LOW FLOW LOW GRADIENT AORTIC STENOSIS

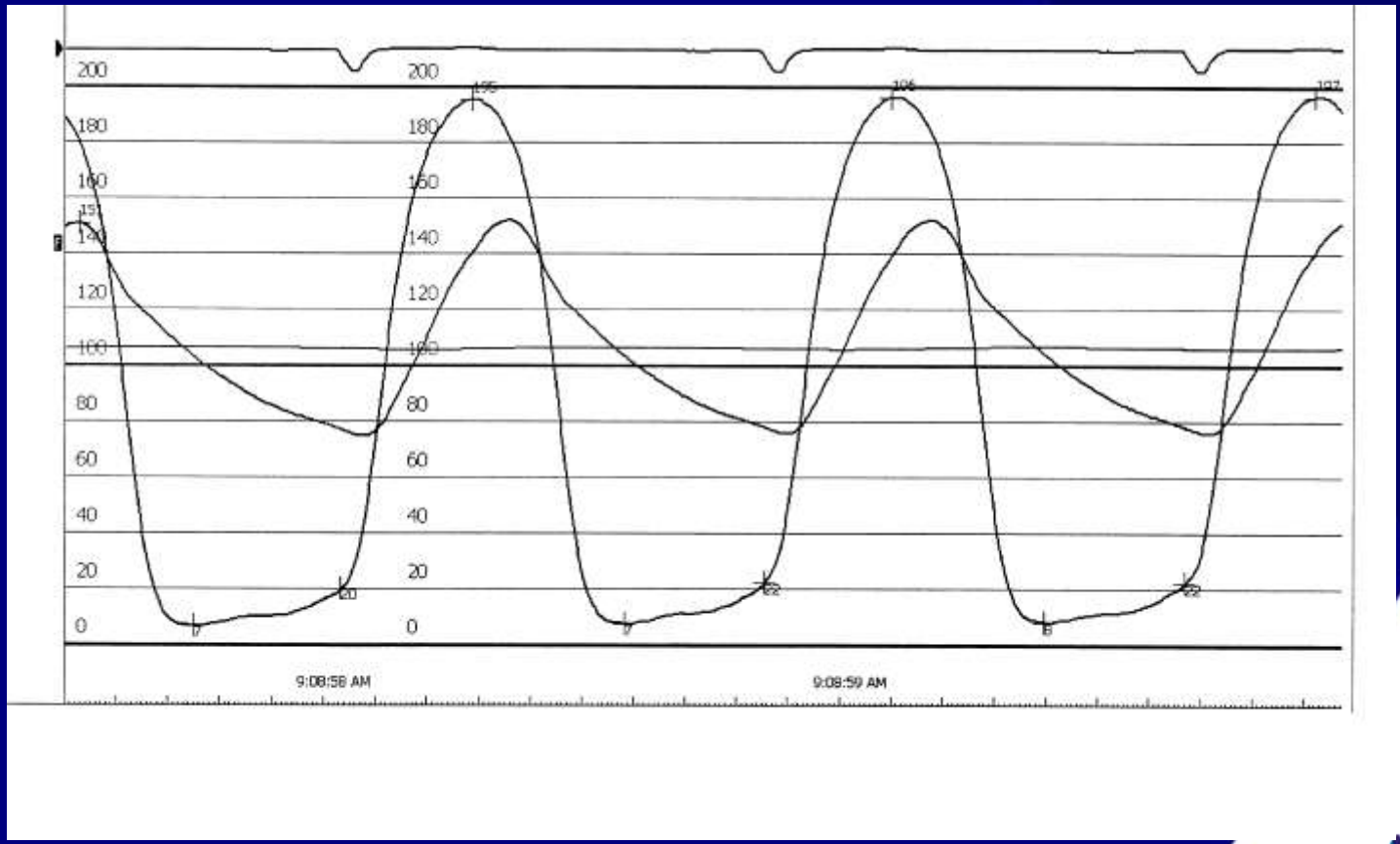
HOW MANY DISEASES ARE WE TALKING ABOUT?

Mount Sinai Beth Israel

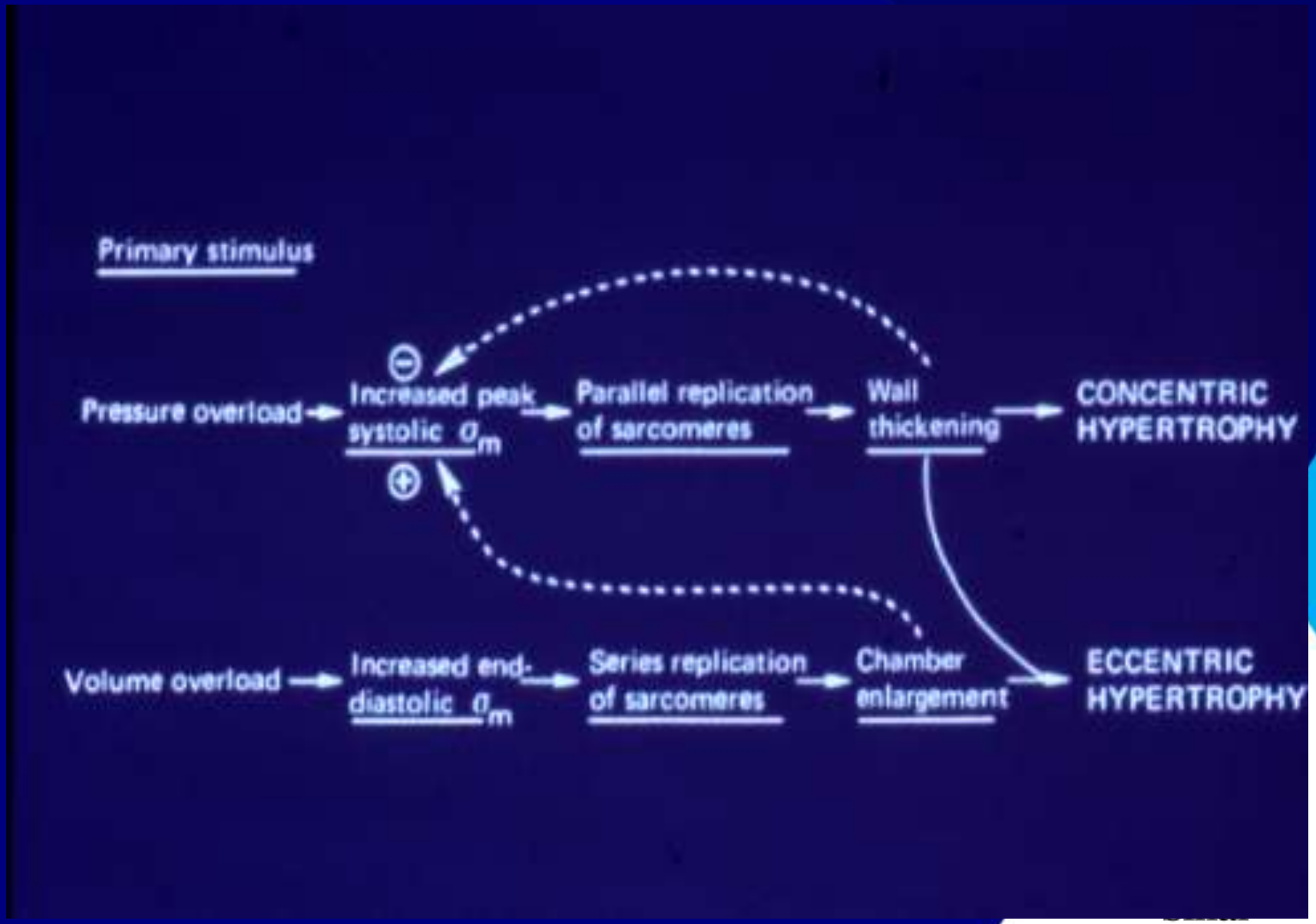
BACKGROUND

- THE LV’s RESPONSE TO PRESSURE OVERLOAD IS WANTONLY CAPRICIOUS .

Mount Sinai Beth Israel



Mount Sinai Beth Israel


Primary stimulus
Pressure overload
Increased peak systolic σ_m
Parallel replication of sarcomeres
Wall thickening
CONCENTRIC HYPERTROPHY
Volume overload
Increased end-diastolic σ_m
Series replication of sarcomeres
Chamber enlargement
ECCENTRIC HYPERTROPHY

Beth Israel

- $\sigma = P \times r / 2th$

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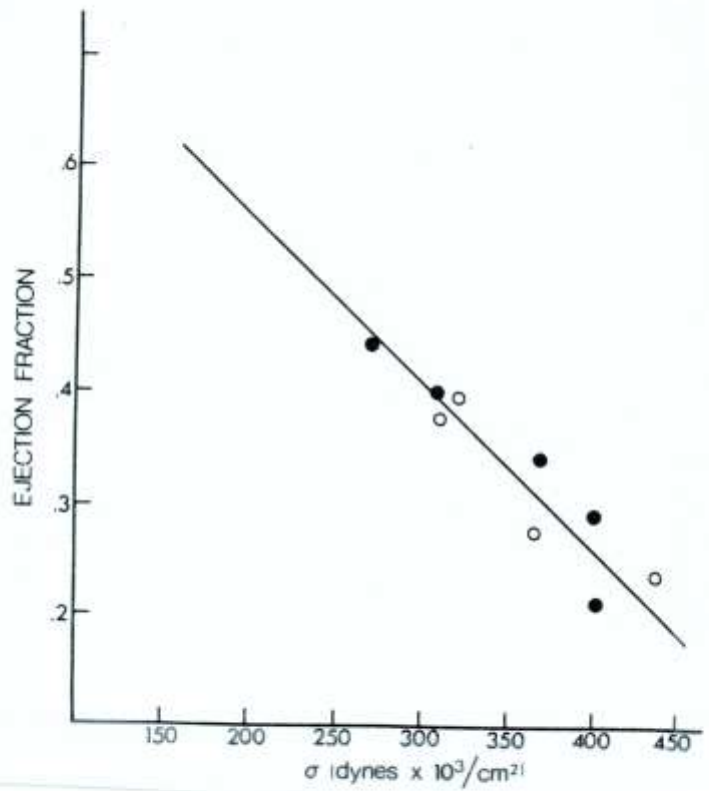
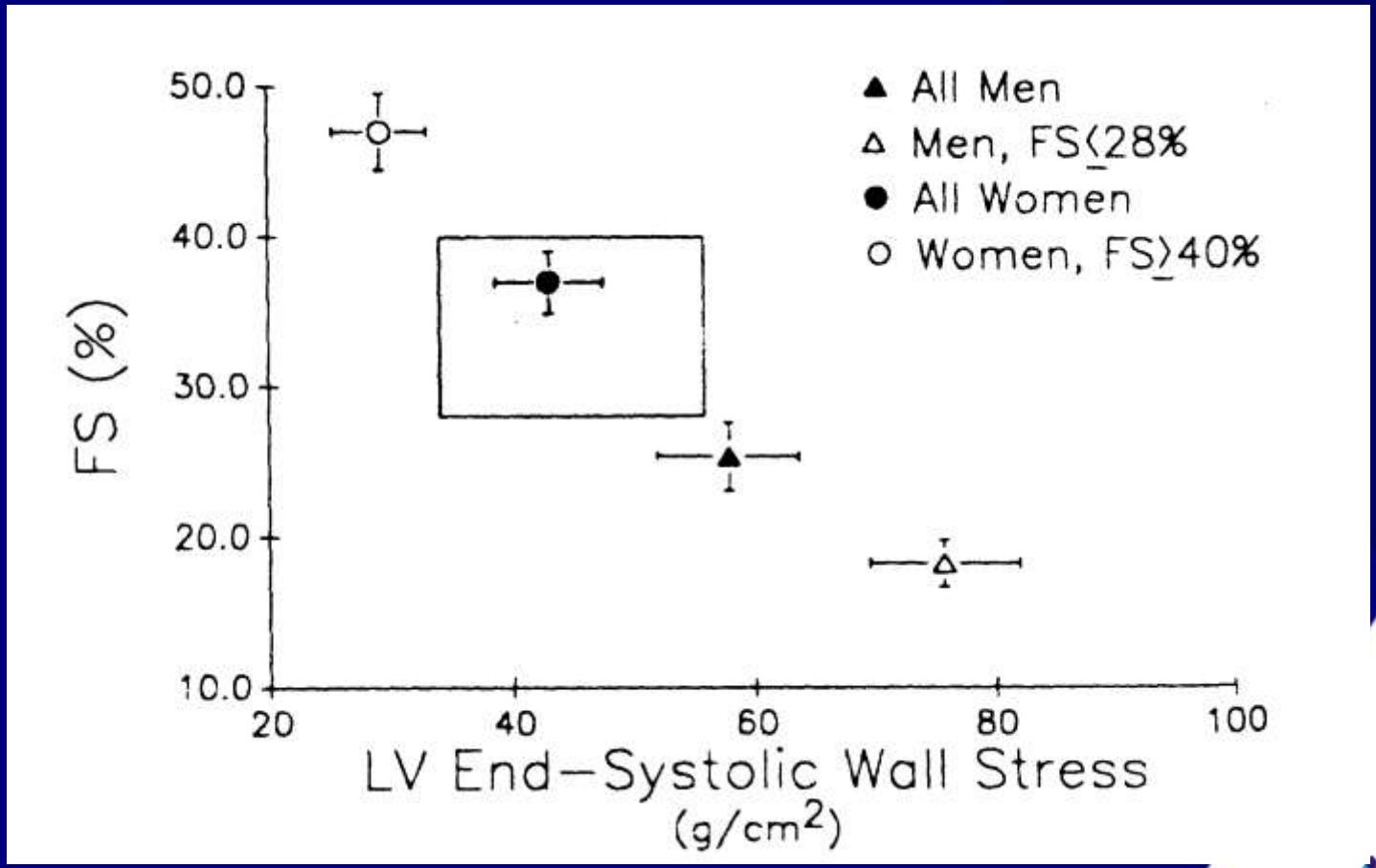


Carabello BA, Green LH, Gross W, et al. Hemodynamic determinants of prognosis of aortic valve replacement in critical aortic stenosis and advanced congestive heart failure. Circulation 1980;62:42-48.

CARABELLO et al CIRC 1980

Mount Sinai Beth Israel



CARROLL et al CIRC 1992

Mount Sinai Beth Israel

80 Y/O WOMAN

- CLASS III Sx OF DYSPNEA
- 3/6 SEM; DELAYED CAROTIDS
- ABSENT A_2

Mount Sinai Beth Israel

ECHO

- 1.7 cm LV WALL
- EF 0.62
- MEAN GRADIENT 24 mm Hg
- AVA 0.8 cm^2

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CONCENTRIC REMODELING WITHOUT LVH

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- SMALL THICK VENTRICLES
- NO ROOM FOR THE BLOOD
- LOW STROKE VOL, NL EF
- LOW GRADIENT

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WHY CAUSES THIS HETEROGENEITY IN RESPONSE ?

STENOSIS SEVERITY ?

PATIENT FACTORS (BODY HABITUS, ACTIVITY etc ?

RATE OF ORIFICE NARROWING ?

GENETIC BACKGROUND ?

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CANINE MODEL OF AS

- CONTROLLABLE AORTIC BAND
- DOGS OUTWARDLY SIMILAR
- BROWN, MALE, 25 kg

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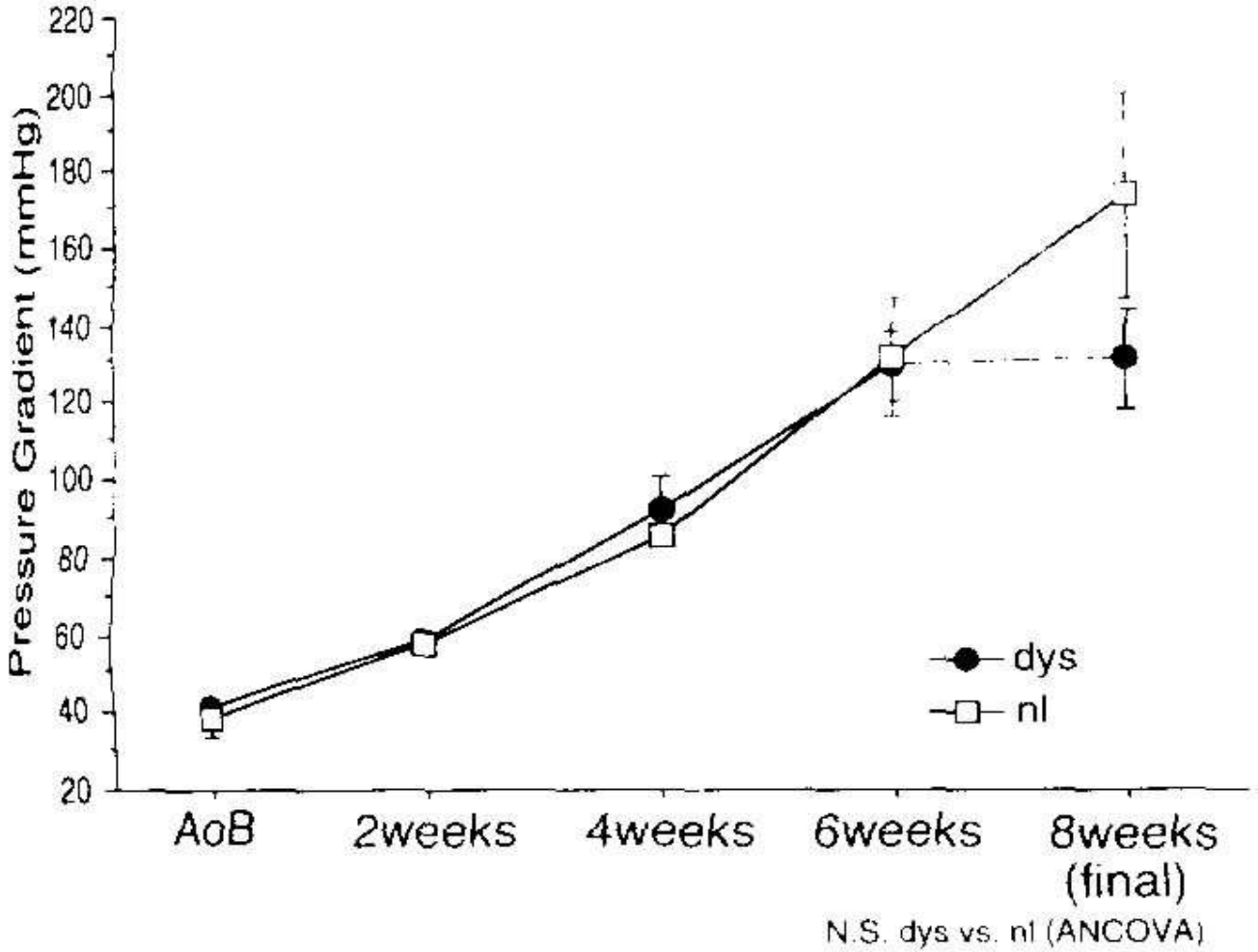

KOIDE, CARABELLO et al CIRC 1997

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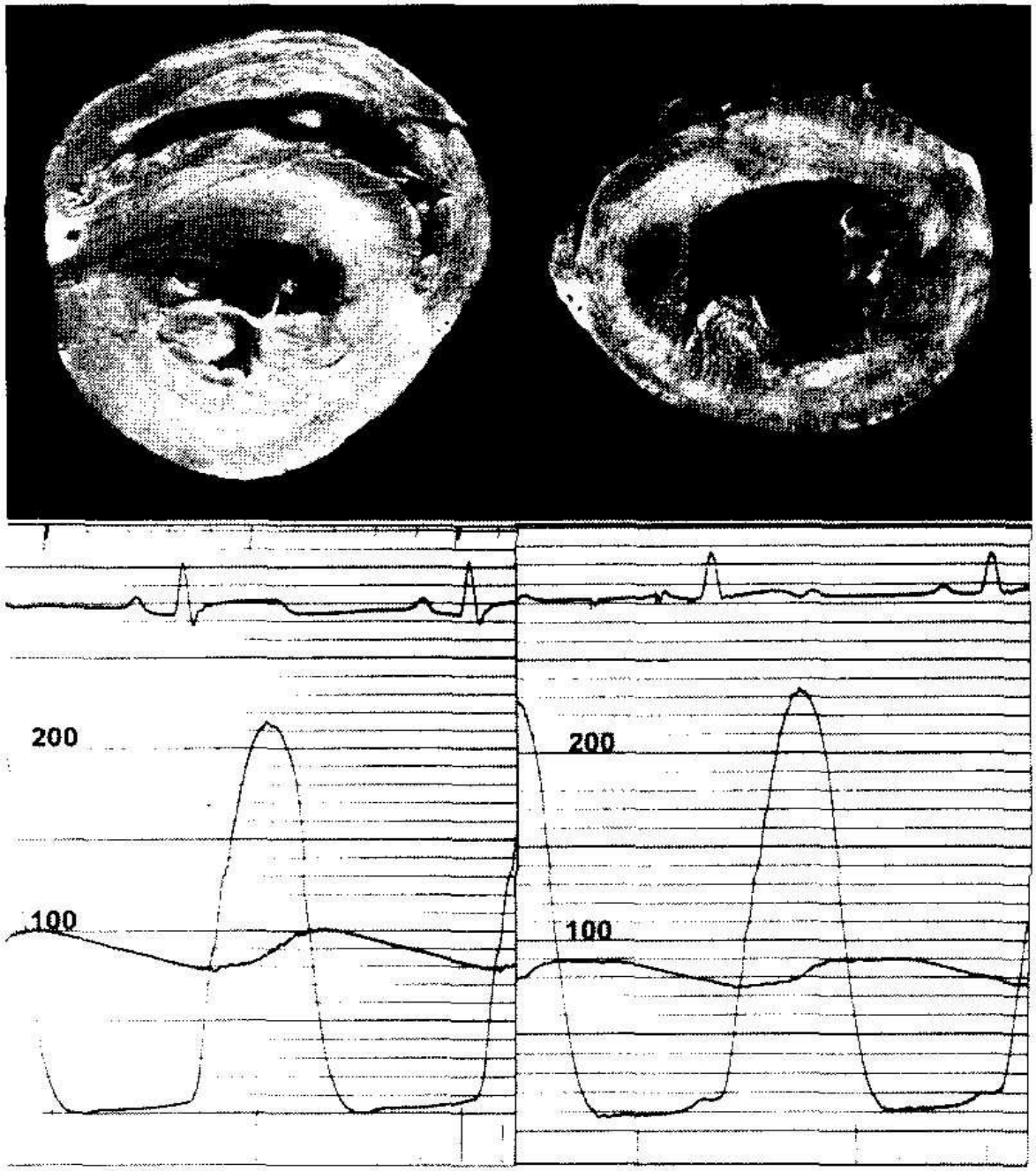
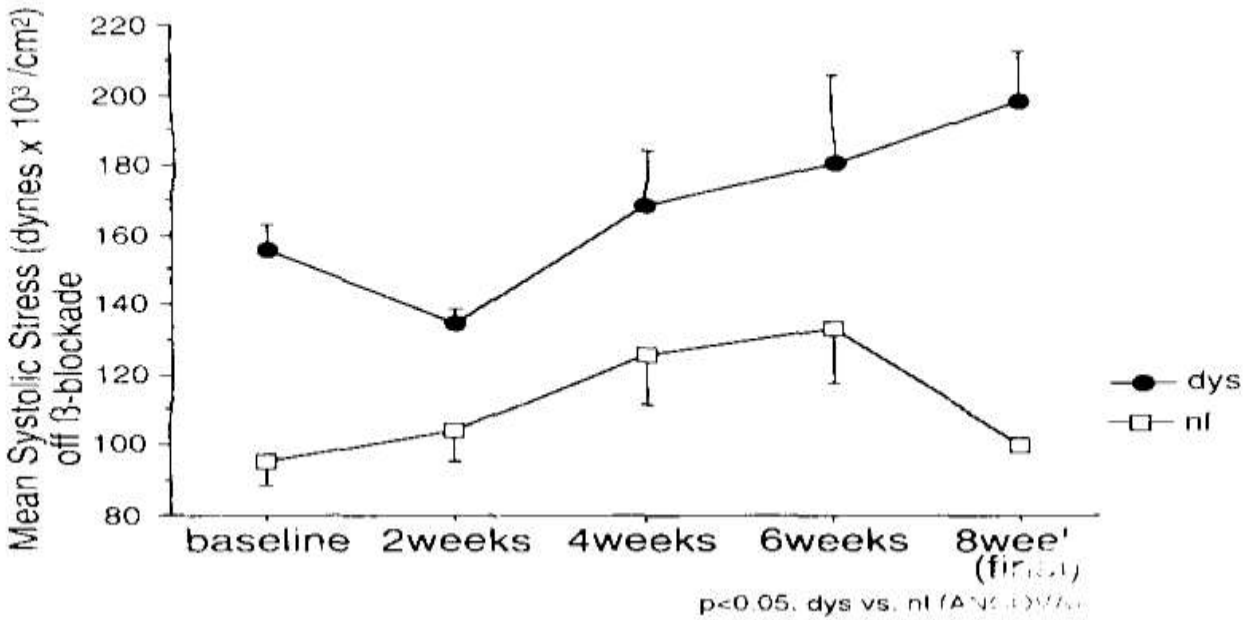
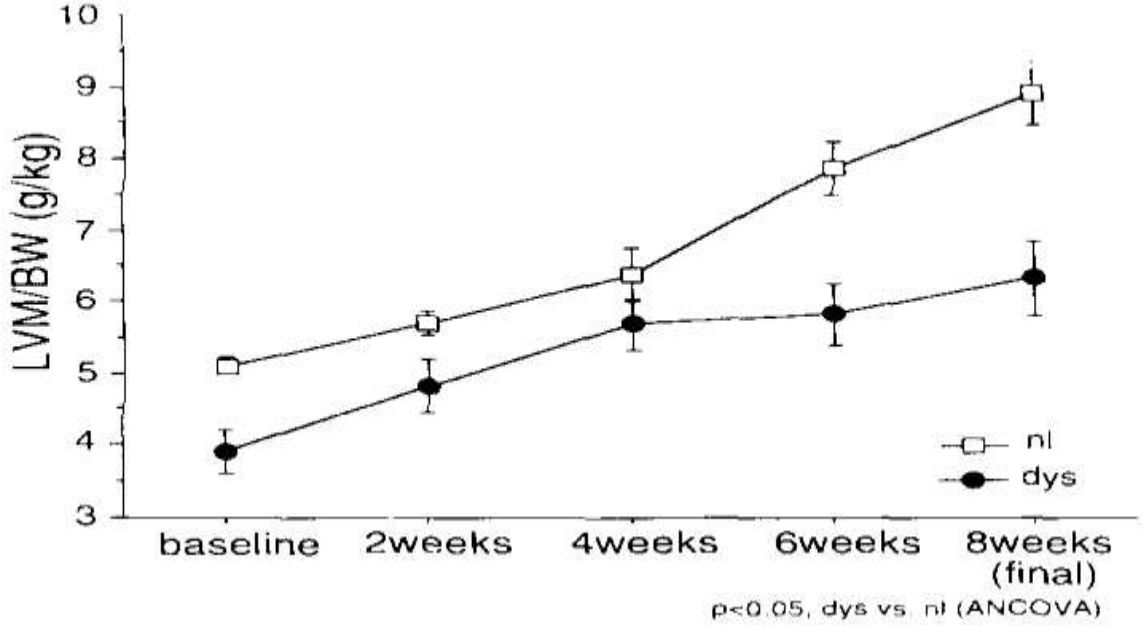

200
100
200
100


Mean Systolic Stress (dynes x 10³ /cm²)
off β-blockade
220
200
180
160
140
120
100
80
baseline
2weeks
4weeks
6weeks
8wee'
dys
nl
p<0.05, dys vs. nl


LVM/BW (g/kg)
10
9
8
7
6
5
4
3
baseline
2weeks
4weeks
6weeks
8weeks
(final)
nl
dys
p<0.05, dys vs. nl (ANCOVA)

IS LVH GOOD OR BAD

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Sinai
Beth Israel

YES

Mount
Sinai
Beth Israel

WELL-KNOWN

- LVH INCREASES MORTALITY, ESPECIALLY IN THE FACE OF ISCHEMIA

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DUNCAN et al ATS 2008

AVR MORTALITY

- CONC GEO NO CONC GEO
- 38/964 (3.9%) 18/964 (1.9%)

- MORBIDITY
- 33/964 (3.4%) 17/964 (1.8%)

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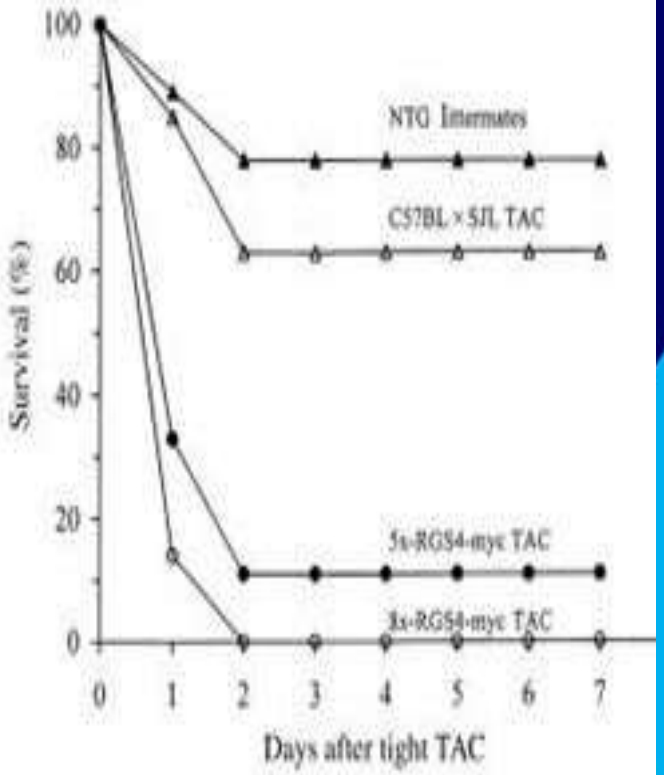
	Total "tight" TAC	1 day survival	3 day survival	7 day survival
NTG littermates (of 5x-RGS4-myc mice)	9	8 (89%)	7 (78%)	7 (78%)
NTG C57BL × SJL	48	41 (85%)	30 (63%)	30 (63%)
5x-RGS4-myc	18	6 (33%)	2 (11%)	2 (11%)
8x-RGS4-myc	14	2 (14%)	0 (0%)	0 (0%)



Rogers et al JCI 1999

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WHAT IS SEVERE AS

WHEN YOU FIND OUT YOU TELL ME

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Sinai
Beth Israel

SEVERE AS

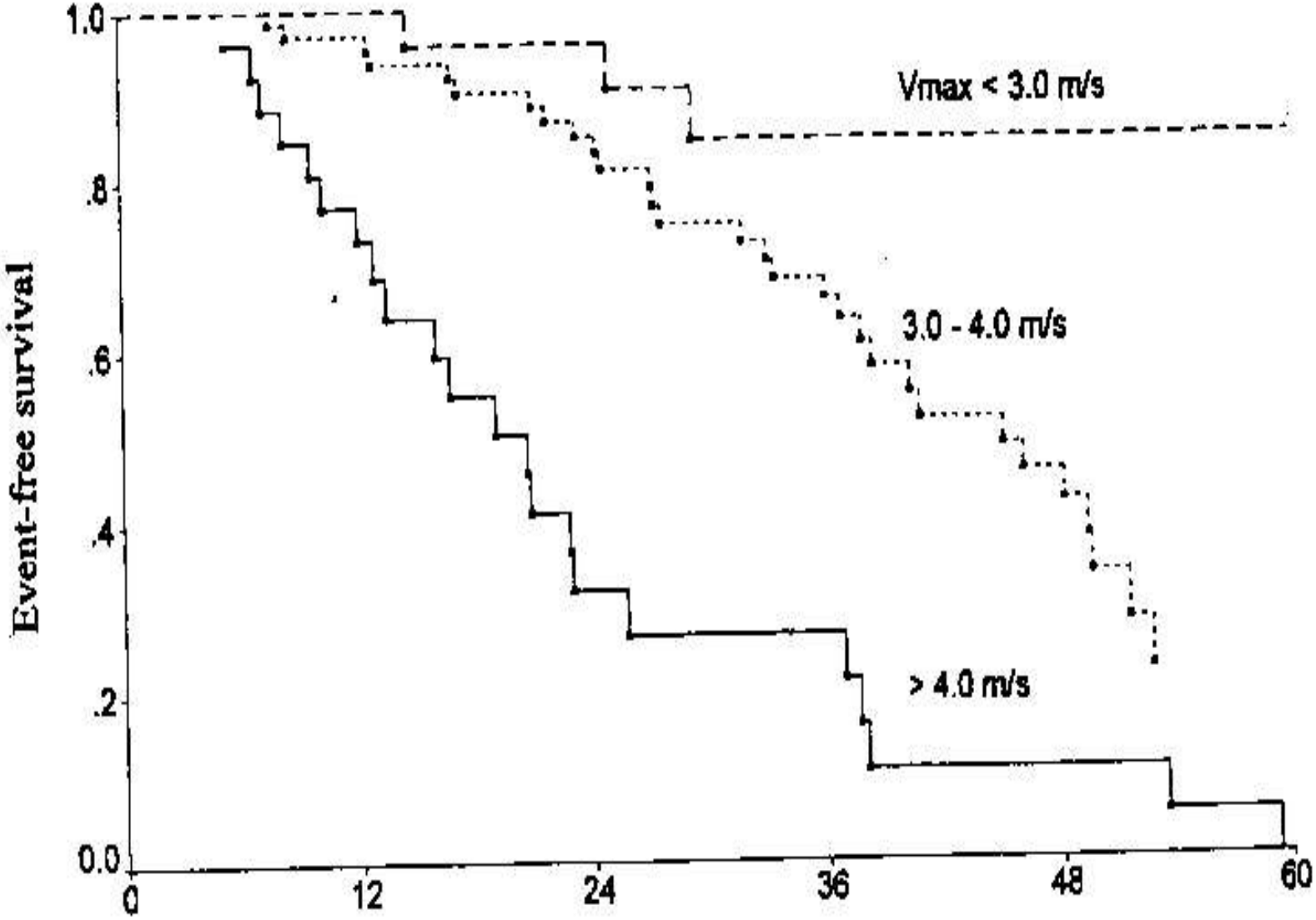
- 1/4/40

Mount Sinai Beth Israel

1.0

- WIGGERS EXPERIMENTS IN RUBBER TUBES, CIRCA 1938

Mount Sinai Beth Israel


Event-free survival
1.0
.8
.6
.4
.2
0.0
0
12
24
36
48
60
Vmax < 3.0 m/s
3.0 - 4.0 m/s
> 4.0 m/s

Beth Israel

40 mm Hg

- 1998 ACC/AHA GUIDELINES: 50 mm Hg

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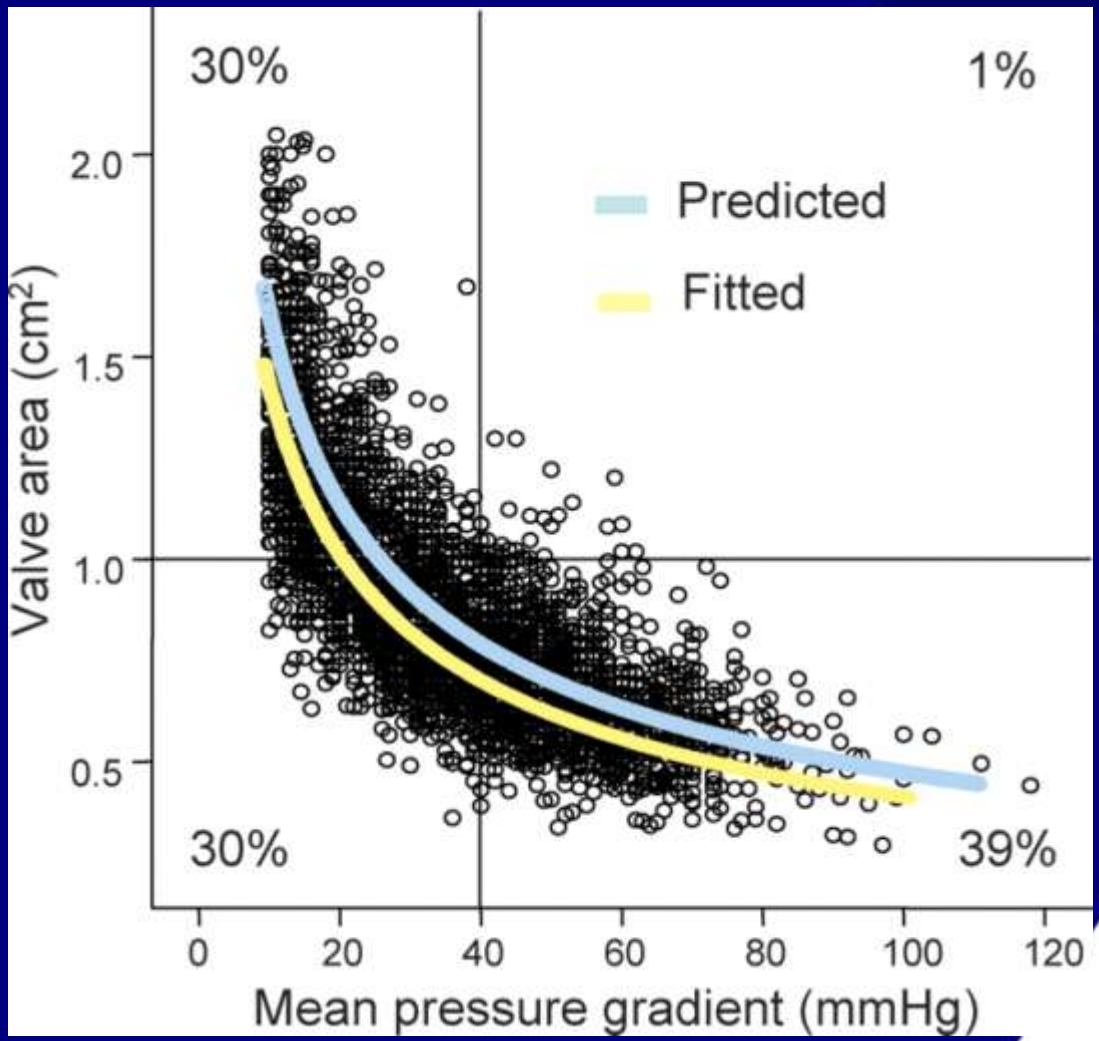
Valve area vs. mean pressure gradient of 3483 echocardiographic studies in patients with aortic valve stenosis and normal left ventricular function.



Minners J et al. Eur Heart J 2008;29:1043-1048

Mount Sinai
European Heart Journal

AND THEN THERE IS INDEXING

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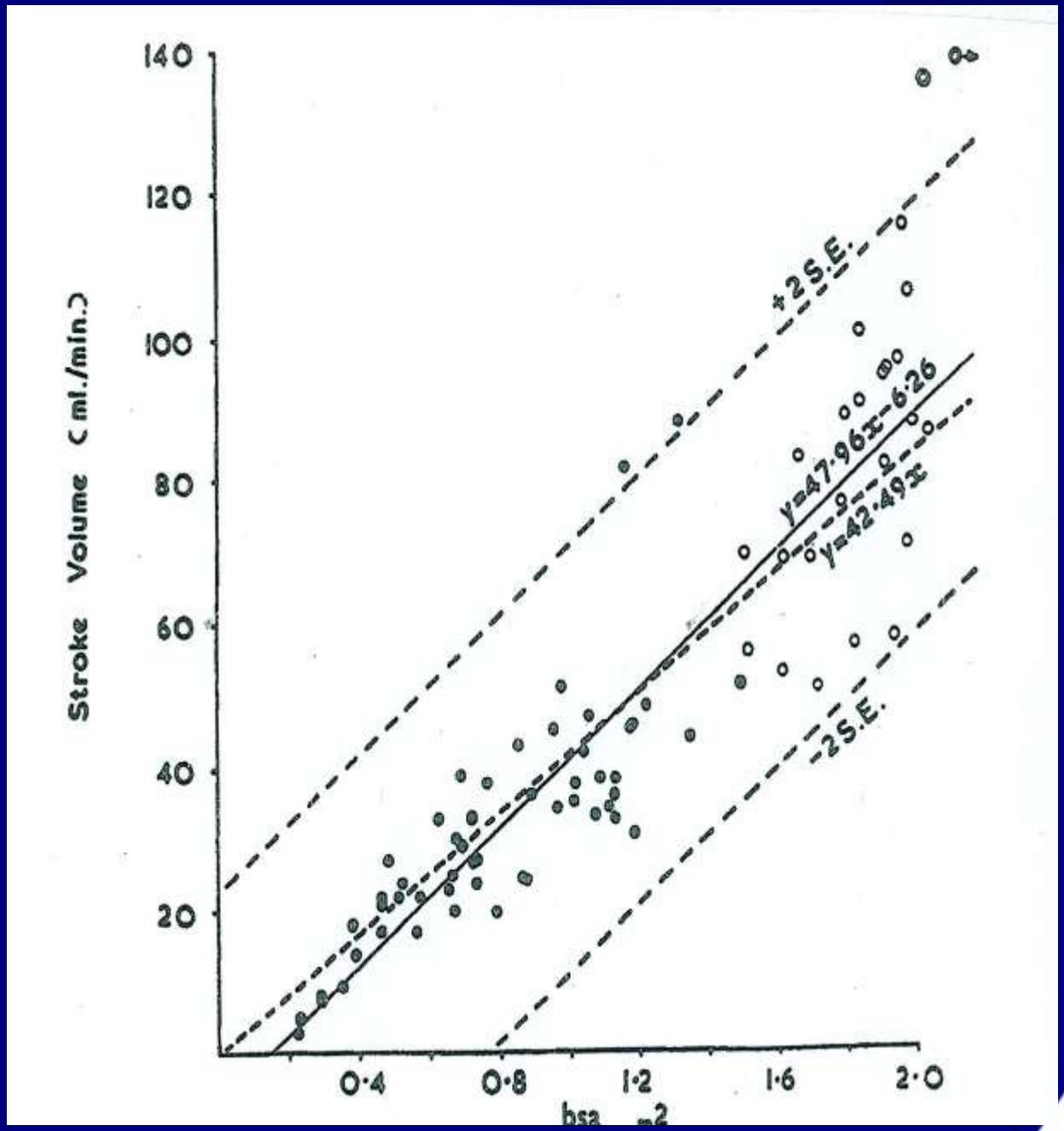
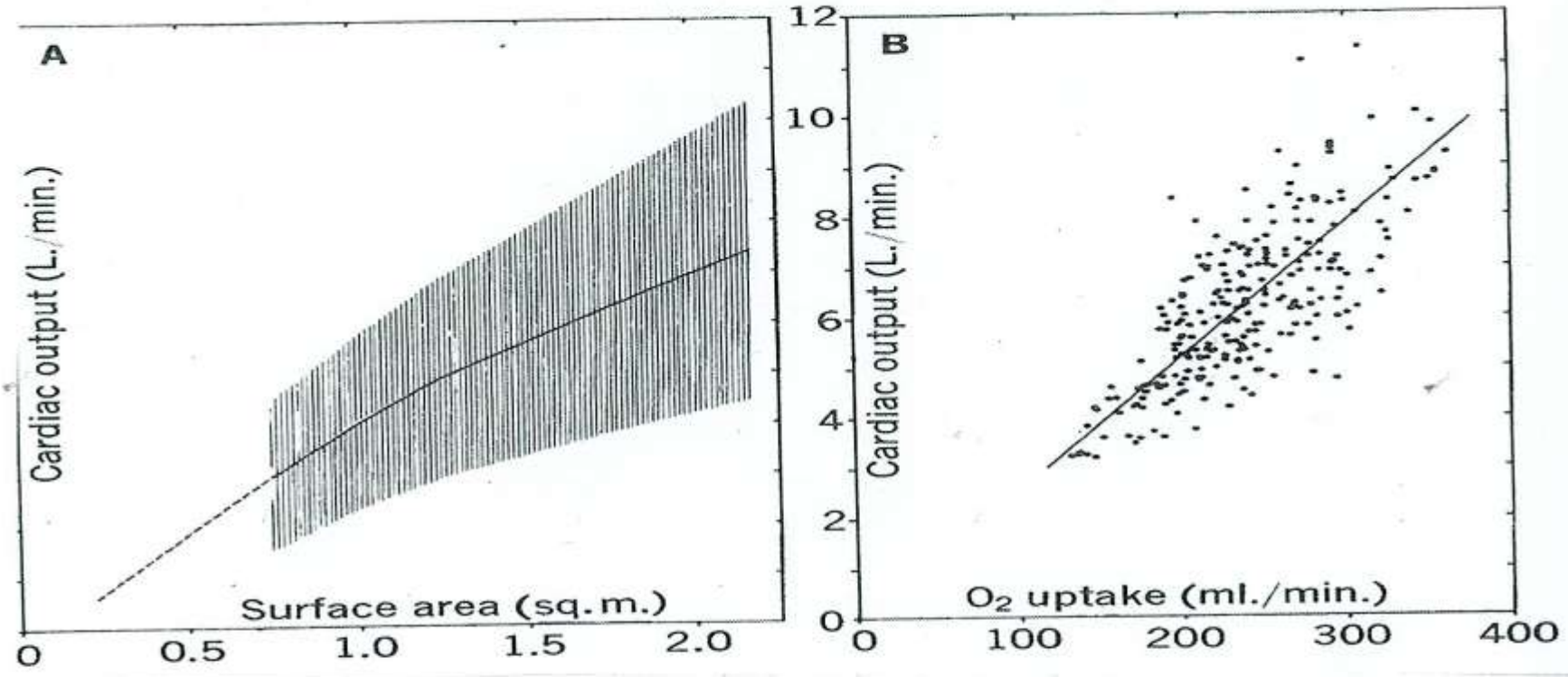
Sinai
Beth Israel



REEVES et al J APPL PHYS 1961

Mount Sinai Beth Israel


A
Cardiac output (L./min.)
Surface area (sq. m.)
0
0.5
1.0
1.5
2.0
B
Cardiac output (L./min.)
O_2 uptake (ml./min.)
0
2
4
6
8
10
12
0
100
200
300
400

AS HAS CHANGED

AND WE CHANGED IT

Mount
Sinai
Beth Israel

Mount
Sinai
Beth Israel

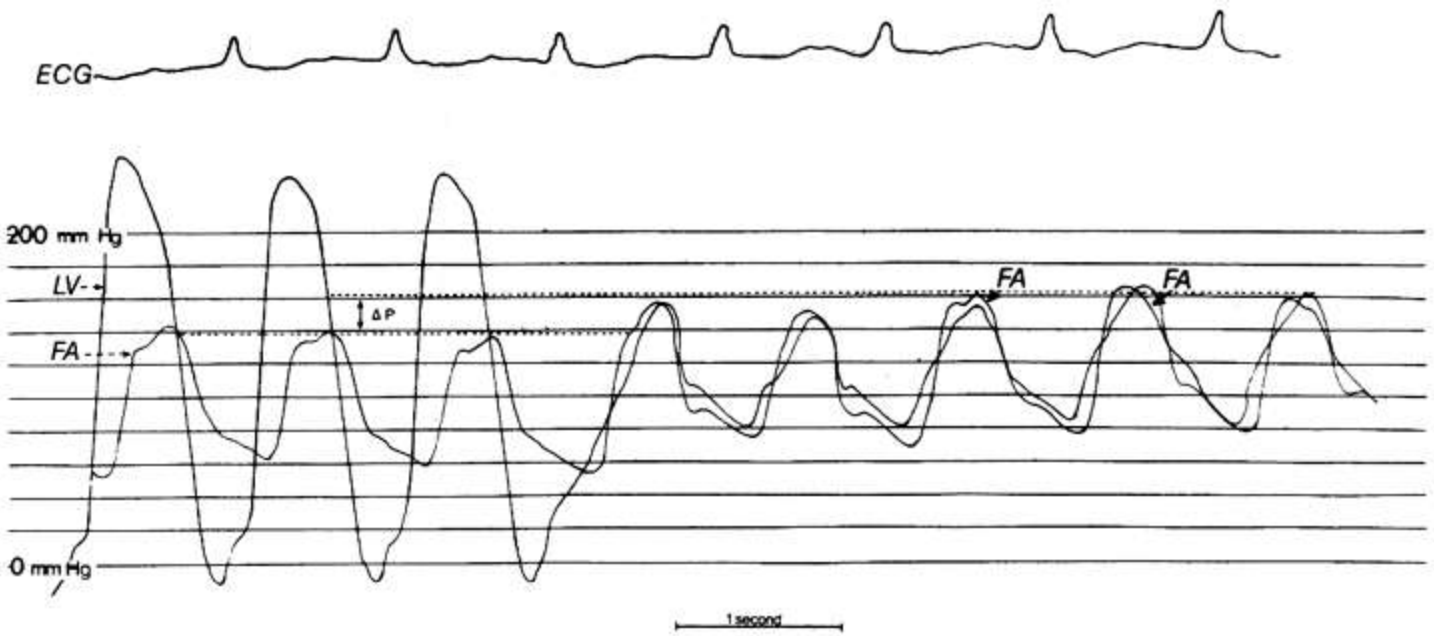
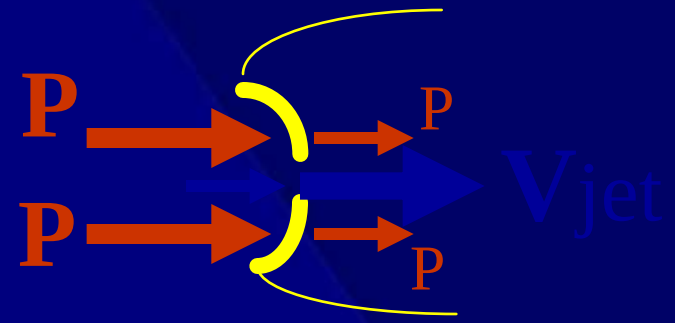
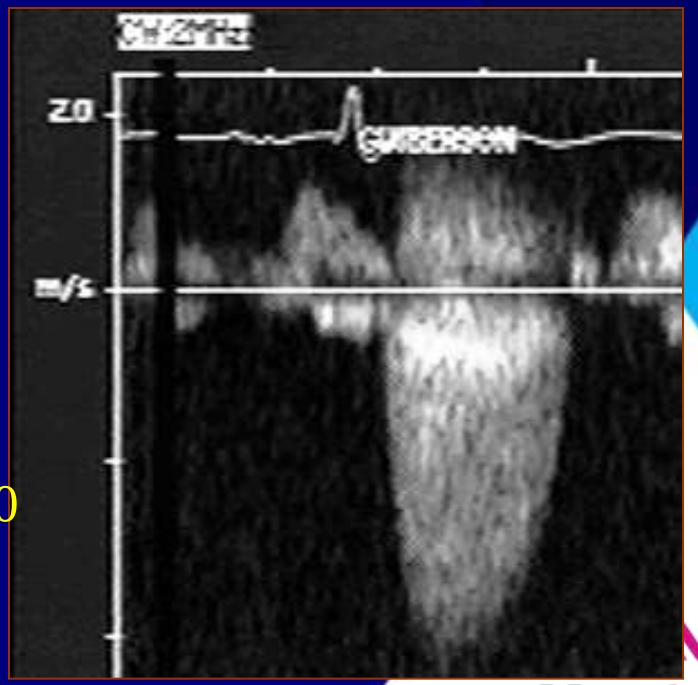


Figure 28.7 Left ventricular (LV) and femoral artery (FA) pressure tracings in a patient with severe aortic stenosis (aortic valve area 0.4 cm^2). During pullback of the retrograde catheter from LV to ascending aorta, the peak systolic femoral artery pressure can be seen to increase (ΔP) by approximately 20 mm Hg. This sign is seen only in patients with aortic valve areas <0.6 cm^2. The mechanism of this phenomenon is believed to be partial obstruction of an already narrowed aortic orifice by the retrograde catheter and relief of this obstruction with catheter withdrawal. (From Carabello BA, et al. Changes in arterial pressure during left heart pullback in patients with aortic stenosis. *Am J Cardiol* 1979;44:424.)

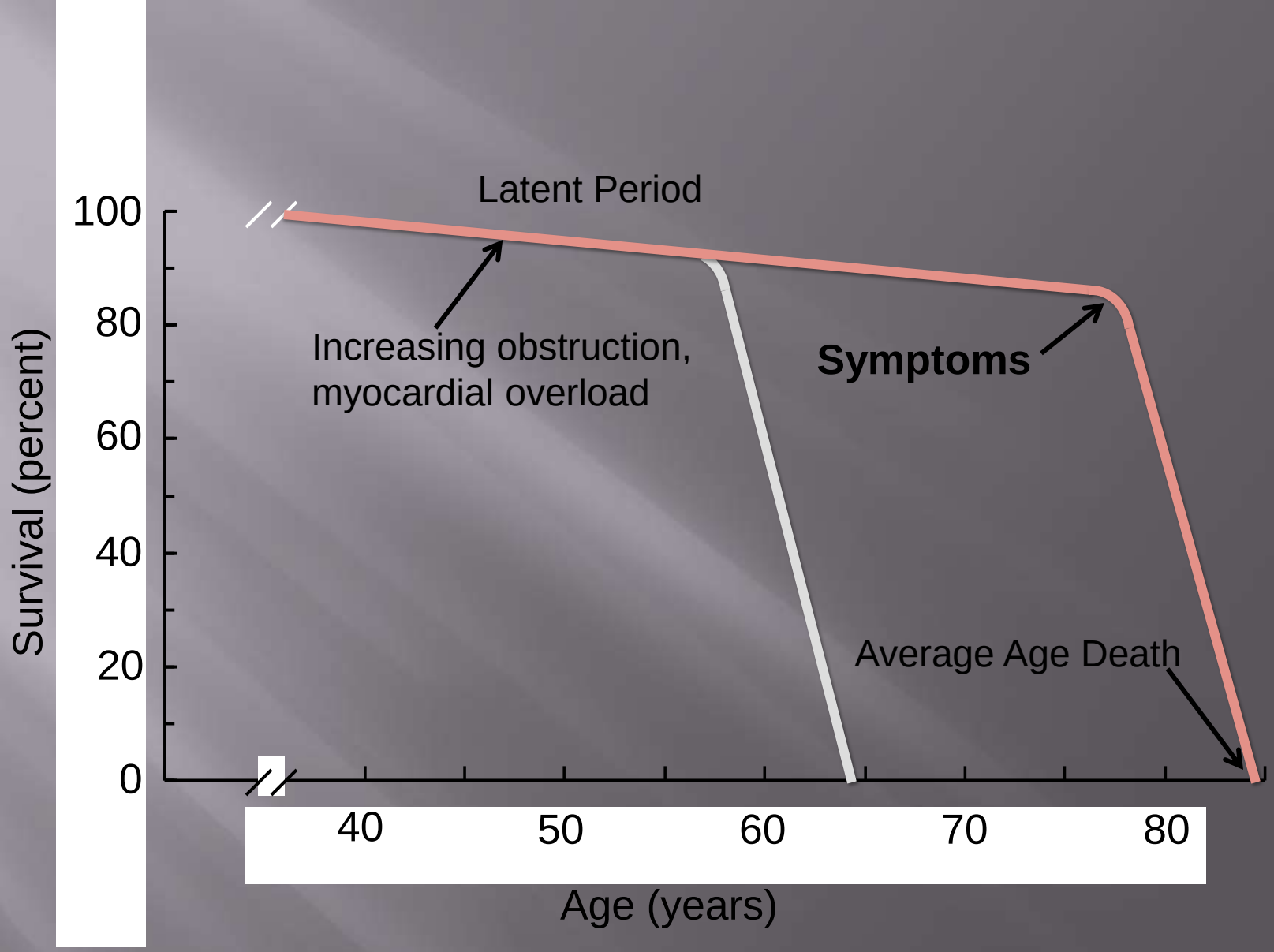
Mount Sinai Beth Israel

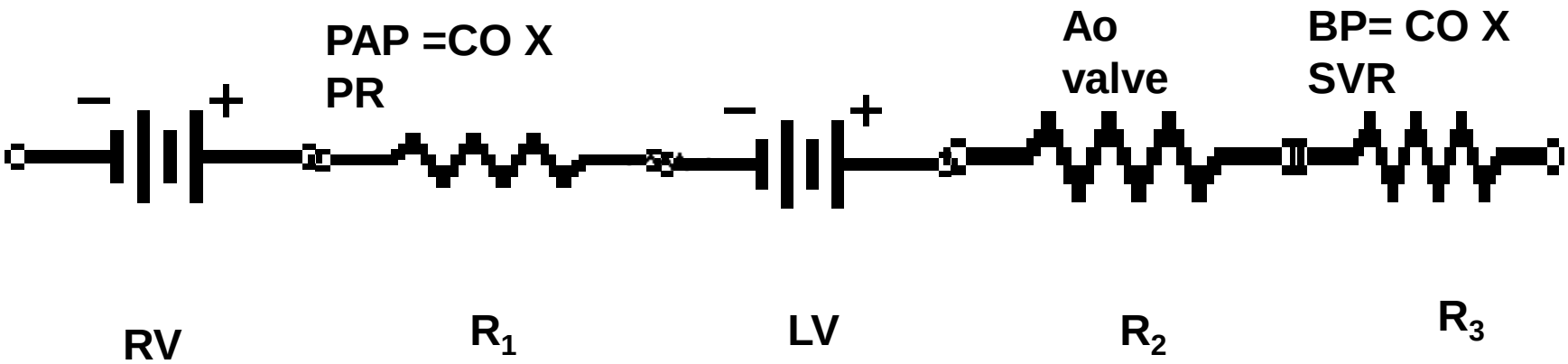
- Velocity increases as blood passes through the stenosis
- Pressure Gradient = $4V^2$

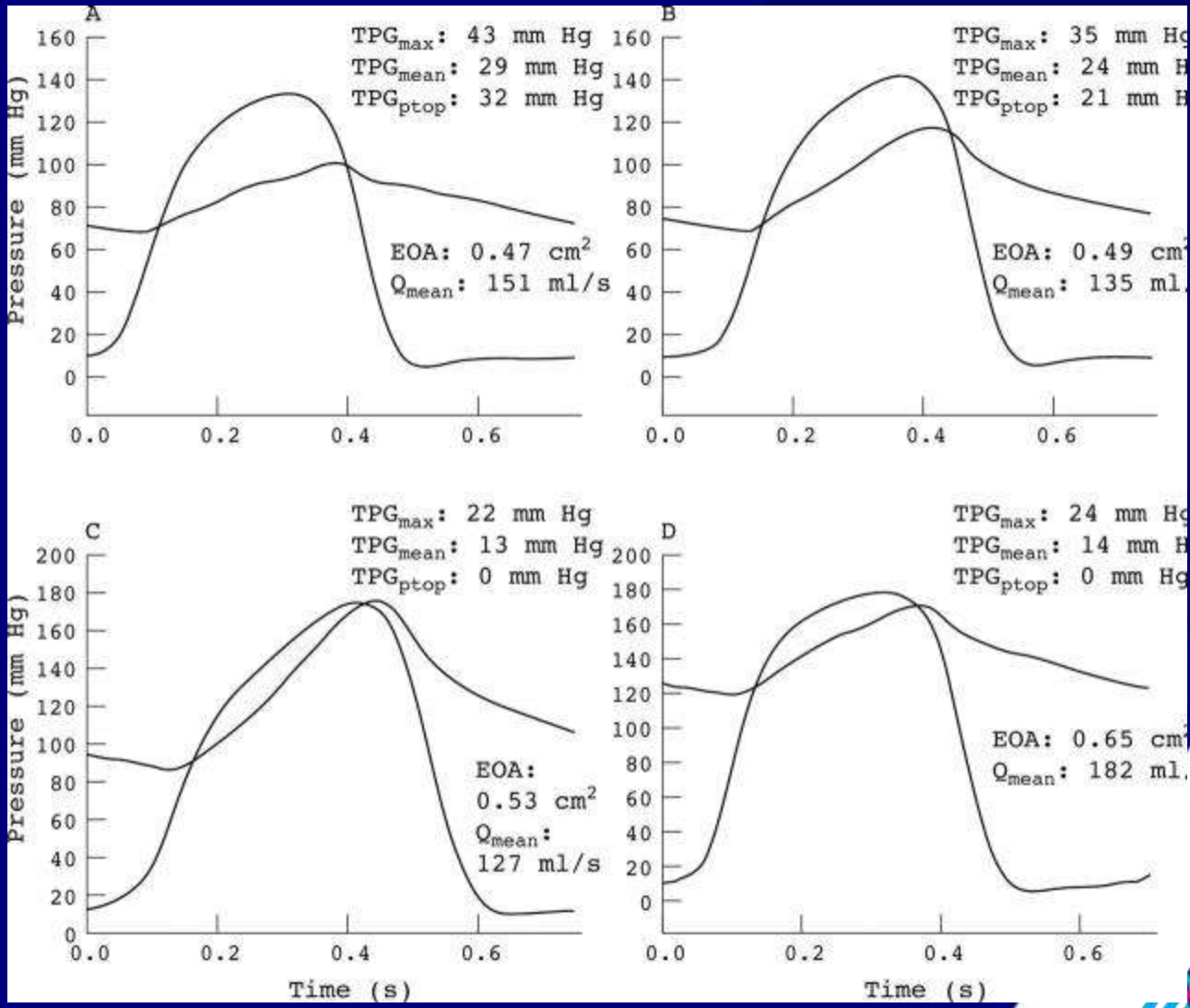




Mount Sinai Beth Israel


Latent Period
Increasing obstruction,
myocardial overload
Symptoms
Average Age Death
Survival (percent)
100
80
60
40
20
0
40
50
60
70
80
Age (years)


PAP =CO X
PR
Ao
valve
BP= CO X
SVR
RV
R1
LV
R2
R3



KADEM et al HEART;2005, 91:374

Mount Sinai Beth Israel

TAKING CARE OF THE LOW GRADIENT LOW FLOW SEVERE AS PATIENT

- 1. THE DEFINITION OF SEVERE IS SHAKY
- 2. THE RESPONSE OF THE LV IS MANIFOLD
- 3. IT'S NOT SURPRISING THAT ONE SIZE DOESN'T FIT ALL

Mount Sinai Beth Israel

72 Y/O MAN

- DYSPNEA WALKING 50 ft. TO GET THE NEWSPAPER IN THE MORNING
- 3 PILLOW ORTHOPNEA
- WITHOUT SYNCOPE OR ANGINA

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PE

- BP 110/80 P84
- EST CVP: 10 cm H_2O
- BILAT BASILAR RALES
- 2/6 MID-LATE PEAKING SEM
- CAROTIDS WEAK, ? DELAYED

Mount Sinai Beth Israel

ECHO

- EF 0.22
- Pk JET vel 2.8 m/sec
- MEAN GRADIENT 22 mm Hg
- AVA 0.9 cm^2
- DIMENSIONLESS INDEX 0.27

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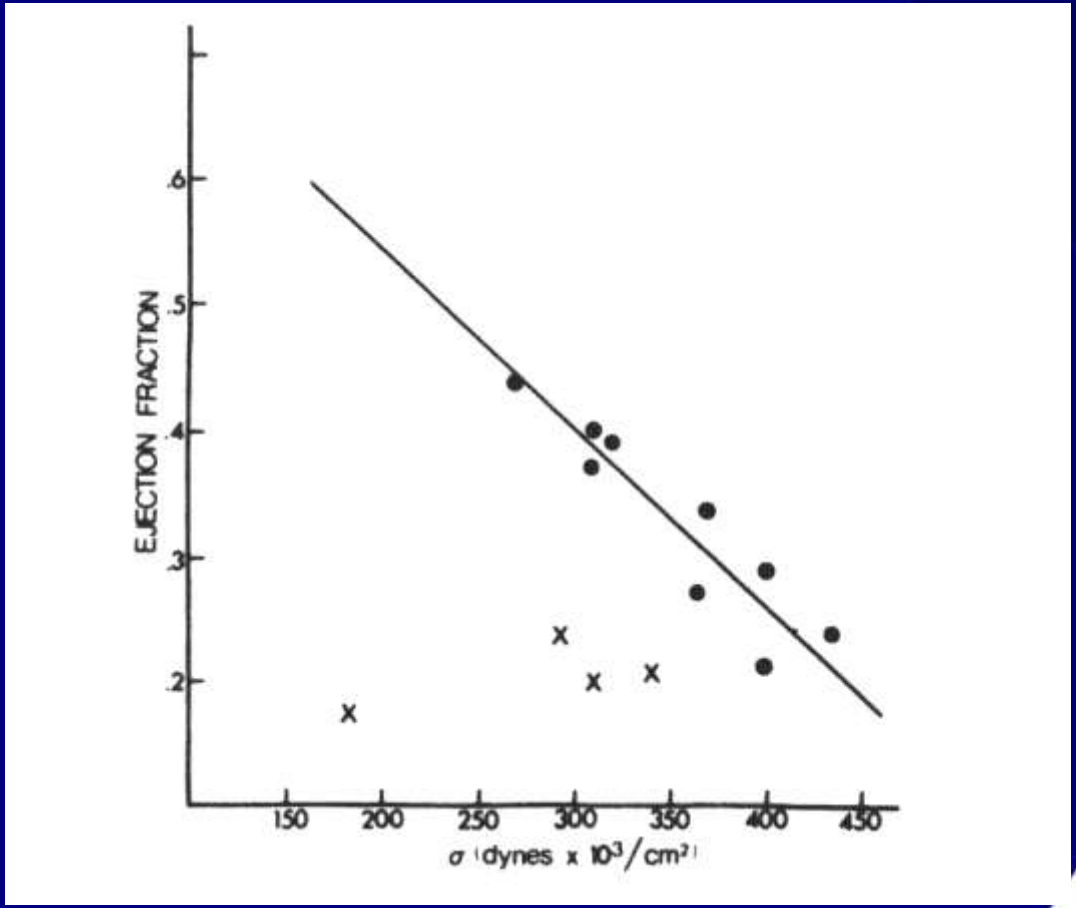
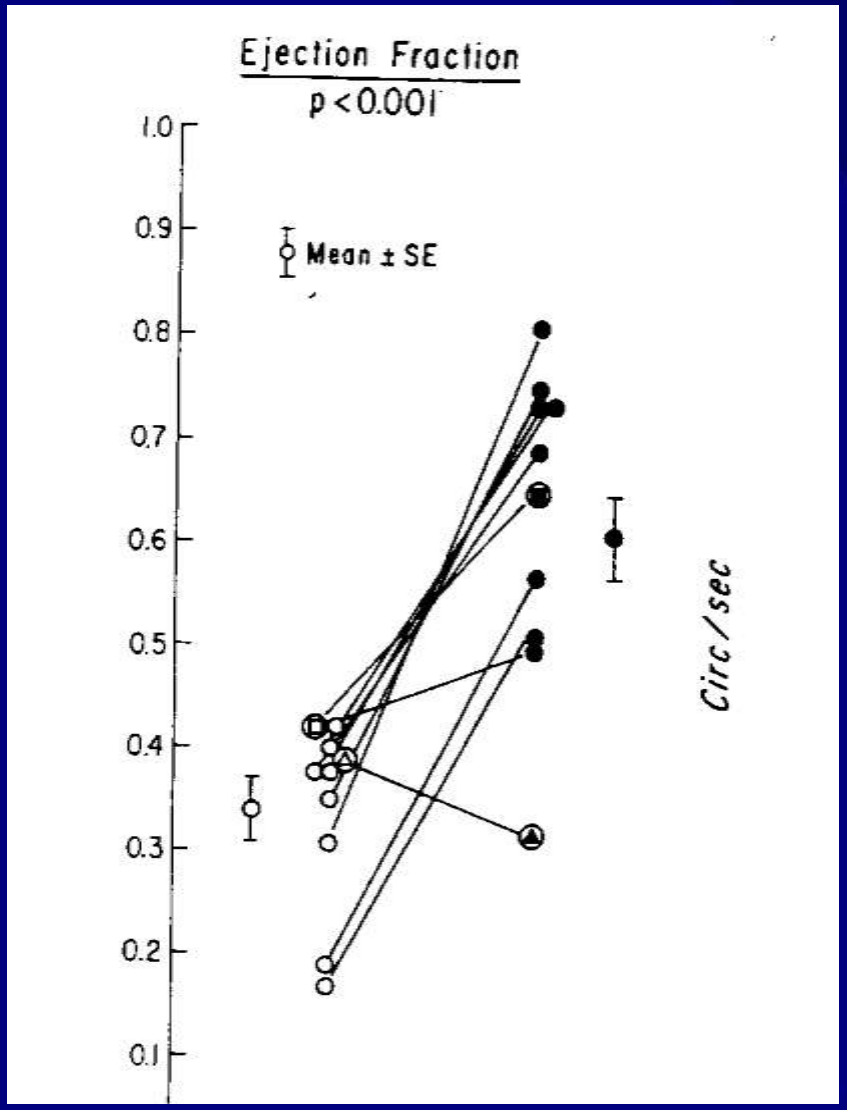


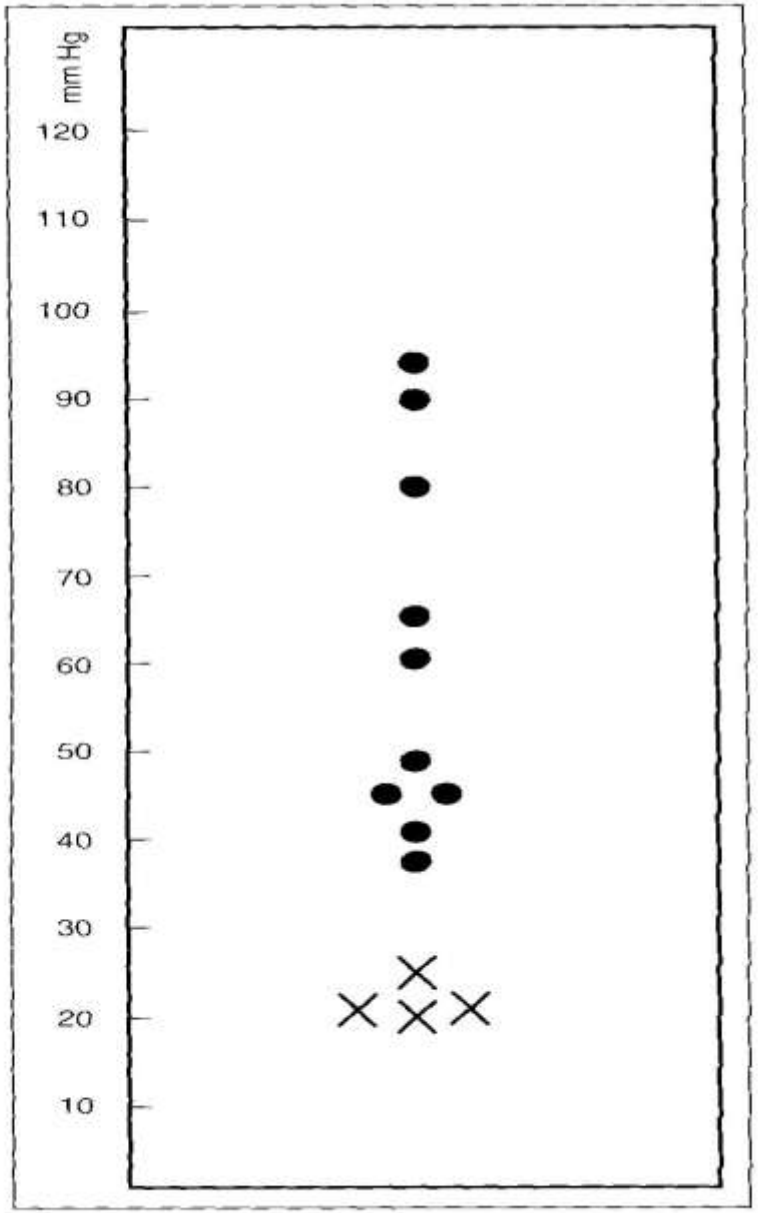
CARABELLO etl al CIRC, 1980

Mount Sinai Beth Israel

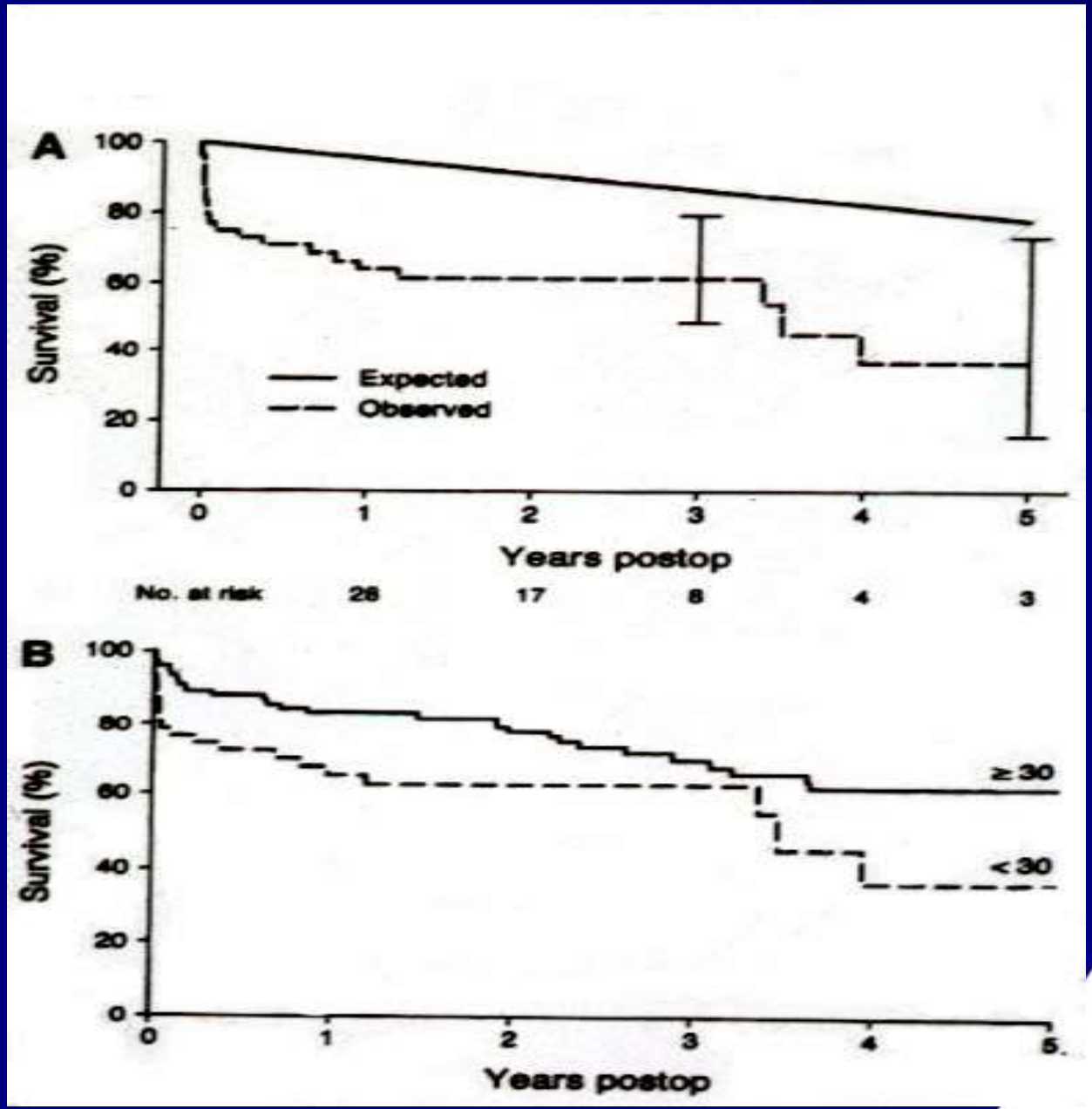


SMITH et al Circulation 1978

Mount Sinai Beth Israel

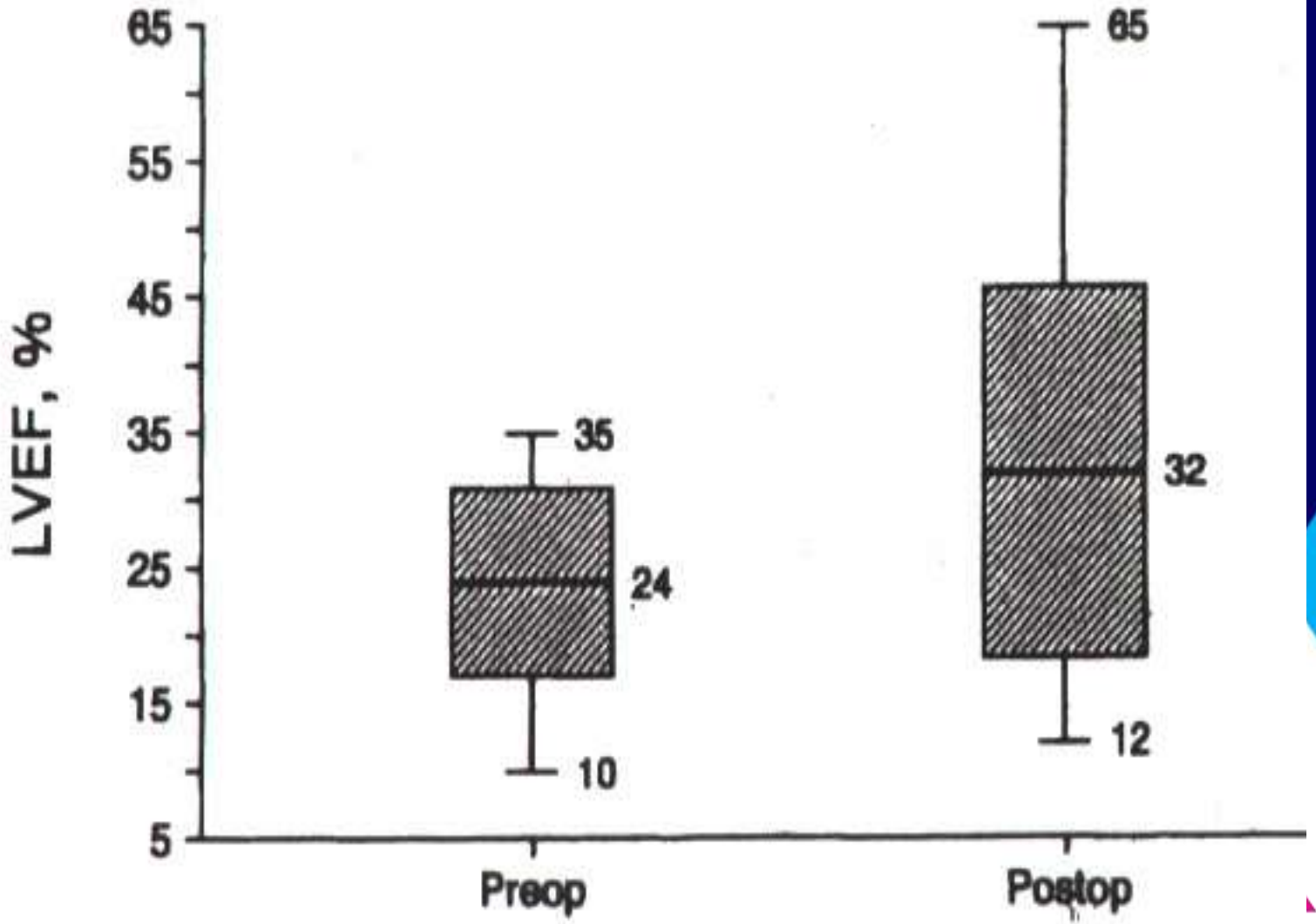


Mount Sinai Beth Israel



CONNOLLY et al CIRCULATION; 2000

Mount Sinai Beth Israel



CONNOLLY et al; CIRC 2000

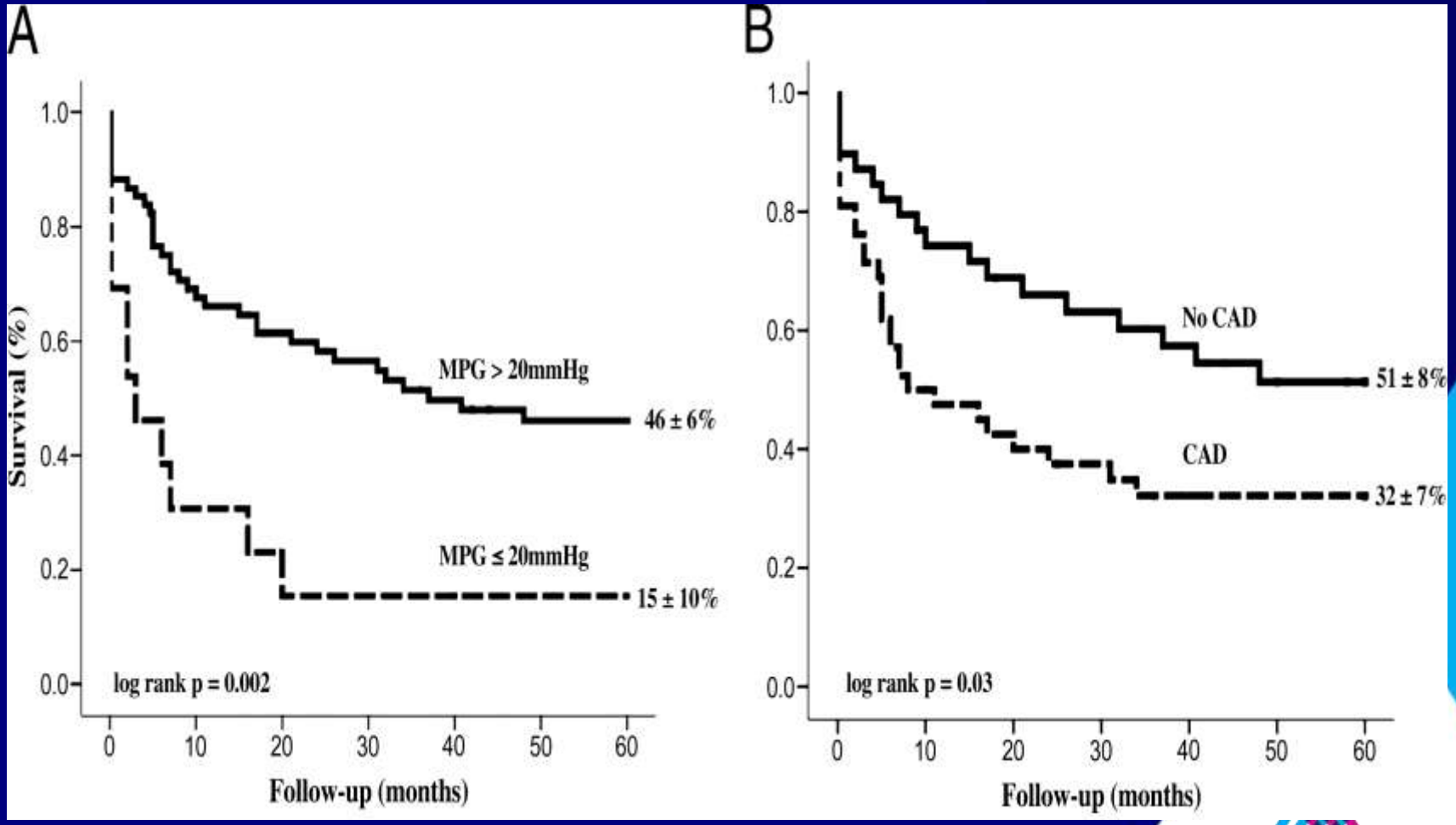
Beth Israel

- WHO’S GOING TO DIE?; WHO’S GOING TO GET BETTER?

Mount Sinai Beth Israel

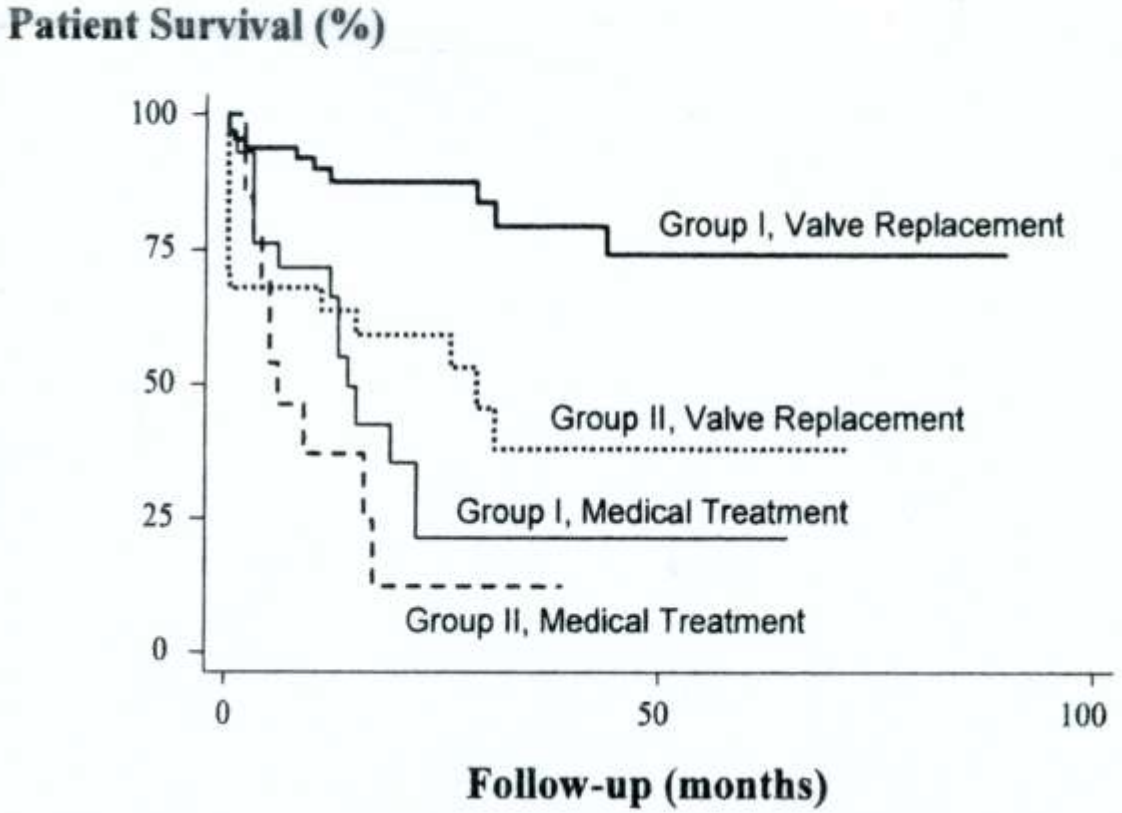
NOT VERY WORRIED ABOUT THE 35/40 PATIENT

Mount Sinai Beth Israel



TRIBOUILLOY et al JACC 2009

Mount Sinai Beth Israel



Kaplan-Meier survival estimates by group and treatment.

Monin J-L, Quere J-P, Monchi M, et al. Low-gradient aortic stenosis: operative risk stratification and predictors for long-term outcome: a multicenter study using dobutamine stress hemodynamics. Circulation 2003;108:319-324.

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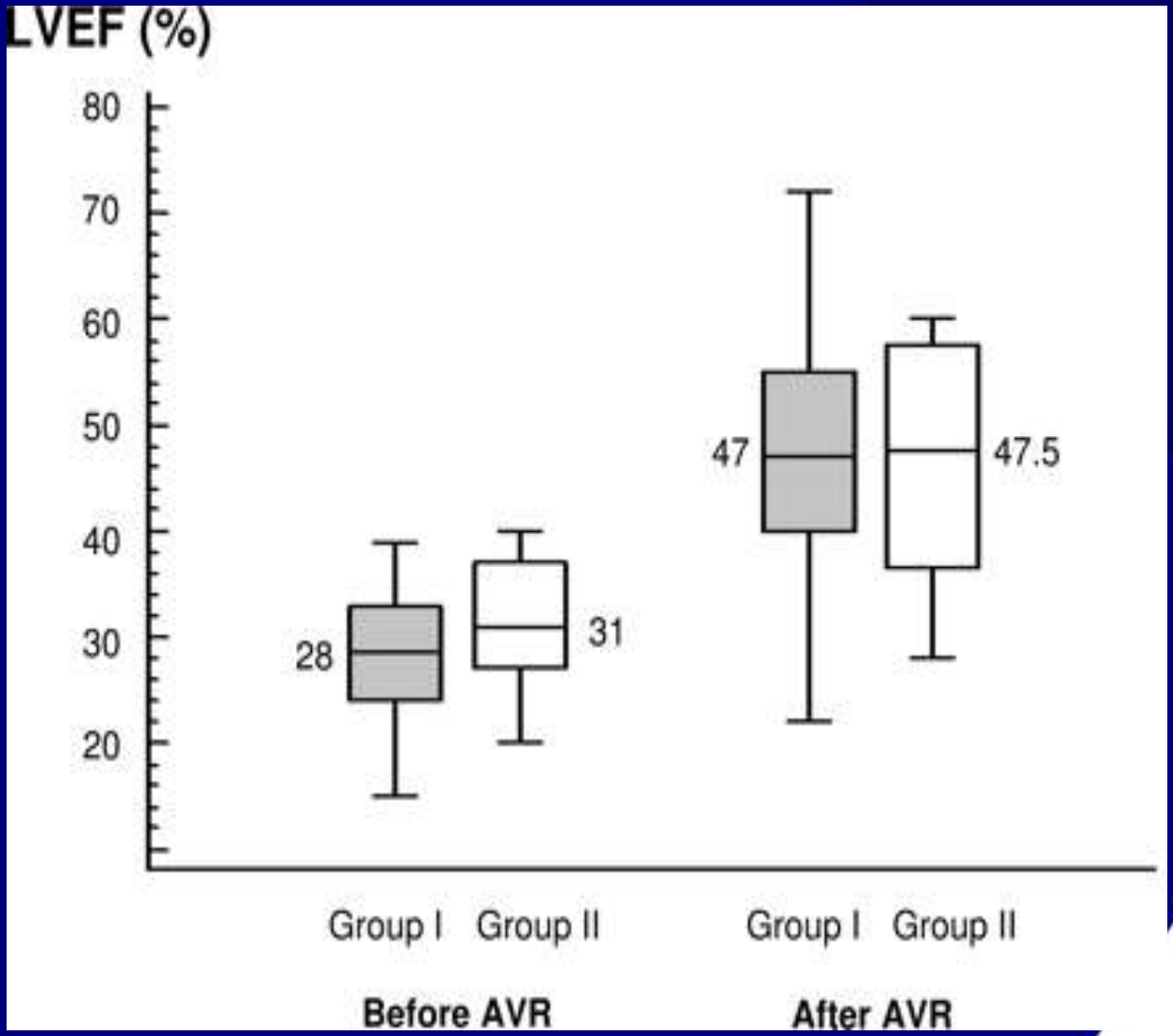

QUERE et al Circ, 2006

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72 Y/O MAN

- DYSPNEA WALKING 50 ft. TO GET THE NEWSPAPER IN THE MORNING
- 3 PILLOW ORTHOPNEA
- WITHOUT SYNCOPE OR ANGINA

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- NEGATIVE INJOTROPIC RESERVE

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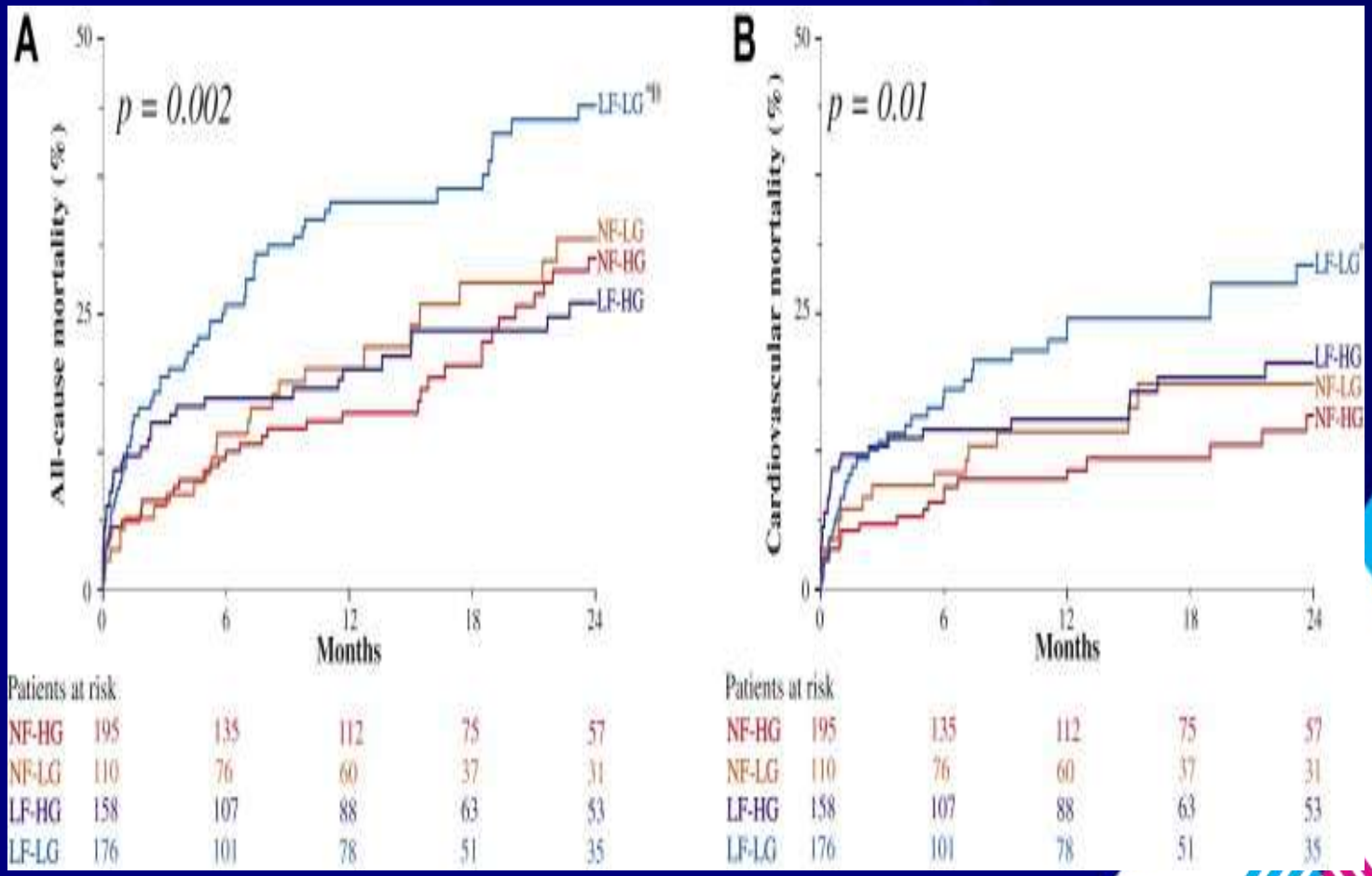

Le Ven et al JACC ‘13

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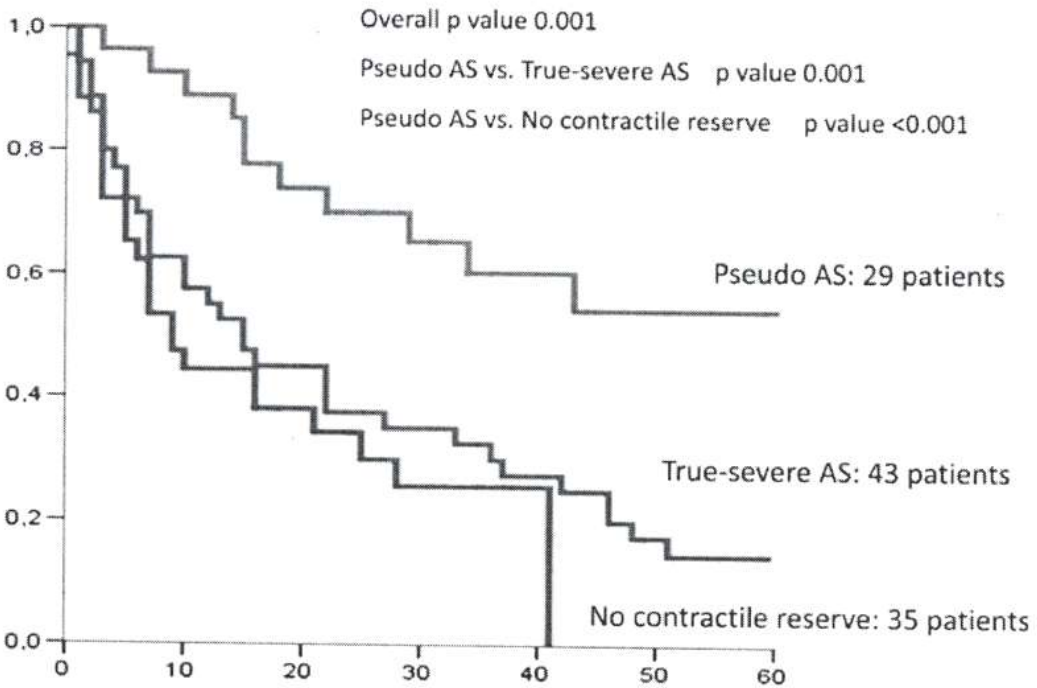
INFUSION OF SNP AT 25 mcg/min

Mount Sinai Beth Israel

	REST	SNP
MAP mmHg	68	62
CO l/min	3.5	5.0
M G mm Hg	20	19
AVA cm^2	0.8	1.2



Patients at risk							
True-severe AS	43	24	18	14	11	6	4
Pseudo AS	29	25	19	14	10	7	5
No contractile reserve	35	15	10	6	1	0	0

FOUGERES et al EUR HJ 33:2426, 2012

Mount Sinai Beth Israel

80 Y/O WOMAN

- CLASS III Sx OF DYSPNEA
- 3/6 SEM; DELAYED CAROTIDS
- ABSENT A_2

Mount Sinai Beth Israel

ECHO

- 1.7 cm LV WALL
- EF 0.62
- MEAN GRADIENT 24 mm Hg
- AVA 0.8 cm^2

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NORMAL EF BUT NOT NORMAL SYSTOLIC FUNCTION

Mount Sinai Beth Israel

- **NORMAL SARCOMERE SHORTENING IS 0.10-0.12%**
- **NORMAL EF IS 0.60**

Mount Sinai Beth Israel

Mount
Sinai
Beth Israel

- SUBNORMAL SARCOMERE SHORTENING CAN STILL YIELD A NORMAL EF

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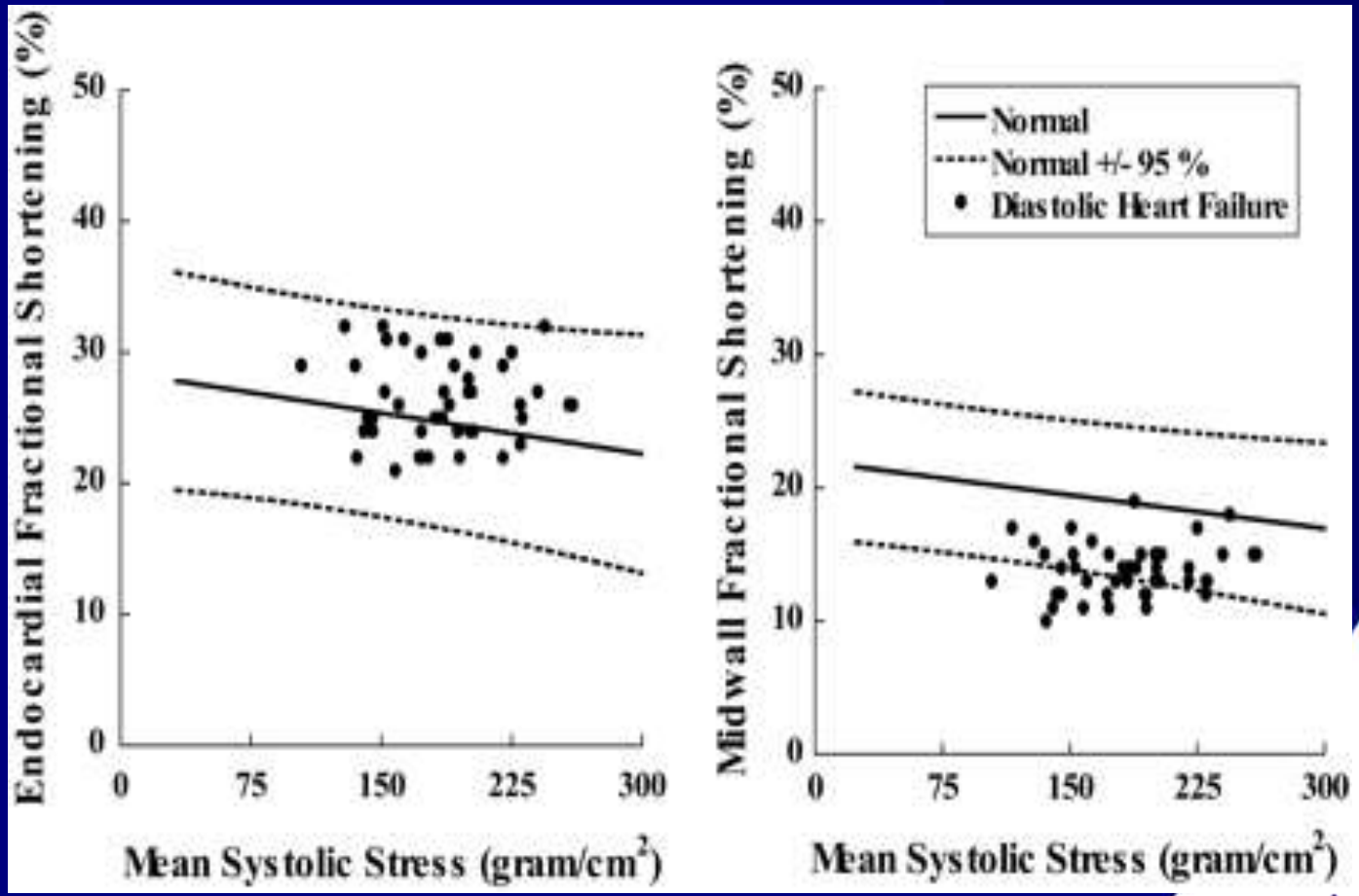

BAICU, ZILE et al CIRC: 2005

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SEVERE LOW GRADIENT NL EF AS

TALK ABOUT APPLES AND FREIGHT TRAINS

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STUDY MISCONSTRUCTIONS

- COMPARING SYMPTOMATIC TO ASYMPTOMATIC PATIENTS
- ADMIXING CAD AND THOSE WITH CLEAN CORONARIES
- USING AVA ALONE TO DEFINE AS

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DOES THE Pt REALLY HAVE SEVERE AS TO BEGIN WITH

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Beth Israel

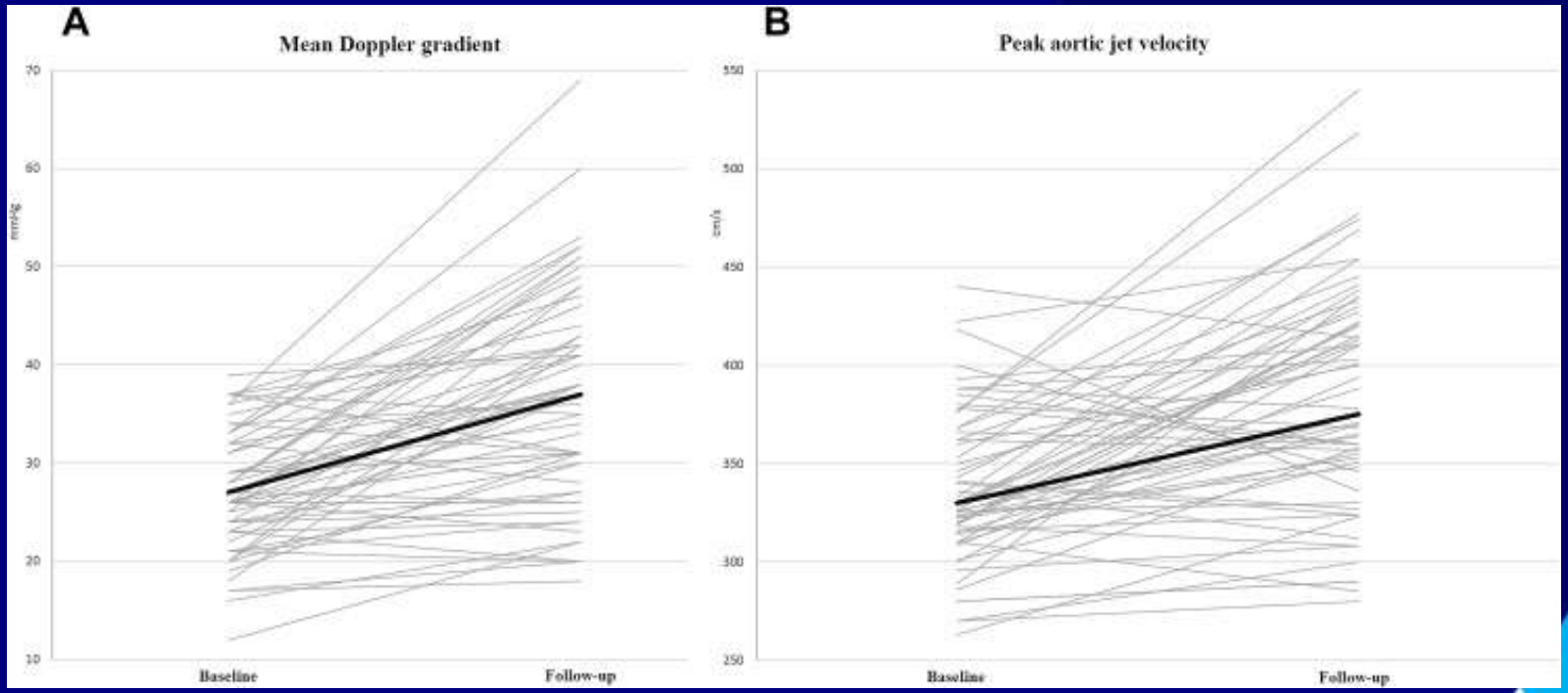

Figure 1. Individual and median changes in mean Doppler gradient (A) and peak aortic jet velocity (B) showing significant increase for both parameters compared to baseline (p <0.001). Dark solid lines represent median changes.

Christophe Tribouilloy, Dan Rusinaru, Vincent Charles, Jamila Boulif, Frédéric Maes, Franck Lévy, Agnès Pasquet, Sylvestre Maréchaux, Jean-Louis Vanoverschelde

Progression of Low-Gradient, Low-Flow, Severe Aortic Stenosis With Preserved Left Ventricular Ejection Fraction

The American Journal of Cardiology, Volume 116, Issue 4, 2015, 612–617

http://dx.doi.org/10.1016/j.amjcard.2015.05.023

Mount Sinai Beth Israel

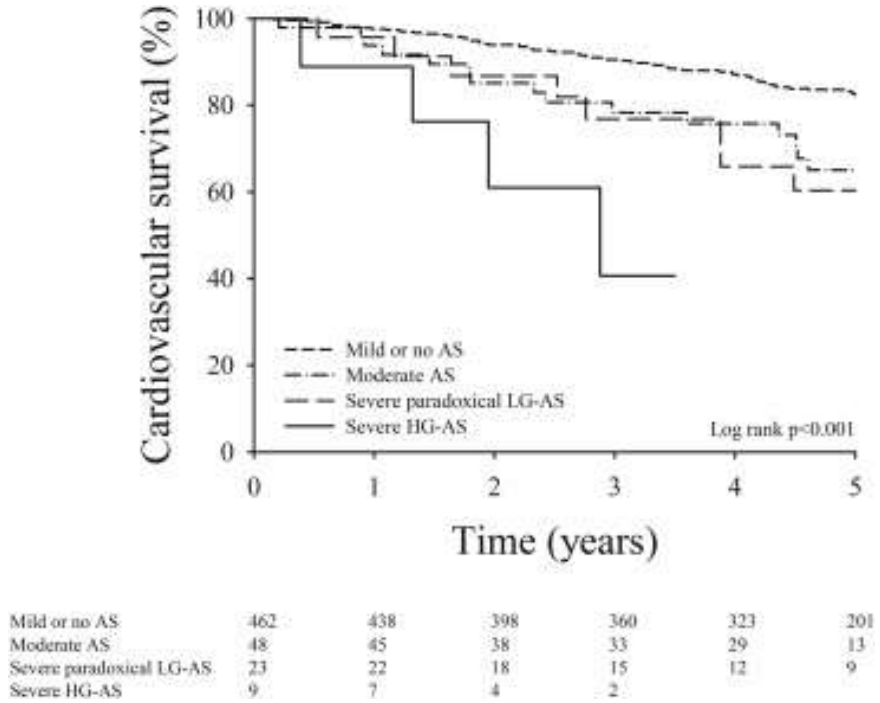

Figure 3. Kaplan-Meier survival curves comparing cardiovascular survival in patients with mild or no AS (short dashed line), moderate AS (medium dashed line), severe paradoxical LG-AS (dashed and dotted line), and severe HG-AS (solid line). Numbers at bottom i...

Nawel Rezzoug, Bert Vaes, Agnès Pasquet, Bernhard Gerber, Christophe de Meester, Gijs Van Pottelbergh, Wim Adriaensen, Catharina Matheï, Jan DeGryse, Jean-Louis Vanoverschelde

Prevalence and Prognostic Impact of Valve Area—Gradient Patterns in Patients ≥80 Years With Moderate-to-Severe Aortic Stenosis (from the Prospective BELFRAIL Study)

The American Journal of Cardiology, Volume 116, Issue 6, 2015, 925–932

http://dx.doi.org/10.1016/j.amjcard.2015.05.062

- MODERATE AS USING ONLY AVA FOR DEFINITION

- ALL AS IS NOT ALIKE

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IT'S ALL GOT TO FIT

- PHYSICAL EXAM
- AVA,JET
- VALVE MOVEMENT
- CALCIFICATION

Mount Sinai Beth Israel

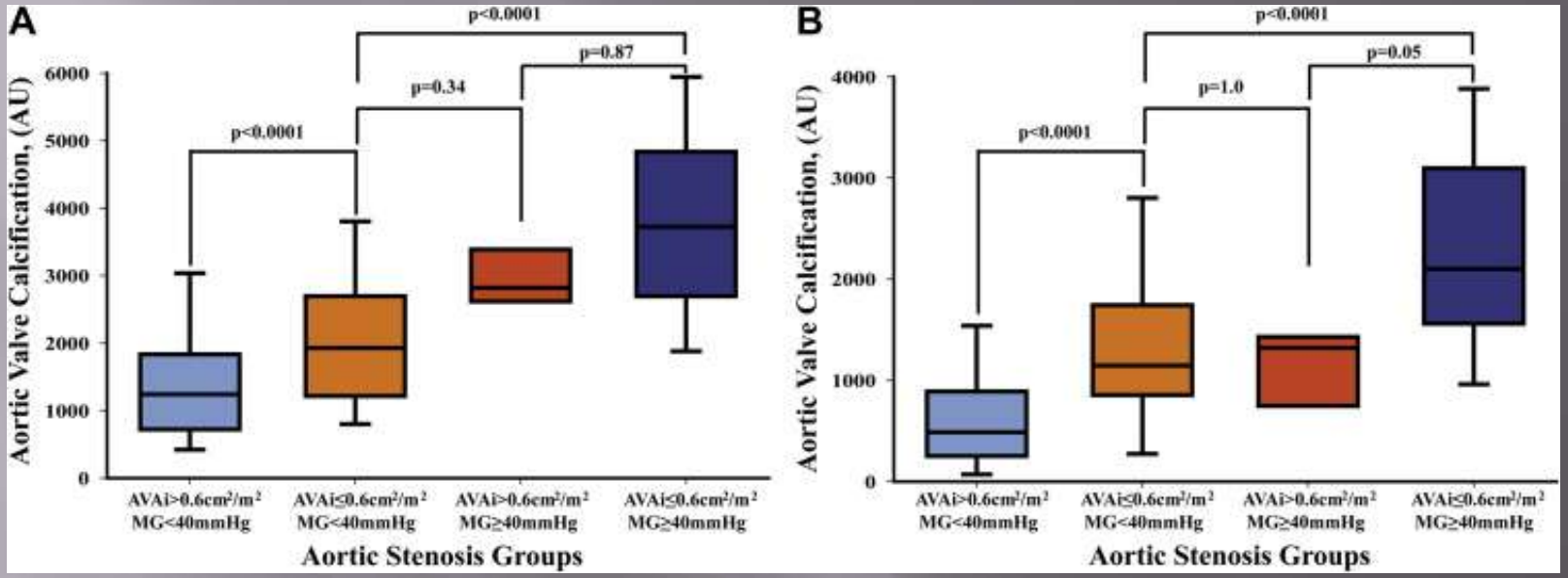


Figure 1. Distribution of Aortic Valve Calcification by Sex in the Various AS GroupsConcordant grading-moderate aortic stenosis (AS), discordant grading with low mean gradient (MG), discordant grading with high MG, and concordant grading-severe AS; x-axis in b...

Marie-Annick Clavel, David Messika-Zeitoun, Philippe Pibarot, Shivani R. Aggarwal, Joseph Malouf, Phillip A. Araoz, Hector I. Michelena, Caroline Cueff, Eric Larose, Romain Capoulade, Alec Vahanian, Maurice Enriquez-Sarano

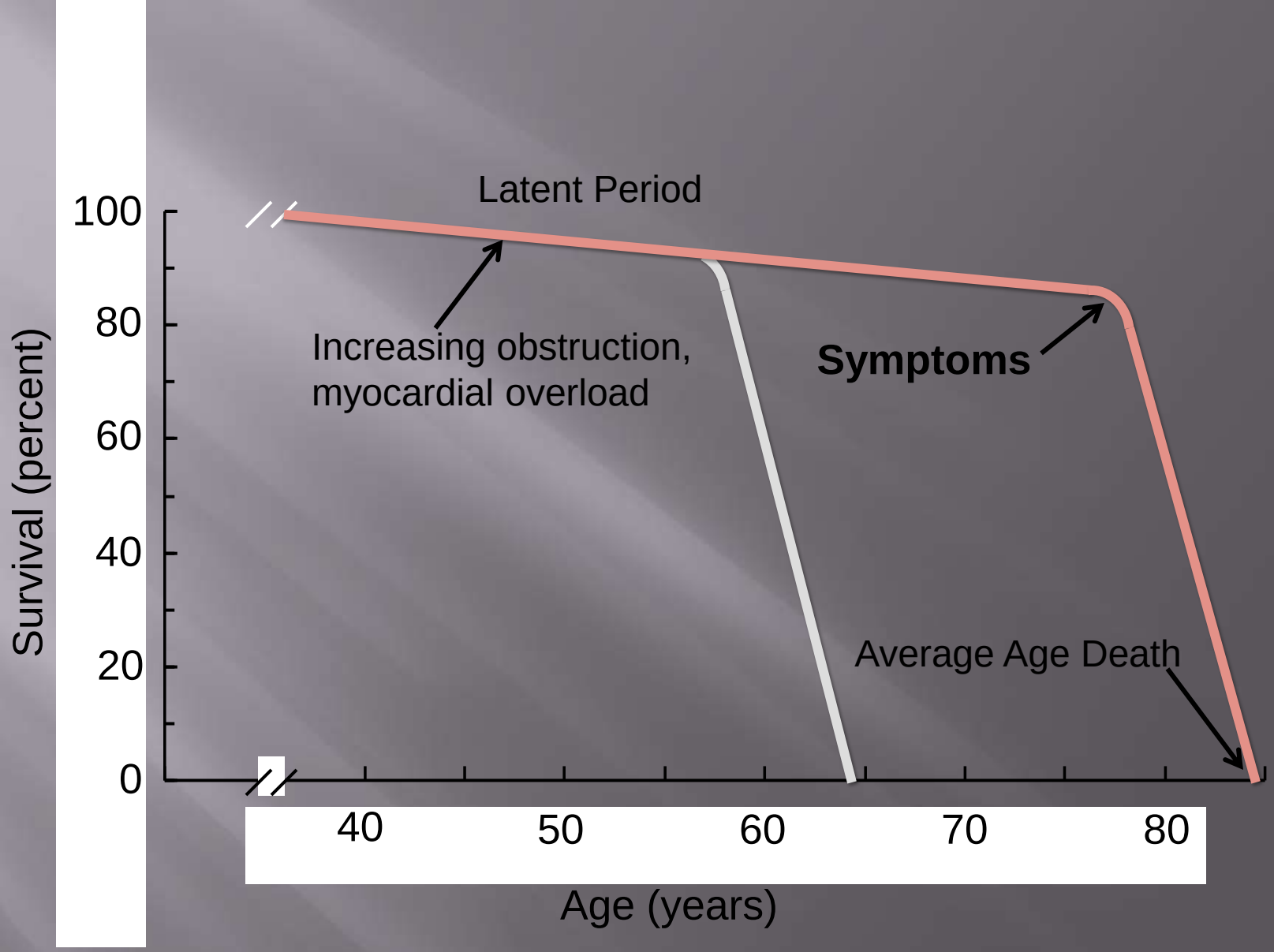
The Complex Nature of Discordant Severe Calcified Aortic Valve Disease Grading : New Insights From Combined Doppler Echocardiographic and Computed Tomographic Study

Journal of the American College of Cardiology, Volume 62, Issue 24, 2013, 2329–2338

http://dx.doi.org/10.1016/j.jacc.2013.08.1621

- YOU CAN NEVER COMPARE ASYMPTOMATIC PATIENTS TO SYMPTOMATIC PATIENTS NO MATTER WHAT THE AVA

Mount Sinai Beth Israel


Latent Period
Increasing obstruction,
myocardial overload
Symptoms
Average Age Death
Survival (percent)
100
80
60
40
20
0
40
50
60
70
80
Age (years)

LOW FLOW, LOW GRADIENT SEVERE AS IS REAL

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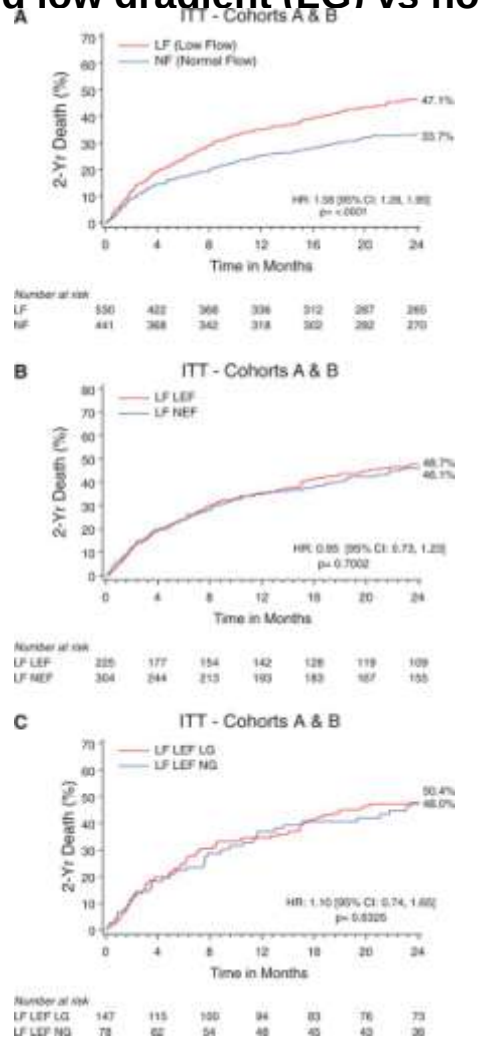
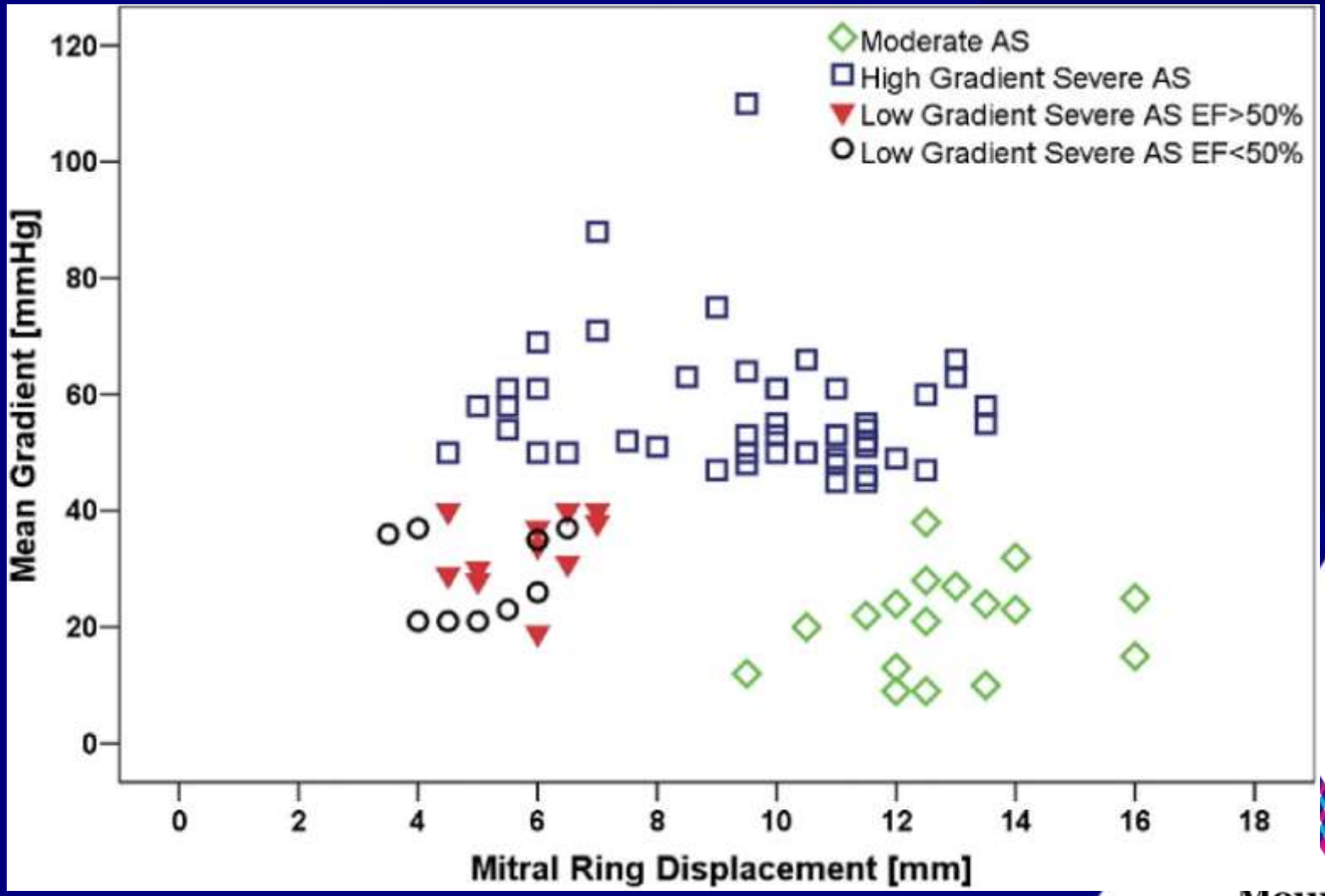
Beth Israel

Kaplan–Meier all-cause mortality analysis to 2 years is shown for patients with low flow (LF) vs normal flow (NF; A), LF with low ejection fraction (LEF) vs normal ejection fraction (NEF; B), and LF with LEF and low gradient (LG) vs normal gradient (NG; C).



Herrmann H C et al. *Circulation*. 2013;127:2316-2326



HERRMANN et al JACC , 58:402, 2011

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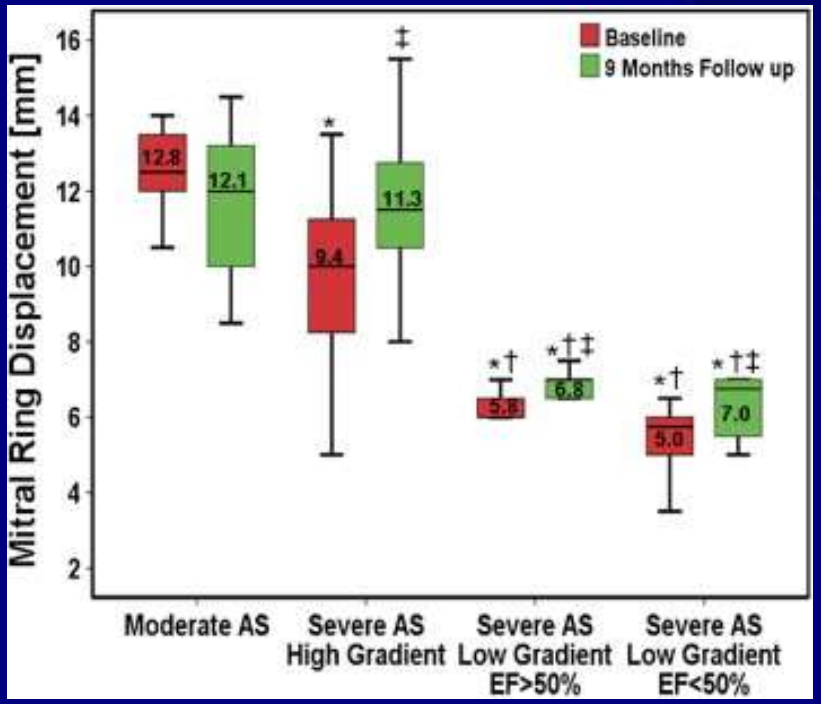

Figure 4. Baseline and 9-Month Follow-Up of Mitral Ring Displacement Data According to the 4 Groups StudiedPatients with moderate AS showed higher values both at baseline and follow-up compared with patients with low-gradient AS, irrespective of ejection fract...

Sebastian Herrmann, Stefan Störk, Markus Niemann, Volkmar Lange, Jörg M. Strotmann, Stefan Frantz, Meinrad Beer, Stefan Gattenlöhner, Wolfram Voelker, Georg Ertl, Frank Weidemann

<img height="20" border="0" style="vertical-align:bottom" width="39" alt="CME article" title="CME article" src="http://eresources.library.mssm.edu:3160/content/image/1-s2.0-S073510971101566X-cme_o.gif">Low-Gradient Aortic Valve Stenosis : Myocardial Fibrosis and Its Influence on Function and Outcome

Journal of the American College of Cardiology, Volume 58, Issue 4, 2011, 402–412

http://dx.doi.org/10.1016/j.jacc.2011.02.059

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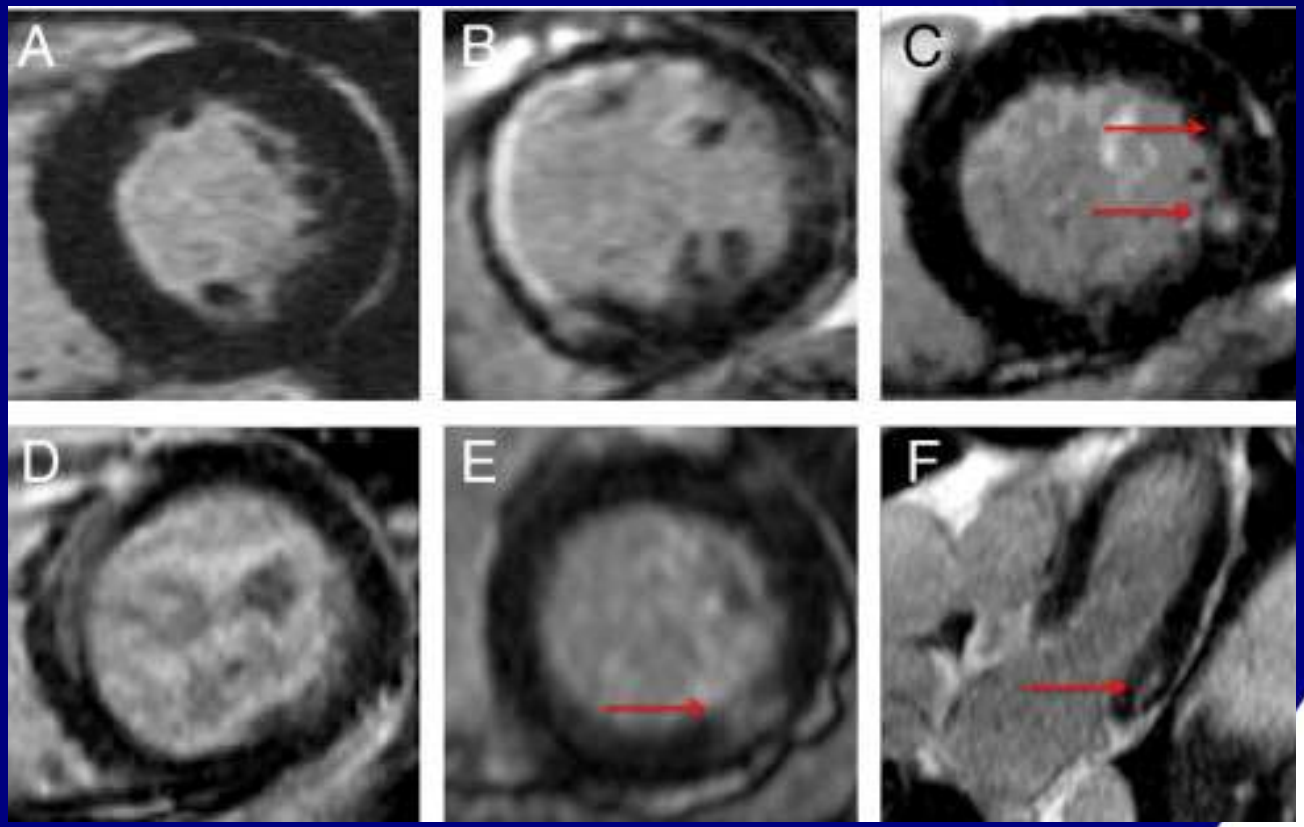


Dweck et al JACC 2011

Mount Sinai Beth Israel

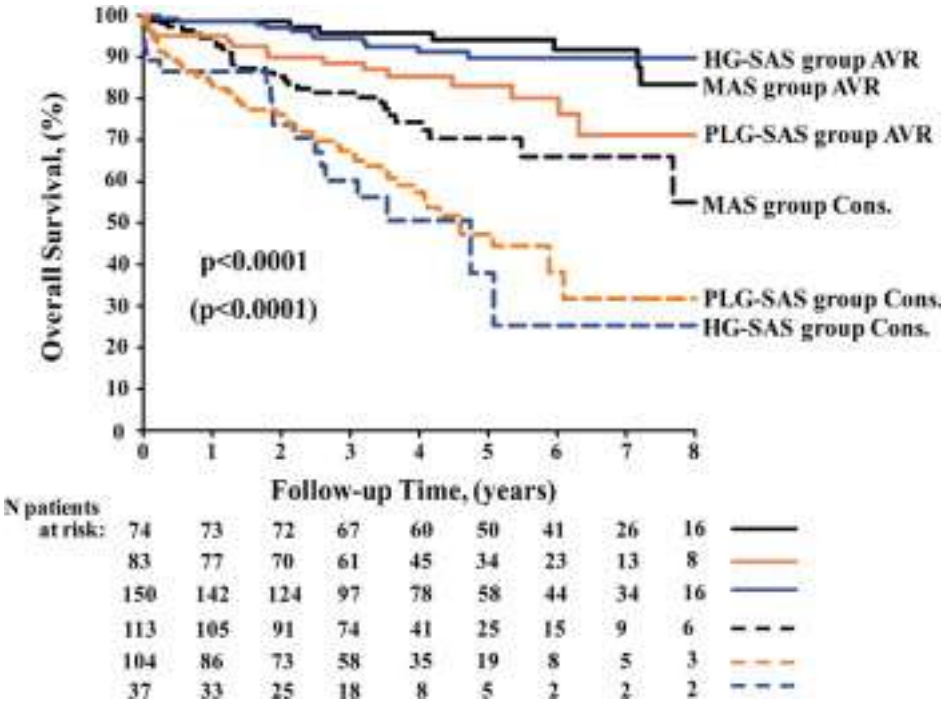


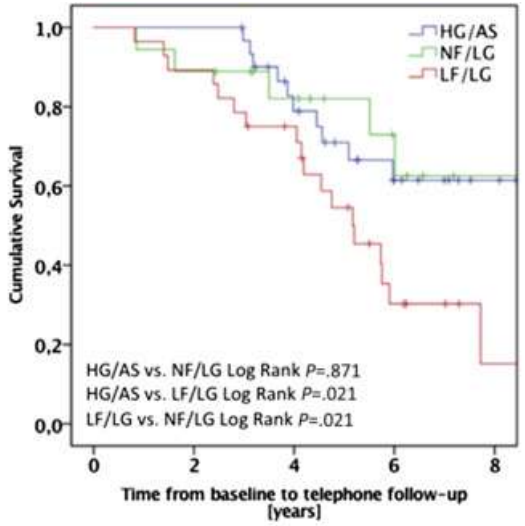
Figure 3 Kaplan-Meier Curves of Overall Survival According the Group of Patients and Type of Treatment Kaplan-Meier curves of overall survival according the group of patients and type of treatment: AVR versus Conservative (Cons). Abbreviations a...

Marie-Annick Clavel , Jean G. Dumesnil , Romain Capoulade , Patrick Mathieu , Mario S?n?chal , Philippe Pibarot

Outcome of Patients With Aortic Stenosis, Small Valve Area, and Low-Flow, Low-Gradient Despite Preserved Left Ventricular Ejection Fraction

Journal of the American College of Cardiology Volume 60, Issue 14 2012 1259 - 1267

http://dx.doi.org/10.1016/j.jacc.2011.12.054



# at risk	0 y	2 y	4 y	6 y	8 y
HG/AS	31	29	21	10	4
NF/LG	18	16	12	7	3
LF/LG	28	25	19	6	1

Figure 6. Kaplan-Meier survival plot for overall survival of the three different groups. Note the worst survival in AS patients with LF/LG physiology.

Sebastian Herrmann, Bastian Fries, Dan Liu, Kai Hu, Stefan Stoerk, Wolfram Voelker, Catharina Ruppert, Kristina Lorenz, Georg Ertl, Frank Weidemann

Differences in Natural History of Low- and High-Gradient Aortic Stenosis from Nonsevere to Severe Stage of the Disease

Journal of the American Society of Echocardiography, 2015, Available online 28 August 2015

http://dx.doi.org/10.1016/j.echo.2015.07.016

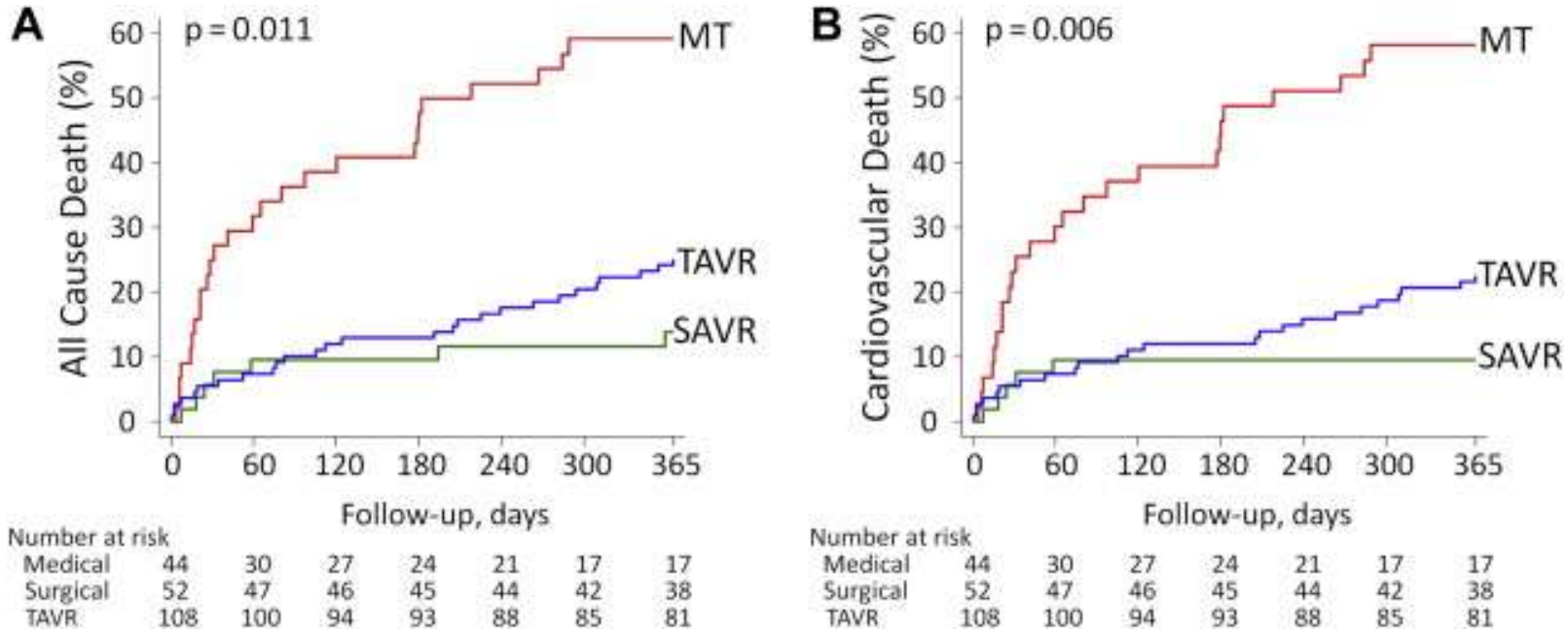


Figure 2. Kaplan-Meier Curves for Clinical Outcomes According to Assigned Treatment ModalityKaplan-Meier analysis of death (A) and cardiovascular death (B) at 1 year according to the assigned treatment modality. Abbreviations as in Figure 1.

Crochan J. O'Sullivan, Lars Englberger, Nicola Hosek, Dik Heg, Davide Cao, Giulio G. Stefanini, Stefan Stortecky, Steffen Gloekler, Ernest Spitzer, David Tüller, Christoph Huber, Thomas Pilgrim, Fabien Praz, Lutz Buellesfeld, Ahmed A. Khattab, Thierry Carrel, Bernhard Meier, Stephan Windecker, Peter Wenaweser

Clinical Outcomes and Revascularization Strategies in Patients With Low-Flow, Low-Gradient Severe Aortic Valve Stenosis According to the Assigned Treatment Modality

JACC: Cardiovascular Interventions, Volume 8, Issue 5, 2015, 704–717

http://dx.doi.org/10.1016/j.jcin.2014.11.020

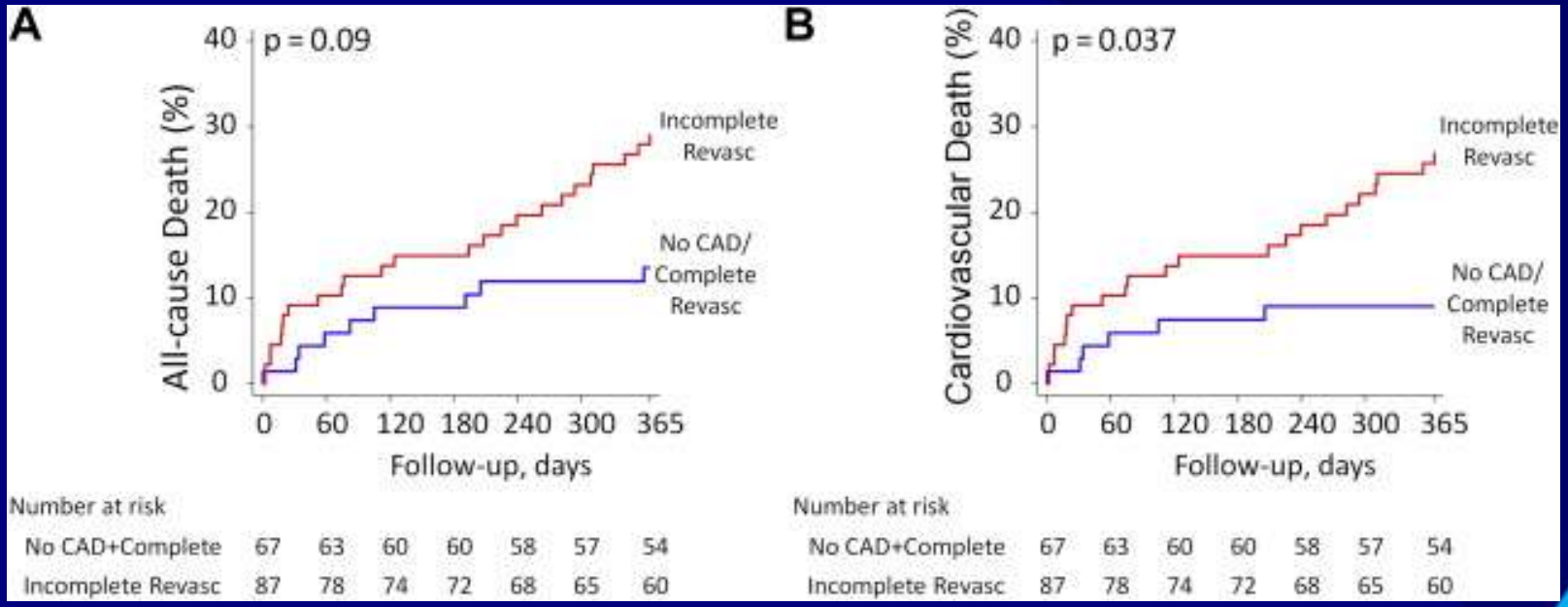


Figure 4. Kaplan-Meier Curves for Clinical Outcomes Stratified by Completeness of Revascularization Among TAVR and SAVR Patients OnlyKaplan-Meier analysis of death (A) and cardiovascular death (B) at 1 year according to the completeness of revascularization am...

Crochan J. O'Sullivan, Lars Englberger, Nicola Hosek, Dik Heg, Davide Cao, Giulio G. Stefanini, Stefan Stortecky, Steffen Gloekler, Ernest Spitzer, David Tüller, Christoph Huber, Thomas Pilgrim, Fabien Praz, Lutz Buellesfeld, Ahmed A. Khattab, Thierry Carrel, Bernhard Meier, Stephan Windecker, Peter Wenaweser

Clinical Outcomes and Revascularization Strategies in Patients With Low-Flow, Low-Gradient Severe Aortic Valve Stenosis According to the Assigned Treatment Modality

JACC: Cardiovascular Interventions, Volume 8, Issue 5, 2015, 704–717

http://dx.doi.org/10.1016/j.jcin.2014.11.020

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AND IF SYMPTOMATIC MUST BE TREATED AS SUCH

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SUMMARY

- LOW FLOW LOW GRADIENT LOW EF AORTIC STENOSIS IS THE PRODUCT OF A VERY SICK HEART, ESPECIALLY 20/20.
- INOTROPIC RESERVE IS IMPORTANT IN SURGICAL RISK STRATIFICATION BUT NOT IN PREDICTING POST- OP OUTCOME
- BAV MAY BE A USEFUL BRIDGE IN SUCH PAITENTS

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LOW FLOW NORMAL EF SEVERE AORTIC STENOSIS

- MAKE SURE THEY'VE GOT IT

- PROGNOSIS REDUCED BUT BETTER OUTCOME WITH AVR. ? TAVR

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SINGLE MOST IMPORTANT GUIDELINES

- HEART TEAM
- INTEGRATIVE APPROACH

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- IF YOU FOLLOW THESE GUIDELINES WITHOUT FAIL

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YOU'RE NOT DOING YOUR JOB

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