

Update on Evaluation and Nonsurgical Treatment Strategies for the Symptomatic Patient with HCM

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DISCLOSURE

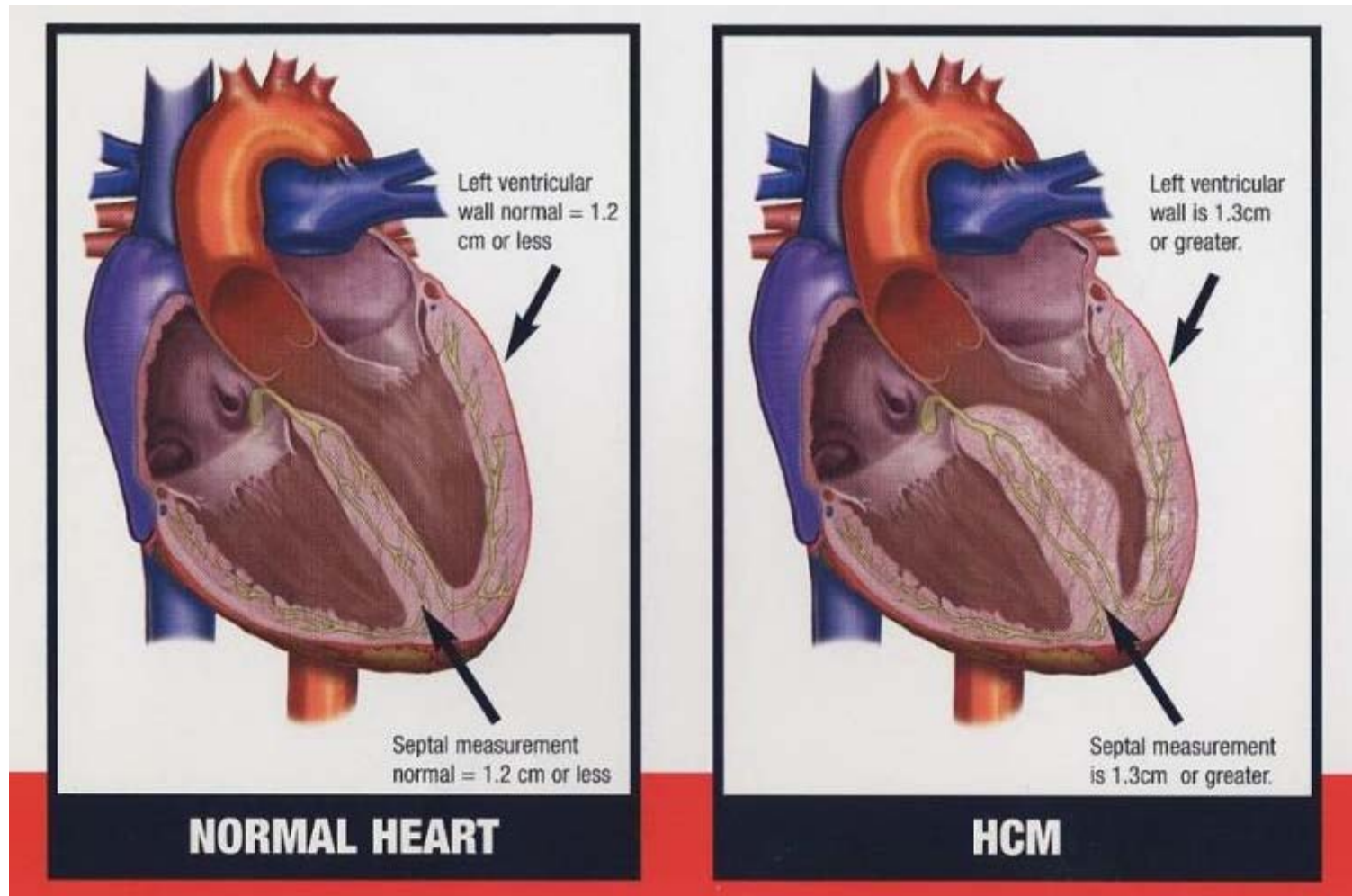
Affiliation/Financial Relationship

- Grant/Research Support
- Consulting Fees/Honoraria
- Major Stock Shareholder/Equity
- Royalty Income
- Ownership/Founder
- Intellectual Property Rights
- Other Financial Benefit

Company

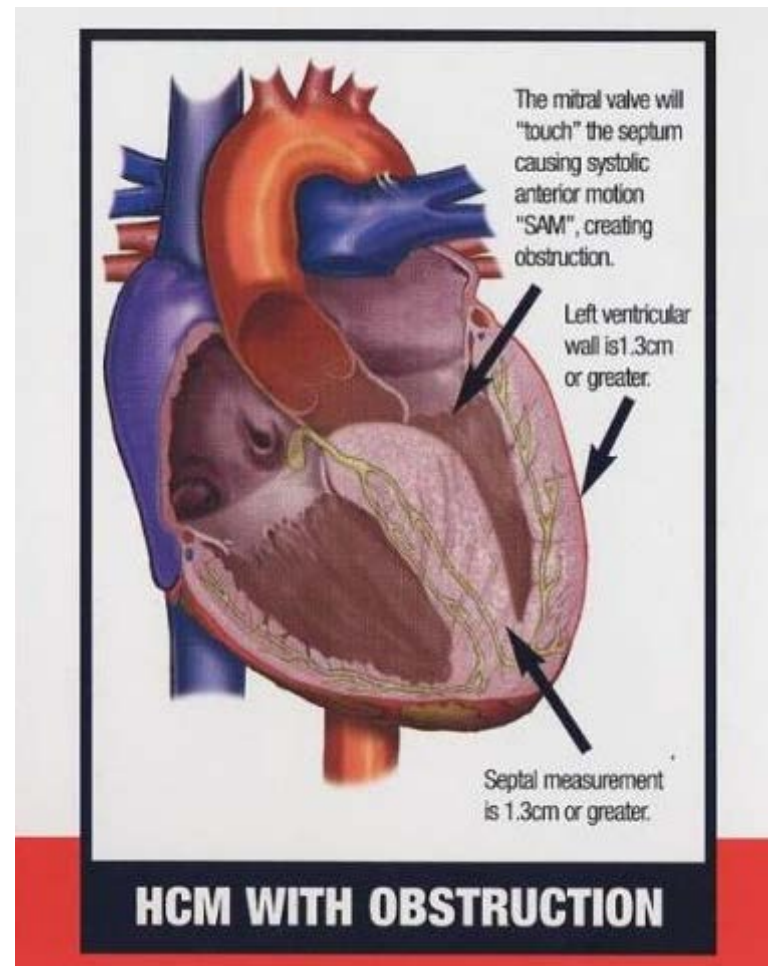
- Astra-Zeneca, Eli Lilly, Gilead, GSK, Merck
- Lilly, Novo Nordisk
- None
- None
- None
- None
- None

Hypertrophic Cardiomyopathy (HCM)



Hypertrophic Cardiomyopathy

- Approximately 70% of pts with HCM have significant resting or provokable left ventricular outflow tract obstruction



Hypertrophic Cardiomyopathy: Clinical Manifestations

- Heart Failure
- Angina
- Syncope
- Sudden Death

Hypertrophic Cardiomyopathy

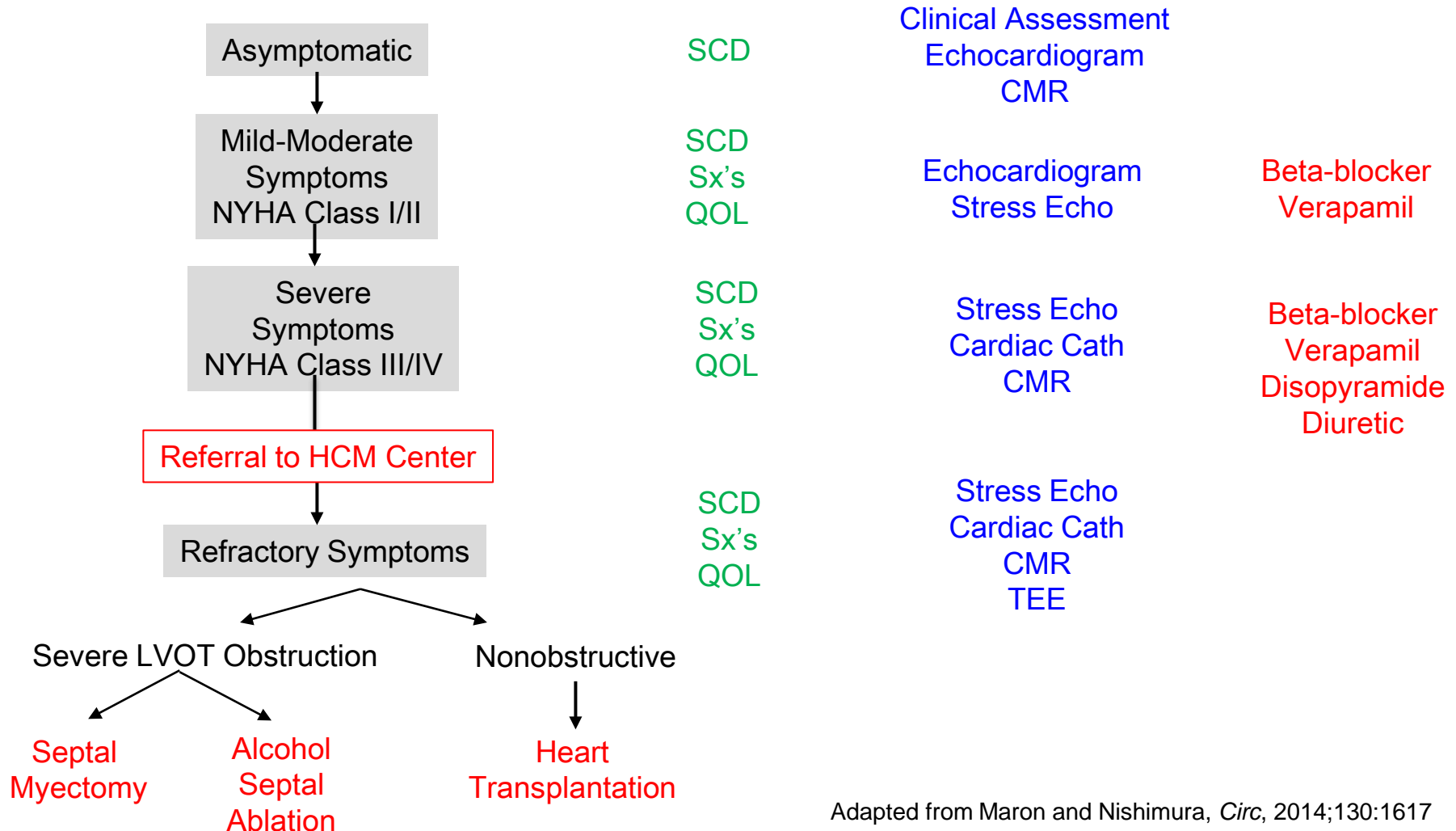
Treatment Goals

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graph TD; A[Treatment Goals] --> B[Symptom Relief]; A --> C[Prevent Sudden Death];
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**Symptom
Relief**

**Prevent
Sudden Death**

Evaluation and Treatment Algorithm for HCM Patients



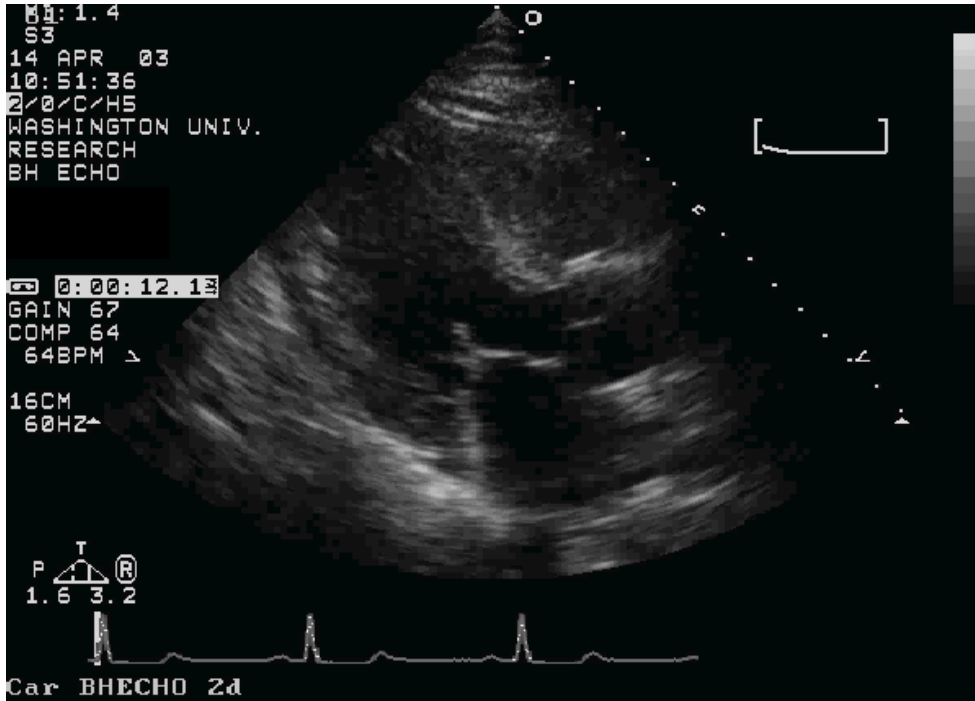
Evaluating the Symptomatic Patient with HCM

- Specialized Evaluation
 - Stress Echocardiography
 - Cardiac Cath
 - Cardiac MRI
 - TEE

Patient A: History

- 29 yr old male
 - SOB/chest discomfort on exertion increasing in frequency and severity over the last several months
 - SOB with walking < 1 block
 - chest pressure at rest after heavy meals
 - multiple episodes of lightheadedness and near syncope.
- Social History
 - Former construction worker, now on disability
- Exam
 - Regular S1 and S2, harsh III/VI systolic murmur that increases with Valsalva maneuver, otherwise unremarkable.

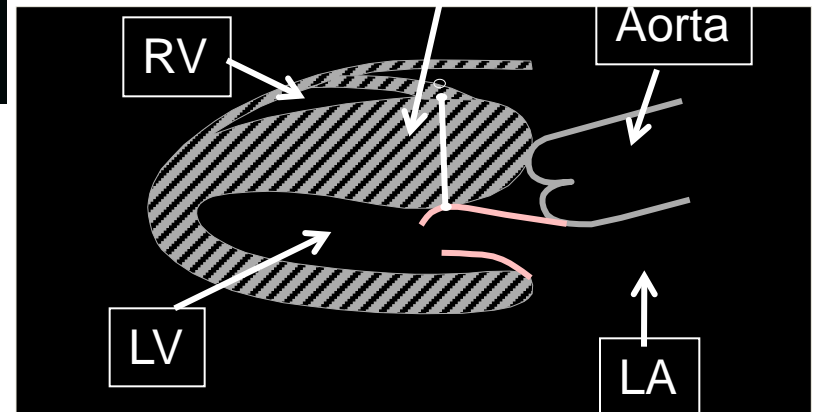
Echocardiogram



Septum	2.57 cm
Post Wall	1.6 cm
LA	5.7 cm
SAM	Present

“Asymmetric Septal Hypertrophy”

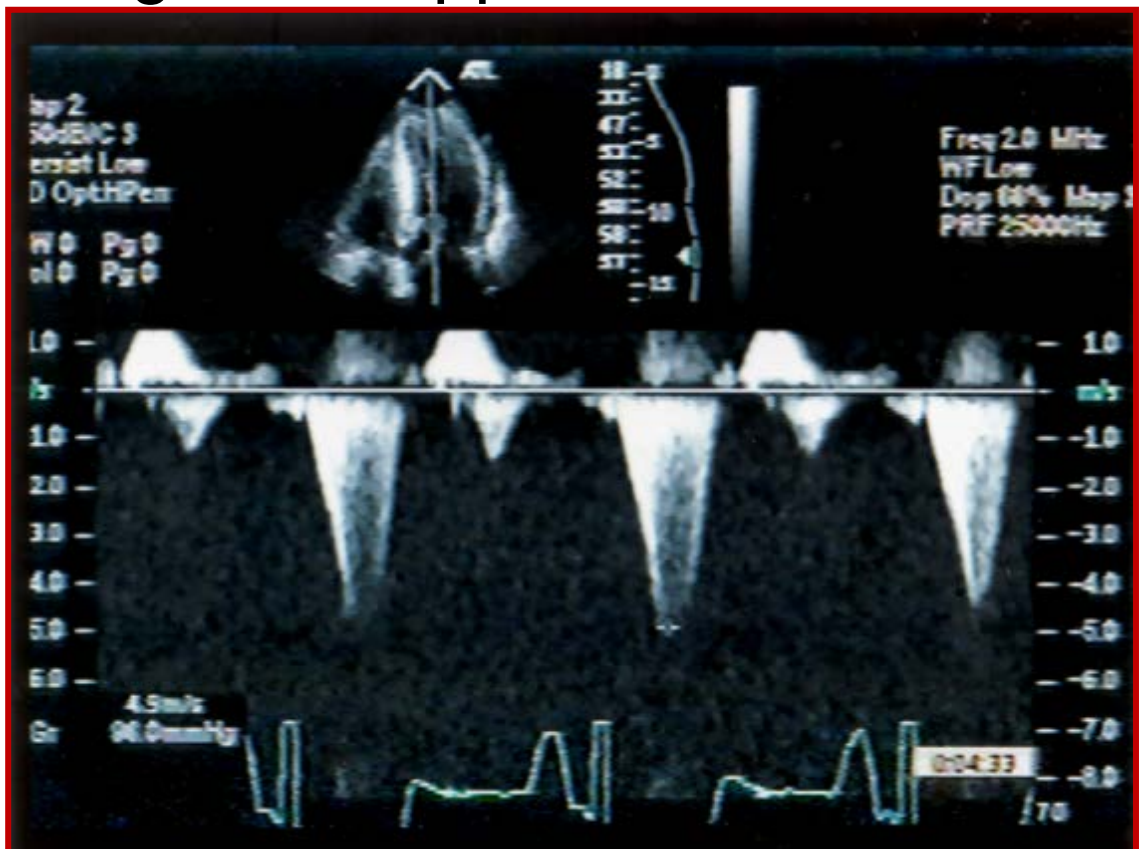
“Systolic Anterior Motion”



Patient A

Resting CW Doppler in Outflow Tract

- 29 yr old WM
- Severe DOE
Pre-syncope
CP after meals
- CHF NYHA Class III
Angina Class III-IV



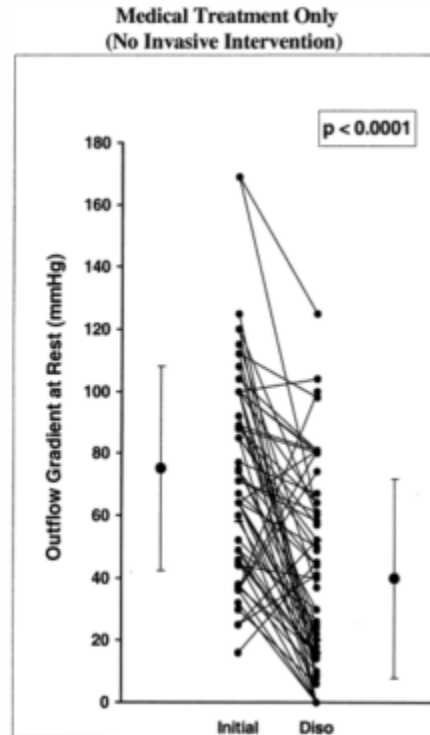
Peak Outflow Velocity = 4.9 m/s
Resting LVOT Gradient = 96 mmHg

Patient A: Treatment Algorithm

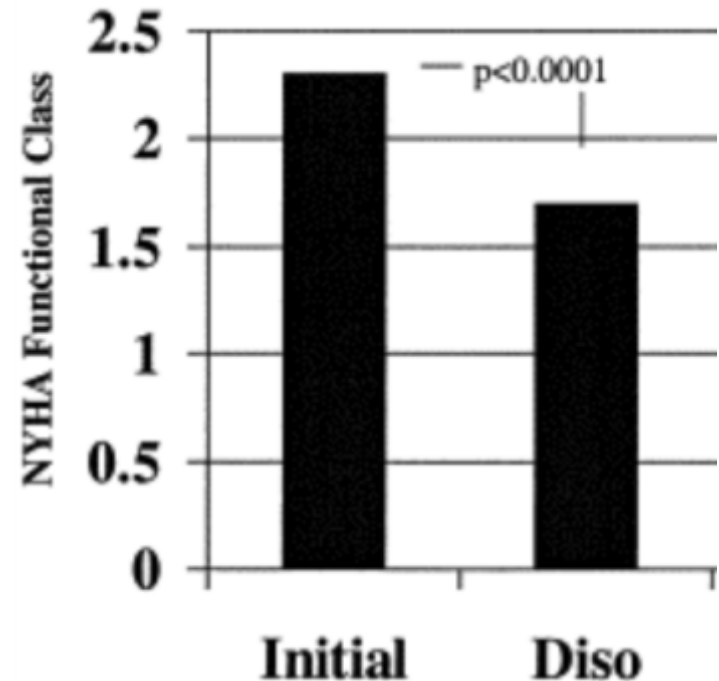
- 29 yr old male with HCM
 - Severe LVOT obstruction
 - Class III CHF
 - Class III-IV angina
- Treated with metoprolol...
- Only minor improvement in symptoms...

Disopyramide for HCM

- 118 Patients with HCM and Severe LVOT Obstruction
- Treated with disopyramide and followed for 3 years



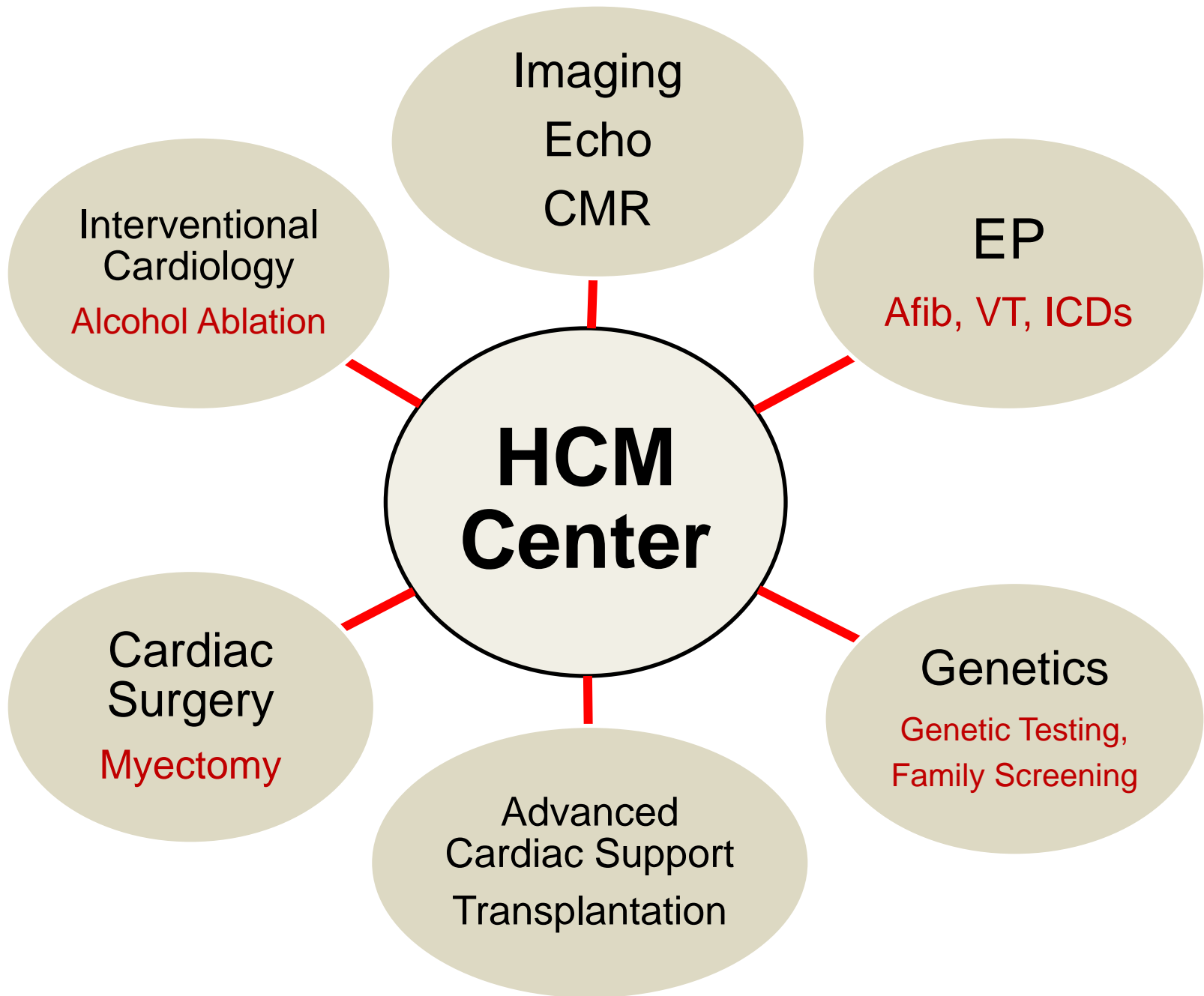
Effect on
LVOT Gradient



Effect on Symptoms
(NYHA Class)

Patient A: History

- 29 yr old male with HCM
 - Severe LVOT obstruction
 - Class III CHF
 - Class III-IV angina
- Treated with metoprolol...
- Only minor improvement in symptoms...
- Treated with disopyramide...
- Did not tolerate due to dry mouth, malaise...



Evaluating the Patient with HCM For Symptomatic Patients:

I. Specialized HCM-Protocol Stress Echo

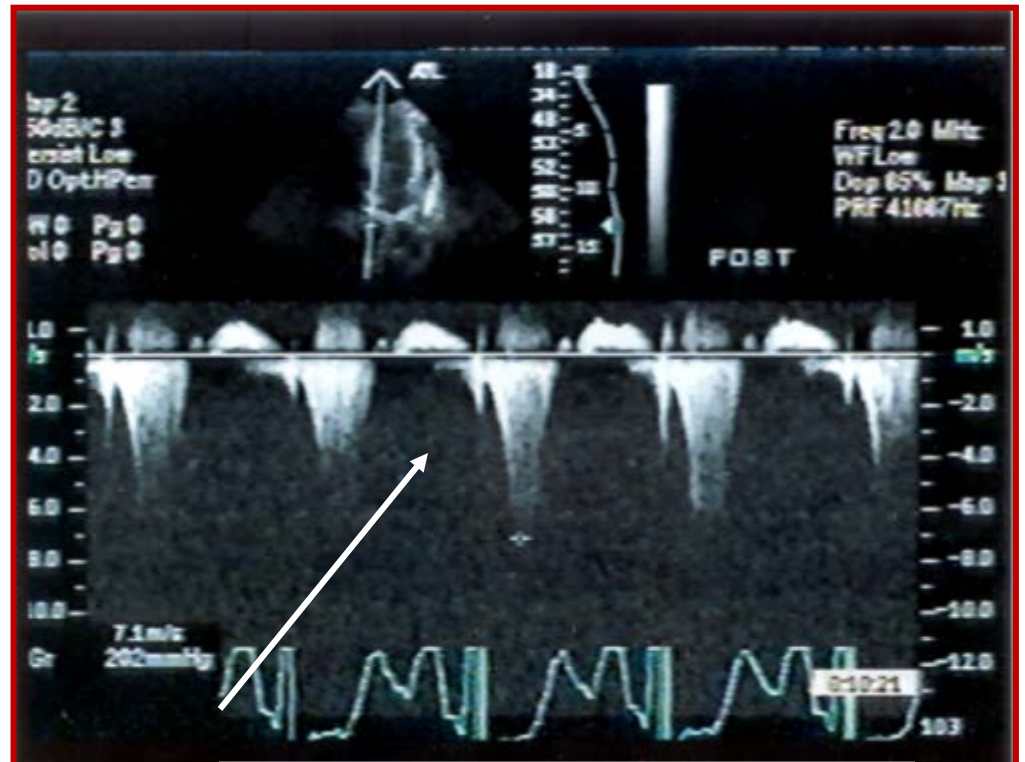
- Resting 2D Imaging
 - LV shape, wall thickness, ASH, SAM
 - Tissue Doppler
 - LVOT Velocity
 - At rest
 - + Valsalva
 - + Amyl nitrite
 - Peak exercise

Patient A

Specialized HCM-Protocol Echocardiogram

- Treadmill Exercise Study
 - Bruce Protocol
 - 3 min 56 sec
 - 5 METS
 - Stopped due to SOB, chest heaviness and lightheadedness
 - BP 120/60 → 90/50

Peak Exercise CW Doppler



Peak Exercise Velocity = 7.1 m/s
Peak LVOT Gradient = 202 mmHg

Patient A

Dx:

- HCM with Severe LVOT Obstruction
- Congestive Heart Failure, NYHA Class III
- Angina, CCS Class III-IV

- Sxs refractory to medical therapy...

Treatment Recommendation?

Further Evaluation?

Evaluating the Patient with Suspected HCM For Patients with LVOT Obstruction:

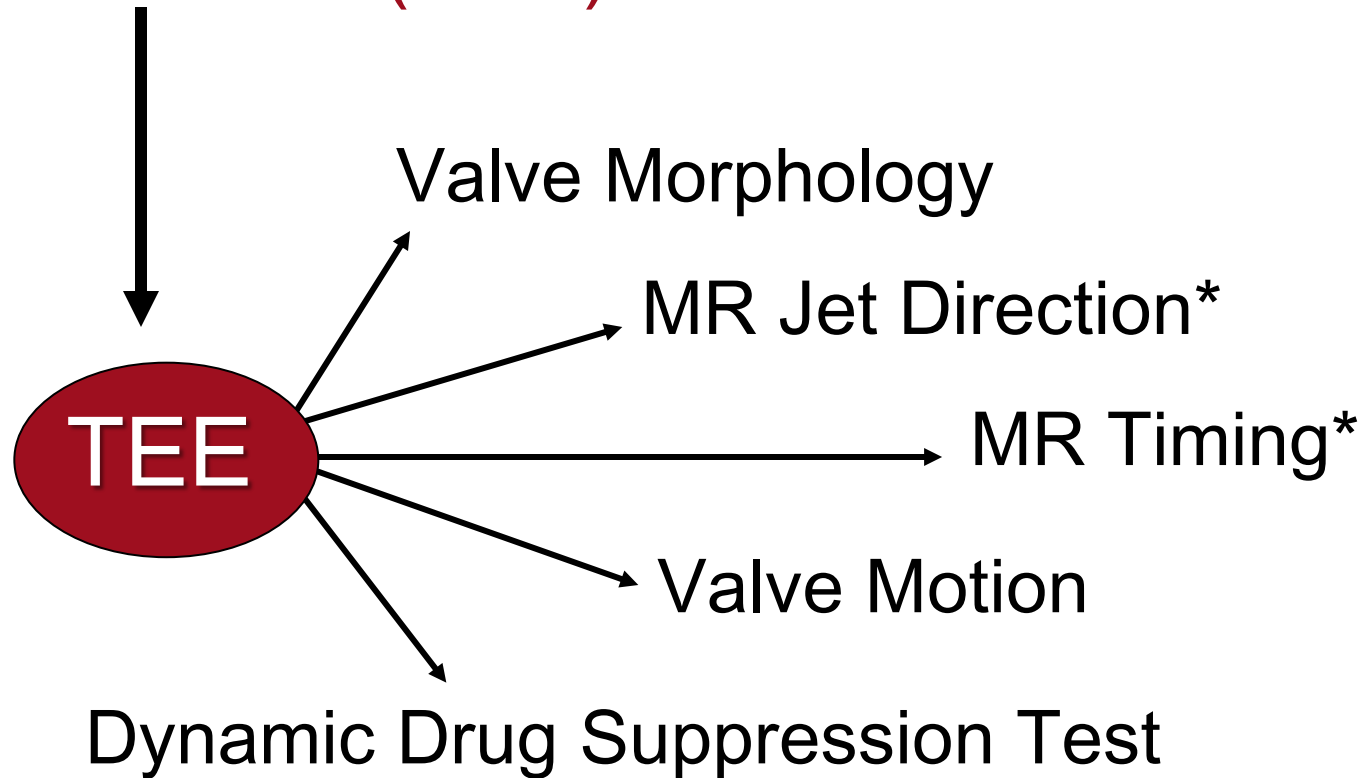
II. Specialized HCM-Protocol TEE

- Assess the LVOT:
 - Exclude fixed LVOT obstruction
- Assess Mitral regurgitation

Evaluating the Patient with Suspected HCM

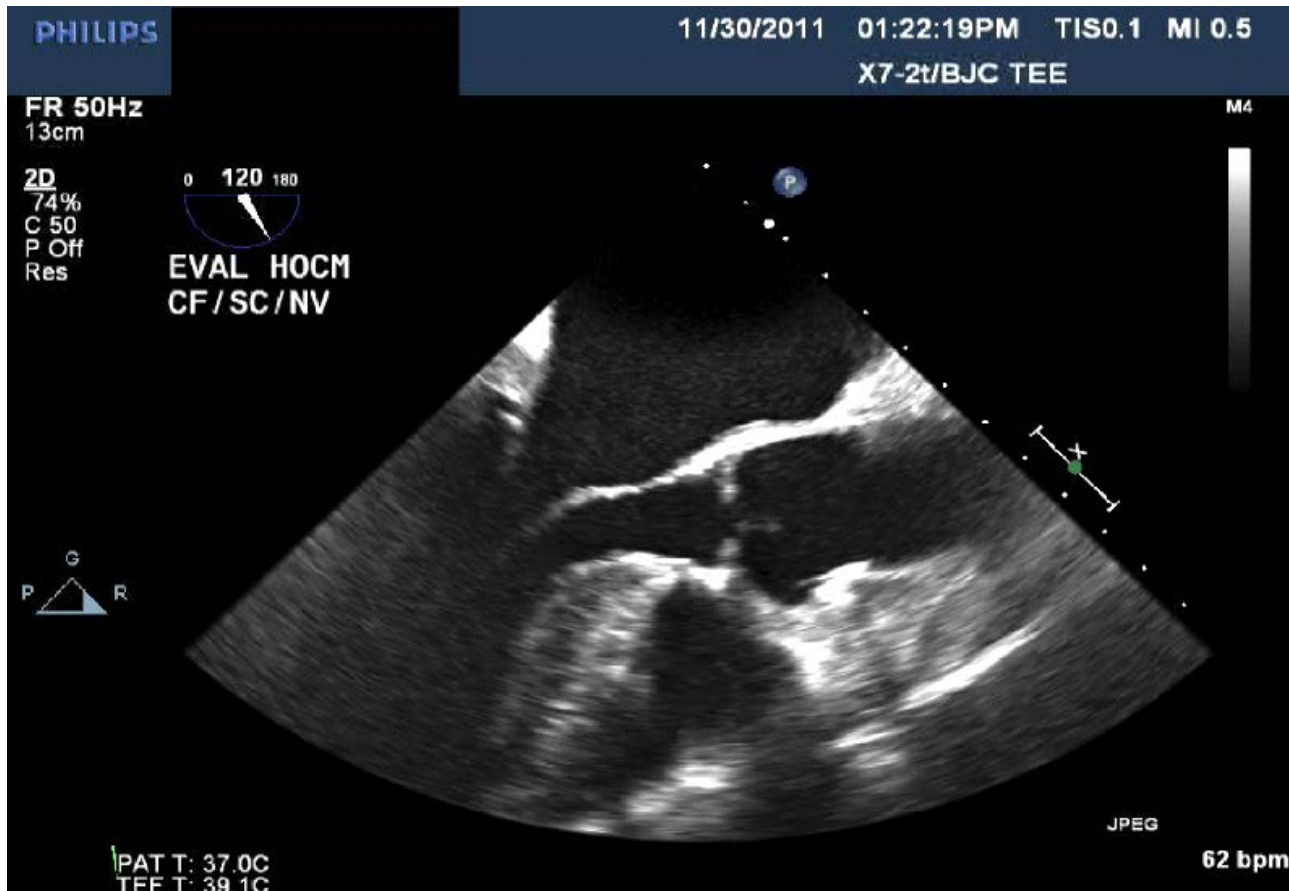
Patients with LVOT Obstruction:

TTE with Severe (3-4+) MR



Evaluating the Patient with Suspected HCM

- Specialized TEE Evaluation



Evaluating the Patient with Suspected HCM

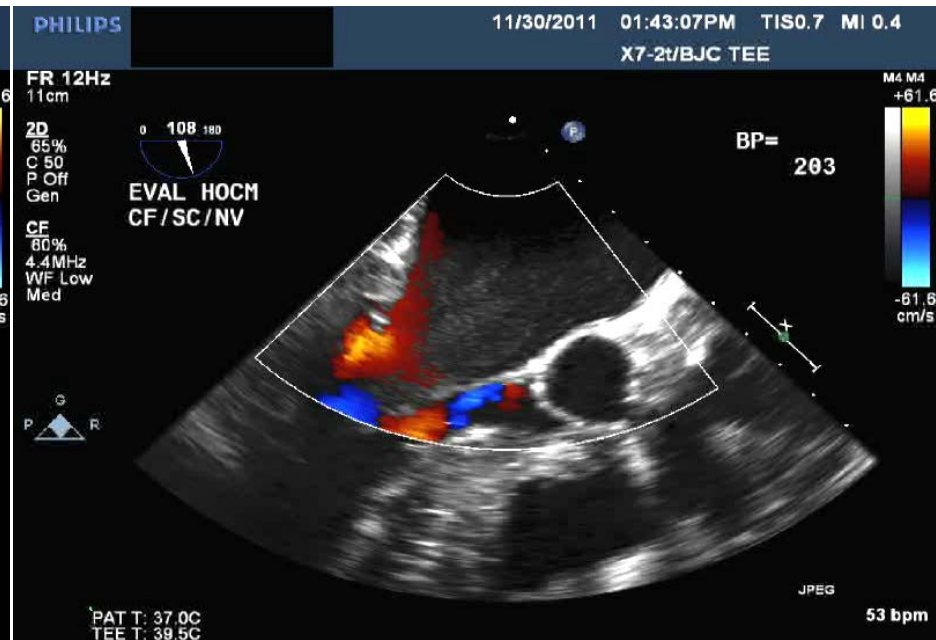


- MR: Posteriorly directed
- Related to SAM

Before and After IV Phenylephrine

Systolic BP = 120

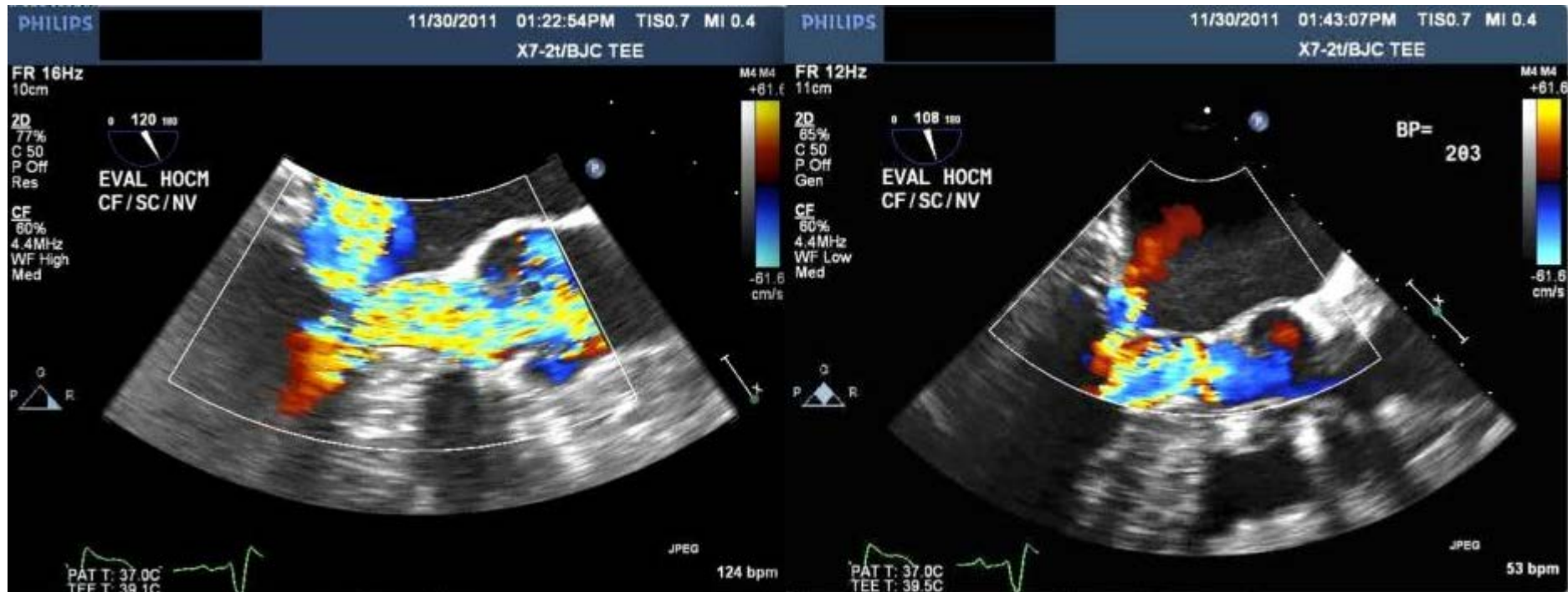
Systolic BP = 203



Before and After IV Phenylephrine

Systolic BP = 120

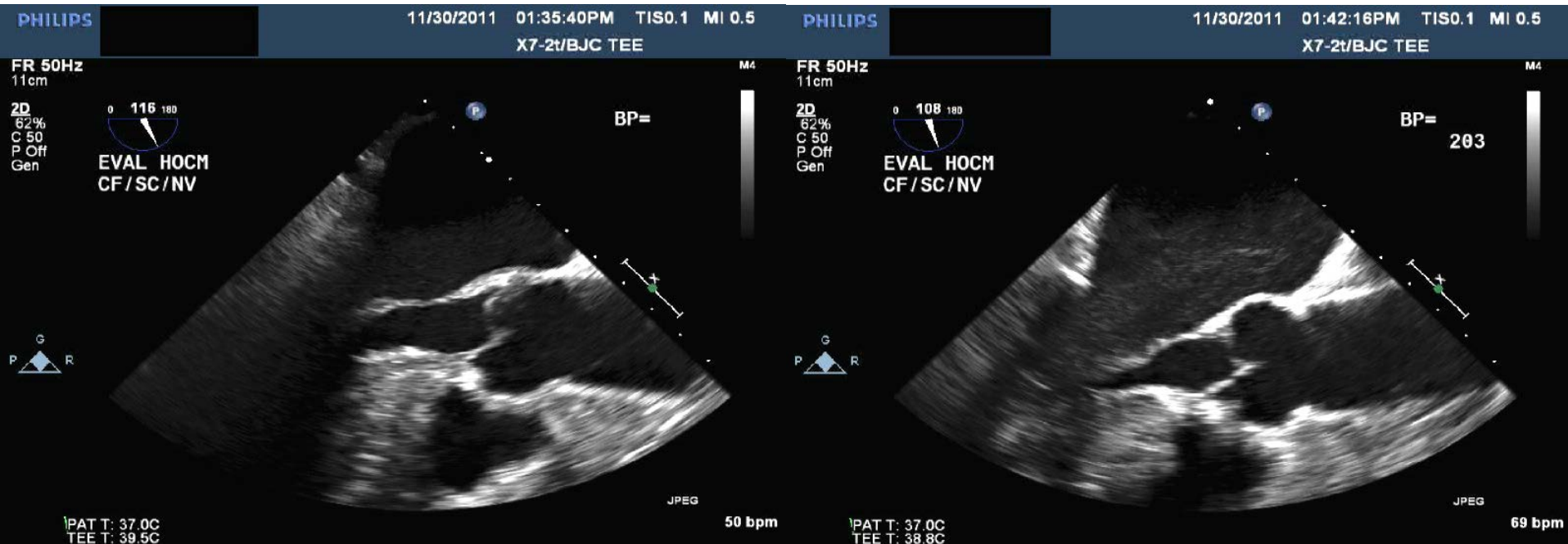
Systolic BP = 203



Before and After IV Phenylephrine

Systolic BP = 120

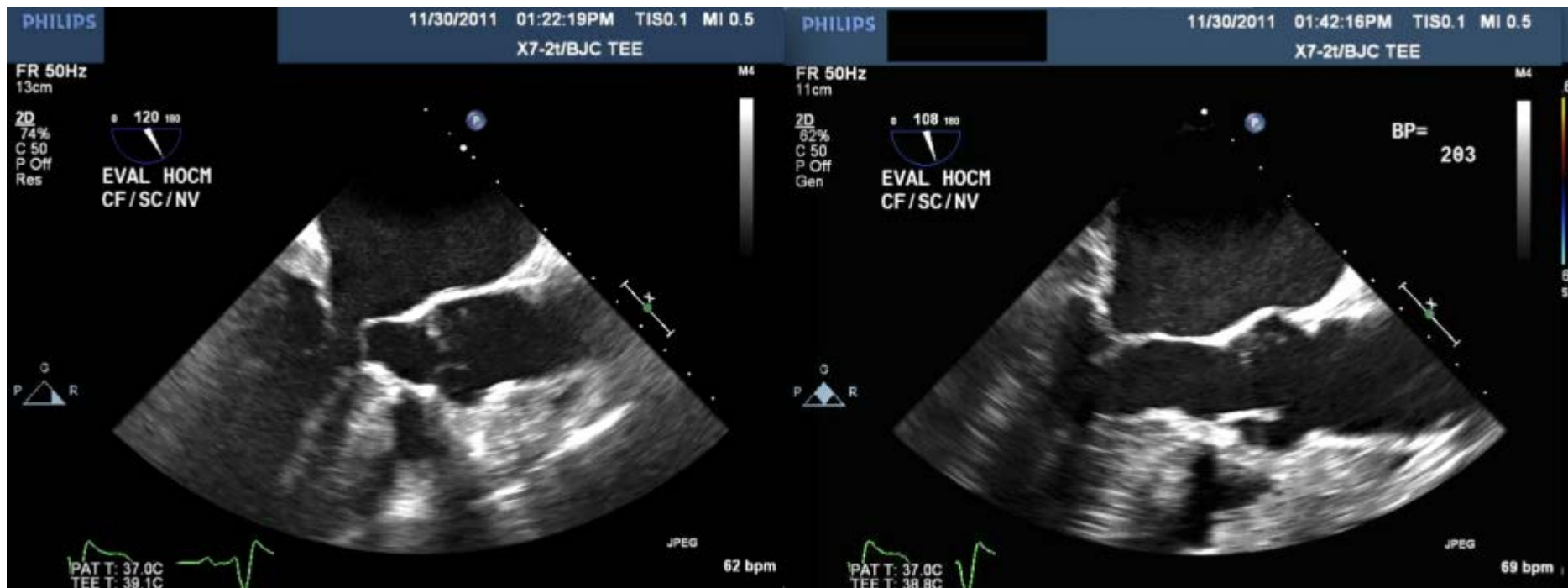
Systolic BP = 203



Before and After IV Phenylephrine

Systolic BP = 120

Systolic BP = 203



Evaluation for Candidacy for Septal Reduction is Key: Not ALL LVOT Obstruction is Due to HOCM!

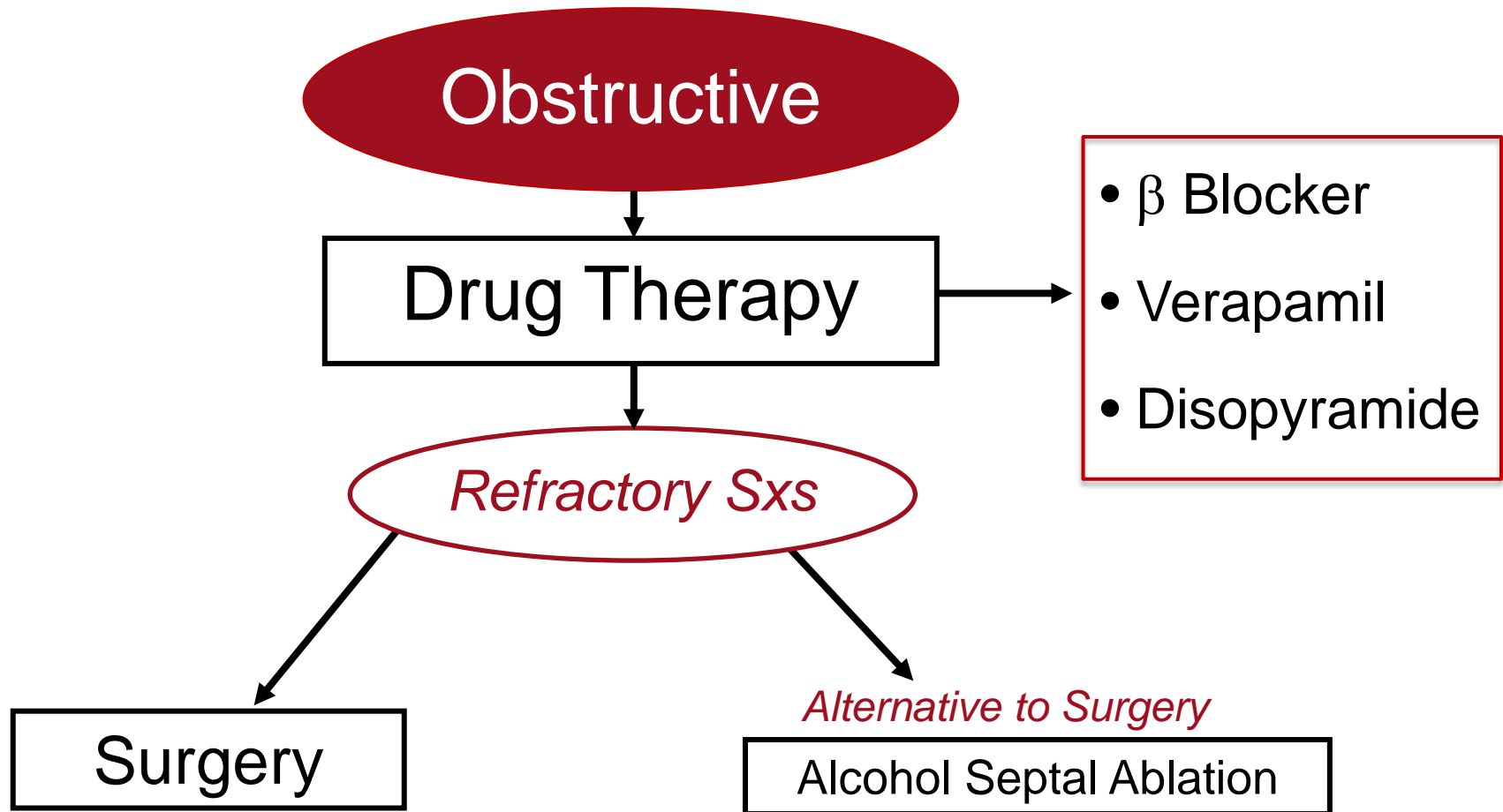
- **Mayo Clinic Experience**

- Bruce et al. *Ann Thorac Surg* 1999;68:100
- 4 cases referred to Mayo Clinic with presumed dx HOCM found to have fixed LVOT obstruction
 - 1 subaortic fibrous ring + accessory mitral valve
 - 2 fixed tunnel stenoses
 - 1 subaortic ridge

- **Washington University Experience**

- 175 pts with dx HCM referred for alcohol septal ablation
- 8 pts (4.5%) with unexpected fixed cause of LVOTO
 - 6 subaortic membrane or tunnel lesions
 - 2 accessory mitral valves
 - Of these, 4 had classic TTE features of HCM with ASH and SAM...diagnosed at TEE

Evaluation for Candidacy for Septal Reduction is Key: Not ALL LVOT Obstruction is Due to HOCM!

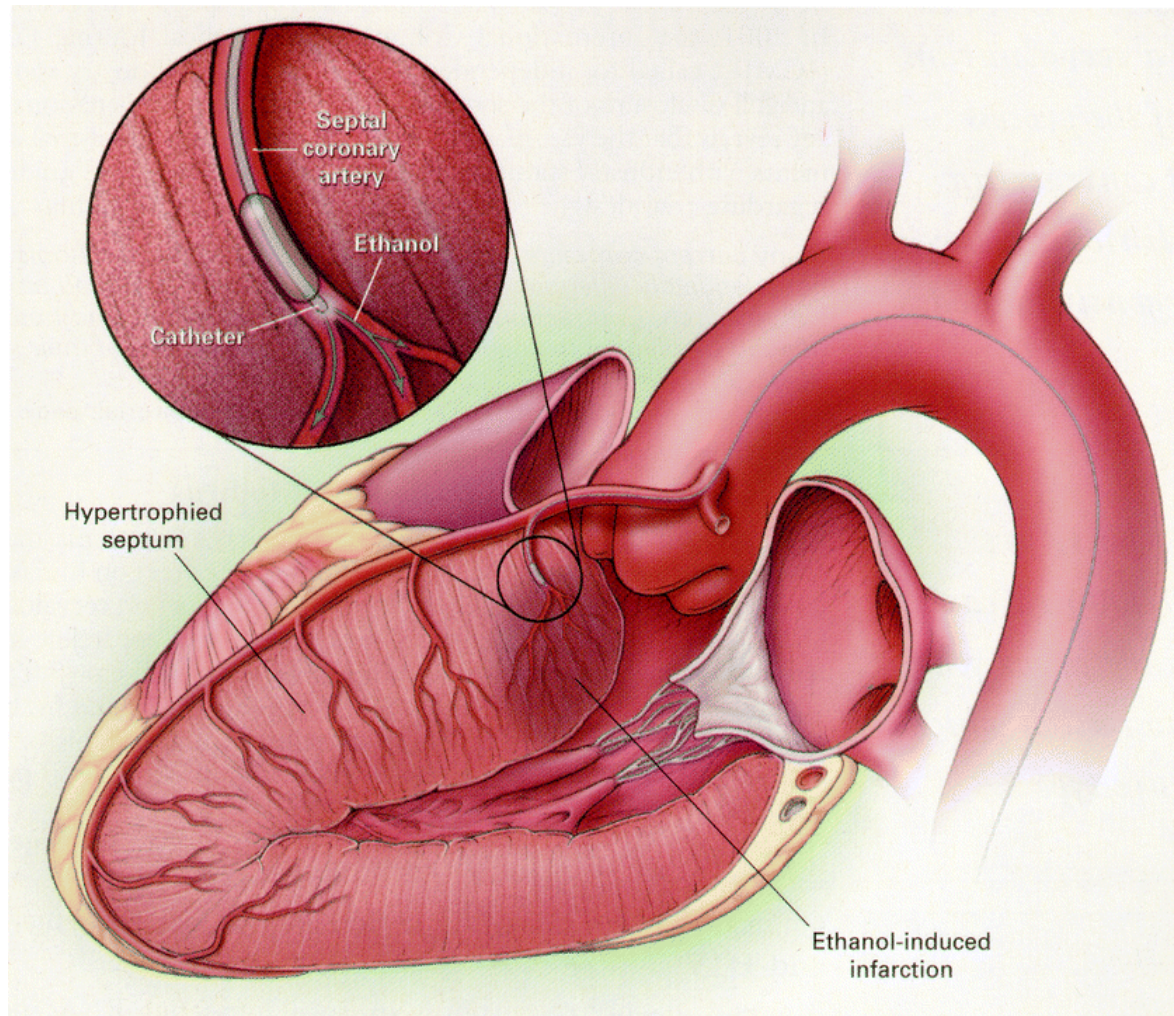


Patient A

- Treatment by Alcohol Septal Ablation

Treatment of Drug-Refractory HOCM

Septal Reduction by Transcatheter Alcohol Septal Ablation



385-1000-015

Patient: [REDACTED]

79 BPM

Status: ROOM AIR, REST

Proc. No: 65937

03/07/00

17:16

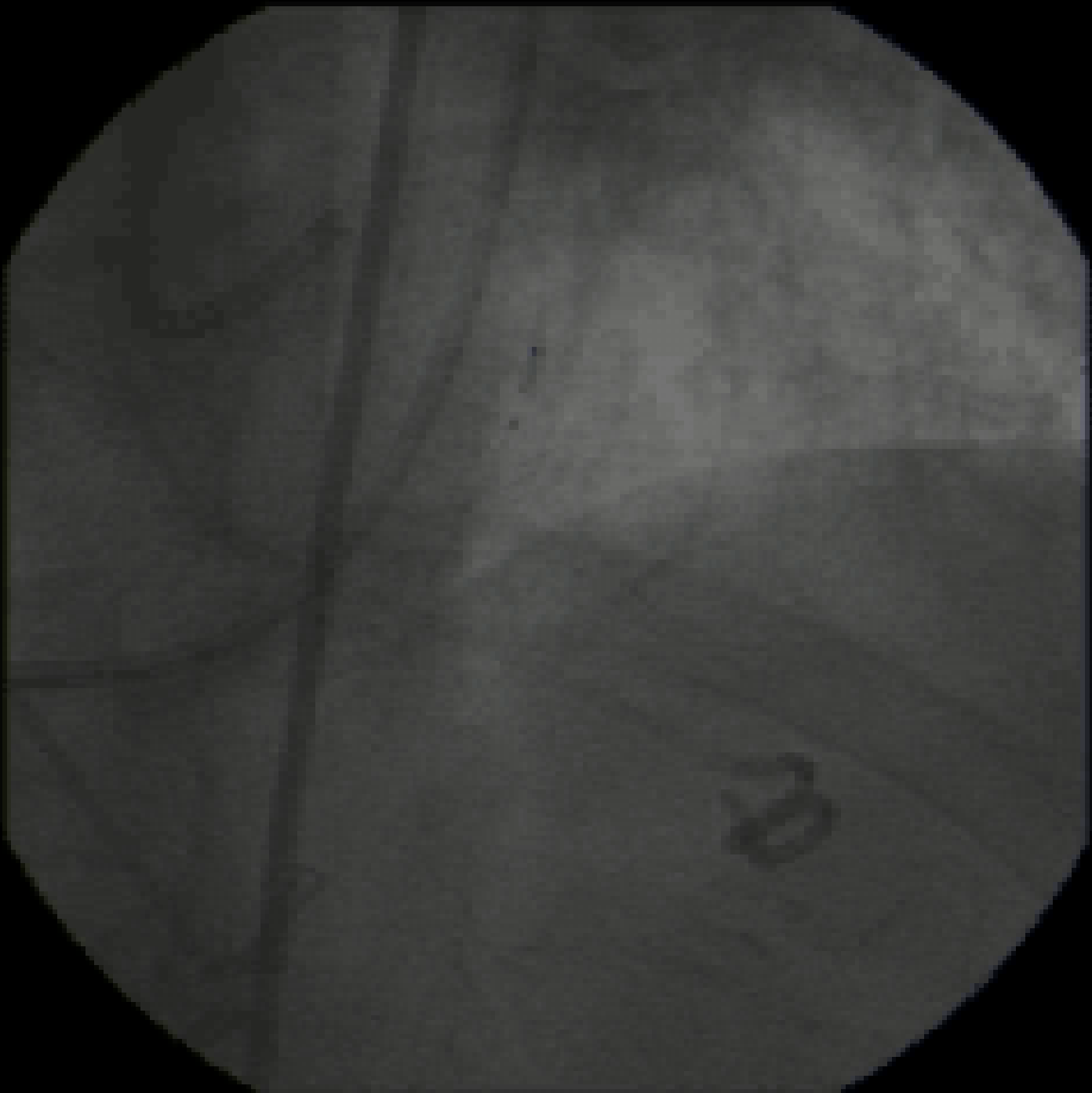


ET1: 00:00:00	AO	Sys	AO	Dias	AO	Mean	R-R
ET2: 00:00:00	111	mmHg	76	mmHg	92	mmHg	761 ms

Paper Speed: 50 mm/sec

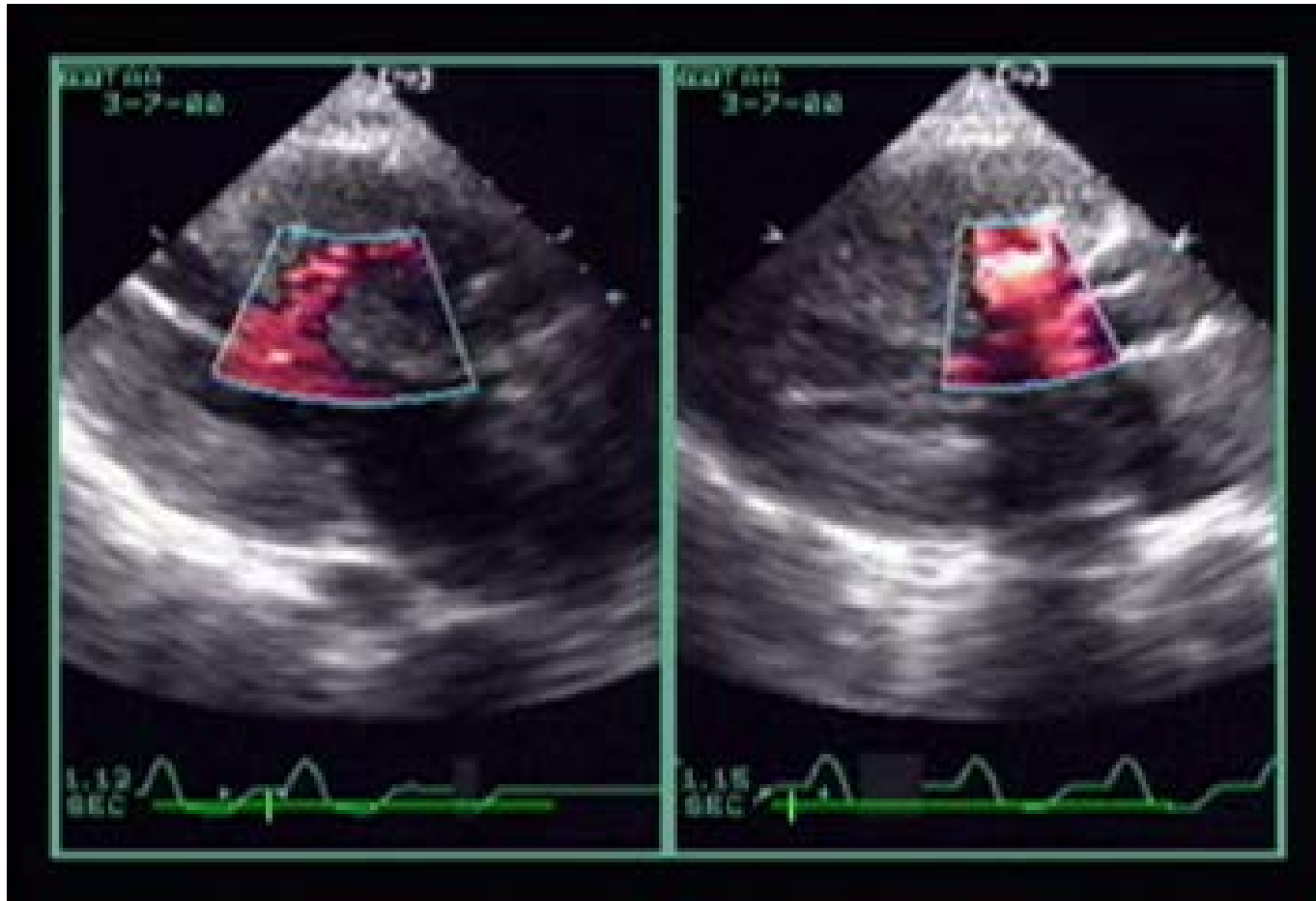
Timing: 0.10 seconds

BARNES HOSP • WASH U MED CENTR
ST. LOUIS, MO. 63110

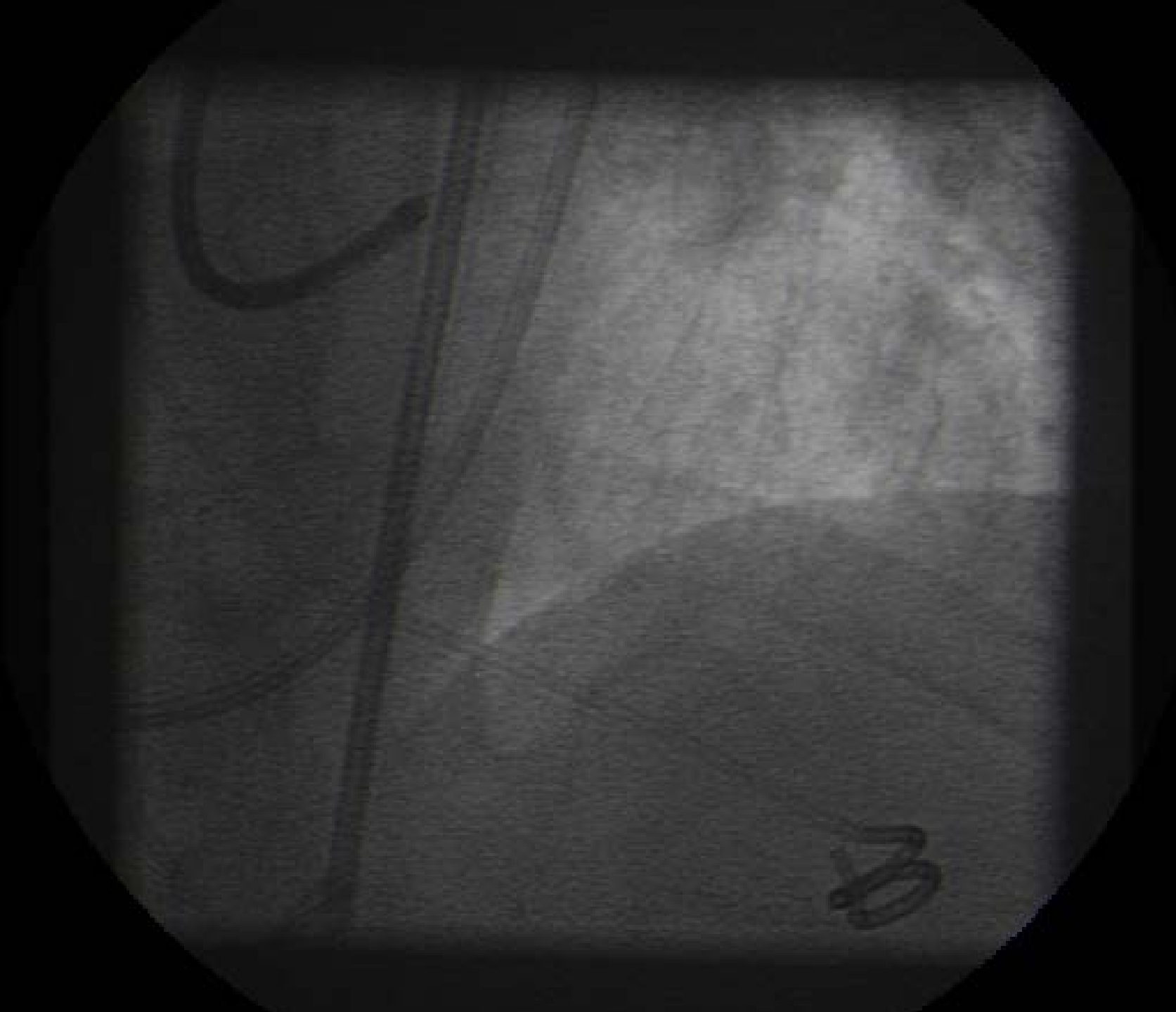


Contrast Echo Guidance for Alcohol Septal Ablation

Low Mechanical Index Real Time Imaging



Second Septal vs. First Septal



Baseline

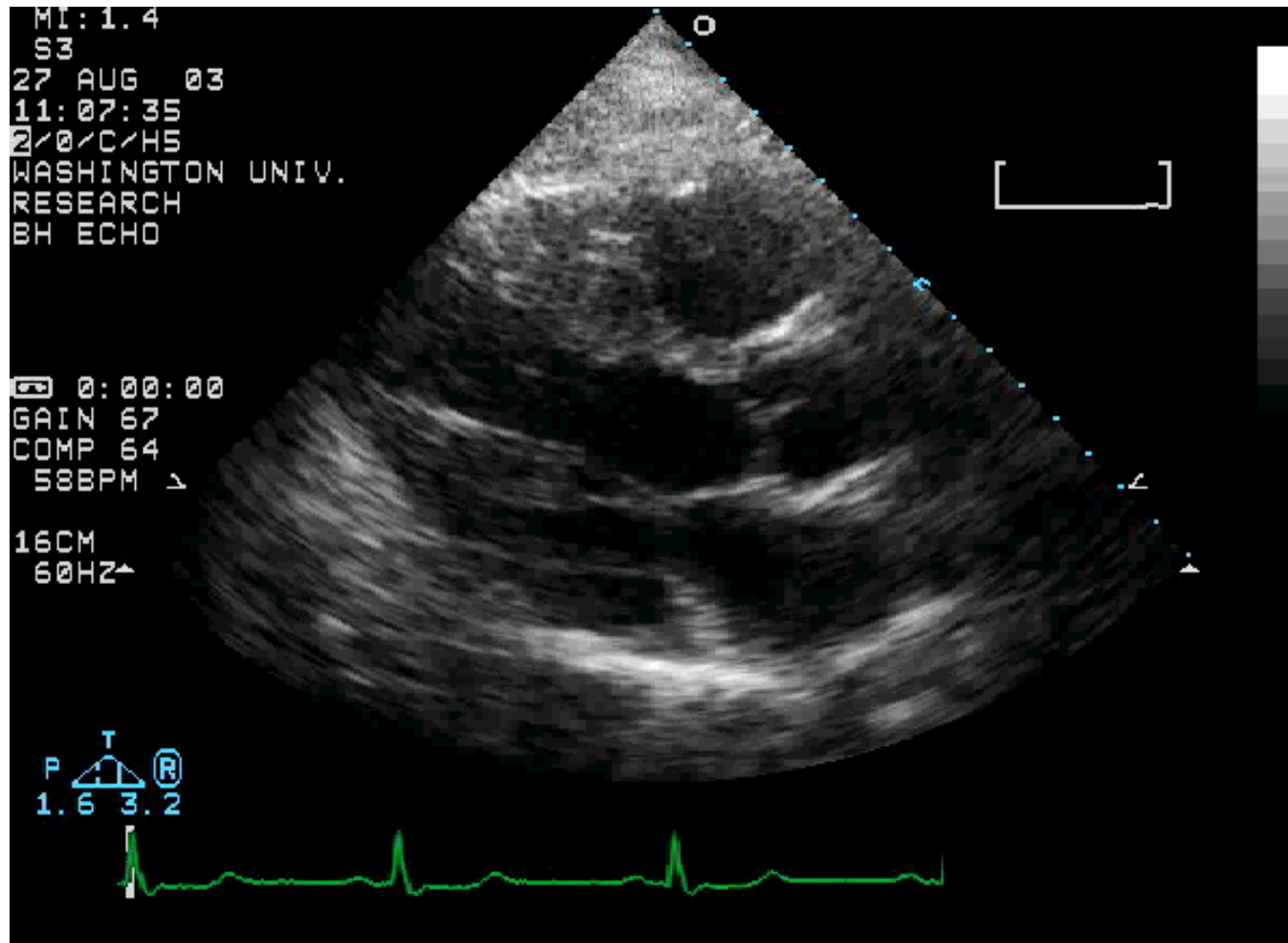


Immediately-Post Alcohol



Echo Follow-Up 3 Months After Alcohol Septal Ablation

Parasternal Long Axis View

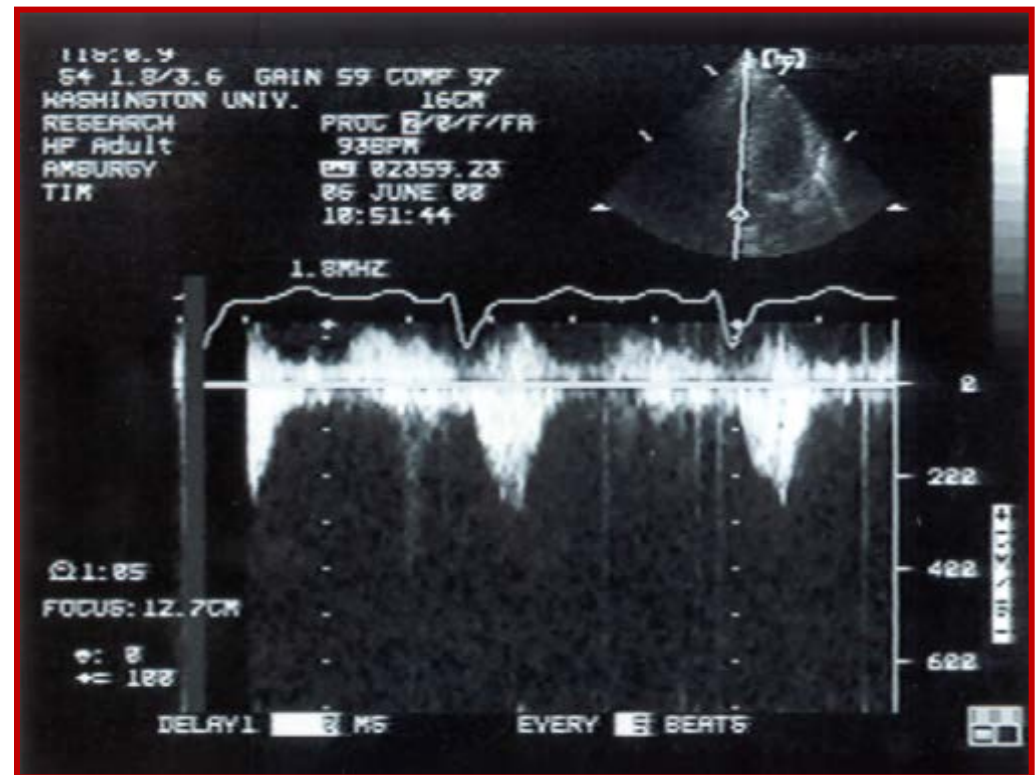


Patient A - 3 Months Post-Septal Ablation

Treadmill Exercise Study

- Bruce Protocol
 - 7 min 24 sec
 - 9 METS
- Stopped due to fatigue
- BP 130/70 → 170/60

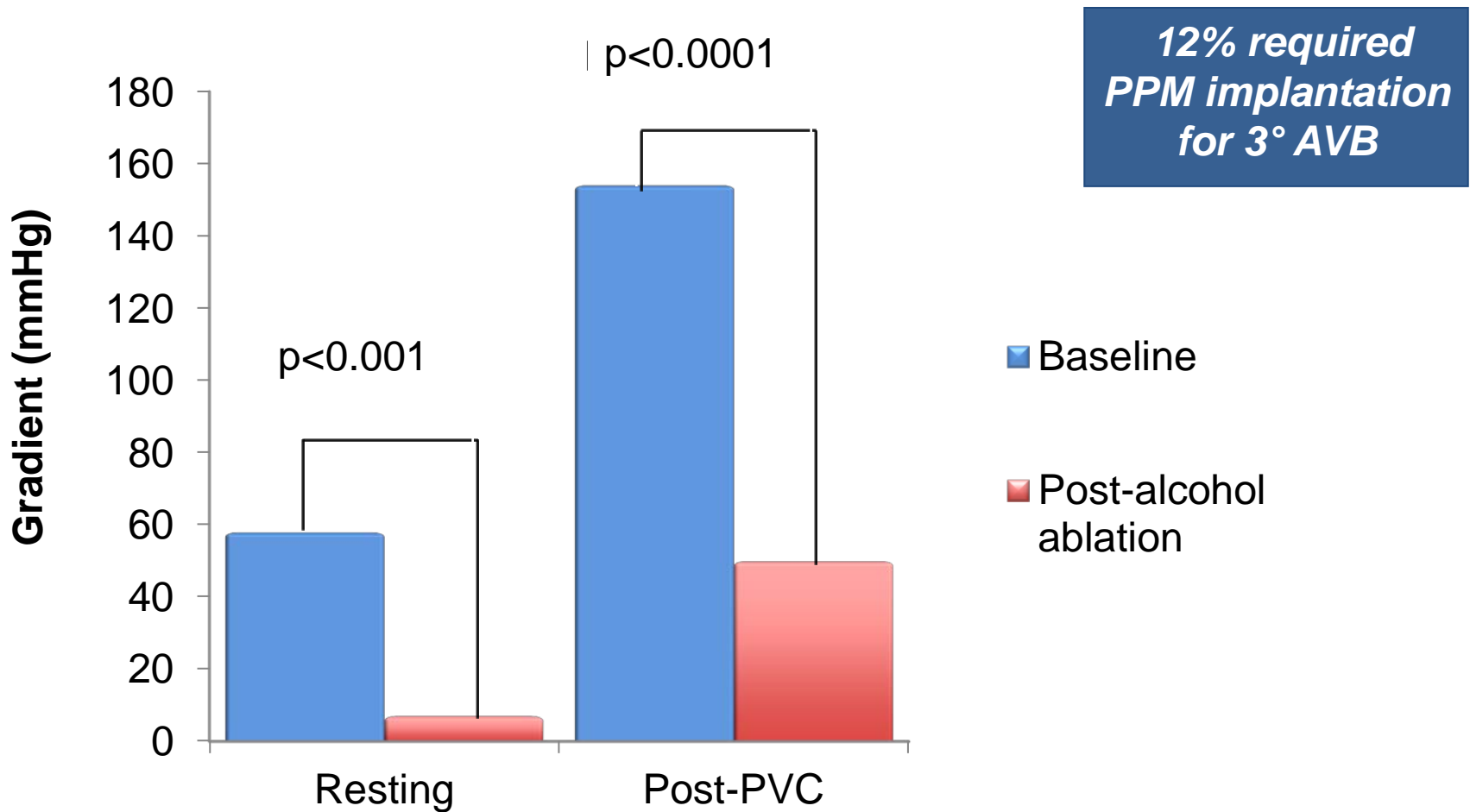
Peak Exercise CW Doppler



Resting LVOT Gradient = 12 mmHg

Peak Exercise LVOT Gradient = 33 mmHg

Effect of Alcohol Septal Ablation on LVOT gradient



Alcohol Septal Ablation for HOCM at Washington University

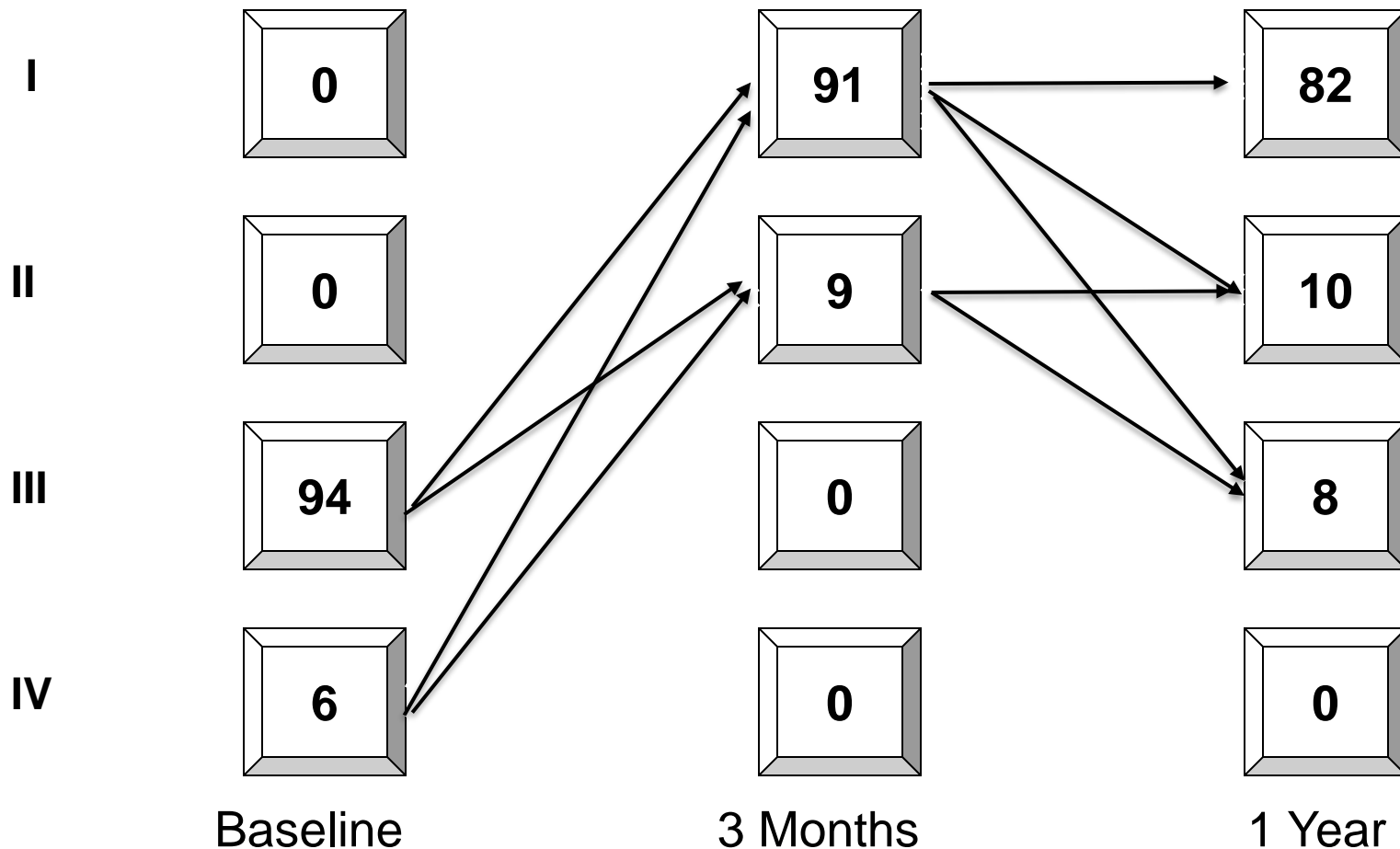
100 Patients: NYHA Functional Class

Procedural Success: 100%

Procedural Deaths: None

Permanent PM for AV Block: 12 (12%)

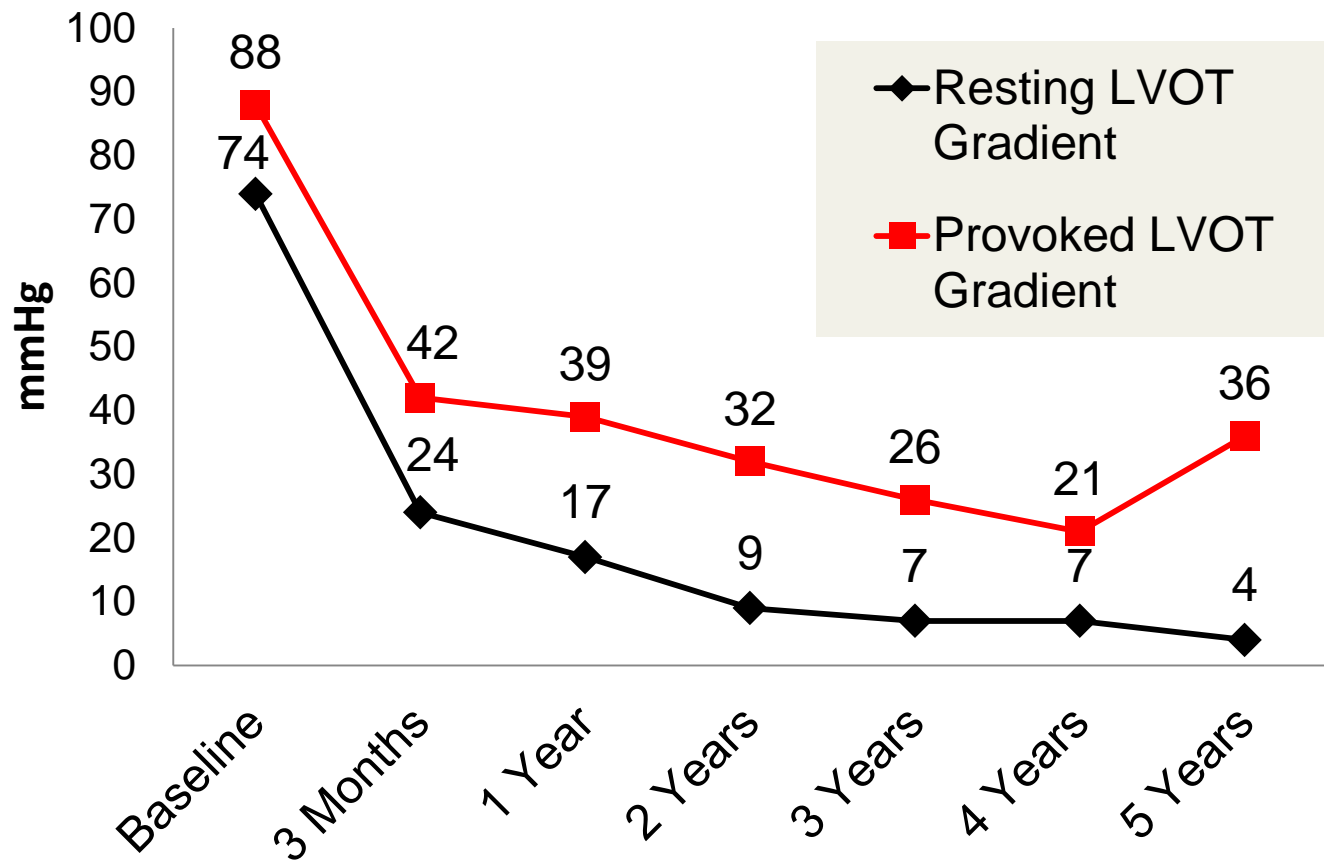
92% Class I or II at 1 Year



Alcohol Septal Ablation: 5-Year Follow-Up

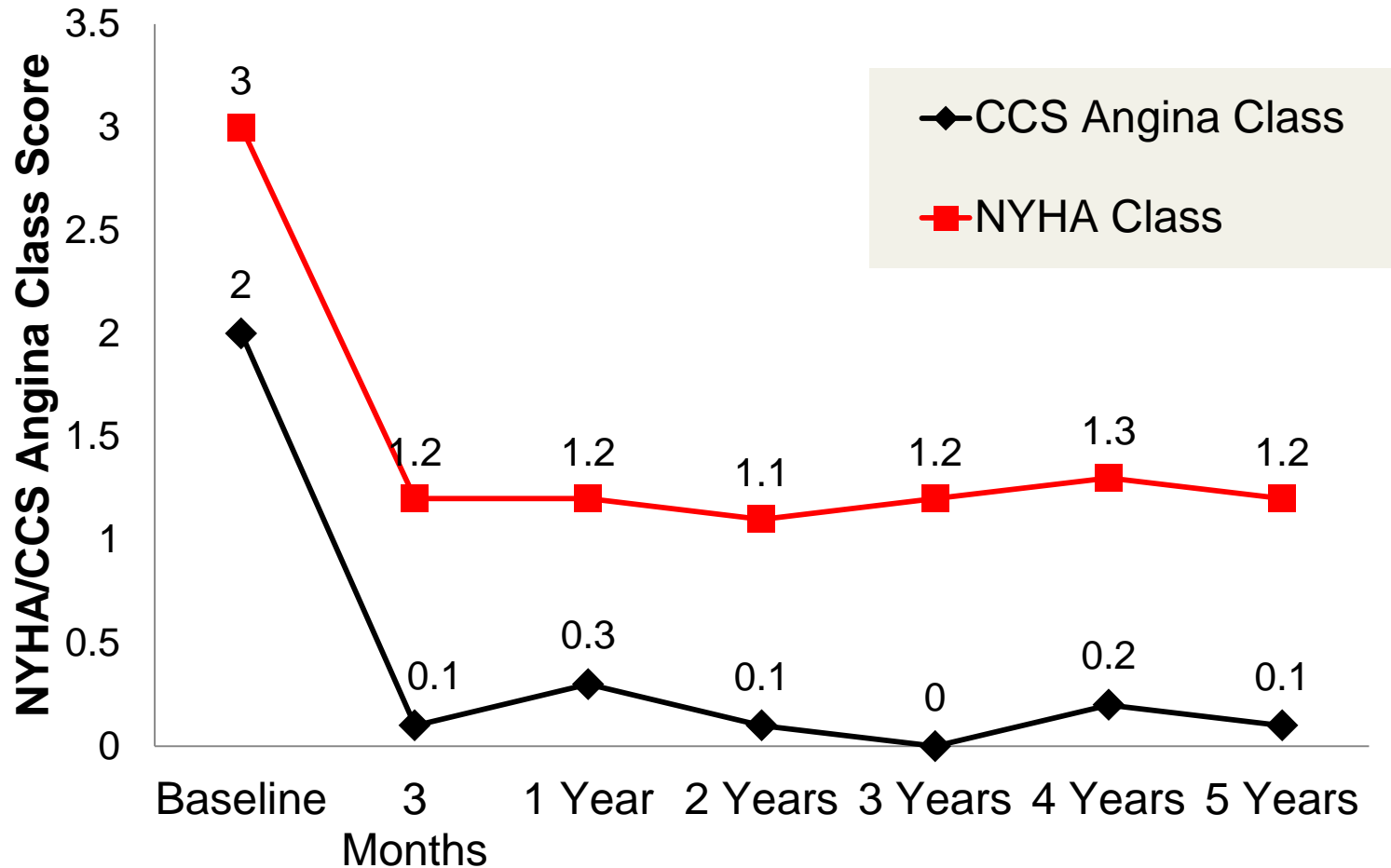
Reduction of LVOT Gradient by Alcohol Septal Ablation

N = 130 pts; 2 (1.5%) deaths, 17 (13%) PPM for AVB
Cardiac mortality 0.6% per year



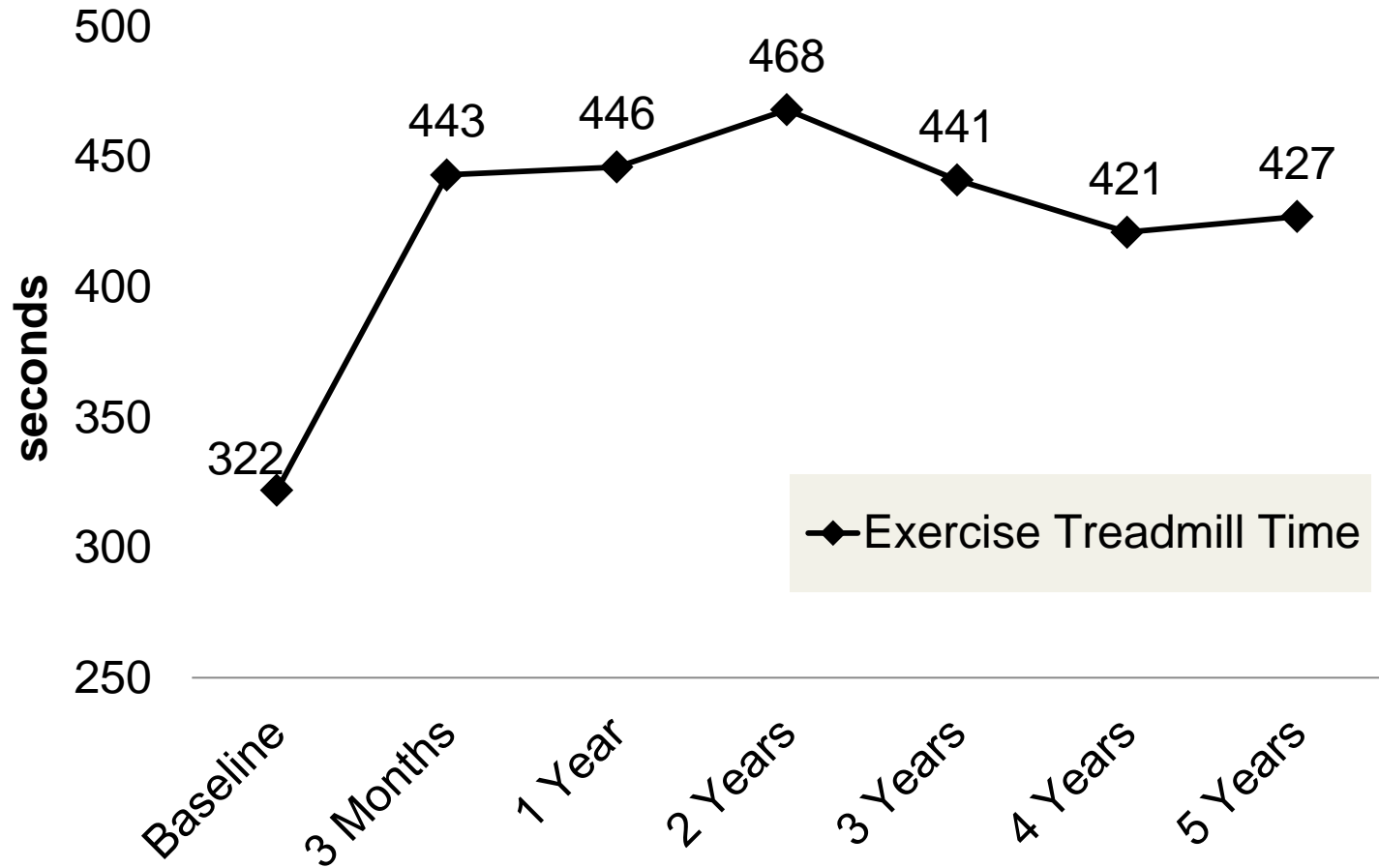
Alcohol Septal Ablation: 5-Year Follow-Up

Symptomatic Response



Alcohol Septal Ablation: 5-Year Follow-Up

Improvement in Exercise Capacity



Long Term Outcomes of Alcohol Septal Ablation

AUTHOR	CENTER	PRESENTED/ PUBLICATION	N	F/U	%NYHA Class I/II	CARD MORT/YR
Fernandes, et al.	MUSC+Baylor Charleston, SC Houston, TX	Clin Cardiol 2005	137	5 yrs	96%	0.6%
Welge, et al.	Ruhr U Bochum Bad Oeynhausen Germany	ACC 2008 Dtsch Med Wochen	347	5 yrs	89%	1%
Sorajja, et al.	Mayo Clinic Rochester, MN	AHA 2007 Circ	140	5 yrs	81%	2%
Chawla, et al.	Institut CV Paris Massy, France	ACC 2008	104	3 yrs	>90%	1.5%
ten Cate, et al.	Thoraxcenter Rotterdam, Netherlands	Circ Hrt Fail 2010	91	5.4 yrs	NR	4.4%* (*or ICD shock)
Kuhn, et al.	Bielefeld, Germany	Clin Res Cardiol 2008	644	1.4 yrs	NR	3.2%

Multicenter North American Registry

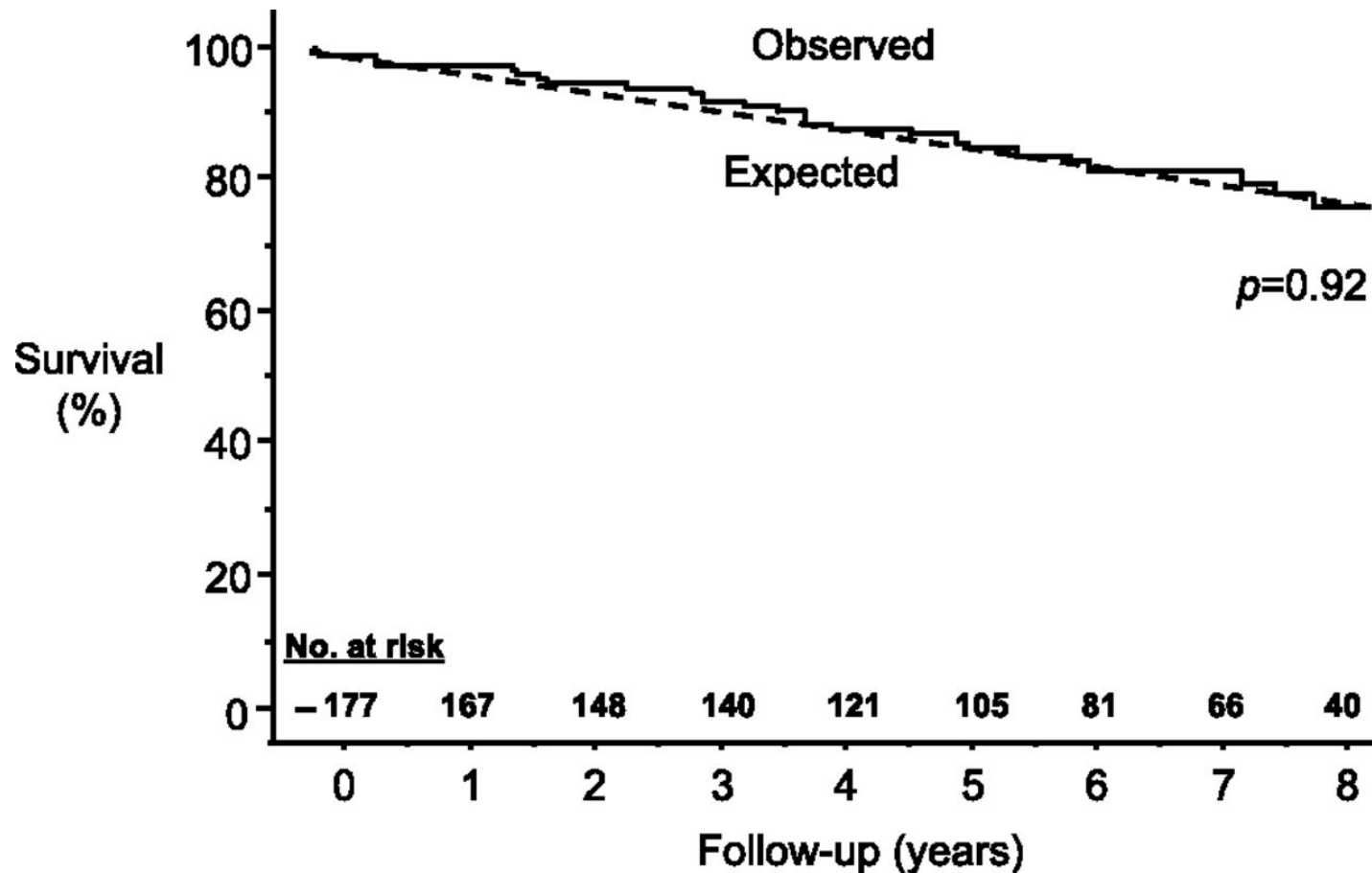
- Prospective, Initiated in 2000
- Uniform Criteria for Case Selection,
- Standardized Procedural and Follow-up Protocols
- 9 Institutions, 874 patients
 - Methodist Debaquey Heart & Vascular Center..... Nagueh, Buergler
 - Medical University of South Carolina..... Spencer, Nielson
 - University of Colorado..... Groves
 - Washington University in St. Louis..... Bach
 - University of Florida..... Smith
 - Loyola University Medical Center..... Leya
 - Duke University Medical Center..... Wang
 - Heartland Regional Medical Center..... Rowe
 - University of Toronto..... Schwartz, Woo

Long Term Outcomes of Alcohol Septal Ablation Multicenter North American Registry

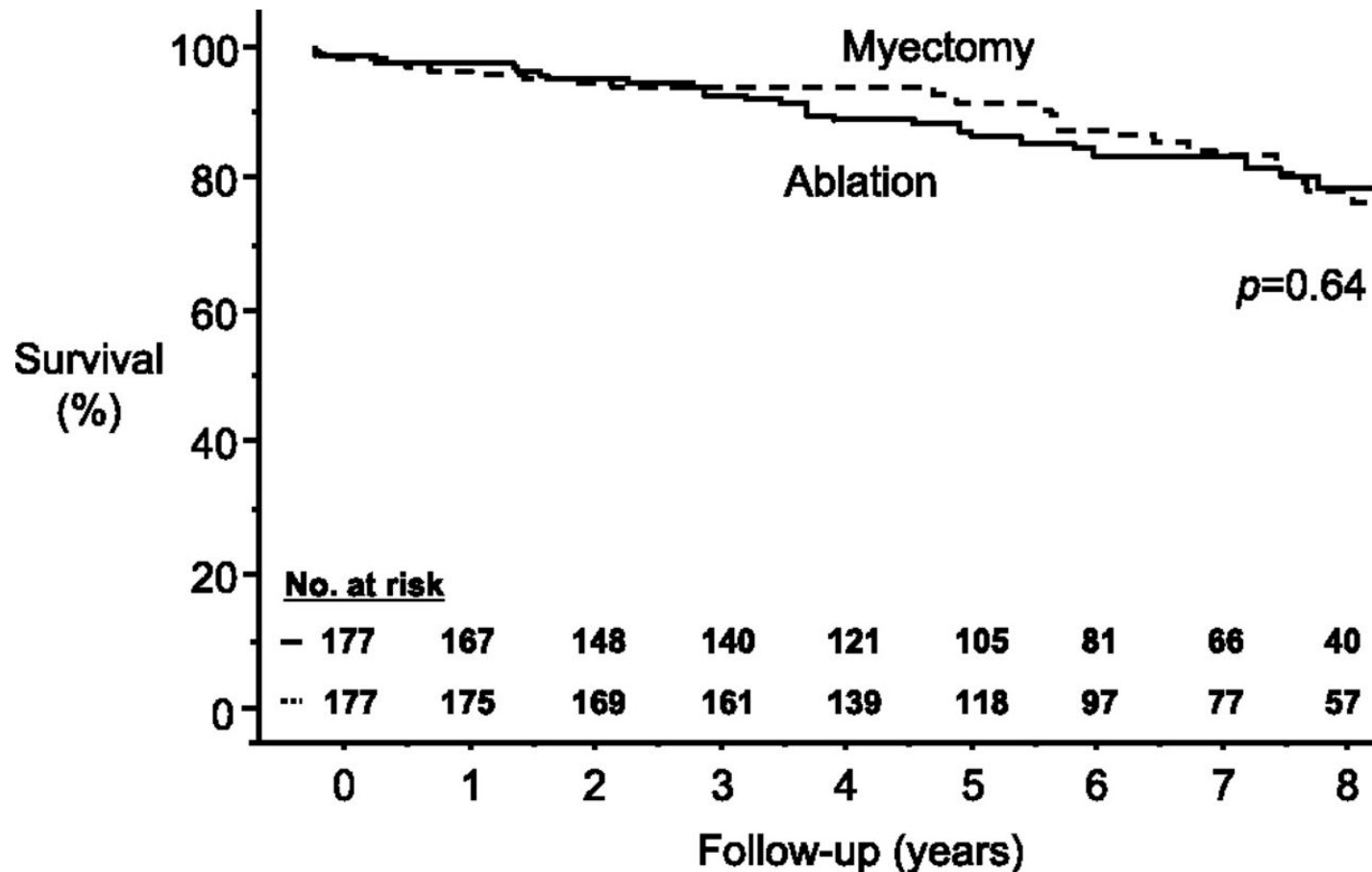
- 874 Patients, 2000 to 2010, 78% NYHA Class III/IV
 - Mean Duration of F/U: 2.1 ± 0.1 yrs
 - NYHA Class I or II: 95%
 - Total Deaths: 81 (9.3%); 25 cardiac, 25 noncardiac, 31 unknown
 - Survival:
 - @ 1 yr: 97% (95% CI, 96%, 98%)
 - @ 5 yr: 86% (95% CI, 81%, 91%)
 - @ 9 yr: 74% (95% CI, 64%, 86%)

“...compared with HCM pts who did not undergo septal reduction therapy included in other series, survival appears better after alcohol septal ablation...(9-10 yrs, 74% vs. 61%)”

Long-Term Survival for Patients with Septal Ablation Mayo Clinic Experience



Long-Term Survival for Patients with Septal Ablation Compared with Myectomy Mayo Clinic Experience

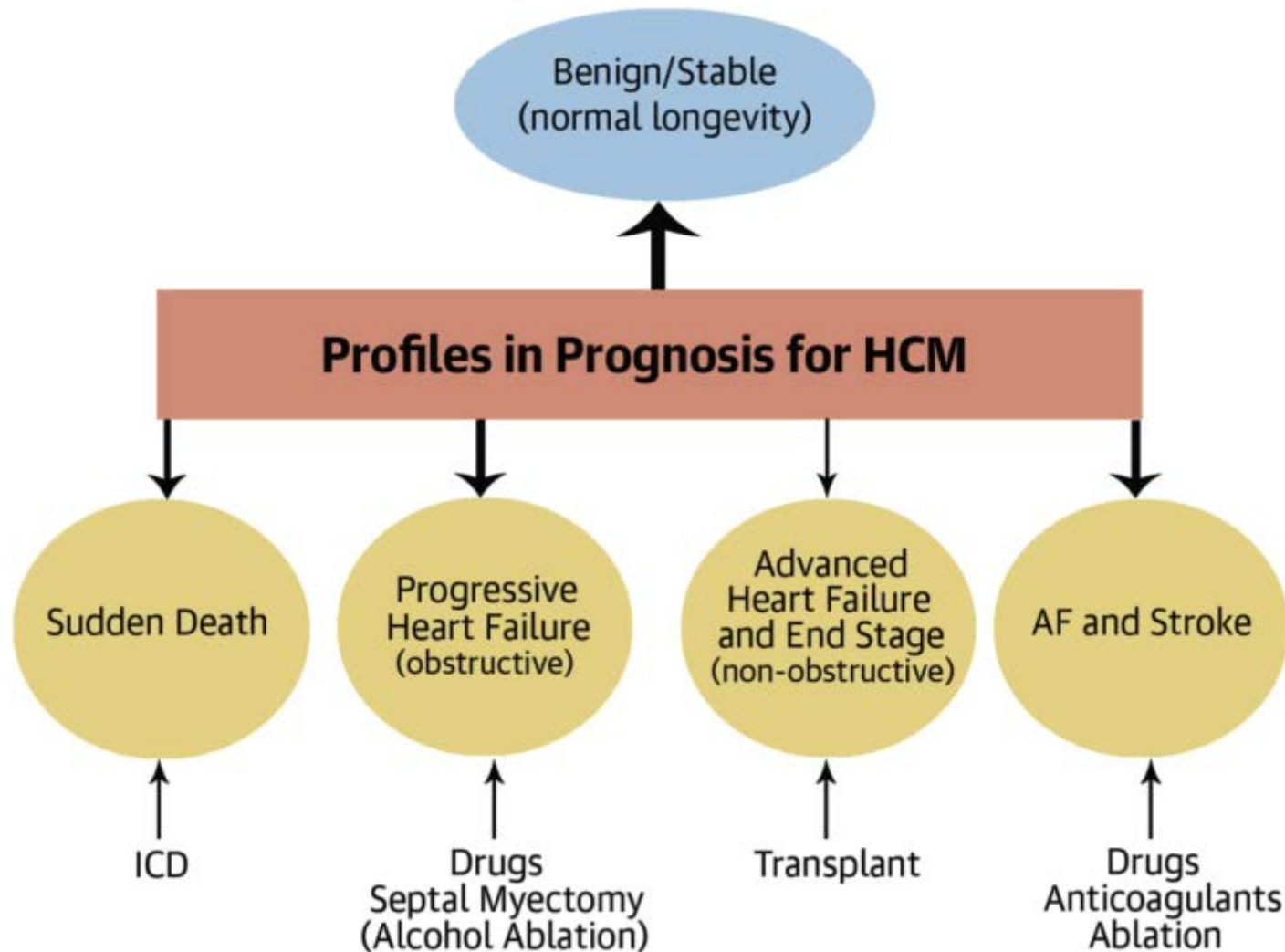


Long Term Outcomes of Alcohol Septal Ablation

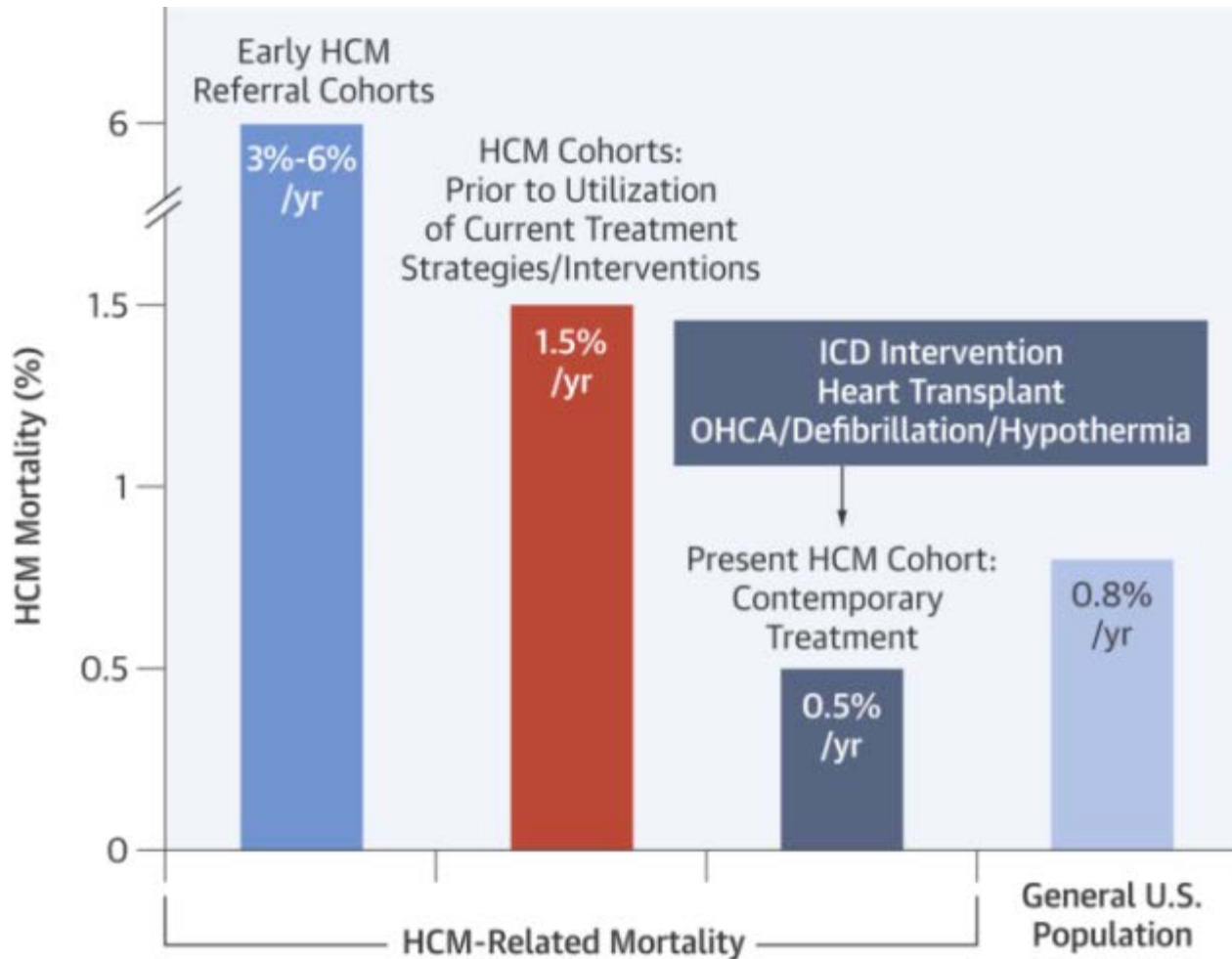
Conclusions

- For severely symptomatic patients with HCM and LVOT obstruction, ASA results in early and sustained hemodynamic and symptomatic improvement.
- ASA, like myectomy, carries risks of death and significant morbidity, mandating careful patient selection and meticulous technique by experienced operators; for appropriately selected patients, long term results of ASA support a highly favorable risk-benefit balance.

Schematic Representation of the Differing Effects of Septal Reduction Therapies



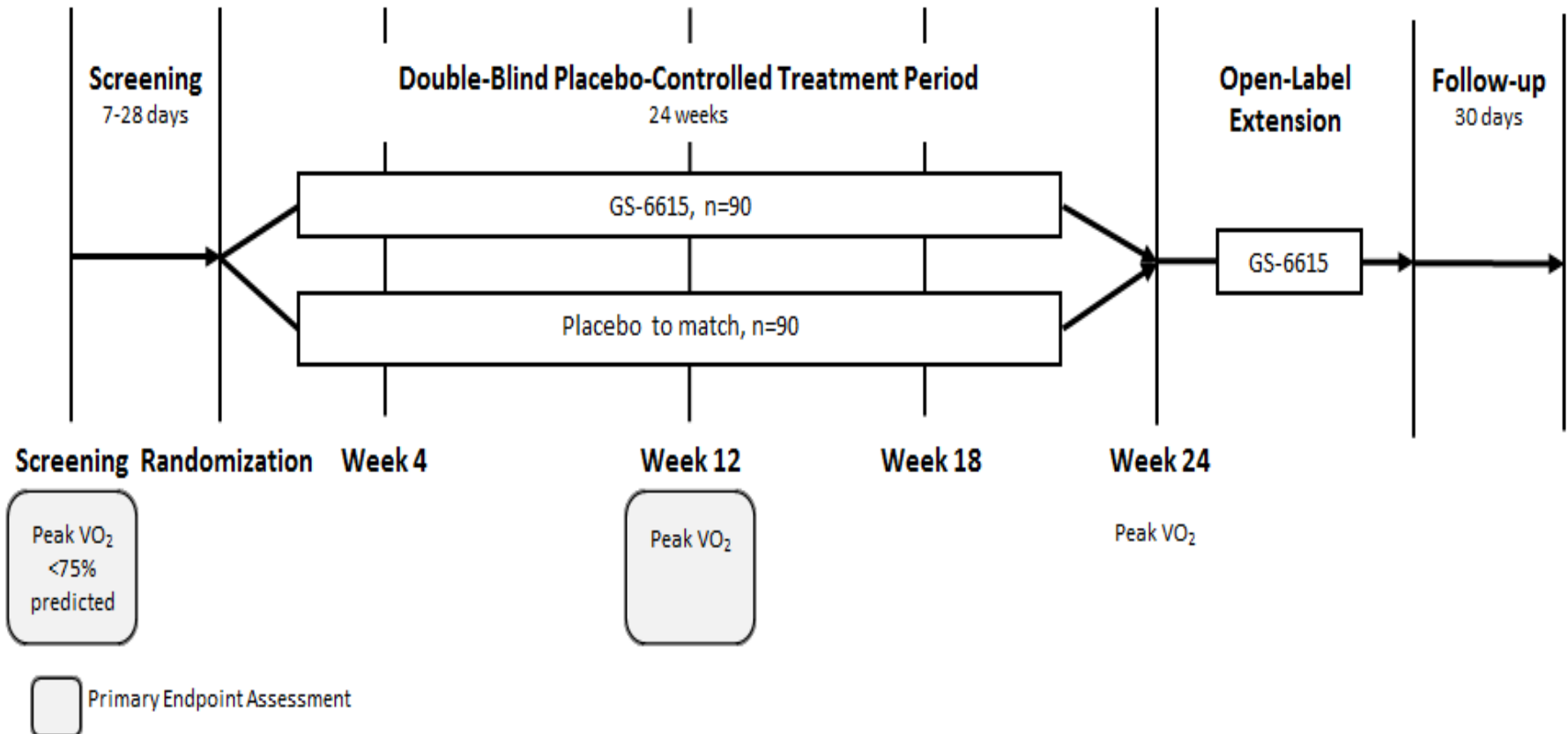
Decreasing Mortality Due to HCM



LIBERTY-HCM

impact of Late sodium current InhiBition on ExeRcise capaciTY in subjects with symptomatic HCM

- Novel late sodium channel inhibitor
- Favorable effects on action potential duration, Ca^{++} overload



Heart & Vascular Center



NATIONAL LEADERS IN MEDICINE