# VHD

## HOW FAR WE'VE COME and WHERE WE ARE GOING

# AORTIC STENOSIS

THE VALVE

ITS NATURAL HISTORY

ITS DEFINITION

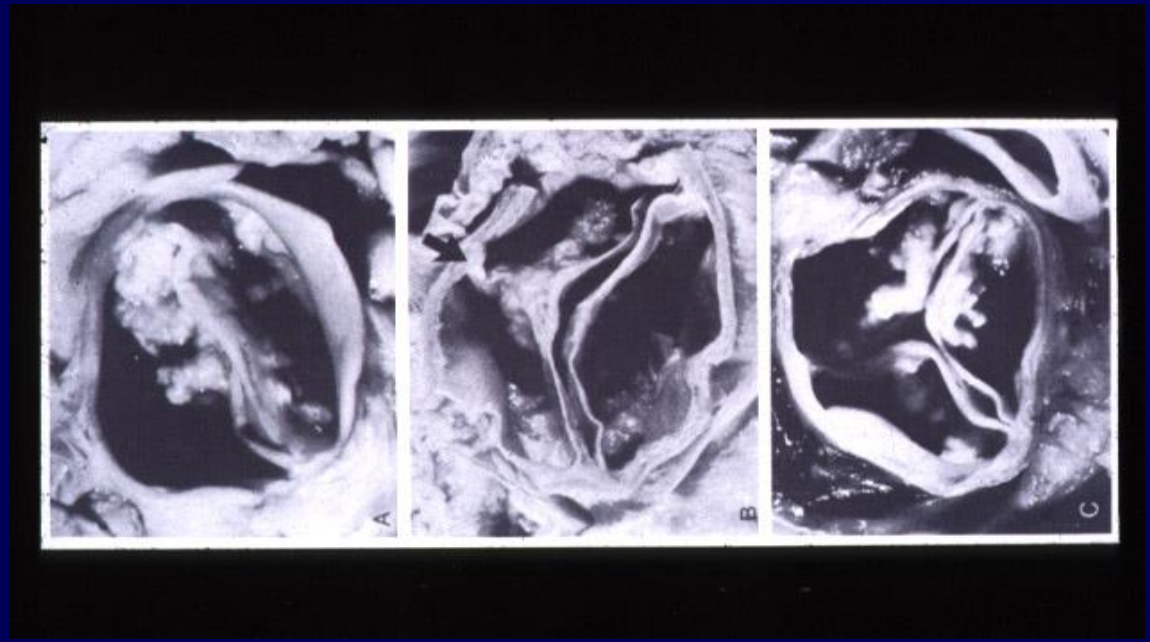
ITS EFFECTS

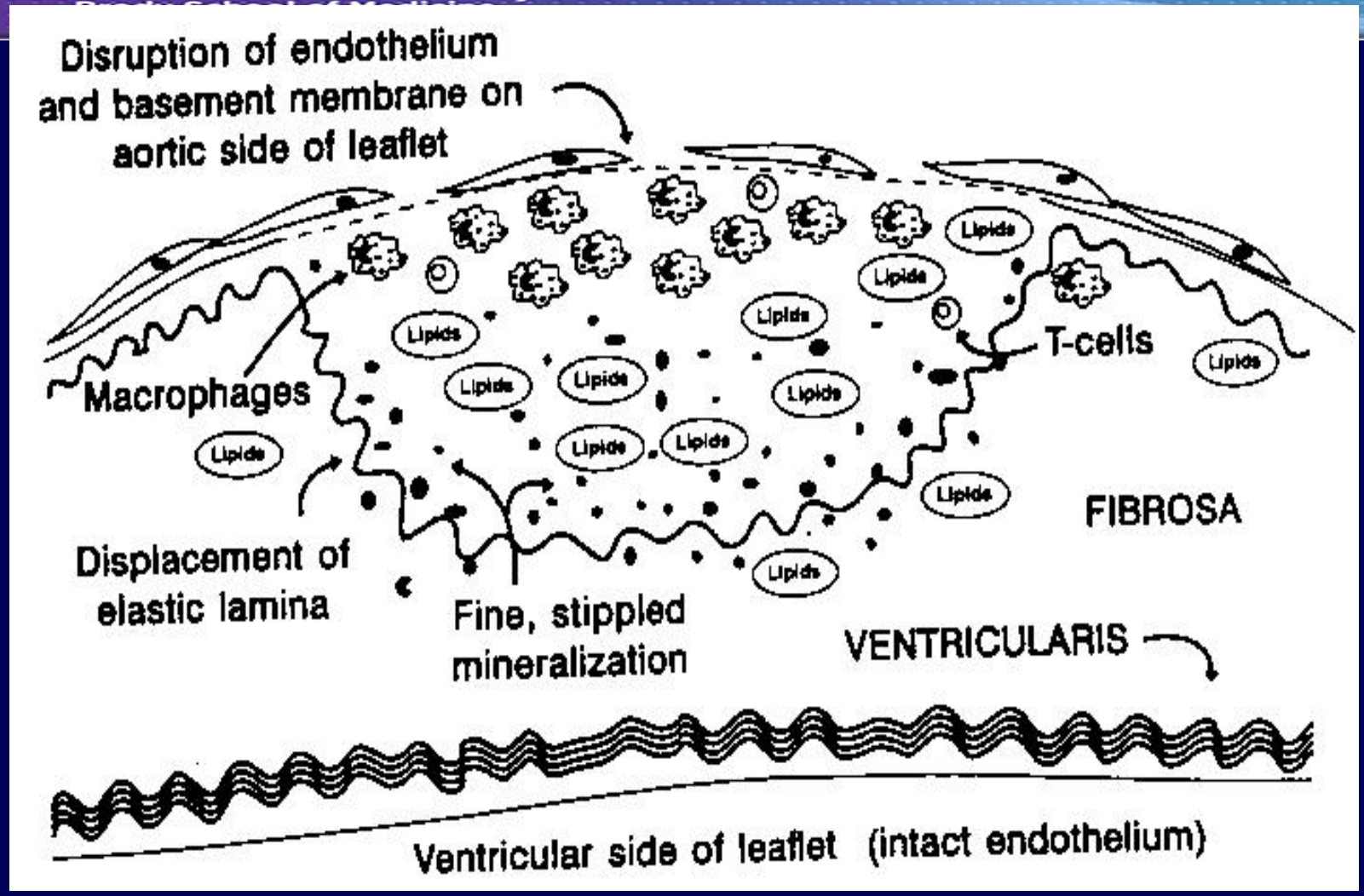
ITS THERAPY

ITS OUTCOME

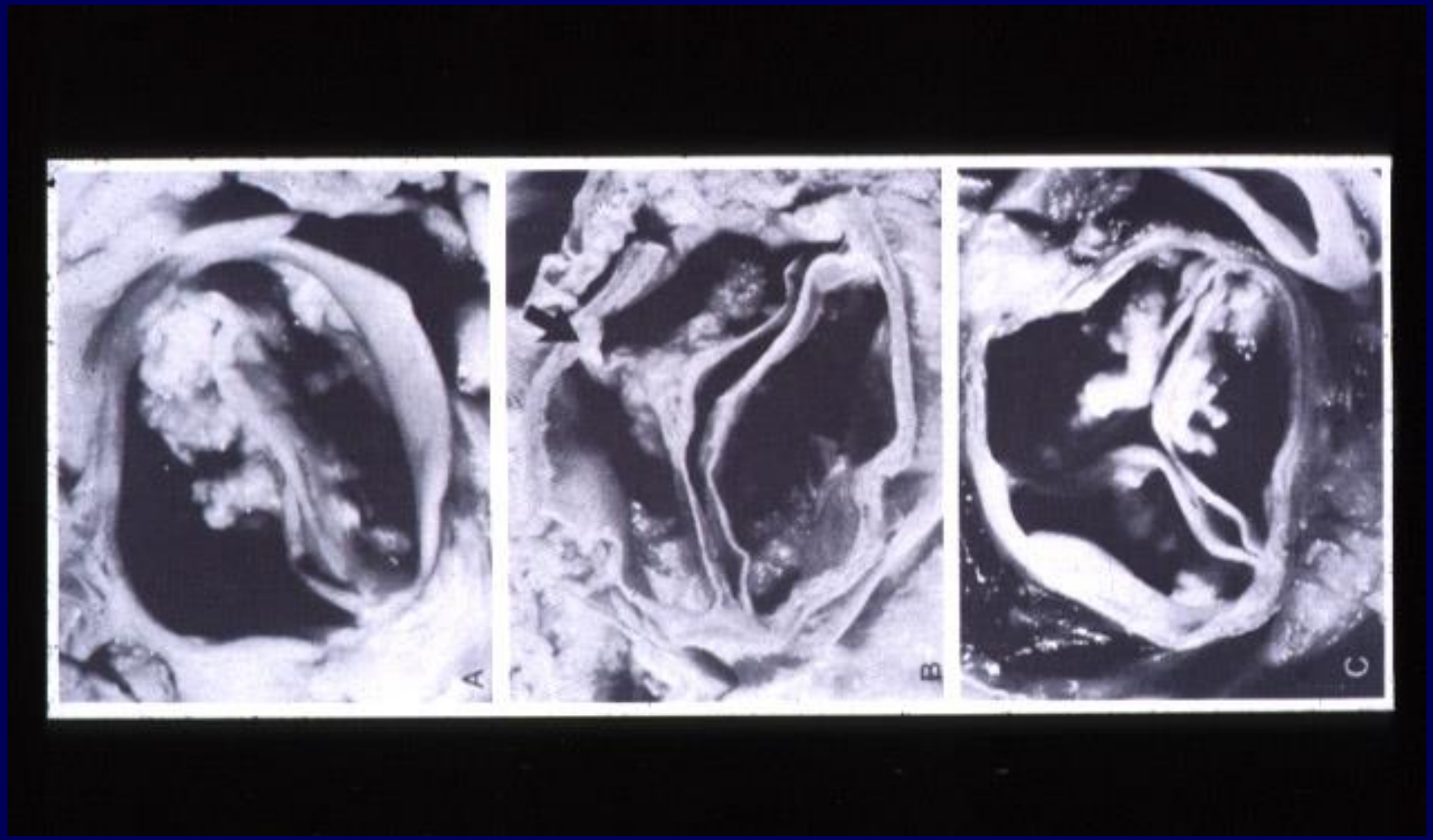
# THE VALVE

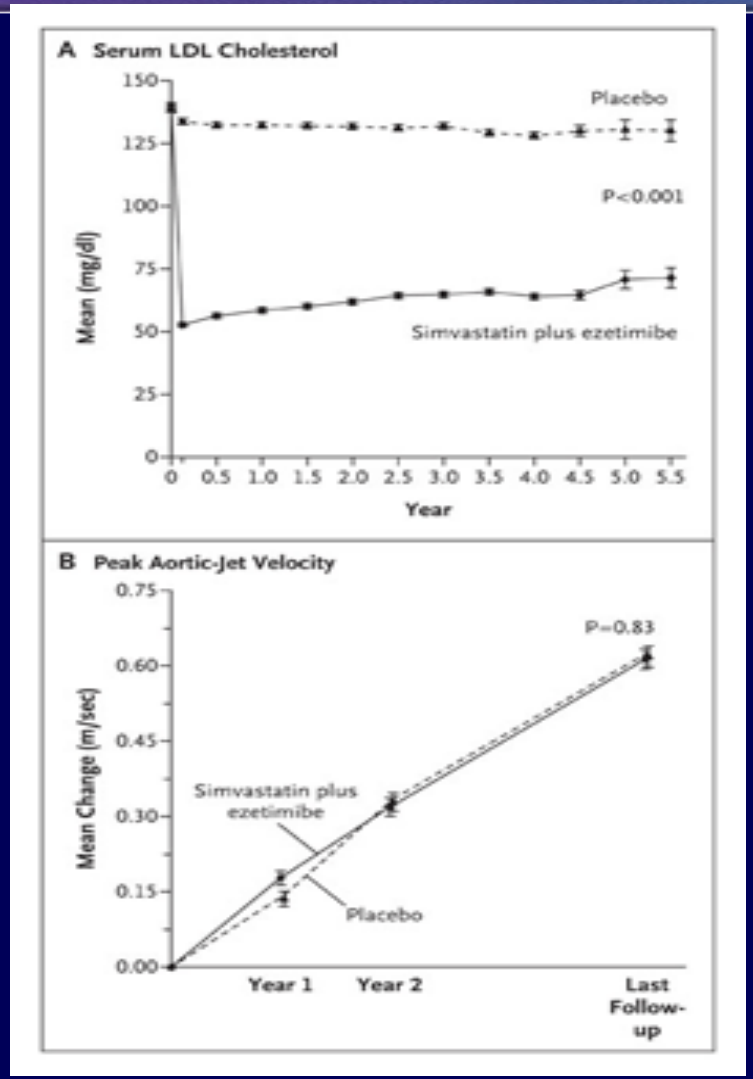
# A0RTIC STENOSIS



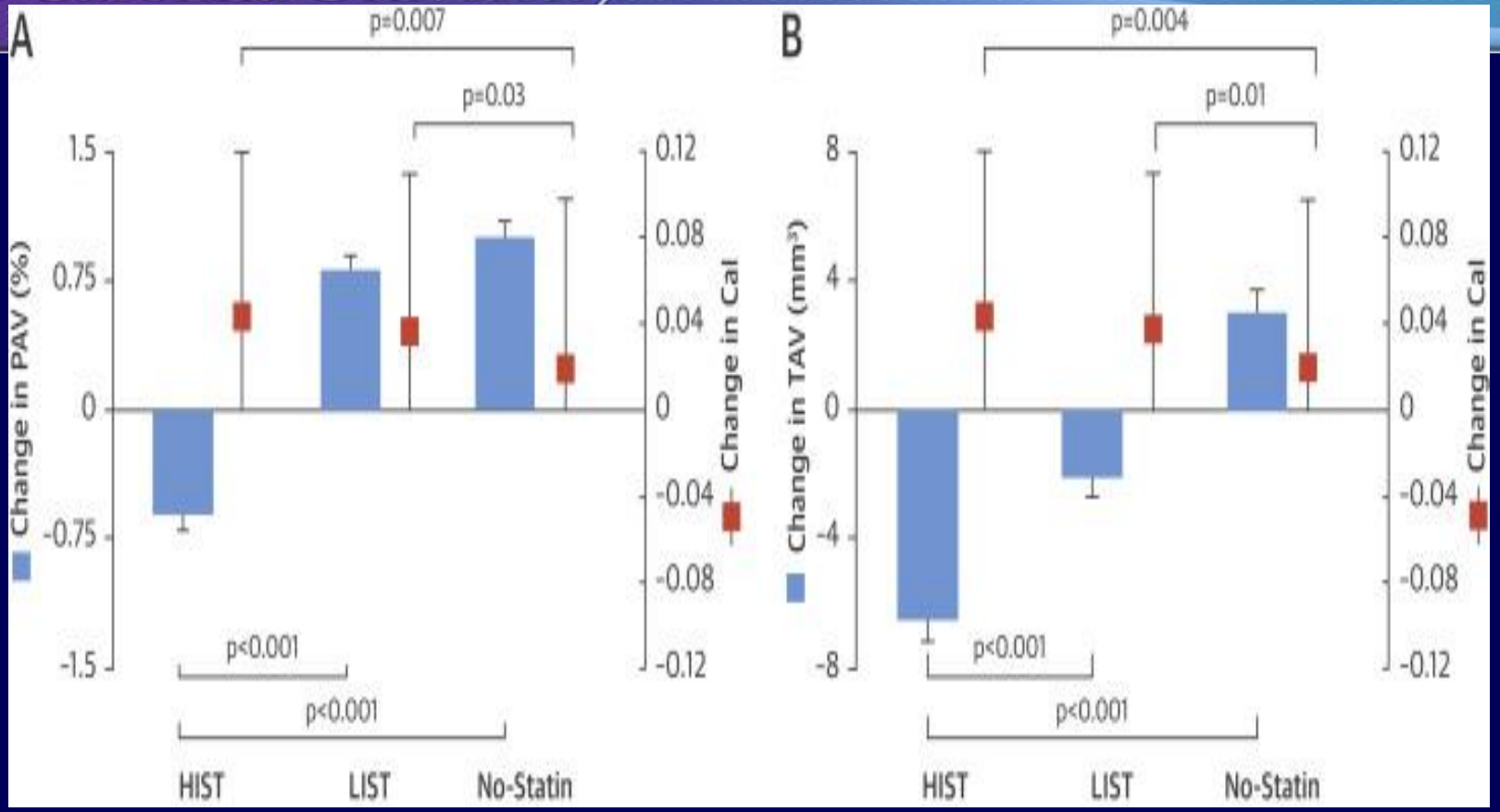



Authors: Otto CM, Kuusisto J, Reichenbach DD, et al


A
B
C




SEAS Tria NEJ 2008




Rishi Puri, Stephen J. Nicholls, Mingyuan Shao, Yu Kataoka, Kiyoko Uno, Samir R. Kapadia, E. Murat Tuzcu, Steven E. Nissen

**>Impact of Statins on Serial Coronary Calcification During Atheroma Progression and Regression**

Journal of the American College of Cardiology, Volume 65, Issue 13, 2015, 1273–1282

http://dx.doi.org/10.1016/j.jacc.2015.01.036

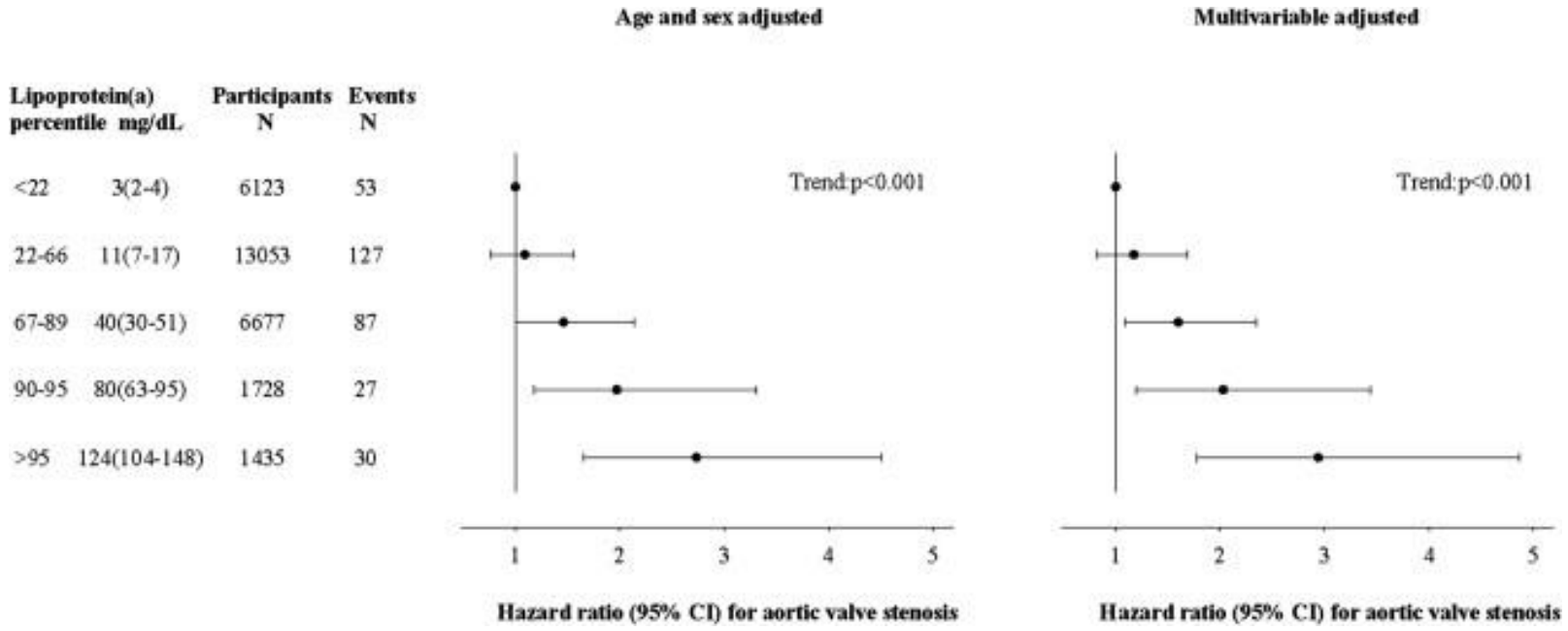



Figure 1. Risk of Aortic Valve Stenosis as Function of Elevated Lp(a) LevelsAnalyses were adjusted for (left) age and sex or (right) multivariable adjusted additionally for total cholesterol, high-density lipoprotein cholesterol, systolic blood pressure, smoki...

Pia R. Kamstrup, Anne Tybjærg-Hansen, Børge G. Nordestgaard

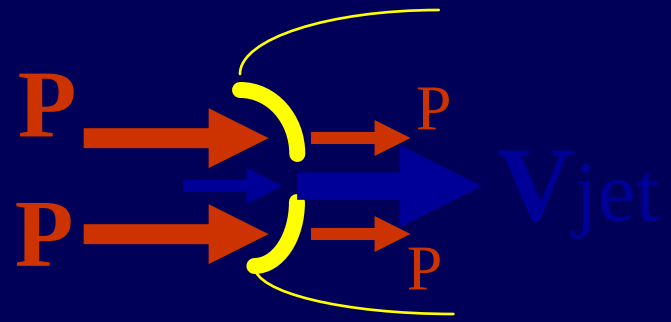
**Elevated Lipoprotein(a) and Risk of Aortic Valve Stenosis in the General Population**

Journal of the American College of Cardiology, Volume 63, Issue 5, 2014, 470–477

http://dx.doi.org/10.1016/j.jacc.2013.09.038

# NATURAL HISTORY

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



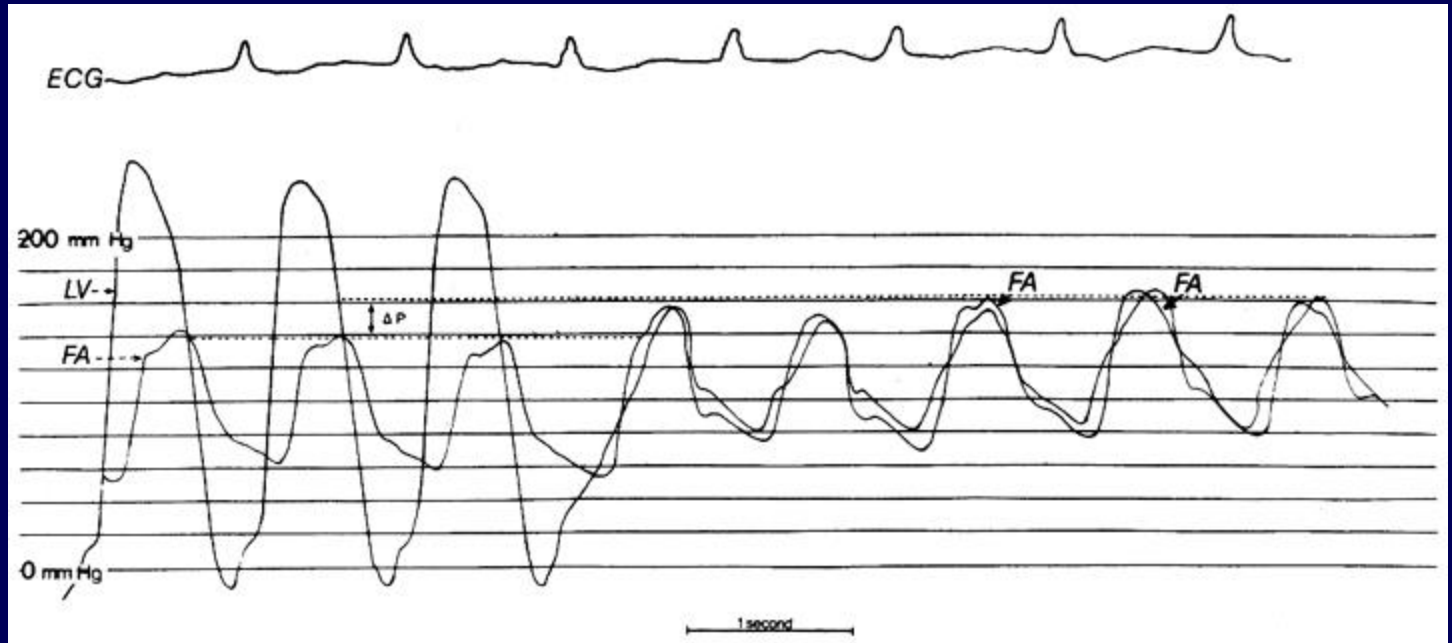
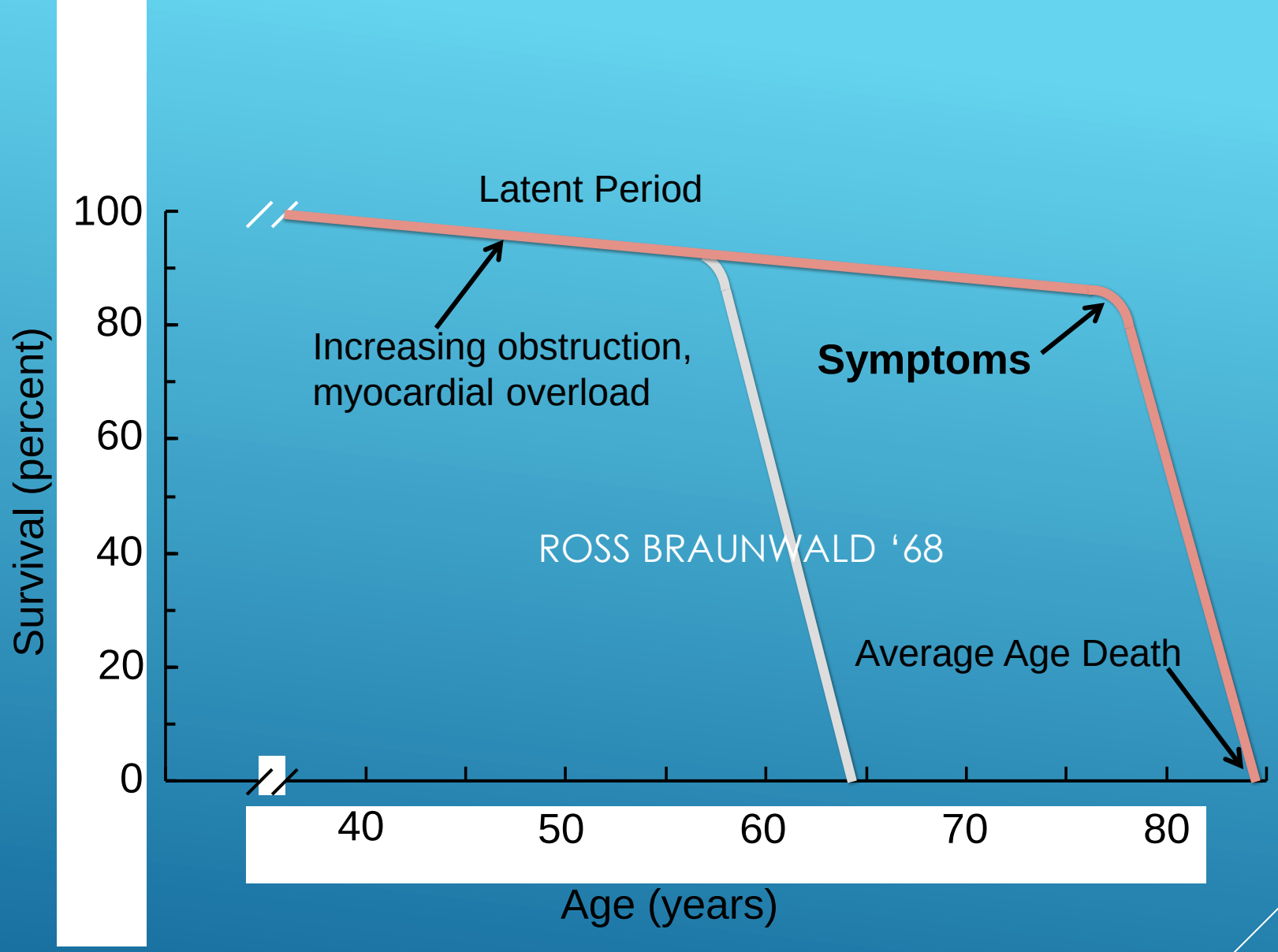
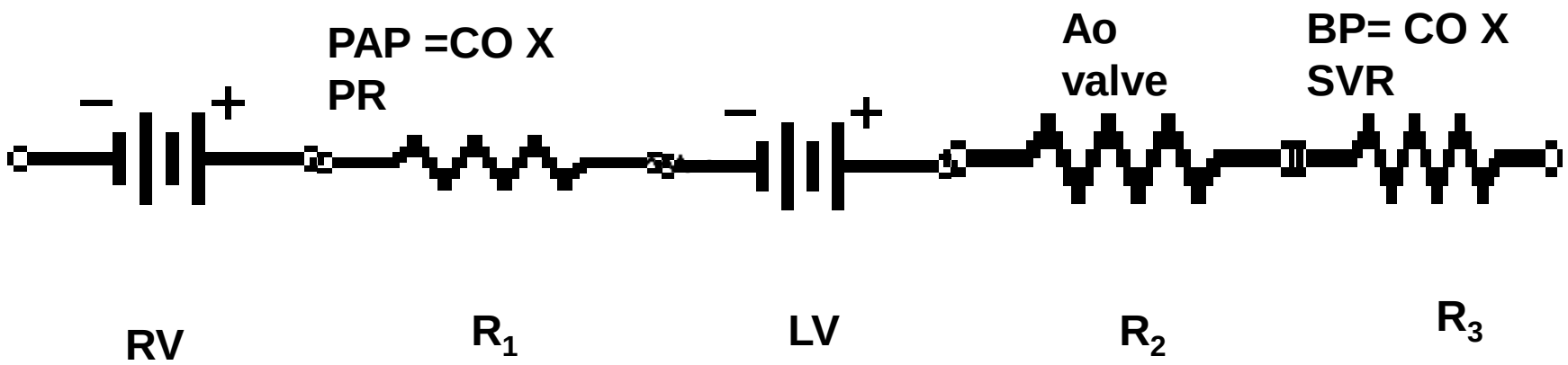
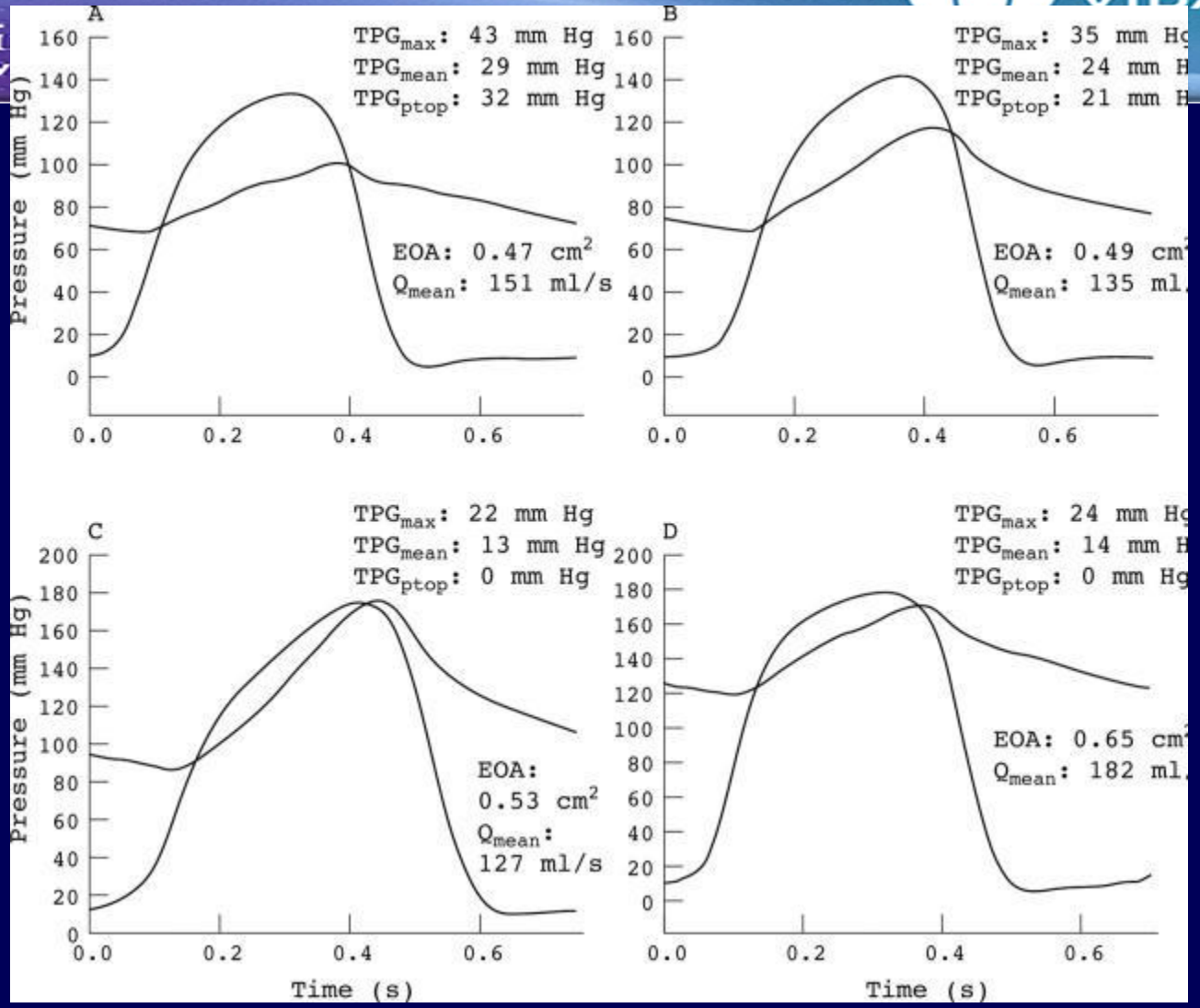




**Figure 28.7** Left ventricular (LV) and femoral artery (FA) pressure tracings in a patient with severe aortic stenosis (aortic valve area 0.4 $cm^2$). During pullback of the retrograde catheter from LV to ascending aorta, the peak systolic femoral artery pressure can be seen to increase (ΔP) by approximately 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.)


Latent Period
Increasing obstruction,
myocardial overload
Symptoms
ROSS BRAUNWALD '68
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

# DEFINITION OF "SEVERE"

MANMADE AND FRAUGHT

# THE REAL DEFINITION OF SEVERE AS

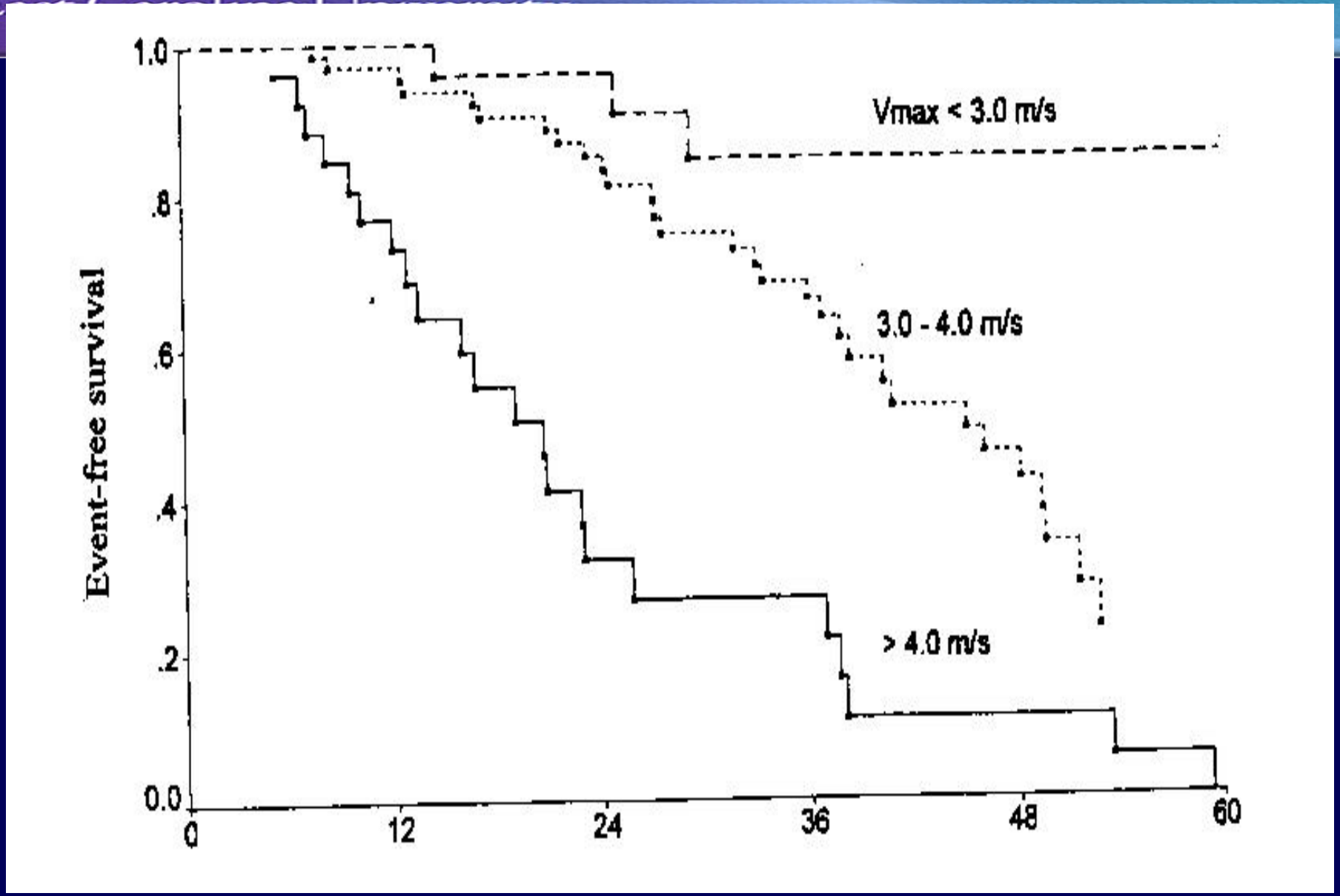
- THE AMOUNT OF OBSTRUCTION TO LV OUTFLOW THAT CAUSES ILLNESS

# THE ASSESSMENT STARTS WITH THE PHYSICAL EXAM

- WHEN DOES THE MURMUR PEAK
- CAROTID DELAY
- FORCEFUL APICAL BEAT
- [SSSS]

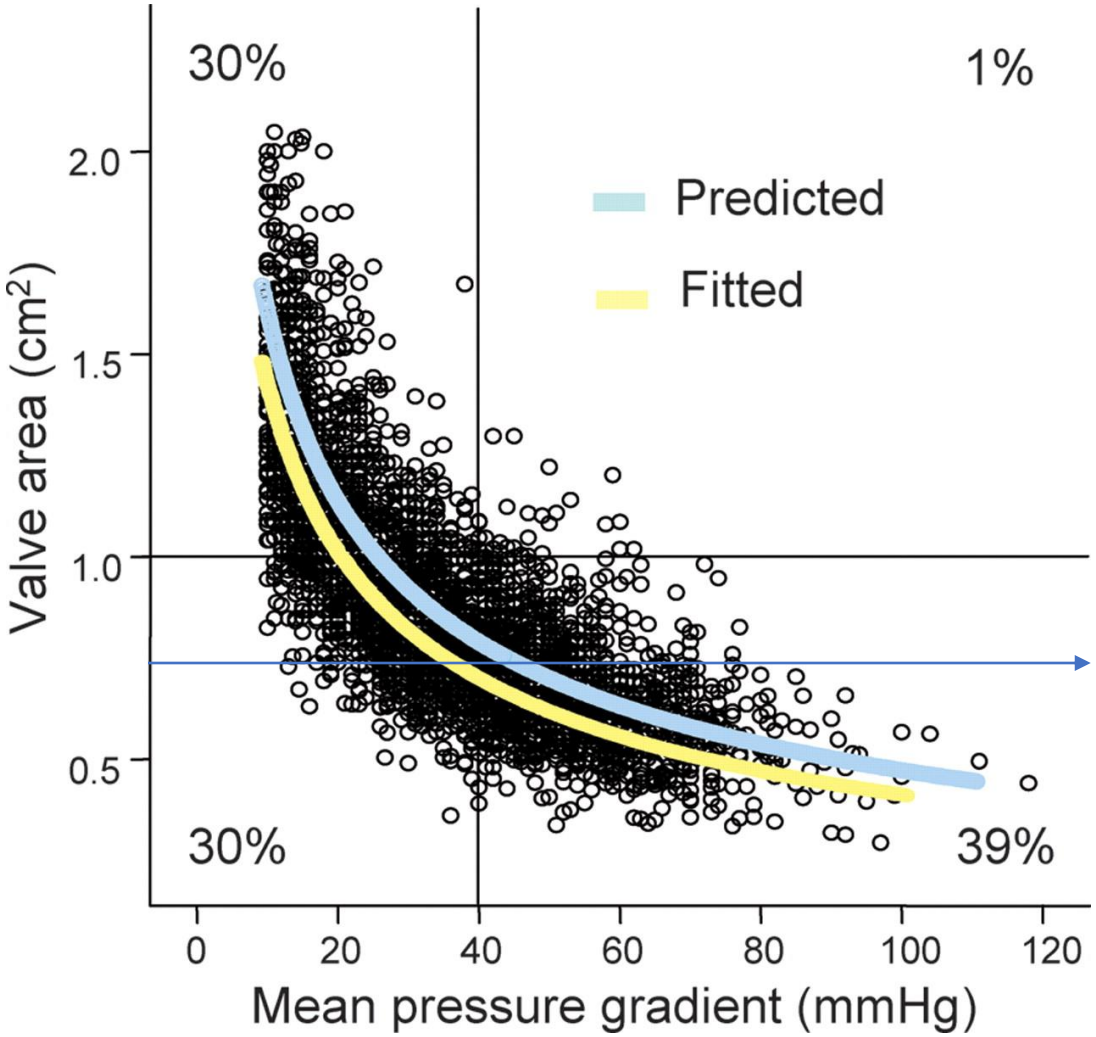
# SEVERE AS

- 4/40/1/0.6




OTTO et al CIRC '97

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



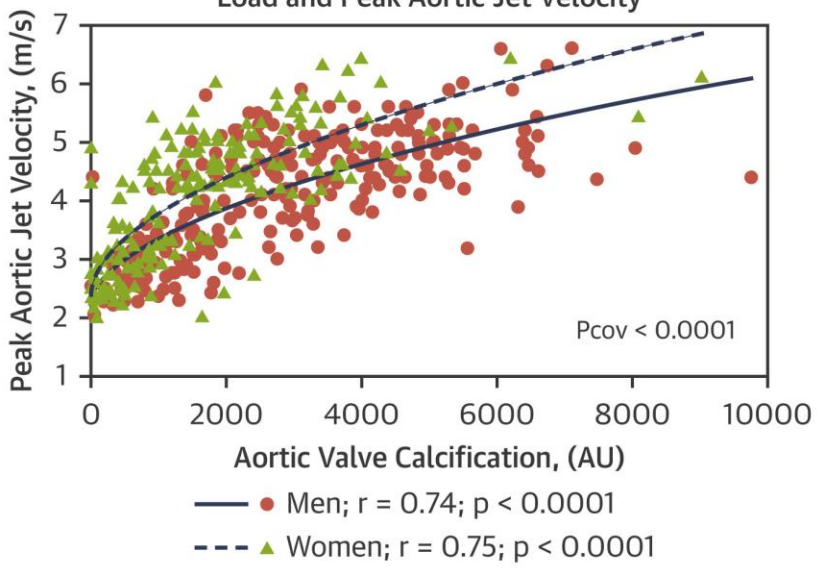

**Minners J et al. Eur Heart J 2008;29:1043-1048**



European Heart Journal

# ADDITIONAL HELP

A

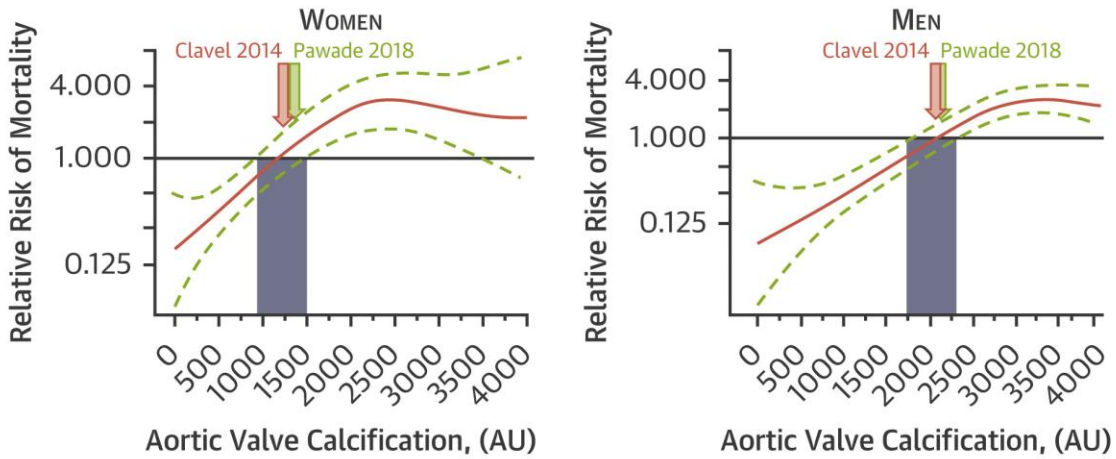



B

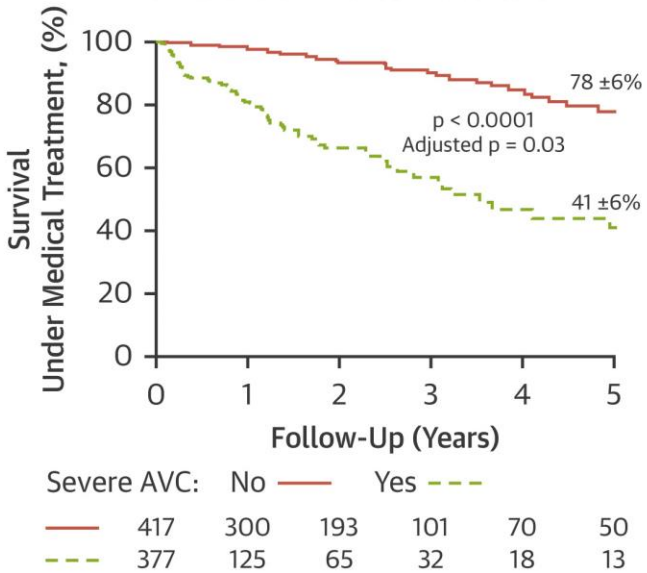
Thresholds Identifying Severe Aortic Stenosis in Women and Men

| Sex | AUC | AVC Thresholds | Reference |
|---|---|---|---|
| Women | 0.91 | 1,274 AU | Clavel 2014 |
| | 0.92 | 1,377 AU | Pawade 2018 |
| | - | 1,200 AU | ESC/EACTS Guidelines |
| Men | 0.90 | 2,065 AU | Clavel 2014 |
| | 0.89 | 2,062 AU | Pawade 2018 |
| | - | 2,000 AU | ESC/EACTS Guidelines |

C




D



# HUGE BIOLOGIC VARIABILITY

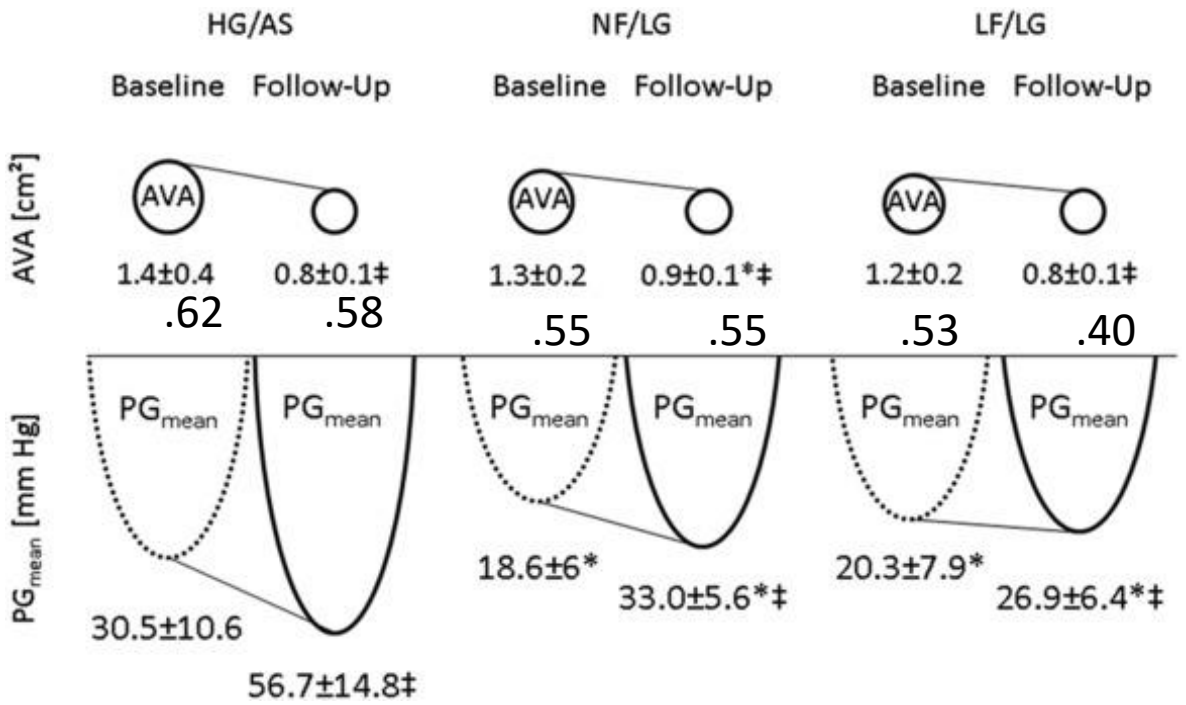



Figure 3. Progression of AVA and PGmean from baseline to follow-up. ∗P < .05, HG/AS versus NF/LG and LF/LG. ‡P < .05, follow-up versus baseline values, compared using Wilcoxon signed rank test.

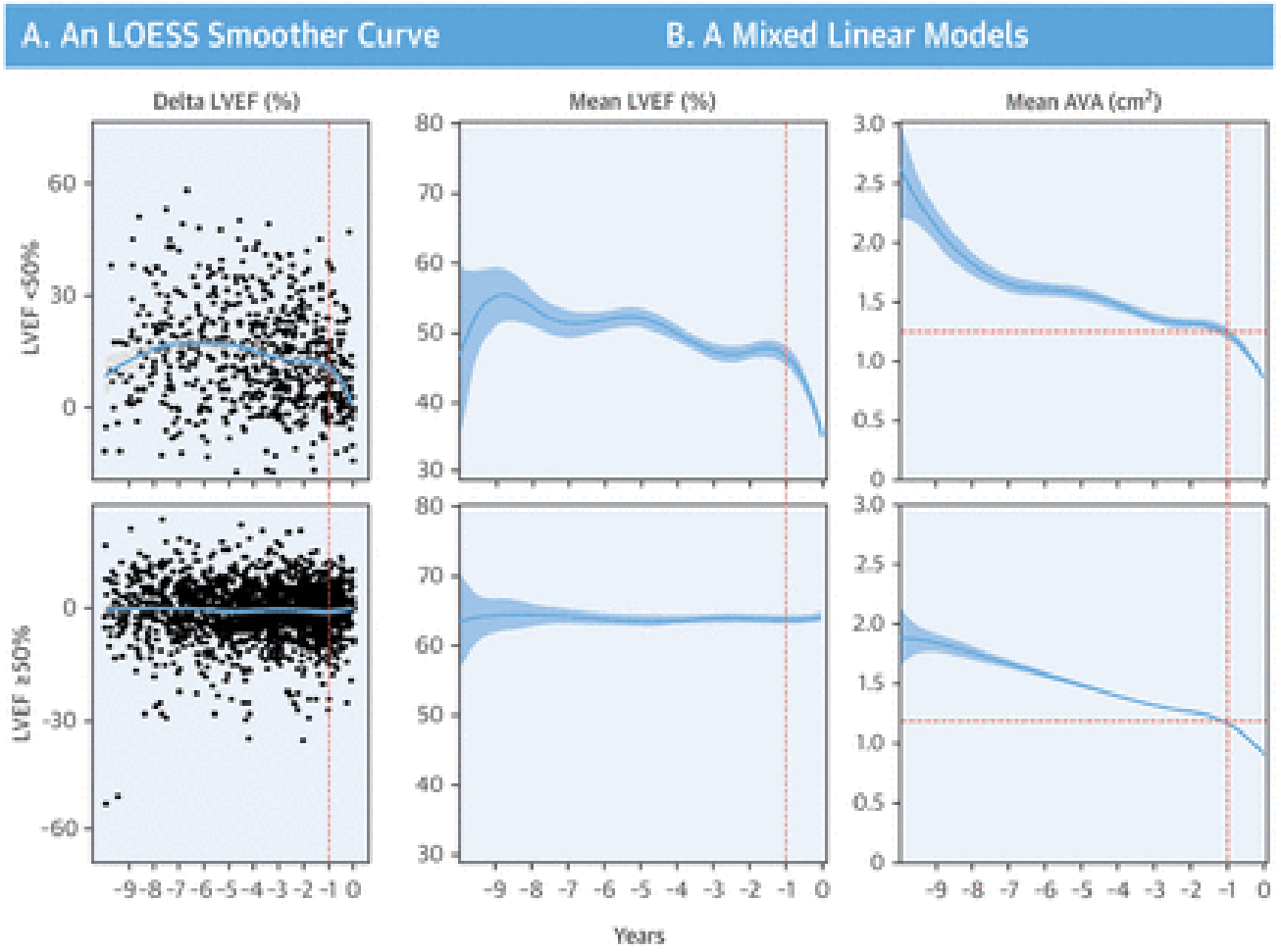
Sebastian Herrmann, Bastian Fries, Dan Liu, Kai Hu, Stefan Stoerk, Wolfram Voelker, Catharina Ruppert, Kristina Lorenz, Georg Ertl, Frank Weidemann

**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

**CENTRAL ILLUSTRATION: Time Course of Left Ventricular Ejection Fraction and Aortic Valve Area**



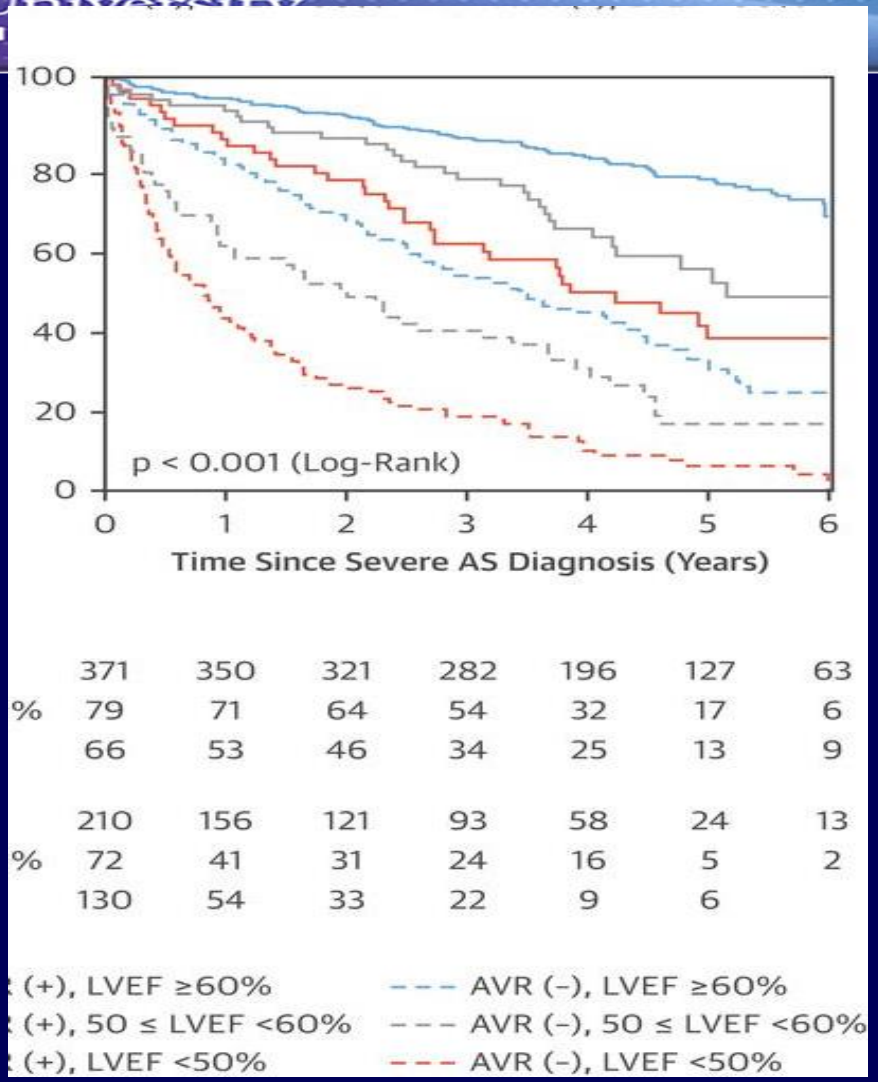

Ito, S. et al. J Am Coll Cardiol. 2018;71(12):1313-21.

- Aortic Vmax ≥ 4 m/s or mean ΔP ≥40 mm Hg
- AVA typically is ≤1.0 cm2 (or AVAi 0.6 cm2/m2) but not required to define severe AS
- Very severe AS is an aortic Vmax ≥5 m/s or mean P ≥60 mm Hg

# AVA IS INSTRUCTIVE BUT IMPERATIVE

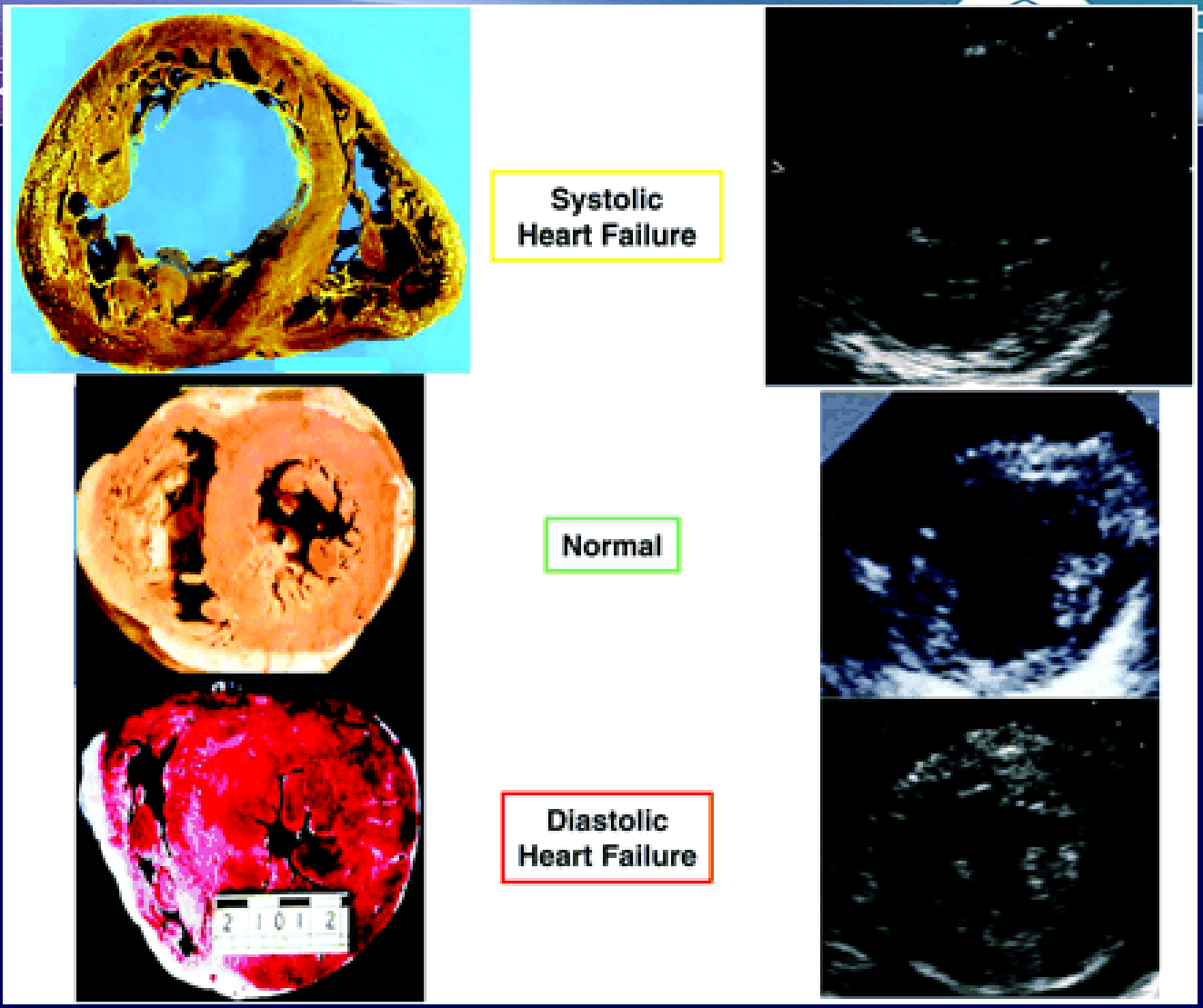
# CLASS I

- AVR FOR LV DYSFUNCTION
- But then you'd actually have to measure LV function



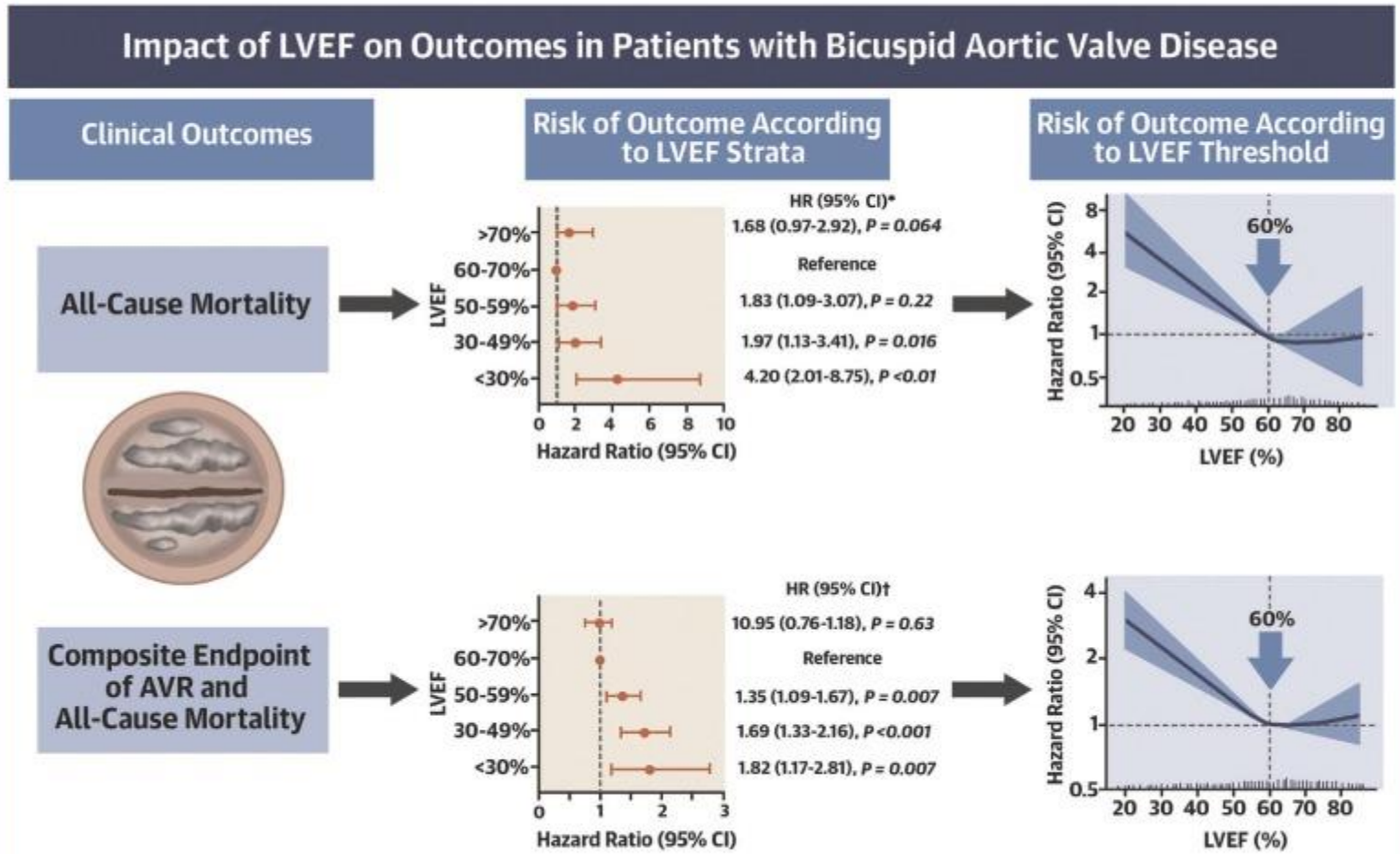

ITO et al JACC 2018


ITO et al JACC 2018




AURIGEMMA et al CIRC 113: 296

## CENTRAL ILLUSTRATION: Impact of Left Ventricular Ejection Fraction on Clinical Outcomes in Bicuspid Aortic Valve Disease




Hecht S, et al. J Am Coll Cardiol. 2022;80(11):1071-1084.

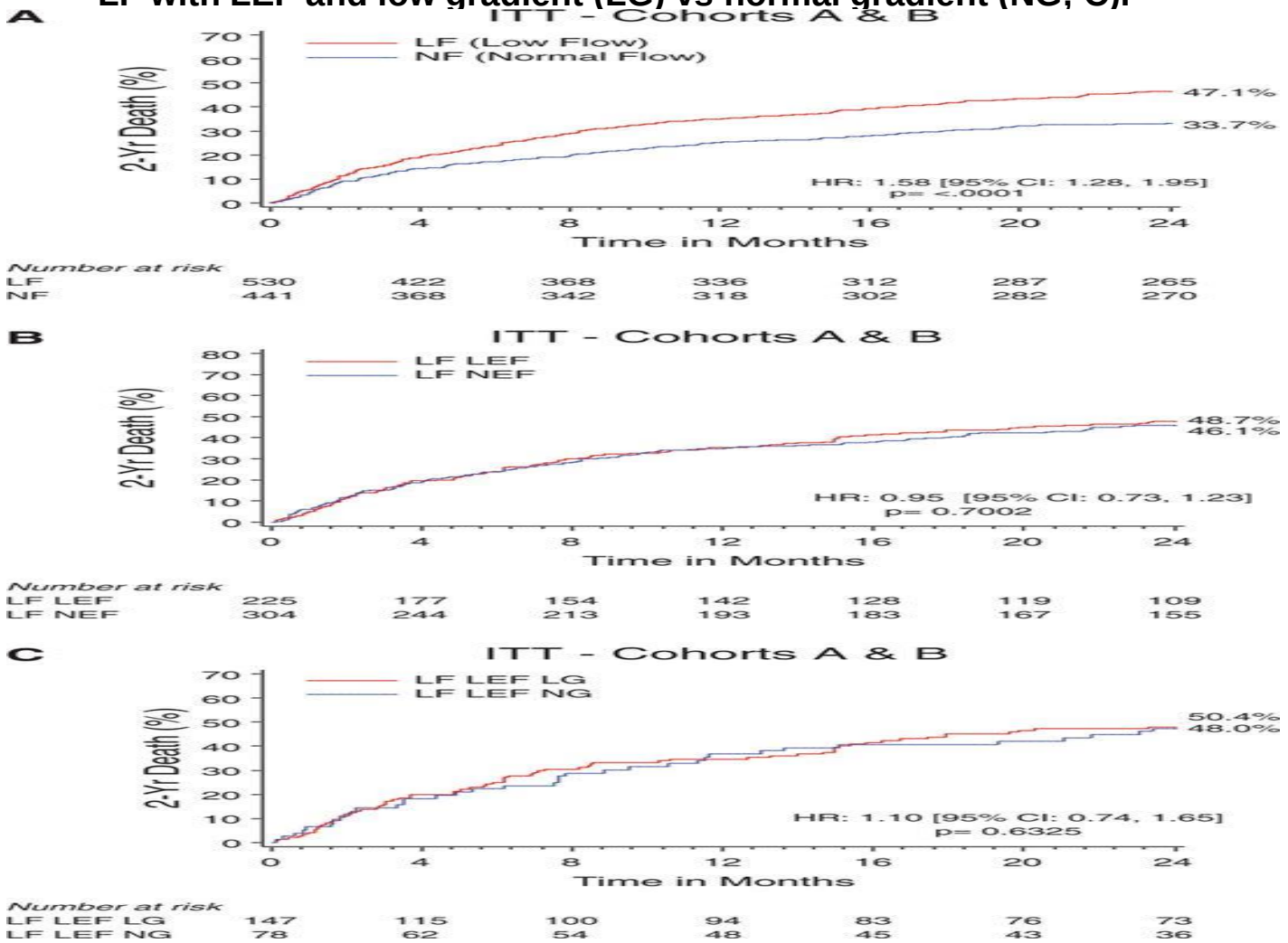
# LOW FLOW-LOW GRADEINT LOW EF AS

LOUSY SYSTOLE

LOUSY DIASTOLE

BOTH

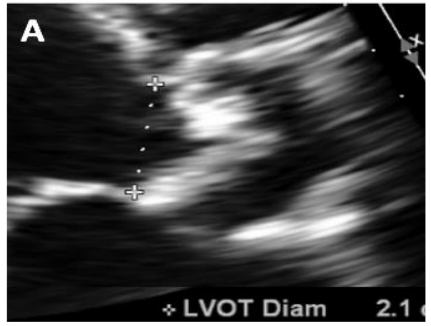
**Kaplan–Meier all-cause mortality analysis to 2 years is shown for patients with low flow (LF) vs normal flow (NF; A), LF with low ejection fraction (LEF) vs normal ejection fraction (NEF; B), and LF with LEF and low gradient (LG) vs normal gradient (NG; C).**



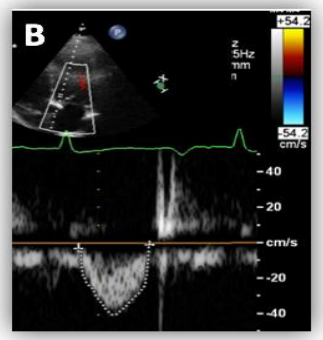

Howard C. Herrmann et al. Circulation. 2013;127:2316-2326

76 year old Male
Blood pressure: 111/67

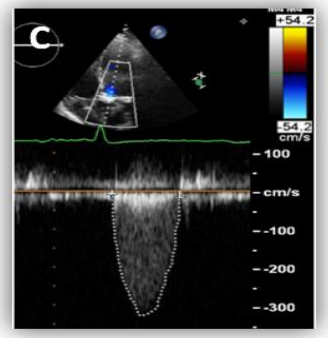
CAD s/p CABG
Diabetes mellitus
Hypertension
NYHA class: III
LVEF: 20%




REST

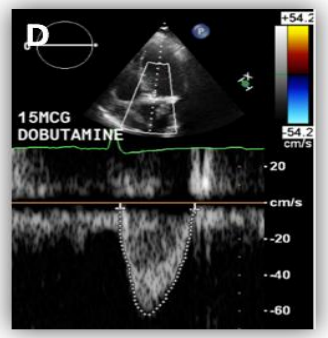



SV: 30 ml

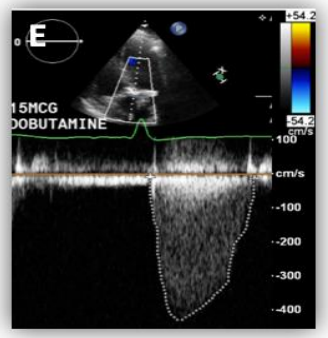



MG: 26 mmHg
AVA: 0.5 cm²

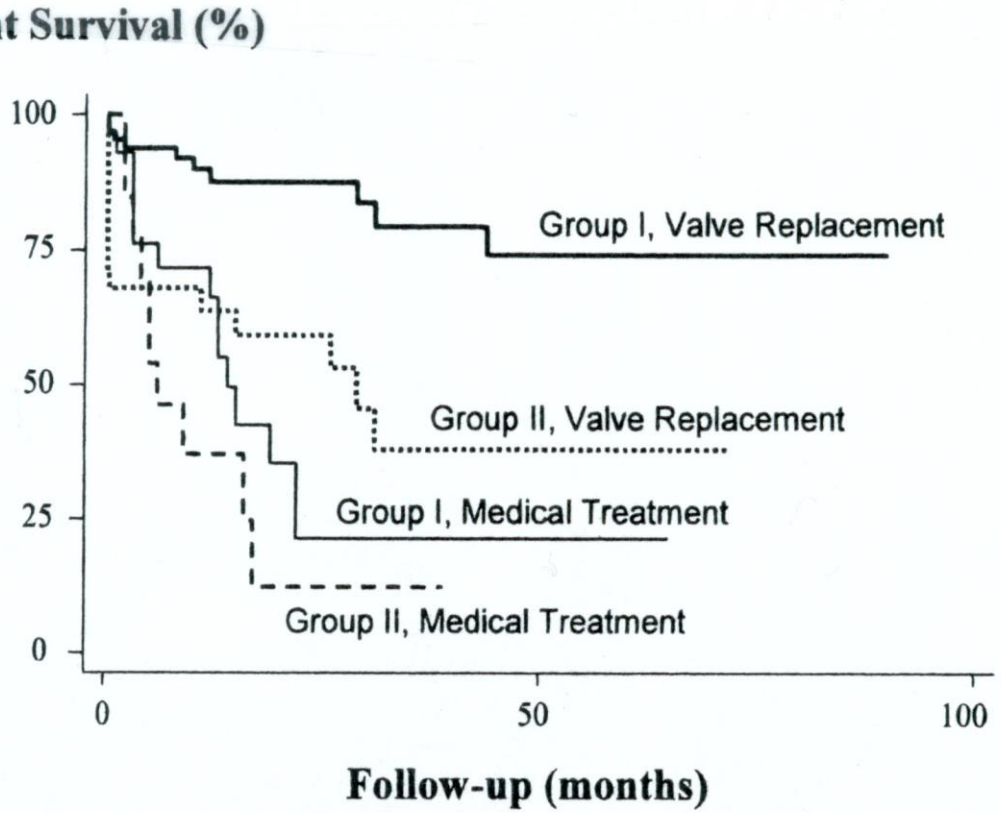
Dobutamine




SV: 45 ml




MG: 43 mmHg
AVA: 0.5 cm²

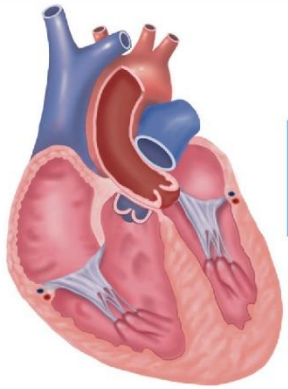



Kaplan-Meier survival estimates by group and treatment.

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.

**CENTRAL ILLUSTRATION: Clinical Outcomes and LV Changes Following TAVR in Patients With LFLG-AS**

## TAVR in Patients with Low-Flow, Low-Gradient Aortic Stenosis



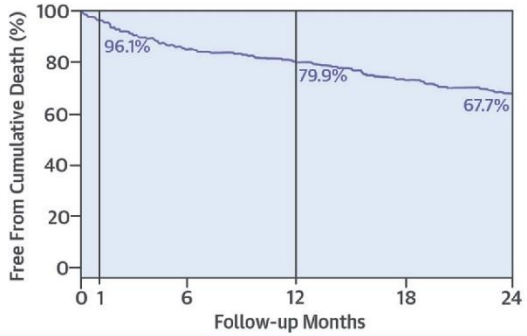
- LVEF ≤40%
- ΔP <35 mmHg
- AVA <1.0 cm²

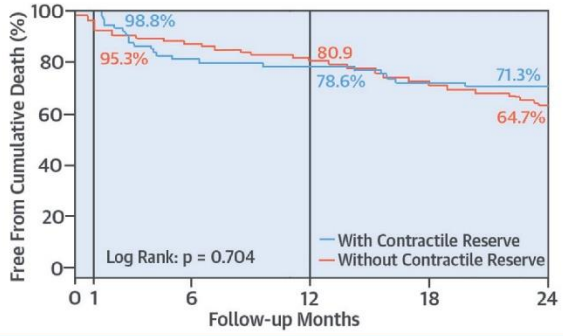
n = 287

Dobutamine Stress-Echo
n = 234

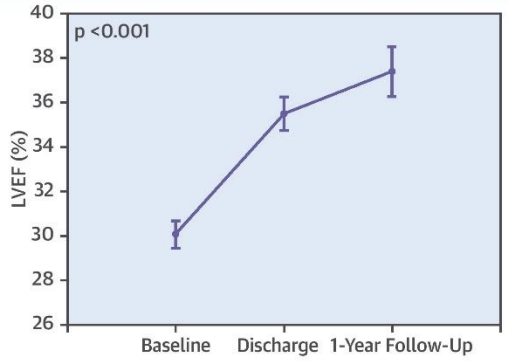
Contractile (Flow) Reserve
↑SV ≥20%
(45%)

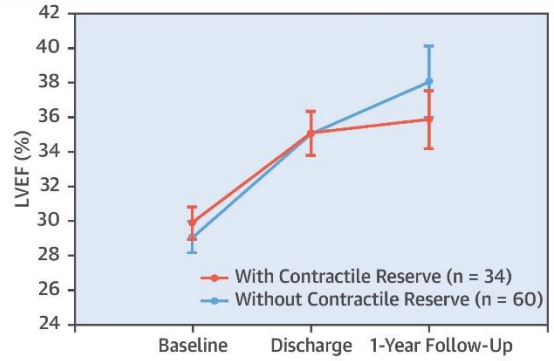
No Contractile (Flow) Reserve
↑SV <20%
(55%)




## Changes in LVEF Over Time

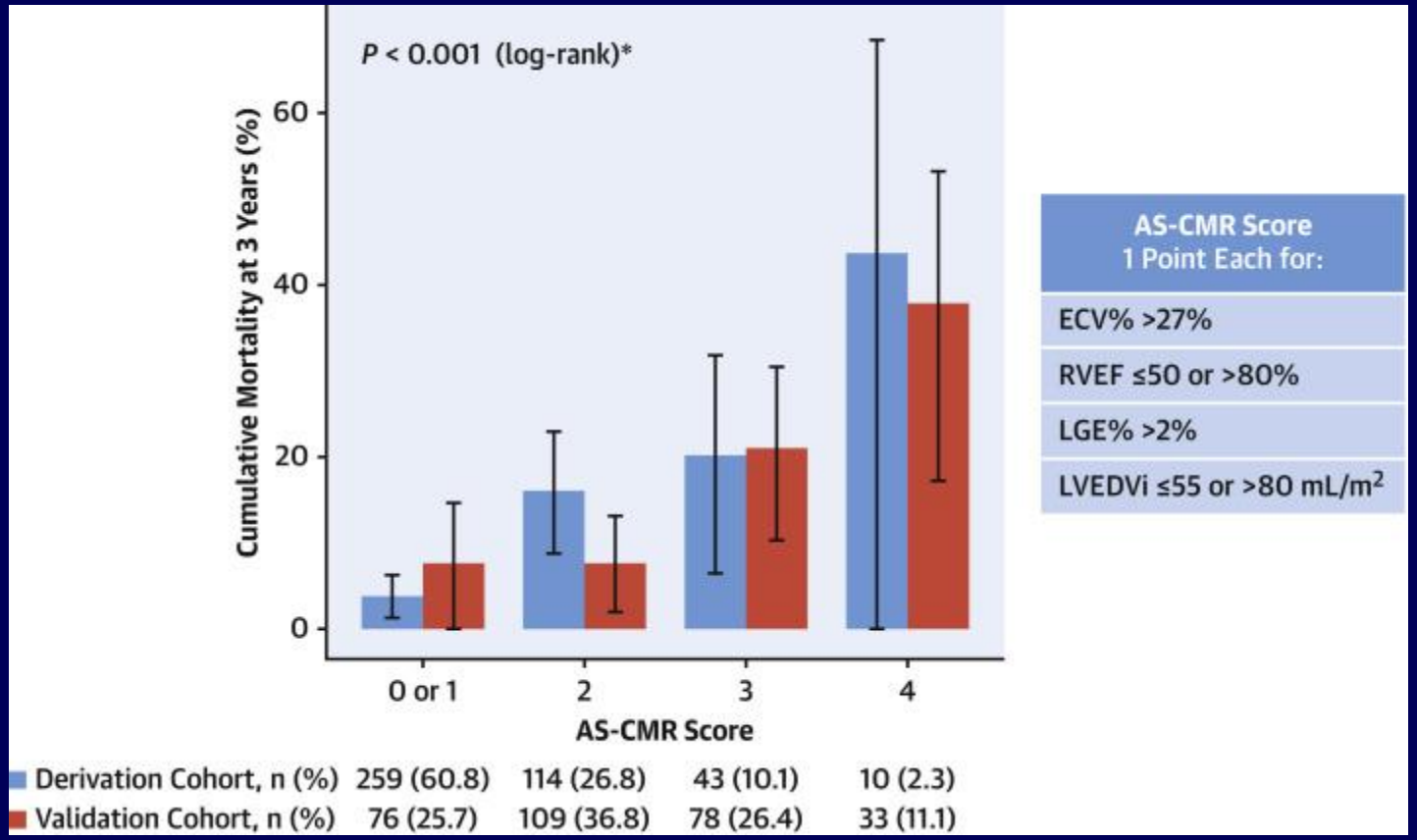



Ribeiro, H.B. et al. J Am Coll Cardiol. 2018;71(12):1297-308.

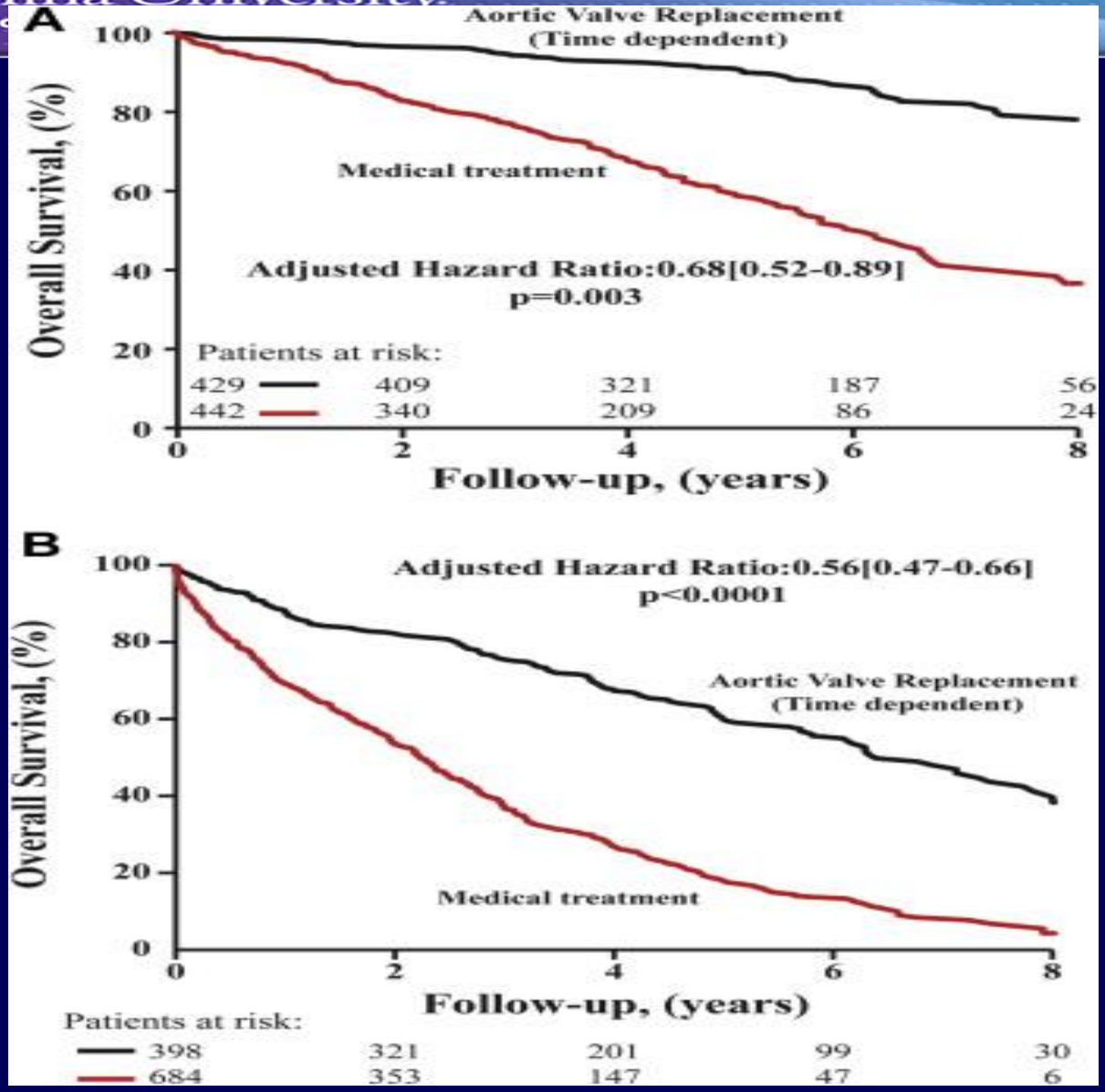
# WE NEED BETTER TOOLS

- MRI
- BIOMARKERS
- BAV




KWAK et al JACC 2021

# BIOMARKERS




CLAVEL et al JACC 2014

# CONCLUSION (AS)

- ASSESSMENT OF SEVERITY IS EASY WHEN A 60 y/o HAS ANGINA AND A GRADIENT OF 80 mm Hg

- FOR AN 80y/o WITH DOE AND AND A GRADIENT OF 32 IT TAKES EVERY PIECE OF DATA YOU'VE GOT STARTING WITH THE PE

- YOU CANNOT RELY UPON ANY SINGLE VARIABLE TO DECIDE ON AVR

# MR

- PRIMARY MR: IT'S THE VALVE THAT MAKES THE HEART SICK
- SECONDARY MR: IT'S THE HEART THAT MAKES THE VALVE SICK

# PRIMARY MR

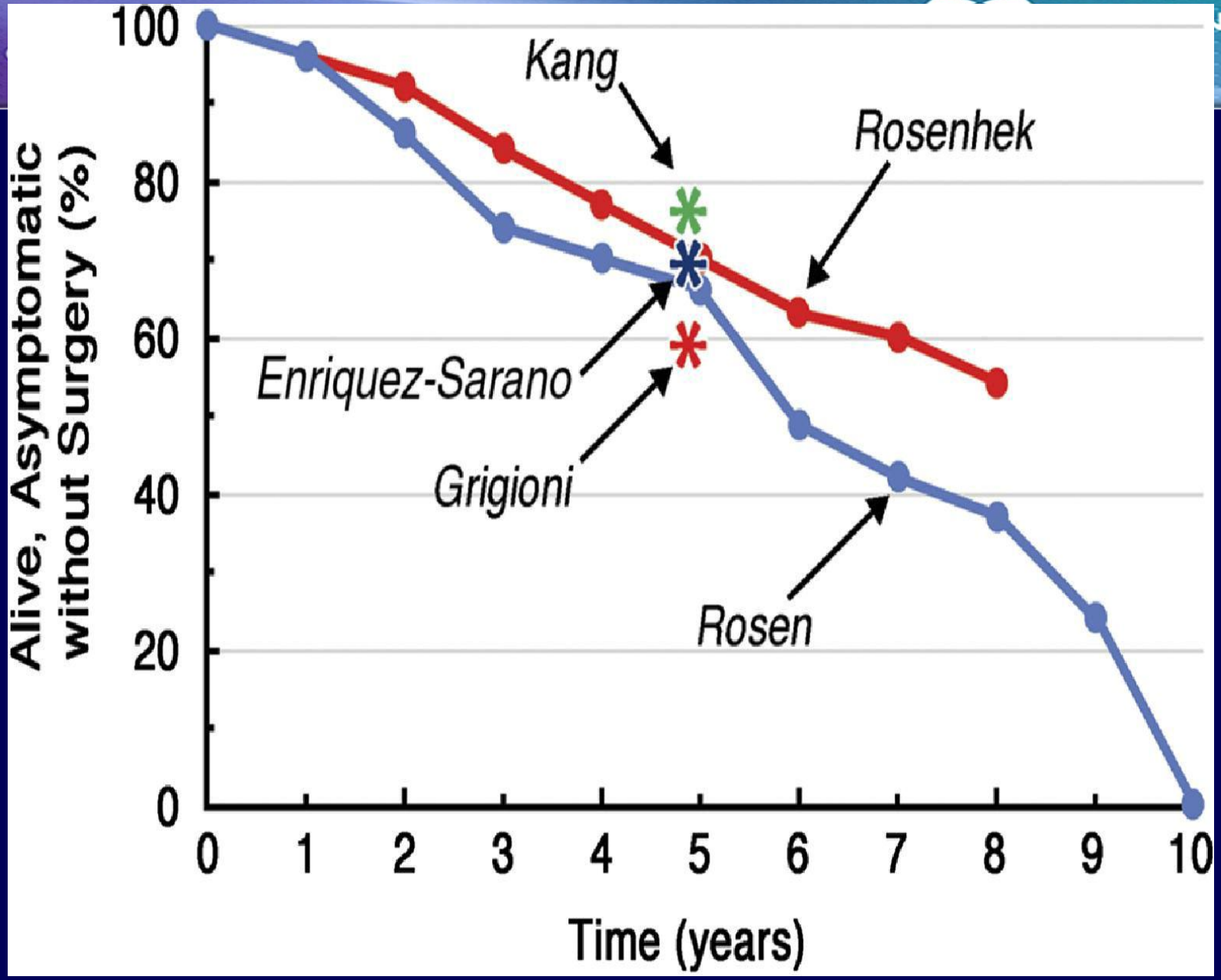
# SEVERE MR

BIG JET

ROA >0.4 $CM^2$

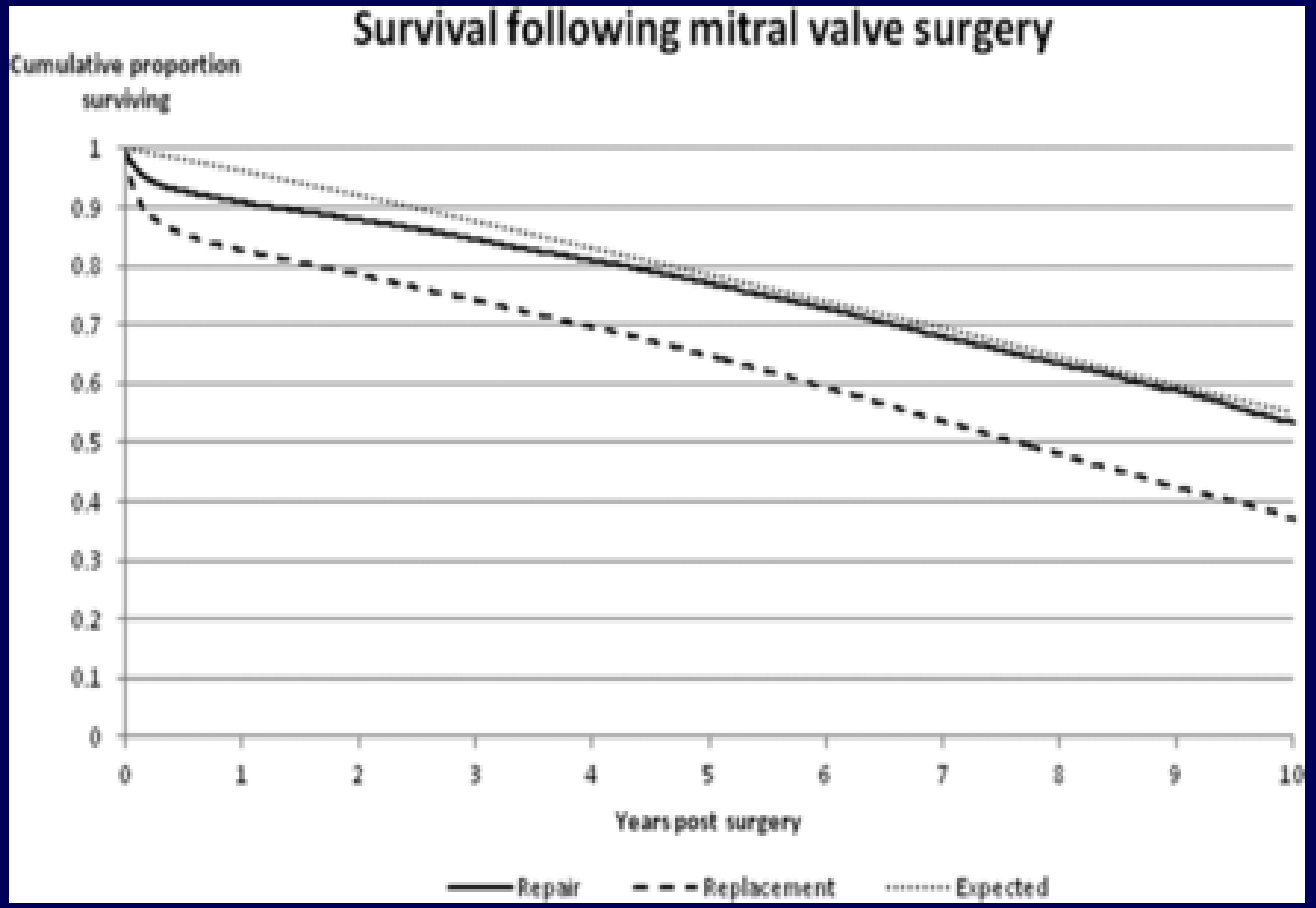
REGURGITANT Fx >/= 50%

REGURGITANT VOLUME >/= 60 cc


Alive, Asymptomatic without Surgery (%)
100
80
60
40
20
0
0
1
2
3
4
5
6
7
8
9
10
Time (years)
Kang
Rosenhek
Enriquez-Sarano
Grigioni
Rosen

# SEVERE MR

- REPAIR
- REPAIR
- REPAIR




VASSILEVA et al CIRC: 2013

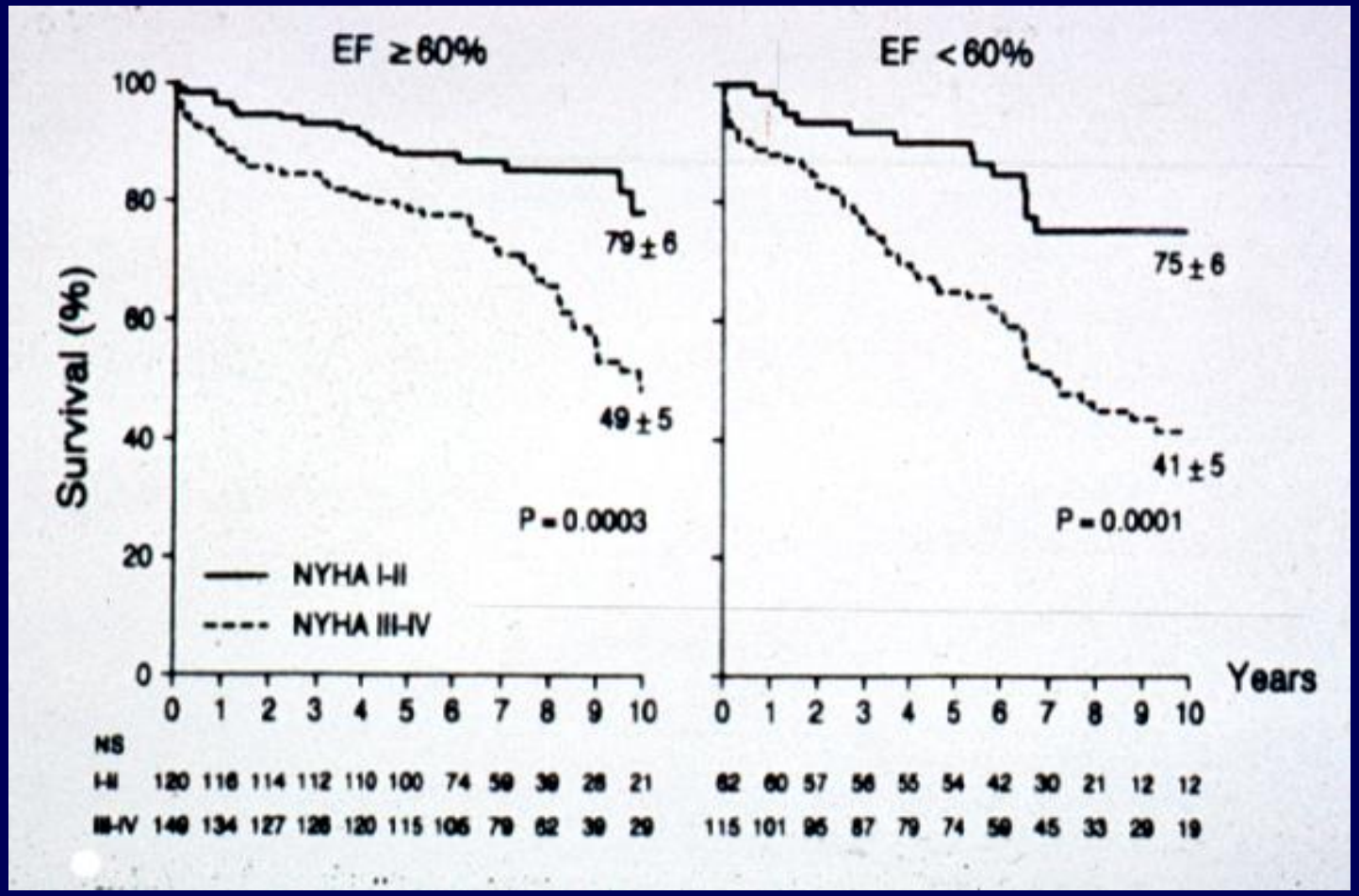
# 55 Y/O ASYMPTOMATIC MAN

- MVP WITH SEVERE MR ($P_2$ PRO)
- EF 65 %
- ESD 38 mm

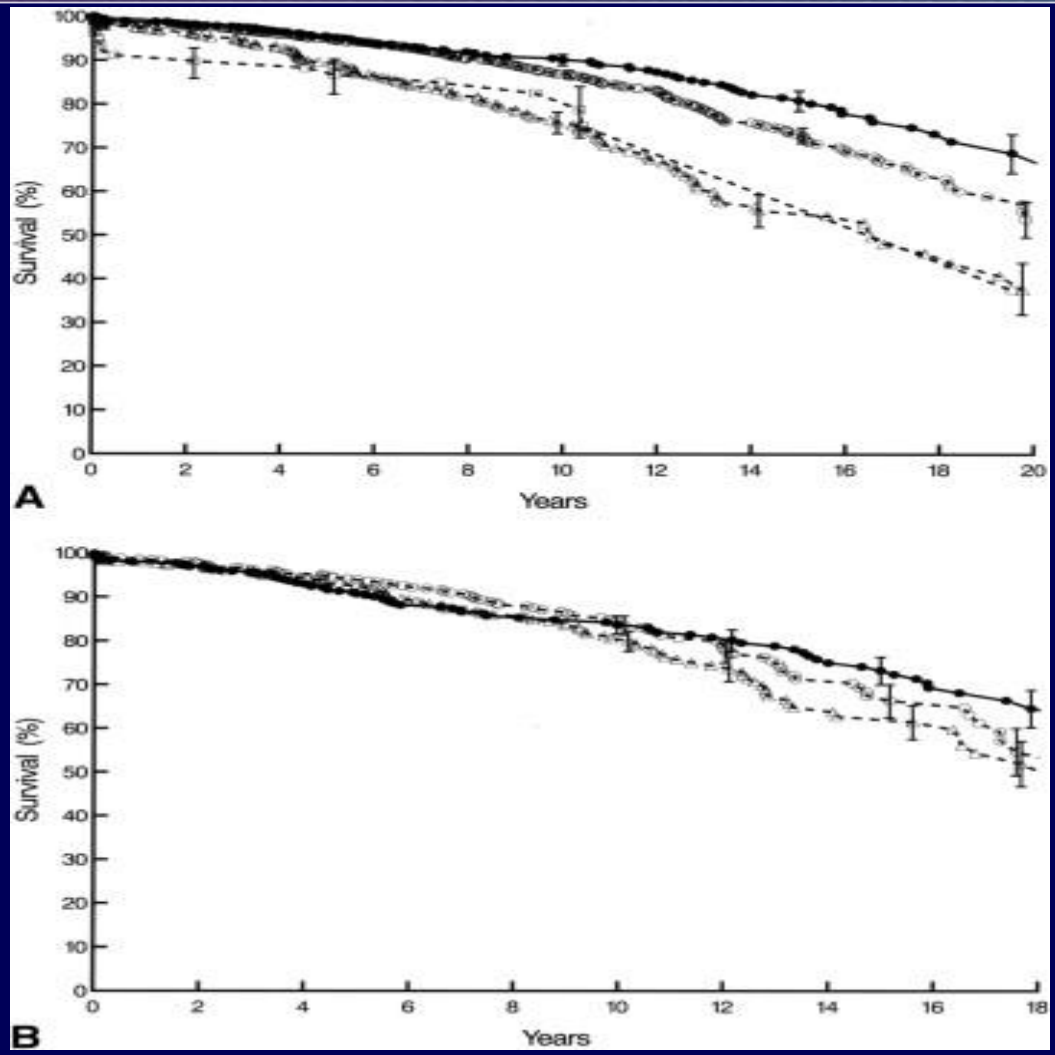
# TRIGGERS FOR PRIMARY MR INTERVENTION

- CLASS 1 **Sx/ 60/40**

# WHERE DID THE TRIGGERS COME FROM




TRIBOUILLOY etal, CIRC 99:400,1999




CLASS II

GILLINOV et al ANN THOR SURG 90 :481 , 2010

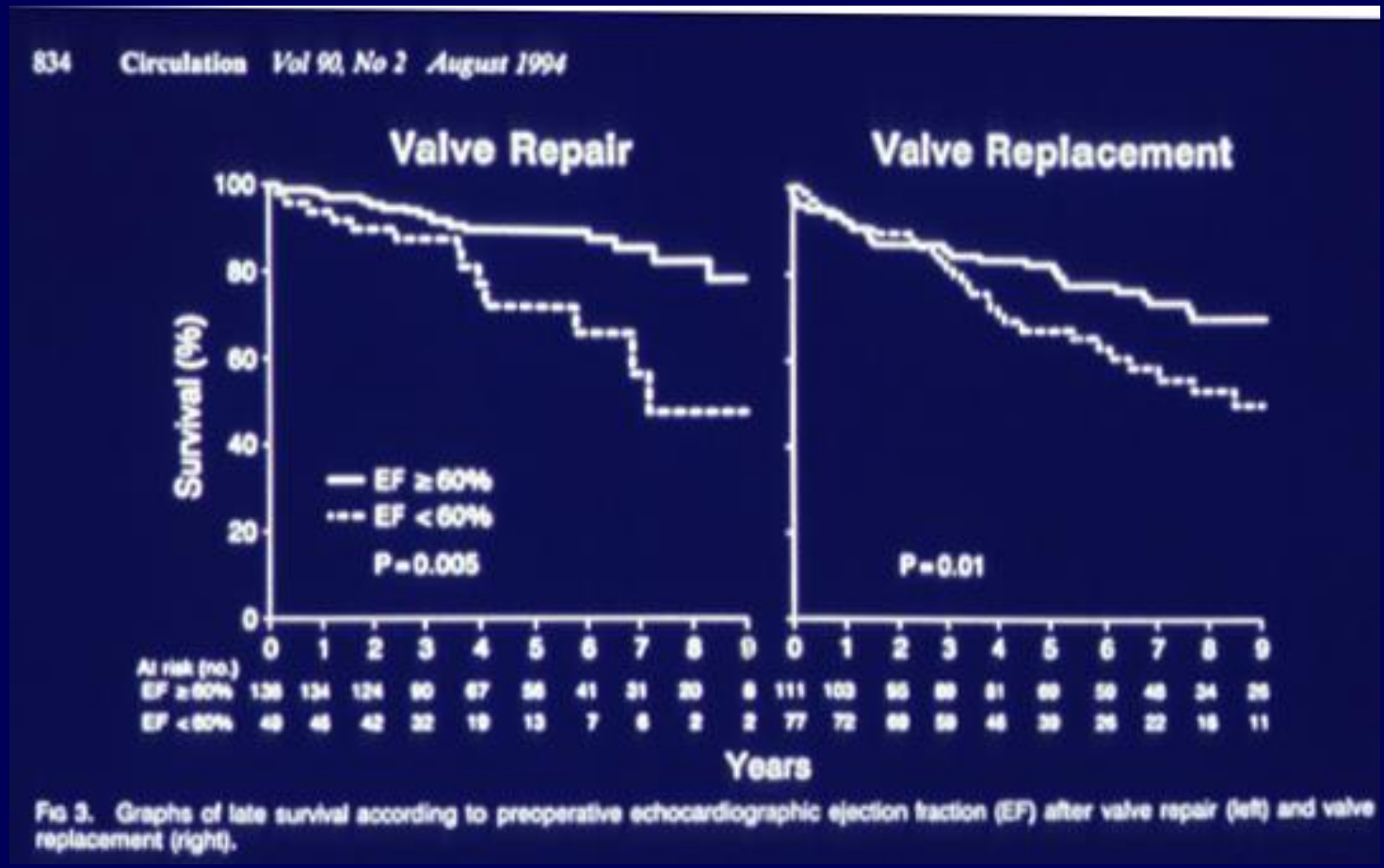
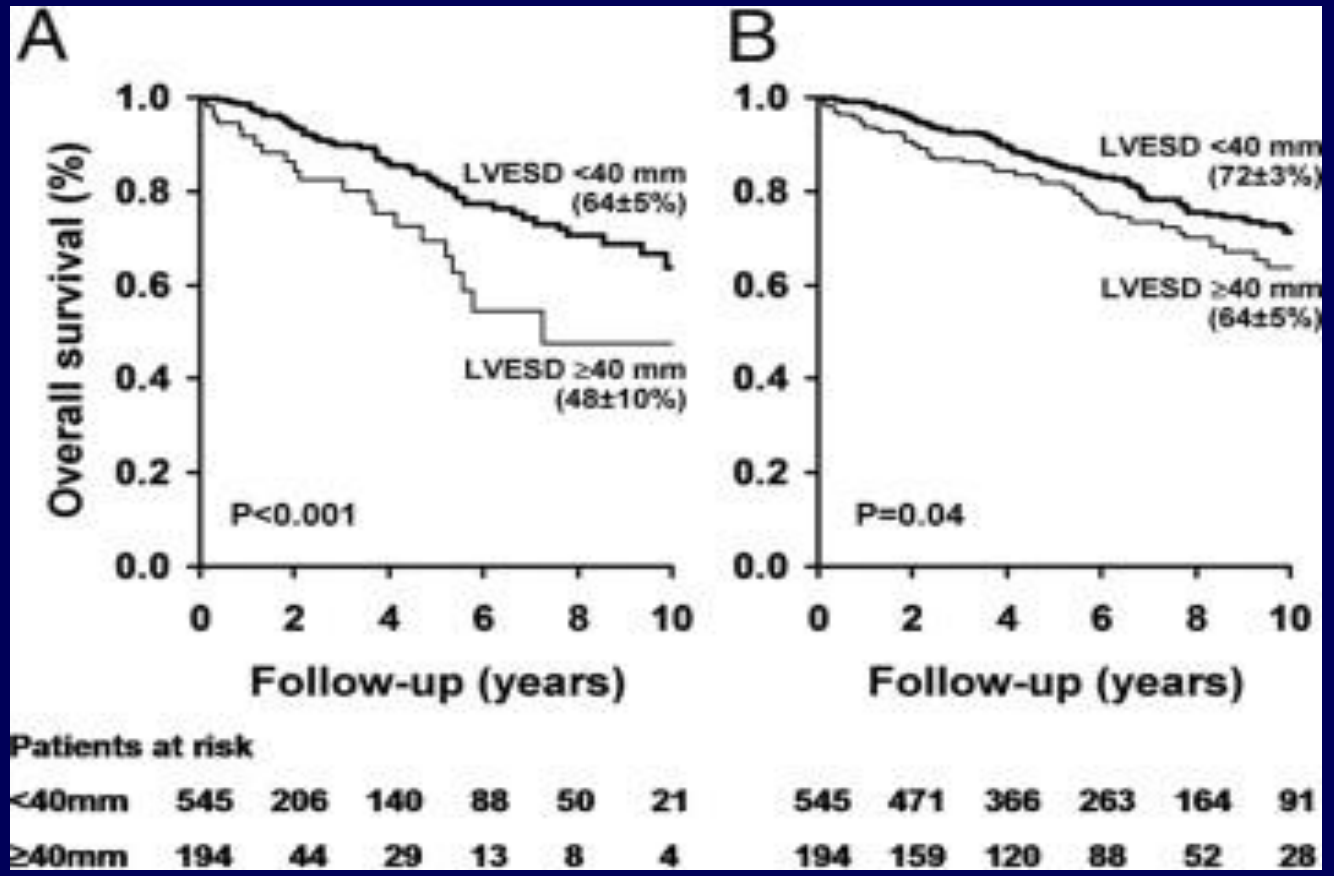
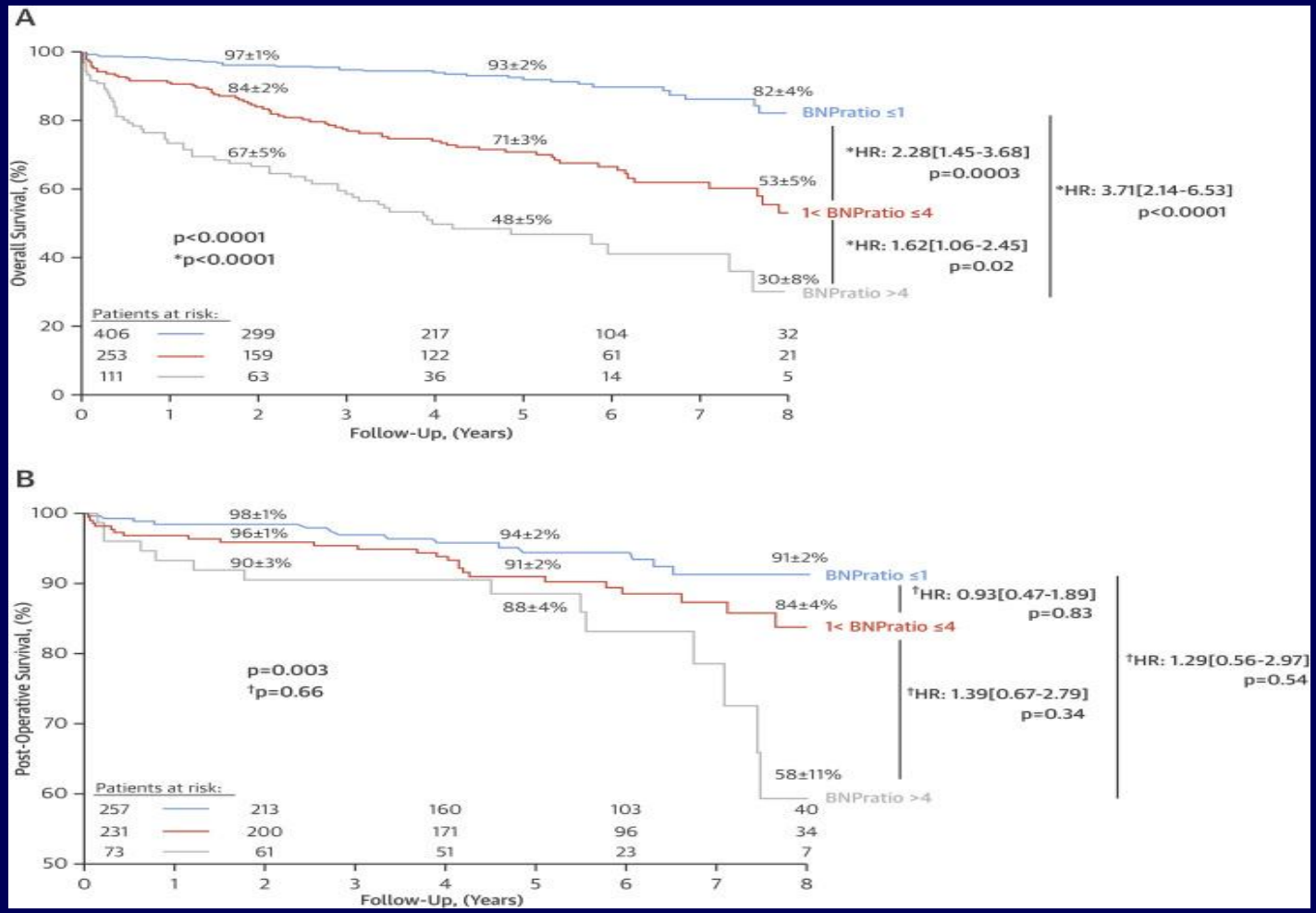



Fig 3. Graphs of late survival according to preoperative echocardiographic ejection fraction (EF) after valve repair (left) and valve replacement (right).

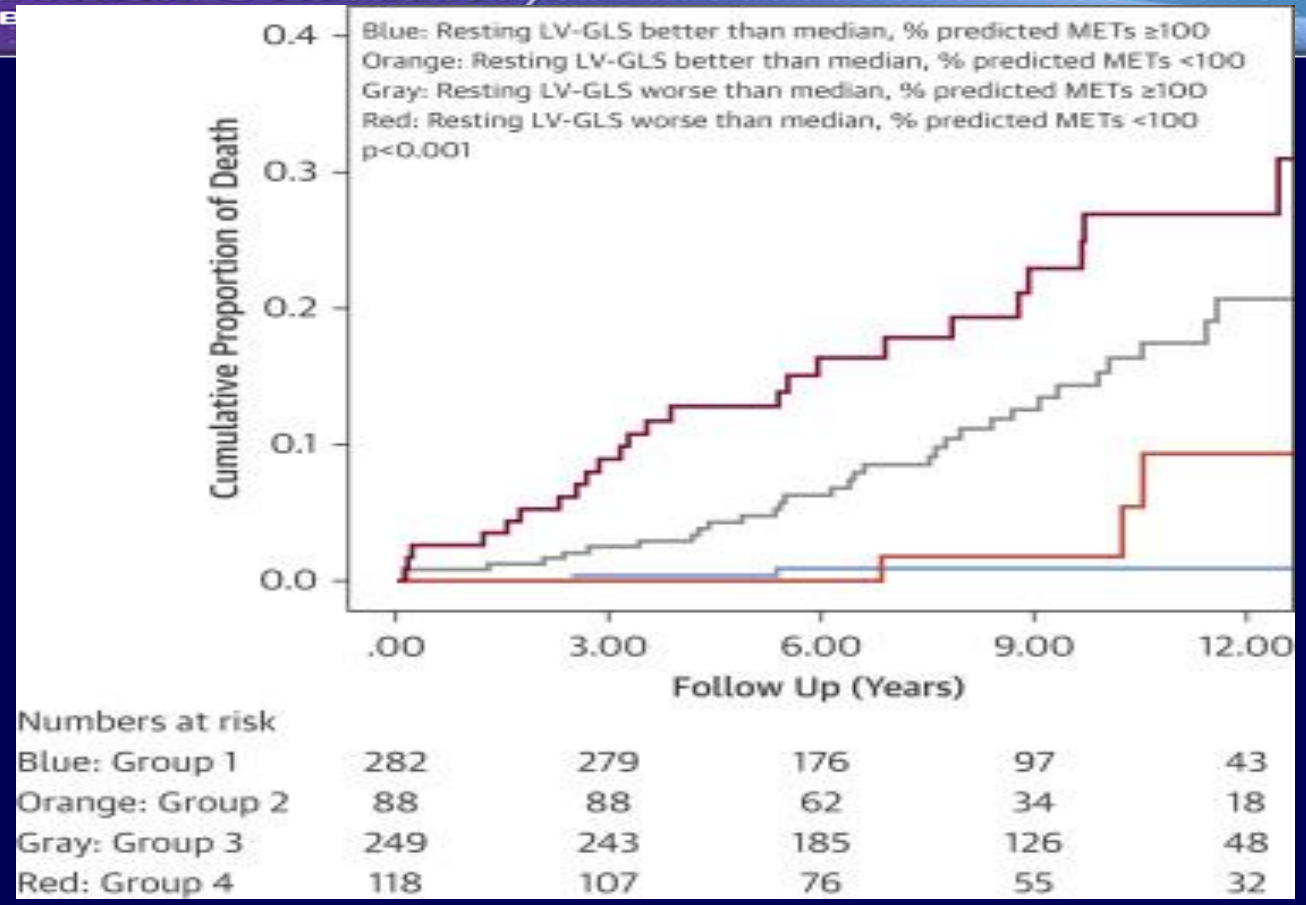
ENRIQUEZ-SARANO etal CIRC, 90:830, 1994




TRIBOUILLOY et al JACC 2009




CLAVEL et al JACC 20166




| Numbers at risk | | | | | |
|---|---|---|---|---|---|
| Blue: Group 1 | 282 | 279 | 176 | 97 | 43 |
| Orange: Group 2 | 88 | 88 | 62 | 34 | 18 |
| Gray: Group 3 | 249 | 243 | 185 | 126 | 48 |
| Red: Group 4 | 118 | 107 | 76 | 55 | 32 |

Amgad Mentias, Peyman Naji, A. Marc Gillinov, L. Leonardo Rodriguez, Grant Reed, Tomislav Mihaljevic, Rakesh M. Suri, Joseph F. Sabik, Lars G. Svensson, Richard A. Grimm, Brian P. Griffin, Milind Y. Desai

Journal of the American College of Cardiology, Volume 68, Issue 18, 2016, 1974–1986

http://dx.doi.org/10.1016/j.jacc.2016.08.030

| | | |
|---|---|---|
| 2a | B-NR | 1. In asymptomatic patients with severe primary MR and normal LV systolic function (LVEF ≥ 60% and LVESD ≤ 40mm) (stage C1) mitral valve repair is reasonable when the likelihood of a successful and durable repair without residual MR is greater than 95% with an expected mortality rate of less than 1% when performed at a Primary or Comprehensive Valve Center . |

# SURGERY IN ASYMPTOMATIC MR WITH NL LVF THE BIG 5

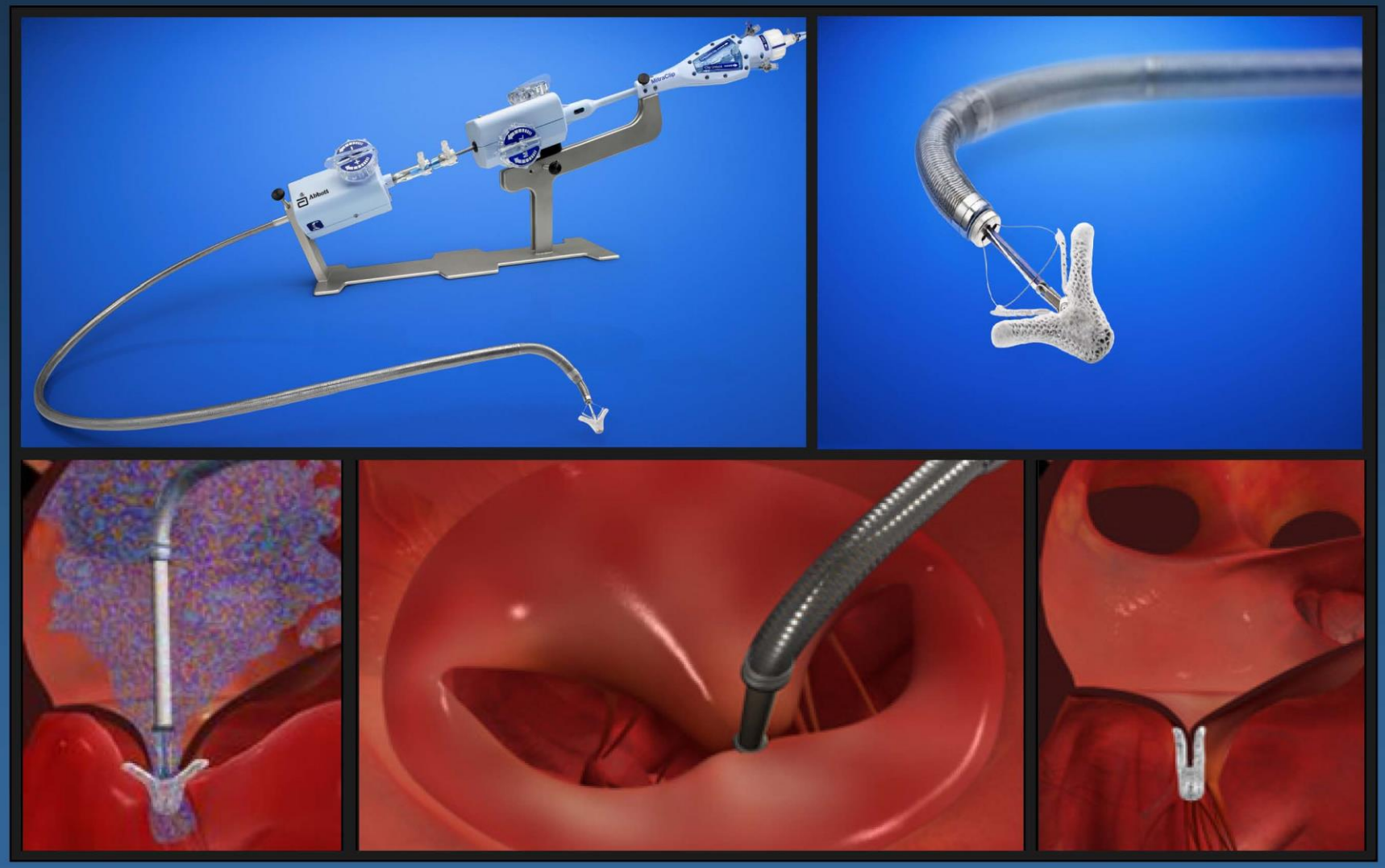
- IT'S THERE AND IT'S NOT GOING AWAY (ASD ANALOGY)
- REVEALING TREADMILL
- HIGH BNP
- IMPAIRED GLS
- IT CAN BE REPAIRED

# 55 Y/O ASYMPTOMATIC MAN

- MVP WITH SEVERE MR ($P_2$ PRO)
- EF 65 %
- ESD 38 mm

# Percutaneous Mitral Valve Repair

## MitraClip® System

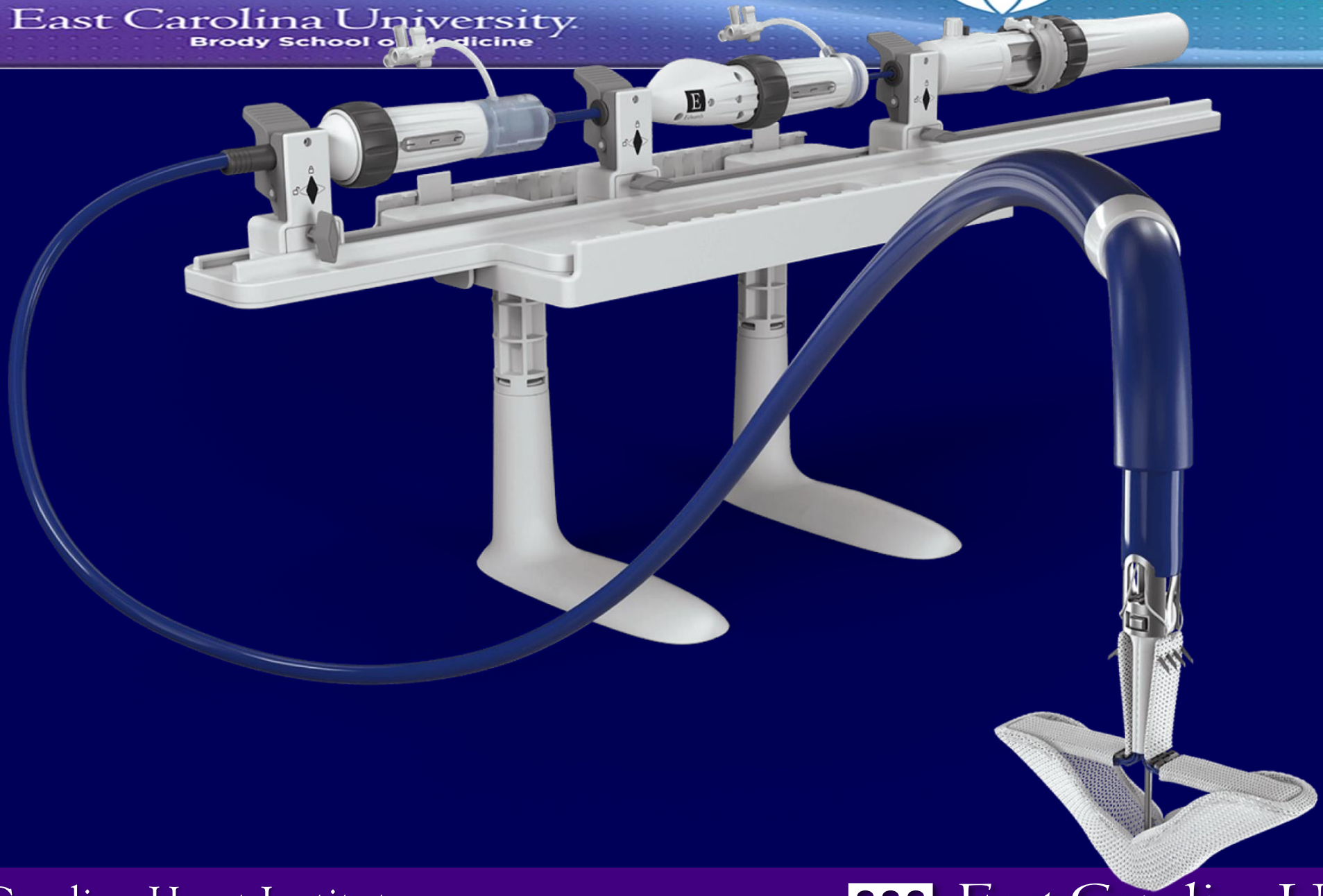


EVEREST II RCT – ACC 2011

Investigational Device only in the U.S. Not available for sale in the U.S.

East Carolina University
Brody School of Medicine

VIDANT HEALTH

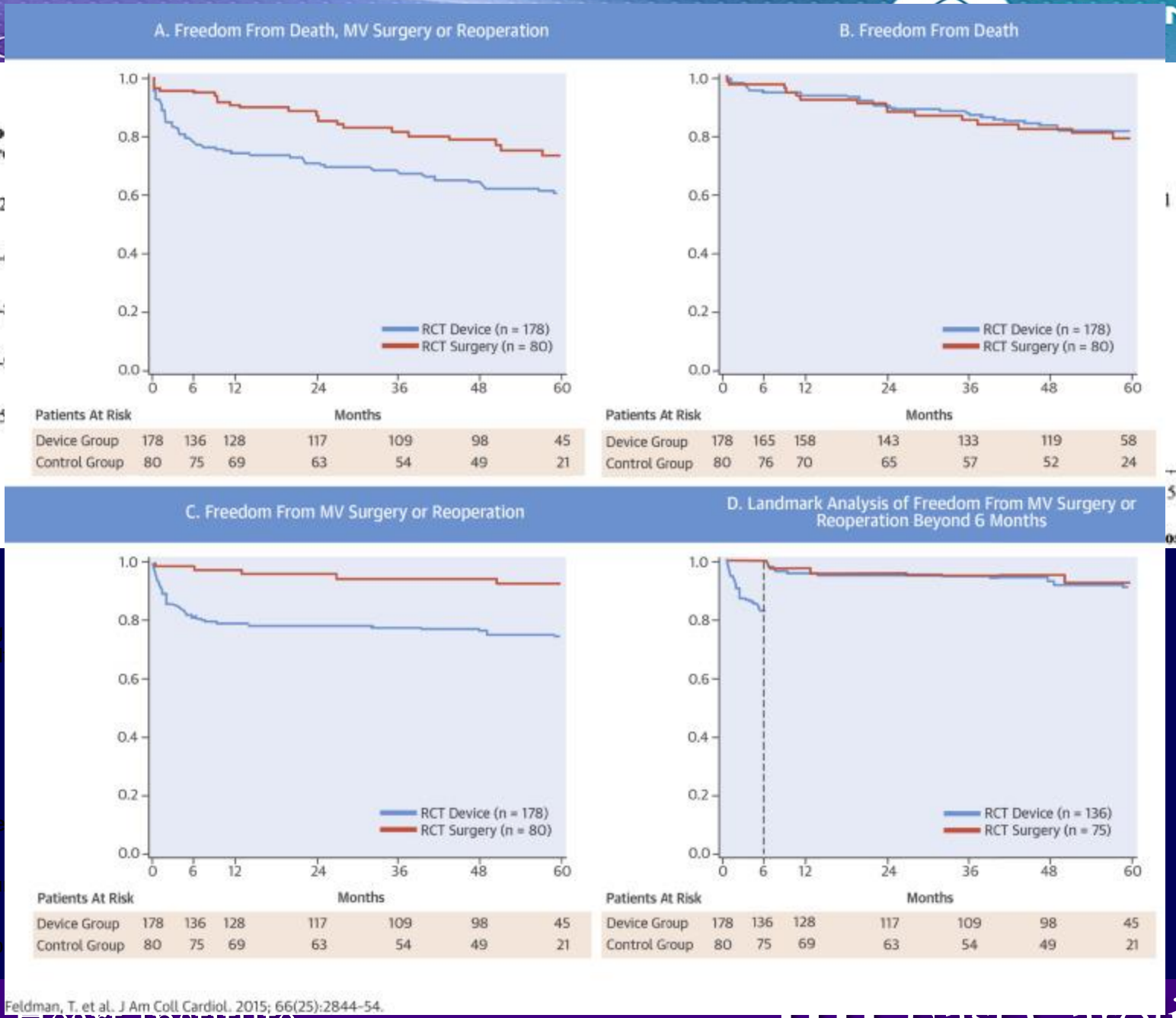


East Carolina Heart Institute

East Carolina University

# MITRALCLIP IN PRIMARY MR

- FOR HIGH RISK PATIENTS
- MORE DURABLE THAN PREDICTED




Feldman, T. et al. J Am Coll Cardiol. 2015; 66(25):2844-54.

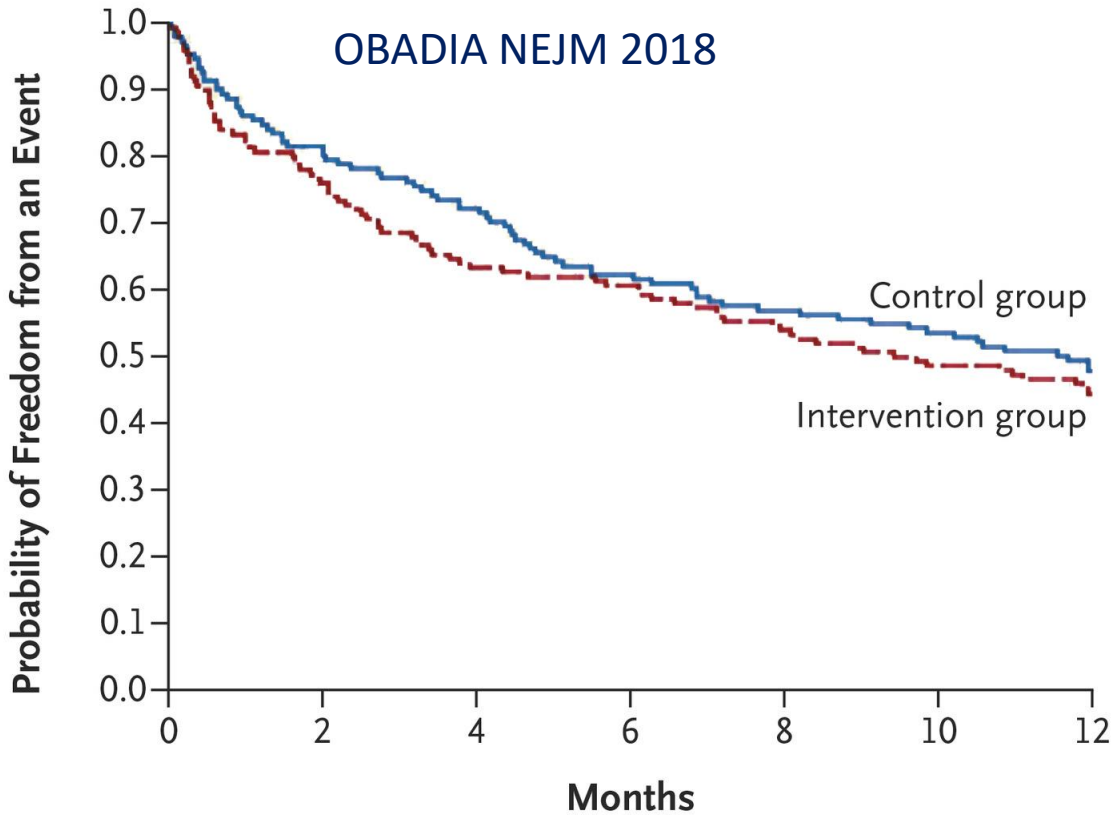
# SECONDARY MR

## IT'S THE HEART THAT MAKES THE VALVE SICK

# 75 Y/O MAN

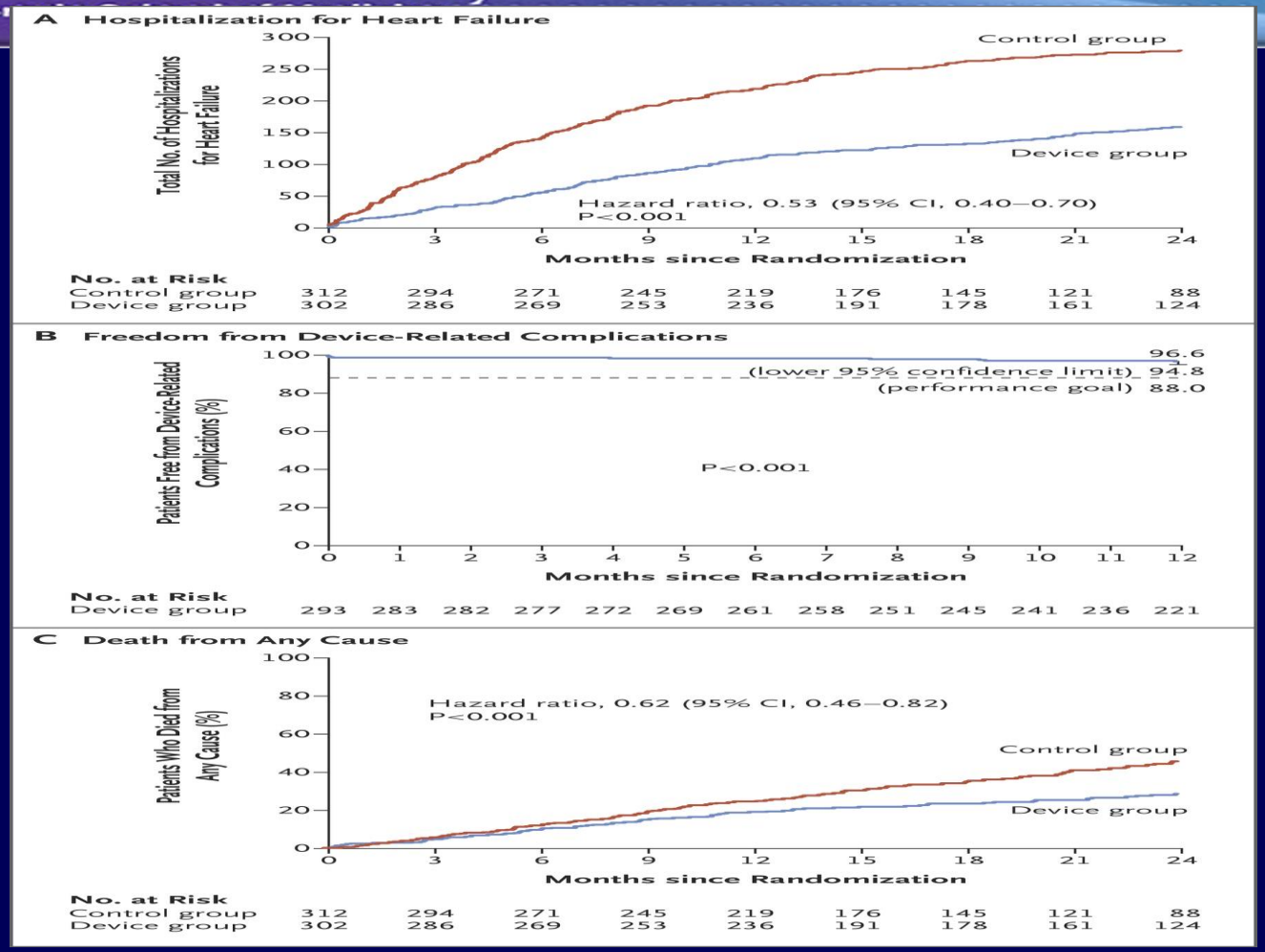
- S/P 3 MIs
- CLASS III HF
- EF 0.22 (POP-OFF CONCEPT IS H--S-S–T)
- SEVERE MR

## OBADIA NEJM 2018



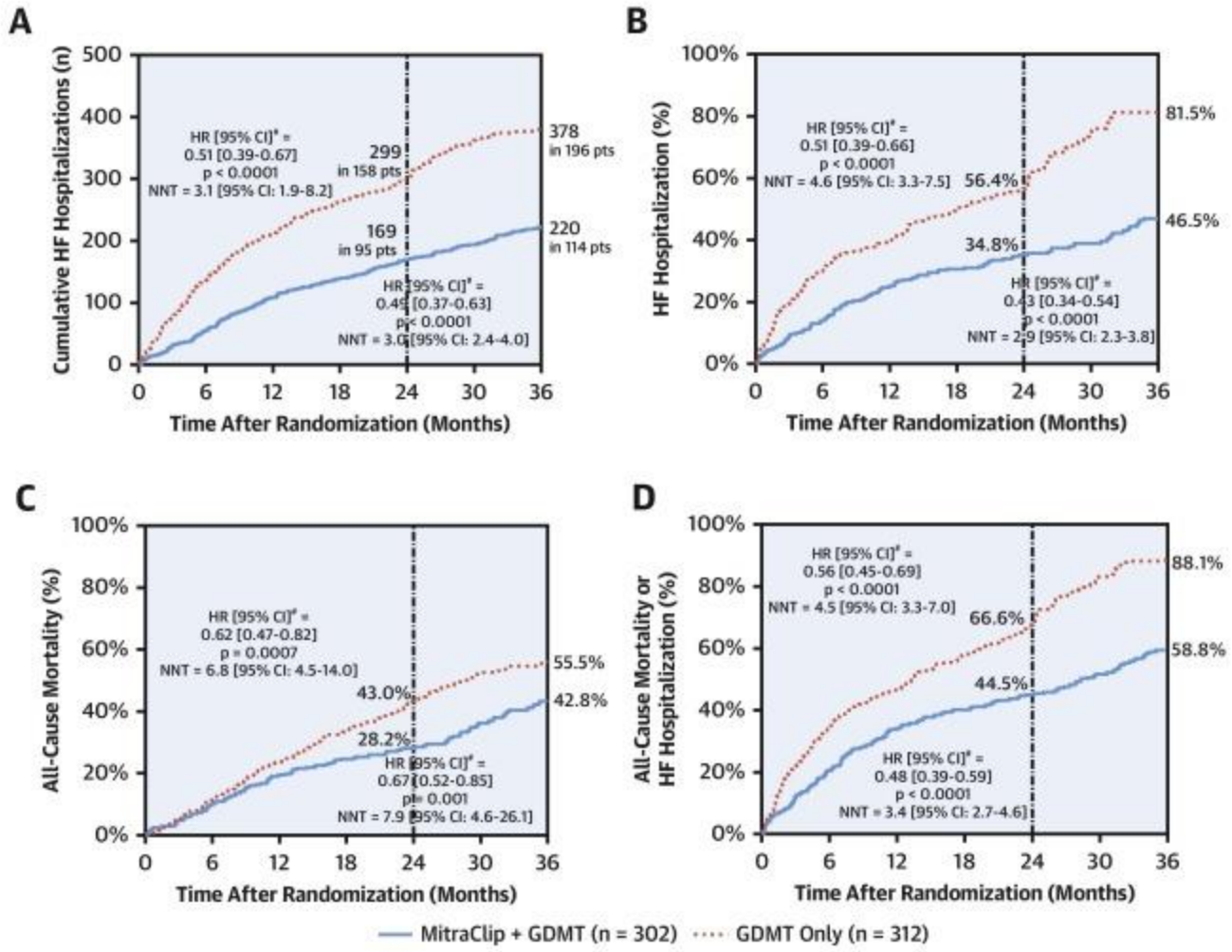

**No. at Risk**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Control group | 152 | 123 | 109 | 94 | 86 | 80 | 73 |
| Intervention group | 151 | 114 | 95 | 91 | 81 | 73 | 67 |




STONE et al NEJM 2019

## CENTRAL ILLUSTRATION: Outcomes Through 3-Year Follow-Up in the Intention-to-Treat Population




Mack, M.J. et al. J Am Coll Cardiol. 2021;77(8):1029-40.

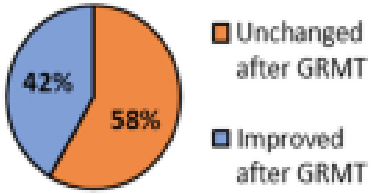
# GDMT WORKS

# Impact of changes in MR severity after GRMT in HF

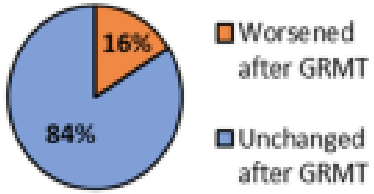
## *An analysis on 1,022 patients from BIOSTAT-CHF*

### *MR evolution after GRMT*

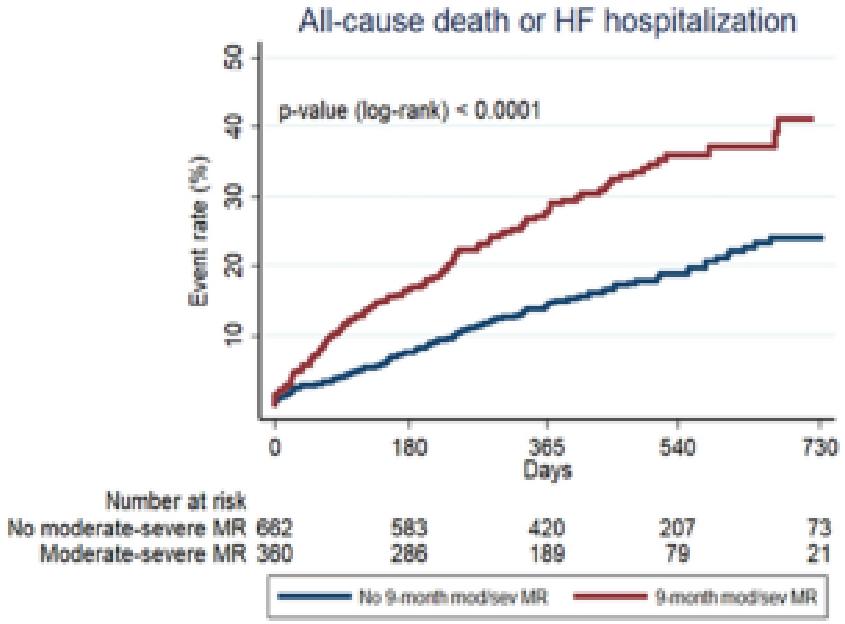
**Moderate-severe MR at baseline (n=462)**




**No moderate-severe MR at baseline (n=560)**




### *Impact of significant MR after GRMT*

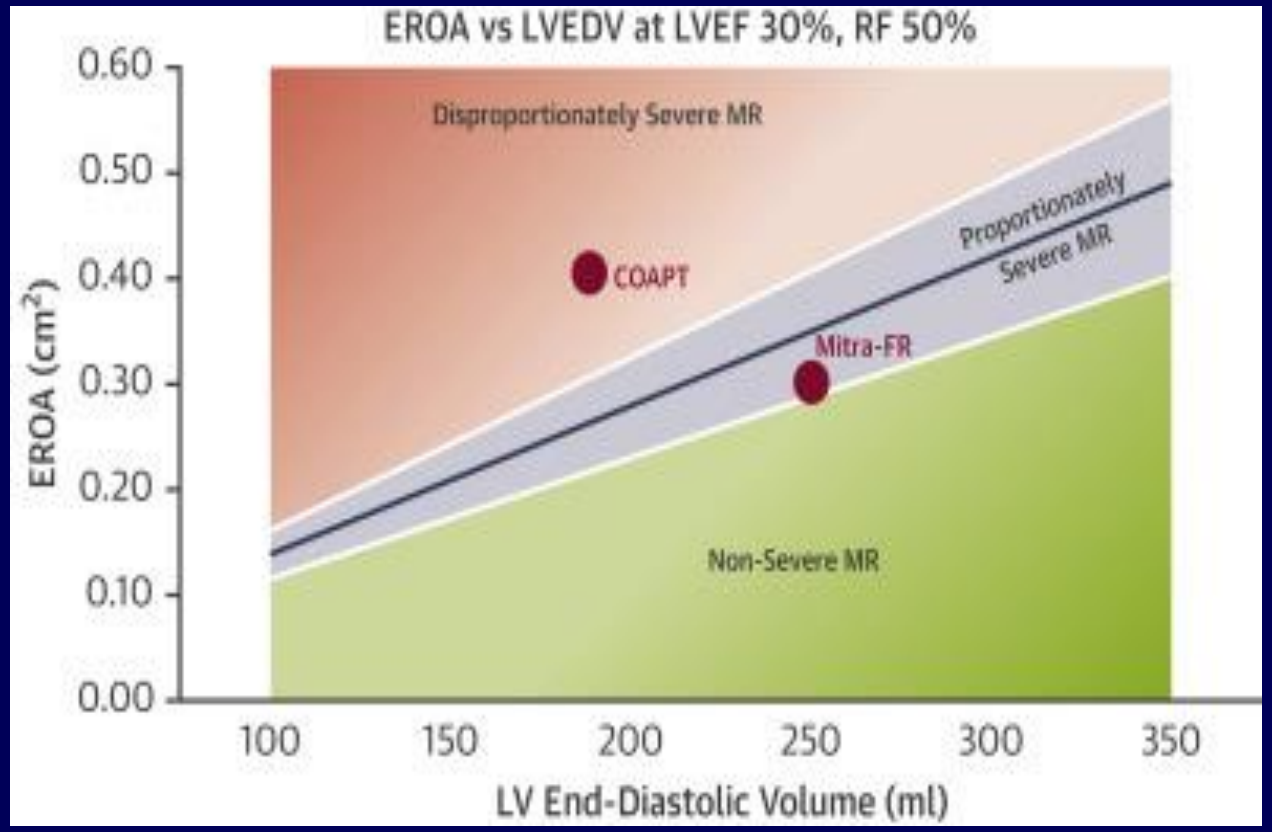



**Adjusted HR 1.85 (95% CI 1.43-2.39)**

### *Independent predictors of significant MR after GRMT*

| | |
|---|---|
| **Age**<br>OR 1.03 (95% CI 1.02-1.05) | **Baseline significant MR**<br>OR 6.96 (95% CI 4.96-9.78) |
| **HFpEF**<br>OR 0.36 (95% CI 0.16-0.85) | **ACEi/ARB up-titration**<br>OR 0.60 (95% CI 0.39-0.93) |

| | MITRA FR | COAPT |
|---|---|---|
| • AGE | 70.5 | 72 |
| • ERO | 0.31 | 0.41 |
| • EDVI | 135 | 100 e |
| • EF | 0.33 | 0.31 |




GRAYBURN et al JACC IMAG 2019

| | MITRA FR | COAPT |
|---|---|---|
| • AGE | 70.5 | 72 |
| • ERO | 0.31 | 0.41 |
| • EDVI | 135 | 100 e |
| • EF | 0.33 | 0.31 |

**Predictors of Clinical Response to Transcatheter Reduction of Secondary Mitral Regurgitation: The COAPT Trial**

Author links open overlay panelPaul A.GrayburnMD[a]AnnaSanninoMD[a]David J.CohenMD, MSc[b]SaibalKarMD[cd]D. ScottLimMD[e]Jacob M.MishellMD[f]Brian K.WhisenantMD[g]Michael J.RinaldiMD[h]Samir R.KapadiaMD[i]VivekRajagopalMD[j]AaronCrowley MA[k]Lak N.KotinkaduwaPhD[k]JoAnnLindenfeldMD[l]William T.AbrahamMD[m]Michael J.MackMD[a]Gregg W.StoneMD JACC 2020

| • | SR (>20K) | R(5-20k) | NON |
|---|---|---|---|
| ERO$cm^2$ | 0.39 | 0.39 | 0.41 |
| EDV ml | 187 | 181 | 198 |
| ERO/EDV | 0.0021 | 0.0021 | 0.0021 |

# BOTTOM LINE (MR)

- IS THIS PRIMARY OR SECONDARY MR?
- PRIMARY: IS IT SEVERE? IF SO: CONSIDER EARLY REPAIR EVEN IF ASYMPTOMATIC. GLS AND BNP HELPFUL
- SECONDARY: GDMT
- STILL SYMPTOMATIC: CLIP

# AR

- CURRENTLY ASYMPTOMATIC Pts
- SURGERY: EF <0.55  ESD >50 mm

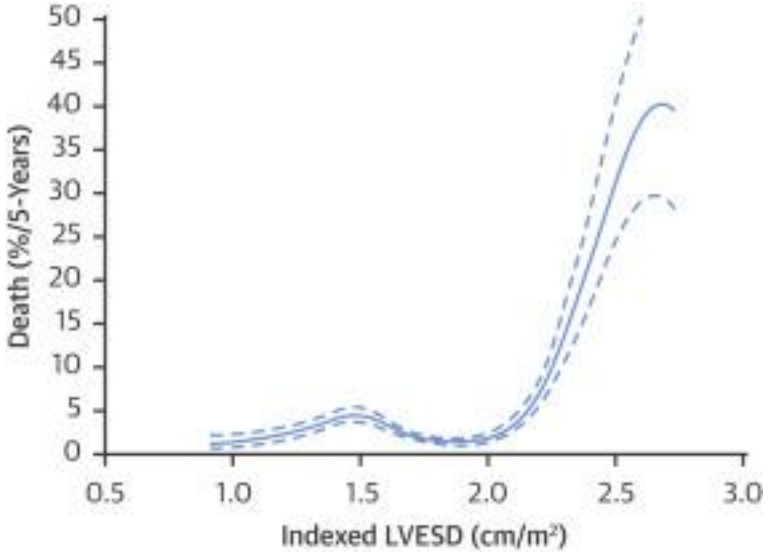



Figure 1. Mortality RiskIn the subgroup that did not undergo aortic valve surgery, in order to assess the possible nonlinear relationship between iLVESD and risk of death, we modeled the covariate predicted iLVESD as a quadratic spline. Based upon the visual a...

Amgad Mentias, Ke Feng, Alaa Alashi, L. Leonardo Rodriguez, A. Marc Gillinov, Douglas R. Johnston, Joseph F. Sabik, Lars G. Svensson, Richard A. Grimm, Brian P. Griffin, Milind Y. Desai

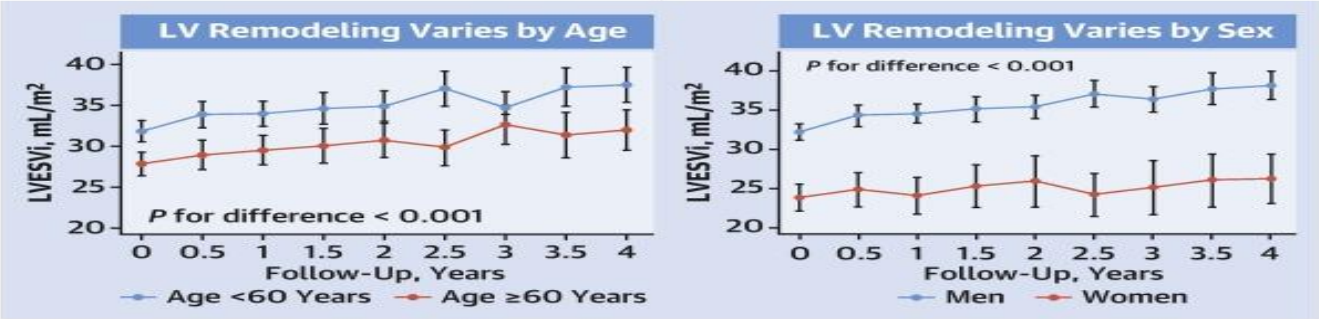
**Fraction**

Journal of the American College of Cardiology, Volume 68, Issue 20, 2016, 2144–2153

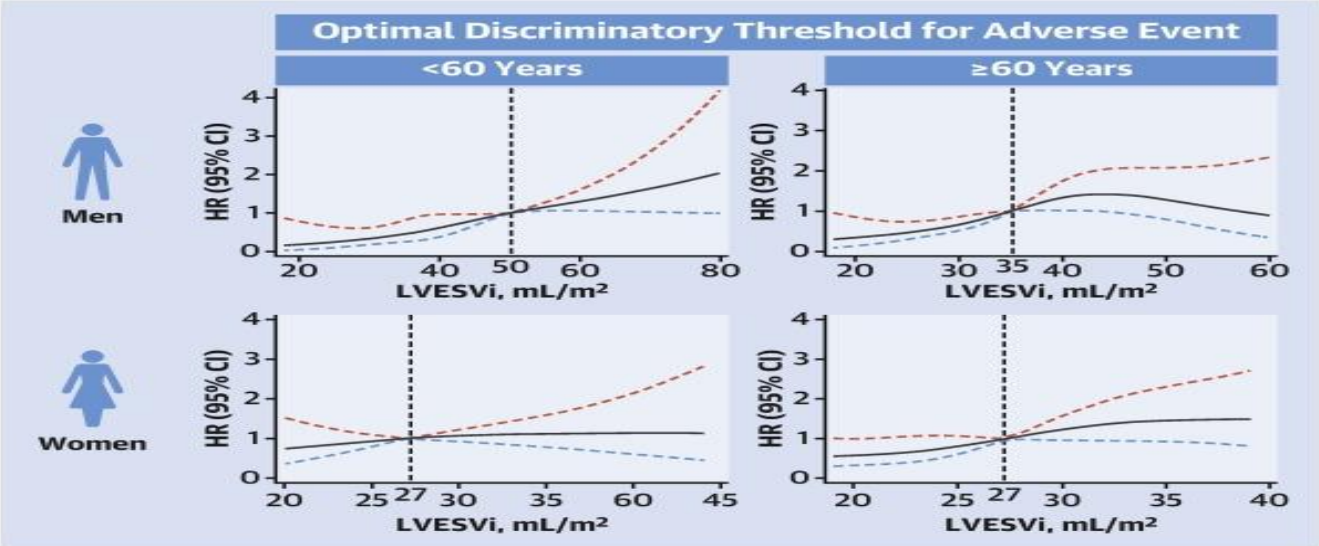
http://dx.doi.org/10.1016/j.jacc.2016.08.045

## CENTRAL ILLUSTRATION: Age and Sex Effect on Remodeling and Outcomes in Aortic Regurgitation

- 525 Patients with severe aortic regurgitation
- Median echocardiogram follow-up of 2.0 years (IQR: 1.0-3.6 years)




- Older patients maintained smaller LV volumes compared to younger patients
- Women maintained smaller LV volumes compared to men




- Rate of adverse events significantly increased at a lower LV volume threshold in older men compared to younger men
- Rate of adverse events significantly increased at a lower LV volume threshold in women compared to men

Akintoye E, et al. J Am Coll Cardiol. 2023;81(15):1474–1487.

AKINTOYE JACC 2023

# "PREDICTIONS ARE HARD TO MAKE ESPECIALLY ABOUT THE FUTURE"

- PREVENTION A REAL POSSIBILITY
- MYOCARDIAL ASSESSMENT
- PROGRESSIVELY SAFER THERAPIES