

# Mitral Regurgitation

## *2016-Lugano*

Maurice E. Sarano, MD  
Mayo Clinic, Rochester, MN,

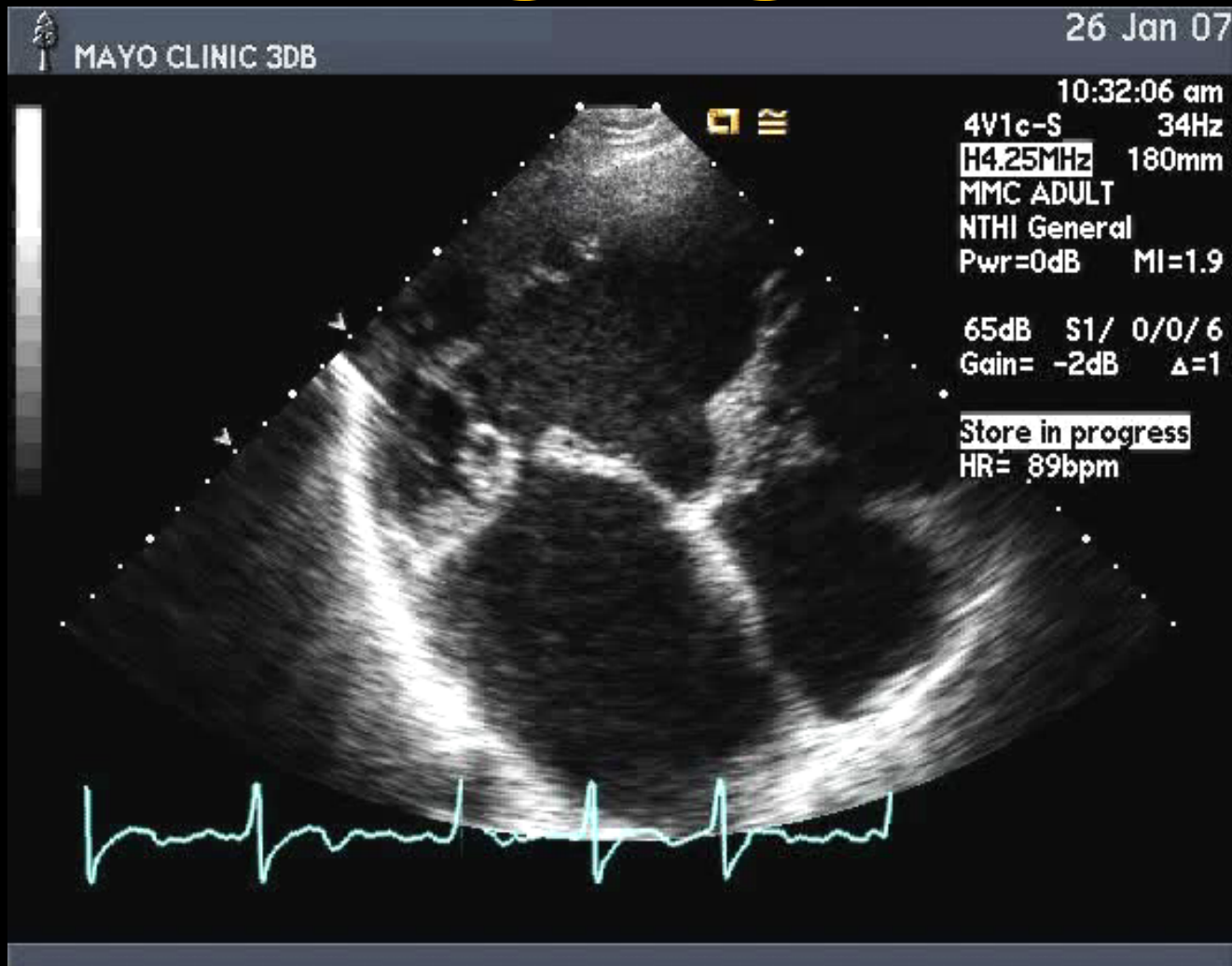


# Mitral Regurgitation

Which of these circumstances does not represent a high-risk MR:

- MVP with MR and LA volume 60 mL/m<sup>2</sup>
- MVP with mid-late systolic MR and ERO 60 mm<sup>2</sup>
- Bileaflet prolapse with regurgitant volume 60 mL
- MVP-MR with end-systolic LV dimension 42 mm
- MVP holosystolic MR and EF 56%

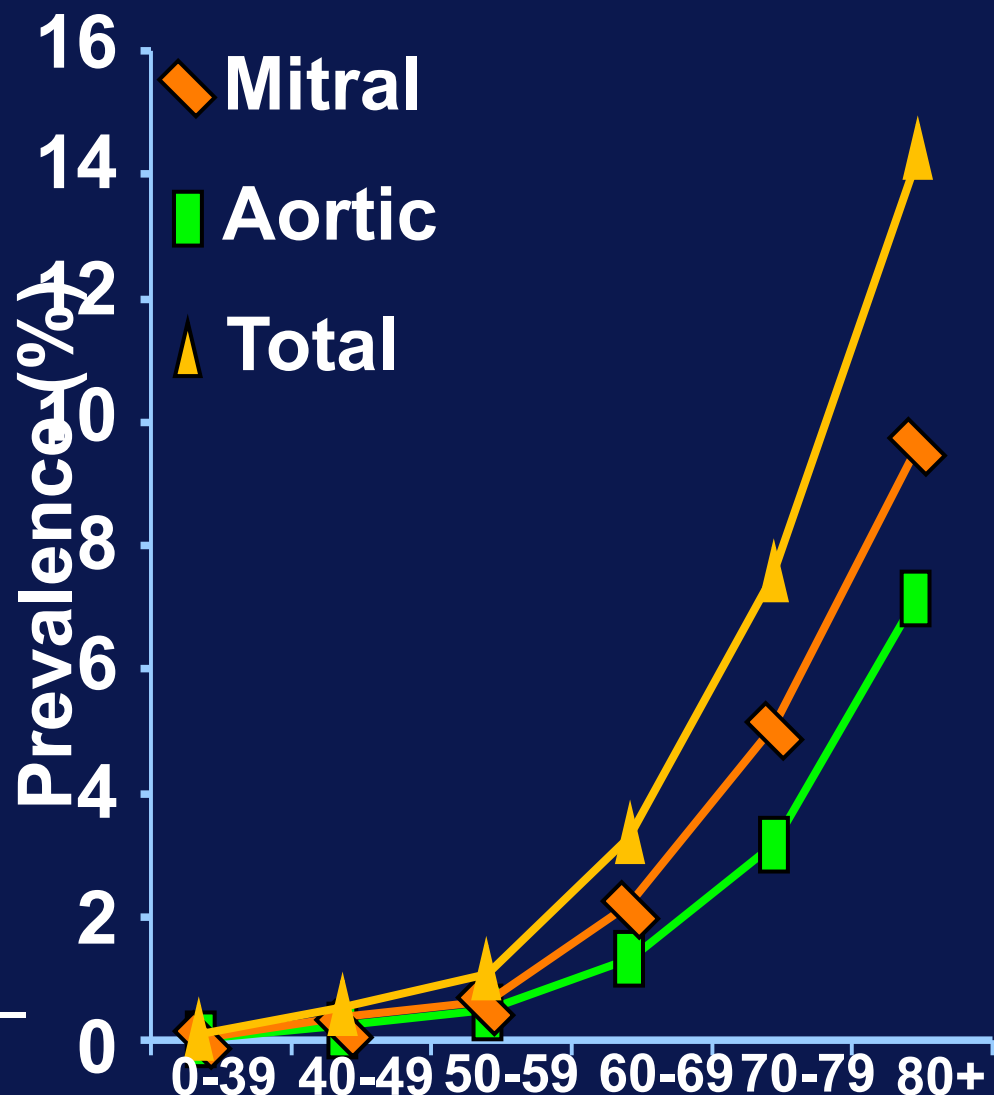
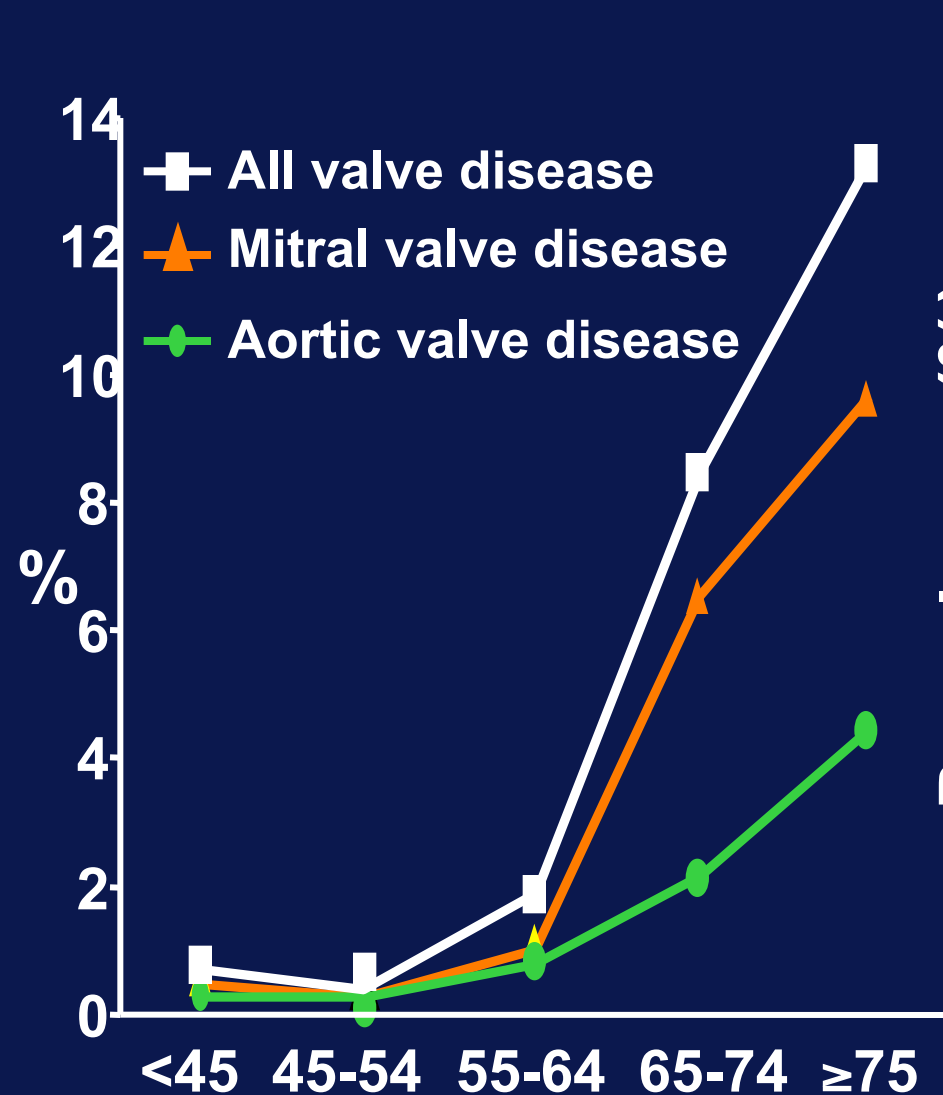
# Why are we interested in Mitral Regurgitation ?



# Prevalence of Valve Diseases

**Population-NIH series**

**Olmsted County**





# Burden of valvular heart diseases: a population-based study



Vuyisile T Nkomo, Julius M Gardin, Thomas N Skelton, John S Gottdiener, Christopher G Scott, Maurice Enriquez-Sarano

**Background** Valvular heart diseases are not usually regarded as a major public-health problem. Our aim was to assess their prevalence and effect on overall survival in the general population.

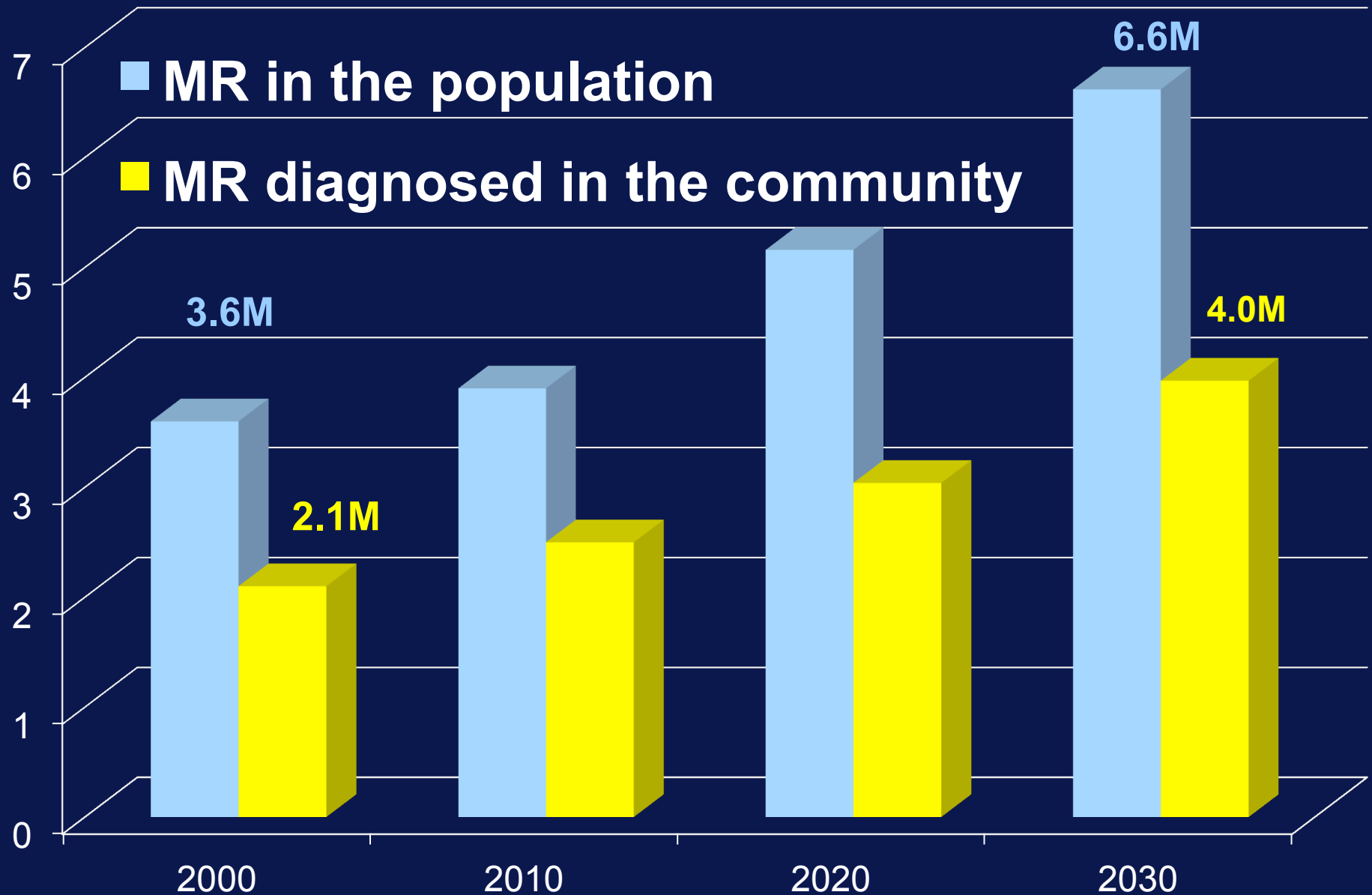
*Lancet* 2006; 368: 1005-11  
Published Online  
August 18, 2006  
DOI:10.1016/S0140-6736(06)69208-8  
See [Comment](#) page 969  
Mayo Clinic, Rochester, MN,

**Methods** We pooled population-based studies to obtain data for 11911 randomly selected adults from the general population who had been assessed prospectively with echocardiography. We also analysed data from a community study of 16 501 adults who had been assessed by clinically indicated echocardiography.

	Population					p value for trend	Frequency adjusted to 2000 US adult population
	Age (years)						
	18-44	45-54	55-64	65-74	≥75		
Participants (n)	4351	696	1240	3879	1745	..	209 128 094
Male, n (%)	1959 (45%)	258 (37%)	415 (33%)	1586 (41%)	826 (47%)	..	100 994 367 (48%)
Mitral regurgitation (n=449)	23, 0.5% (0.3-0.8)	1, 0.1% (0-0.8)	12, 1.0% (0.5-1.8)	250, 6.4% (5.7-7.3)	163, 9.3% (8.1-10.9)	<0.0001	1.7% (1.5-1.9)
Mitral stenosis (n=15)	0, 0% (0-0.1)	1, 0.1% (0-0.8)	3, 0.2% (0.1-0.7)	7, 0.2% (0.1-0.4)	4, 0.2% (0.1-0.6)	0.006	0.1% (0.02-0.2)
Aortic regurgitation (n=90)	10, 0.2% (0.1-0.4)	1, 0.1% (0-0.8)	8, 0.7% (0.3-1.3)	37, 1.0% (0.7-1.3)	34, 2.0% (1.4-2.7)	<0.0001	0.5% (0.3-0.6)
Aortic stenosis (n=102)	1, 0.02% (0-0.1)	1, 0.1% (0-0.8)	2, 0.2% (0.6-1.9)	50, 1.3% (1.0-1.7)	48, 2.8% (2.1-3.7)	<0.0001	0.4% (0.3-0.5)

	Community					p value for trend
	Age (years)					
	18-44	45-54	55-64	65-74	≥75	
Residents, n	49 957	16 306	10 241	6686	6663	..
Residents examined, n (% men)	4310 (38%)	2737 (48%)	2847 (53%)	2798 (53%)	3851 (41%)	..
Mitral regurgitation (n=874)	57, 0.1% (0.1-0.2)	62, 0.4% (0.3-0.5)	93, 0.9% (0.7-1.1)	186, 2.8% (2.4-3.3)	476, 7.1% (6.5-7.8)	<0.0001
Mitral stenosis (n=33)	5, 0.01% (0-0.02)	3, 0.02% (0-0.05)	3, 0.03% (0.01-0.1)	8, 0.1% (0.05-0.2)	14, 0.2% (0.1-0.4)	<0.0001
Aortic regurgitation (n=282)	55, 0.1% (0.08-0.1)	38, 0.2% (0.2-0.3)	33, 0.3% (0.2-0.5)	41, 0.6% (0.4-0.8)	115, 1.7% (1.4-2.1)	<0.0001
Aortic stenosis (n=547)	51, 0.1% (0.08-0.1)	35, 0.2% (0.2-0.3)	57, 0.6% (0.4-0.7)	96, 1.4% (1.2-1.8)	308, 4.6% (4.1-5.2)	<0.0001

# MR in the Adult Population



**What is the first task  
in patients with MR ?**

**Recognize the  
difference**

**Functional/  
OrganicMR**

# Mitral Regurgitation

**MR**

**Serious Valve  
Lesions**

**Structurally  
Normal Valve**

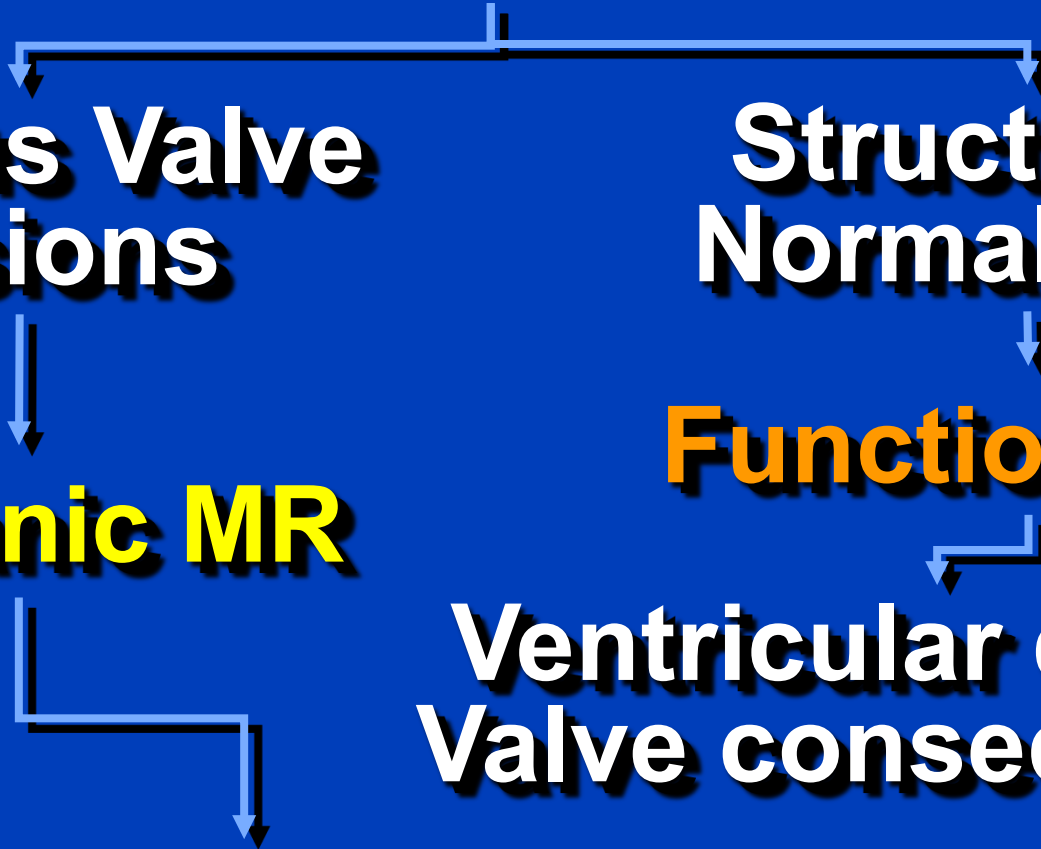
**Organic MR**

**Functional MR**

**Ventricular disease  
Valve consequences**

**Valve Disease**

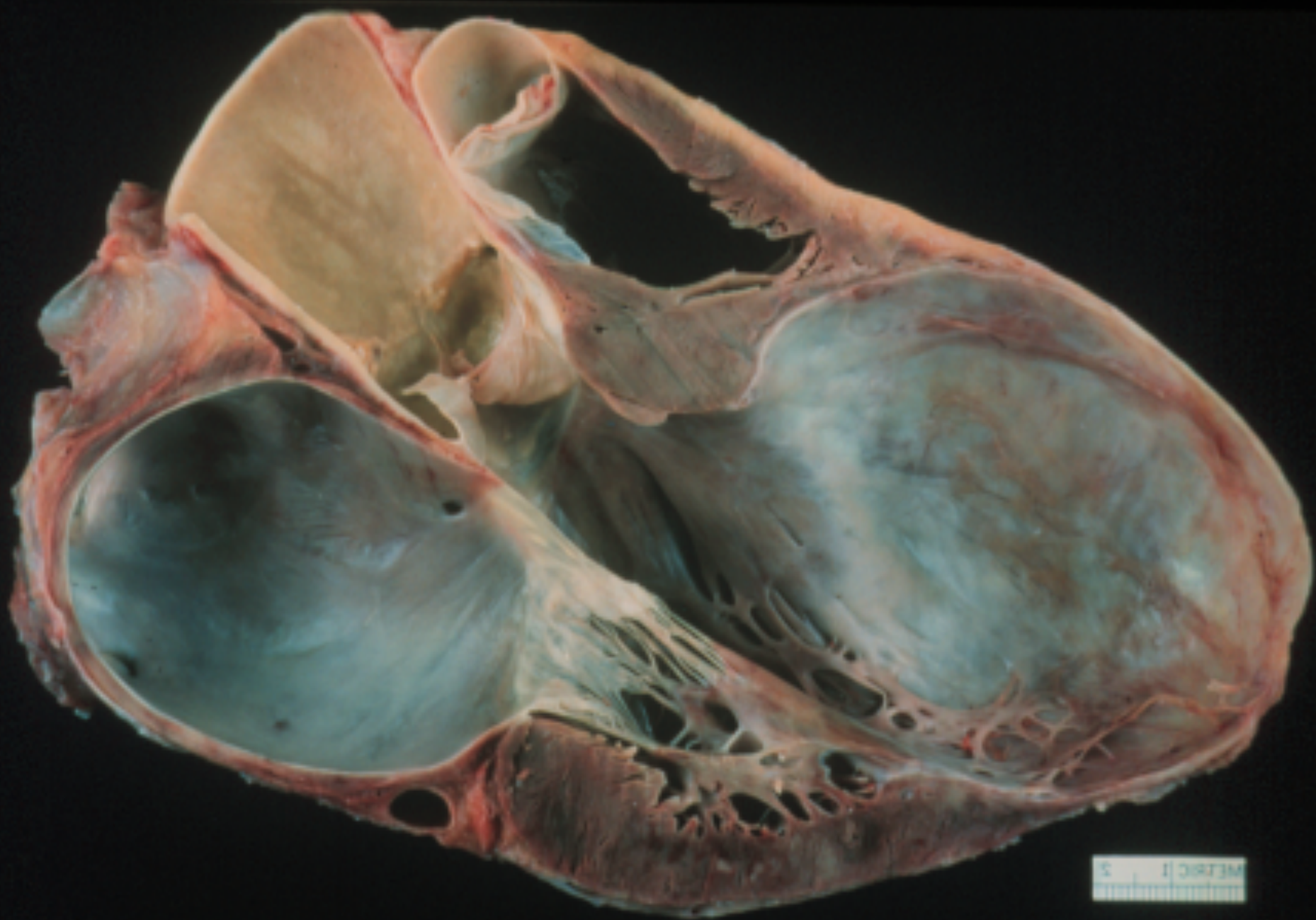
**Ventricular consequences**





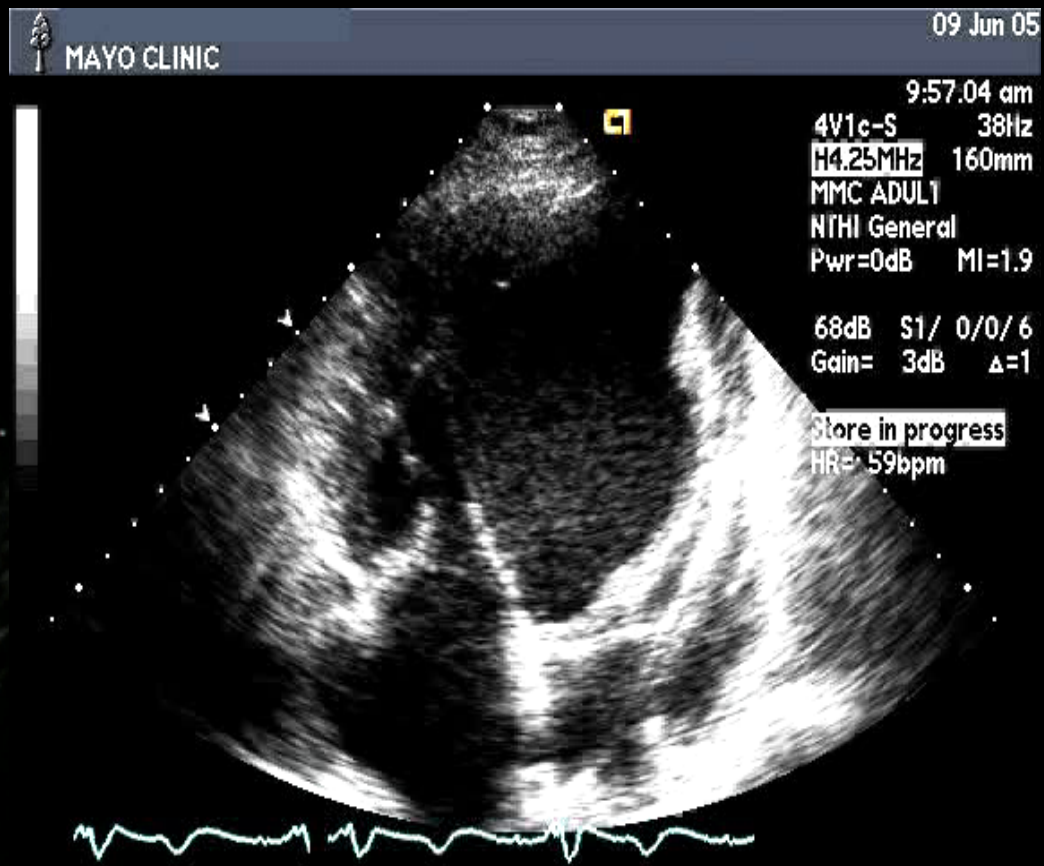
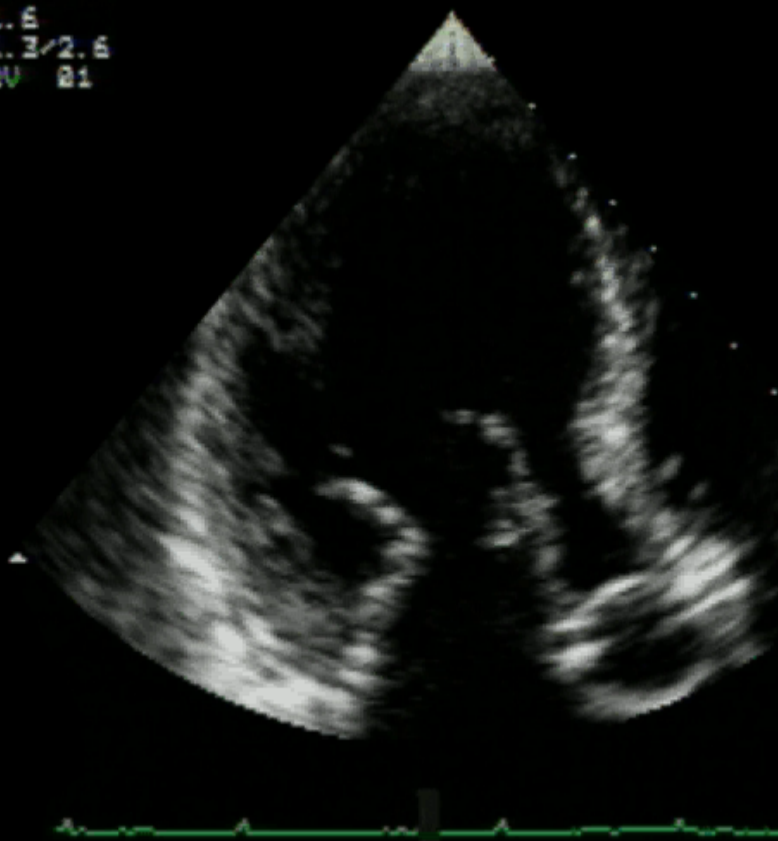


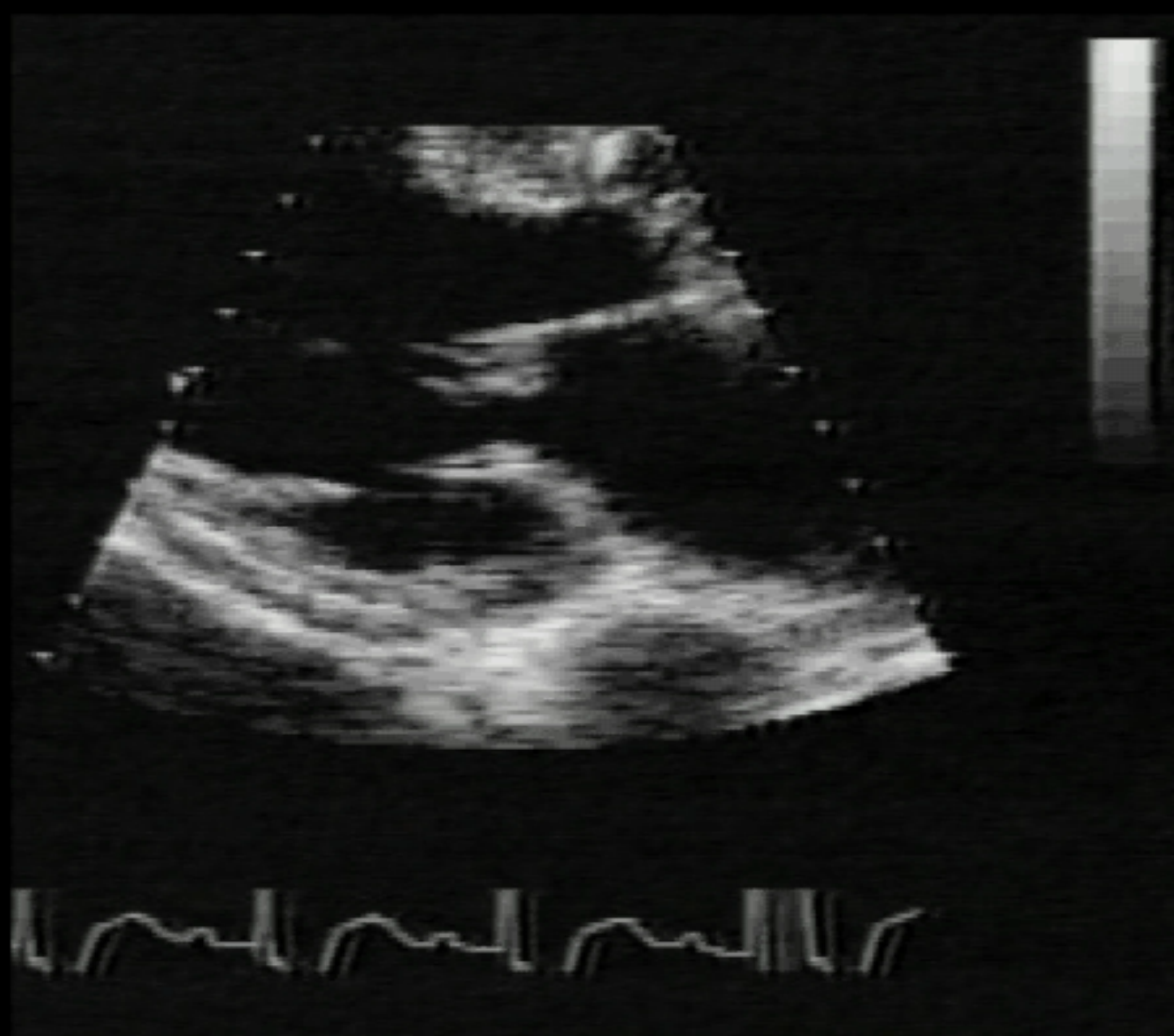




# MR Assessment which disease?

MI: 1.6  
S3 1.3/2.6  
Q1 NOV Q1





# Mitral Regurgitation

Patients with enlarged LV ( $\geq 60$  mm)

	Organic MR	Ischemic MR
RVol, mL	104 $\pm$ 41	26 $\pm$ 16
RF, %	58 $\pm$ 12	29 $\pm$ 14
ERO, mm <sup>2</sup>	71 $\pm$ 32	19 $\pm$ 13
EF, %	65 $\pm$ 9	29 $\pm$ 8

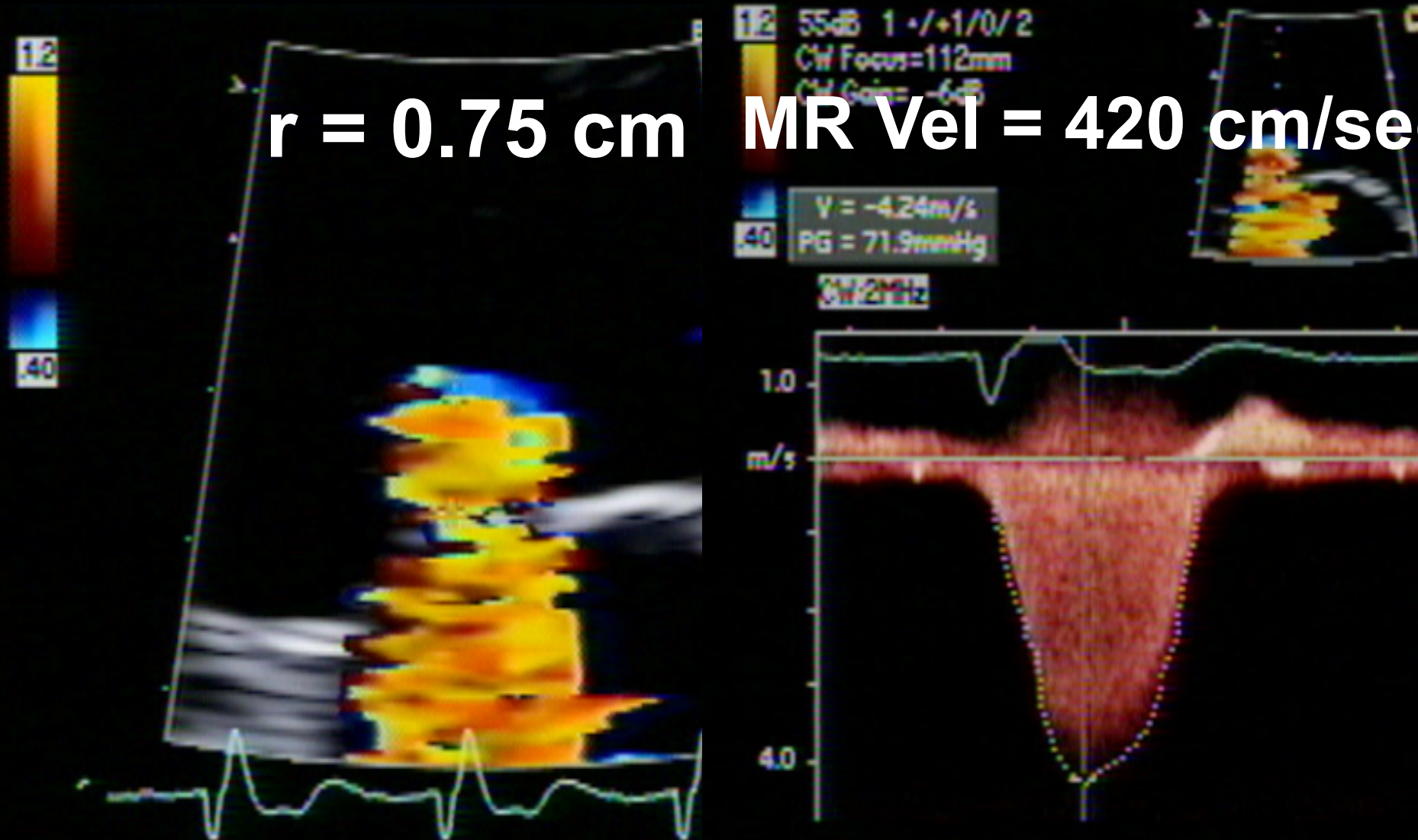


# Functional MR-Quantitation

ERO = 0.34 cm<sup>2</sup> RVol = 46 mL

$r = 0.75$  cm

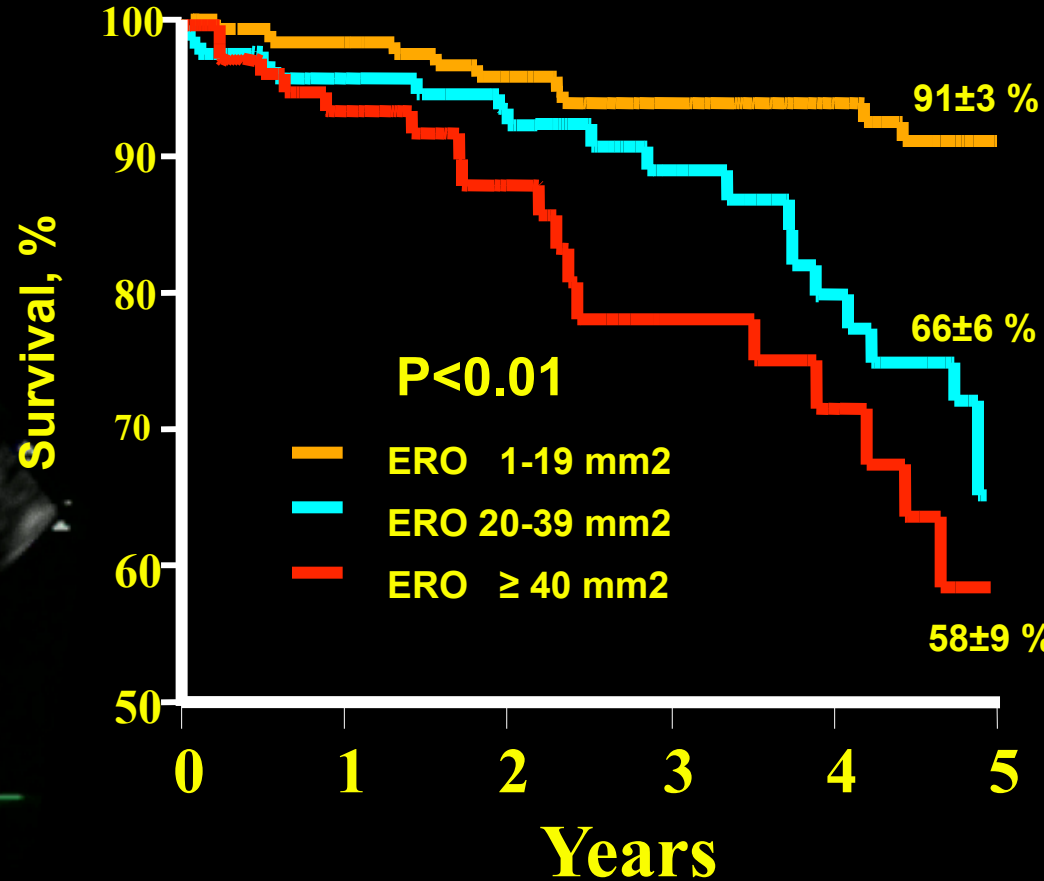
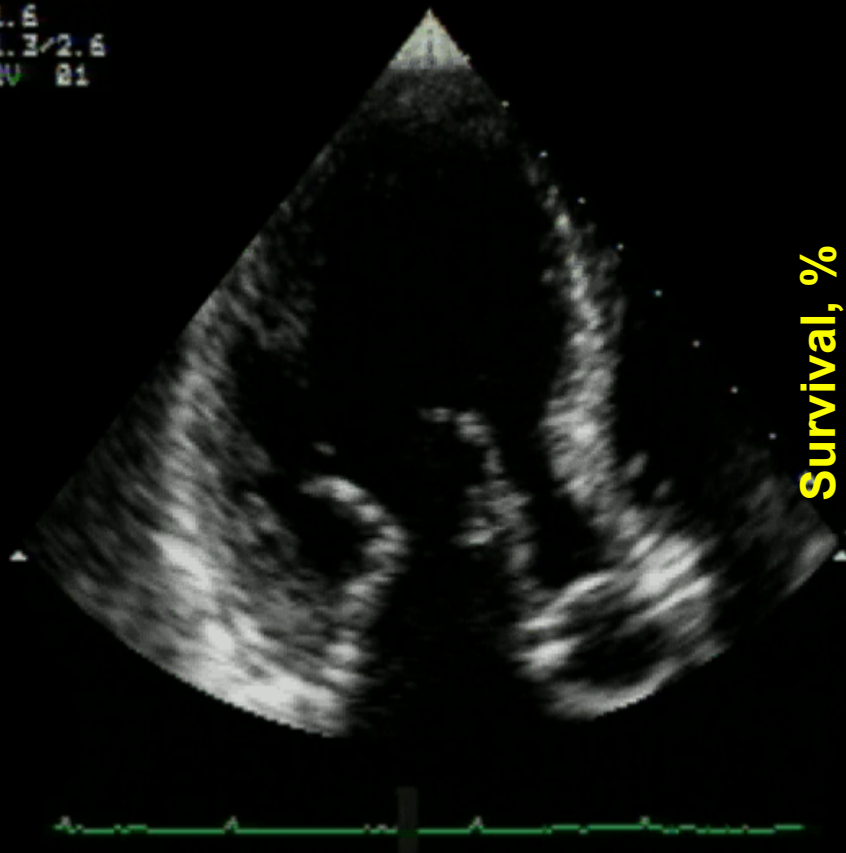
MR Vel = 420 cm/sec



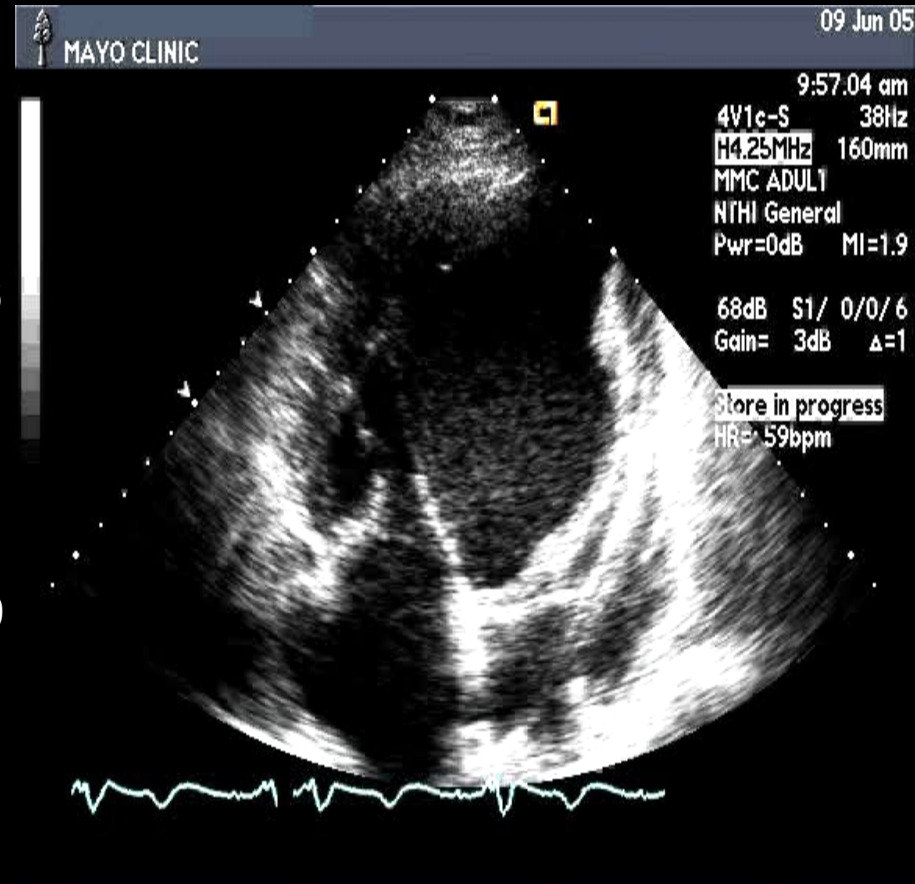
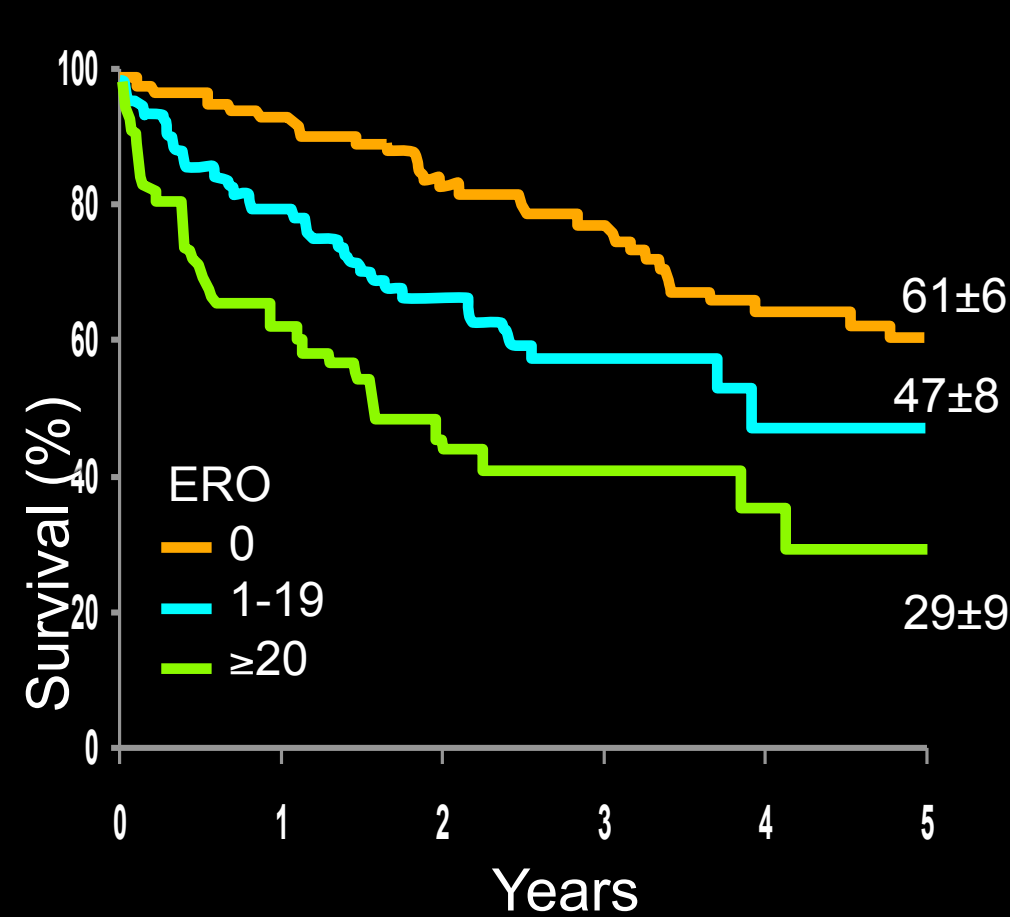


# MR Assessment which disease?

MI: 1.6  
S3 1.3/2.6  
01 NOV 01



# MR Assessment which disease?



# FMR Management

FMR is a low-volume,  
poor outcome MR, which  
has its own grading scale

What to do ?

## ORIGINAL ARTICLE

## Mitral-Valve Repair versus Replacement

**Table 2.** Clinical End Points, Serious Adverse Events, and Hospitalizations at 30 Days and 1 Year.

Clinical end point	30 Days			1 Year		
	Repair Group (N=126)	Replacement Group (N=125)	P Value	Repair Group (N=126)	Replacement Group (N=125)	P Value
	<i>no. of patients (%)</i>			<i>no. of patients (%)</i>		
Death	2 (1.6)	5 (4.0)	0.26	18 (14.3)	22 (17.6)	0.47
Stroke	3 (2.4)	4 (3.2)	0.72	6 (4.8)	5 (4.0)	0.77
Worsening in NYHA class of 1	10 (7.9)	10 (8.0)	0.99	6 (4.8)	6 (4.8)	0.99
Rehospitalization for heart failure	3 (2.4)	7 (5.6)	0.22	17 (13.5)	14 (11.2)	0.58
Mitral-valve reoperation	1 (0.8)	0	1.0	3 (2.4)	0	0.25
Composite major adverse event*	19 (15.1)	24 (19.2)	0.39	41 (32.5)	42 (33.6)	0.86
	<i>no. of events (rate/100 patient-yr)</i>			<i>no. of events (rate/100 patient-yr)</i>		

# **Coronary Artery Bypass Surgery With or Without Mitral Valve Annuloplasty in Moderate Functional Ischemic Mitral Regurgitation**

## **Final Results of the Randomized Ischemic Mitral Evaluation (RIME) Trial**

K.M. John Chan, FRCS CTh; Prakash P. Punjabi, FRCS CTh; Marcus Flather, MD, FRCP; Riccardo Wage, DCR (R); Karen Symmonds, DCR (R); Isabelle Roussin, MD; Shelley Rahman-Haley, MD, FRCP; Dudley J. Pennell, MD, FRCP; Philip J. Kilner, MD, PhD; Gilles D. Dreyfus, MD; John R. Pepper, MChir, FRCS; for the RIME Investigators

**Patients with CAD referred to CABG with moderate MR with EF >30%, NYHA I-III**

**Randomized 1/1 to CABG alone or CABG + Mitral repair**





# Coronary Artery Bypass Surgery With or Without Mitral Valve Annuloplasty in Moderate Functional Ischemic Mitral Regurgitation

## Final Results of the Randomized Ischemic Mitral Evaluation (RIME) Trial

K.M. John Chan, FRCS CTh; Prakash P. Punjabi, FRCS CTh; Marcus Flather, MD, FRCP; Riccardo Wage, DCR (R); Karen Symmonds, DCR (R); Isabelle Roussin, MD; Shelley Rahman-Haley, MD, FRCP; Dudley J. Pennell, MD, FRCP; Philip J. Kilner, MD, PhD; Gilles D. Dreyfus, MD; John R. Pepper, MChir, FRCS; for the RIME Investigators

Variable	CABG (n=39)	CABG+MVR (n=34)	Mitral regurgitation*		
Age, y	70.4±7.9	70.9±10.5	Effective regurgitant orifice area, cm <sup>2</sup>	0.18±0.10	0.21±0.09
Female sex, n (%)	10 (26)	9 (26)	Regurgitant volume, mL/beat	30.3±13.8	35.5±13.3
Body mass index	27.4±5.0	25.3±6.4	Vena contracta width, cm	0.4±0.1	0.4±0.1
Medical history, n (%)			Tricuspid regurgitation,* n (%)		
Atrial fibrillation	4 (10)	2 (6)	None	18 (46)	12 (36)
Previous myocardial infarction	28 (72)	25 (74)	Mild	18 (46)	18 (52)
Previous stroke	1 (3)	2 (6)	Moderate	3 (8)	4 (12)
Peripheral vascular disease	5 (13)	4 (12)	Left ventricle*		
Hypertension	23 (59)	17 (50)	LVEDD, mm	43.3±9.5	45.7±7.4
Diabetic on treatment	15 (38)	12 (35)	LVEDD, mm	56.5±12.0	56.5±12.6
Chronic pulmonary disease	1 (3)	2 (6)	Ejection fraction, %	40.3±16.1	40.0±17.3
NYHA class, n (%)					
I	1 (3)	1 (3)			
II	25 (64)	22 (65)			
III	13 (33)	11 (32)			

# Coronary Artery Bypass Surgery With or Without Mitral Valve Annuloplasty in Moderate Functional Ischemic Mitral Regurgitation

## Final Results of the Randomized Ischemic Mitral Evaluation (RIME) Trial

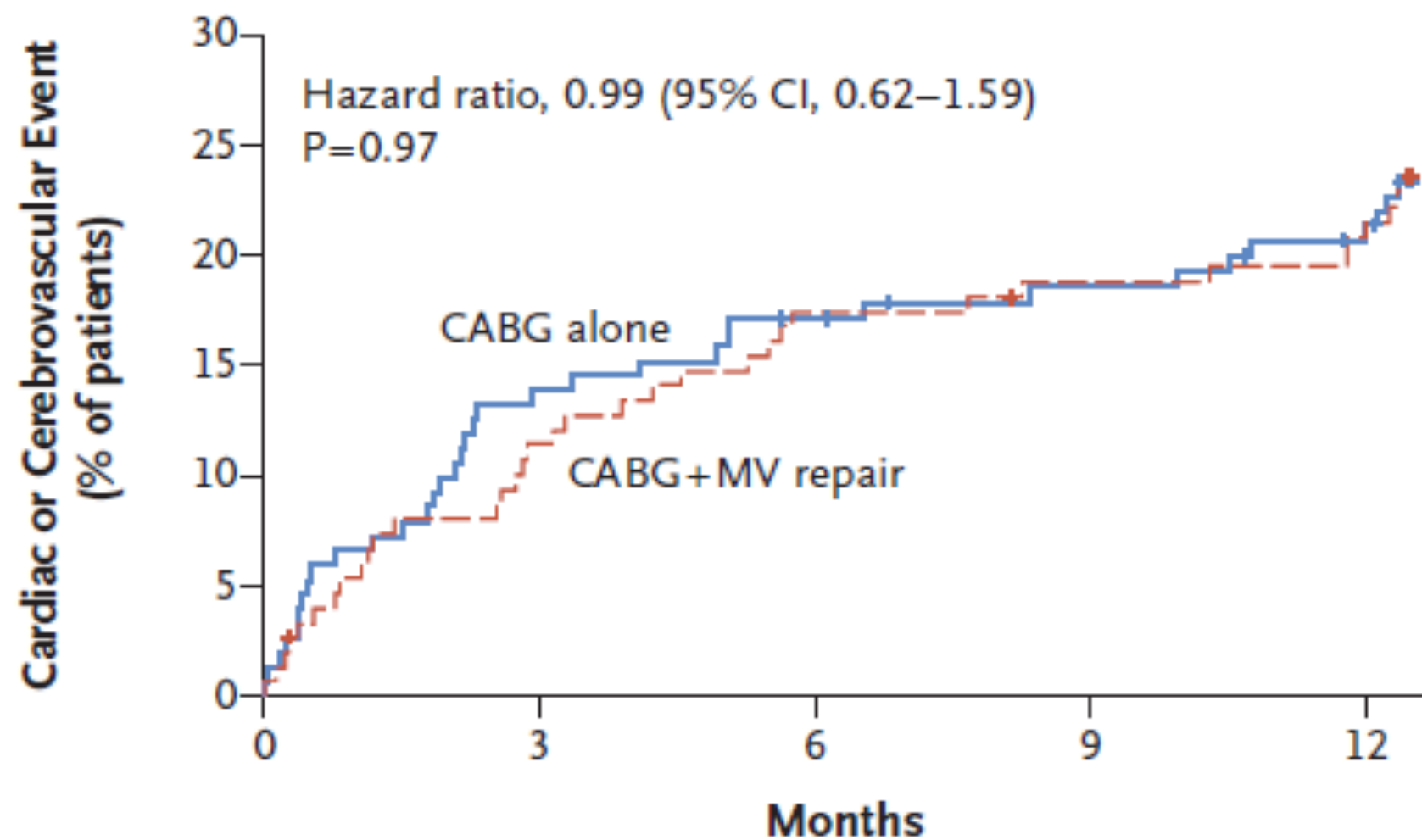
K.M. John Chan, FRCS CTh; Prakash P. Punjabi, FRCS CTh; Marcus Flather, MD, FRCP; Riccardo Wage, DCR (R); Karen Symmonds, DCR (R); Isabelle Roussin, MD; Shelley Rahman-Haley, MD, FRCP; Dudley J. Pennell, MD, FRCP; Philip J. Kilner, MD, PhD; Gilles D. Dreyfus, MD; John R. Pepper, MChir, FRCS; for the RIME Investigators

# Results

**Table 3. Study End Points at 1 Year**

End Points	CABG (n=32)			CABG+MVR (n=27)			P Value*
	Baseline	1 Year	Δ	Baseline	1 Year	Δ	
Primary end point							
Peak VO <sub>2</sub> , ml/kg/min	15.1±3.3	15.9±2.5	0.8±2.9	14.8±3.2	18.1±2.9	3.3±2.3	<0.001
Secondary end points							
LV ESVI, ml/m <sup>2</sup> †	71.8±16.1	67.4±20.4	−4.4±17.4	78.4±26.5	56.2±14.9	−22.2±25.6	0.002
MR volume, ml/beat†	31.9±14.8	22.7±14.6	−9.2±19.1	35.4±24.0	7.2±3.5	−28.2±24.6	0.001
BNP (pg/ml)	681.4±197.3	286.7±132.0	−394.7±213.6	748.1±158.3	190.7±117.8	−557.4±182.9	0.003

## ORIGINAL ARTICLE



# The COAPT trial

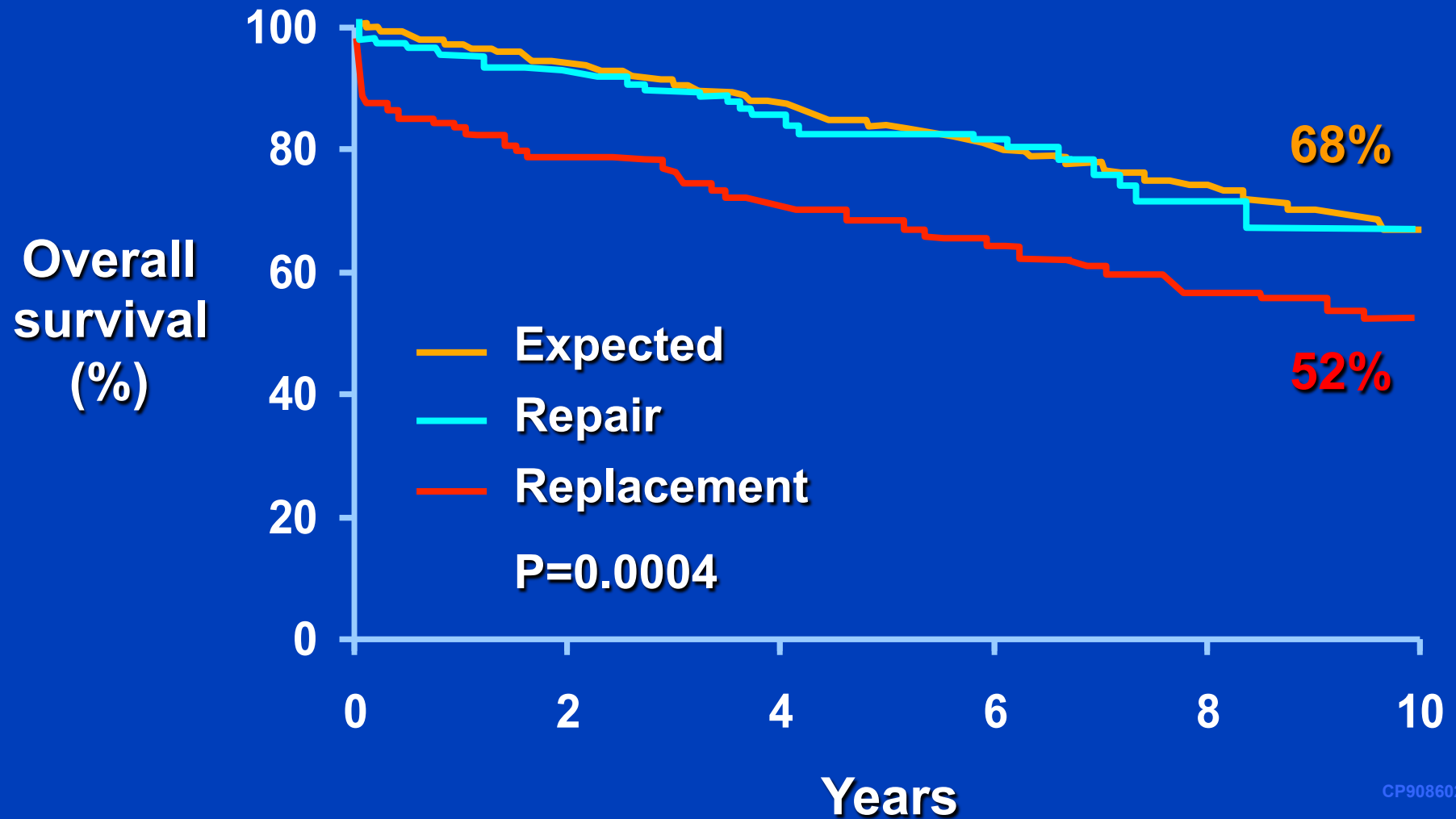
Truly FMR: EF:20-50%,  
Structurally Normal valve,  
Quantified FMR, Low-risk Intervention



# Organic MR



# MR: Mitral Valve Repair

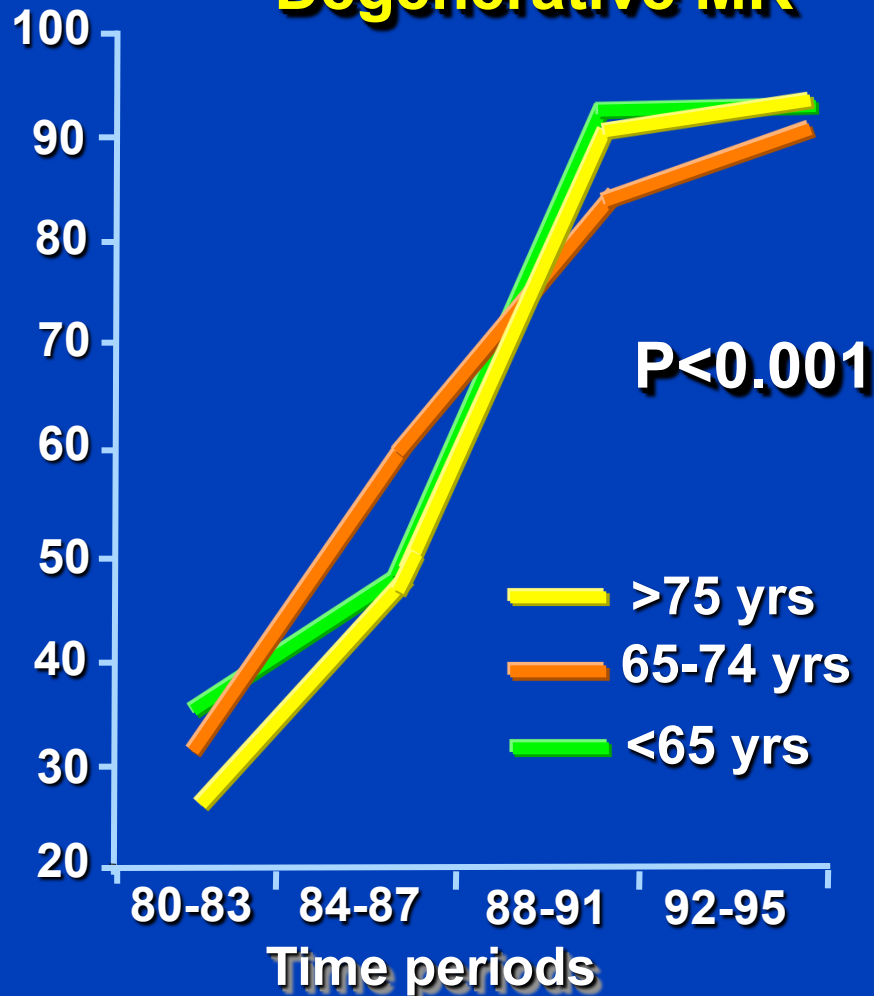


# MR Surgery in the Elderly

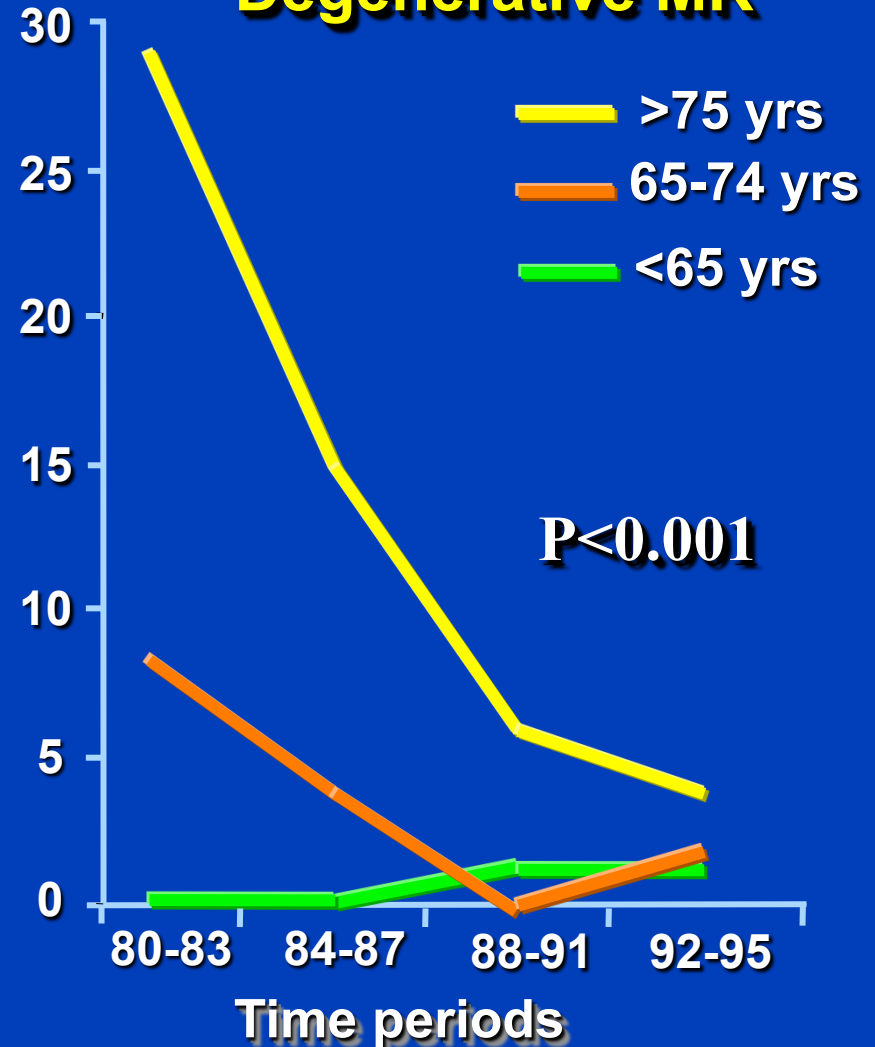
## Feasibility of Valve Repair

## Operative Mortality

### Degenerative MR



### Degenerative MR



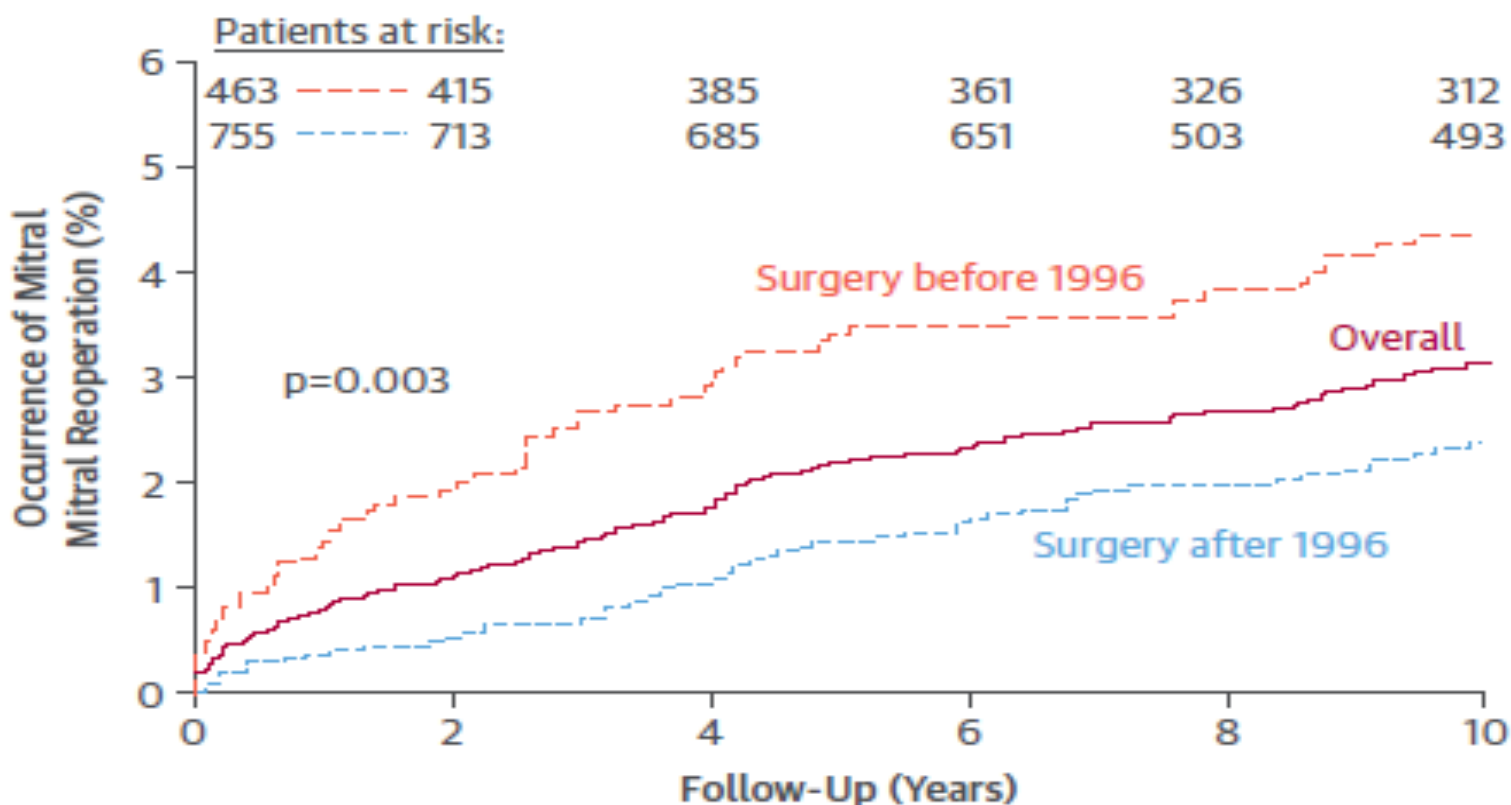
# Effect of Recurrent Mitral Regurgitation Following Degenerative Mitral Valve Repair

## Long-Term Analysis of Competing Outcomes

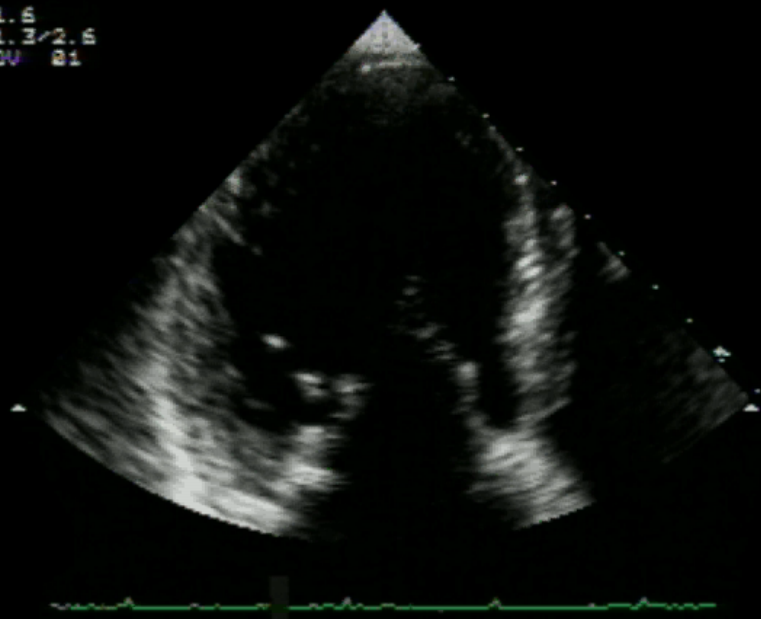


Rakesh M. Suri, MD, DPHIL,<sup>a</sup> Marie-Annick Clavel, DVM, PhD,<sup>b,c</sup> Hartzell V. Schaff, MD,<sup>a</sup> Hector I. Michelena, MD,<sup>b</sup> Marianne Huebner, PhD,<sup>d</sup> Rick A. Nishimura, MD,<sup>b</sup> Maurice Enriquez-Sarano, MD<sup>d</sup>

**FIGURE 4** Incidence of Mitral Valve Reoperation According to Study Period



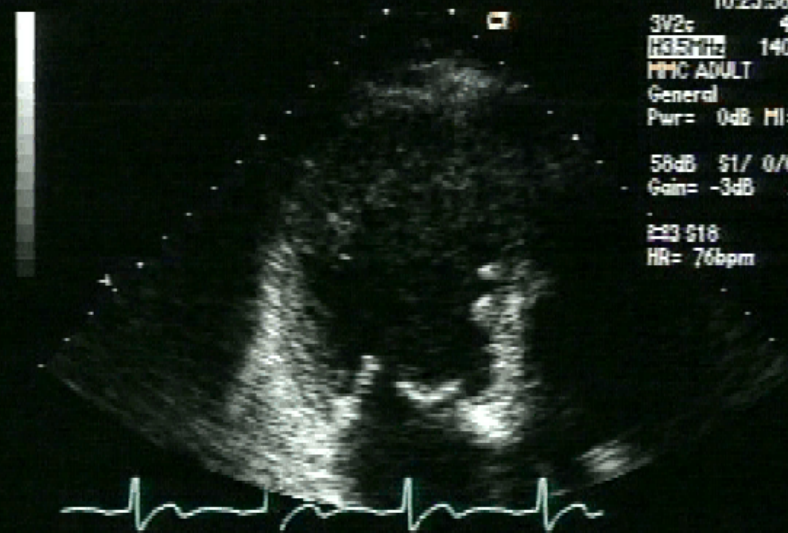
MI: 1.6  
S3 1.3/2.6  
Q1 NOV 81



MAYO CLINIC 52624

13 Apr 00

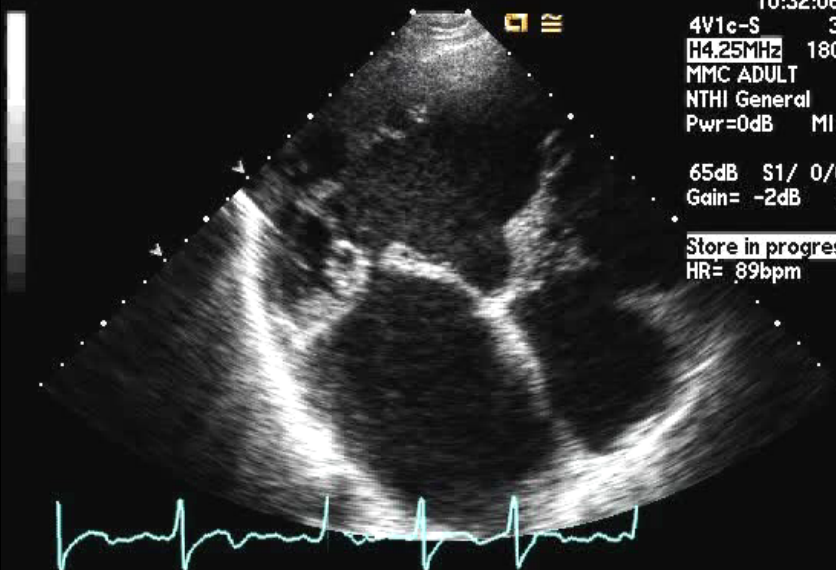
10:23:58 am  
3V2c 42Hz  
H3.5MHz 140mm  
MMC ADULT  
General  
Pwr= 0dB MI=1.3  
58dB S1/ 0/0/6  
Gain= -3dB Δ=1  
HR= 76bpm



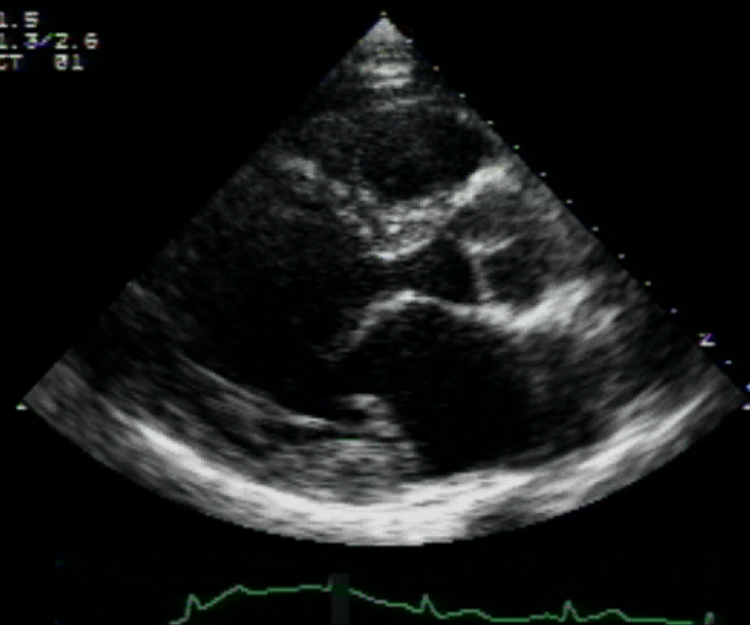
MAYO CLINIC 3DB

26 Jan 07

10:32:06 am  
4V1c-S 34Hz  
H4.25MHz 180mm  
MMC ADULT  
NTHI General  
Pwr=0dB MI=1.9  
65dB S1/ 0/0/6  
Gain= -2dB Δ=1  
Store in progress  
HR= 89bpm



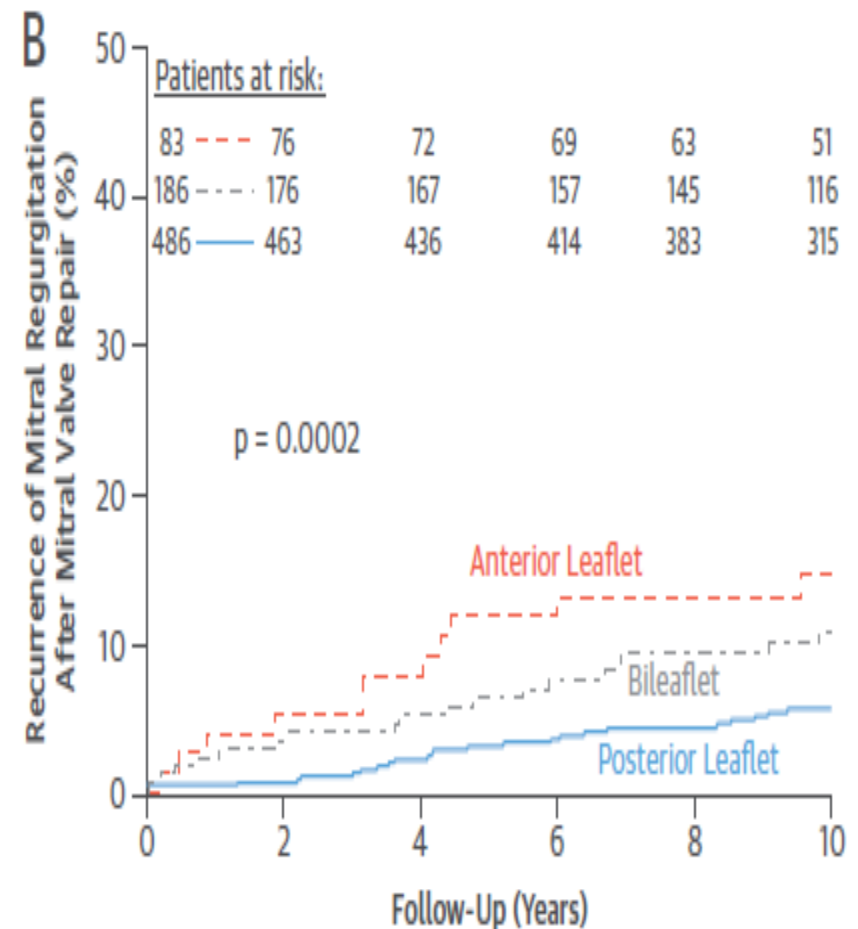
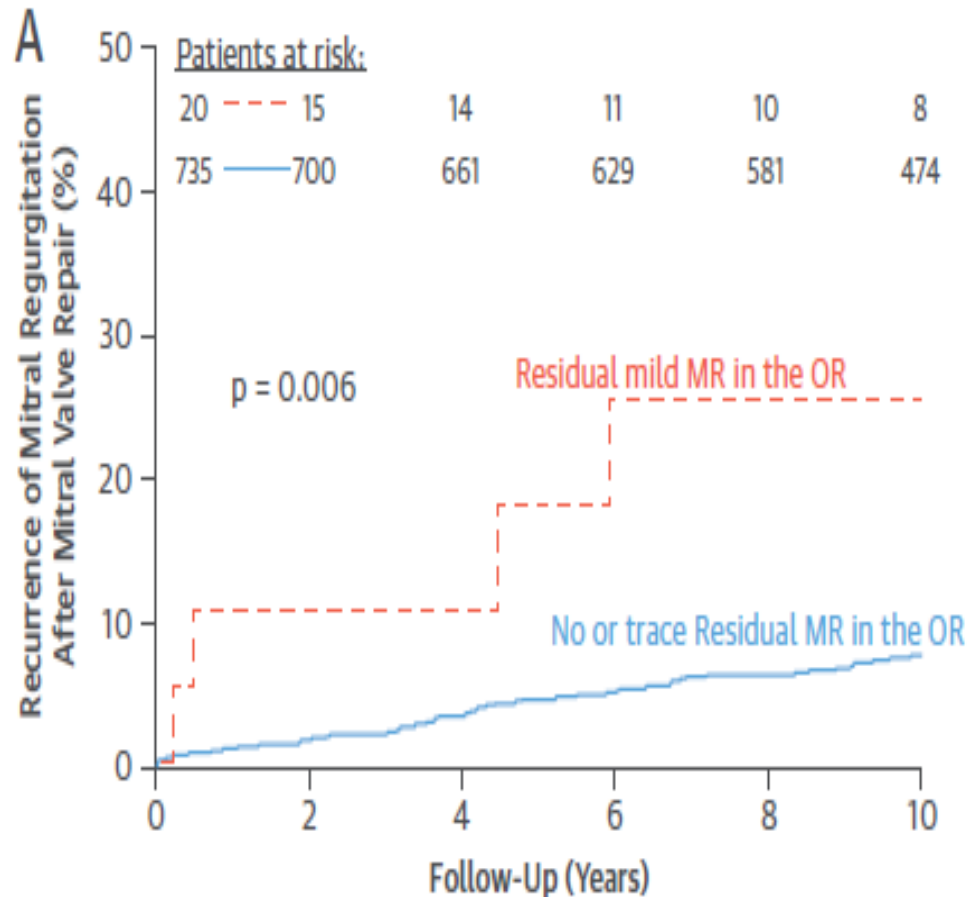
MI: 1.5  
S3 1.3/2.6  
29 OCT 81



# Effect of Recurrent Mitral Regurgitation Following Degenerative Mitral Valve Repair

## Long-Term Analysis of Competing Outcomes

Rakesh M. Suri, MD, DPHIL,<sup>a</sup> Marie-Annick Clavel, DVM, PhD,<sup>b,c</sup> Hartzell V. Schaff, MD,<sup>a</sup> Hector I. Michelena, MD,<sup>b</sup> Marianne Huebner, PhD,<sup>d</sup> Rick A. Nishimura, MD,<sup>b</sup> Maurice Enriquez-Sarano, MD<sup>d</sup>





BP 90/70 mmHG 143/317:  
MAYO CLINIC 3AH

22 Jun 99

11:35:58 am

3V2c 66Hz

HEALTHY 333mm

MHC Adult

Pwr= 0dB MI=1.5

65dB S1/ 0/0/6

Gain= 6dB Δ=2

S1

HR= 80bpm



Exit

Reg Box





BP:100/60MMHG

12:41:52 pm

4V1c-S 55Hz

H3.75MHz R56mm

MMC ADULT

NTHI General

Pwr=0dB MI=1.9

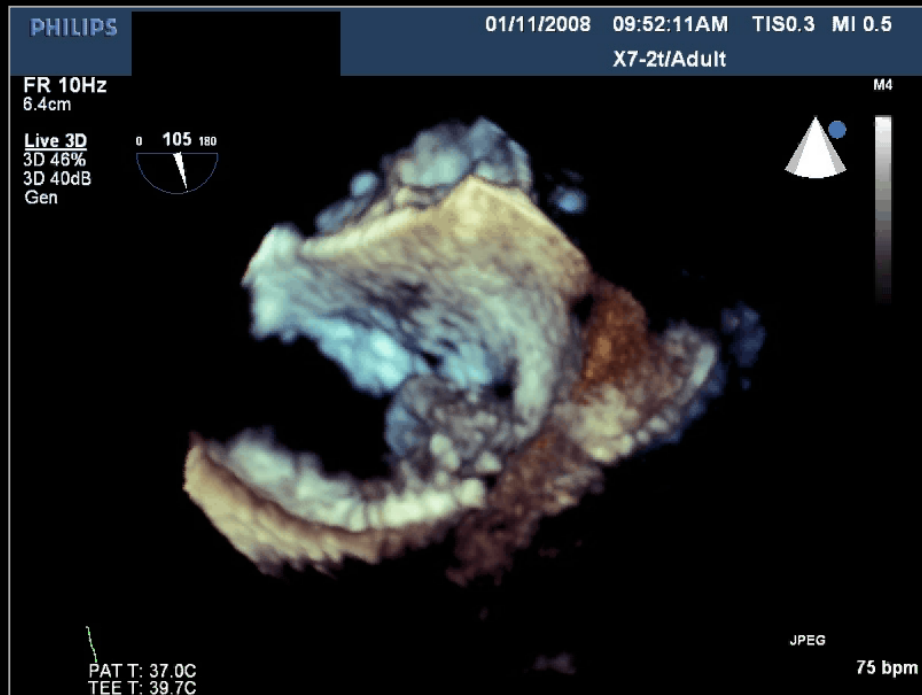
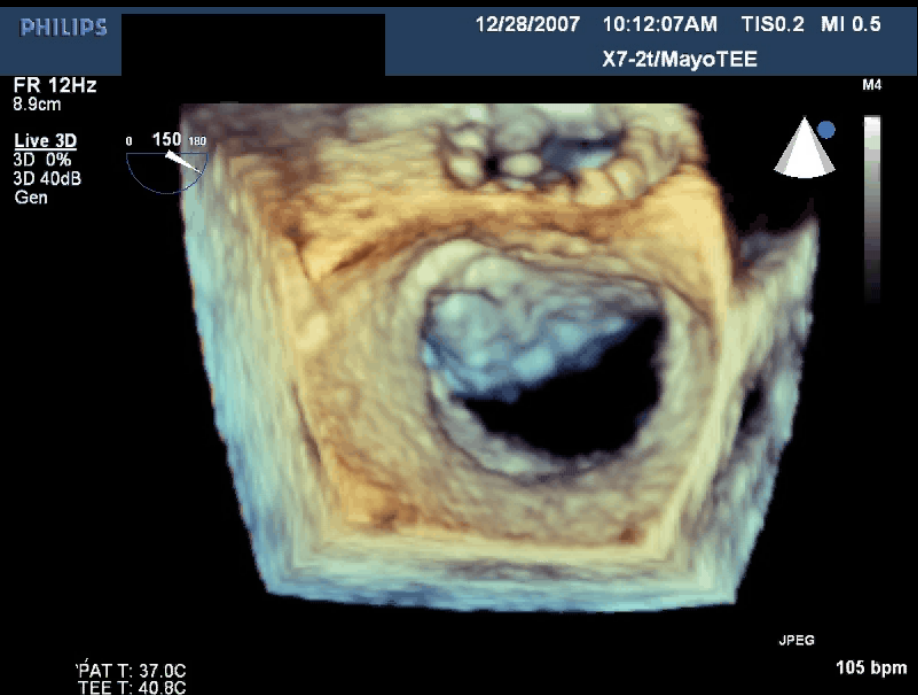
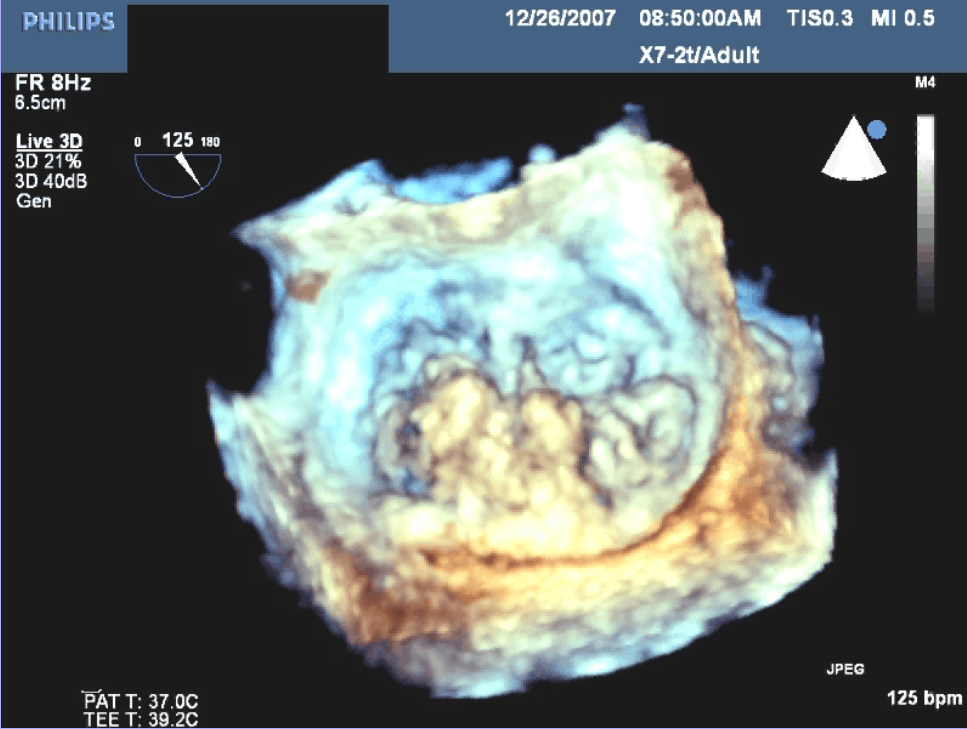
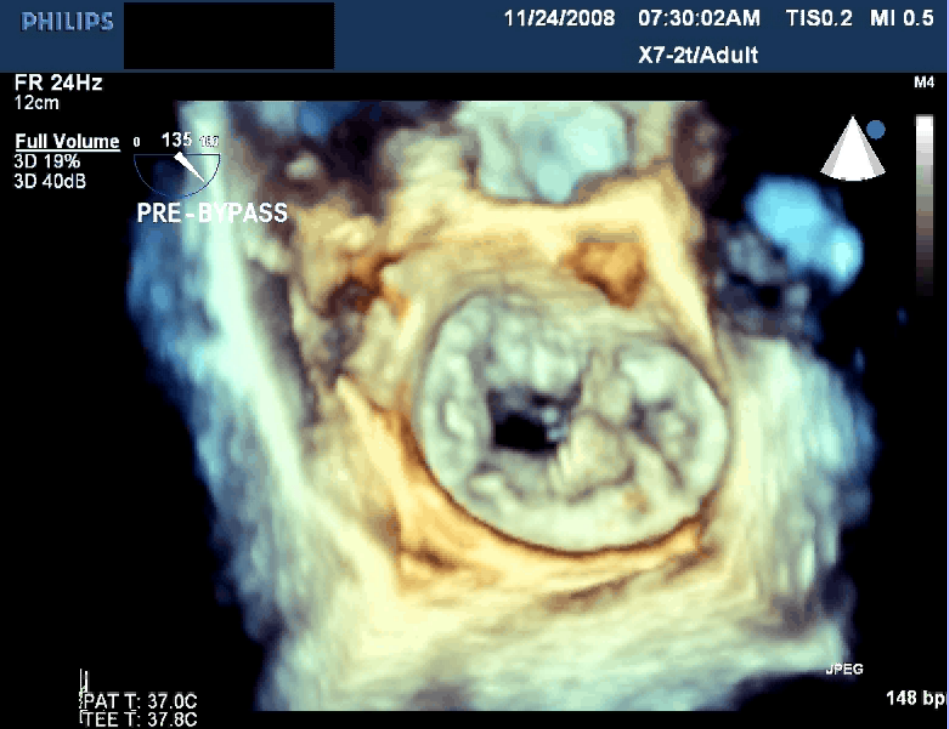
68dB S1/ 0/0/6

Gain= -3dB Δ=1

Store in progress

HR=102bpm





# Mitral Regurgitation

We know how to identify  
mitral lesions and  
valve reparability

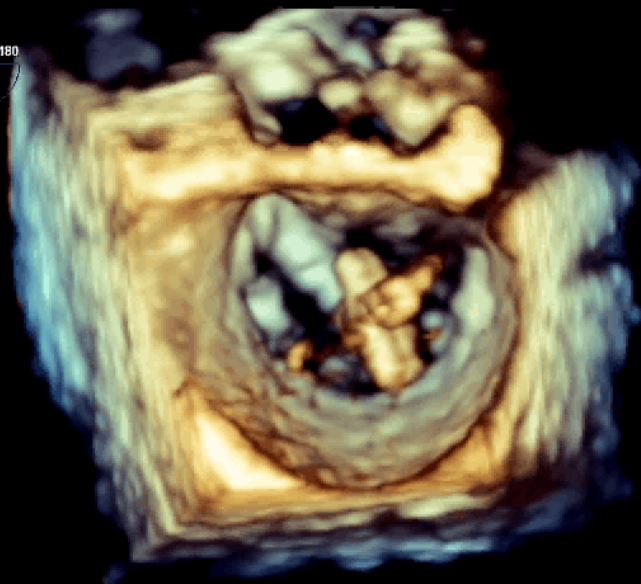
Am I too tough with  
3D Echo ?

...times



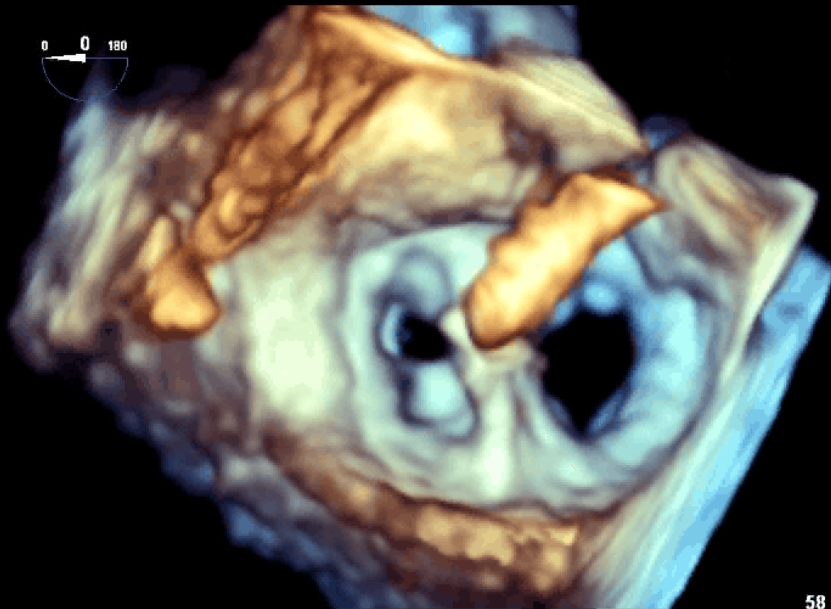
FR 10Hz  
10cm

3D Beats 1



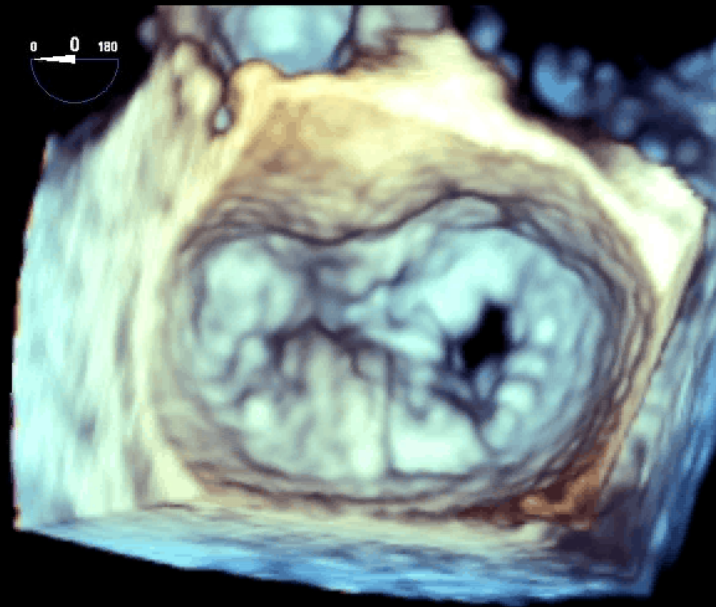
FR 10Hz  
10cm

3D Beats 1



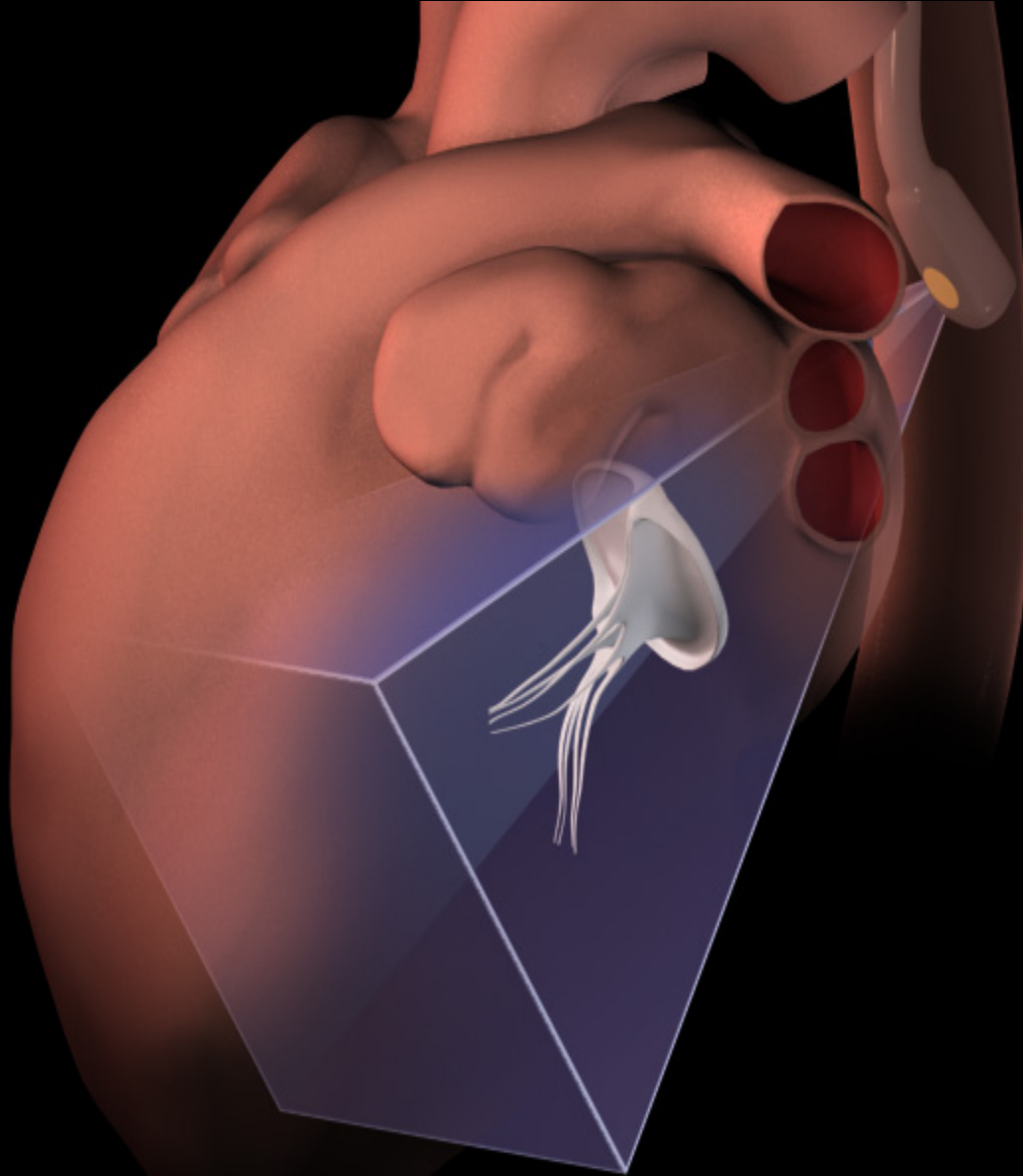
FR 41Hz  
9.2cm

3D Beats 4Q



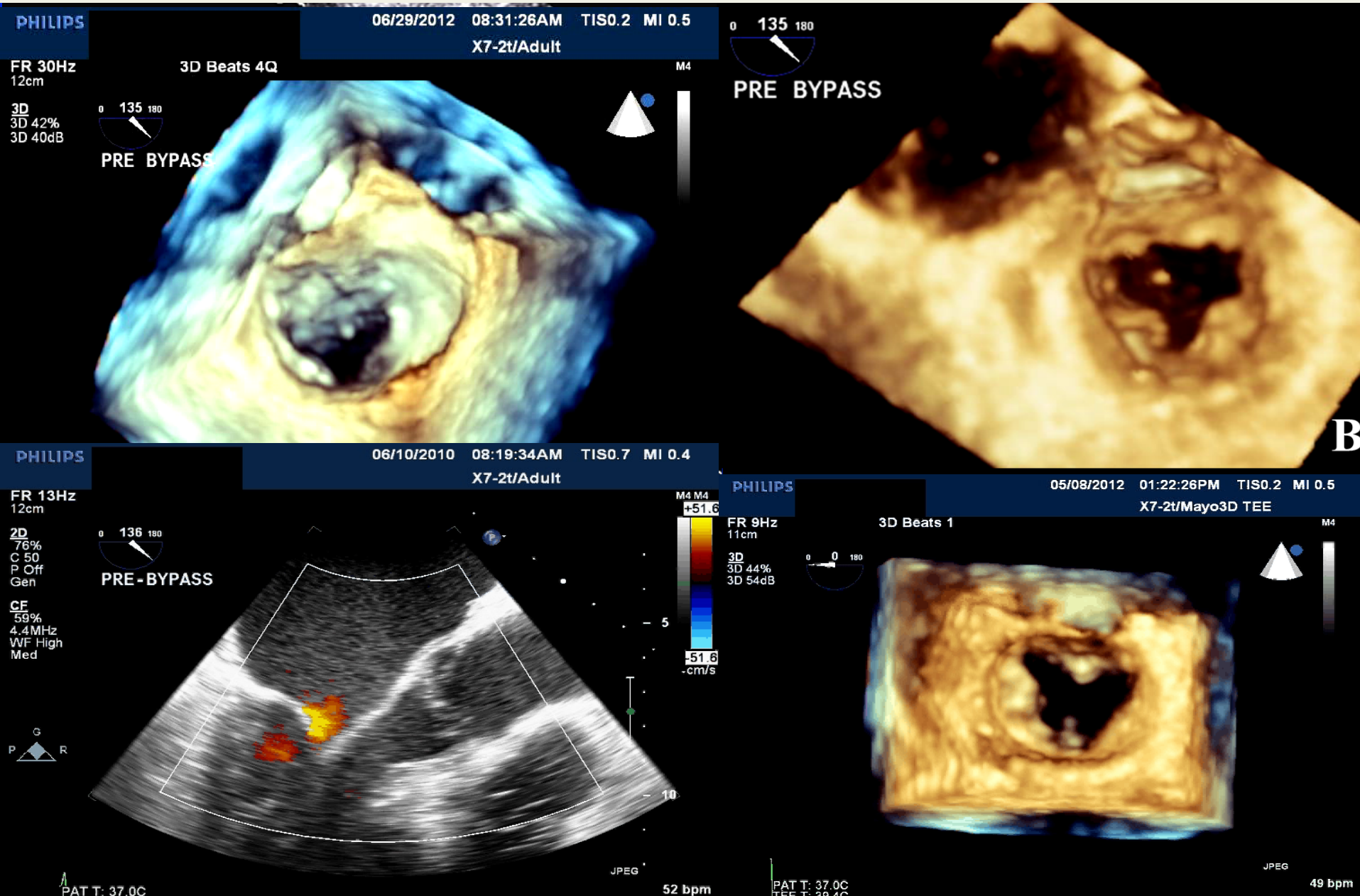


3D Echo allows complete insonation of the Mitral Valve



# Cleft posterior mitral leaflet resembling a tri-leaflet mitral valve: a novel phenotypic association with hypertrophic cardiomyopathy

Hayan Jouni<sup>1†</sup>, Steven L. Driver<sup>2†</sup>, Maurice Enriquez-Sarano<sup>1</sup>, and Hector I. Michelena<sup>1\*</sup>



# Deep Indentation

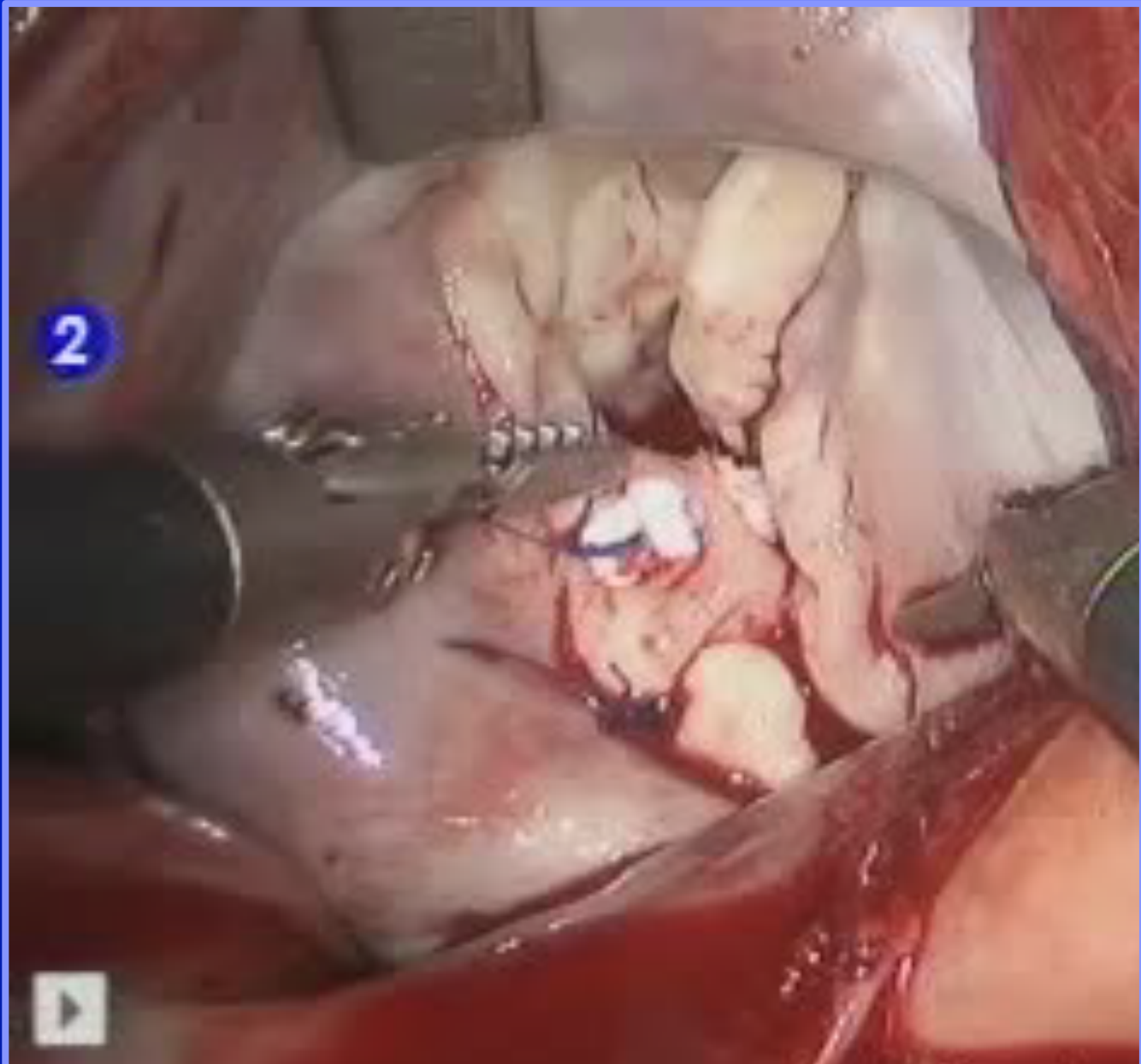


Anterior  
Leaflet

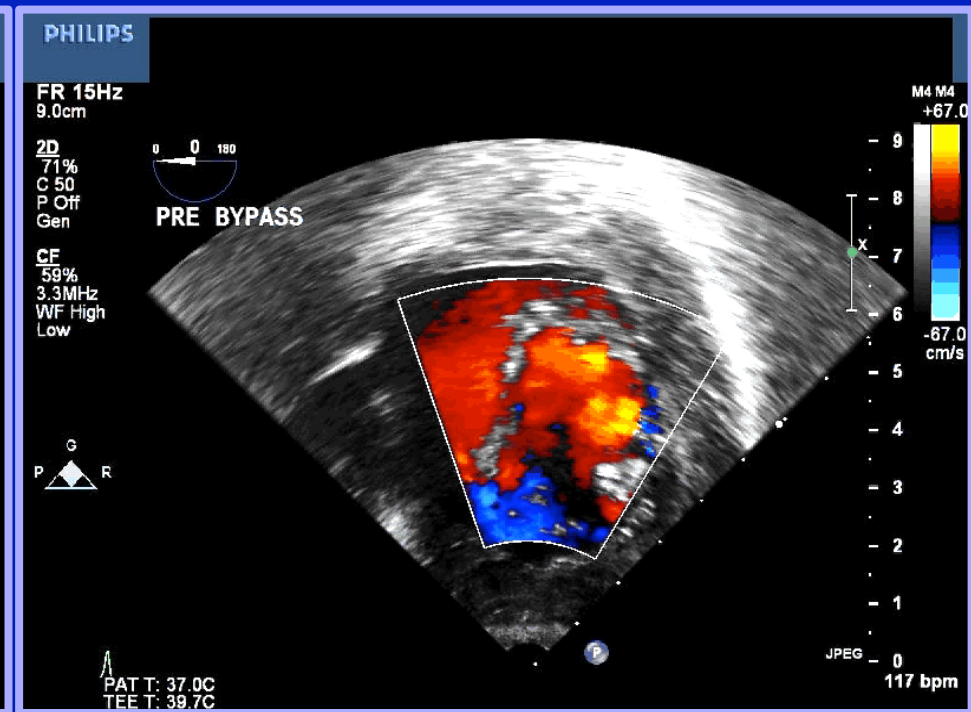
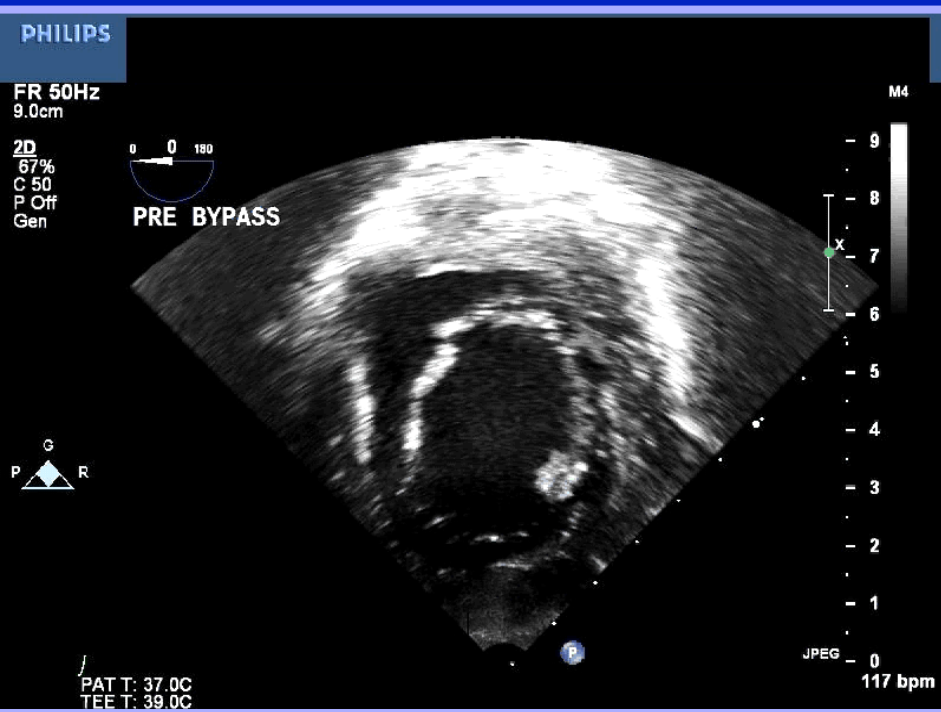
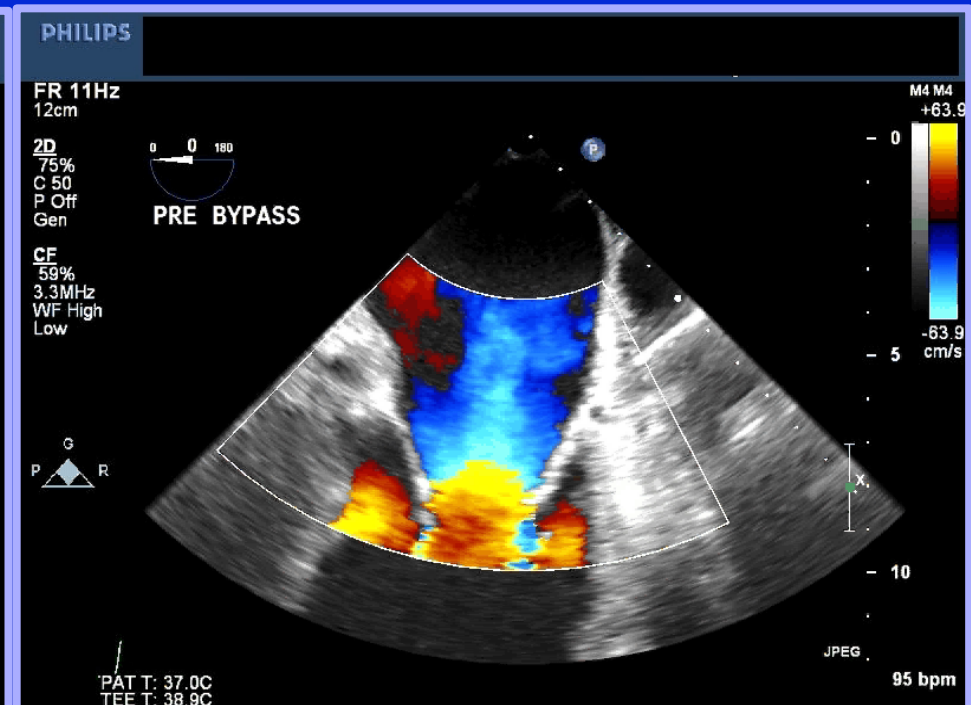
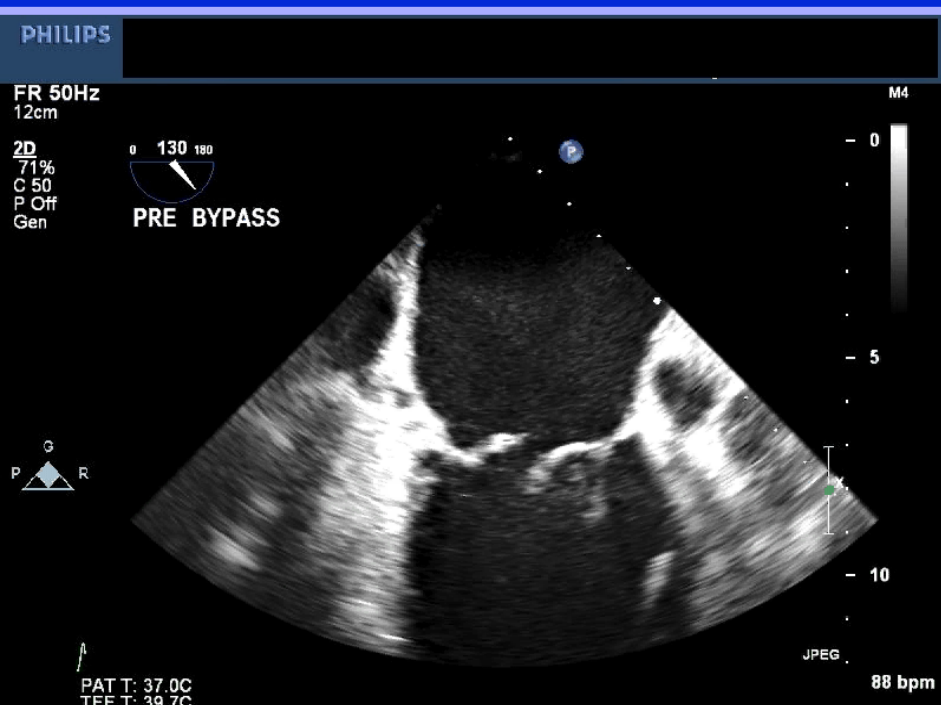
Posterior  
Leaflet



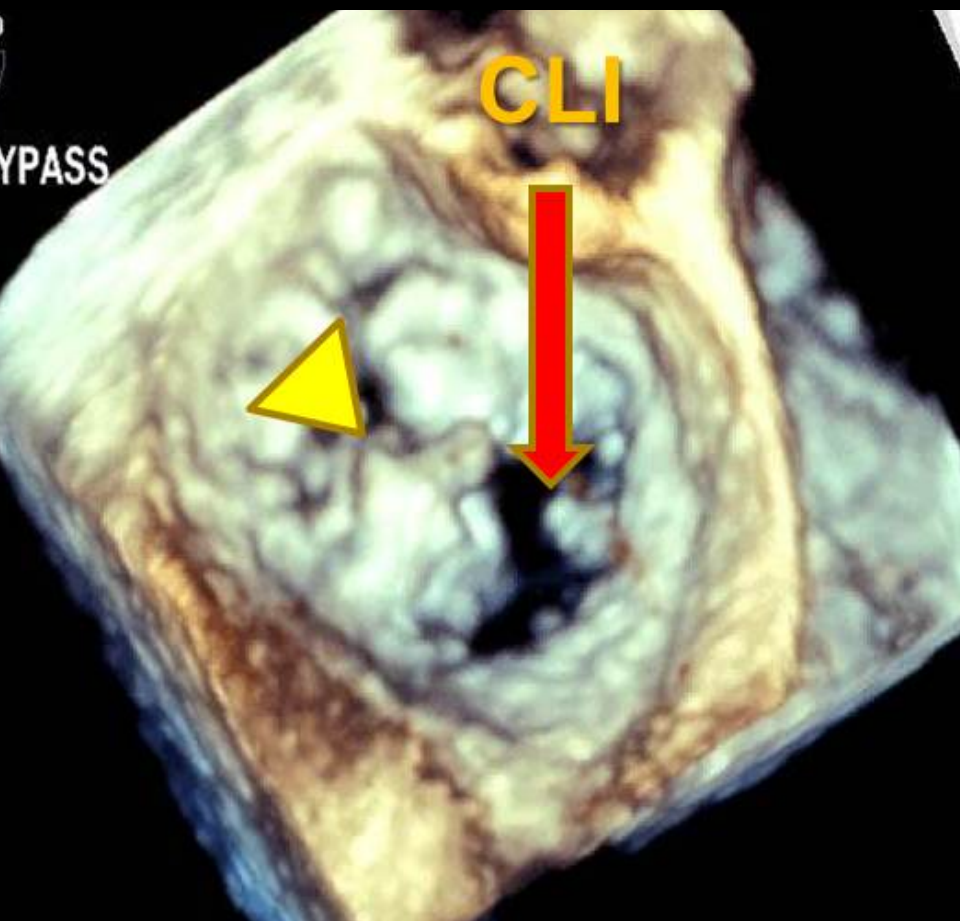
# Cleft-Like Indentations



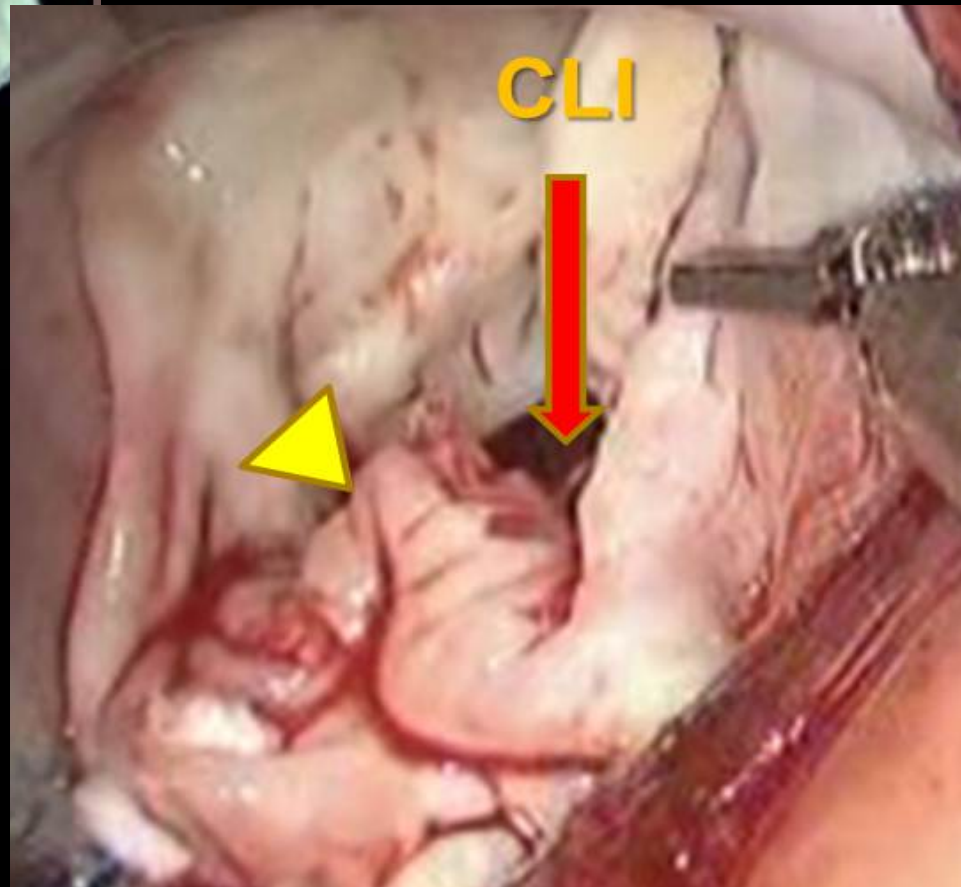








# Cleft-Like Indentations

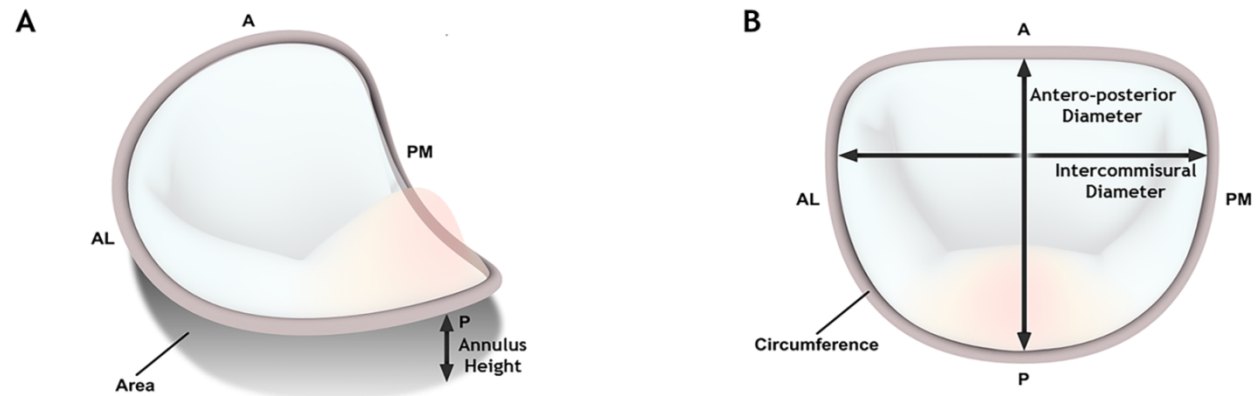


## ORIGINAL ARTICLE

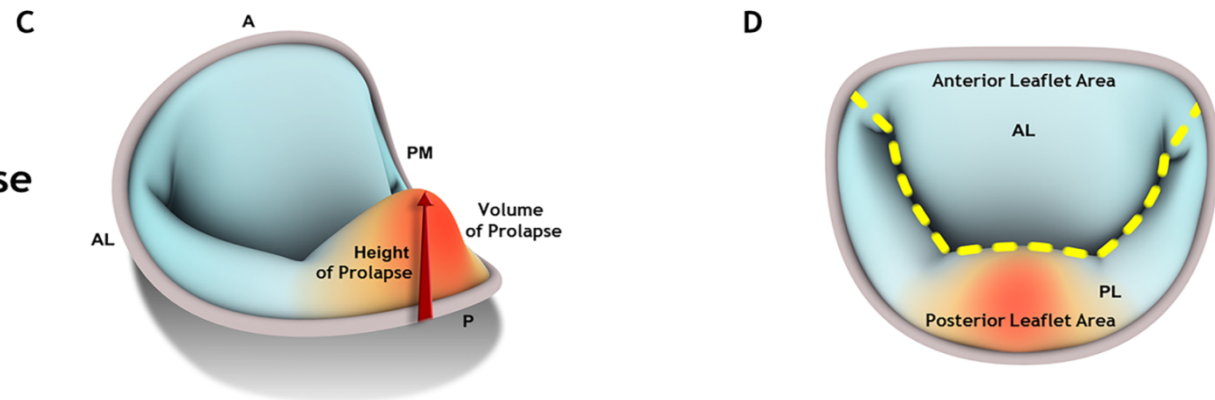
# Cleft-like indentations in myxomatous mitral valves by three-dimensional echocardiographic imaging

Francesca Mantovani,<sup>1,2</sup> Marie-Annick Clavel,<sup>1</sup> Ori Vatury,<sup>1</sup> Rakesh M Suri,<sup>1</sup>  
 Sunil V Mankad,<sup>1</sup> Joseph Malouf,<sup>1</sup> Hector I Michelena,<sup>1</sup> Sonia Jain,<sup>1</sup>  
 Luigi Paolo Badano,<sup>3</sup> Maurice Enriquez-Sarano<sup>1</sup>

## Annulus Measurements



## Leaflets and Prolapse Measurements

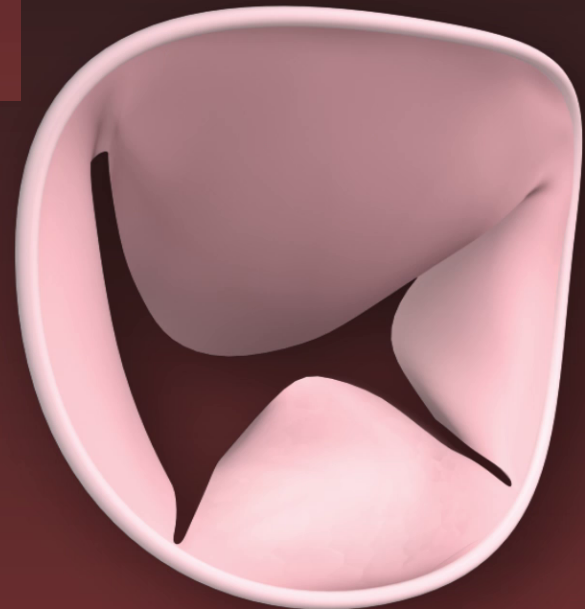




Multi-segment Prolapse  
+  
Excess tissue  
=  
No CLI



Single-segment Prolapse  
+  
Tissue Paucity  
=  
Often CLI



# 3D echo in MR

- 1-An essential **clinical tool** during percutaneous interventions and surgical repair
- 2-A unique **physiologic tool** to understand MV diseases and balance **valve respect vs. resect**
- 3-But **not** the main instrument for clinical decision making

**How do we conduct  
Clinical Decision making ?**



# Is early surgery recommended for mitral regurgitation?

## *Early Surgery Is Recommended for Mitral Regurgitation*

*Maurice Enriquez-Sarano, MD; Thoralf M. Sundt III, MD*

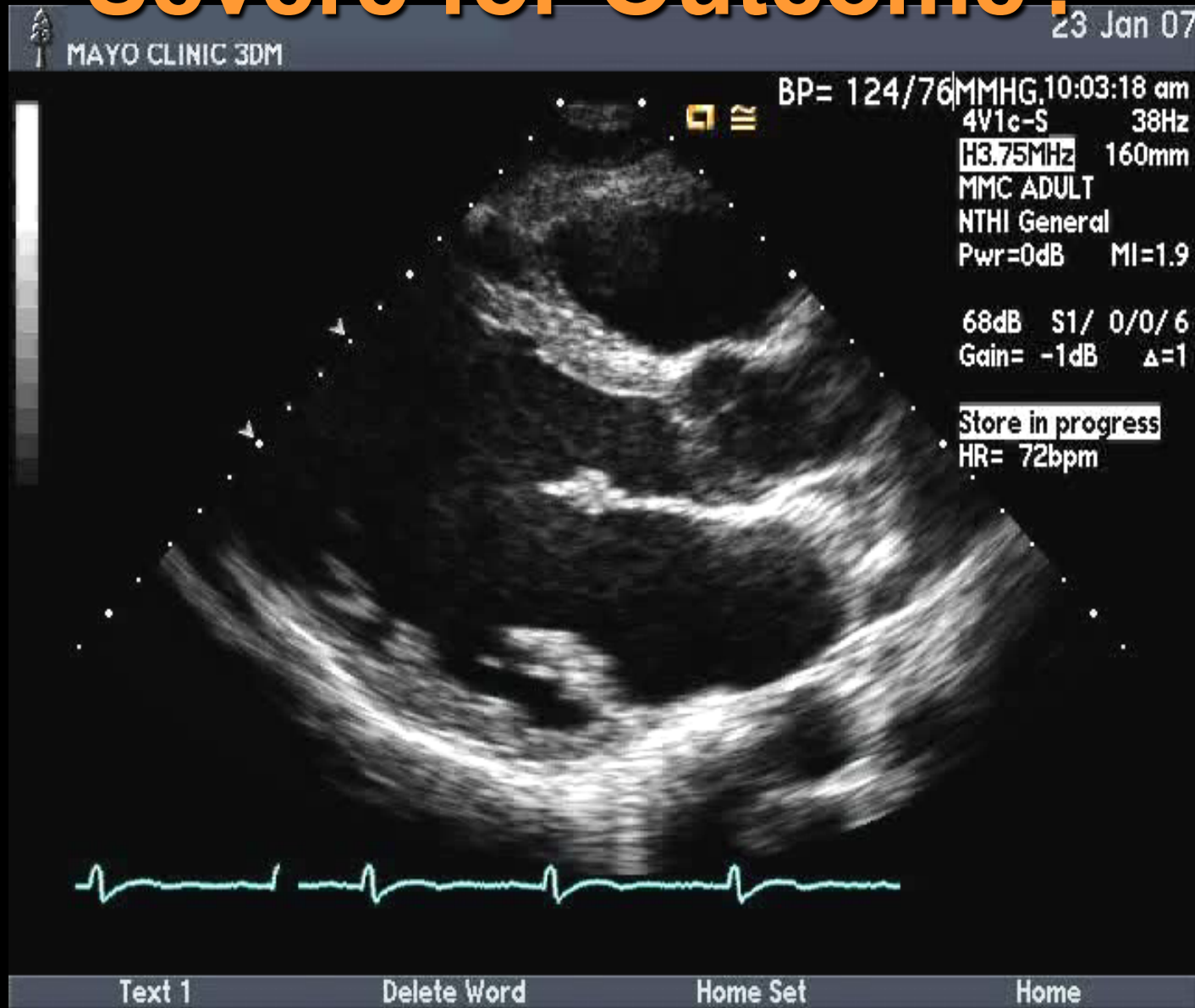
## *Primum Non Nocere*

## The Case for Watchful Waiting in Asymptomatic “Severe” Degenerative Mitral Regurgitation

*Linda D. Gillam, MD; Allan Schwartz, MD*

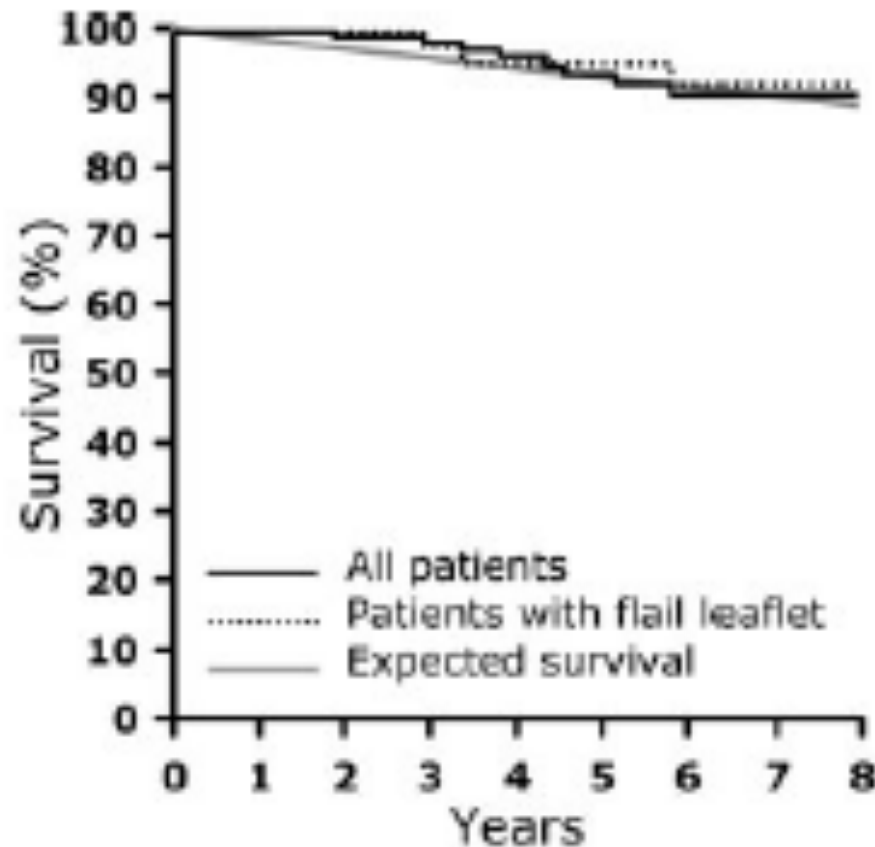


# Is Voluminous Organic MR Severe for Outcome?



# Outcome of Watchful Waiting in Asymptomatic Severe Mitral Regurgitation

Raphael Rosenhek, MD; Florian Rader, MD; Ursula Klaar, MD; Harald Gabriel, MD; Marcel Krejc, PhD; Daniel Kalbeck, PhD; Michael Schemper, PhD; Gerald Maurer, MD; Helmut Baumgartner, MD



## All patients

Pts. at risk: 129 129 118 103 87 70 53 24 10

## Patients with flail leaflet

Pts. at risk: 56 55 53 43 37 32 28 10 4

Circulation,  
2006;113:2228

# Organic MR

## Flail Leaflets



# Asymptomatic MR

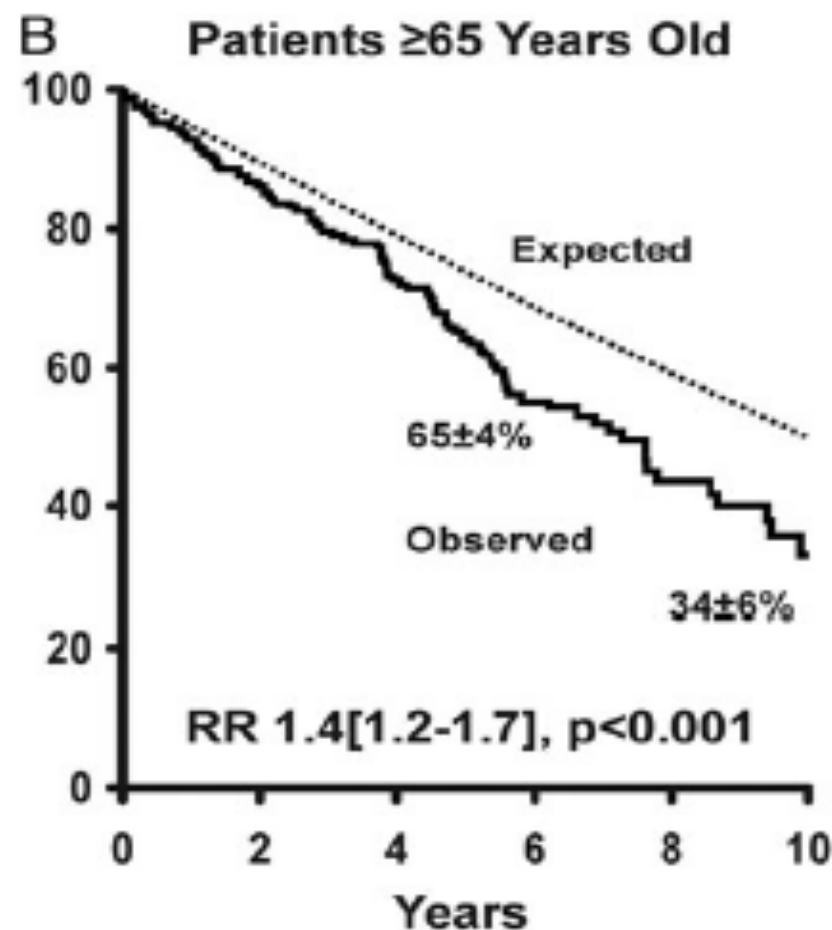
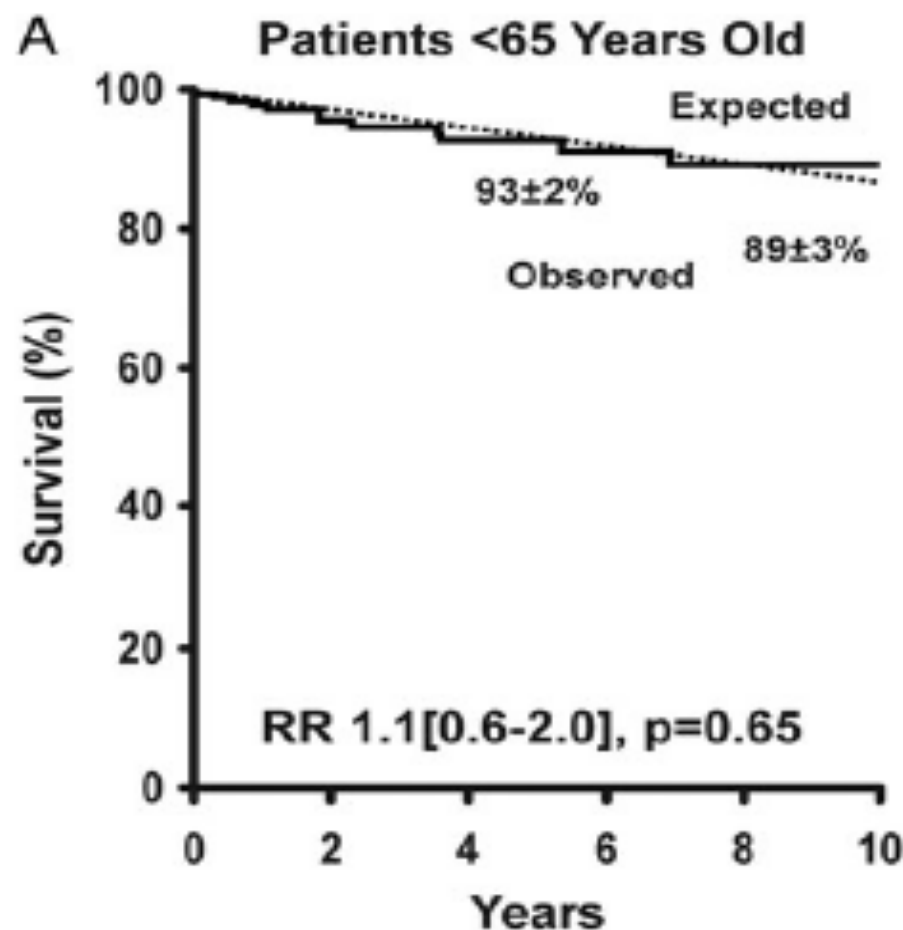
## Baseline Characteristics

<u>Study</u>	<u>Age</u>
Ling, Flail	66±13
MES, MR	63±14
Mohty, Surg MVP	65±13
Rosenhek, MR	56±14

**What is  
the impact  
of enrolling  
too young  
patients ?**

# Impact of ageing on presentation and outcome of mitral regurgitation due to flail leaflet: a multicentre international study

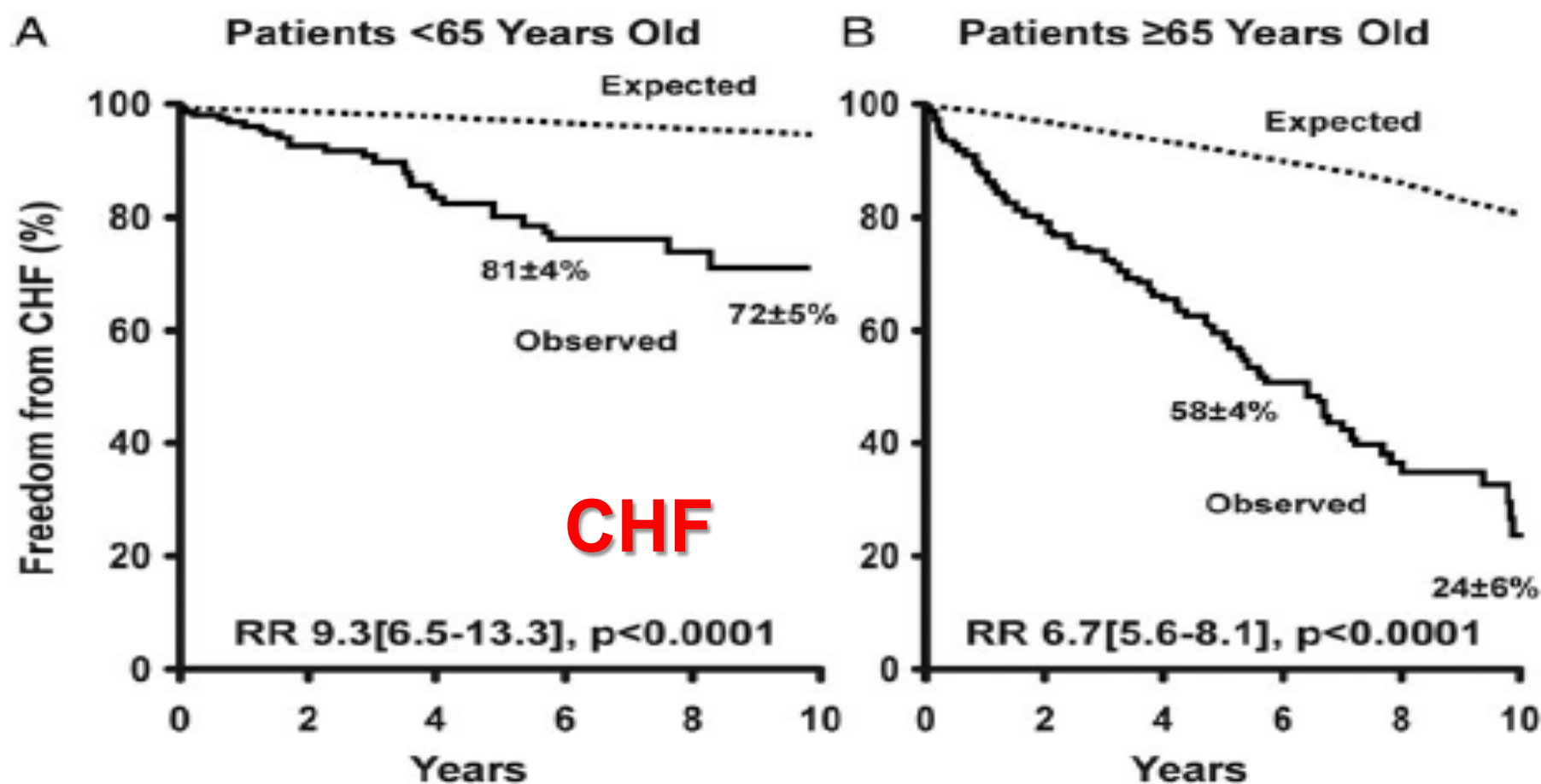
Jean-François Avierinos<sup>1\*</sup>, Christophe Tribouilloy<sup>2</sup>, Francesco Grigioni<sup>3</sup>, Rakesh Suri<sup>4</sup>, Andrea Barbieri<sup>5</sup>, Hector I. Michelena<sup>4</sup>, Teresa Ionico<sup>3</sup>, Dan Rusinaru<sup>2</sup>, Sébastien Analdi<sup>1</sup>, Gilbert Habib<sup>1</sup>, Catherine Szymanski<sup>2</sup>, Roch Giorgi<sup>6</sup>, Douglas W. Mahoney<sup>4</sup>, and Maurice Enriquez-Sarano<sup>4</sup>, on Behalf of the Mitral

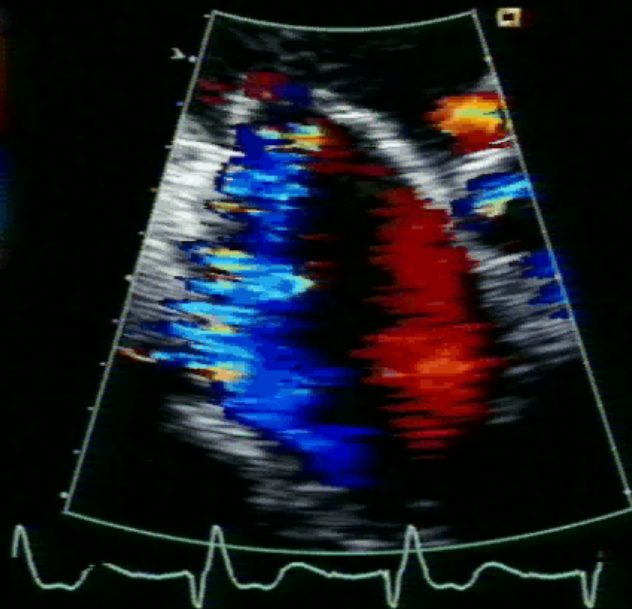




# Impact of ageing on presentation and outcome of mitral regurgitation due to flail leaflet: a multicentre international study

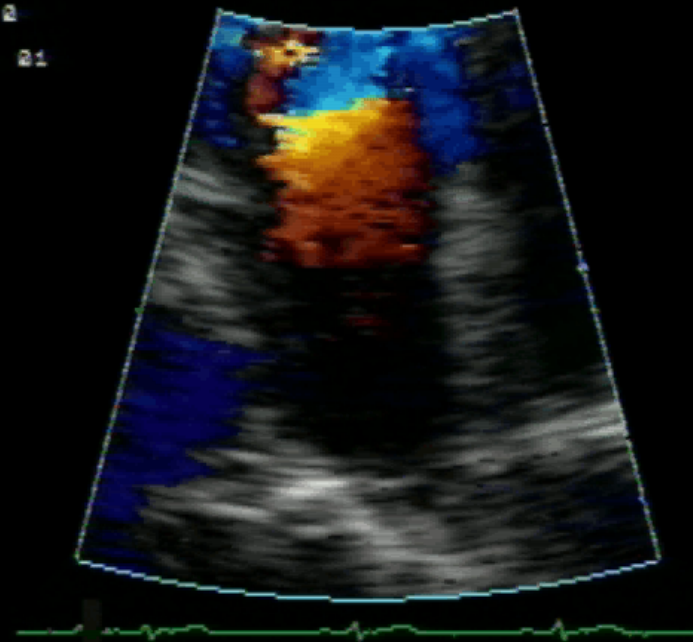
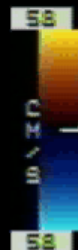
Jean-François Avierinos<sup>1\*</sup>, Christophe Tribouilloy<sup>2</sup>, Francesco Grigioni<sup>3</sup>, Rakesh Suri<sup>4</sup>, Andrea Barbieri<sup>5</sup>, Hector I. Michelena<sup>4</sup>, Teresa Ionico<sup>3</sup>, Dan Rusinaru<sup>2</sup>, Sébastien Ansaldi<sup>1</sup>, Gilbert Habib<sup>1</sup>, Catherine Szymanski<sup>2</sup>, Roch Giorgi<sup>6</sup>, Douglas W. Mahoney<sup>4</sup>, and Maurice Enriquez-Sarano<sup>4</sup>, on Behalf of the Mitral





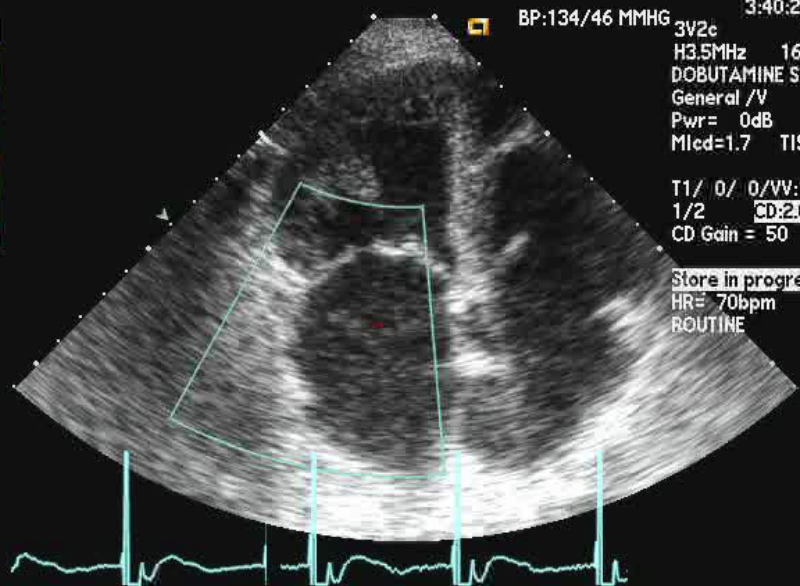
11:06:03 am  
3Y2c 17Hz  
H3.5MHz 388mm  
MMC ADULT  
General  
Pwr= 0dB  
Mlcd=1.8 TIS=1.9  
  
T1/ 0/ 0/VV:1  
1/2 CD:2.0MHz  
CD Gain = 46  
  
S32 S38  
0:15:12  
HR= 57bpm

TIS: 1.8  
S3  
26 AUG 21



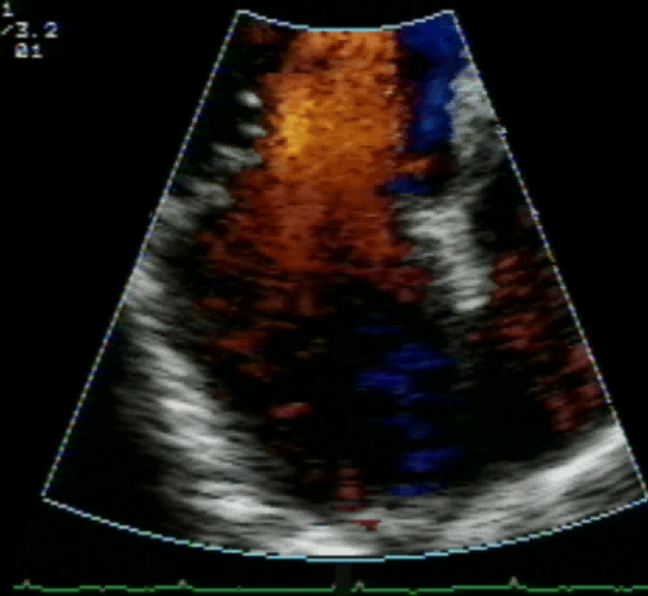
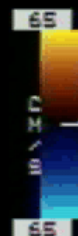
MAYO CLINIC 3BP

01 Jun 04



BP:134/46 MMHG 3:40:26 pm  
3Y2c 19Hz  
H3.5MHz 160mm  
DOBUTAMINE STRESS  
General /V  
Pwr= 0dB  
Mlcd=1.7 TIS=1.7  
  
T1/ 0/ 0/VV:1  
1/2 CD:2.0MHz  
CD Gain = 50  
  
Store in progress  
HR= 70bpm  
ROUTINE

TIS: 1.1  
S3 1.6/3.2  
21 NOV 21

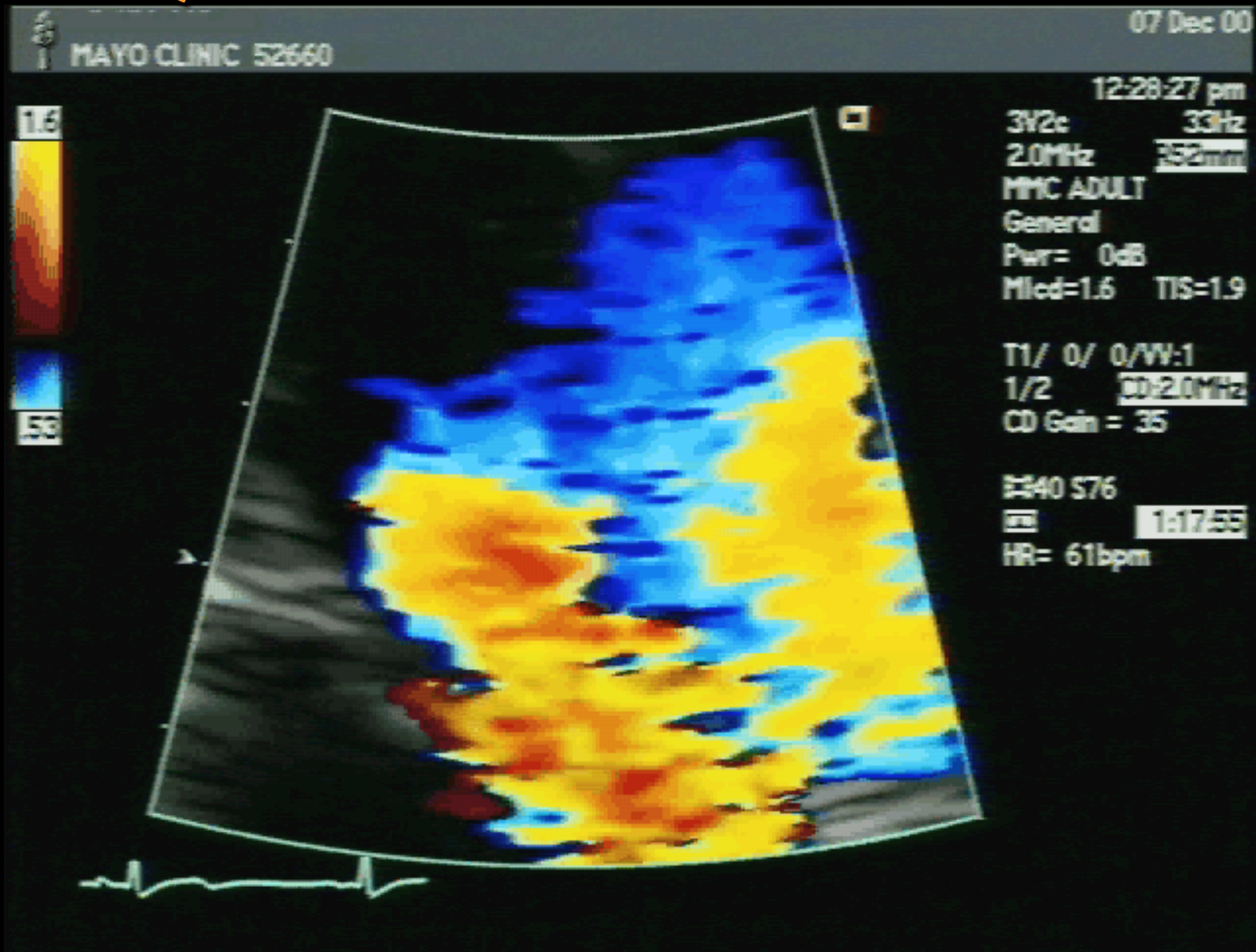


DTV/CDV

CD Pan

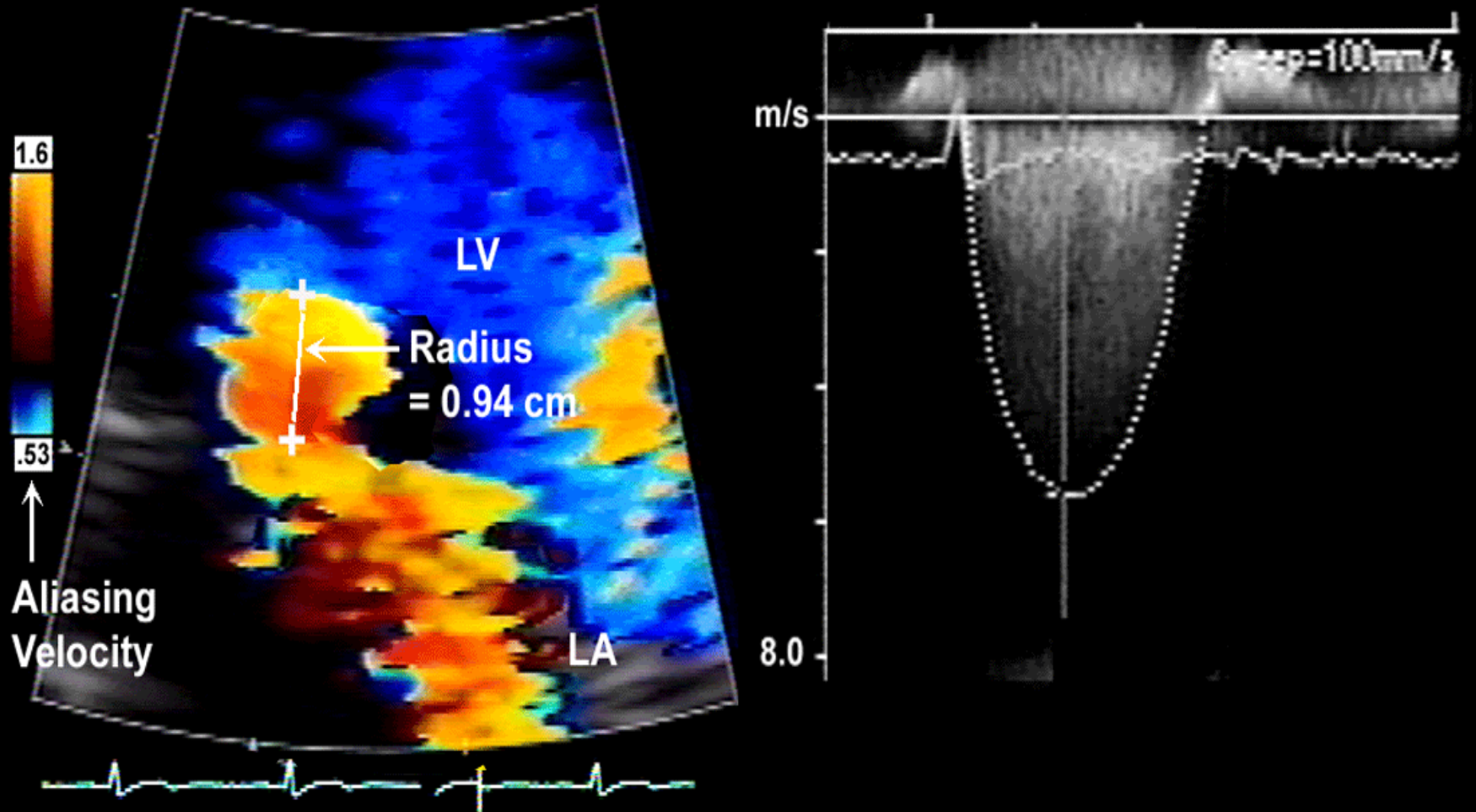
CD Pos/Size

# Quantitation of MR





# ERO Calculation

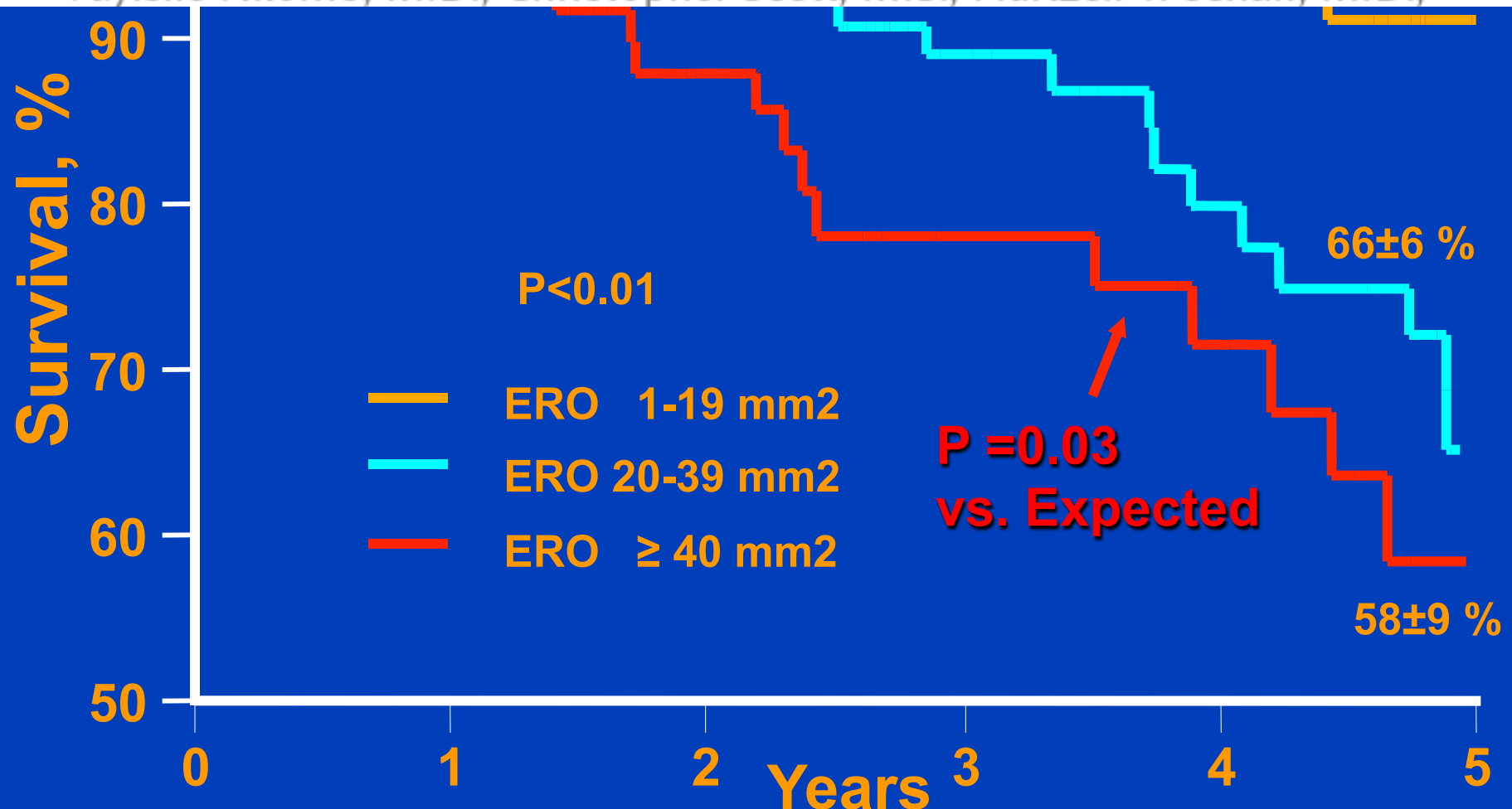


**Flow = 294 mL/sec. MR velocity = 557 cm/sec.**

**$ERO = \text{flow/velocity} = .53 \text{ cm}^2 \text{ or } 53 \text{ mm}^2$**

# Quantitative Determinants of the Outcome of Asymptomatic Mitral Regurgitation

Maurice Enriquez-Sarano, M.D., Jean-François Avierinos, M.D.,  
David Messika-Zeitoun, M.D., Delphine Detaint, M.D., Maryann Capps, R.D.C.S.,  
Vuyisile Nkomo, M.D., Christopher Scott, M.S., Hartzell V. Schaff, M.D.,





# Comparison of Early Surgery Versus Conventional Treatment in Asymptomatic Severe Mitral Regurgitation

Duk-Hyun Kang, MD, PhD; Jeong Hoon Kim, MD; Ji Hye Rim, MD; Mi-Jeong Kim, MD; Sung-Cheol Yun, PhD; Jong-Min Song, MD, PhD; Hyun Song, MD, PhD; Kee-Joon Choi, MD, PhD; Jae-Kwan Song, MD, PhD; Jae-Won Lee, MD, PhD

**Background**—The optimal timing of surgical intervention in asymptomatic patients with severe mitral regurgitation is unclear. We therefore compared the long-term results of early surgery with a conventional treatment strategy.

**Methods and Results**—From 1996 to 2005, 447 consecutive asymptomatic patients (253 men, age  $50 \pm 15$  years) with severe degenerative mitral regurgitation and preserved left ventricular function were evaluated prospectively. The end point was defined as the composite of operative mortality, cardiac death, repeat mitral valve surgery, and urgent admission due to congestive heart failure during follow-up. Early surgery was performed on 161 patients (operated group), and the conventional treatment strategy was used for 286 patients (conventional treatment group). There were no significant differences between the 2 groups in terms of age, gender, euroSCORE (European System for Cardiac Operative Risk Evaluation), or ejection fraction. During a median follow-up of 1988 days, there were 2 repeat surgeries and no cardiac deaths or operative mortality in the operated group compared with 12 cardiac deaths, 1 repeat surgery, and 22 admissions for congestive heart failure in the conventional treatment group. The estimated actuarial 7-year cardiac mortality rate was 0% in the operated group and  $5 \pm 2\%$  in the conventional treatment group ( $P=0.008$ ). In propensity score–matched pairs, the estimated actuarial 7-year event-free survival rate was significantly higher in the operated than in the conventional treatment group ( $99 \pm 1\%$  versus  $85 \pm 4\%$ ,  $P=0.007$ ). In the conventional treatment group, baseline grade of pulmonary hypertension (hazard ratio 1.87, 95% CI 1.22 to 2.87,  $P=0.003$ ), age (hazard ratio 1.02, 95% CI 1.01 to 1.04,  $P=0.005$ ), and effective regurgitant orifice area (hazard ratio 2.06, 95% CI 1.11 to 3.82,  $P=0.02$ ) were independent variables that predicted late development of surgical indications or congestive heart failure on Cox multivariate analysis.

**Conclusions**—Compared with conservative management, the strategy of early surgery was associated with an improved long-term event rate by decreasing cardiac mortality and congestive heart failure hospitalization more effectively in patients with severe degenerative mitral regurgitation. Early surgery may therefore further improve clinical outcomes in asymptomatic severe mitral regurgitation with preserved left ventricular systolic function and a high likelihood of mitral valve repair. (*Circulation*. 2009;119:797-804.)

ERO  
Predictor  
Of Outcome

**Primum non-Nocere ?**

**1-Voluminous MR is**

**Severe**

**2-Large ERO is a**

**marker of poor  
clinical outcome**

# Mitral Regurgitation: The guidelines

## **CLASS I**

1. Mitral valve surgery is recommended for symptomatic patients with chronic severe primary MR (stage D) and LVEF greater than 30% (156,179). (*Level of Evidence: B*)
2. Mitral valve surgery is recommended for asymptomatic patients with chronic severe primary MR and LV dysfunction (LVEF 30% to 60% and/or LVESD  $\geq 40$  mm, stage C2) (150–153,180–182). (*Level of Evidence: B*)
3. Mitral valve repair is recommended in preference to mitral valve replacement (MVR) when surgical treatment is indicated for patients with chronic severe primary MR limited to the posterior leaflet (155,183–198). (*Level of Evidence: B*)
4. Mitral valve repair is recommended in preference to MVR when surgical treatment is indicated for patients with chronic severe primary MR involving the anterior leaflet or both leaflets when a successful and durable repair can be accomplished (195–197,199–203). (*Level of Evidence: B*)
5. Concomitant mitral valve repair or MVR is indicated in patients with chronic severe primary MR undergoing cardiac surgery for other indications (204). (*Level of Evidence: B*)

# Mitral Regurgitation

What is the problem  
with waiting for  
Symptoms  
to operate ?

# Severe Symptomatic MR

## The EuroHeart Survey

Isolated MR  
(n=977)

# What is “Watchful Waiting” ?

No Symptoms  
n=103

Symptoms  
n=437

Angina: 168

No Intervention  
n=226 (52%)

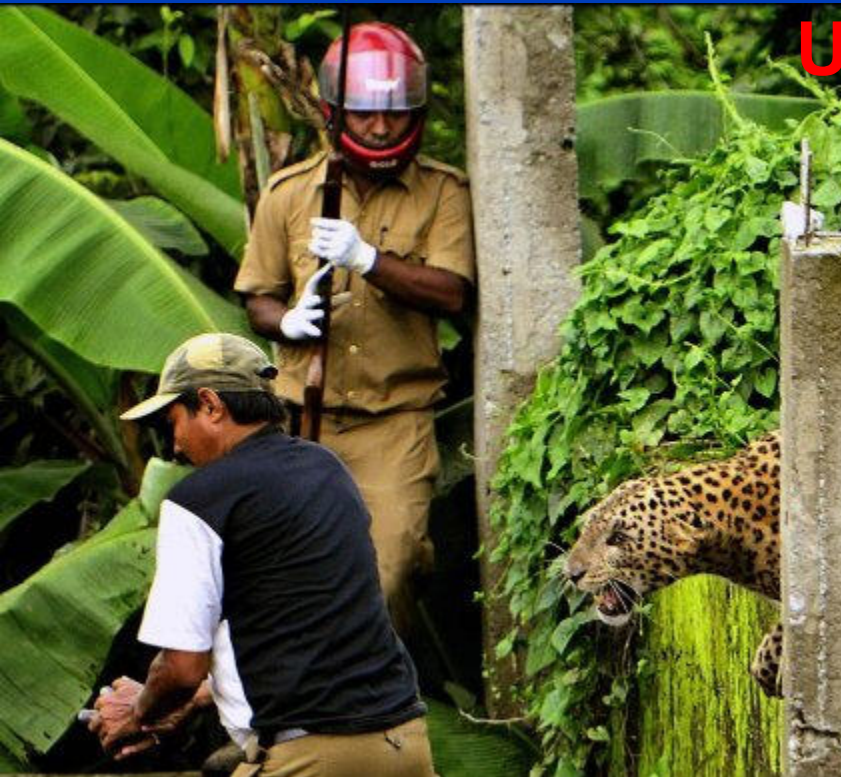
Intervention  
n=211 (48%)



# What is “watchful waiting” ?

Go on, I am watching !

Uh oh, Sorry, I was just waiting



# Should Patients With Severe Degenerative Mitral Regurgitation Delay Surgery Until Symptoms Develop?

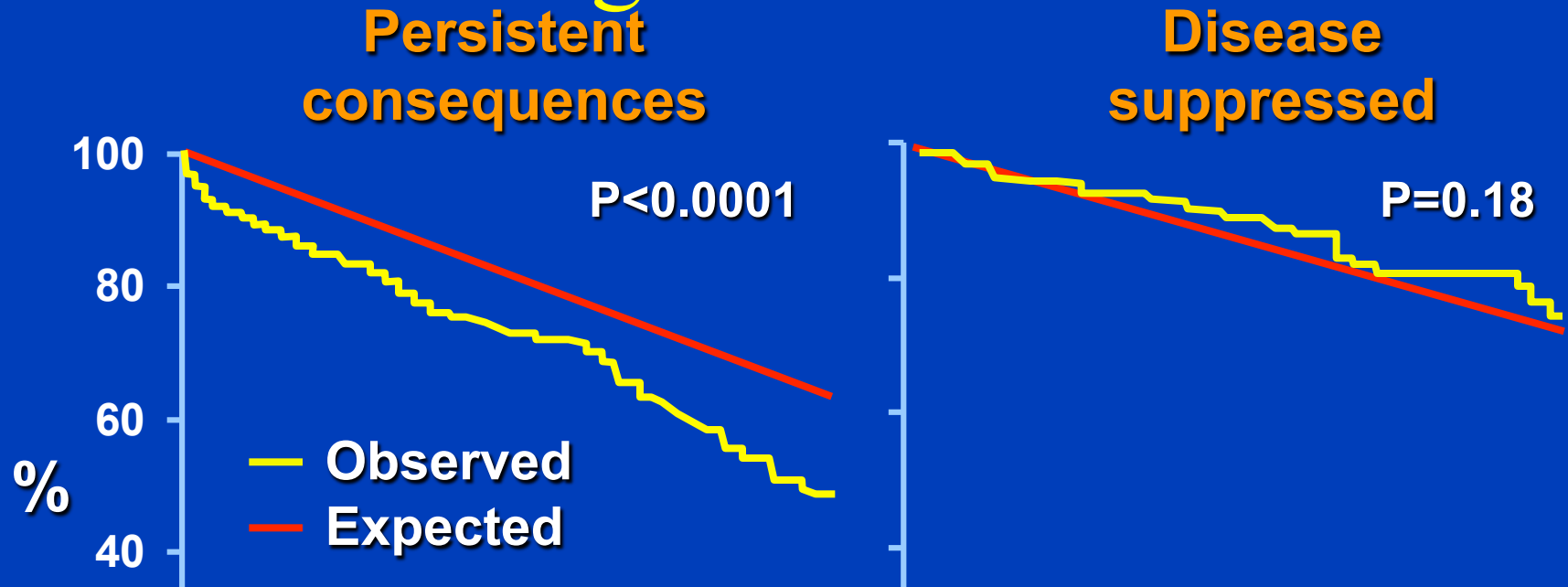
A. Marc Gillinov, MD, Tomislav Mihaljevic, MD, Eugene H. Blackstone, MD, Kristopher George, MD, Lars G. Svensson, MD, Edward R. Nowicki, MD, MS, Joseph F. Sabik III, MD, Penny L. Houghtaling, MS, and Brian Griffin, MD



**Waiting for symptoms  
is causing excess mortality  
even after surgery**

# MIR Postop. Outcome

## Long-term Survival



**Operating on patients with  
no or minimal symptoms  
restores life expectancy**

# Mitral Regurgitation

## Overt LV Dysfunction

**EF <60%**

**What is the problem with  
waiting for EF<60% to  
operate ?**



## Long-Term Mortality Associated With Left Ventricular Dysfunction in Mitral Regurgitation Due to Flail Leaflets

### A Multicenter Analysis

Christophe Tribouilloy, MD, PhD; Dan Rusinaru, MD, PhD; Francesco Grigioni, MD, PhD; Hector I. Michelena, MD; Jean-Louis Vanoverschelde, MD, PhD; Jean-François Avierinos, MD; Andrea Barbieri, MD; Sorin V. Pislaru, MD; Antonio Russo, MD; Agnès Pasquet, MD, PhD; Alexis Théron, MD; Catherine Szymanski, MD, PhD; Franck Lévy, MD; Maurice Enriquez-Sarano, MD; on behalf of the Mitral Regurgitation International Database (MIDA) Investigators\*

**Background**—Ejection fraction (EF) as a marker of left ventricular (LV) dysfunction and the appropriate thresholds for diagnosing severe or mild/moderate LV dysfunction in mitral regurgitation are doubted and poorly followed in clinical practice. We aimed at assessing the role of EF in a large registry of organic mitral regurgitation to objectively establish thresholds for various degrees of LV dysfunction and to analyze whether mitral surgery remains beneficial in those subsets of patients.

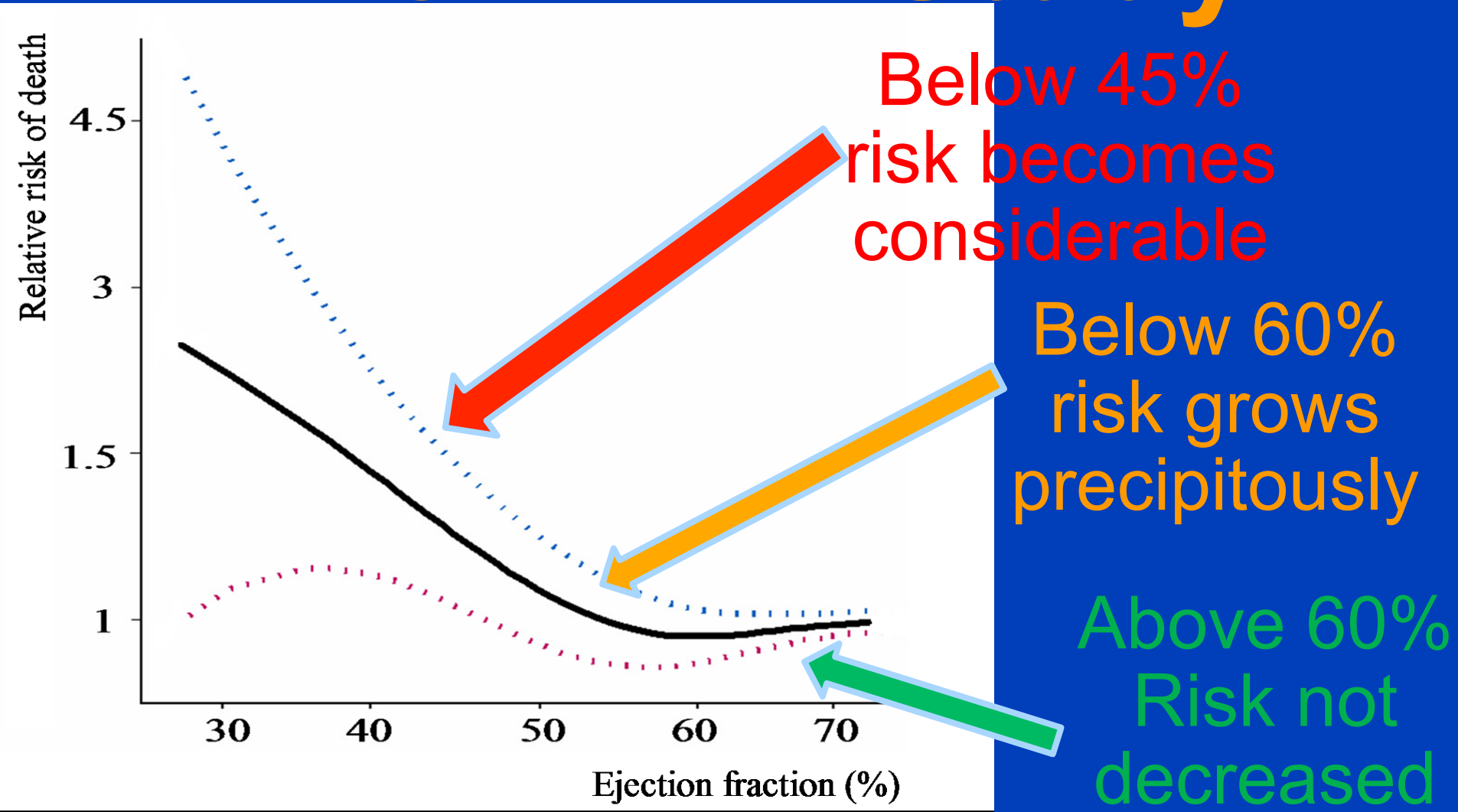
**Methods and Results**—We investigated the relation between EF and mortality in 1875 patients with mitral regurgitation due to flail leaflets in sinus rhythm ( $65 \pm 13$  years; median EF, 66% [60%–71%]) enrolled in the Mitral Regurgitation International Database (MIDA) registry. With EF <60%, mortality after diagnosis increased precipitously under medical management (adjusted hazard ratio [HR], 1.59 [1.19–2.12]) and during the entire follow-up (adjusted HR, 1.51 [1.22–1.87]). Severe LV dysfunction, if defined by EF <30%, would affect a minuscule number of patients (0.3%). Conversely, EF <45% was more frequent (2.9%) and was associated with considerable mortality under medical management (adjusted HR, 2.43 [1.50–3.95]) and during the entire follow-up (adjusted HR, 2.46 [1.67–3.61]). The group with EF of 45% to 60% represented a large proportion of patients (23%), exhibited rarely overt symptoms, and had higher mortality compared with EF >60%. Above 60%, no EF threshold further determined survival. The benefit of surgery remained considerable in the groups with EF <45% (adjusted HR, 0.28 [0.17–0.56]) and with EF of 45% to 60% (adjusted HR, 0.34 [0.21–0.64]).

**Conclusions**—EF is valuable in defining presence and severity of LV dysfunction in organic mitral regurgitation. Patients with EF <45% have severe LV dysfunction, catastrophic outcome under medical management, and should not be denied surgery. Although there is no survival gain with EF ranges >60%, with EF dropping <60%, mortality increases precipitously and prompt surgical referral is critical to outcome. (*Circ Cardiovasc Imaging*. 2014;7:363-370.)



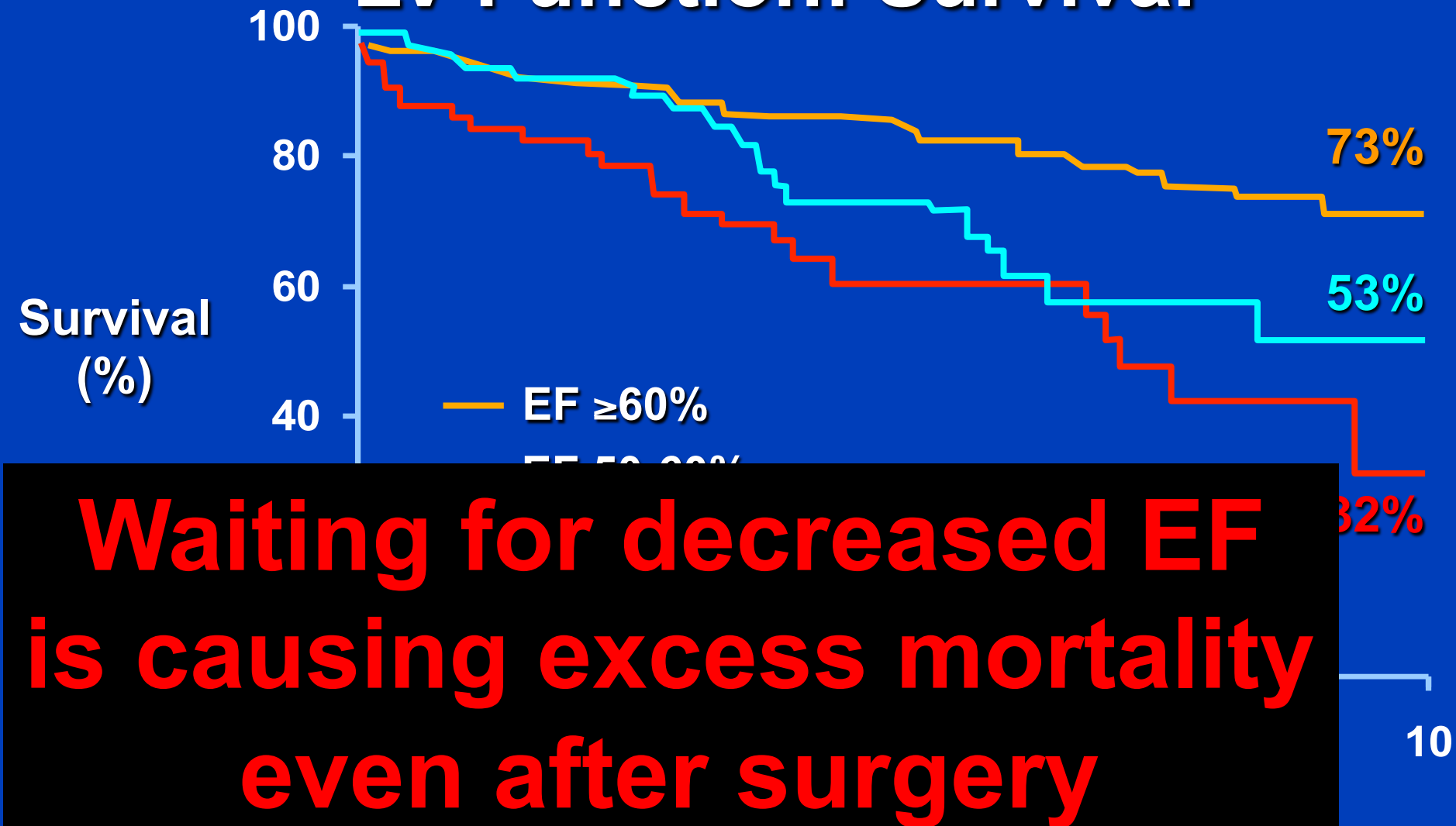
# MR: LV Dysfunction

## The MIDA Study



# MR Postop. Outcome

## LV Function: Survival



# Mitral Regurgitation

## Overt LV Dysfunction

**LVS  $\geq$  40-45 mm**

What is the problem with  
waiting for

**LV ESD  $>40$  mm to operate ?**

# Survival Implication of Left Ventricular End-Systolic Diameter in Mitral Regurgitation Due to Flail Leaflets

## A Long-Term Follow-Up Multicenter Study

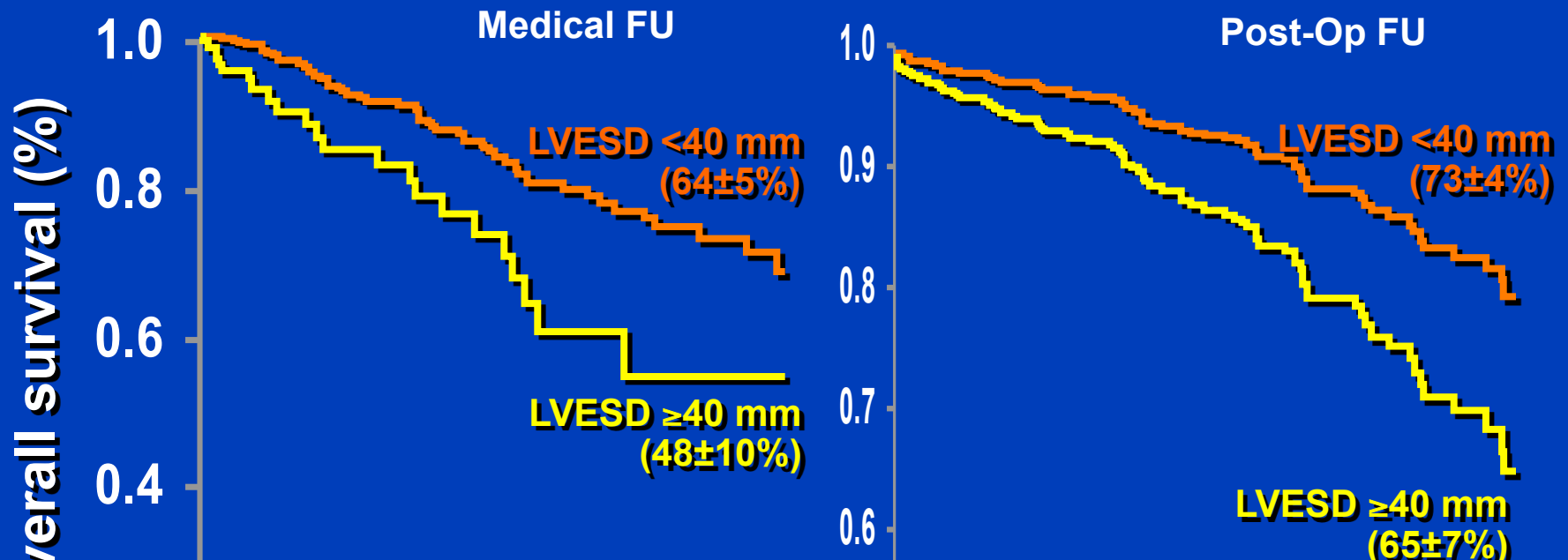
Christophe Tribouilloy, MD, PhD,\* Francesco Grigioni, MD, PhD,† Jean François Avierinos, MD,‡  
 Andrea Barbieri, MD,§ Dan Rusinaru, MD,\* Catherine Szymanski, MD,\* Marinella Ferlito, MD,†  
 Laurence Tafanelli, MD,‡ Francesca Bursi, MD,§ Faouzi Trojette, MD,\* Angelo Branzi, MD,†  
 Gilbert Habib, MD,‡ Maria G. Modena, MD,§ Maurice Enriquez-Sarano, MD,||  
 on behalf of the MIDA Investigators

*Amiens and Marseille, France; Bologna and Modena, Italy; and Rochester, Minnesota*

<b>Objectives</b>	This study analyzed the association of left ventricular end-systolic diameter (LVESD) with survival after diagnosis in organic mitral regurgitation (MR) due to flail leaflets.
<b>Background</b>	LVESD is a marker of left ventricular function in patients with organic MR but its association to survival after diagnosis is unknown.
<b>Methods</b>	The MIDA (Mitral Regurgitation International Database) registry is a multicenter registry of echocardiographically diagnosed organic MR due to flail leaflets. We enrolled 739 patients with MR due to flail leaflets (age $65 \pm 12$ years; ejection fraction: $65 \pm 10\%$ ) in whom LVESD was measured ( $36 \pm 7$ mm).
<b>Results</b>	Under conservative management, 10-year survival and survival free of cardiac death were higher with LVESD $<40$ mm versus $\geq 40$ mm ( $64 \pm 5\%$ vs. $48 \pm 10\%$ ; $p < 0.001$ , and $73 \pm 5\%$ vs. $63 \pm 10\%$ ; $p = 0.001$ ). LVESD $\geq 40$ mm independently predicted overall mortality (hazard ratio [HR]: 1.95, 95% confidence interval [CI]: 1.01 to 3.83) and cardiac mortality (HR: 3.09, 95% CI: 1.35 to 7.09) under conservative management. Mortality risk increased linearly with LVESD $>40$ mm (HR: 1.15, 95% CI: 1.04 to 1.27 per 1-mm increment). During the entire follow-up (including post-surgical), LVESD $\geq 40$ mm independently predicted overall mortality (HR: 1.86, 95% CI: 1.24 to 2.80) and cardiac mortality (HR: 2.14, 95% CI: 1.29 to 3.56), due to persistence of excess mortality in patients with LVESD $\geq 40$ mm after surgery (HR: 1.86, 95% CI: 1.11 to 3.15 for overall death, and HR: 1.81, 95% CI: 1.05 to 3.54 for cardiac death).
<b>Conclusions</b>	In MR due to flail leaflets, LVESD $\geq 40$ mm is independently associated with increased mortality under medical management but also after mitral surgery. These findings support prompt surgical rescue in patients with LVESD $\geq 40$ mm but also suggest that best preservation of survival is achieved in patients operated before LVESD reaches 40 mm. (J Am Coll Cardiol 2009;54:1961–8) © 2009 by the American College of Cardiology Foundation

# MR due to Flail Leaflets

Long-term survival according to **LV-ESD**



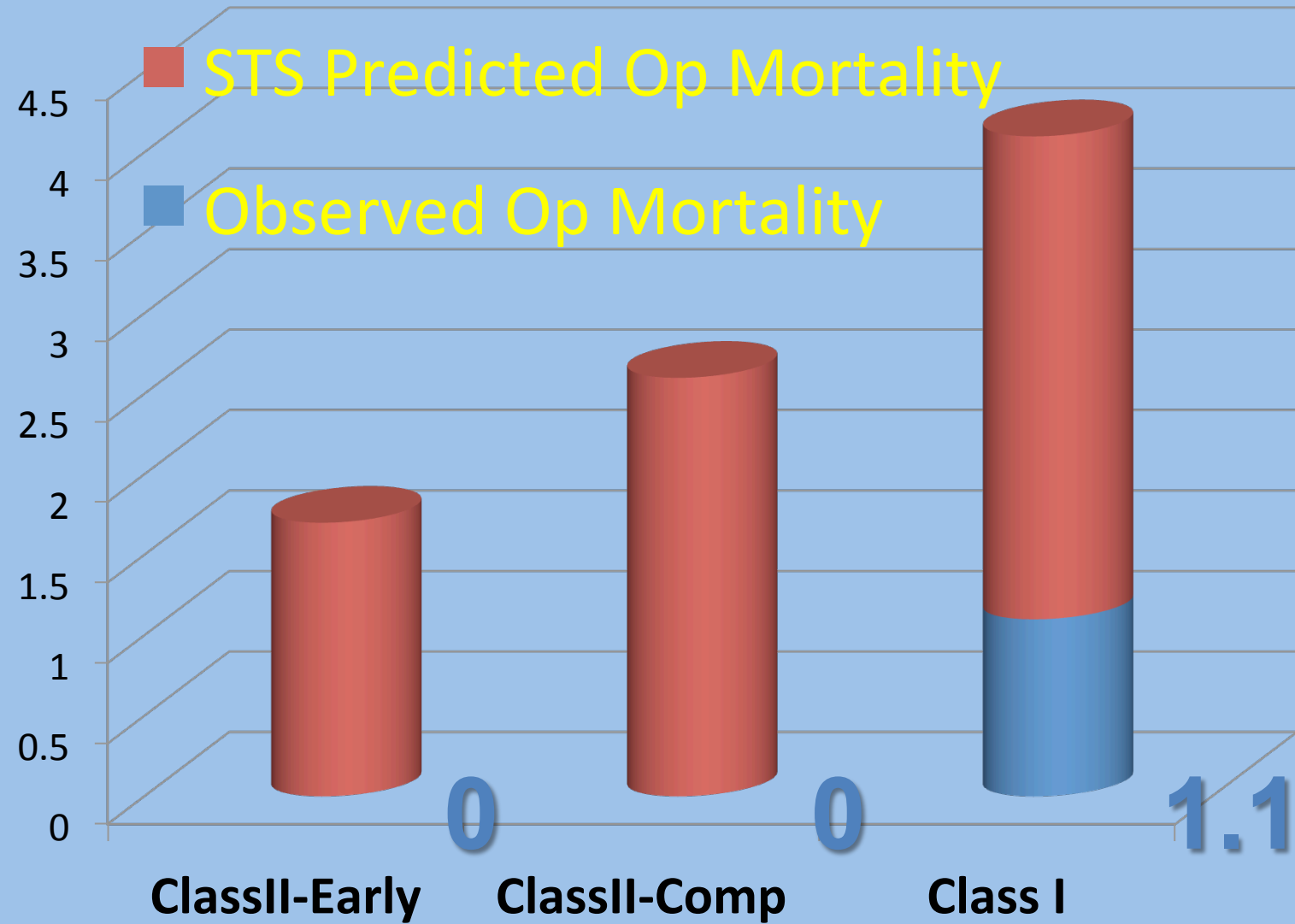
**Waiting for LVS ≥40 mm  
is causing excess mortality  
even after surgery**



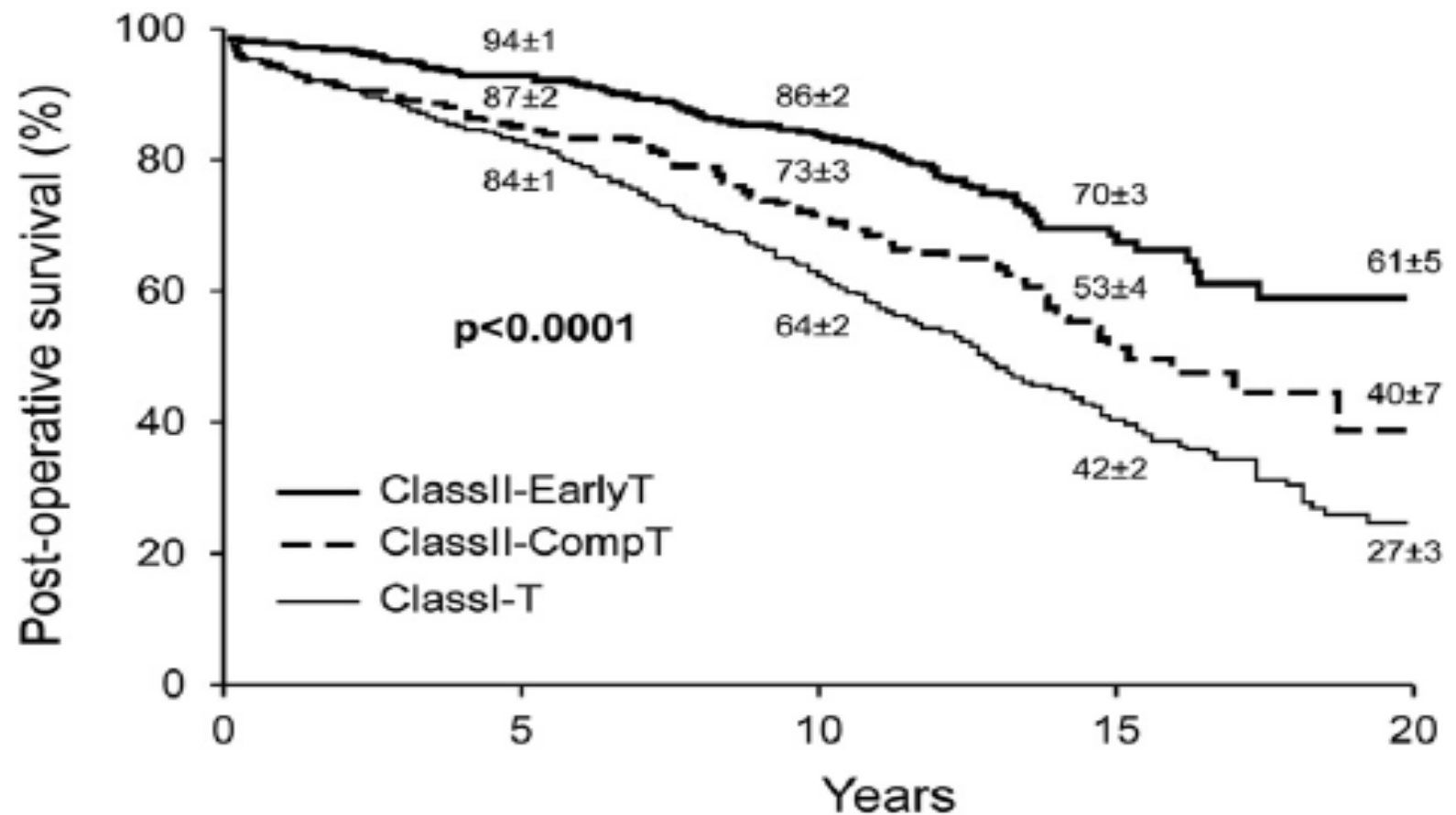
**Most data regarding the outcome implications of mitral surgical indications are based on patients operated in the 1980s with a high proportion of valve replacement**

**Is it true that waiting for guideline-based indications leads to poor outcomes in the repair era?**

# Operative Mortality



# Long-term survival



Triggers					
ClassII-EarlyT	523	488	403	68	6
ClassII-CompT	195	168	127	38	3
ClassI-T	794	664	461	135	13

# Mitral Regurgitation

## Surgical Treatment ?

**MR**

```
graph TD; MR[MR] --> Symptoms; MR --> EarlySurgery[Early Surgery]; Symptoms --> RescueSurgery[Rescue Surgery]; EarlySurgery --> RestorativeSurgery[Restorative Surgery];
```

**Symptoms**  
**LV Dysfunction**  
**AF/PHTN**

**Rescue Surgery**  
**Relieves pts but**  
**poor outcome**

**Early**  
**Surgery**

**Restorative Surgery**  
**No relief but**  
**restores life expectancy**

We should do:

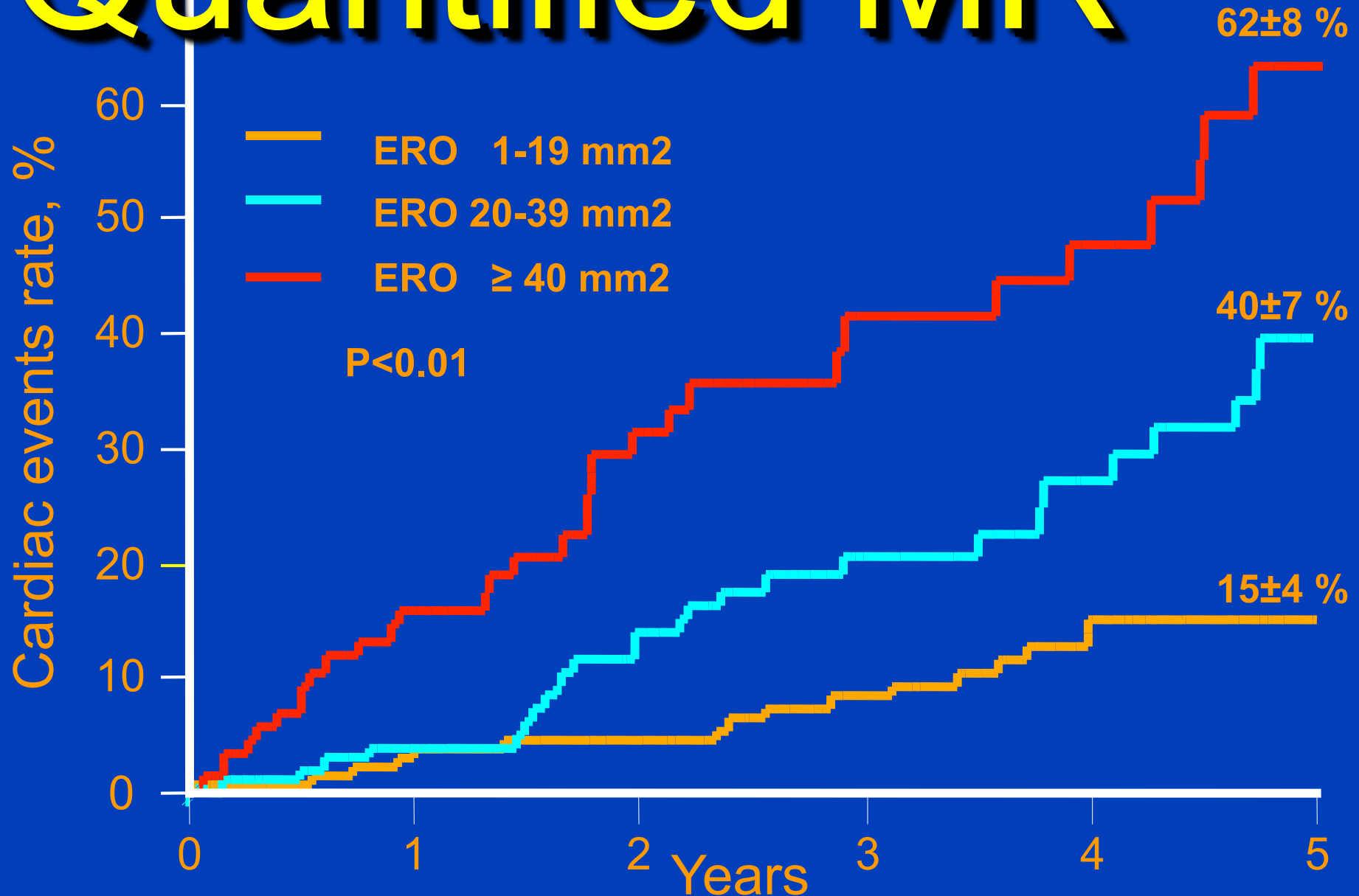
- MR Rescue Surgery  
when we have to

- MR Early Surgery with  
objective risk-markers

**1-MR Severity**



# Quantified MR



# Mitral Regurgitation

## Grading of Severity

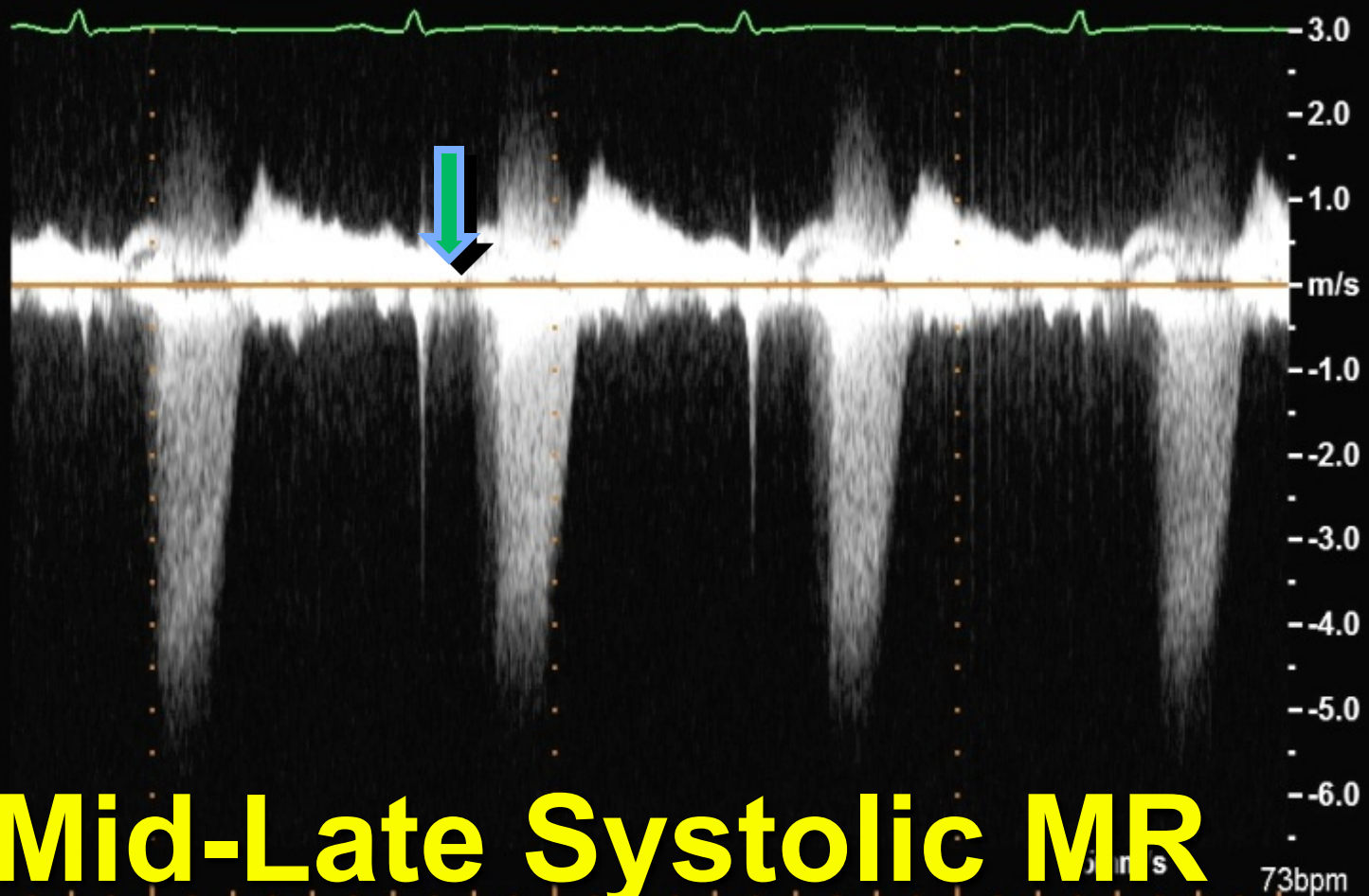
ASE Grade		RVol (mL)	ERO (mm <sup>2</sup> )
Mild	Grade I	<30	<20
Moderate	Grade II	30-44	20-29
	Grade III	45-59	30-39
Severe	Grade IV	≥60	≥40

Excess risk with  $ERO \geq 0.40 \text{ cm}^2$   
is relieved by surgical repair

# Mitral Valve Prolapse With Mid-Late Systolic Mitral Regurgitation

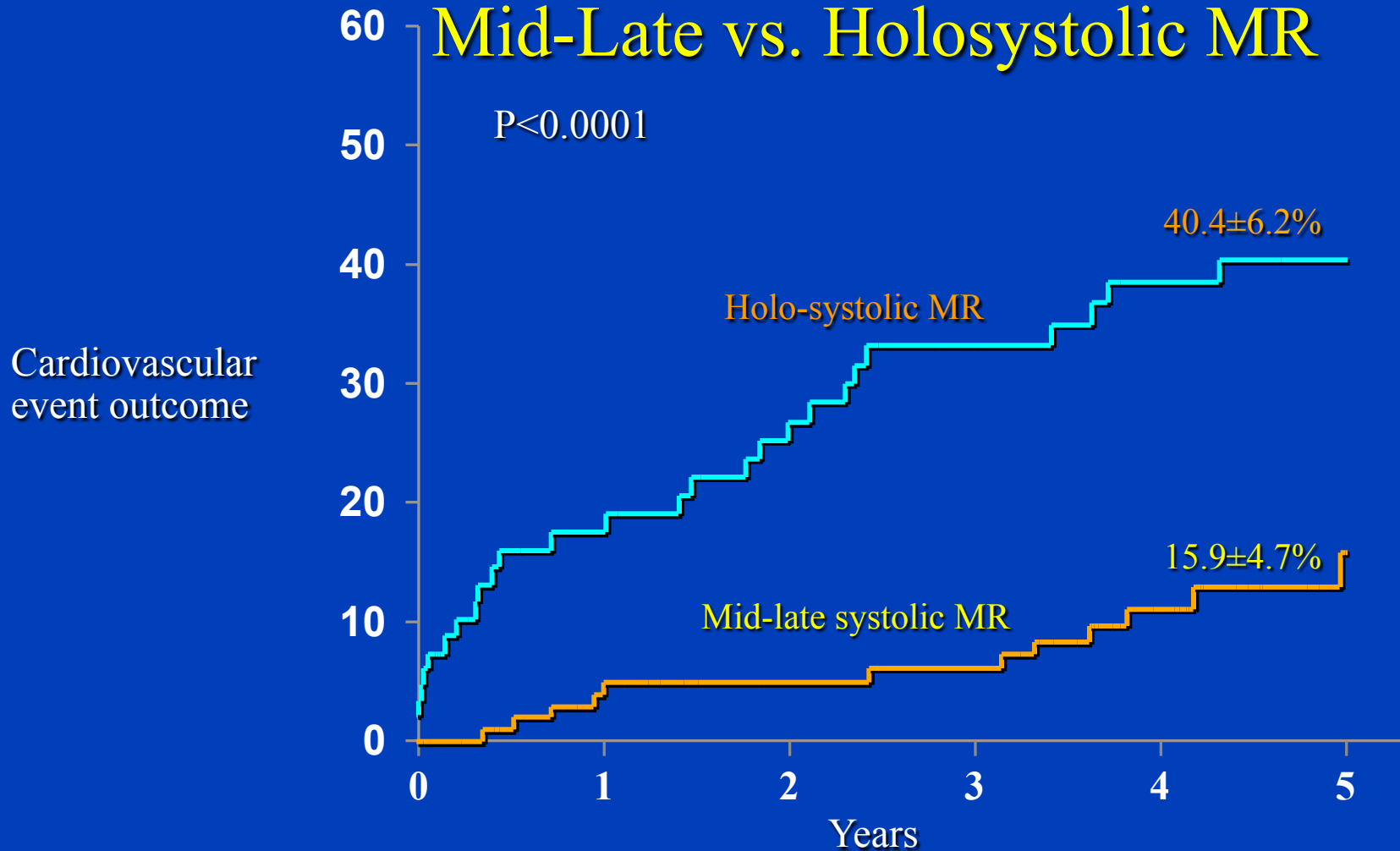
## Pitfalls of Evaluation and Clinical Outcome Compared With Holosystolic Regurgitation

Yan Topilsky, MD; Hector Michelena, MD; Valentina Bichara, MD; Joseph Maalouf, MD;  
Douglas W. Mahoney, MS; Maurice Enriquez-Sarano, MD



# Clinical Outcome

## Mid-Late vs. Holosystolic MR



MLS No at risk	111	94	87	84	59	25
HS No at risk	90	56	48	38	34	31

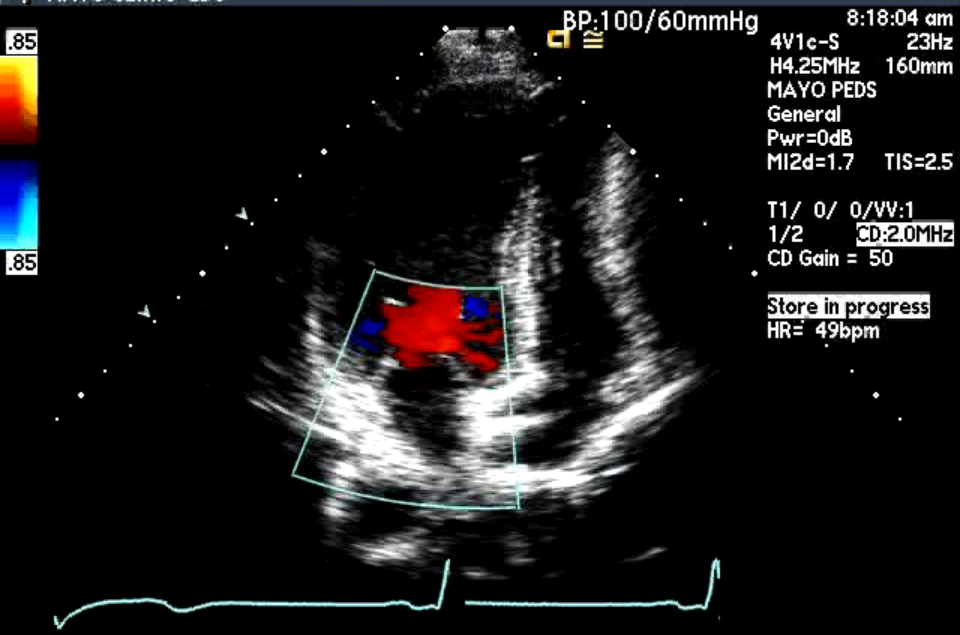
We should do:

- MR Rescue Surgery  
when we have to

- MR Early Surgery with  
objective risk-markers

2-Left Atrium



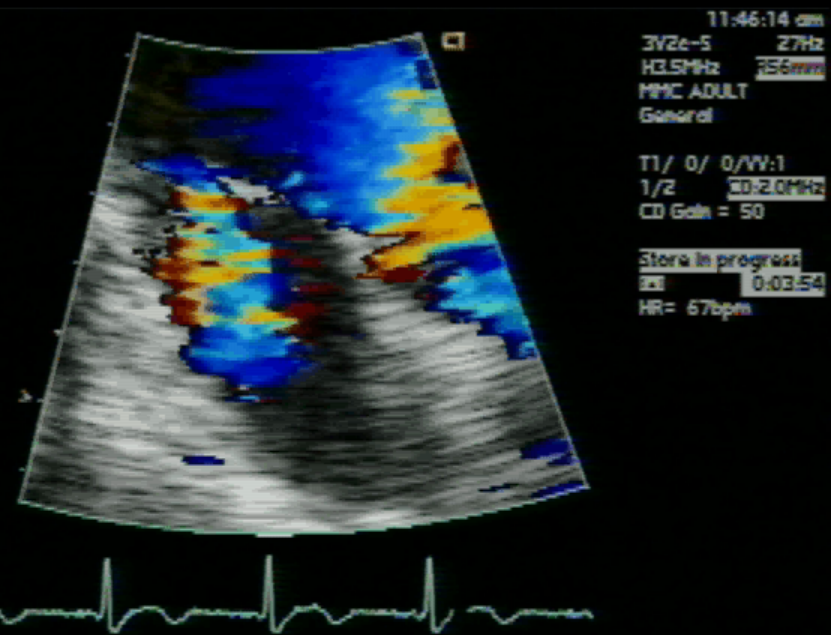
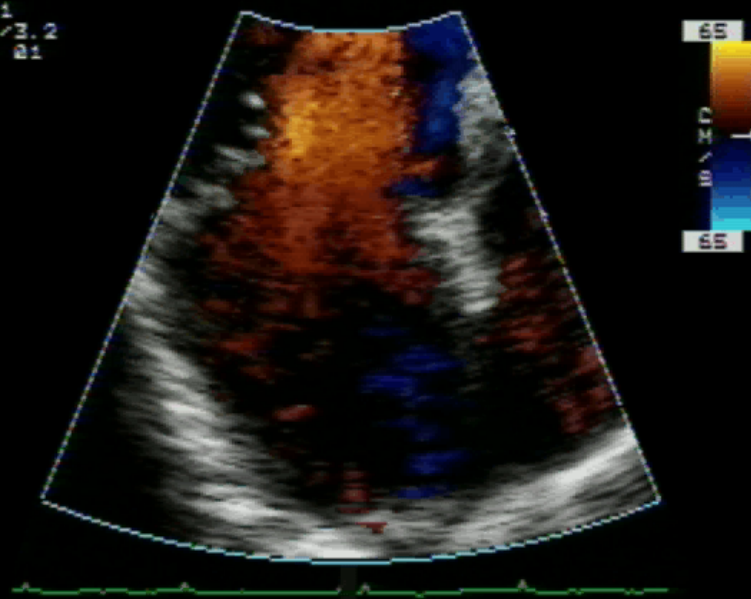


DTV/CDV

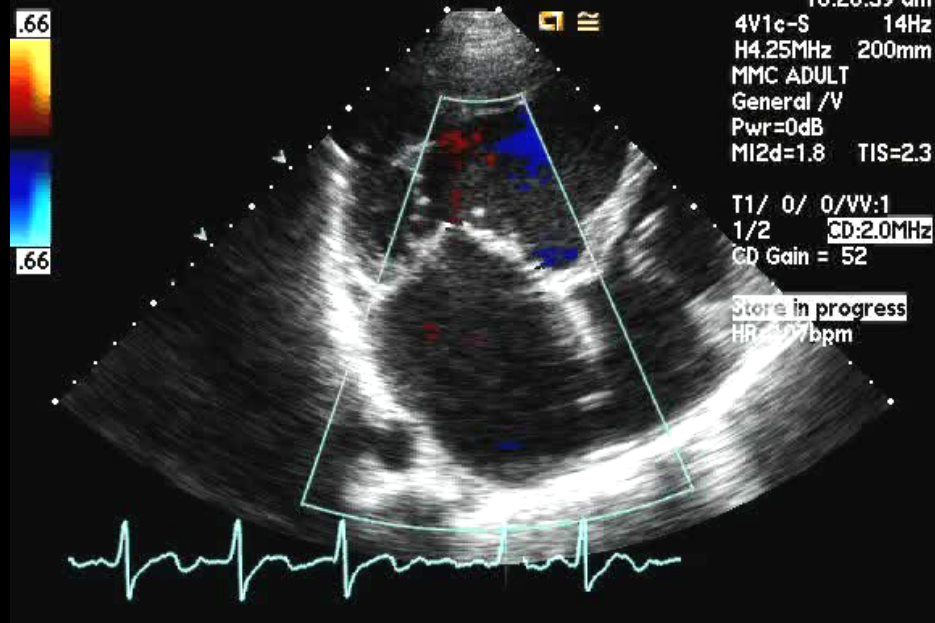
CD Pan

CD Pos/Size

TIS: 1.1  
 S3 1.6/3.2  
 21 NOV 21



MAYO CLINIC 3DB

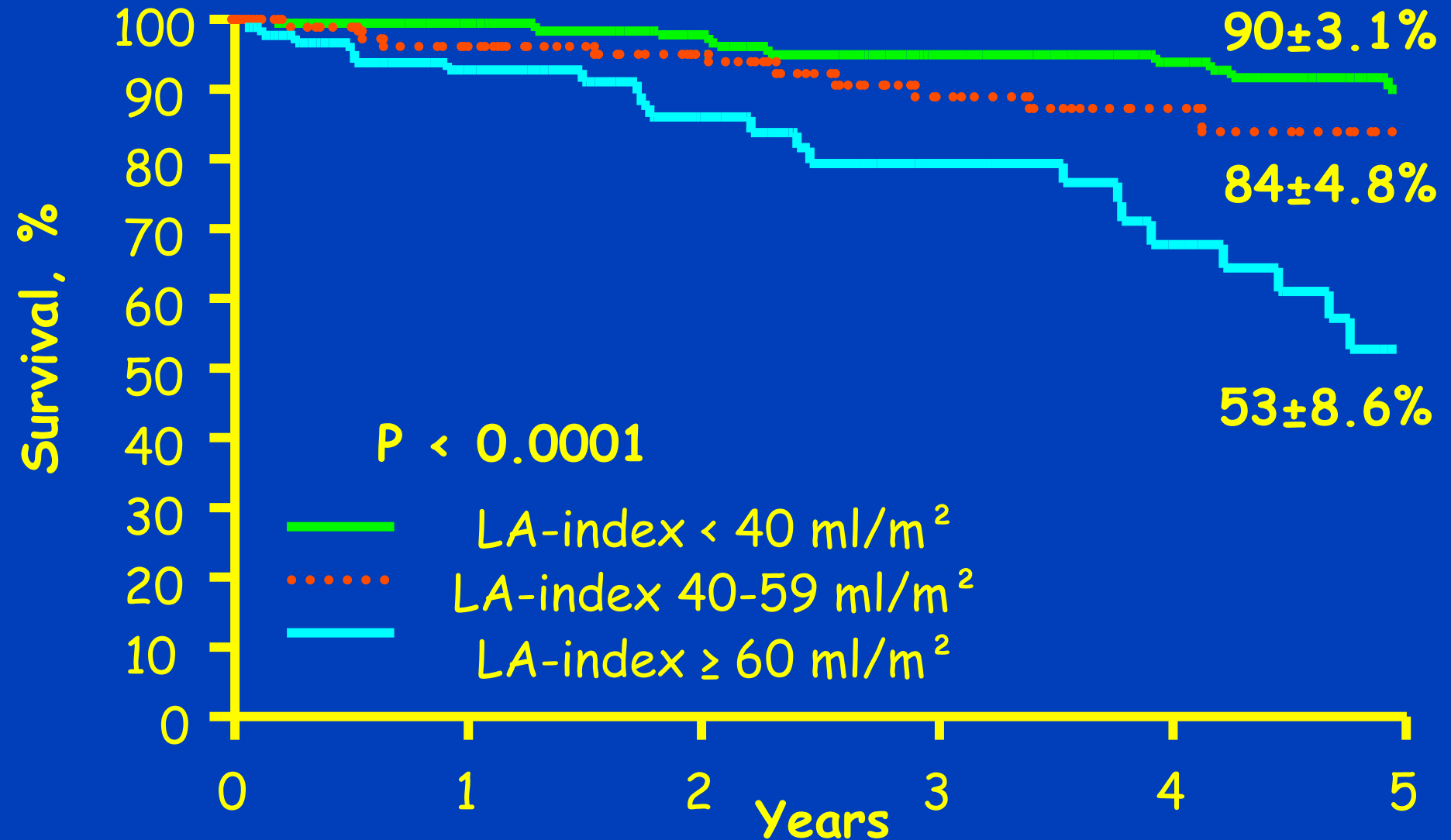


CD Pan

CD Pos/Size

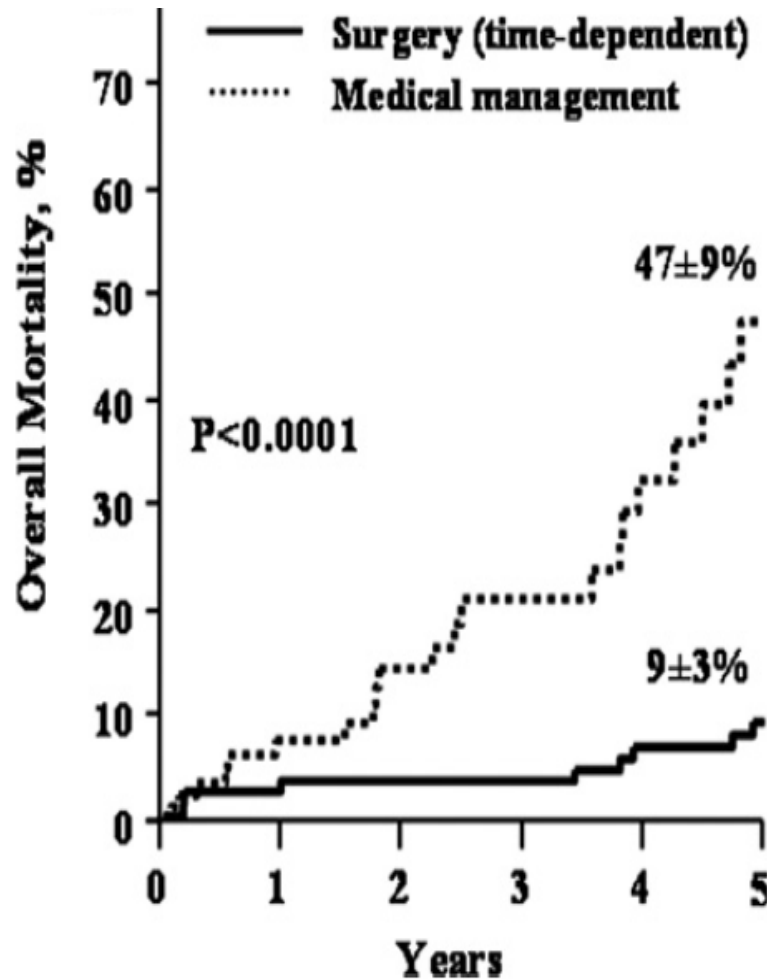
# Left Atrium in MR

Overall Survival (Medical Management)

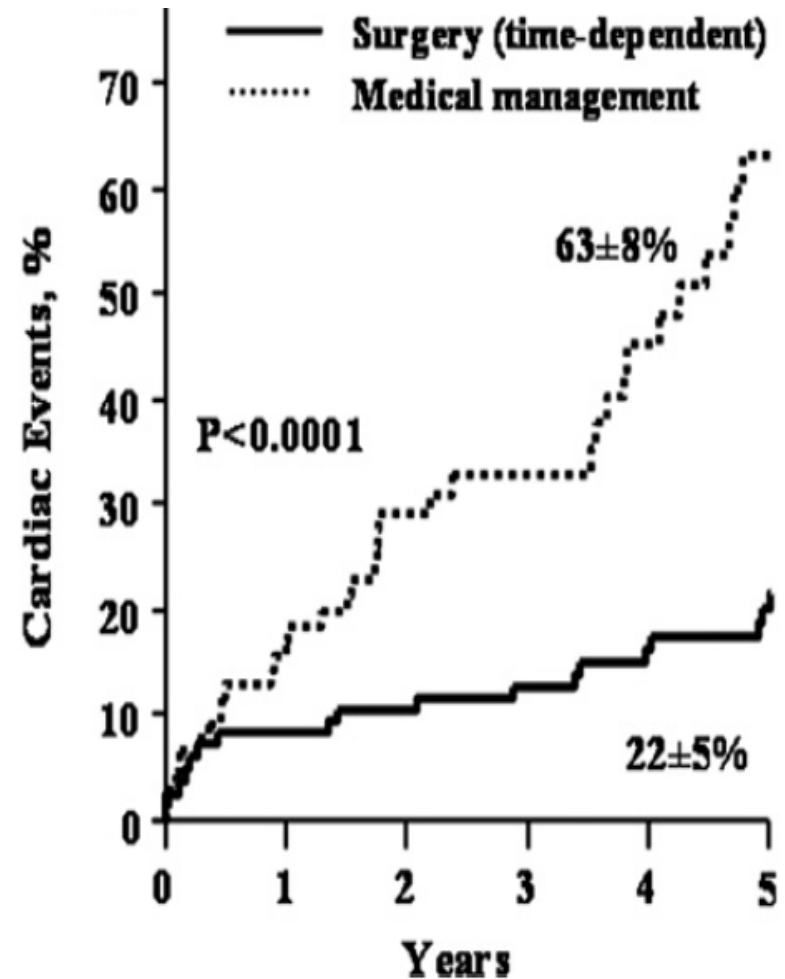


# Surgery Eliminates the risk associated with markedly enlarged LA ( $\geq 60$ mL/m<sup>2</sup>)

## Mortality



## Cardiac Events



Outcome in Patients With Markedly Enlarged LA Compared Between Surgical and Medical Management

# MR Evaluation

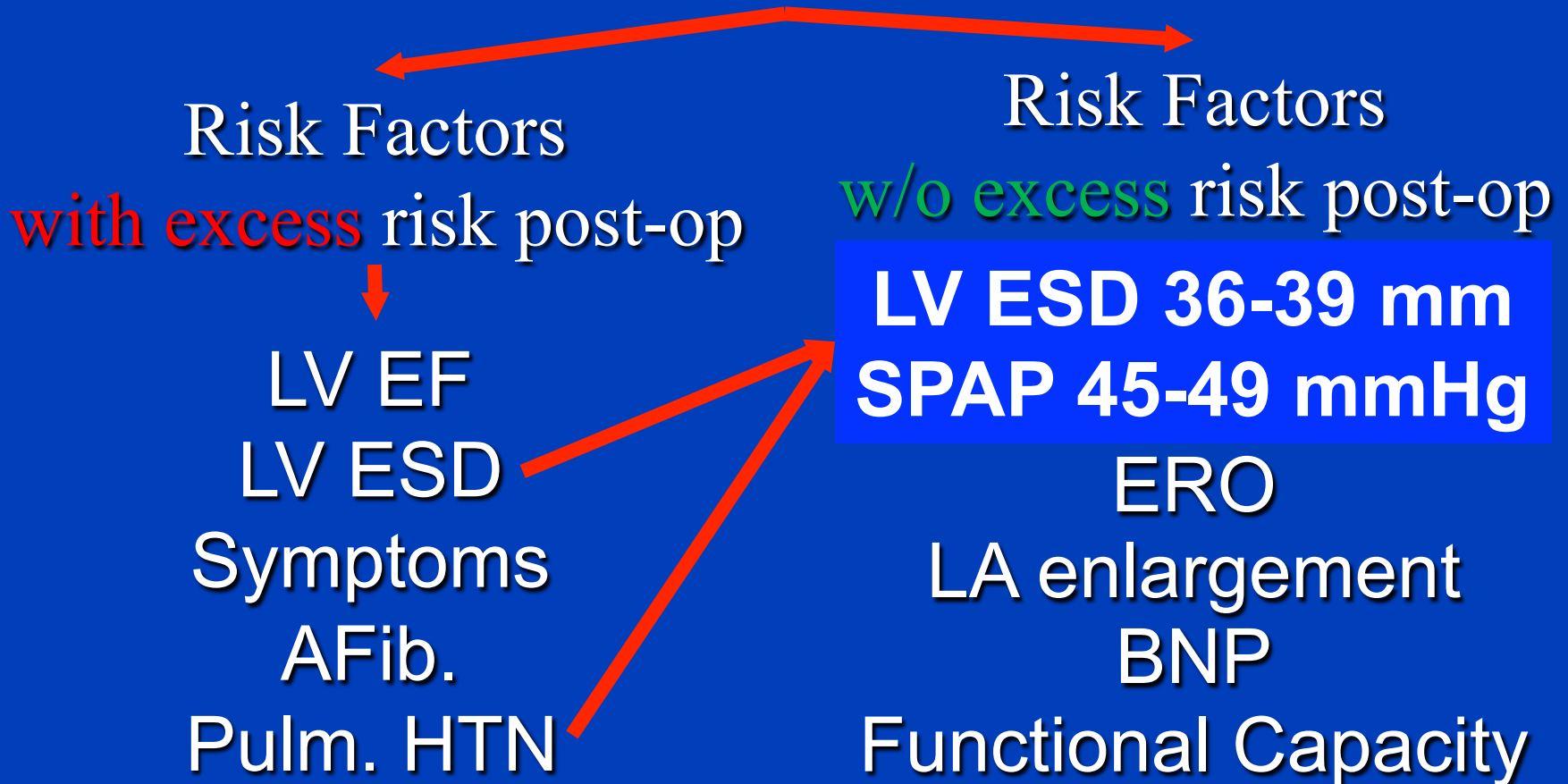
## 3-Other predictors?

- SPAP
- BNP
- Ex testing

# Mitral Regurgitation

A Strategy of Multiple Risk Predictors

## MR





MR Management

Early Surgery  
beneficial ?

# Asymptomatic MR

*Offer **Early Surgery** to  
asymptomatic MR patients in  
Advanced repair centers:*

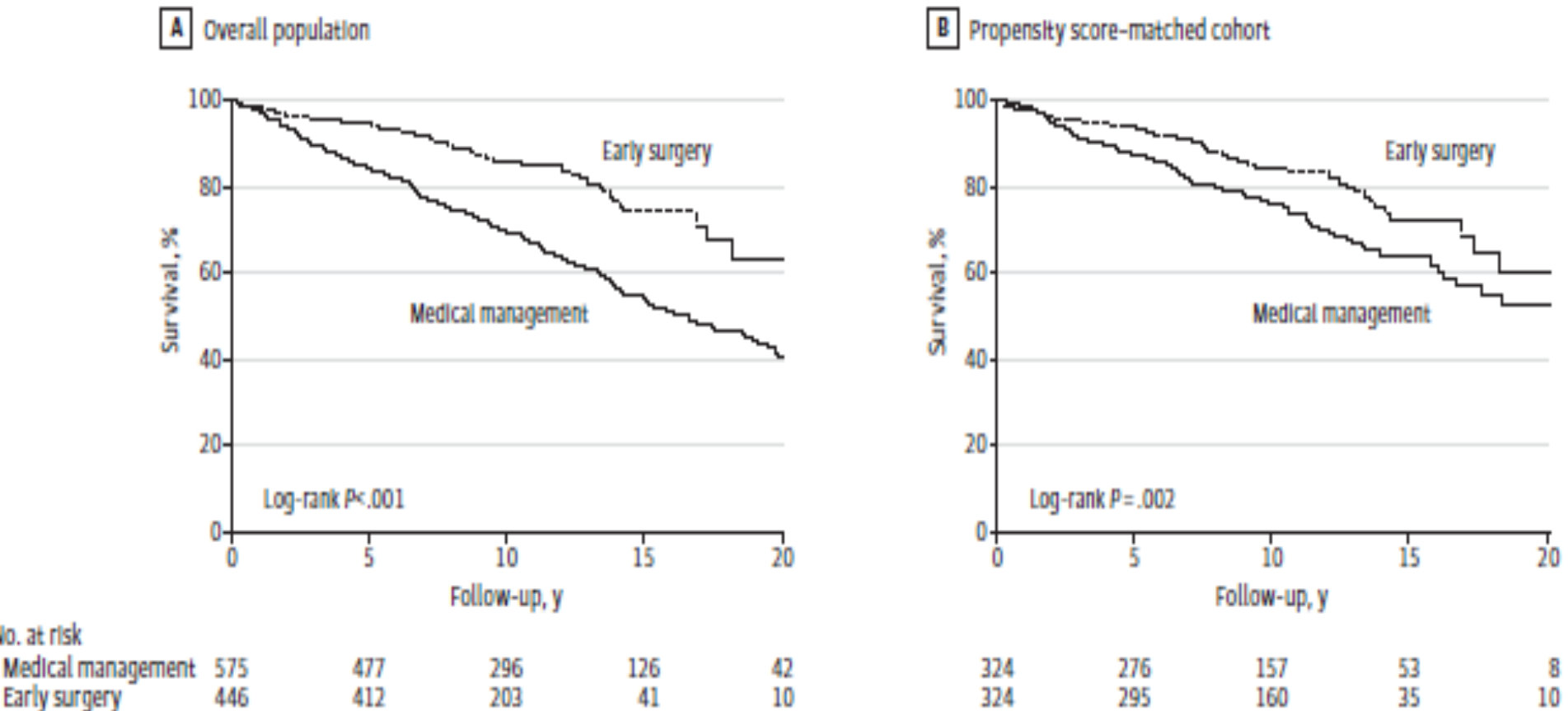
- *Low risk*
- *Excellent Doppler-Echo*
  - *High repair rates*
  - *High repair quality*

# MR due to Flail leaflets: Early surgery candidates

No Heart failure symptoms,  $EF \geq 60$ ,  $LVS < 40\text{mm}$

RR 0.55 0.52

Figure 1. Survival After Diagnosis of Mitral Regurgitation Due to Flail Mitral Leaflet According to Initial Treatment Strategy

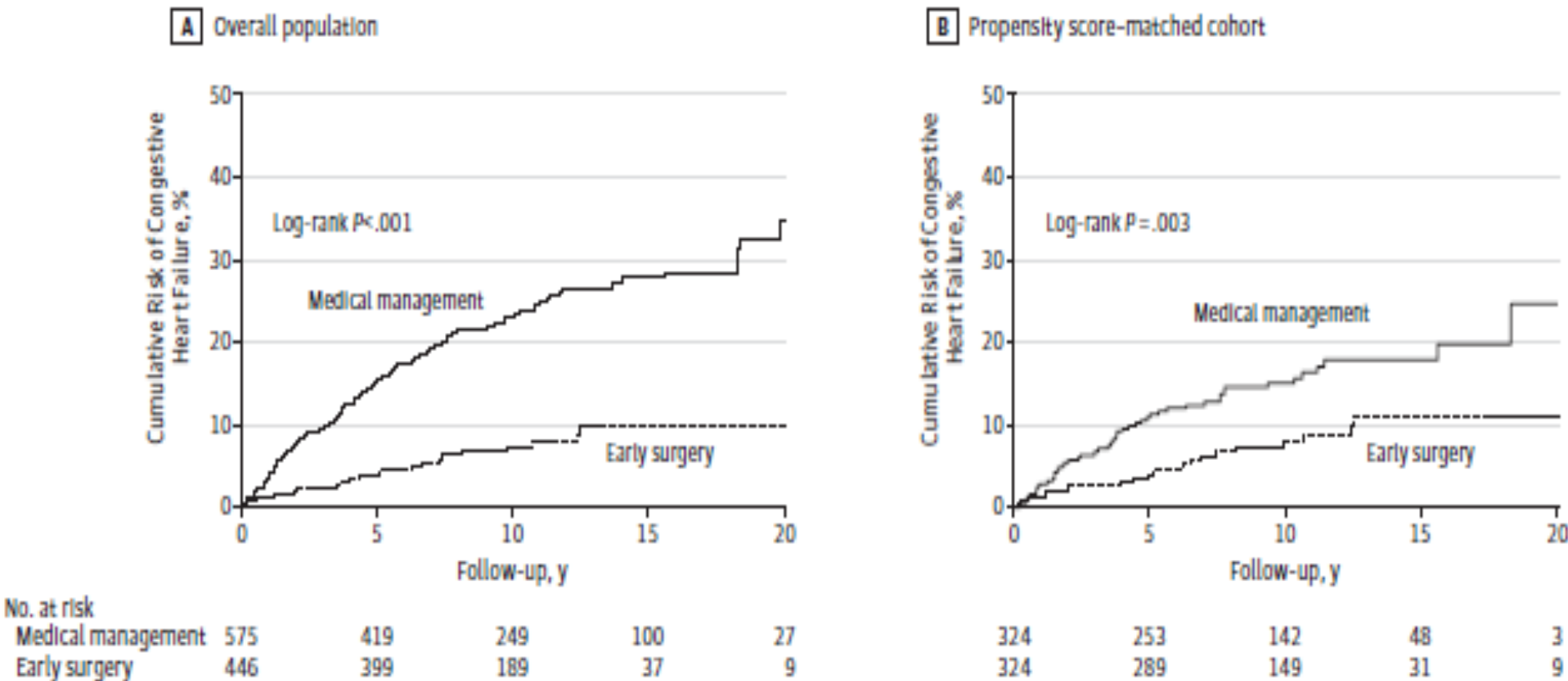


# MR due to Flail leaflets: Early surgery candidates

## No Heart failure symptoms, $EF \geq 60$ , $LVS < 40\text{mm}$

RR 0.29 0.44

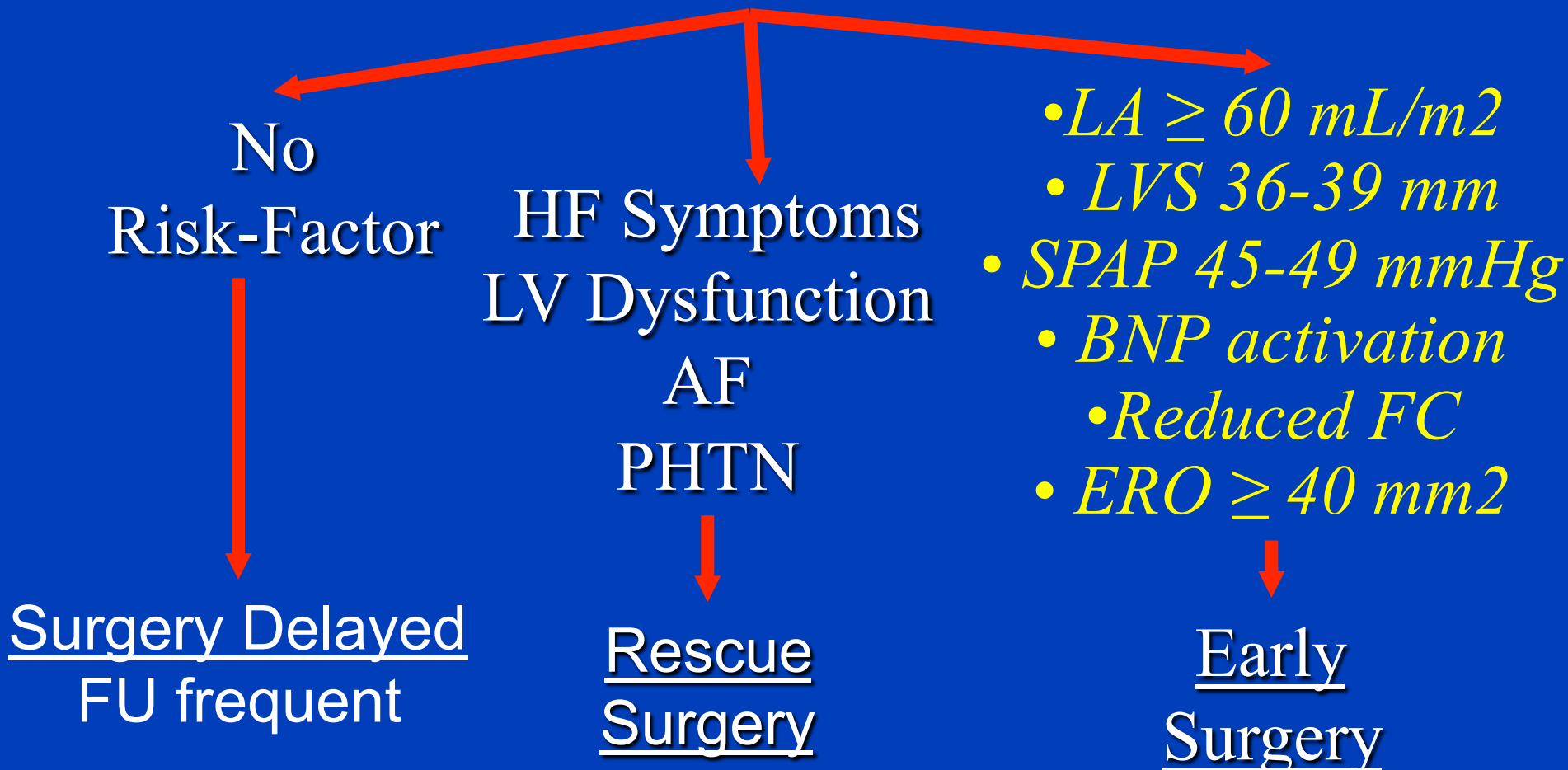
Figure 2. Heart Failure Incidence After Diagnosis of Mitral Regurgitation Due to Flail Mitral Leaflet According to Initial Treatment Strategy



Long-term heart failure risk following early surgery vs initial medical management overall (A) and in the propensity score-matched cohort (B).

# Organic MR

## MR Evaluation





# MR Evaluation for therapeutic strategy

- Comprehensive **assessment of lesions**
- Comprehensive **LV, hemodynamic and LA assessment**: direct MR consequences
- **BNP and exercise testing**: Physiologic MR consequences
- **MR Quantitation** should be the rule: It defines superiorly **severity, outcome and strategy for surgery/intervention**

# Mitral Regurgitation

Which of these circumstances does not represent a high-risk MR:

- MVP with MR and LA volume 60 mL/m<sup>2</sup>
- MVP with mid-late systolic MR and ERO 60 mm<sup>2</sup>
- Bileaflet prolapse with regurgitant volume 60 mL
- MVP-MR with end-systolic LV dimension 42 mm
- MVP holosystolic MR and EF 56%

# Mitral Regurgitation

Which of these circumstances does not represent a high-risk MR:

- MVP with MR and LA volume 60 mL/m<sup>2</sup>
- MVP with mid-late systolic MR and ERO 60 mm<sup>2</sup>
- Bileaflet prolapse with regurgitant volume 60 mL
- MVP-MR with end-systolic LV dimension 42 mm
- MVP holosystolic MR and EF 56%

**THANK  
YOU**