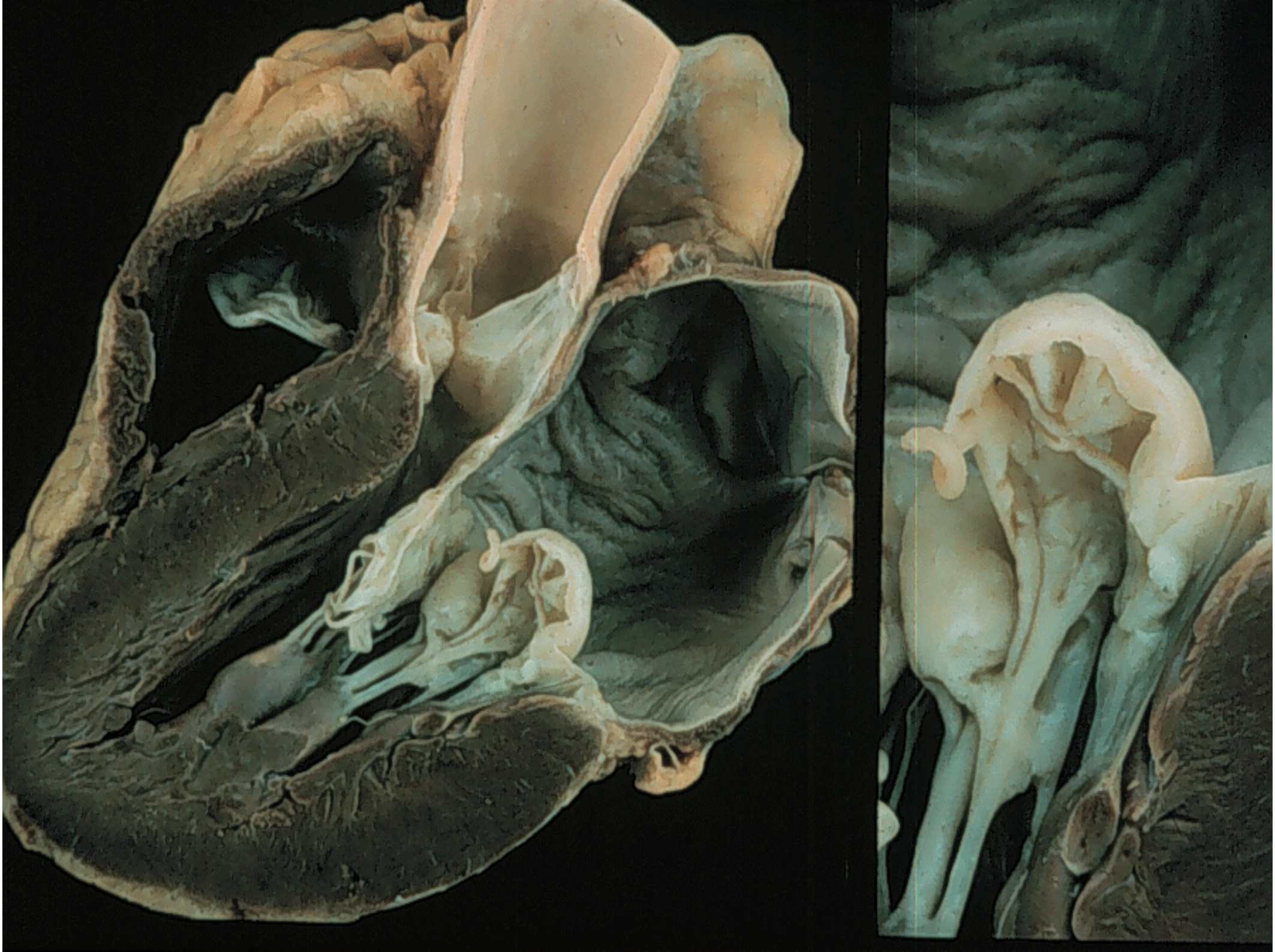
# Mitral Regurgitation

## Turin-*2010*

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



# MR in the 21th century

## What are the guidelines in 2010 ?

# Mitral Regurgitation: The guidelines

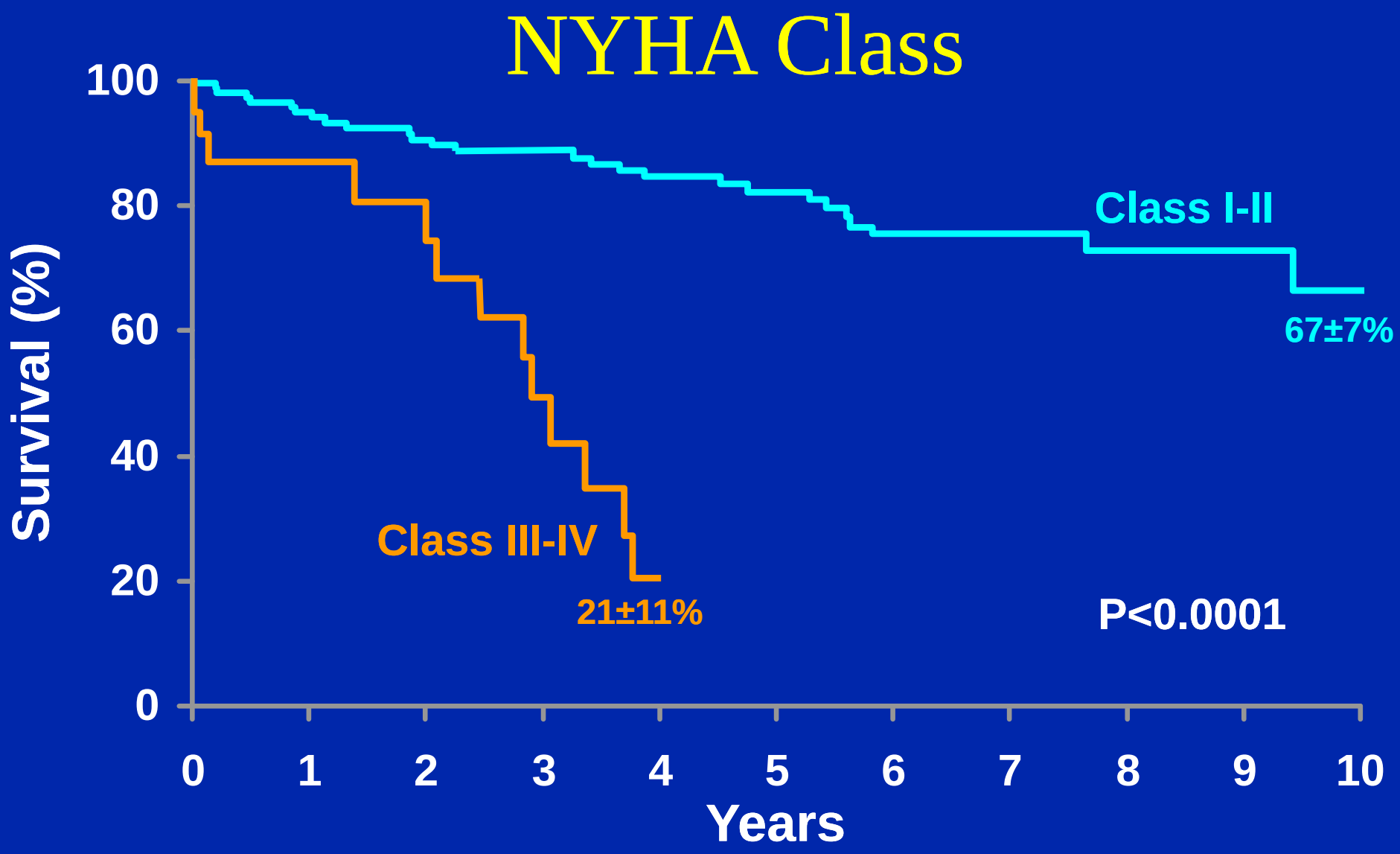
Class I

1. MV surgery is recommended for the [redacted] patient with acute severe MR.* *(Level of Evidence: B)*
2. MV surgery is beneficial for patients with chronic severe MR* and [redacted] symptoms in the absence of severe LV dysfunction (severe LV dysfunction is defined as ejection fraction less than 0.30) and/or end-systolic dimension greater than 55 mm. *(Level of Evidence: B)*
3. MV surgery is beneficial for asymptomatic patients with chronic severe MR* and [redacted], ejection fraction 0.30 to 0.60, and/or end-systolic dimension greater than or equal to 40 mm. *(Level of Evidence: B)*
4. MV repair is recommended over MV replacement in the majority of patients with severe chronic MR* who require surgery, and patients should be referred to

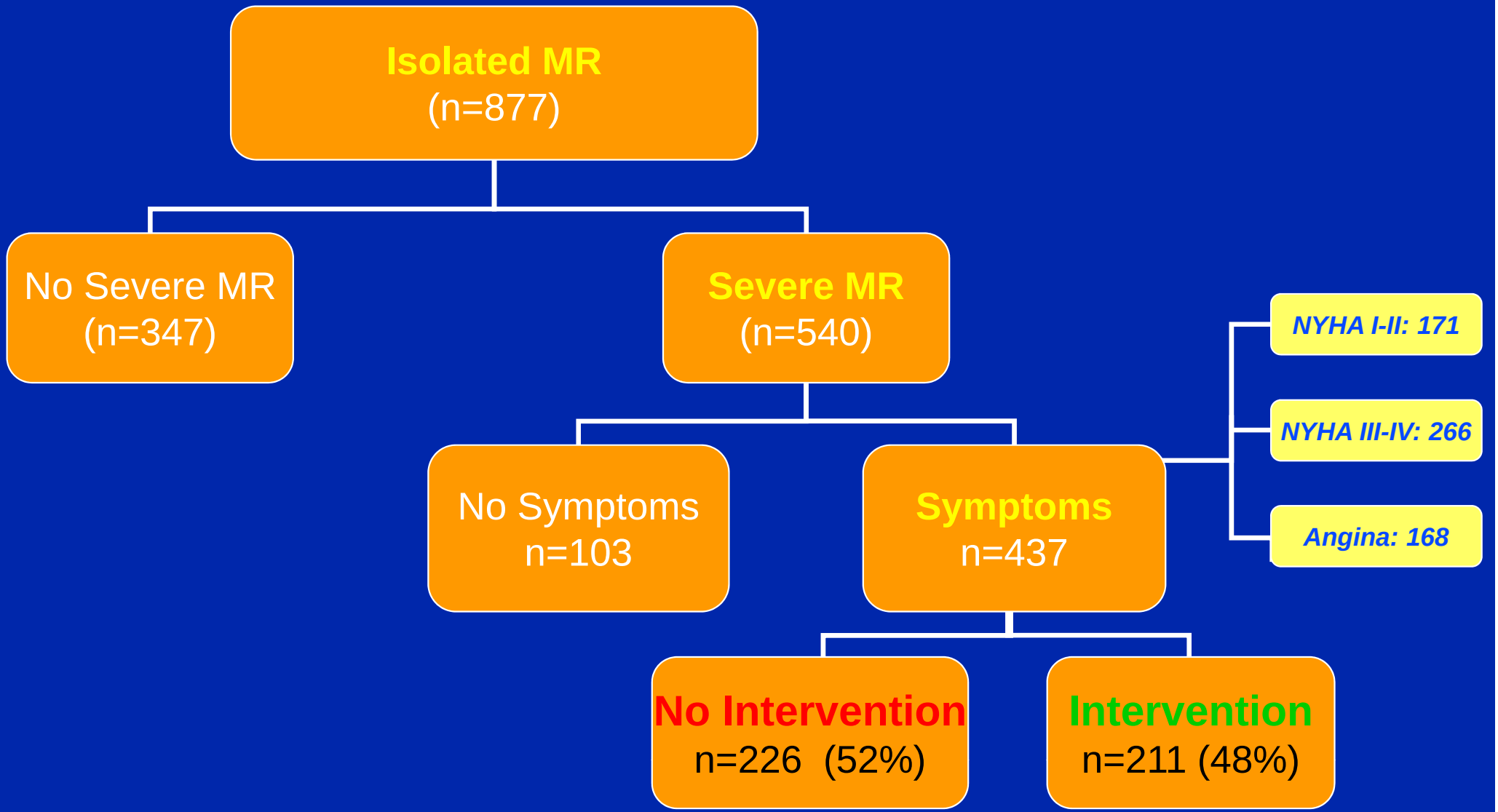
# Mitral Regurgitation

## What is the problem with waiting for Symptoms to operate ?

# MR Natural History



# Severe Symptomatic MR
# The EuroHeart Survey




Mirabel M et al *Eur Heart J.* 2007;28(11):1358-1365.

**Table 4** Prevalence of Indications for Surgical Intervention for Chronic Severe Mitral Regurgitation in Patients With Organic Mitral Regurgitation Based on the 1998 ACC/AHA Guidelines*

| | All Patients | Operated | Unoperated | p Value |
|---|---|---|---|---|
| n | 112 | 59 | 53 | |
| Symptoms | 53 (47%) | 29 (49%) | 24 (45%) | 0.68 |
| LVIDS ≥45 mm | 11 (10%) | 5 (8%) | 6 (11%) | 0.61 |
| LVEF ≤60% | 50 (45%) | 26 (44%) | 24 (45%) | 0.90 |
| Atrial fibrillation | 26 (23%) | 14 (24%) | 12 (23%) | 0.89 |
| RVSP >50 mm Hg | 25 (22%) | 9 (15%) | 16 (30%) | 0.06 |
| Any indication | 96 (86%) | 57 (97%) | 39 (74%) | <0.0001 |

| Rationale | n | Death | Cardiac Death | Interval to Cardiac Death (days) |
|---|---|---|---|---|
| Asymptomatic | 9 (17%) | 1 | 0 | — |
| Stable LVEF, stable chambers | 17 (32%) | 3 | 3 | 186, 839, 855 |
| MR improved on subsequent echocardiogram | 6 (11%) | 1 | 1 | 213 |
| Comorbidities/risk | 10 (19%) | 7* | 4 | 3, 5, 26, 43 |
| Patient refused | 4 (%) | 2 | 2 | 3, 32 |
| Died before planned evaluation | 1 (%) | 1 | 1 | 5 |
| MR unrecognized | 4 (%) | 1† | 0 | — |
| MR ignored | 2 (%) | 1 | 1 | 232 |

Bach et al
JACC 2009

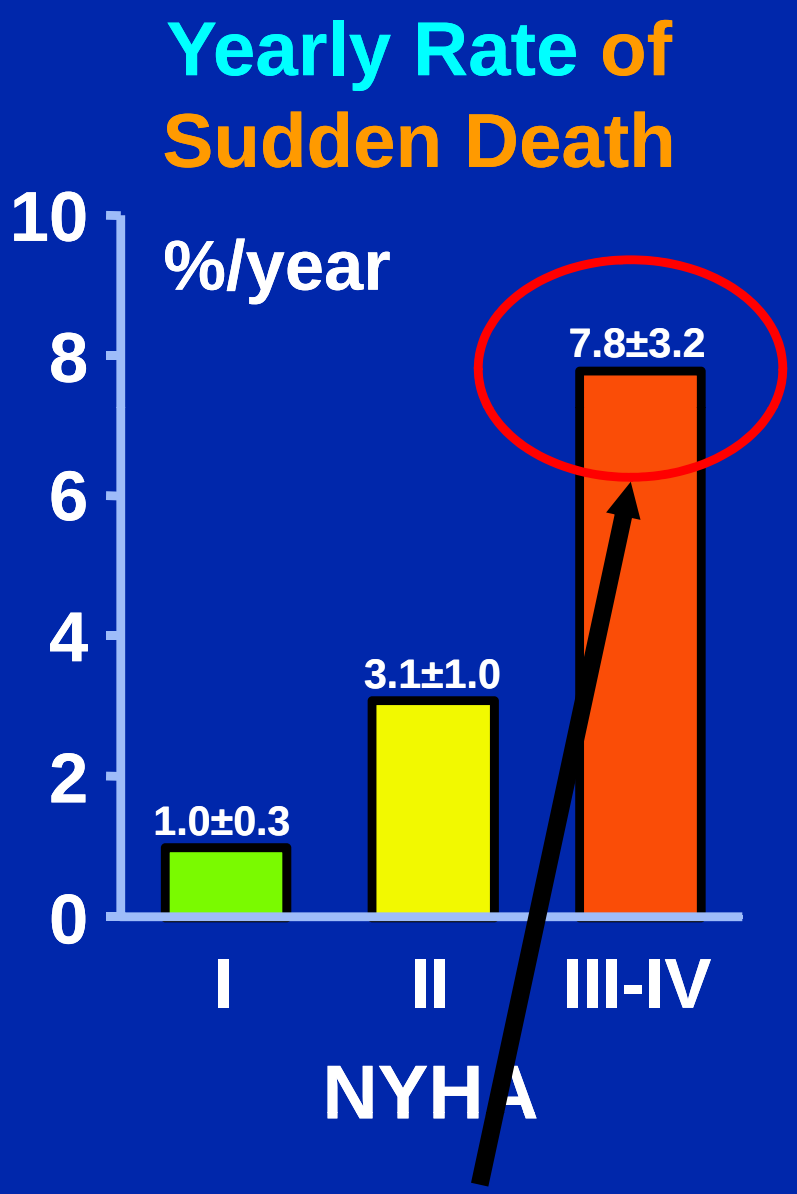
# MR in the Elderly

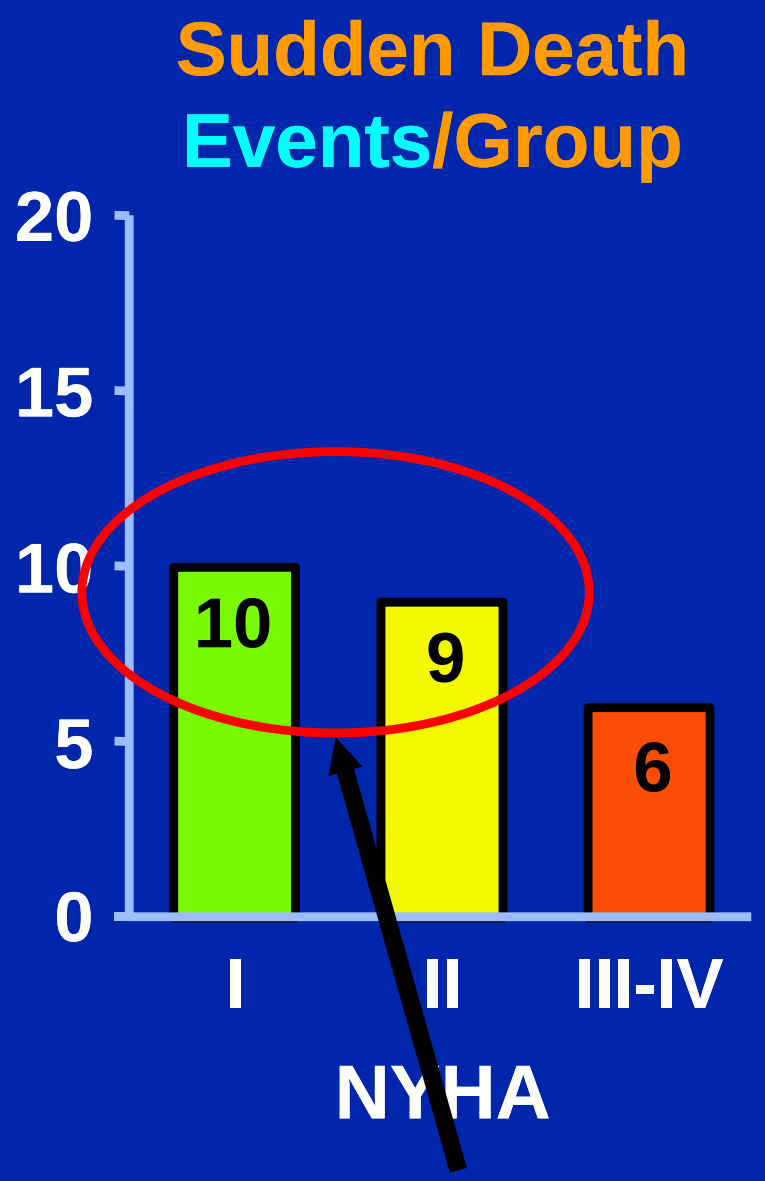
## Usual Management

- **Asymptomatic elderly with severe MR: "You are doing too well to consider a risky surgery"**

- **Symptomatic elderly with MR: "You are too old to be operated"**

# MR Natural History

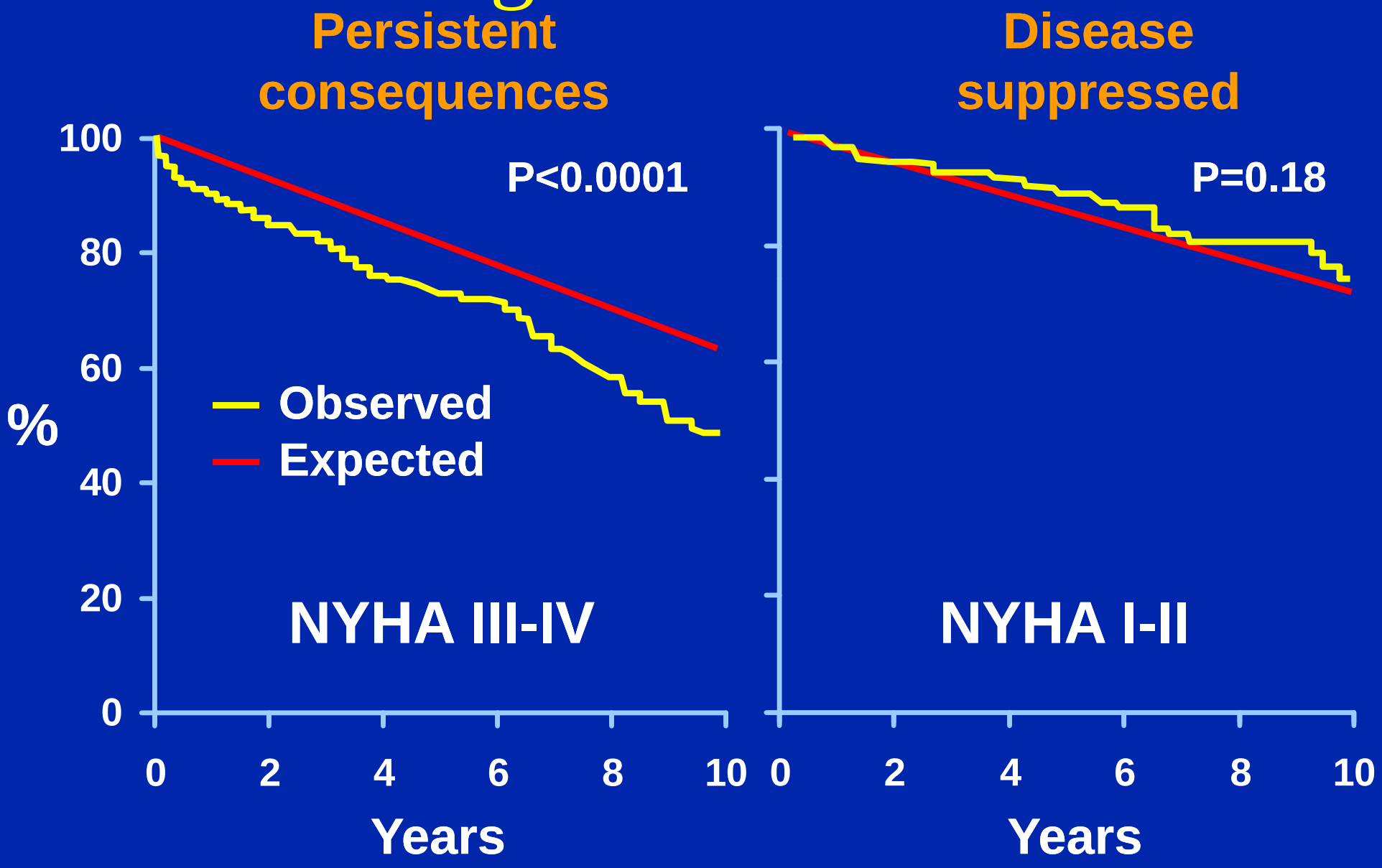



**Symptoms are specific of SD risk..but are not sensitive**

# MR Postop. Outcome

## Long-term Survival



# Mitral Regurgitation

## What are the implications of Symptoms ?

- Symptoms are often neglected
- Symptoms are insensitive markers of risk
- Symptoms are associated with poor post-operative outcome

# Mitral Regurgitation

## What is the problem with waiting for LV Dysfunction to operate ?

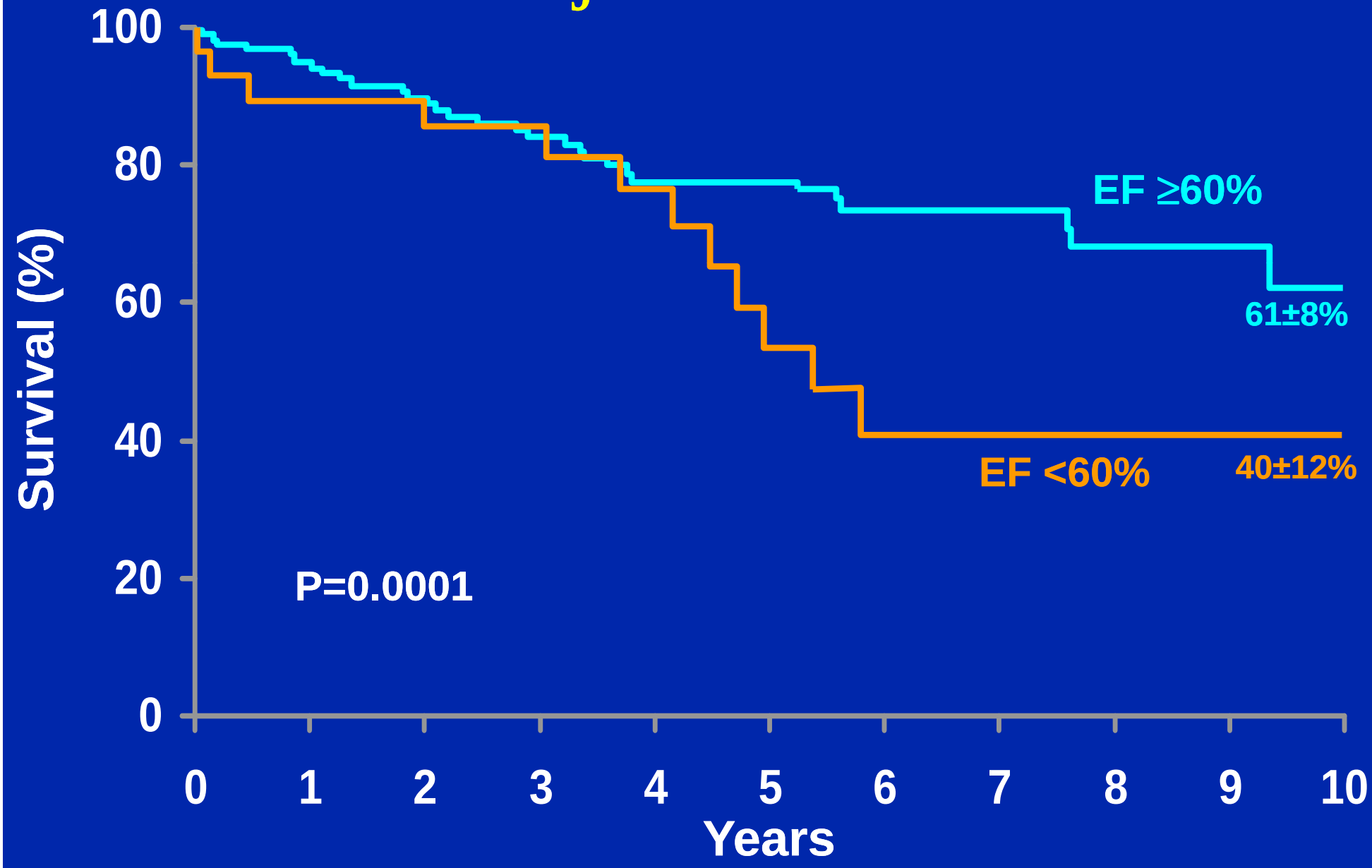
# Mitral Regurgitation

## Overt LV Dysfunction

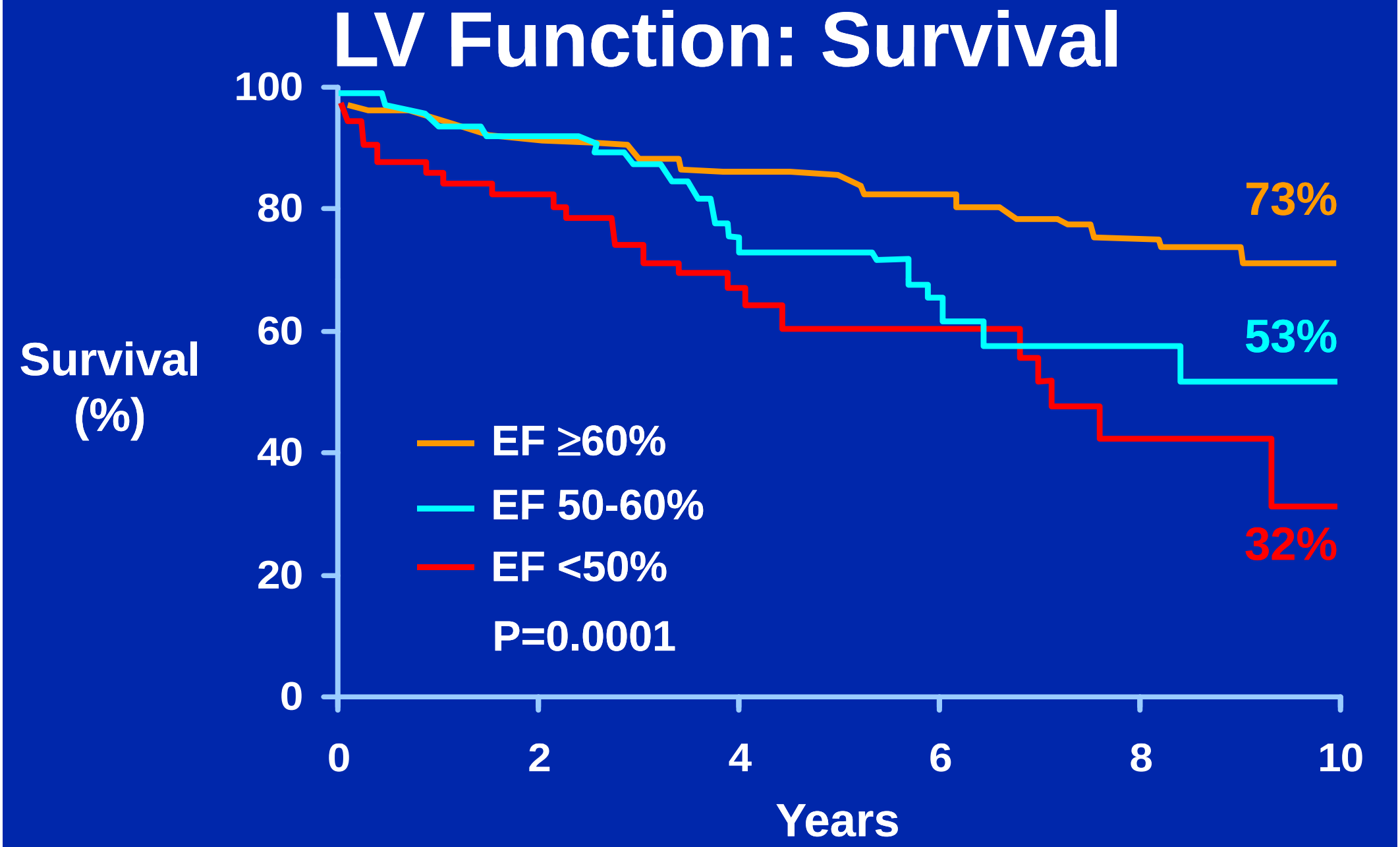
## EF <60%

# MR Natural History

## LV Ejection Fraction



# MR Postop. Outcome



# Mitral Regurgitation

## LV Enlargement

## LVS ≥ 40-45 mm

# 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*

**Objectives** 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.

**Background** LVESD is a marker of left ventricular function in patients with organic MR but its association to survival after diagnosis is unknown.

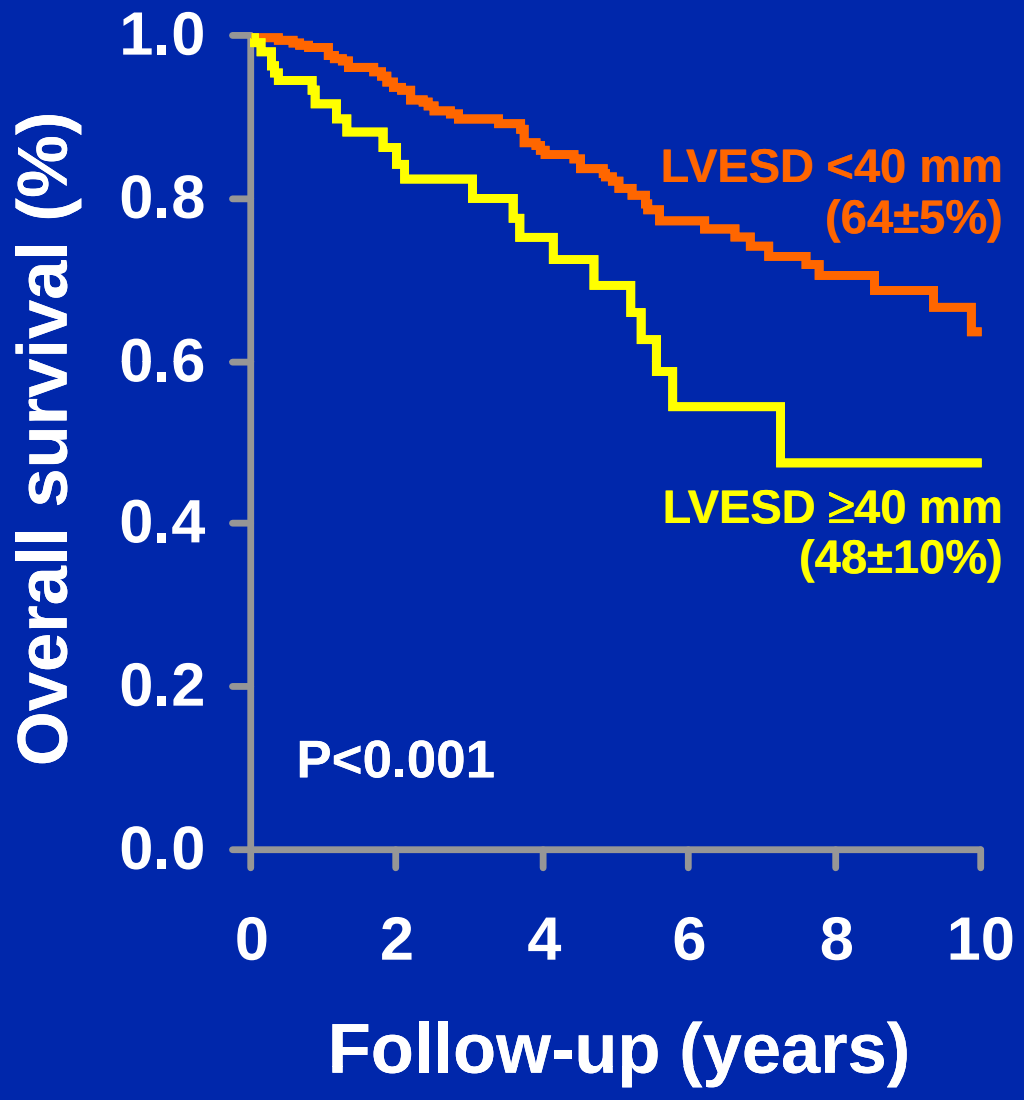
**Methods** The MIDA (Mitral Regurgitation International Database) registry is a multicenter registry of echocardiographically diagnosed organic MR due to flail leaflets. We enrolled 739 patients with MR due to flail leaflets (age 65 ± 12 years; ejection fraction: 65 ± 10%) in whom LVESD was measured (36 ± 7 mm).

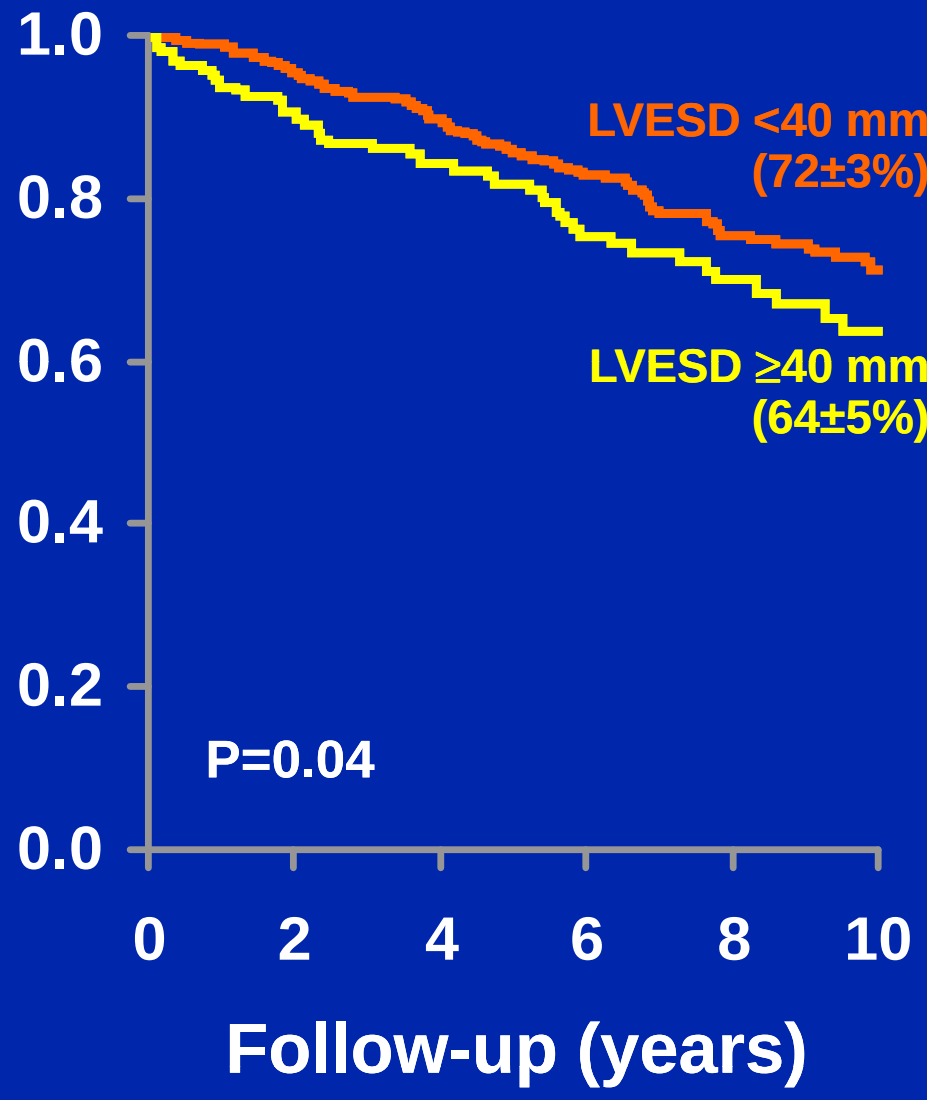
**Results** Under conservative management, 10-year survival and survival free of cardiac death were higher with LVESD <40 mm versus ≥40 mm (64 ± 5% vs. 48 ± 10%; $p < 0.001$, and 73 ± 5% vs. 63 ± 10%; $p = 0.001$). LVESD ≥40 mm independently predicted overall mortality (hazard ratio [HR]: 1.95, 95% confidence 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 ≥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 ≥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).

**Conclusions** In MR due to flail leaflets, LVESD ≥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 ≥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

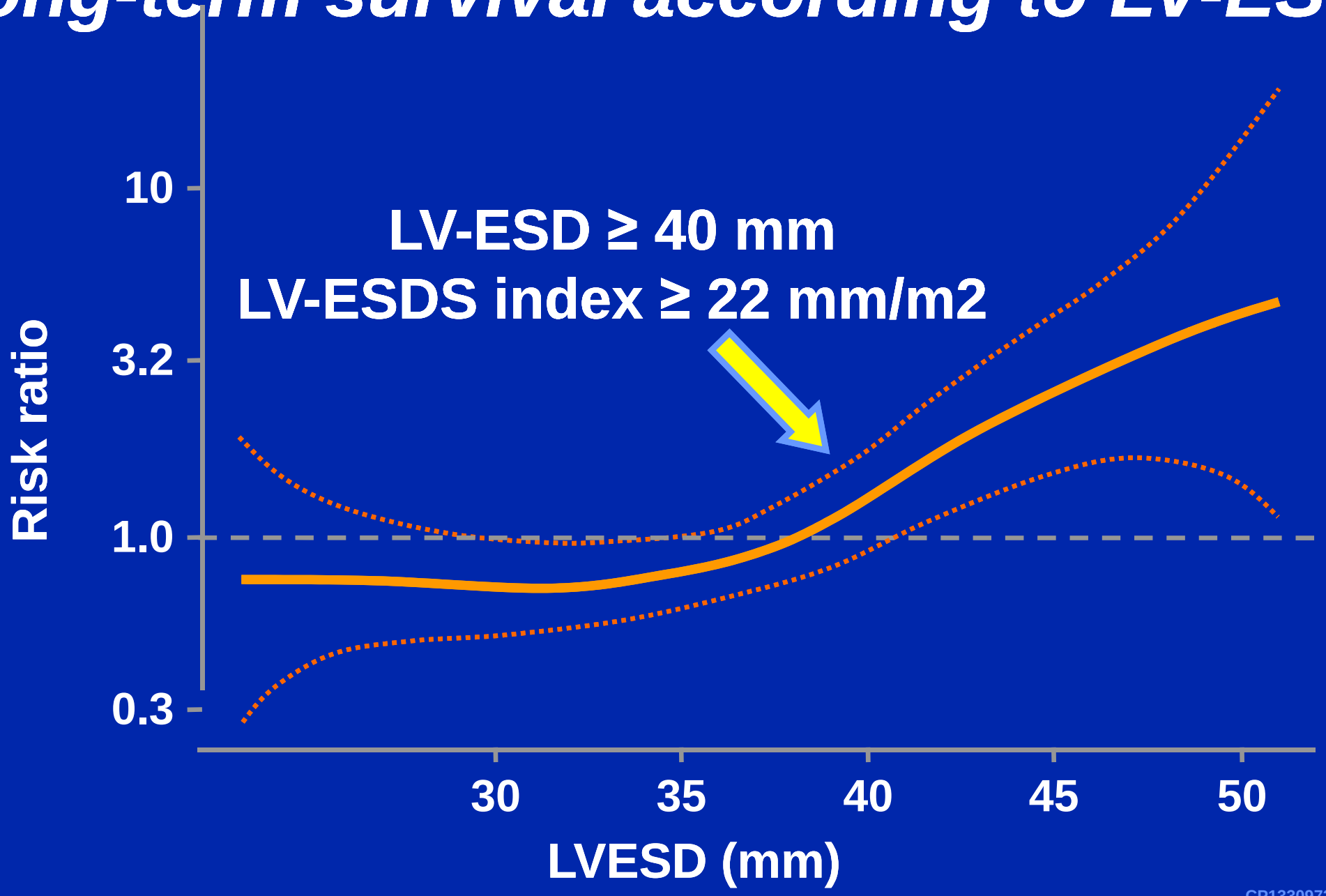
## Long-term survival according to LV-ESD



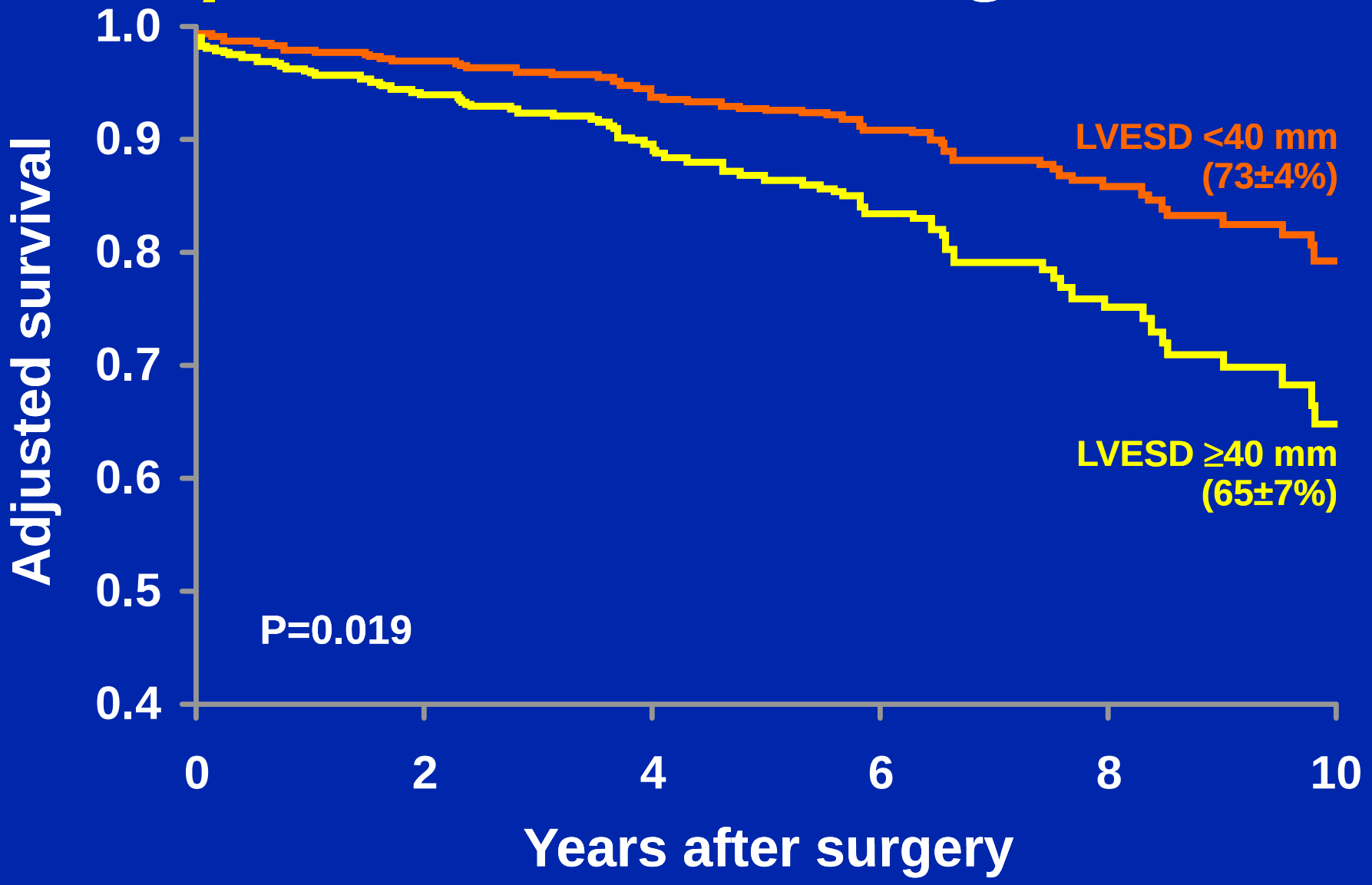
# MR due to Flail Leaflets

## Long-term survival according to LV-ESD



# MR due to Flail Leaflets

## Post-op survival according to LV-ESD



# Mitral Regurgitation

## Surgical Treatment ?

**MR**

**Symptoms**
**LV Dysfunction**

**Rescue Surgery**

**Relieves pts but poor outcome**

**Early**
**Surgery**

**Restorative Surgery**

**No relief but**
**restores life expectancy**

# Mitral Regurgitation

## Can we define MR subsets at high-risk ?

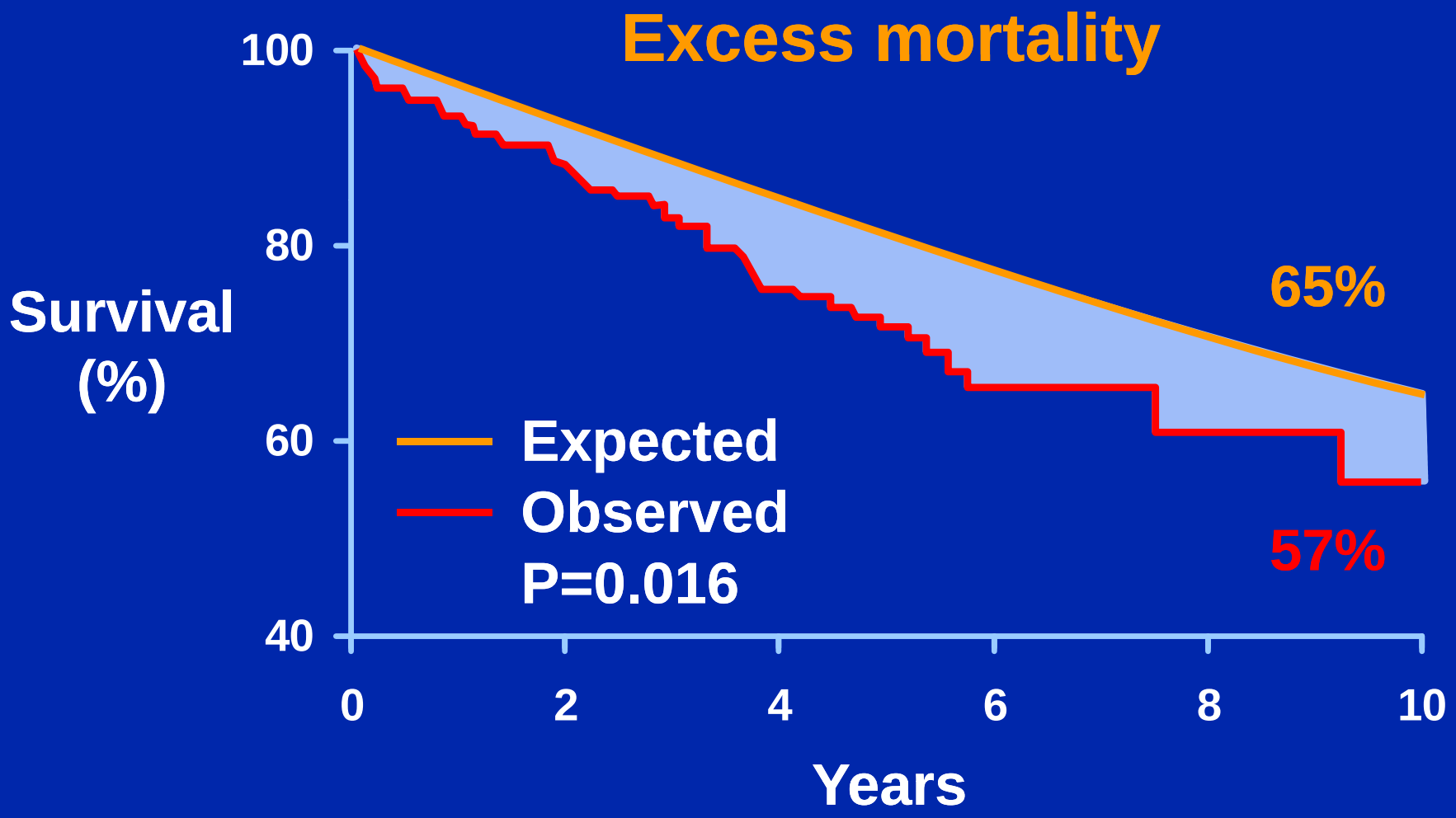
## MR Severity

# MR Severity Assessment

# Is Voluminous MR Severe ?

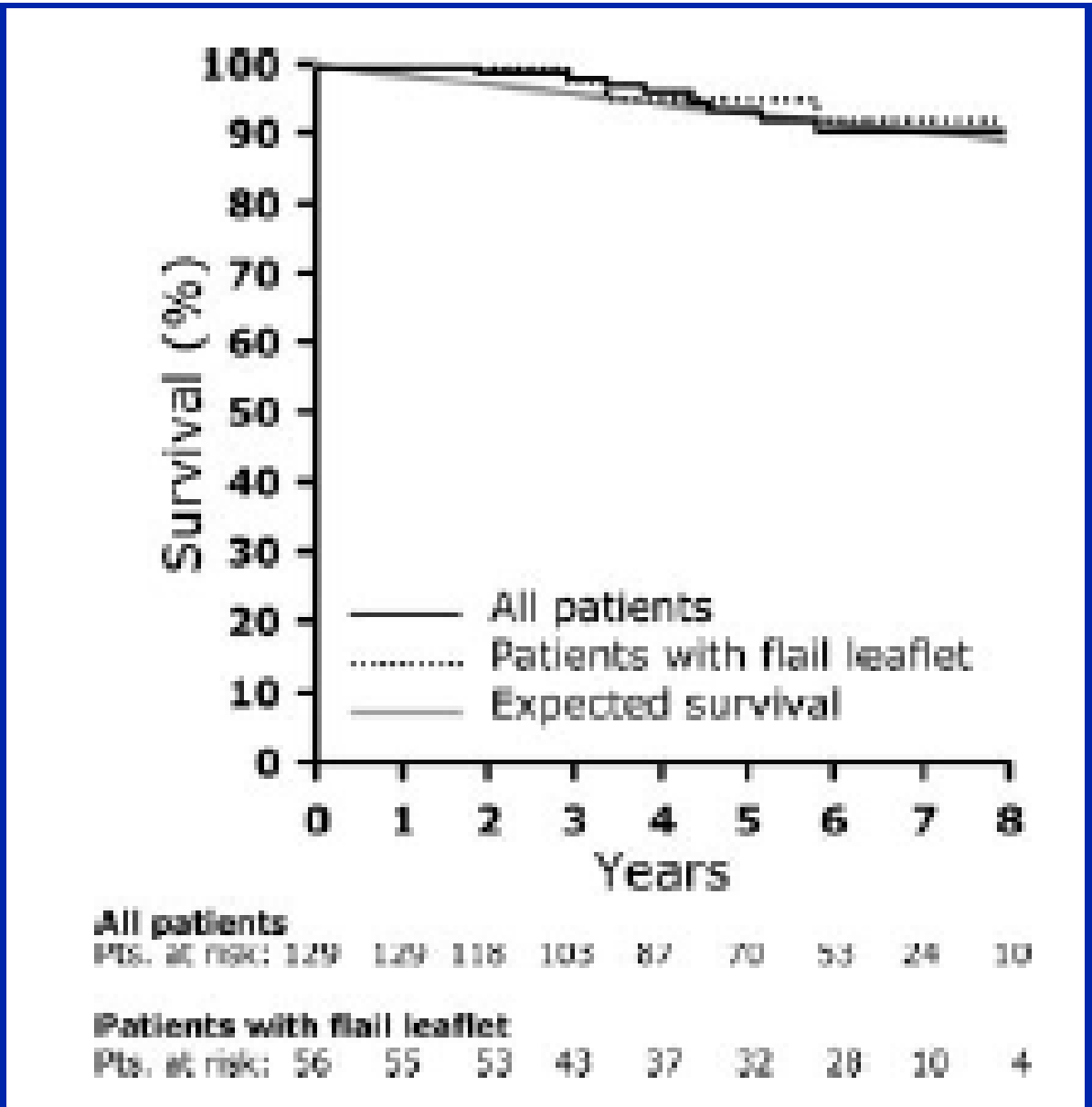
# Organic MR

## Flail Leaflets



# 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

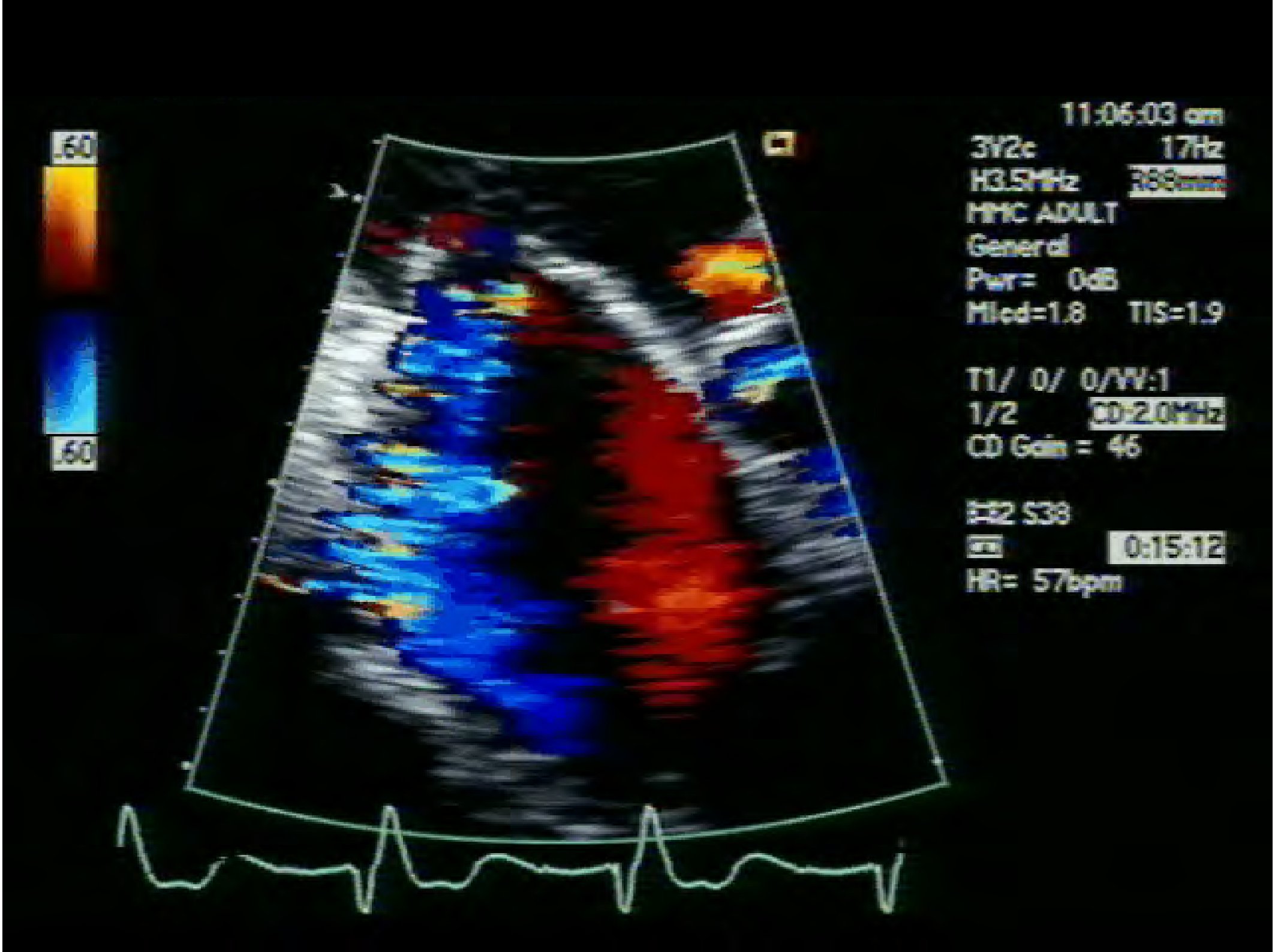



Circulation, 2006;113:2228

# Asymptomatic MR

## Baseline Characteristics

| Study | Age | LV diast. Dia |
|---|---|---|
| Ling, Flail | 66±13 | 34±5 mm/m2 |
| MES, MR | 63±14 | Mod: 54±6<br>Severe: 61±6 |
| Mohty, Surg MVP | 65±13 | 62±9 |
| Rosenhek, MR | 56±14 | MVP: 56±6<br>Flail: 30±4 mm/m2 |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60
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3V2c
17Hz
MYC ADULT
General
Pwr= 0dB
MIed=1.8
TIS=1.9
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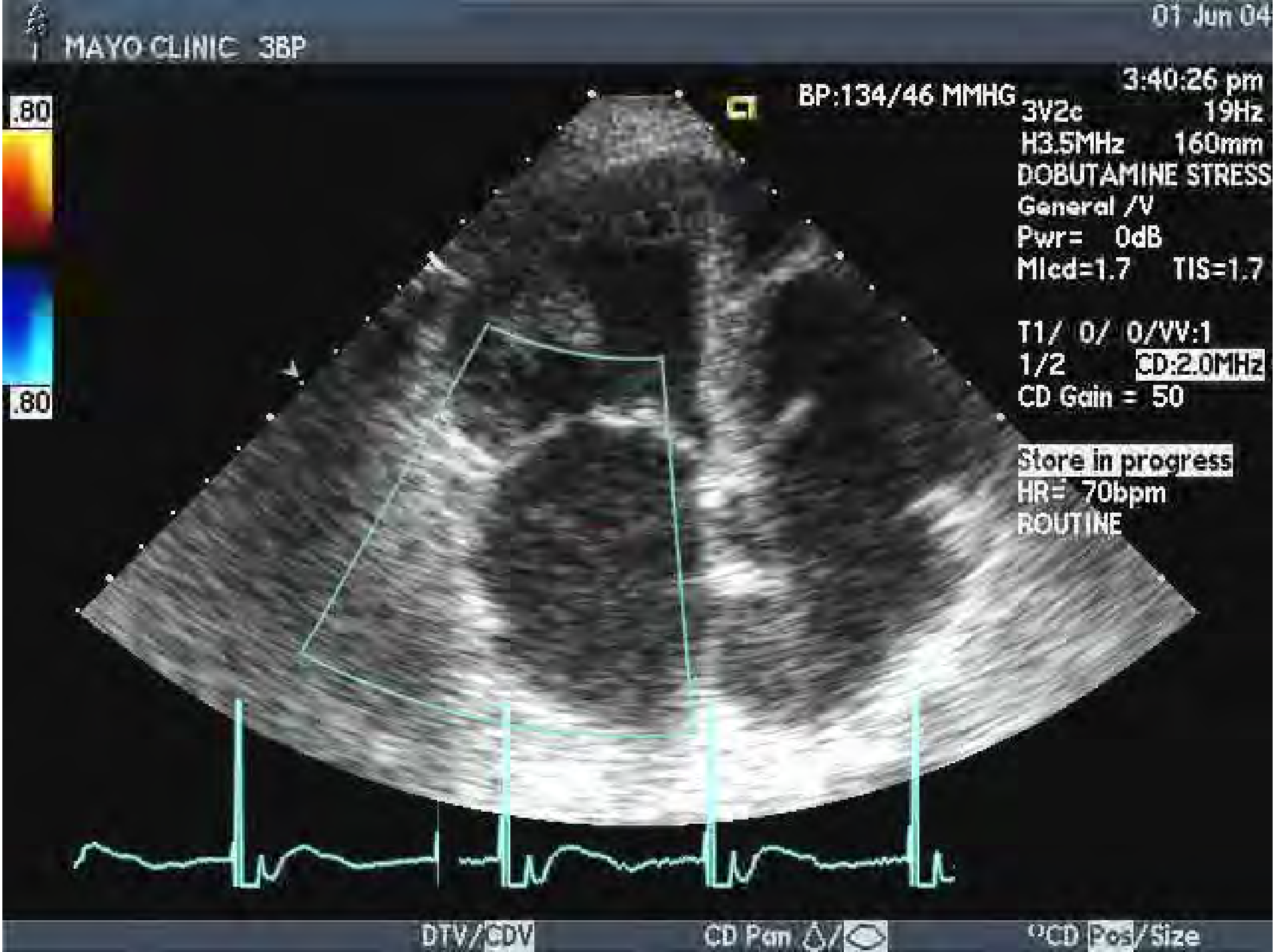
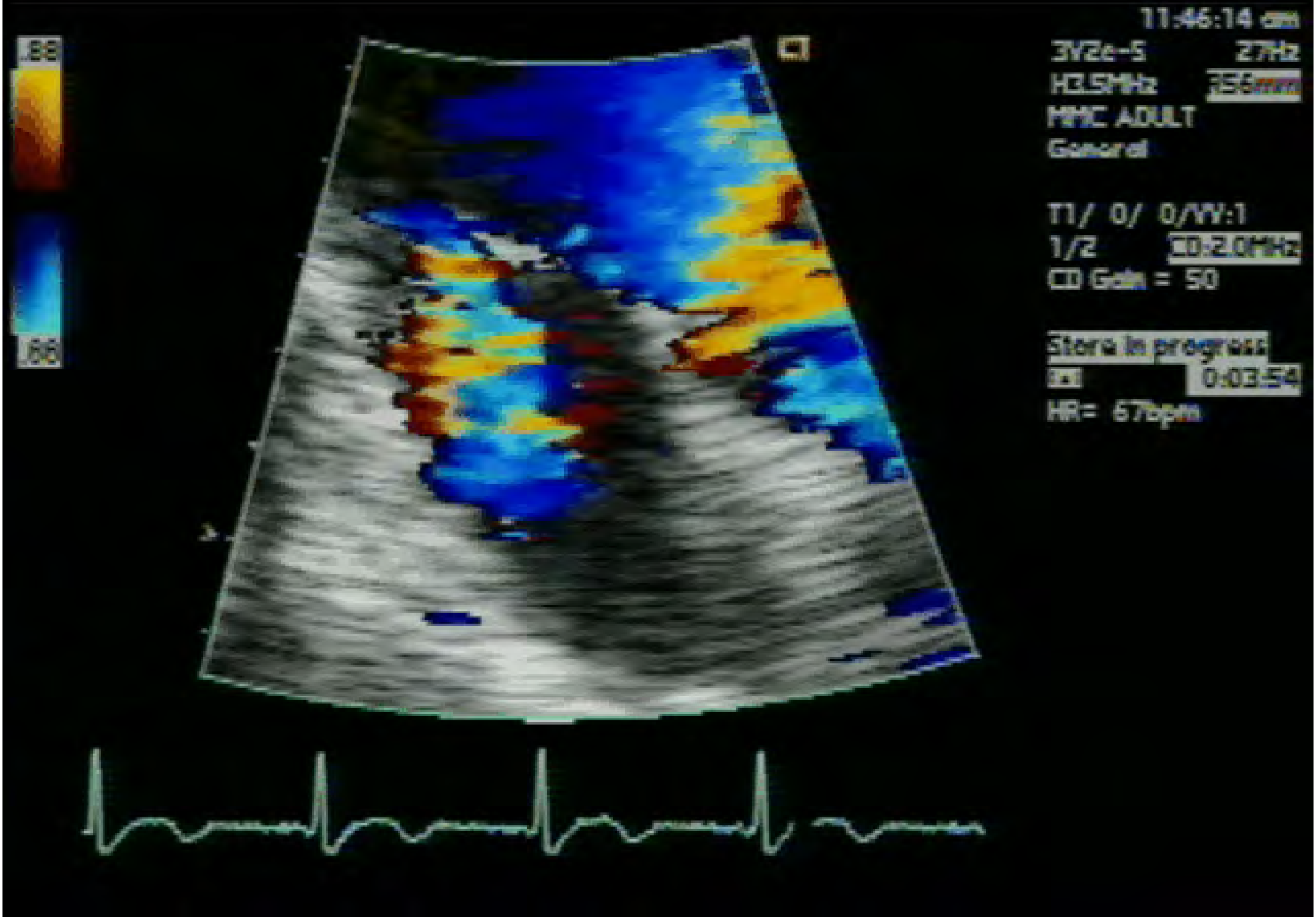
1/2
CD Gain = 46
0:15:12
HR= 57bpm

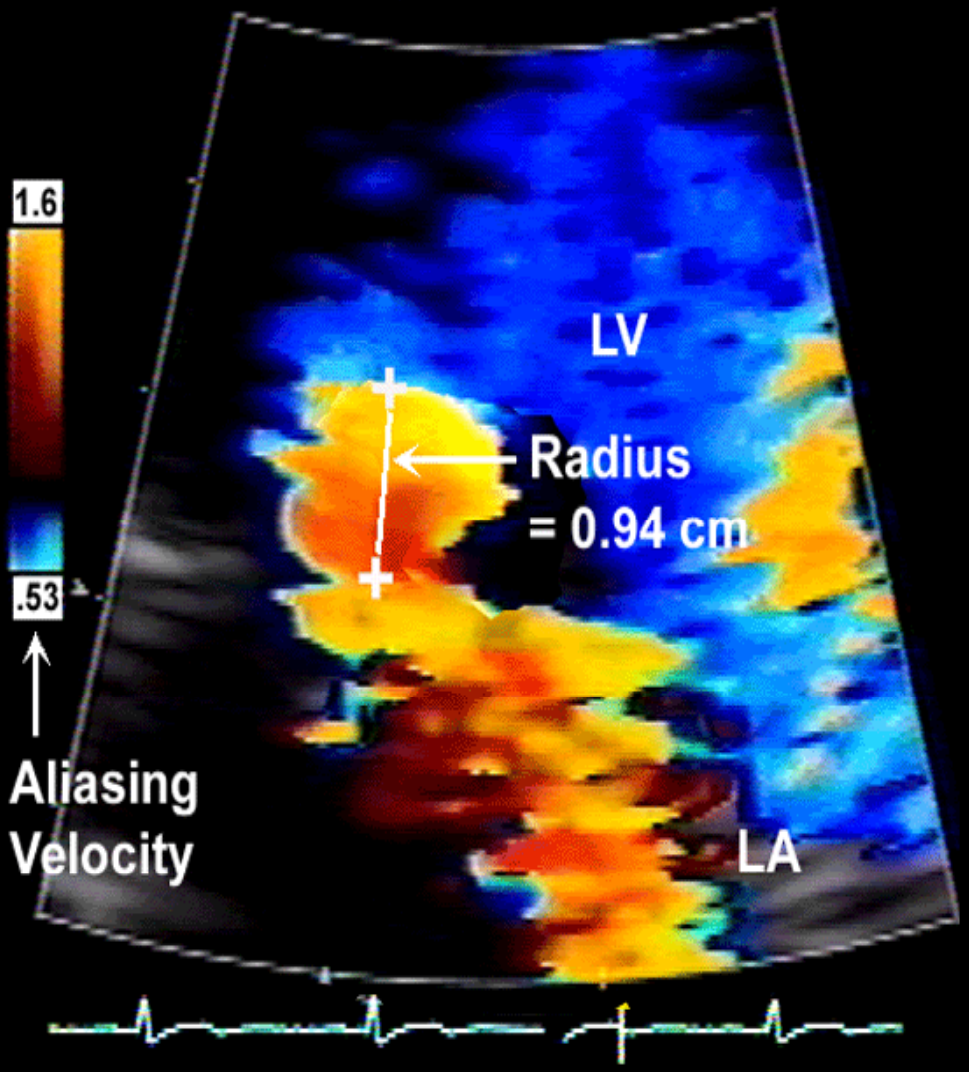

MAYO CLINIC 3BP
01 Jun 04
3:40:26 pm
BP:134/46 MMHG
3V2c 19Hz
H3.5MHz 160mm
DOBUTAMINE STRESS
General /V
Pwr= 0dB
MIcd=1.7 TIS=1.7
T1/ 0/ 0/VV:1
1/2 CD:2.0MHz
CD Gain = 50
Store in progress
HR= 70bpm
ROUTINE
.80
.80
DTV/CDV
CD Pan
CD Pos/Size

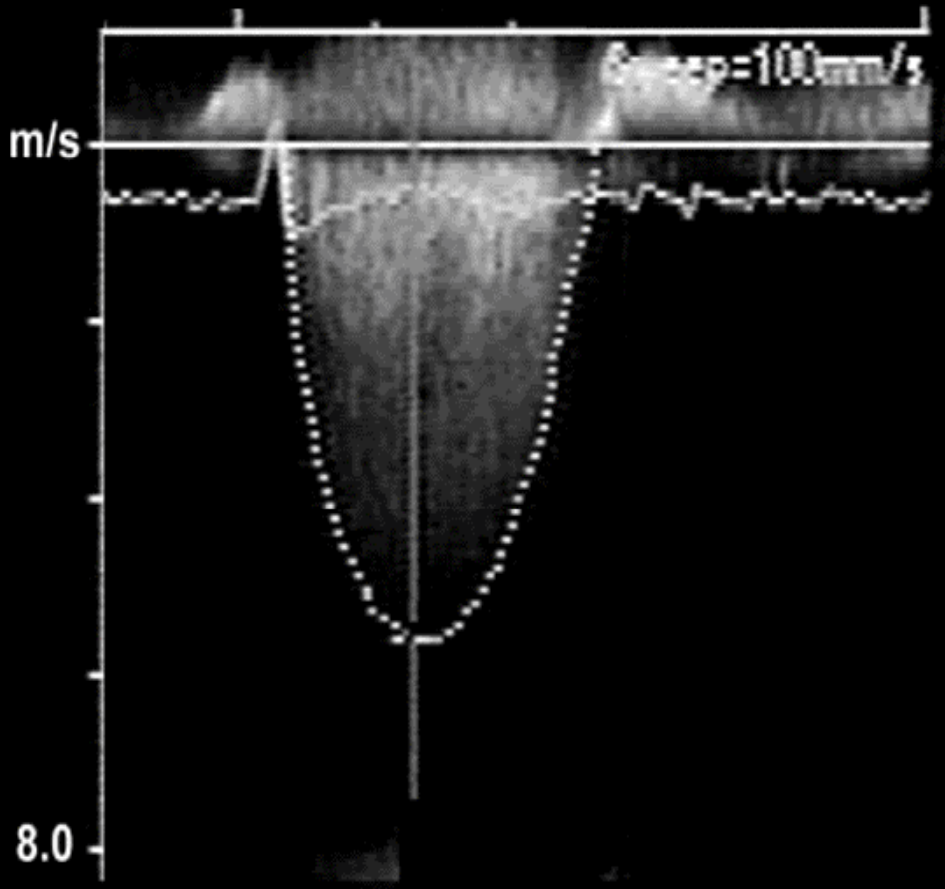

11:46:14
3V2c-5
27Hz
MMC ADULT
General
T1/ 0/ 0/W:1
1/2
Gain = 50
Store in progress
0:03:54
HR= 67bpm

# Valvular Regurgitations Severity Assessment

# Quantitation of Regurgitation

# ERO Calculation




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

**ERO = flow/velocity = .53 $cm^2$ or 53 $mm^2$**

EL064.16.025A-22B

# Mitral Regurgitation

## Grading of Severity

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

The NEW ENGLAND JOURNAL of MEDICINE

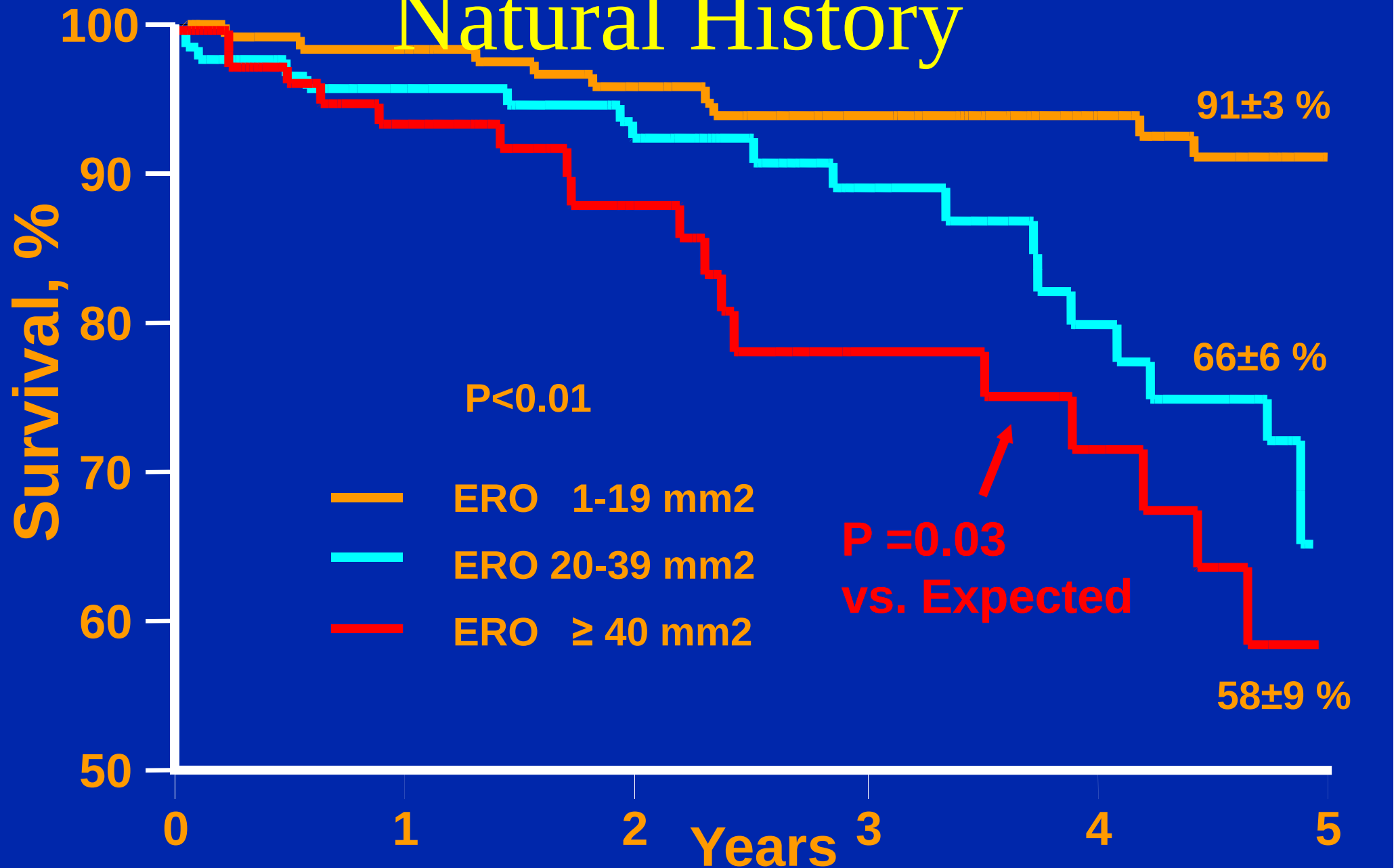
ORIGINAL ARTICLE

# 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., and A. Jamil Tajik, M.D.

# Asymptomatic MR

## Natural History



# 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±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±2% in the conventional treatment group ($P=0.008$). After 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±1% versus

ERO Predictor Of Outcome

***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.)

# Prospective Validation of the Prognostic Usefulness of Brain Natriuretic Peptide in Asymptomatic Patients With Chronic Severe Mitral Regurgitation

Rodolfo Pizarro, MD, Oscar O. Bazzino, MD, Pablo F. Oberti, MD, Mariano Falconi, MD, Federico Achilli, MD, Anibal Arias, MD, Juan G. Krauss, MD, Arturo M. Cagide, MD

*Buenos Aires, Argentina*

(J Am Coll Cardiol 2009;54:1099–106)

**Table 3** Multivariate Analysis to Predict the Combined End Point (Derivation Set)

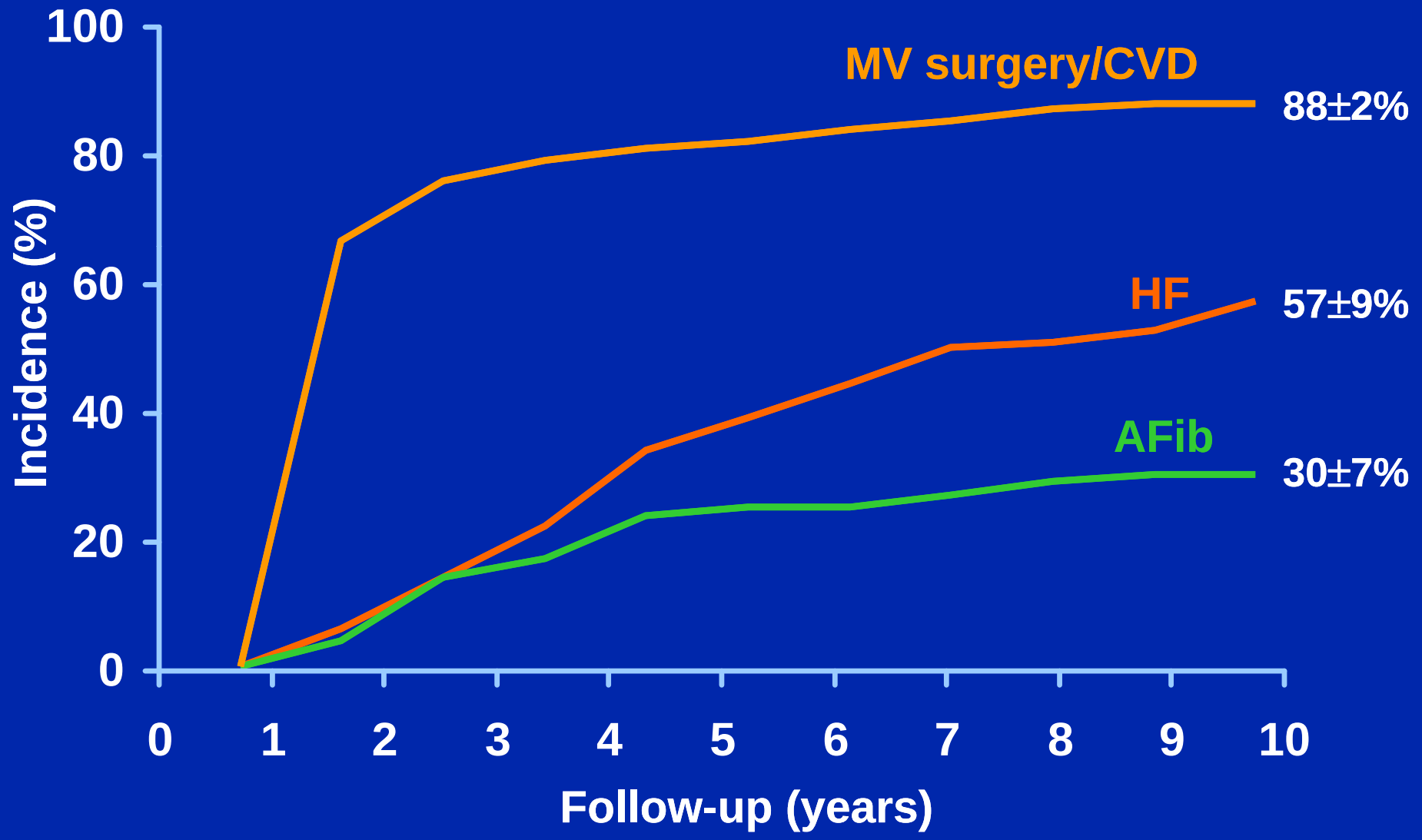
| | OR (95% CI) | p Value |
|---|---|---|
| BNP ≥105 pg/ml | 4.6 (2.7–11.6) | <0.0001 |
| End-systolic diameter/BSA >22 mm/m$^2$ | 3.4 (1.6–10.7) | 0.01 |
| EROA >55 mm$^2$ | 4.2 (2.1–11.4) | 0.001 |

ERO Predictor Of Outcome

# MR Quantitation

**There are now 3 studies, large (total >1000 patients), prospective, showing ERO predictive of clinical outcome**

# MR due to Flail Leaflet: Multicenter European Experience

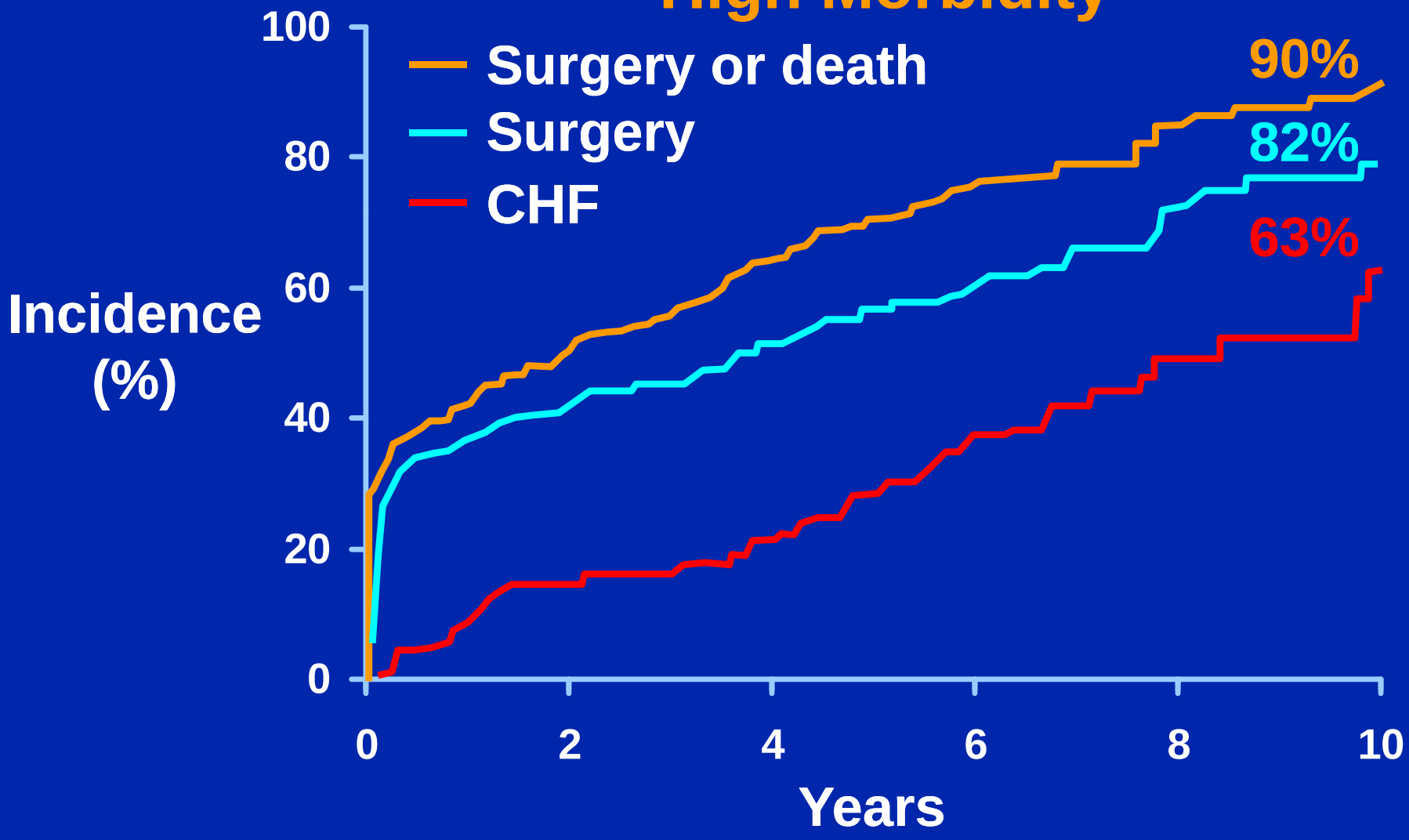



Grigioni F et al. J Am Coll Cardiol Img 2008;1:133-141

# Mitral Regurgitation

## Natural History

### High Morbidity



# MR Severity Assessment

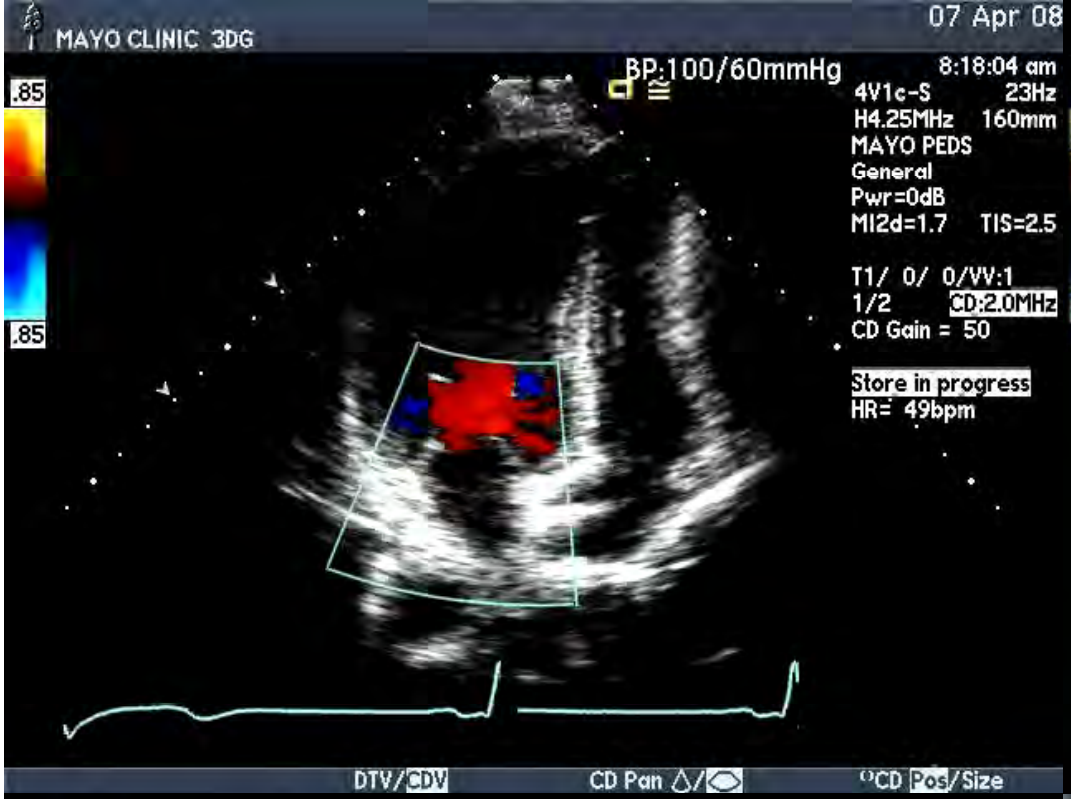
## Voluminous MR is Severe in the USA and in Europe

# Mitral Regurgitation

## Can we define

## MR subsets at high-risk without excess post-op mortality ?

## Left Atrium ?


MAYO CLINIC 3DG
07 Apr 08
BP:100/60mmHg
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4V1c-S 23Hz
H4.25MHz 160mm
MAYO PEDS
General
Pwr=0dB
MI2d=1.7 TIS=2.5
T1/ 0/ 0/VV:1
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CD Gain = 50
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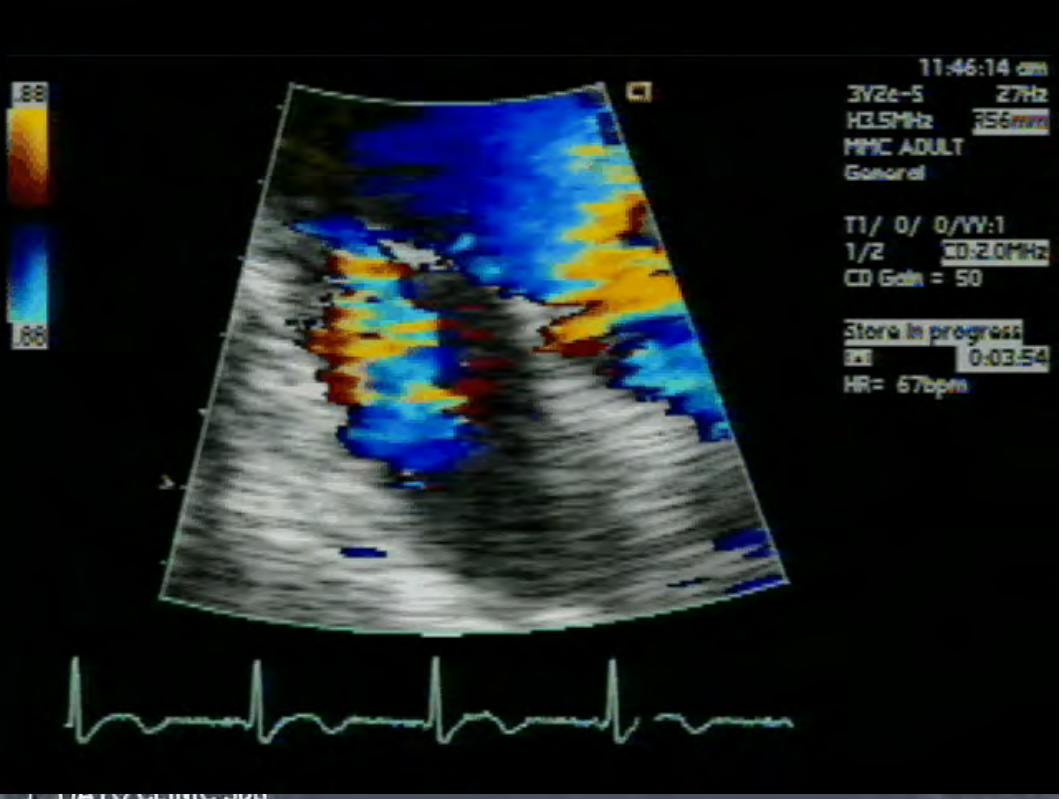
HR= 49bpm
.85
.85
DTV/CDV
CD Pan
CD Pos/Size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3V2c-S 27Hz
H3.5MHz 156mm
MMC ADULT
General
T1/ 0/ 0/VV:1
1/2 CD:2.0MHz
CD Gain = 50
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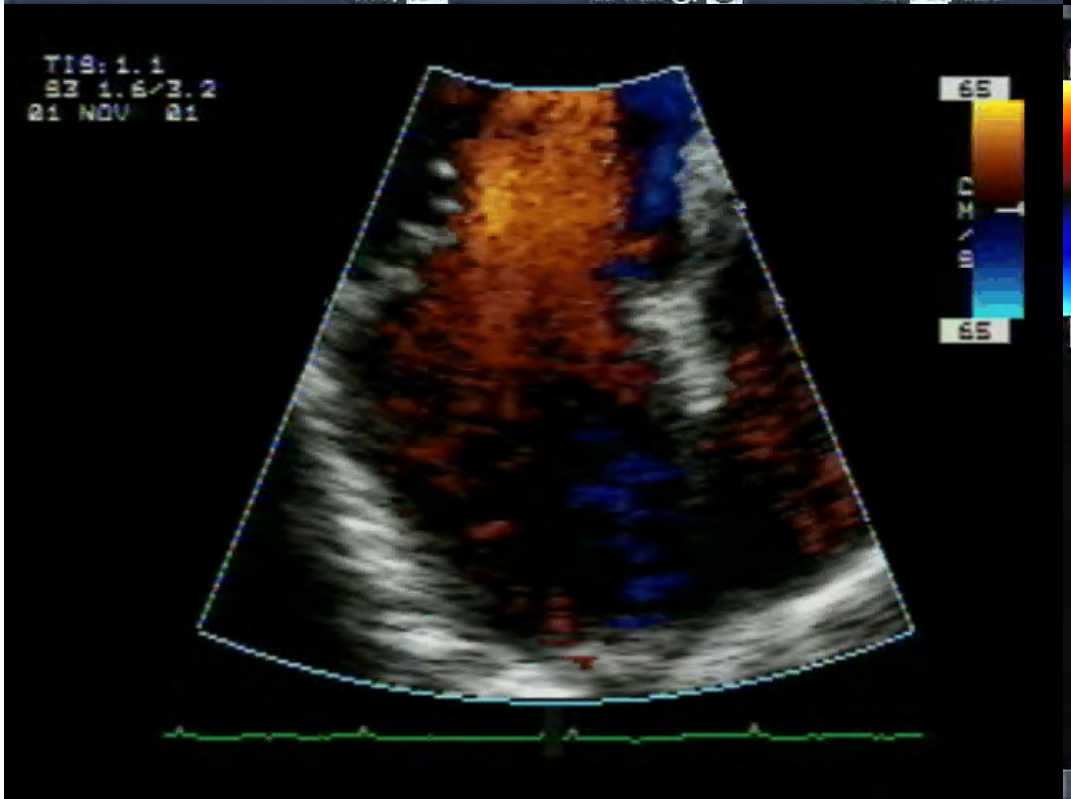
0:03:54
HR= 67bpm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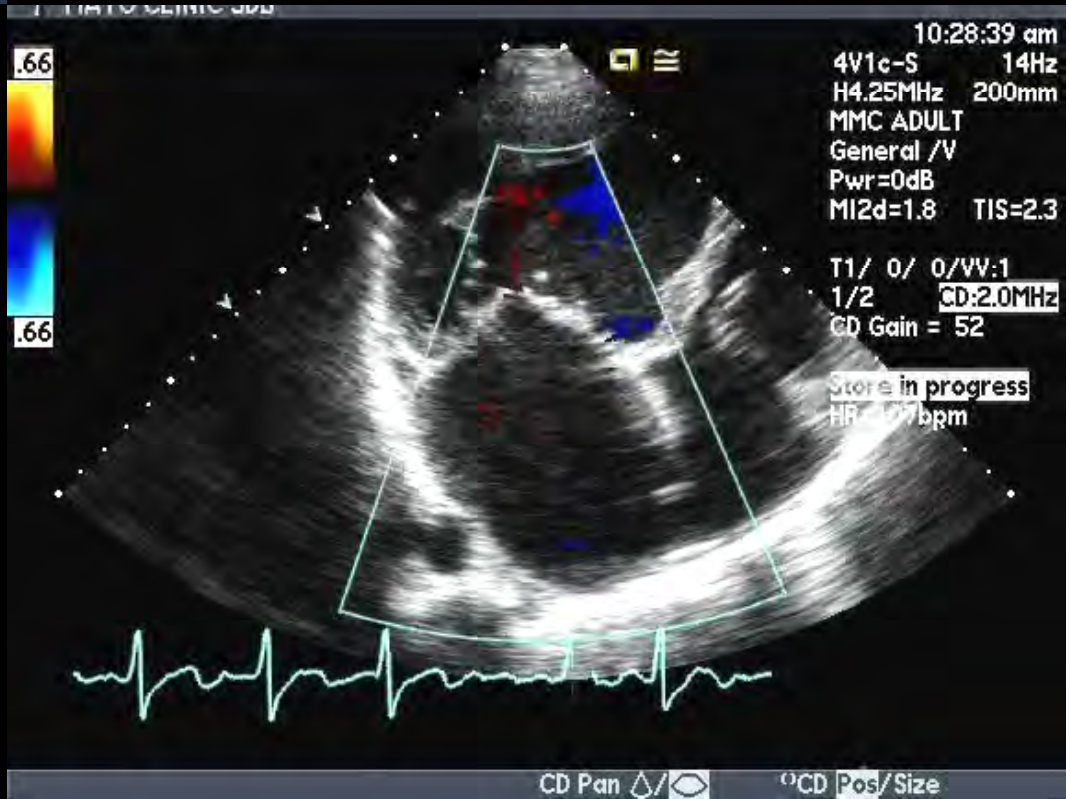
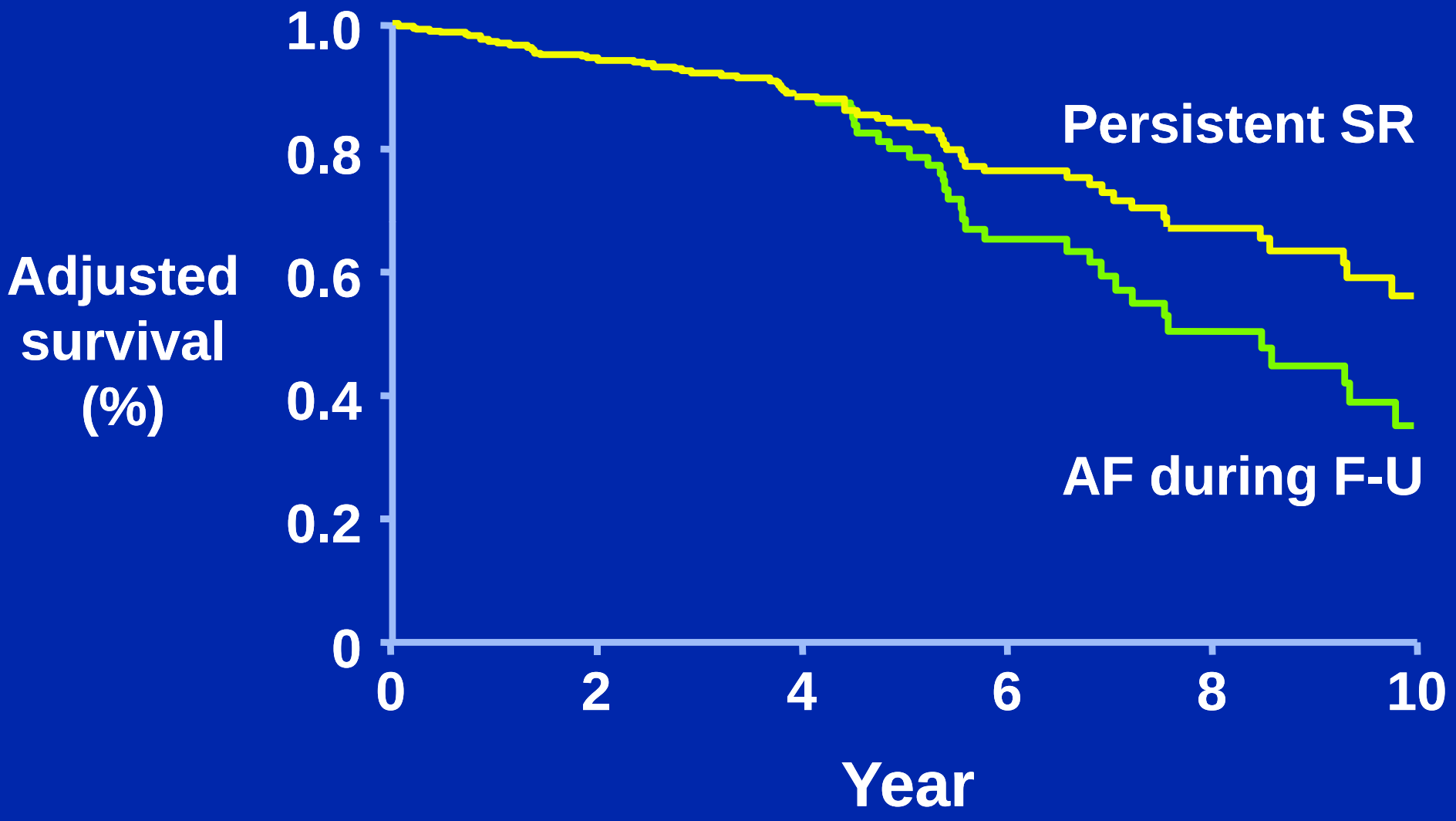
@3 1.6/3.2
@1 NOV @1
65
65

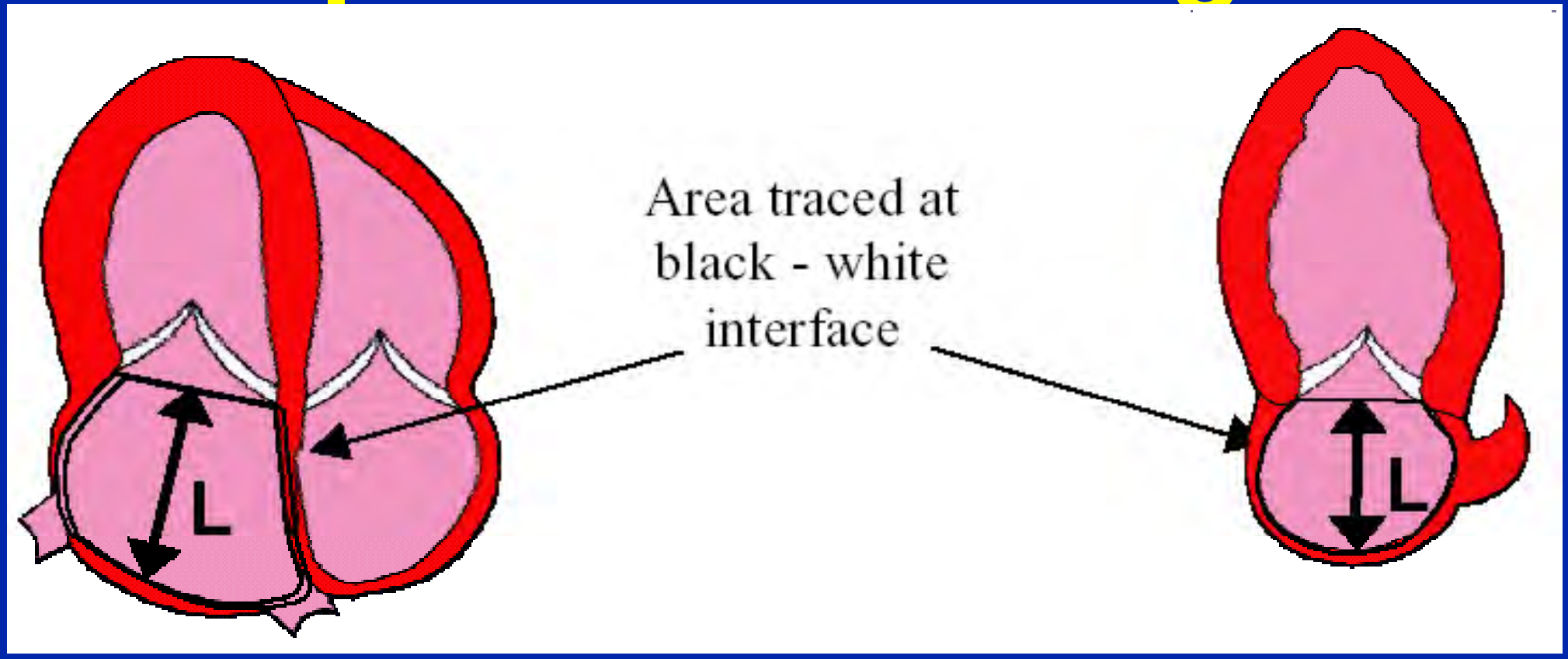

10:28:39 am
4V1c-S 14Hz
H4.25MHz 200mm
MMC ADULT
General /V
Pwr=0dB
MI2d=1.8 TIS=2.3
T1/ 0/ 0/VV:1
1/2 CD:2.0MHz
CD Gain = 52
Store in progress
.66
.66
CD Pan
CD Pos/Size

# MR Natural History

## Impact of AF on Survival



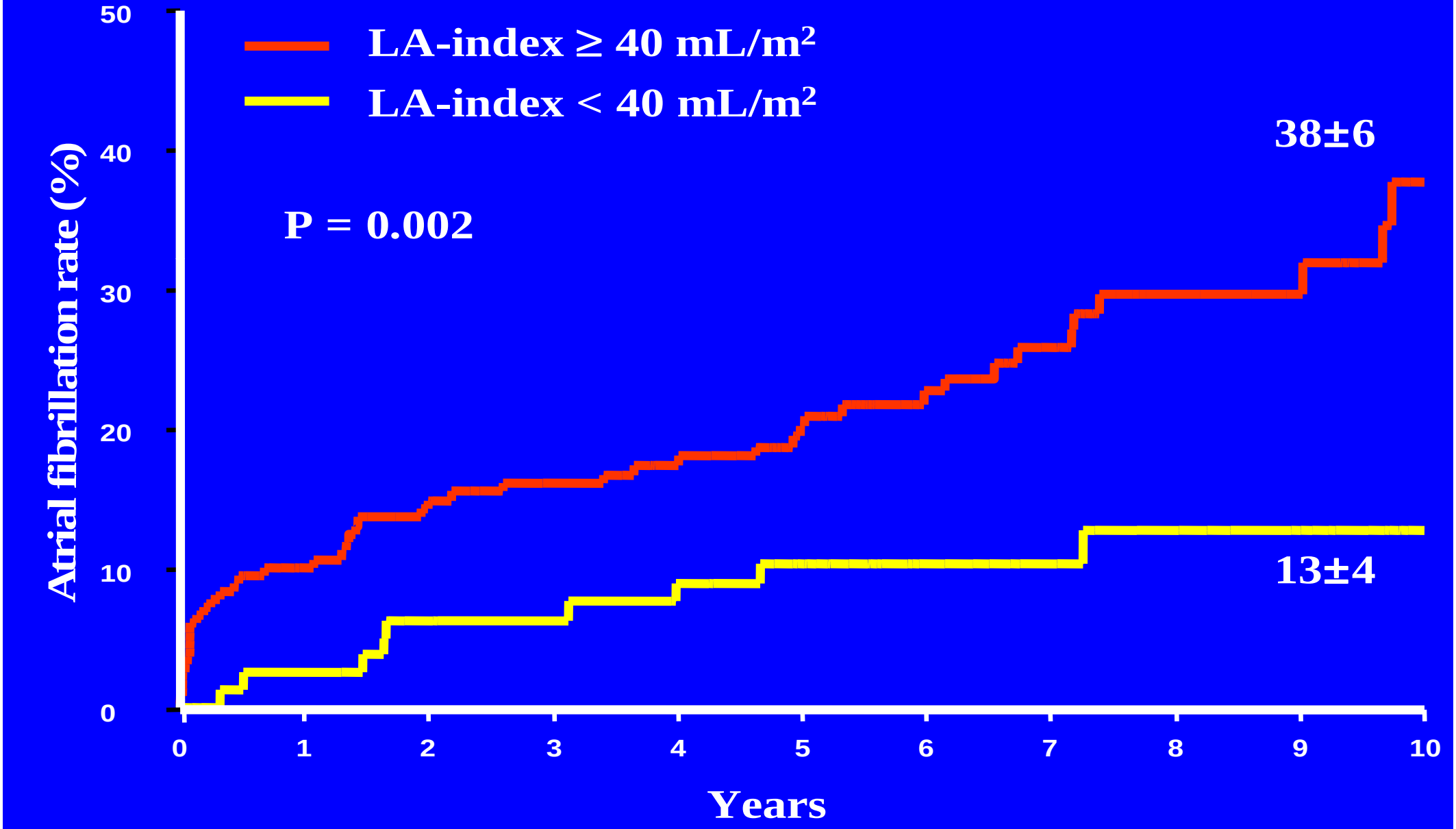
# LA Volume Index (LAVI)
# Biplane Area-length




**Vol = 0.85 * A1 * A2 / L**

**Where A1 and A2 = areas from orthogonal views**

# Mitral Regurgitation : LA Volume



# Impact of Left Atrial Volume on Clinical Outcome in Organic Mitral Regurgitation

Thierry Le Tourneau, MD, David Messika-Zeitoun, MD, Antonio Russo, MD, Delphine Detaint, MD, Yan Topilsky, MD, Douglas W. Mahoney, MS, Rakesh Suri, MD, DPHIL, Maurice Enriquez-Sarano, MD

*Rochester, Minnesota*

**Objectives** The purpose of this paper was to assess the link between left atrial (LA) volume at diagnosis and outcome of patients with mitral regurgitation (MR).

**Background** Left atrial enlargement is a consequence of organic MR, but its association with clinical outcome independently of MR severity is uncertain.

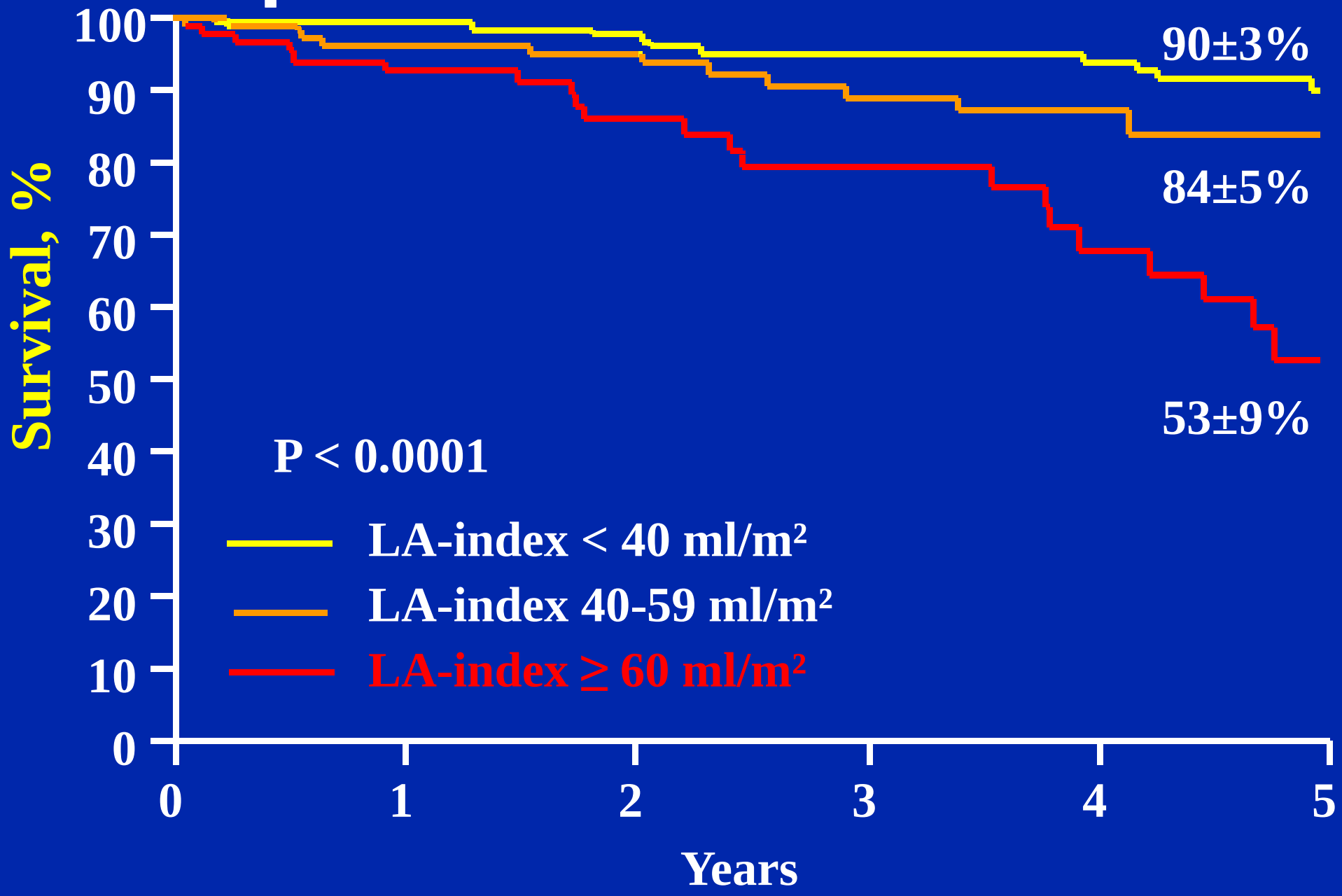
**Methods** We prospectively enrolled 492 patients (age 63 ± 15 years, 60% men) in sinus rhythm with organic MR (regurgitant volume 68 ± 42 ml/beat) and performed at baseline triple echocardiographic quantitation (MR severity, LA volume, and left ventricular characteristics). Outcome with medical and surgical management was analyzed.

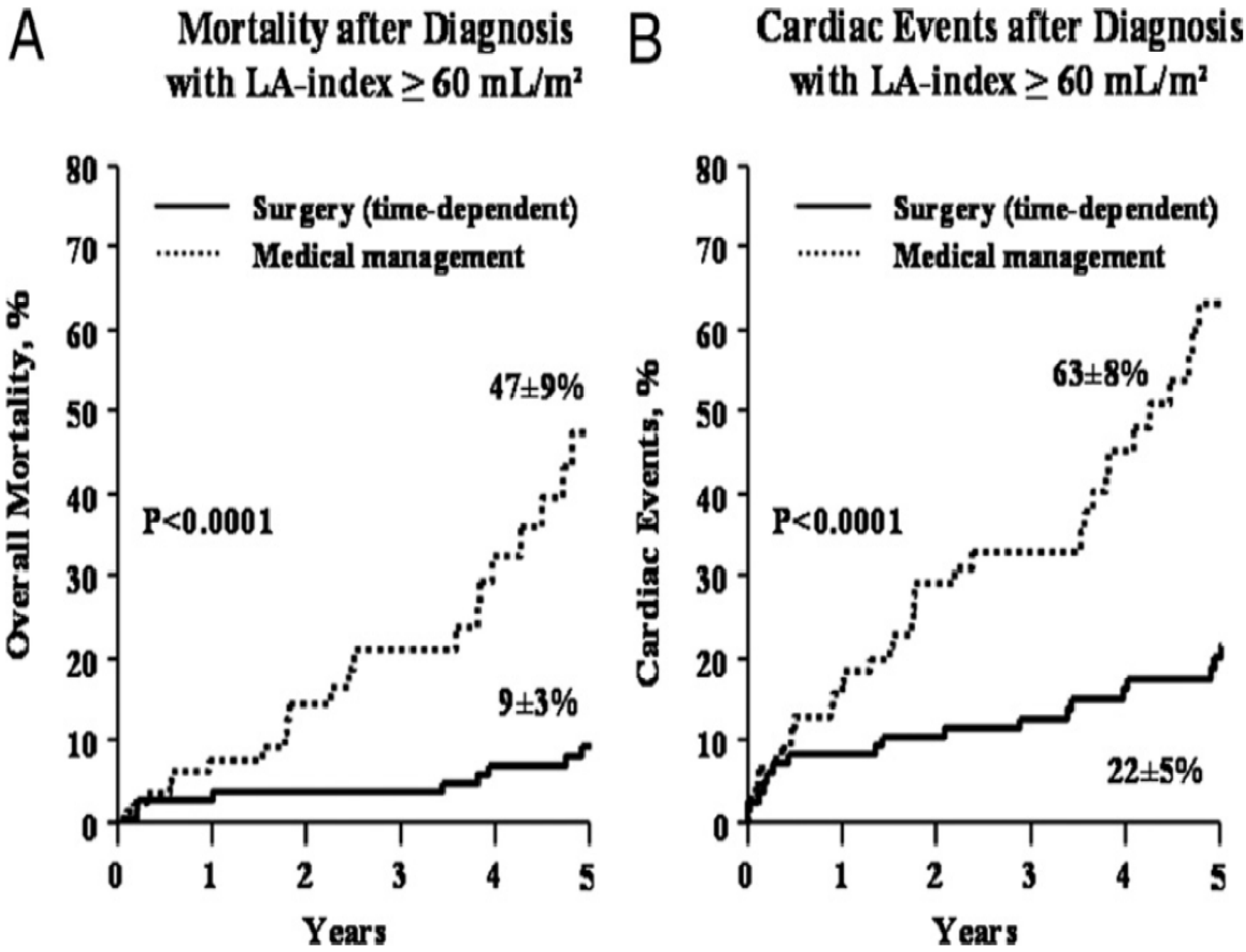
**Results** Left atrial volume indexed to body surface area (LA index) was 55 ± 26 ml/m² (<40 ml/m² in 158 patients, 40 to 59 ml/m² in 160 patients, and ≥60 ml/m² in 174 patients). Under medical management, 5-year survival was 80 ± 2.9% and cardiac events 28 ± 3%. Adjusting for established predictors of outcome, LA index was independently associated with survival after diagnosis (hazard ratio [HR]: 1.3 [95% confidence interval (CI): 1.1 to 1.5] per 10 ml/m² increment, $p = 0.001$). Patients with LA index ≥60 ml/m² had lower 5-year survival than those with no or mild LA enlargement ($p < 0.0001$) and than the rates of survival expected in the U.S. population (53 ± 8.6% vs. 76%, $p = 0.017$). Compared with patients with LA index <40 ml/m², those with LA index ≥60 ml/m² had increased mortality (HR: 2.8 [95% CI: 1.2 to 6.5], $p = 0.016$) and cardiac events (HR: 5.2 [95% CI: 2.6 to 10.9], $p < 0.0001$) with medical management. Mitral surgery was associated with decreased mortality (HR: 0.46 [95% CI: 0.26 to 0.84], $p = 0.01$) and cardiac events (HR: 0.38 [95% CI: 0.23 to 0.62], $p = 0.0001$) and after surgery patients with LA index ≥60 ml/m² versus <60 ml/m² did not incur excess mortality or cardiac events (both $p > 0.30$).

**Conclusions** In organic MR, LA index at diagnosis predicts long-term outcome, incrementally to known predictors of outcome. This marker of risk is particularly important because mitral surgery in these patients markedly improves outcome and restores life expectancy. LA index should be measured in routine clinical practice for risk-stratification and for clinical decision making in patients with organic MR. (J Am Coll Cardiol 2010;56:570–8) 

# Survival after MR diagnosis

## Implications of LA Volume





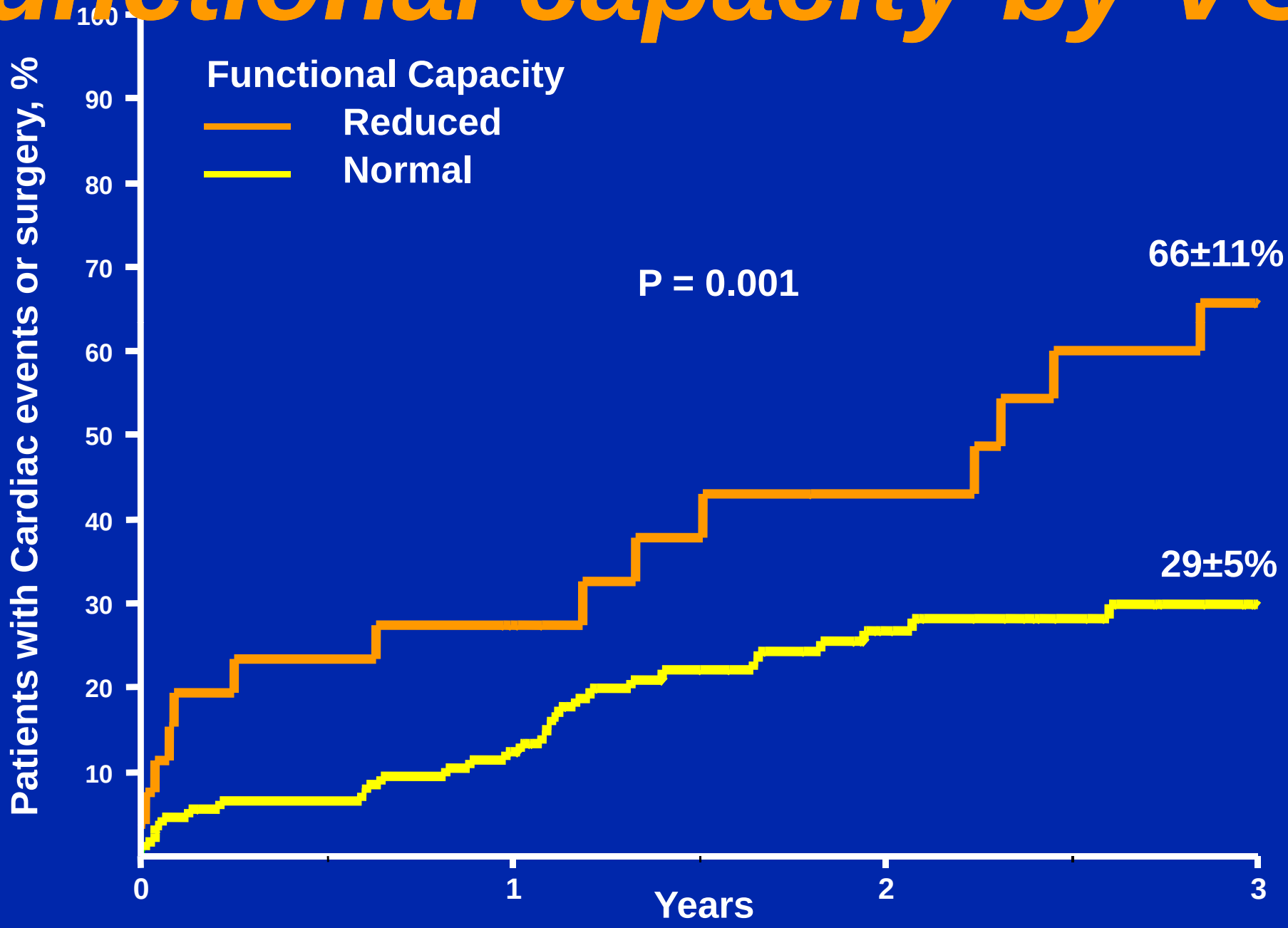

Outcome in Patients With Markedly Enlarged LA Compared Between Surgical and Medical Management

# Mitral Regurgitation

## Can we define MR subsets at high-risk ?

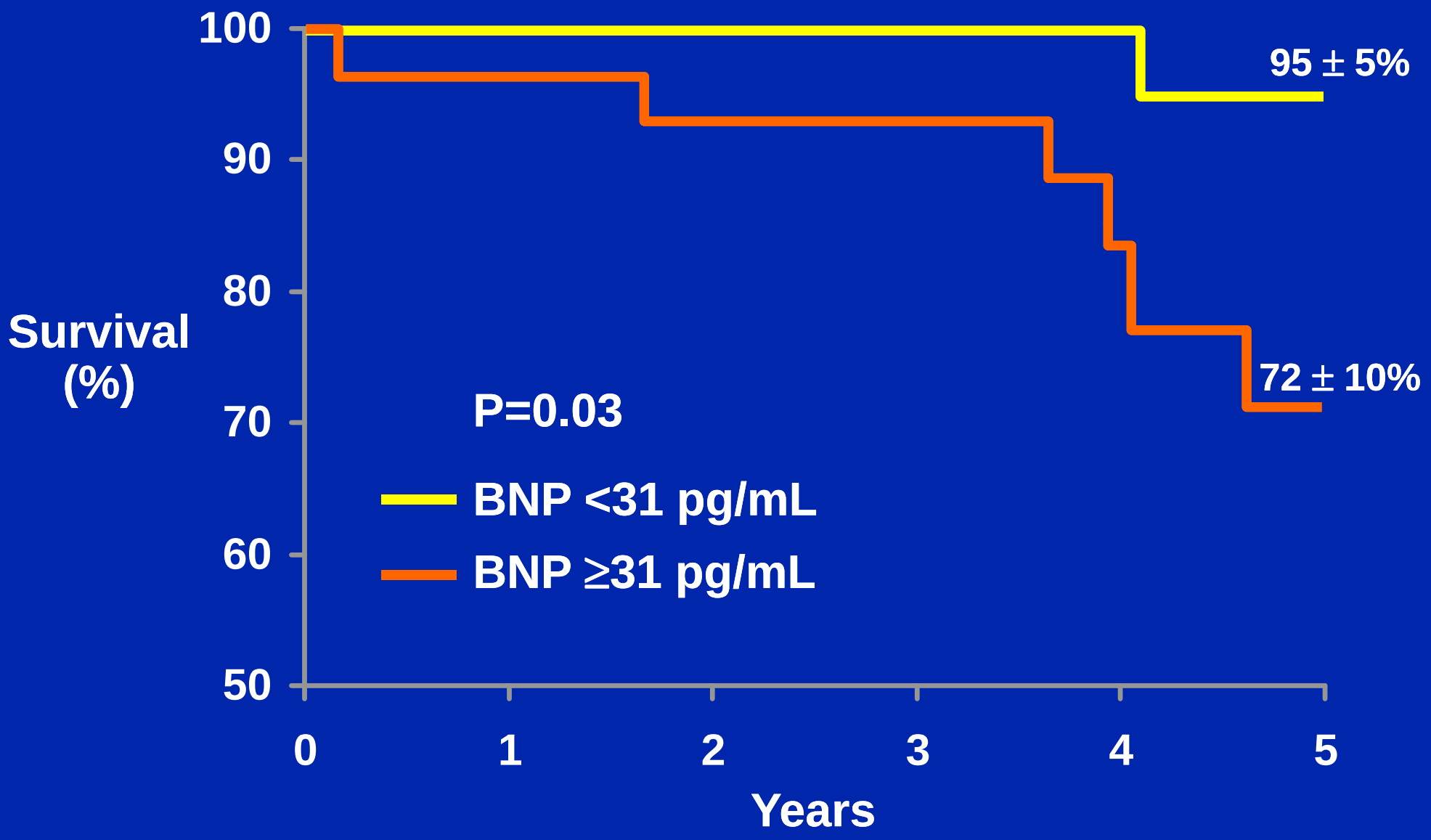
## Other predictors ?

# Mitral Regurgitation : Functional capacity by VO2



# *Mitral Regurgitation : BNP*

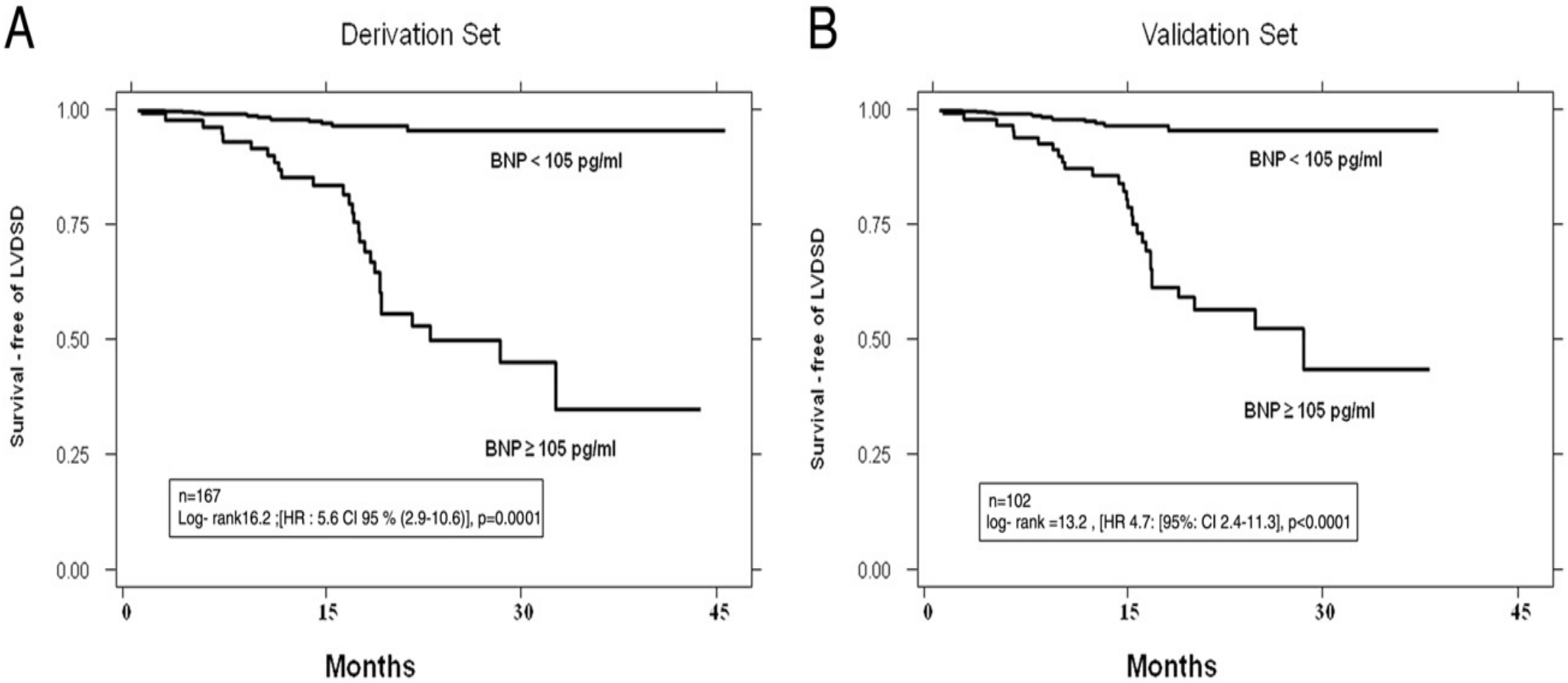
## BNP level and post-diagnosis survival



# Prospective Validation of the Prognostic Usefulness of Brain Natriuretic Peptide in Asymptomatic Patients With Chronic Severe Mitral Regurgitation

Rodolfo Pizarro, MD, Oscar O. Bazzino, MD, Pablo F. Oberti, MD, Mariano Falconi, MD, Federico Achilli, MD, Anibal Arias, MD, Juan G. Krauss, MD, Arturo M. Cagide, MD

*Buenos Aires, Argentina*



European Heart Journal
doi:10.1093/eurheartj/ehq294

CLINICAL RESEARCH

# Prognostic and therapeutic implications of pulmonary hypertension complicating degenerative mitral regurgitation due to flail leaflet: A Multicenter Long-term International Study

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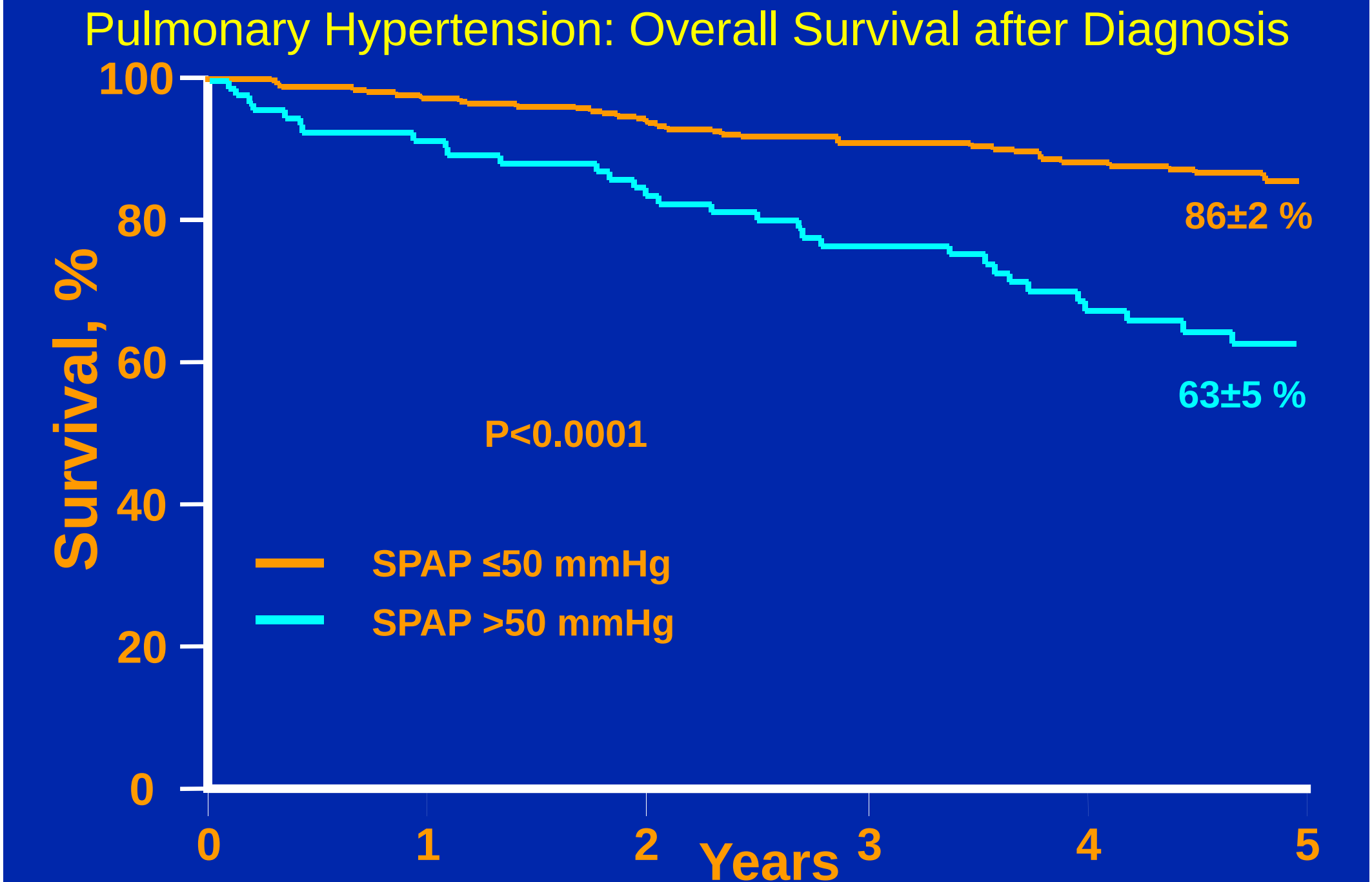
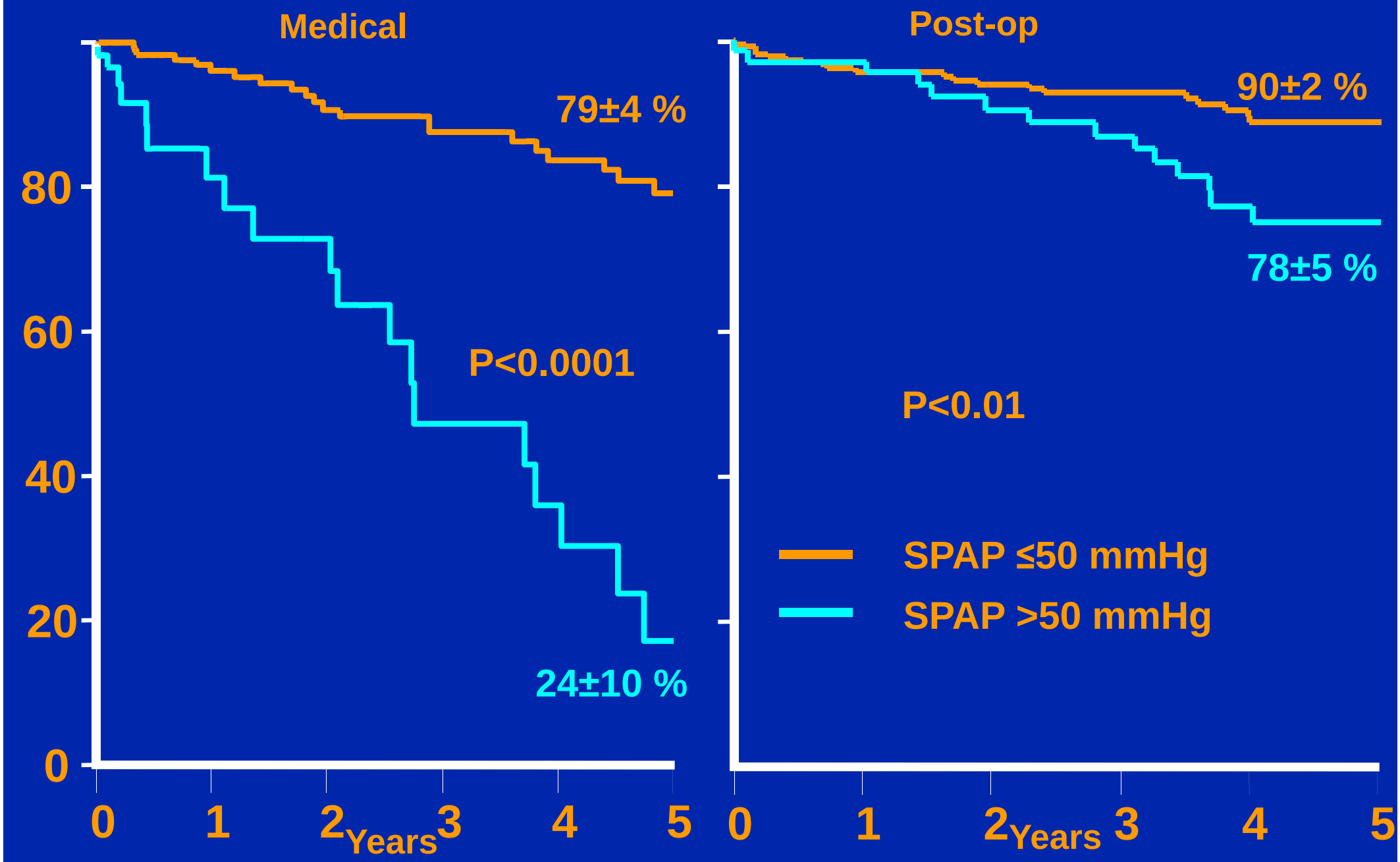
*Received 15 December 2009; revised 18 June 2010; accepted 23 July 2010*

# MR due to Flail Leaflets



# MR due to Flail Leaflets

## Pulmonary Hypertension: Survival after diagnosis



# Mitral Regurgitation

## Risk Factors

## MR

**Risk Factors with excess risk post-op**

↓

**LV EF**
**LV ESD**
**Symptoms**
**AFib.**
**Pulm. HTN**

**Risk Factors w/o excess risk post-op**

↓

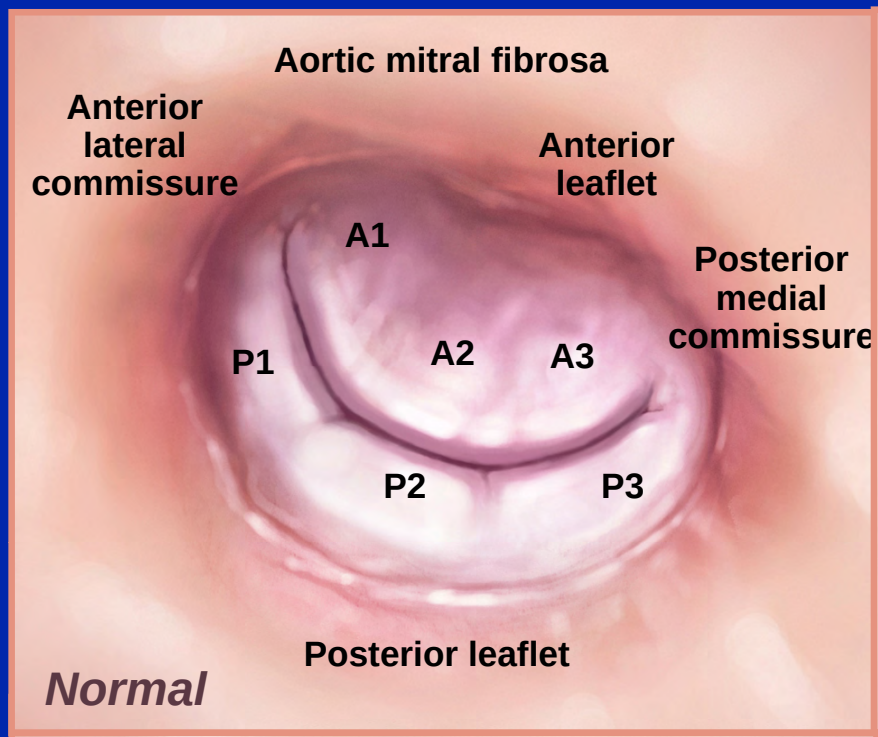
**ERO**
**LA enlargement**
**BNP**
**Functional Capacity**

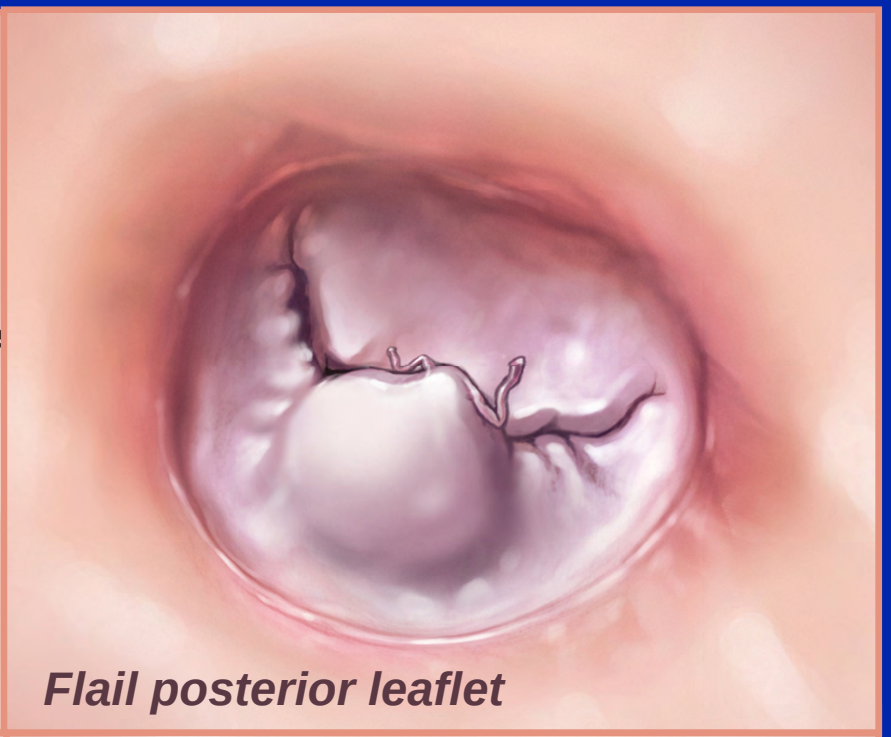
# Mitral Regurgitation

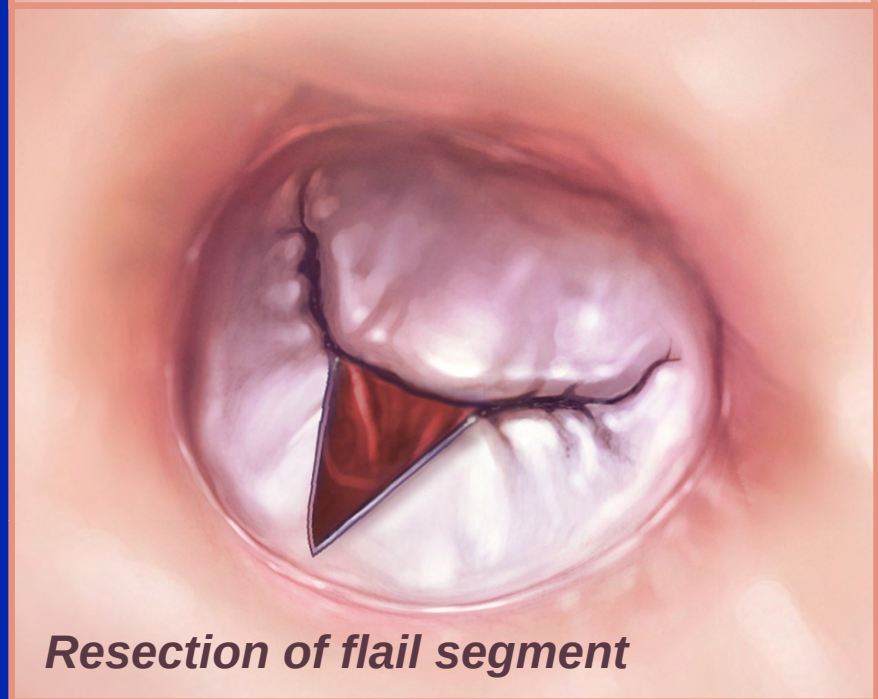
## We have markers of high-risk in asymptomatic patients

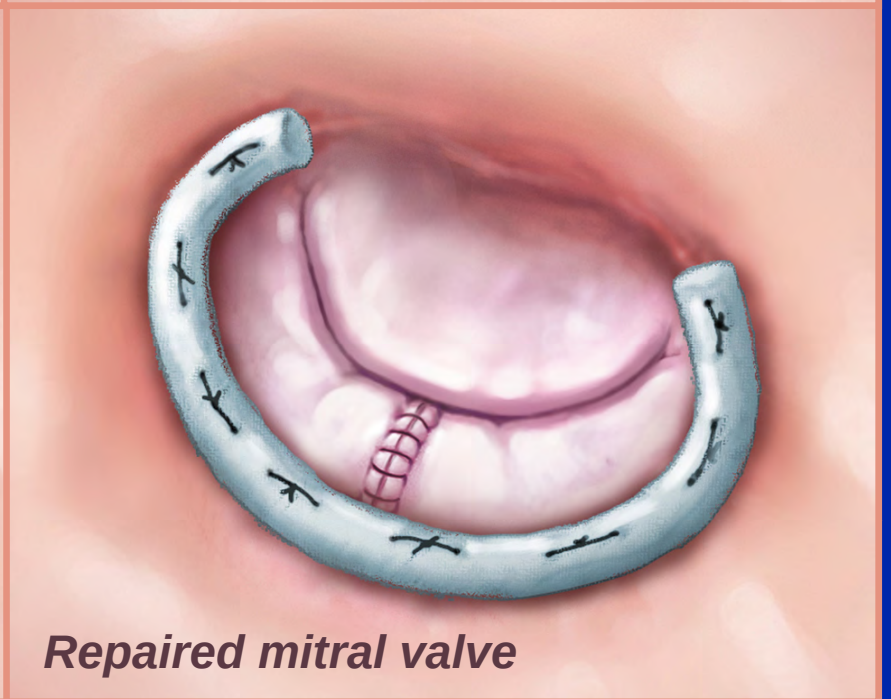
## Can we do a restorative surgery ?

# Mitral Valve Repair



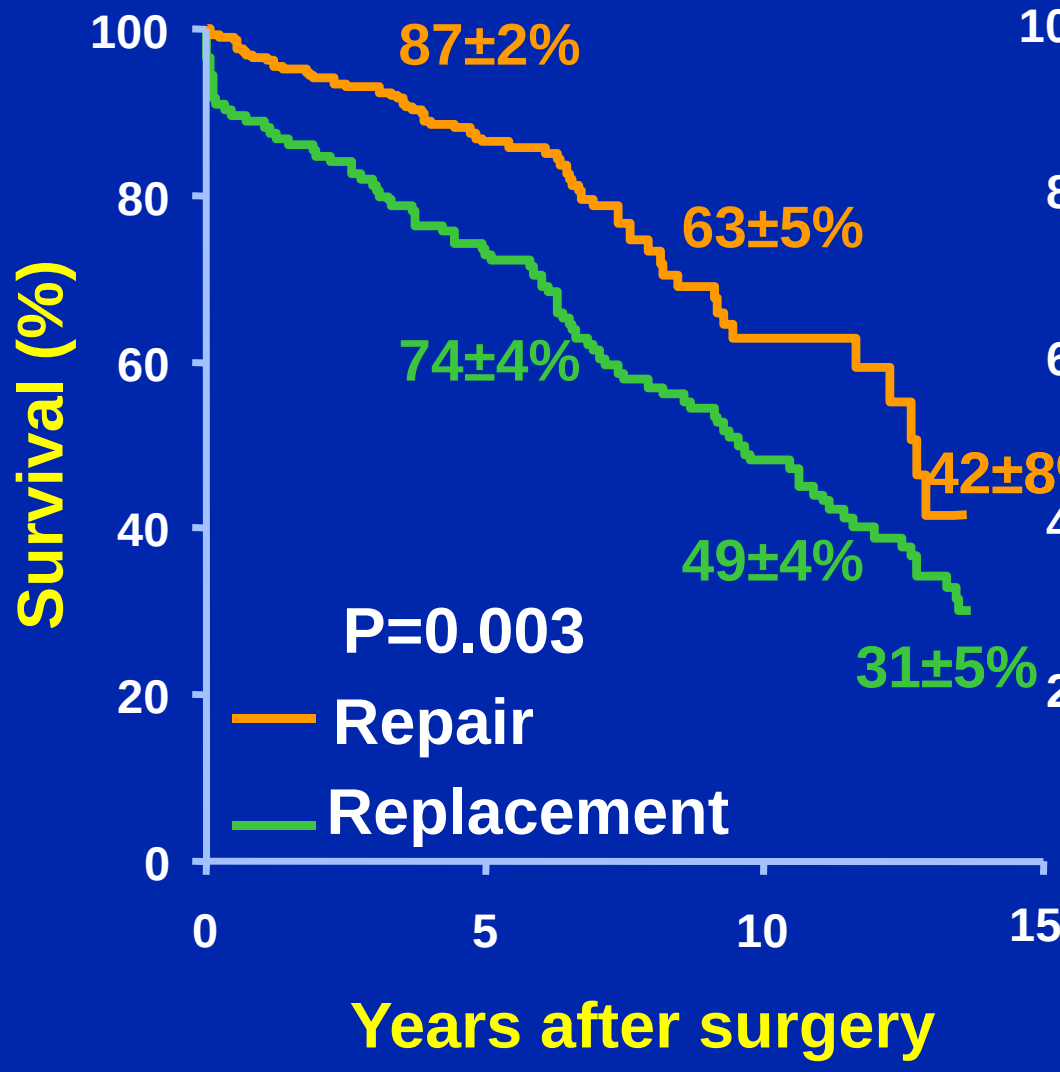



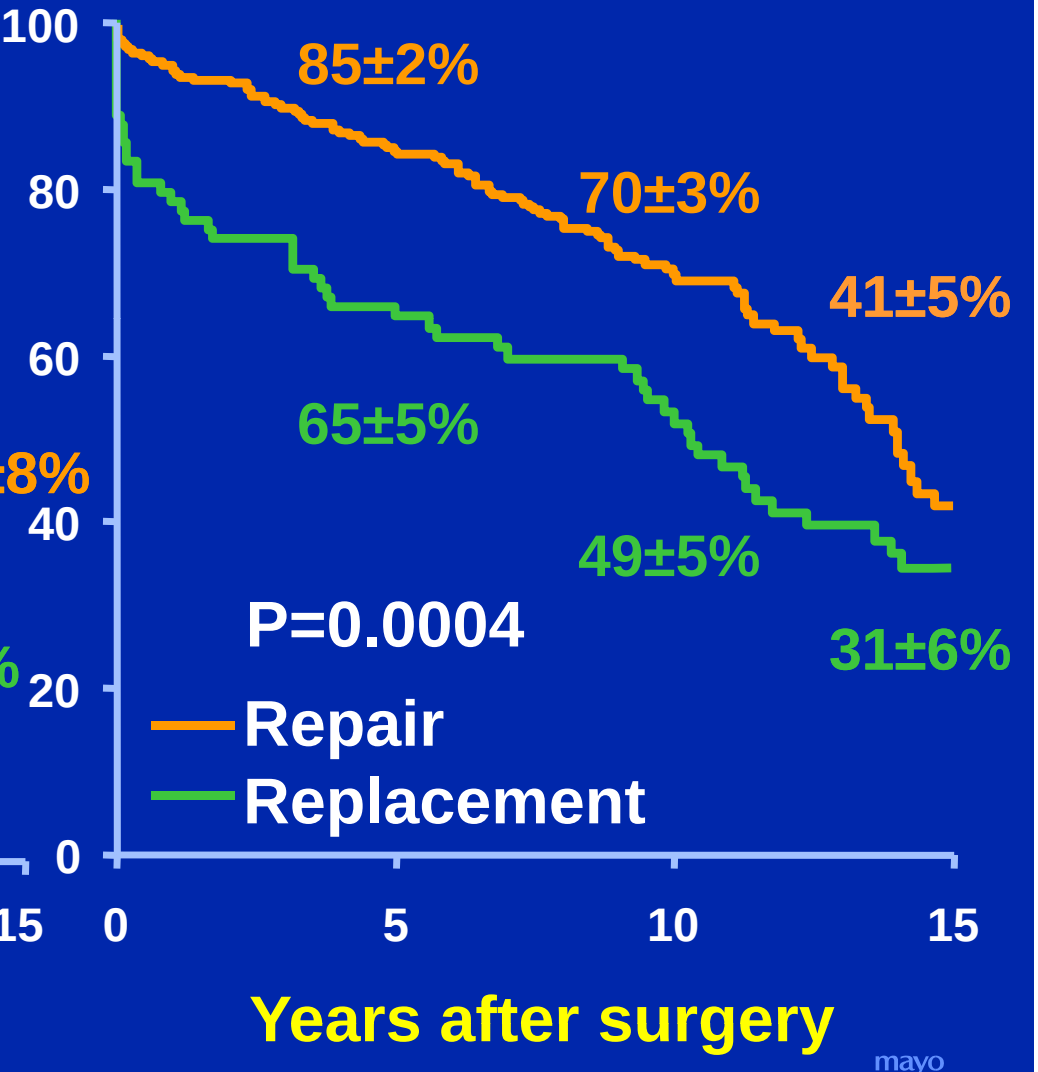



# Better Survival after Valve Repair

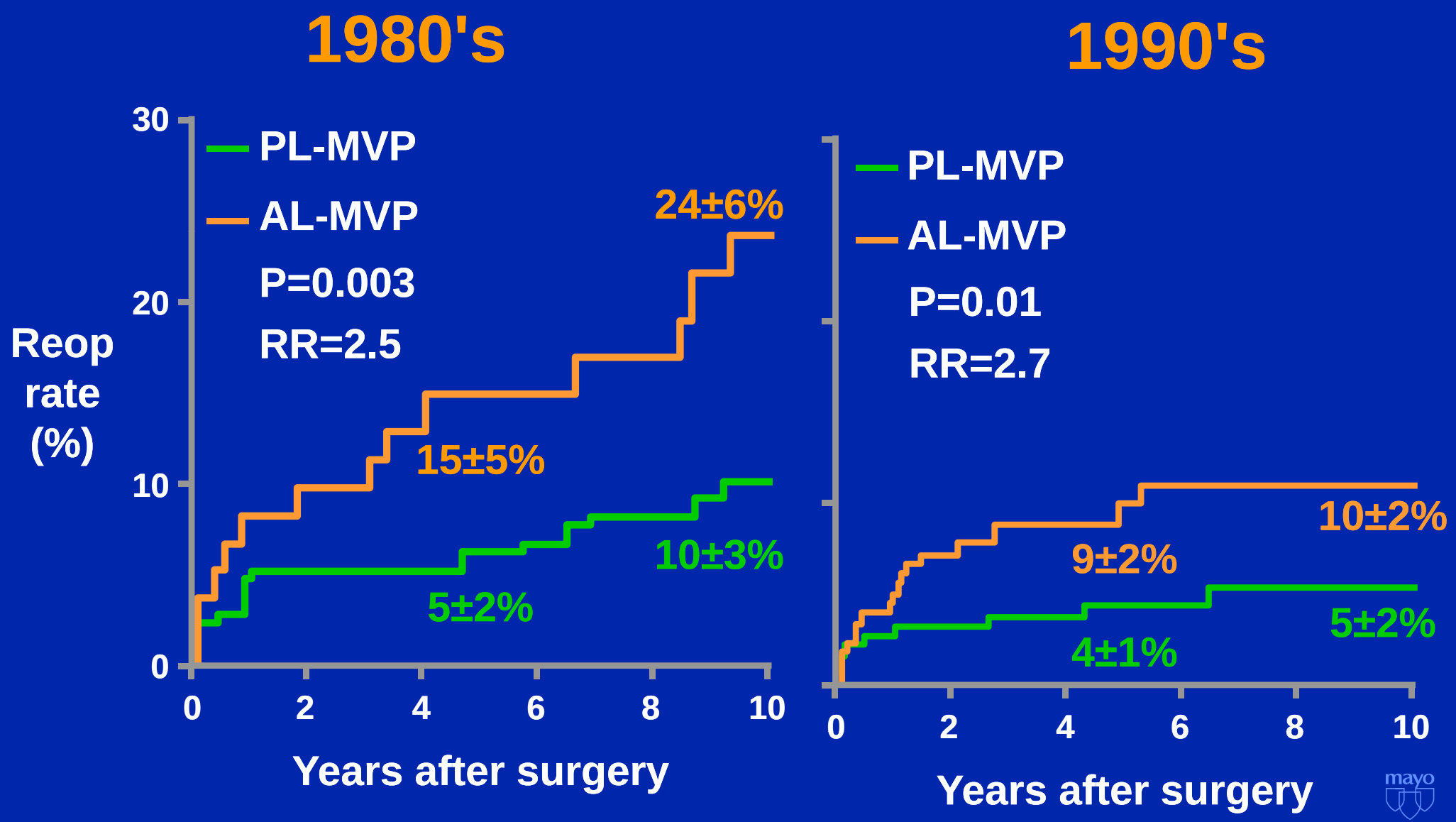
## Anterior vs. Posterior MVP



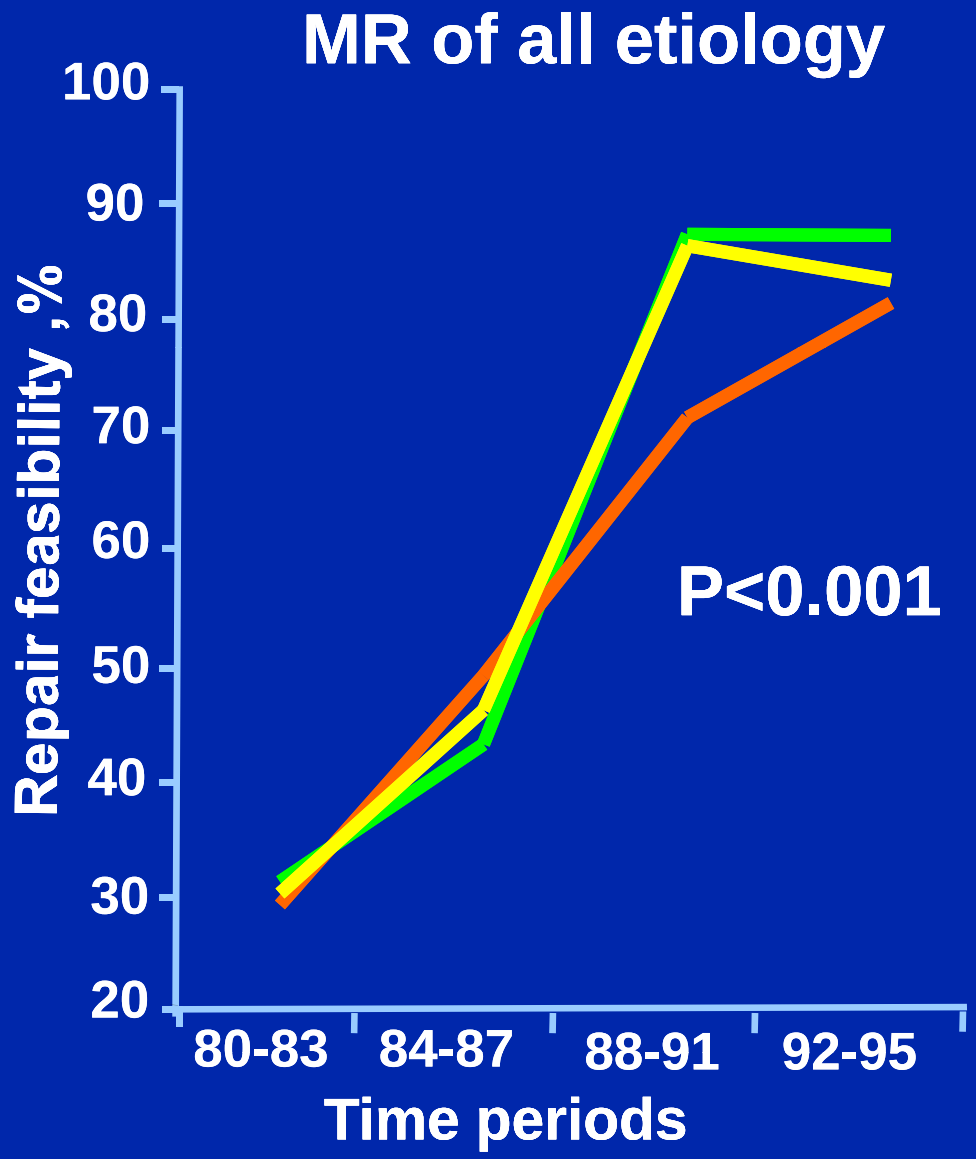
# Reoperation after Valve Repair

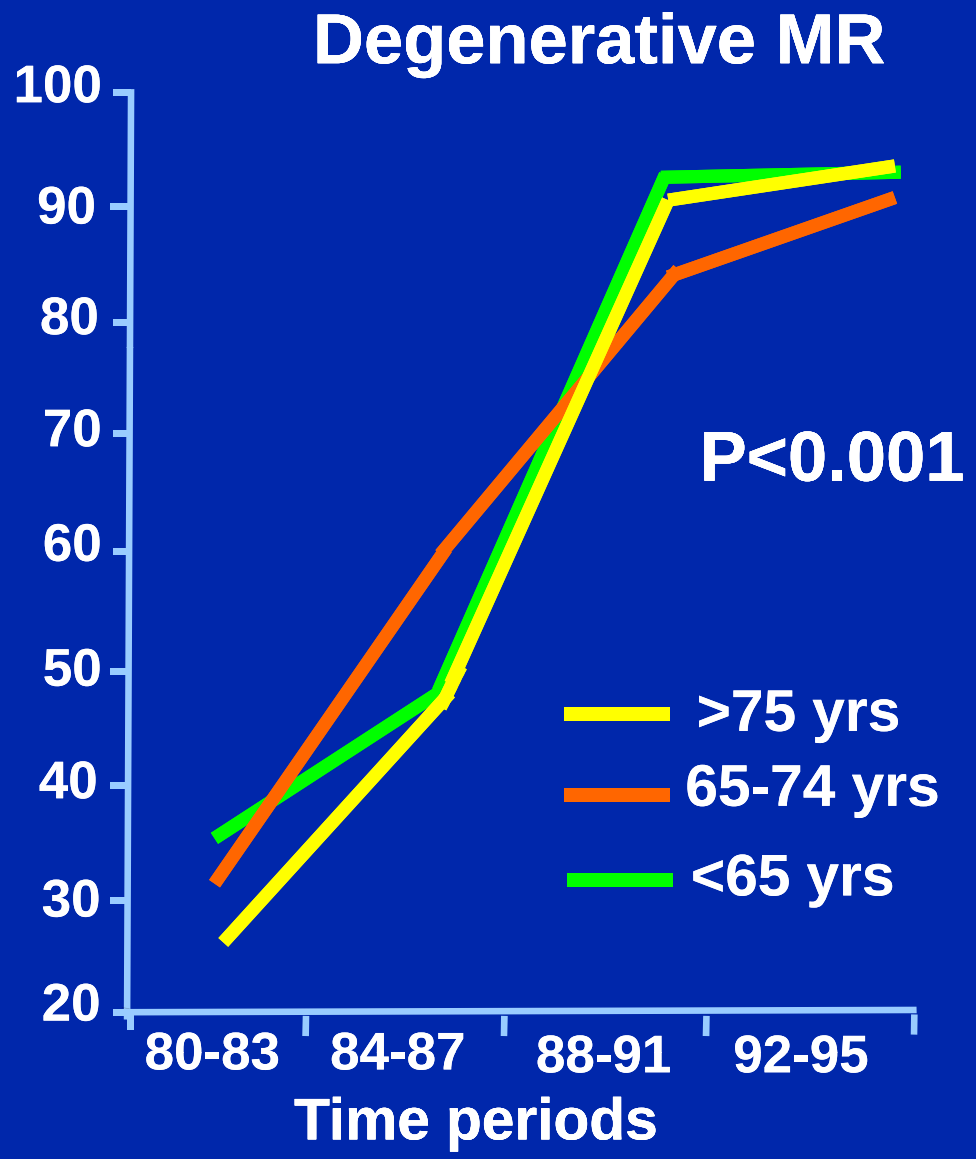
## Improving Results

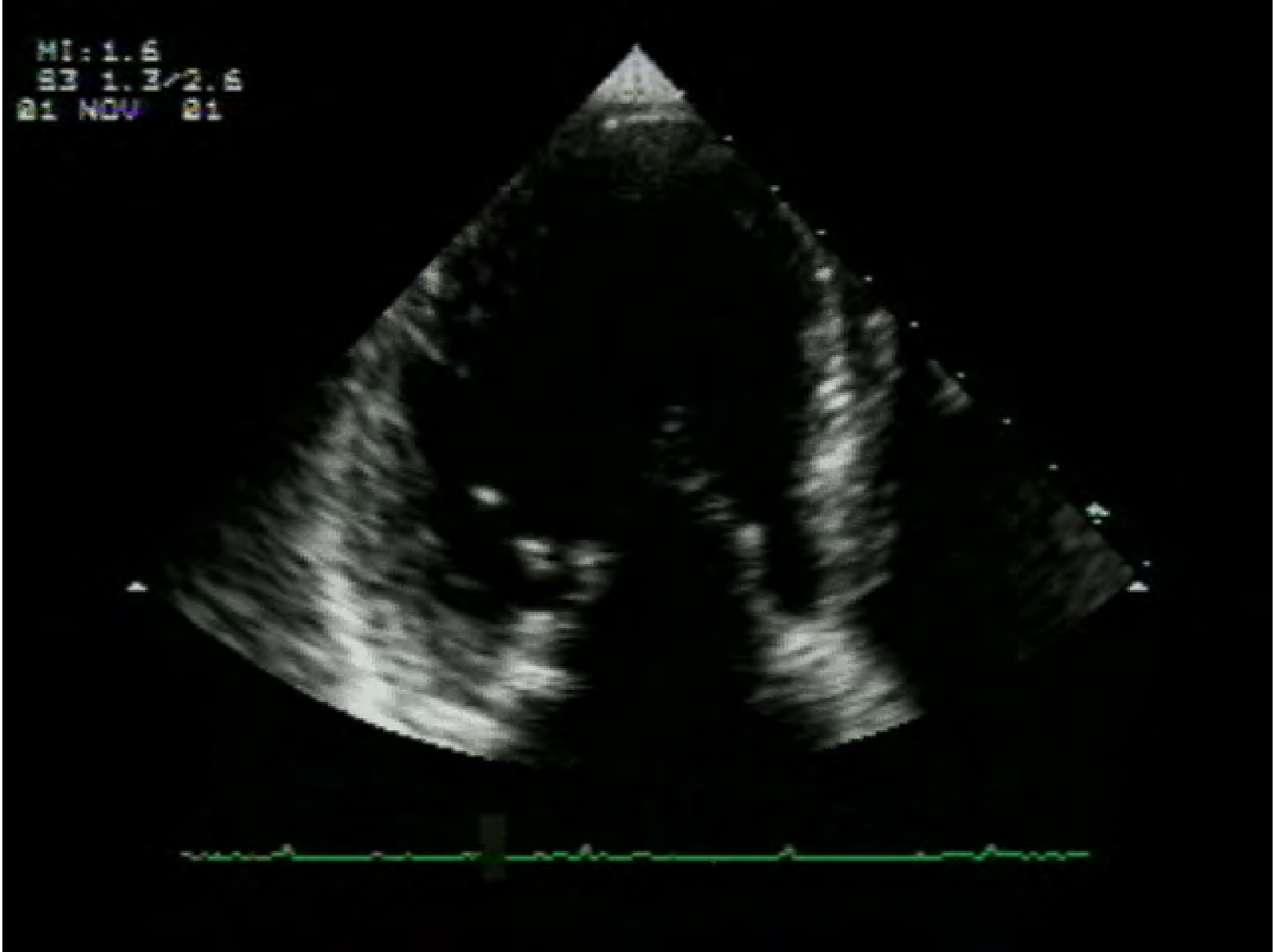


# MR Surgery in the Elderly

## Recent Improvement: Feasibility of Valve Repair

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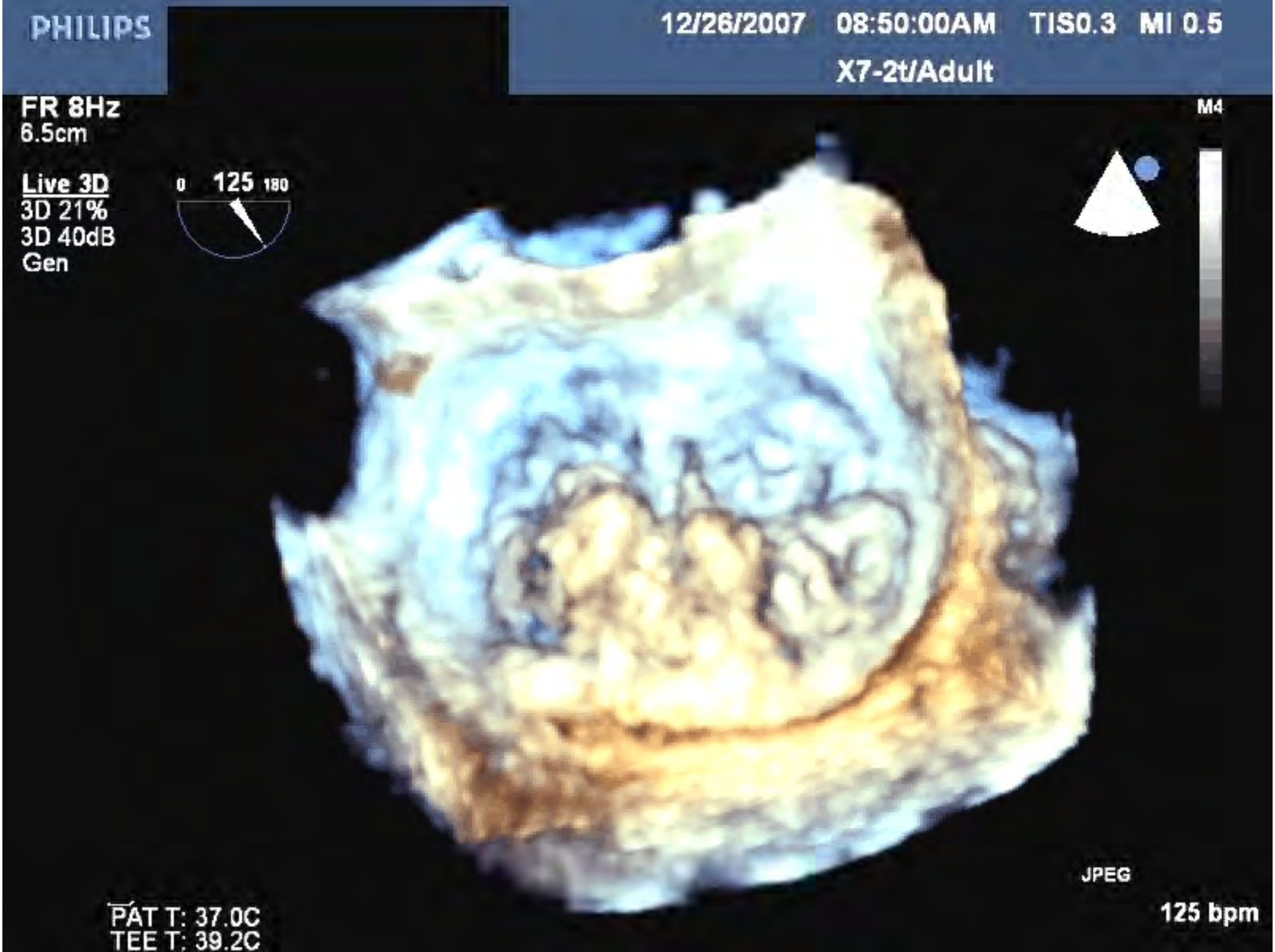
S3 1.3/2.6
21 NOV 21


PHILIPS
12/26/2007 08:50:00AM TIS0.3 MI 0.5
X7-2t/Adult
FR 8Hz
6.5cm
Live 3D
3D 21%
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Gen
0 125 180
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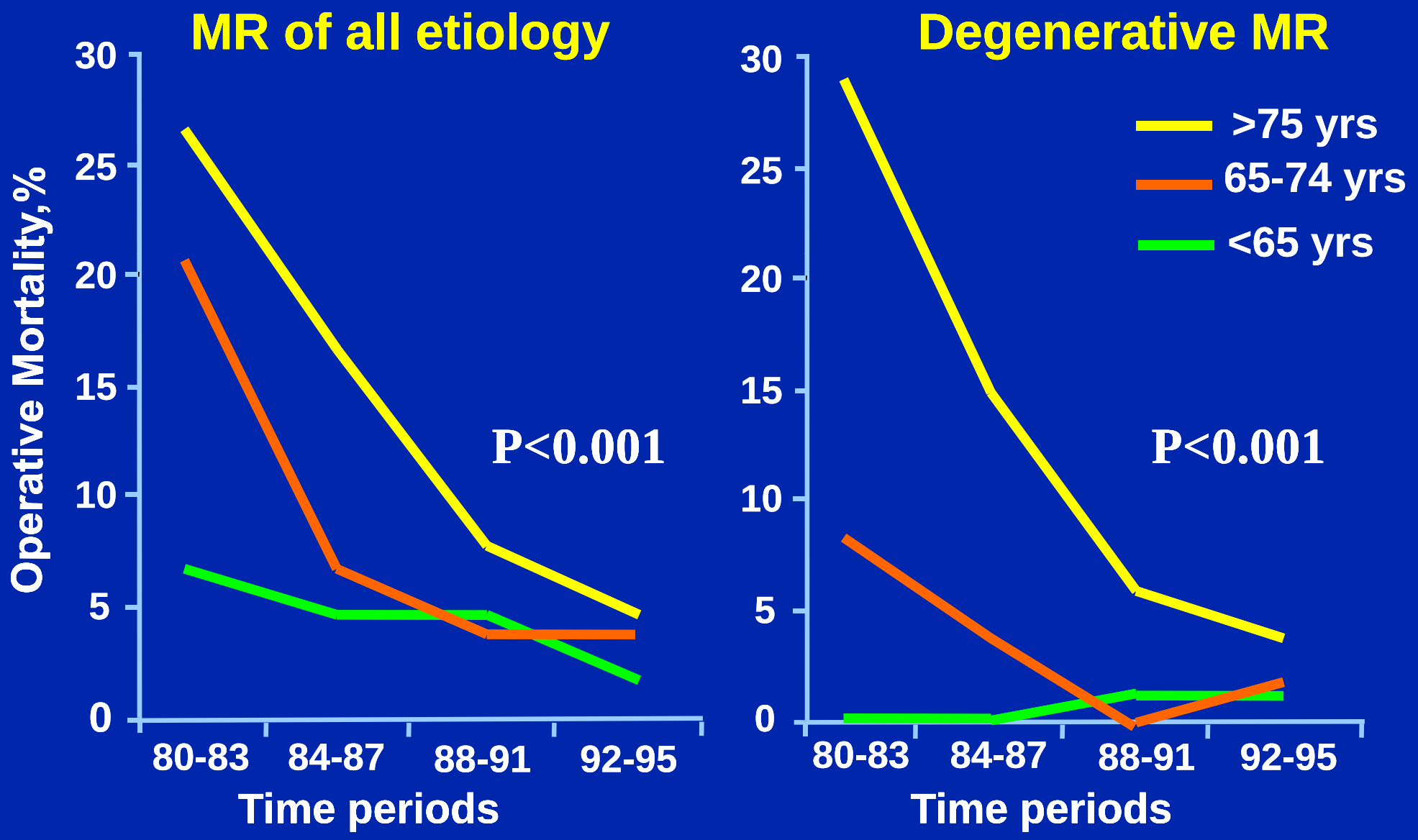
PAT T: 37.0C
TEE T: 39.2C
125 bpm

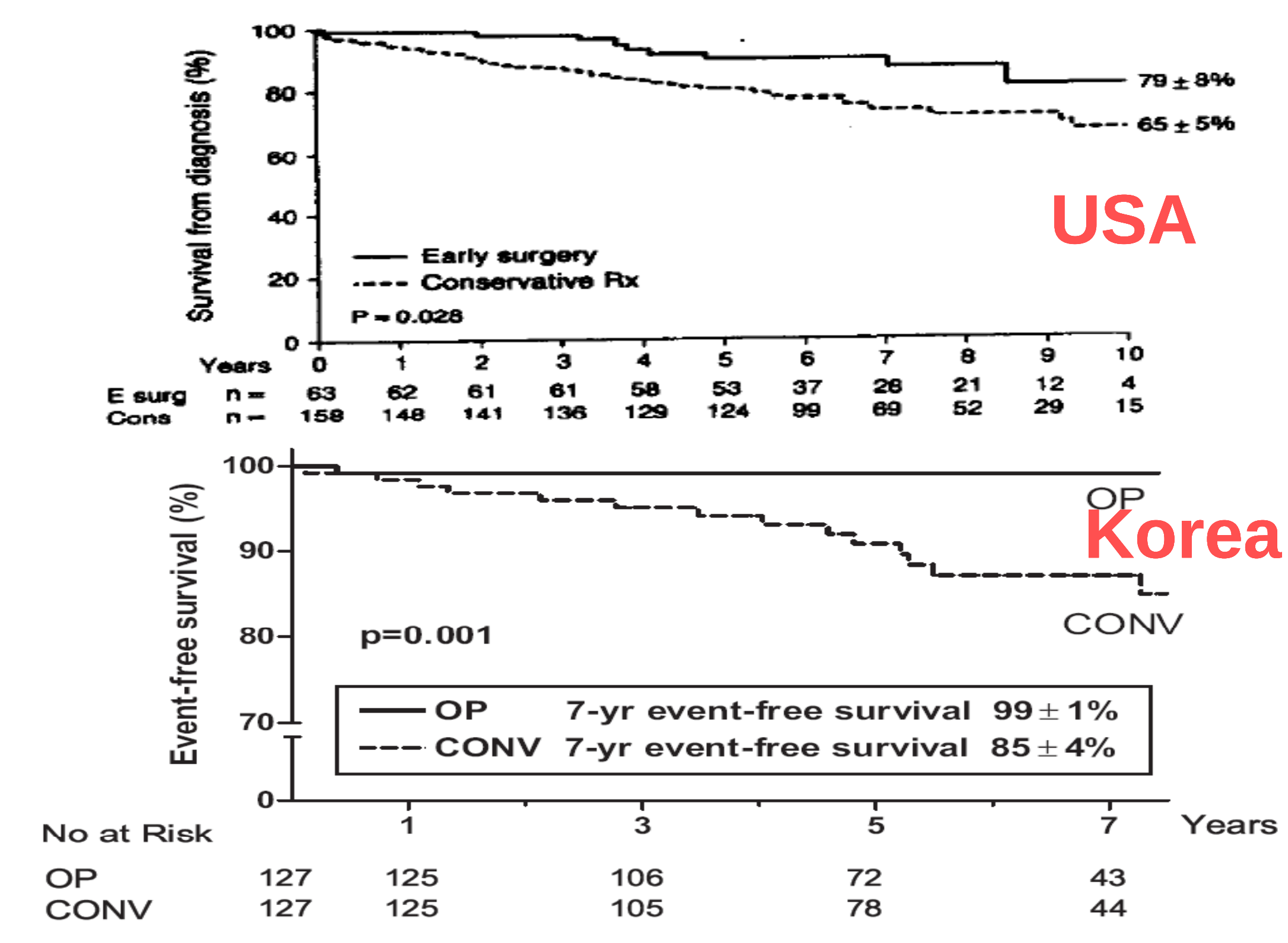
# MR Surgery in the Elderly

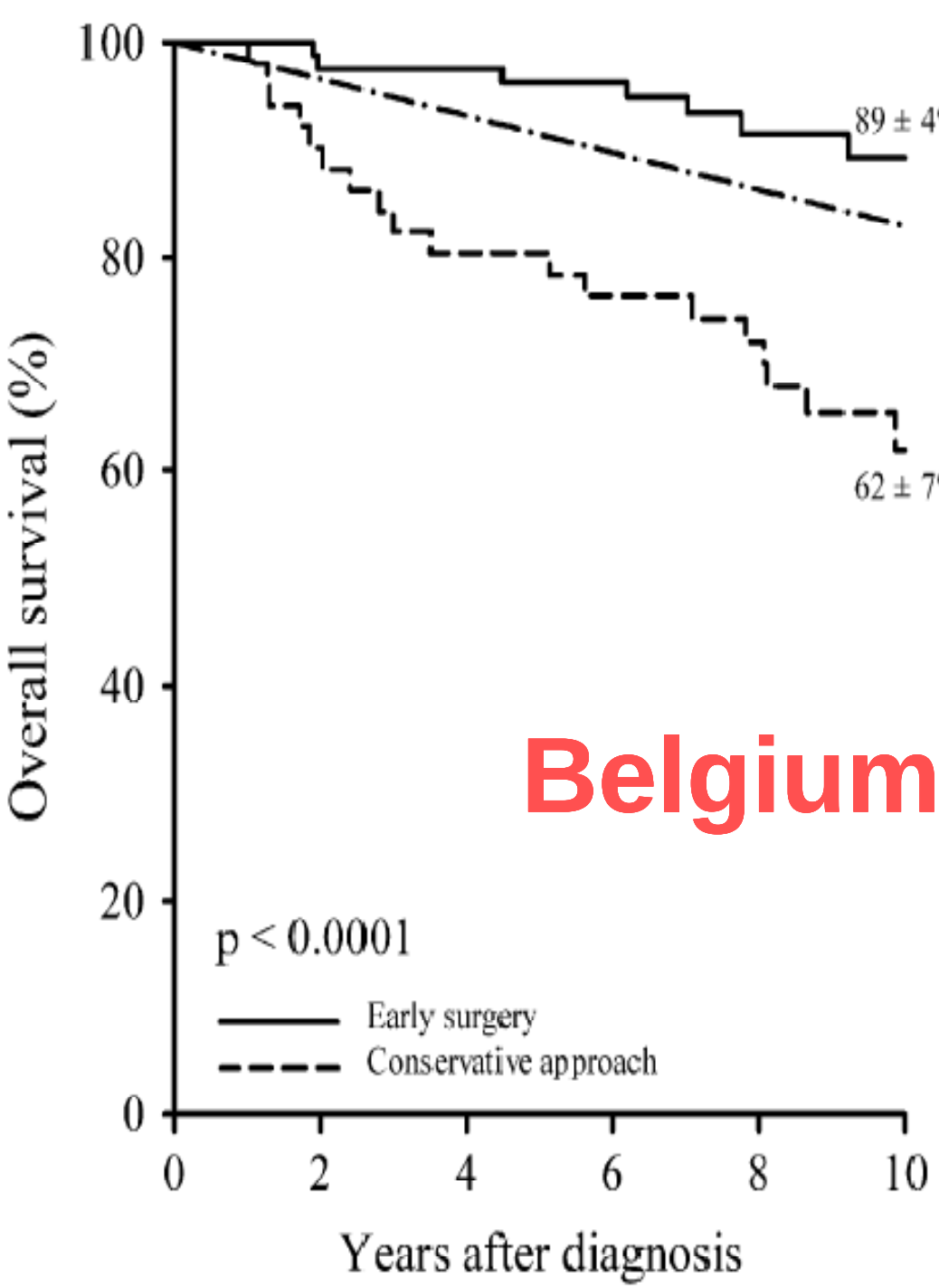
## Recent Improvement: Operative Mortality



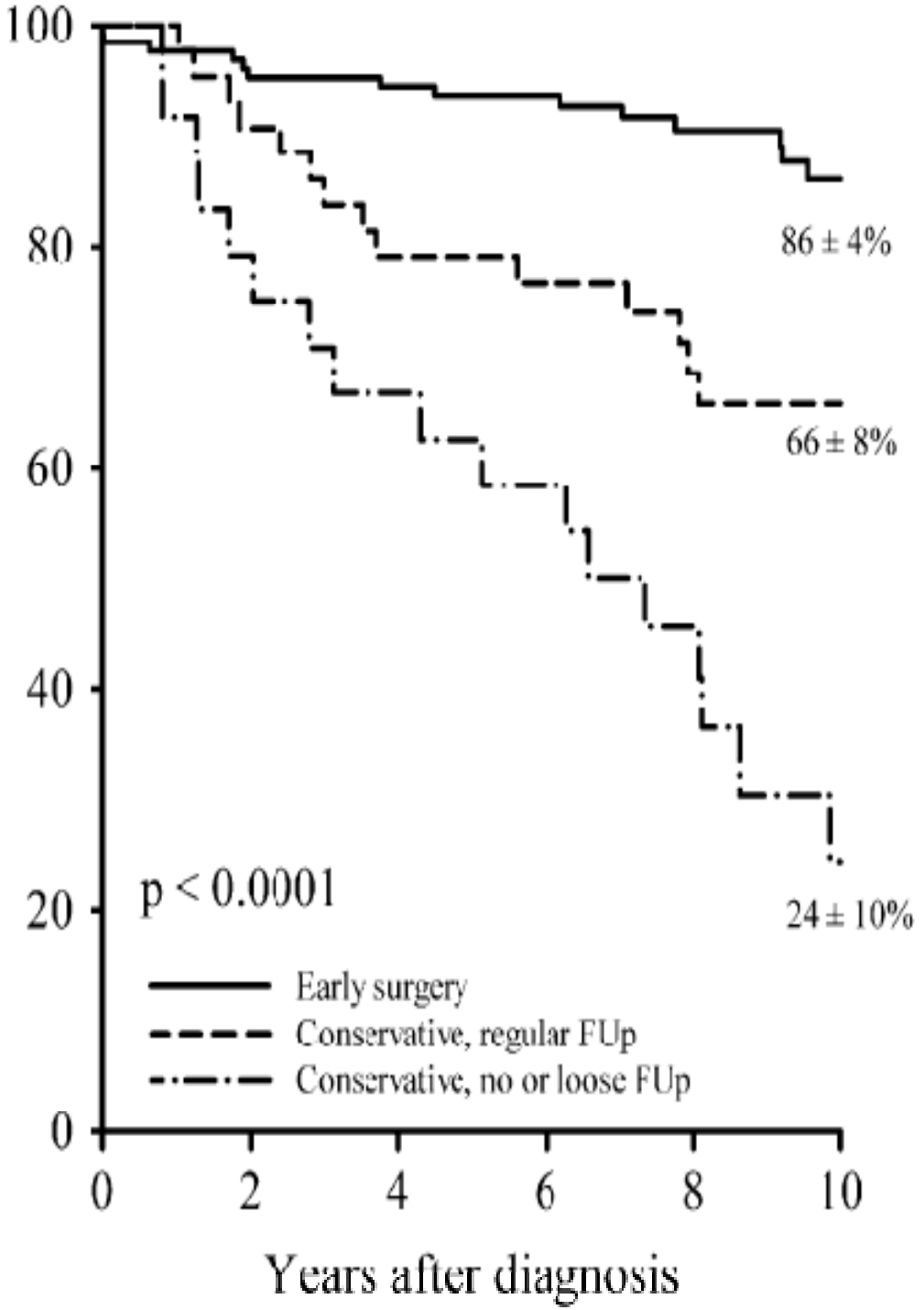
# Mitral Regurgitation

## Is Early Surgery beneficial ?


Survival from diagnosis (%)
100
80
60
40
20
0
79 ± 8%
65 ± 5%
Early surgery
Conservative Rx
P = 0.028
USA
Years 0 1 2 3 4 5 6 7 8 9 10
E surg n = 63 62 61 61 58 53 37 28 21 12 4
Cons n = 158 148 141 136 129 124 99 89 52 29 15
Event-free survival (%)
100
90
80
70
0
OP
CONV
Korea
p=0.001
OP 7-yr event-free survival 99 ± 1%
CONV 7-yr event-free survival 85 ± 4%
No at Risk
1 3 5 7 Years
OP 127 125 106 72 43
CONV 127 125 105 78 44




**Belgium**




Montant et al JTCVS 2009;1339

# Asymptomatic Mitral Regurgitation

*Strategy for treatment ?*

# Asymptomatic MR

*Why not operate :*

- *Normal LV (LVS<35, EF>60)*
- *Normal LA and sinus R*
- *Normal VO2*
- *Normal BNP*
- *ERO < 40 mm2*

# Asymptomatic MR

## Why operate ?

*Offer early surgery to asymptomatic MR patients in*

*Advanced repair centers:*

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

# Asymptomatic MR

## Why operate ?

***Offer early surgery to high-risk MR:***

- *LV Dysfunction (late)*
- *AFib (late)*
- *LA enlargement ≥ 60 mL/m2*
- *BNP activation*
- *Reduced FC*
- *ERO ≥ 40 mm2*

# Mitral Regurgitation

## Management

- Quantify MR
- Think Repair Now


Thank
You