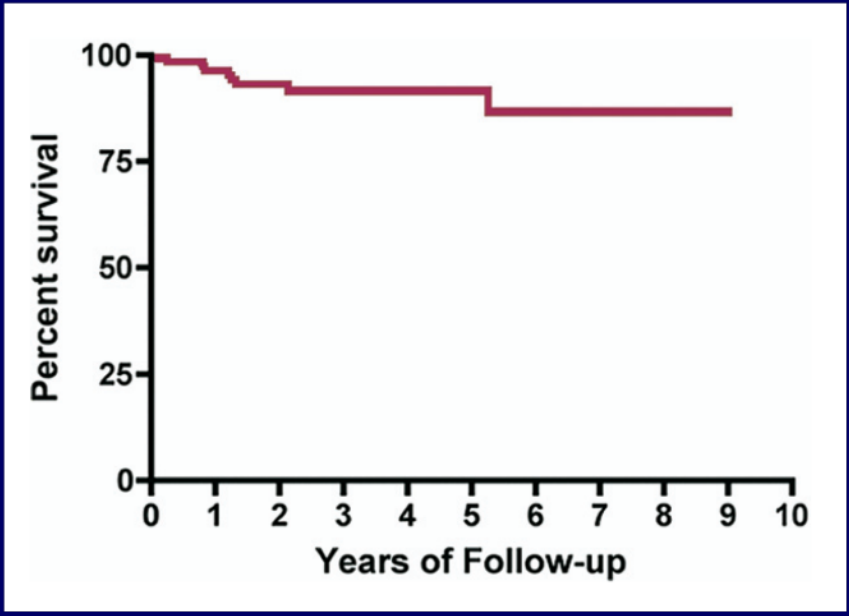
ten Cate FJ Circ Heart Fail 2010;

Is There an Arrhythmogenic Scar After ASA?

Cuoco FA, Spencer WH, Fernandes VL et al. J Am Coll Cardiol 2008;52:1718-1723

123 consecutive pts with ASA with ICD for primary prevention

2.8% annual event **rate (1.5 mean risk factors/pt for SCD)**



"The results suggest that ASA is not proarrhythmic"

Gietzen FH Eur heart J 1999; Lawrenz T Pacing Clin Electrohysiol 2005; Noseworthy PA Am J Cardiol 2009; Agarwal S J Am Coll Cardiol 2010; Leonardi RA Circ Cardiovascular Intrerv 2010

Major Points to be Discussed

- Indications and Main Results of ASA
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Alcohol Septal Ablation vs Myectomy: the Mayo Clinic Experience

Table 1. Baseline Variables

	Ablation Patients (n=177)	Myectomy Patients (n=177)	*P*
Age, y	63±13	62±12	0.17
Women, n (%)	102 (58)	102 (58)	0.99
NYHA class III/IV, n (%)	177 (100)	133 (75)	<0.0001
CCS class III/IV, n (%)	34 (19)	50 (28)	0.07
Syncope, n (%)	27 (15)	30 (17)	0.78
Past medical history, n (%)			
Atrial fibrillation	28 (16)	22 (12)	0.29
Previous stroke	4 (2)	2 (1)	0.23
Hypertension	91 (51)	27 (15)	<0.0001
Diabetes mellitus	13 (7)	3 (2)	0.02
Coronary artery disease	24 (14)	7 (4)	0.002
Previous myectomy	3 (2)	0 (0)	0.08
Previous septal ablation	0 (0)	1 (1)	0.32
Family history of HCM, n (%)	31 (18)	23 (13)	0.18
Family history of sudden death due to HCM, n (%)	10 (6)	17 (10)	0.20
Morphology, n (%)			0.15
Asymmetric hypertrophy	130 (73)	120 (68)	
Concentric hypertrophy	41 (23)	57 (32)	
Maximum ventricular wall thickness, mm	23±5	22±7	0.05
End-diastolic diameter, mm	45±6	45±6	0.07
End-systolic diameter, mm	25±5	24±5	0.53
Resting LVOT gradient, mm Hg	70±40	67±40	0.41
≥50 mm Hg, n (%)	121 (68)	118 (66)	0.73
Internal cardioverter-defibrillator, n (%)	8 (5)	12 (7)	0.40
Permanent pacemaker, n (%)	6 (3)	31 (18)	0.01
Medications, n (%)			
β-receptor antagonist	129 (73)	102 (58)	0.0006
Calcium-channel blocker	66 (37)	86 (49)	0.07
Disopyramide	12 (7)	21 (12)	0.13
Amiodarone	6 (3)	14 (8)	0.08

Sorajja P, Ommen SR, Holmes DR et al. Circulation 2012;126:2374-2380

Alcohol Septal Ablation vs Myectomy: the Mayo Clinic Experience

Table 2. Acute Procedural Results and 30-Day Clinical Events

	Ablation Patients (n=177)	Myectomy Patients (n=177)	*P*
No. septal arteries injected, mean±SD	1.1±0.4	. . .	. . .
Volume of ethanol injected, median (IQR), mL	1.8 (0.5)	. . .	. . .
Residual LVOT gradient at rest, median (IQR), mm Hg	11 (15)	5 (5)	0.001
Reduction in LVOT gradient, %	85±16	88±19	
Procedural and in-hospital complications, n (%)	51 (28.8)	10 (5.6)	<0.0001
Pacemaker dependency	36 (20.3)	4 (2.3)	
Cardiac tamponade	6 (3.3)	1 (0.6)	
Sustained ventricular tachycardia	3 (1.7)	0	
Cardiac surgery	2 (1.1)	2 (0.6)	
Resuscitated sudden cardiac arrest	2 (1.1)	1 (0.6)	
Pneumothorax	1 (0.6)	2 (1.1)	
Stroke	1 (0.6)	0	
Death	2 (1.1)	1 (0.6)	0.32
Sudden cardiac death	1 (0.6)	0	
Heart failure	1 (0.6)	1 (0.6)	

Table 3. Clinical Events During Follow-Up Beyond 30 Days After Procedure

	Ablation Patients (n=177)	Myectomy Patients (n=177)	*P*
Permanent pacemaker implantation, n (%)	3 (1.7)	2 (4.3)	0.65
ICD discharge for VT or VF, n (%)	1 (0.6)	0 (0.0)	
Septal ablation, n (%)	5 (2.8)	0 (0.0)	
Cardiac surgery, n (%)	15 (8.5)	2 (1.1)	0.0001
Surgical myectomy	10 (5.6)	1 (0.6)	
Coronary artery bypass grafting	1 (0.6)	0 (0.0)	
Ascending aortic aneurysm repair	1 (0.6)	0 (0.0)	
Aortic valve replacement	1 (0.6)	1 (0.6)	
Pericardiotomy	1 (0.6)	0 (0.0)	
Mitral valve repair	1 (0.6)	0 (0.0)	
Death, n (%)	24 (13.5)	24 (13.5)	0.99
Noncardiac cause	11 (6.2)	15 (8.5)	
Unknown cause	12 (6.8)	7 (4.0)	
Sudden cardiac death	3 (1.7)	3 (1.7)	

Sorajja P, Ommen SR, Holmes DR et al. Circulation 2012;126:2374-2380

Alcohol Septal Ablation vs Myectomy: the Mayo Clinic Experience

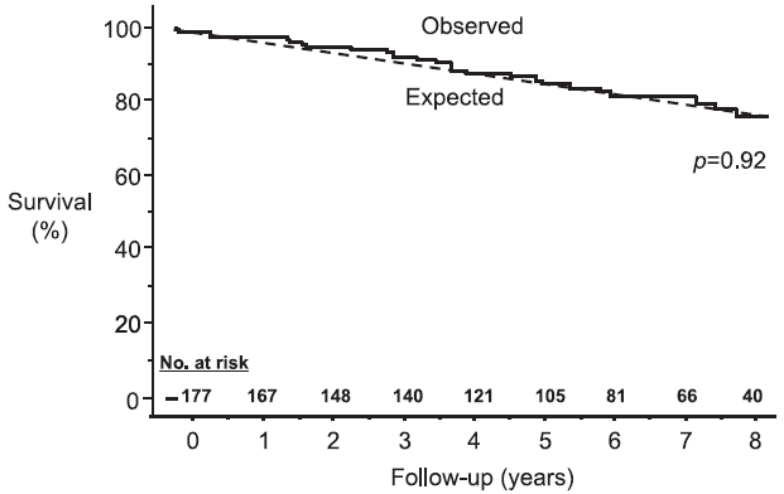


Figure 1. Survival free of all-cause mortality for patients with septal ablation (observed). Expected survival was calculated from age- and sex-specific mortality rates obtained from the US general population.

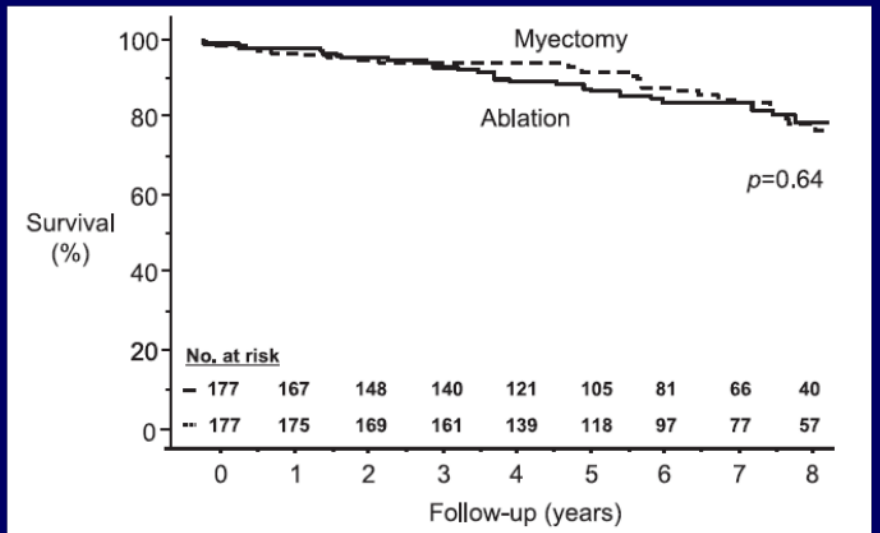


Figure 2. Survival free of all-cause mortality for patients with septal ablation in comparison with age- and sex-matched population of patients who underwent surgical myectomy.

Sorajja P, Ommen SR, Holmes DR et al. Circulation 2012;126:2374-2380

ASA Vs SM: Mortality

Meta-analysis	Inclusion criteria	Number of studies	Number of Patients	In-hospital mortality	
Zeng, Z. *Int.J.Cardiol.* 2006; 112[1]: 80-84.	Case control studies comparing ASA with SM in adult HOCM patients	3	ASA: 86 SM: 91	2.3% Vs 1.1% p=?	
				In-hospital mortality	
Alam, M. *Eur.Heart J.* 2009; 30[9]: 1080-1087.	Case control studies comparing ASA with SM in adult HOCM patients	5	ASA: 183 SM: 168	1.6% Vs 0.6% p=0.2	
				30 day all cause mortality (RD)	**Long term all cause mortality (RD)**
Agarwal, S. *J Am Coll Cardiol* 2010; 55[8]: 823-834.	Cohort and case control studies comparing ASA with SM in adult HOCM patients	9	ASA: 380 SM: 326	0.01 (0.01 to 0.03) p=0.35	0.02 (-0.05 to 0.09) p=0.55
				Annual rate of all cause mortality	**Annual rate of SCD**
Leonardi, R A. *Circ.Cardiovasc.Interv.* 2010; 3[2]: 97-104.	Reports/studies with ≥5 ASA patients or ≥100 SM patients	19 ASA studies (1996-2007)	2207	1.8 (1.2 to 2.6)	0.3 (0.2 to 0.6)
		8 SM studies (1963-2005)	1887 #	2.1 (1.7 to 2.7) p=0.36	0.4 (0.3 to 0.6) p=0.37

Curtsey O'Mahony C

Alcohol Septal Ablation vs Septal Myectomy in HOCM
Meta-Analysis Including 4,094 Patients

Patients: ASA – 2207, SM – 1887;

- **Median *follow up ASA 51 vs SM 1266 pt ys**
- **ASA pts were *older (55 vs 44 years), with less *hypertrophy (21 vs 23 mm)**

*** p<0.001**

	Surgical Myectomy, Median (IQR)	ASA, Median (IQR)
NYHA functional class	1.6 (1.5–1.7)	1.5 (1.3–1.7)
LVOT gradient, mm Hg	3 (2–6)	22 (15–23)
Septal wall thickness, mm	17 (17–19)	16 (15–17)
New permanent pacemaker, %	5 (3–9)	11 (8–15)
Patients with an ICD, %	4 (3–4)	5 (4–8)

Leonardi RA, Circ Cardiovasc Interv 2010;3:97-104

Alcohol Septal Ablation vs Septal Myectomy in HOCM
Meta-Analysis Including 4,094 Patients

	Surgical Myectomy % per Patient-Year, Weighted Mean (95% CI)	ASA % per Patient-Year, Weighted Mean (95% CI)	*P*
All-cause mortality rate	1.8 (1.2–2.6)	2.1 (1.7–2.7)	0.37
SCD rate	0.3 (0.2–0.6)	0.4 (0.3–0.6)	0.36

After adjustment for baseline characteristics, ***odds ratios were lower for ASA than for SM for all-cause mortality 0.28 (95% CI 0.16 to 0.46) and for sudden death 0.32 (95 CI 0.11 to 0.97)***

Leonardi RA, Circ Cardiovasc Interv 2010;3:97-104

Septal Ablation vs Myectomy

- Anatomy
  - Severity of hypertrophy
  - Coronary Arteries
  - Mid-cavity obstruction
  - Intrinsic Mitral Valve abnormalities
  - Subaortic membrane
- Co-morbidities
- Age
- Patient choice
- Medical/Surgical Experience

CONCLUSIONS ON ASA

- Can be alternative to myectomy in selected pts unresponsive to medical therapy

- Has immediate and intermediate term results comparable with myectomy but long term safety is still not known

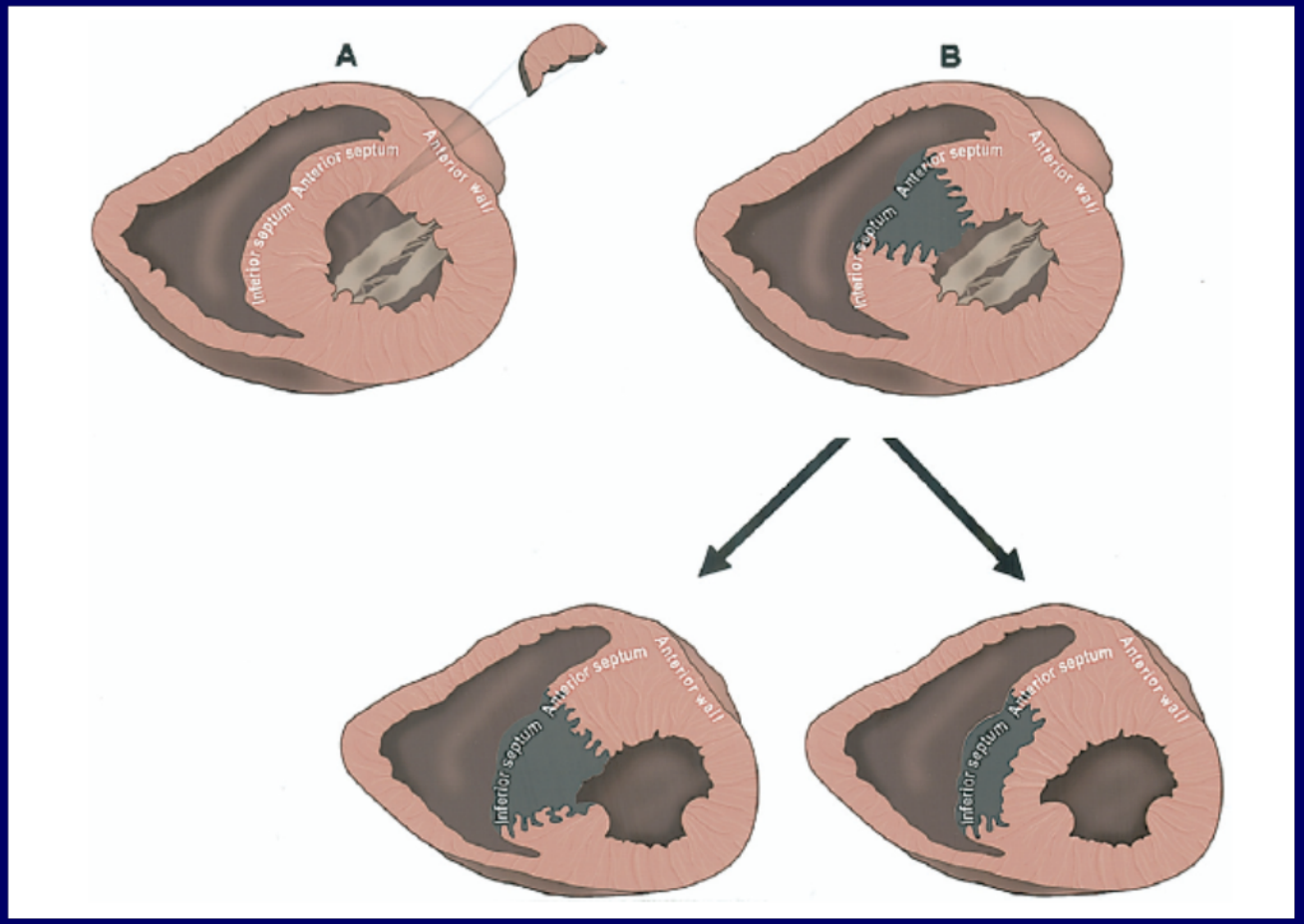
- Current data do not support the hypothesis of increased sudden death rate following ASA

- The 2 procedures are complementary

Thank you

CMR imaging pre/post (3-7 days) SM or ASA (24 pts each group)

In ASA necrotic area was 8+/-4% of LV mass (16+/-7g)



Valeti US, Nishimura RA, Holmes DR et al. J Am Coll Cardiol 2007;49:350-357

Does ASA Shorten Life?

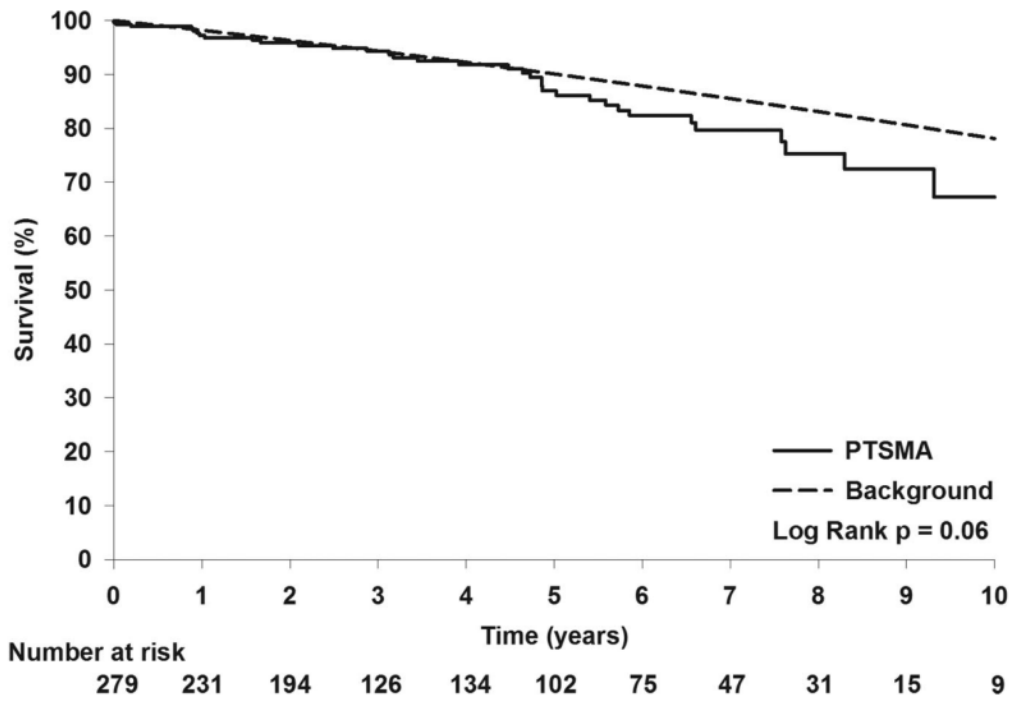


Figure 4. Survival after PTSMA in 279 patients in 4 Scandinavian heart centers (1999 to 2010). Background indicates age- and sex-matched background population; PTSMA, percutaneous transluminal septal myocardial ablation.

The 10-years survival was similar to that in an age and sex matched background population, age was the only predictor of survival

Jensen MK Circ Cardiovasc Interv 2011;4:256-265

ASA vs MYECTOMY: a META-ANALYSIS

-5 CASE CONTROLLED NONRADOMIZED STUDIES

- 183 pts had ASA and 168 SM (total 351 pts), follow up 21 vs 25 months
- ASA pts: older (54 vs 45 MEAN AGE, p=0.02)
- Similar: NYHA 2-4, LVOT gradient (75-80 mmHg)
- Outcome: > pacemakers in ASA (18.4 vs 3.3, p=0.04)

  > LVOT residual gradient in ASA (18 vs 10 mmHg, p<0.001)

  > reinterventions in ASA (5.5% vs 0.6%)

  = ΔNYHA, Δ VO2 max increase on exercise, Survival

Alam M et al. EHJ 2009;30:1080-87

Major Points to be Discussed

- Indications and Main Results of ASA
- Does ASA induce an Arrythmogenic Scar?
- How do the results of ASA compare with SM?
- **Are ASA and SE just competitive or complementary procedures?**

Alternative approaches: old and new

- MVR
  - Z Krajcer. Circ 1989;80:I57-I64
- Alfieri stitch
  - D Sado. Circ 2010;122;938-939
- Papillary muscle re-orientation
  - Kwon DH. J Thor Cardio Surg 2010;140:317-324
- Radiofrequency septal ablation
  - T Lawrenz. JACC 2010: 57;572-576

Endocardial Radiofrequency Septal Ablation

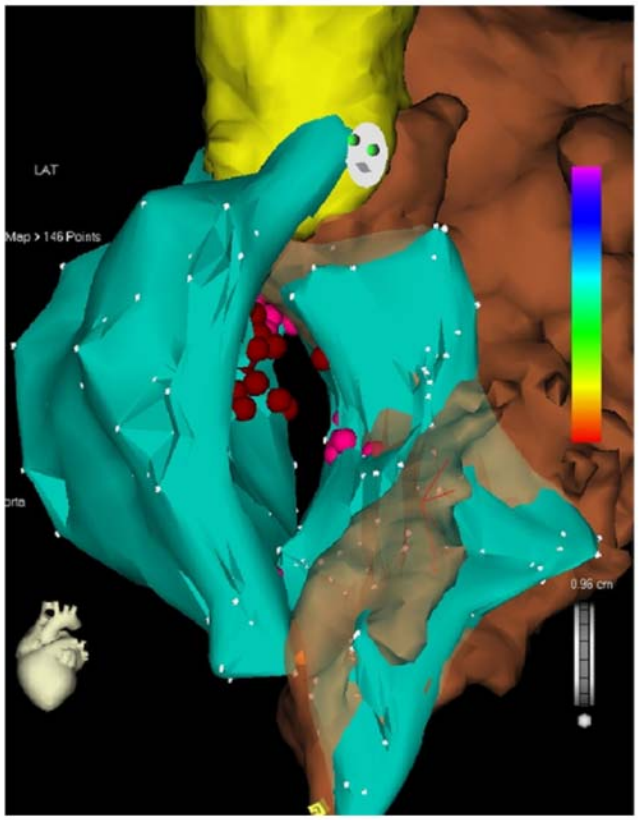


Figure 1 3-Dimensional RV and LV Maps Using the CARTO System With MRI Fusion

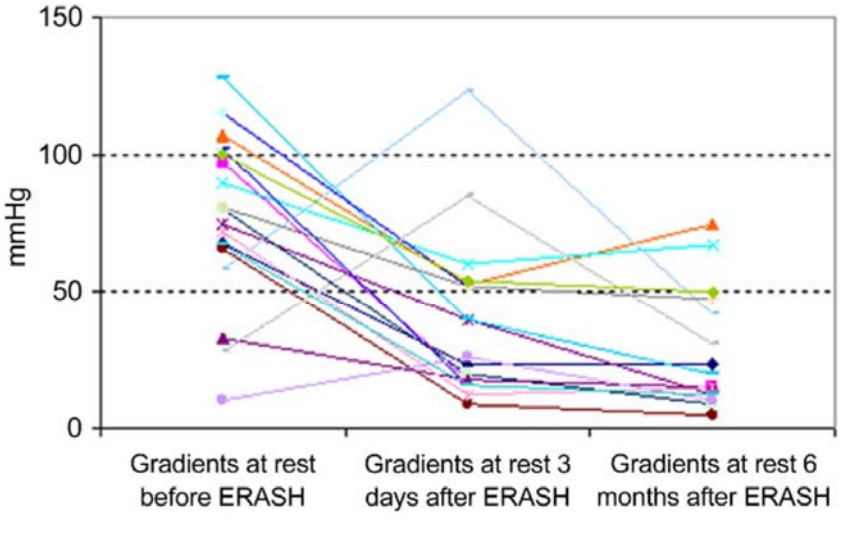
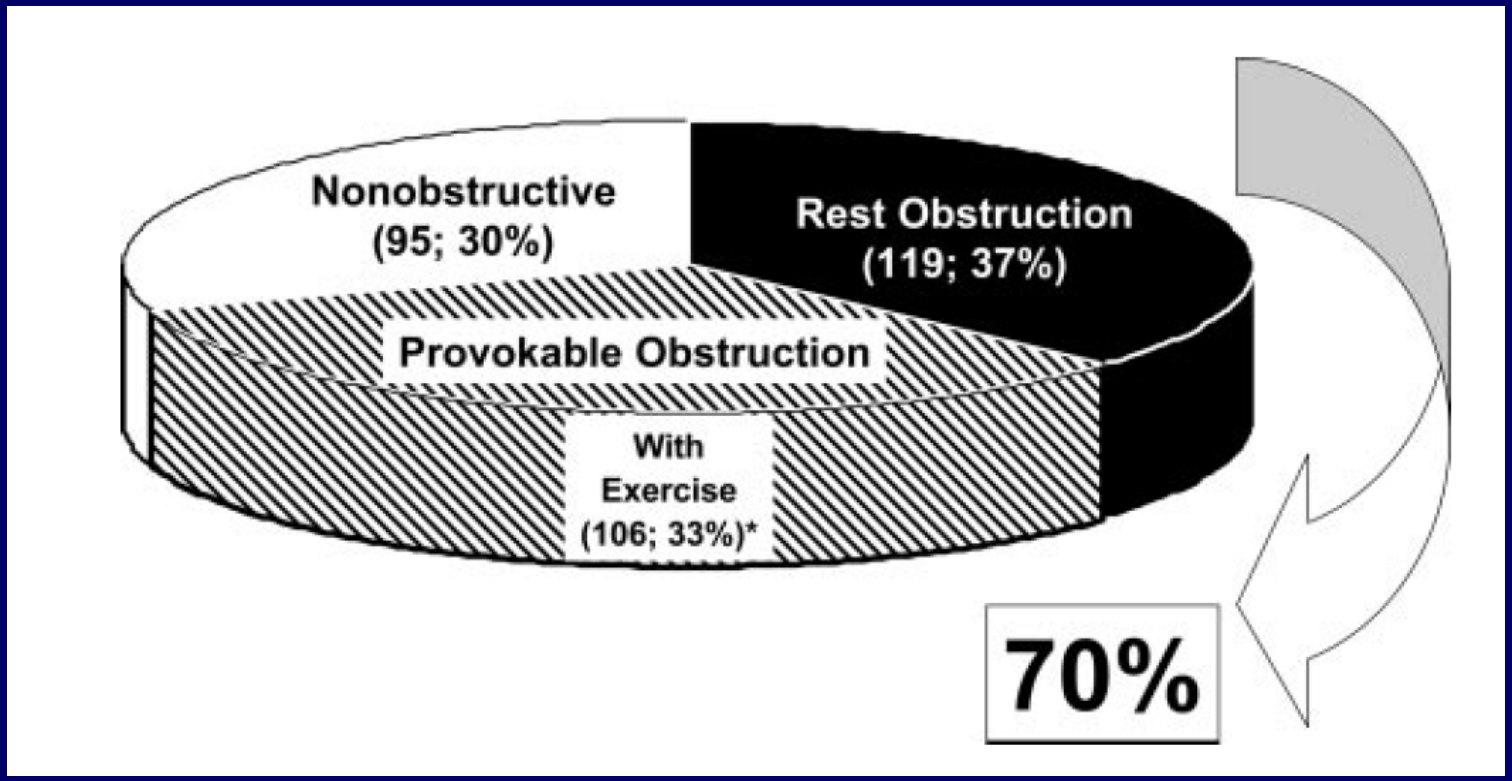


Figure 4 Reduced LVOT Obstruction at Rest

Lawrenz T et al. JACC 2010

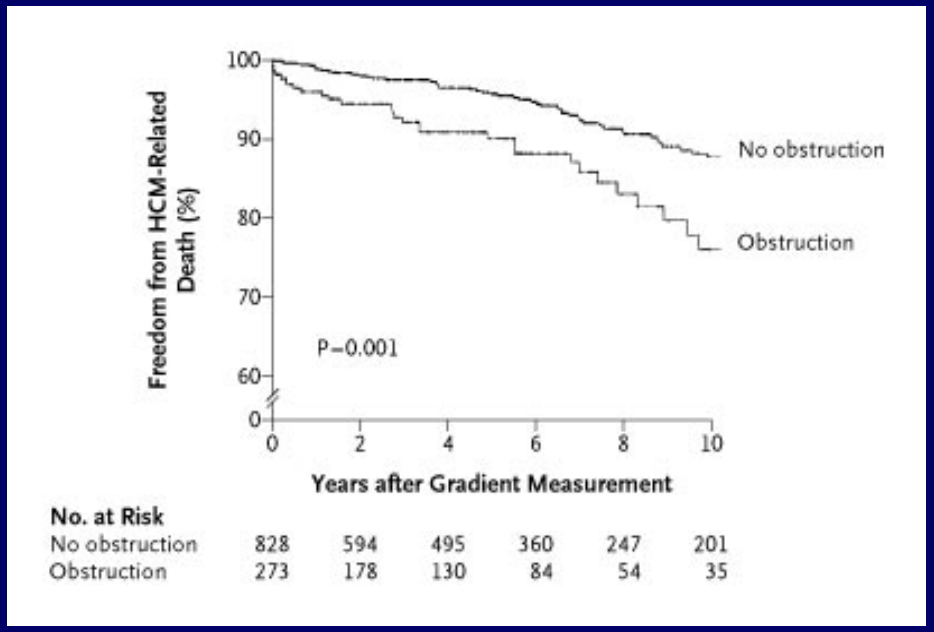
Hypertrophic Cardiomyopathy Is Predominantly a Disease of Left Ventricular Outflow Tract Obstruction

Martin S. Maron, MD; Iacopo Olivotto, MD; Andrey G. Zenovich, MSc; Mark S. Link, MD; Natesa G. Pandian, MD; Jeffery T. Kuvin, MD; Stefano Nistri, MD; Franco Cecchi, MD; James E. Udelson, MD; Barry J. Maron, MD

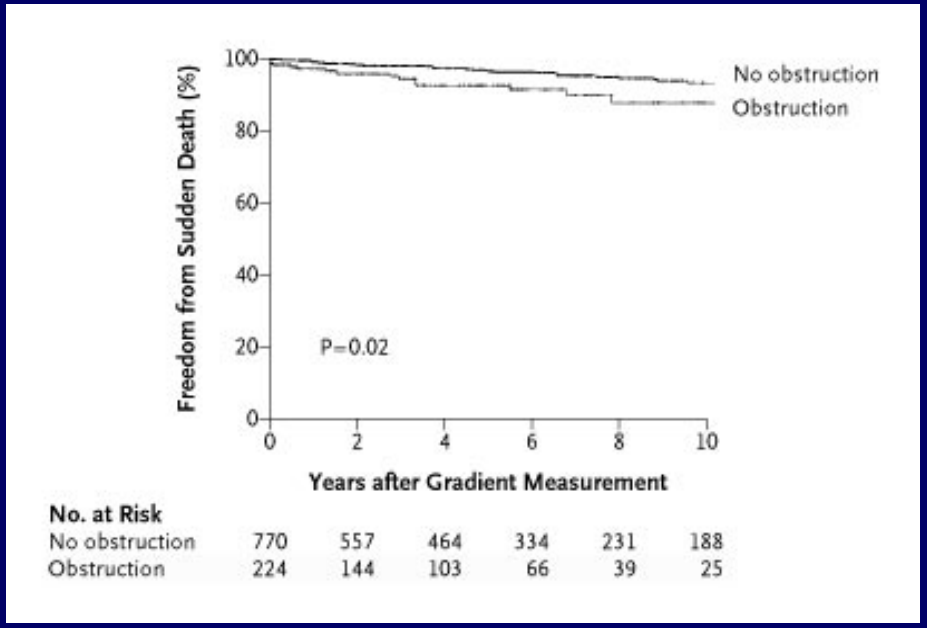


Circulation 2006;114:2232

LVOT Gradient- a Risk Factor with Very Low PPV (~7%)



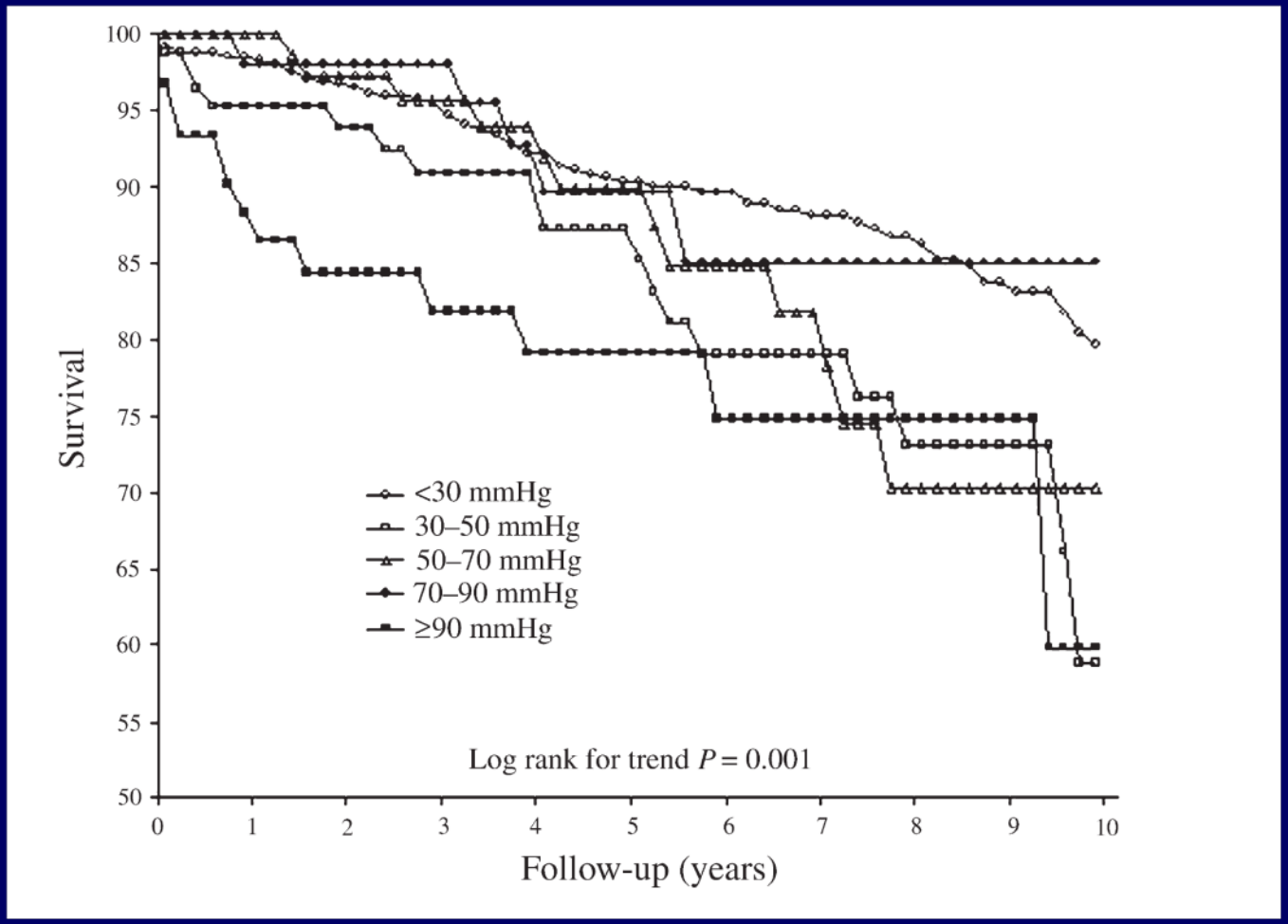
No. at Risk						
No obstruction	828	594	495	360	247	201
Obstruction	273	178	130	84	54	35



No. at Risk						
No obstruction	770	557	464	334	231	188
Obstruction	224	144	103	66	39	25

Maron MS ,Olivotto J et al. NEJM 348 (4): 295, 2003

Presence and Severity of LVOT Gradient Correlate with Survival and Sudden Death



Elliott PM, McKenna WJ et al. Eur Heart J 2006;27:1933