Chronic Primary Mitral Regurgitation

The Case For Early Surgical Intervention

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DISCLOSURES

Relevant Financial Relationship(s)

None

Off Label Usage

None

Watchful Waiting . . .

. . . Is Looking for Trouble

Quantitative Determinants of Outcome of Asymptomatic MR

Initial Patient Characteristics

- 456 Asymptomatic patients with MR
- Mean age 63 ± 14 yrs
- MR regurgitant volume 66 ± 40 cm^3, ERO 40 ± 27 mm^2; (Gr IV/IV in 54%)
- LVEF: 70 ± 8%, LVESD: 34 ± 6 mm
- Systolic PAP: 38 ± 11 mmHg

Sarano ME et al: NEJM 352:875, 2005

Quantitative Determinants of Outcome of Asymptomatic MR

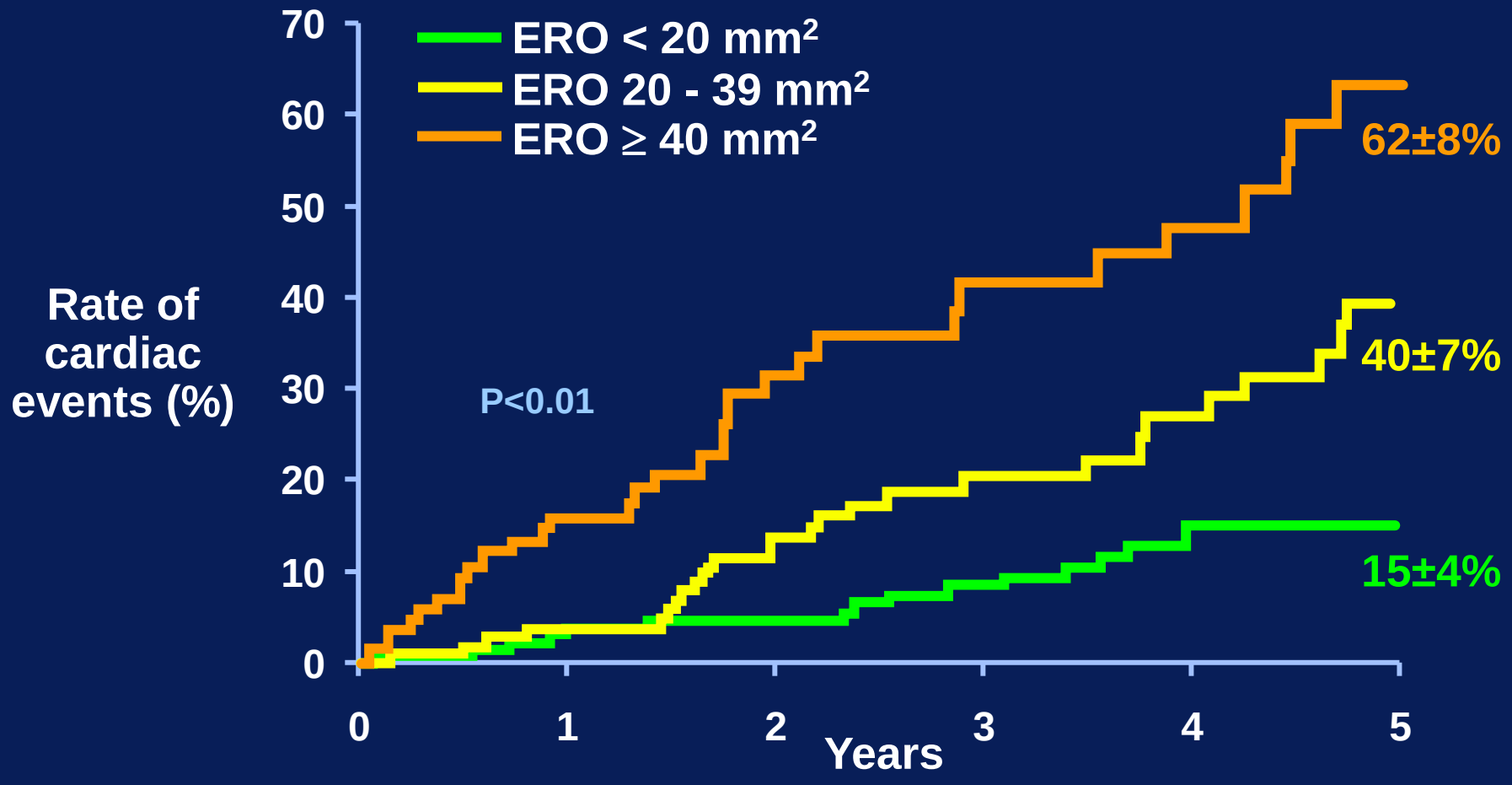
Patient Follow-up

- Follow-up: 5.1 ± 2.9 yrs
- 5 Yr freedom from surgery: 46 ± 3%
- 5 Yr freedom from surgery/death: 36 ± 3%
- Triggers for mitral valve surgery
  - Cardiac symptoms: 41%
  - LVESD ≥ 40 mm: 39%
  - Other: 20%

Sarano ME et al: NEJM 352:875, 2005

Quantitative Determinants of Outcome of Asymptomatic MR

Events: Cardiac Death, CHF, New Atrial Fibrillation



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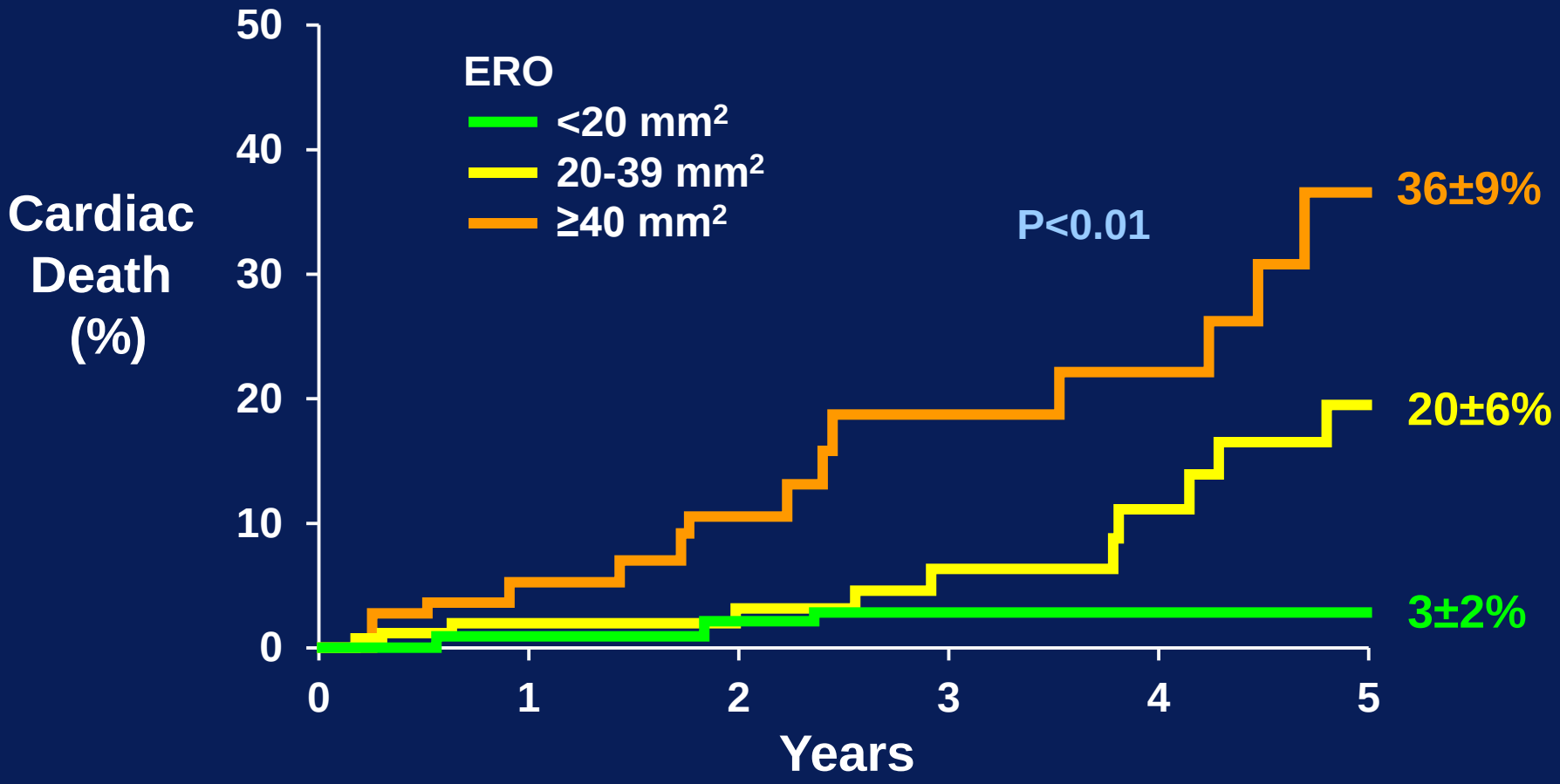
Quantitative Determinants of Outcome of Asymptomatic MR

Death From Cardiac Causes



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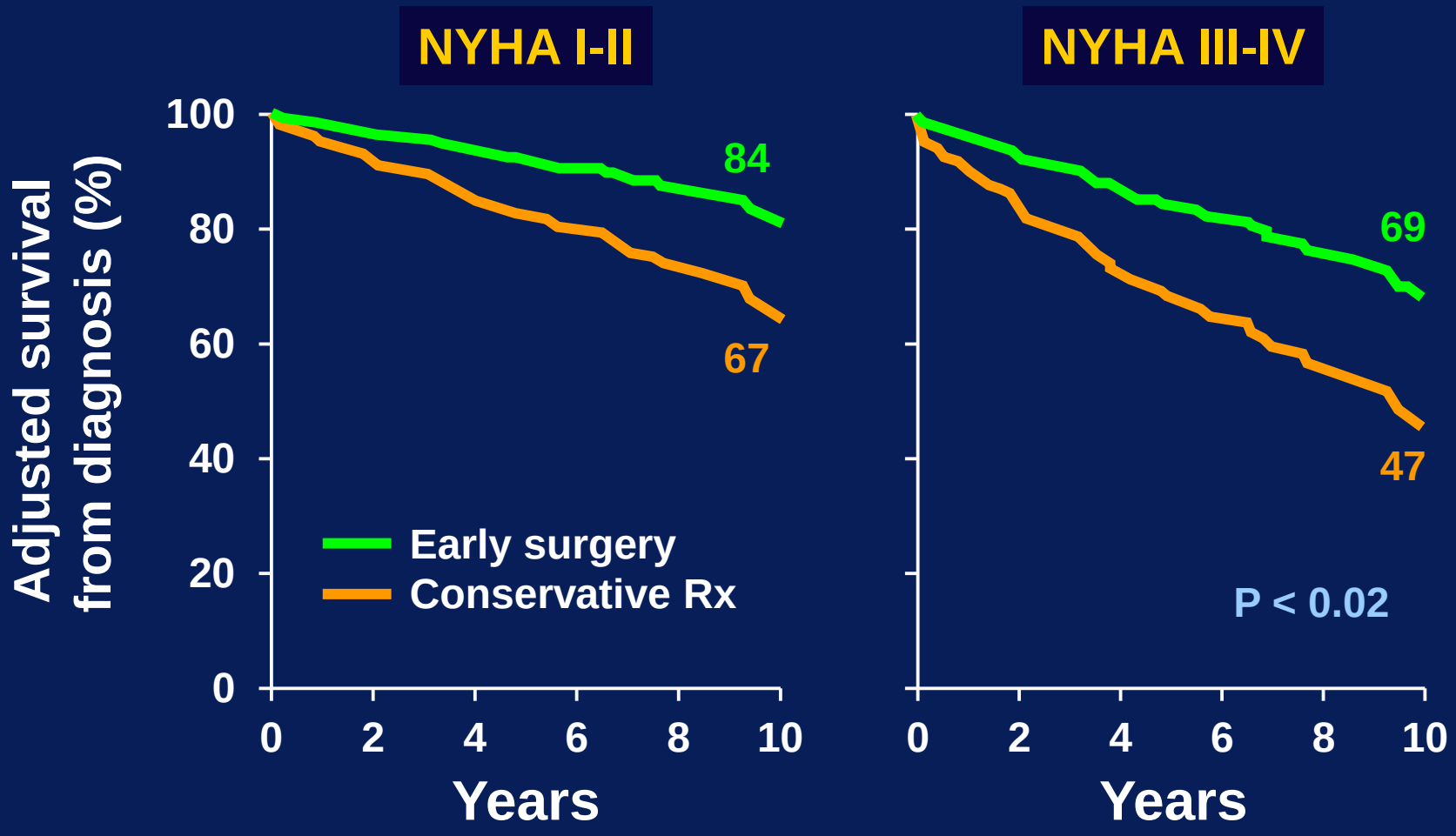
Waiting for Symptoms. . .

. . . Is Asking for Trouble

Early Surgery vs Conservative Therapy For Severe MR

Impact of Preoperative Symptoms



Ling et al: Circulation 1997; 96: 1819

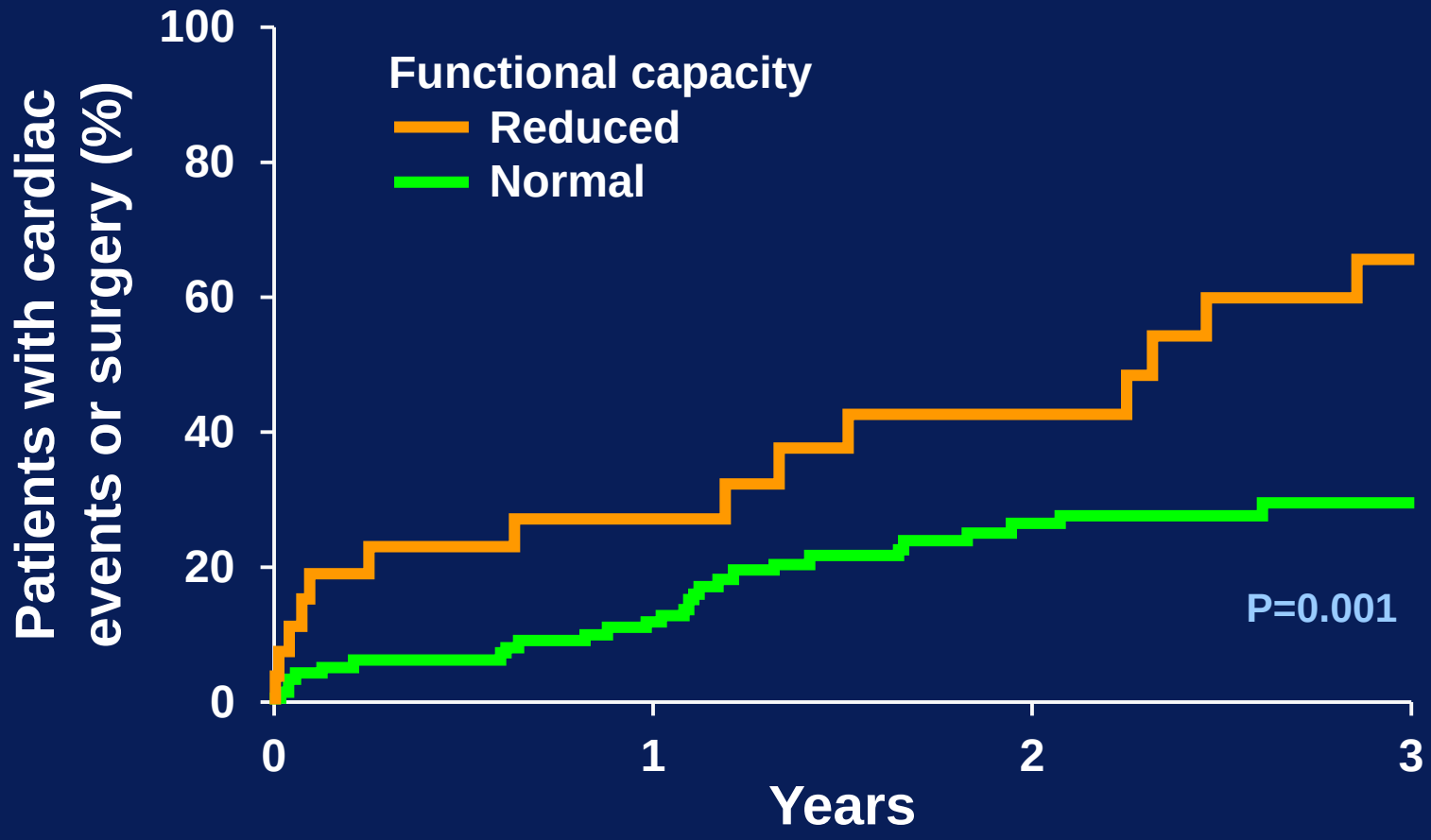
Cardiopulmonary Exercise Testing in "Asymptomatic" MR:
Is the Patient Truly Asymptomatic?

- 134 Asymptomatic patients; 63 ± 14 yrs
- MR regurgitant volume 68 ± 24 cm^3,
  ERO 35 ± 14 mm^2; LVEF 73±6%
- Reduced functional capacity (<84% predicted) related to MR in 19%
  Peak VO_2 22 ± 5 (74 ± 8% Predicted)

Messika-Zeitoun D, et al. JACC 2006; 47: 2521

Cardiopulmonary Exercise Testing in "Asymptomatic" MR

Events: Death, Heart Failure, Surgery, AFib



Messika-Zeitoun et al: JACC 47:2521, 2006

"Asymptomatic" MR: Exercise Induced Pulmonary Hypertension

Is the Patient Truly Asymptomatic?

- 49 Asymptomatic patients with MR
- MR ERO 0.40 ± 0.14 cm^2, RVSP 30 ± 7 mmHg
- LVEF 67 ± 7 %, LVESD 31 ± 6 mm
- Symptom limited exercise echo VO_2 stress
- 24% with <80% functional aerobic capacity (FAC)
- Exercise induced pulmonary hypertension (RVSP ≥ 60 mmHg) the strongest multivariate predictor of poor FAC and onset of symptoms

Suzuki K, et al. J Cardiol 2015; 66: 246

"Asymptomatic" MR: Exercise Induced Pulmonary Hypertension

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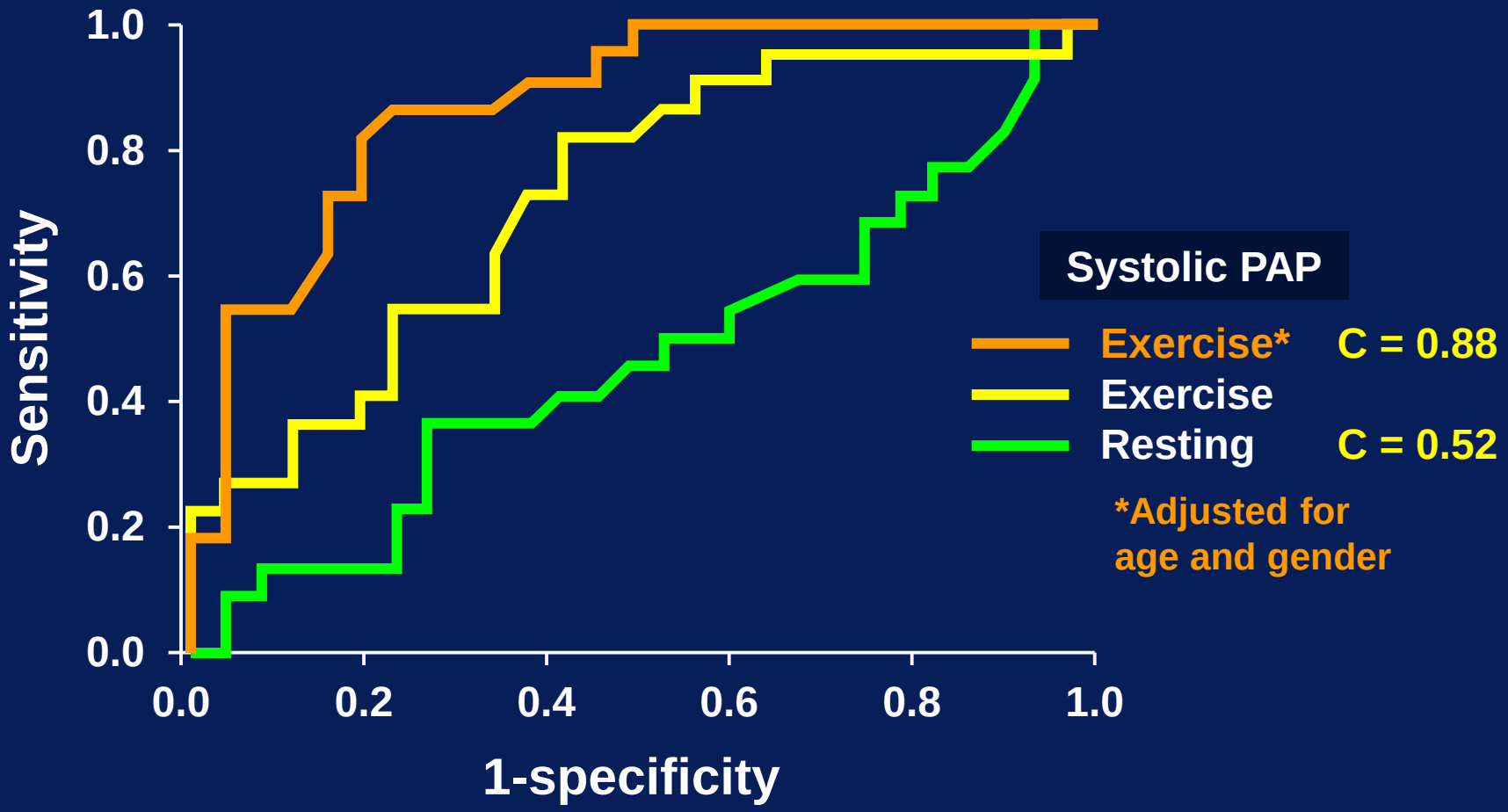

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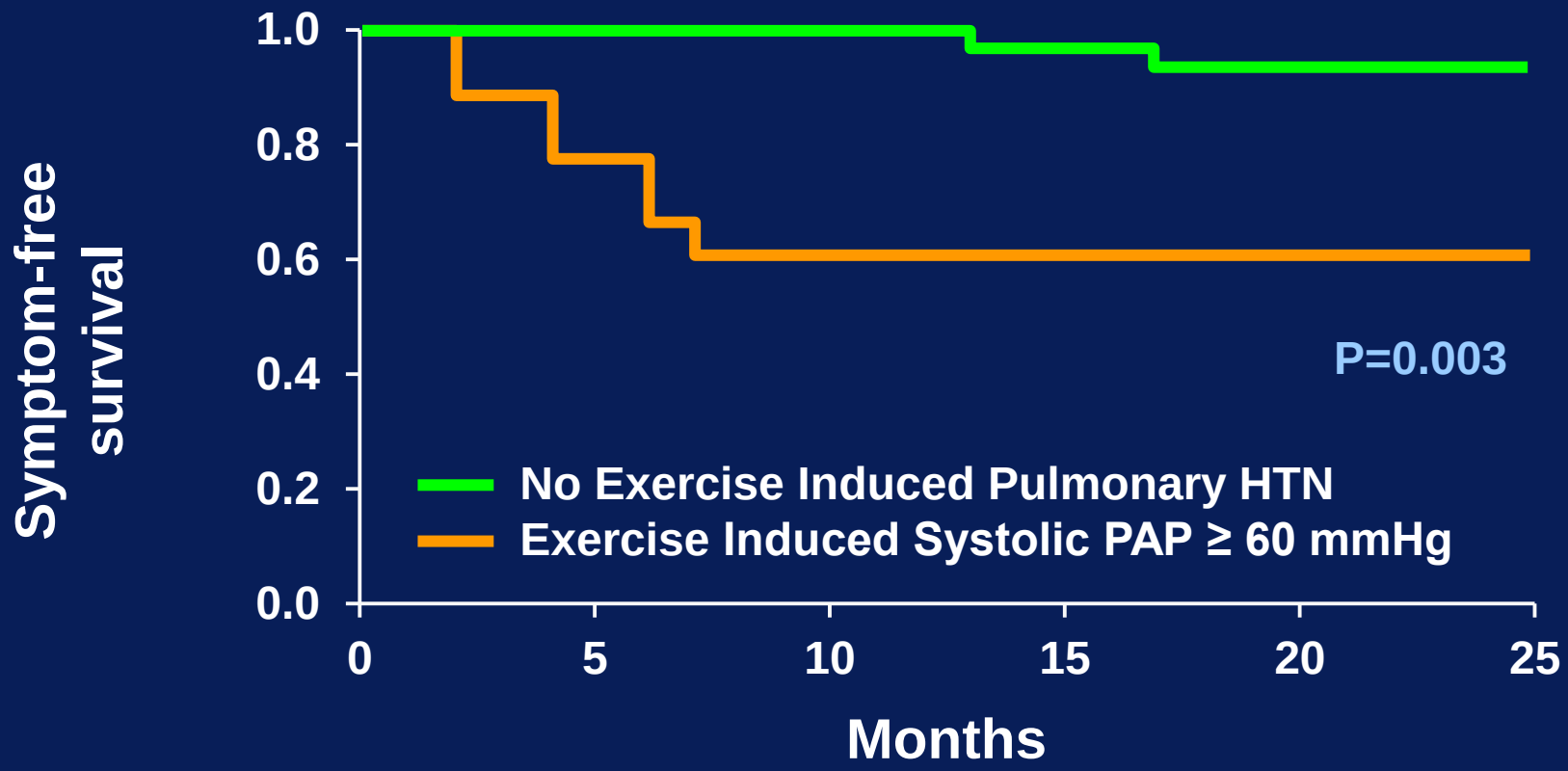


Patients at Risk						
	31	31	31	30	29	29
	18	14	11	11	11	11

Suzuki K, et al. J Cardiol 2015; 66: 246

"Asymptomatic" MR: Exercise Induced Pulmonary Hypertension

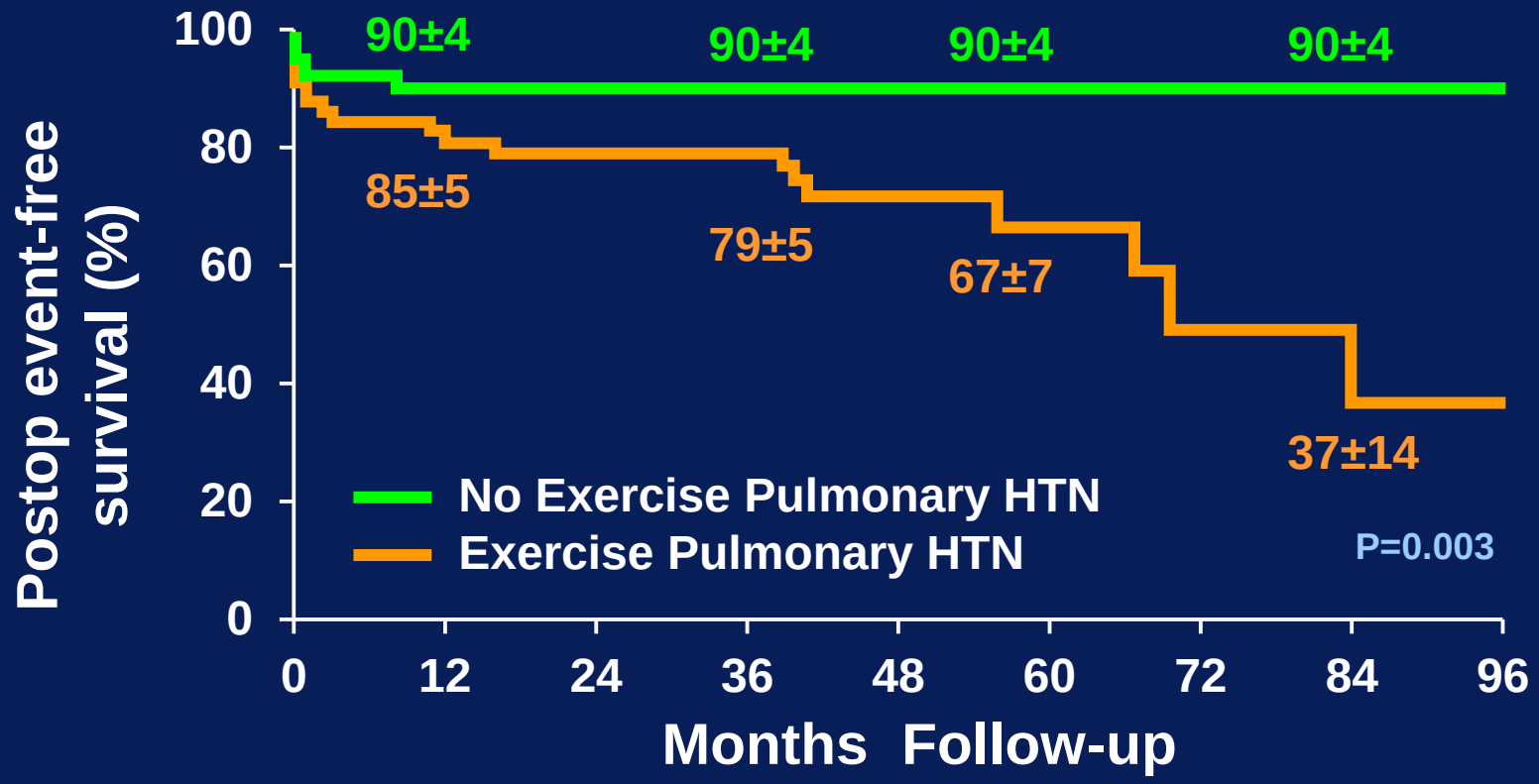
Post-Op Events: Heart Failure, Stroke, Death

- 104 Patients; mean age 64 ± 12 yrs
- MR ERO 0.40 ± 0.07 cm^2, RVSP 36 ± 7 mmHg
- LVEF 71 ± 5 %, LVESD 34 ± 6 mm
- Preoperative exercise echo: **58%** of patients had exercise induced pulmonary HTN (RVSP ≥ 60 mmHg)
- Mitral surgery for isolated primary MR directed by ACC/AHA guideline triggers

Magne J, et al. Heart 2015; 101: 391

"Asymptomatic" MR: Exercise Induced Pulmonary Hypertension

Post-Op Events: Heart Failure, Stroke, Death



Magne J, et al. Heart 2015; 101: 391

And we must be wary . . .

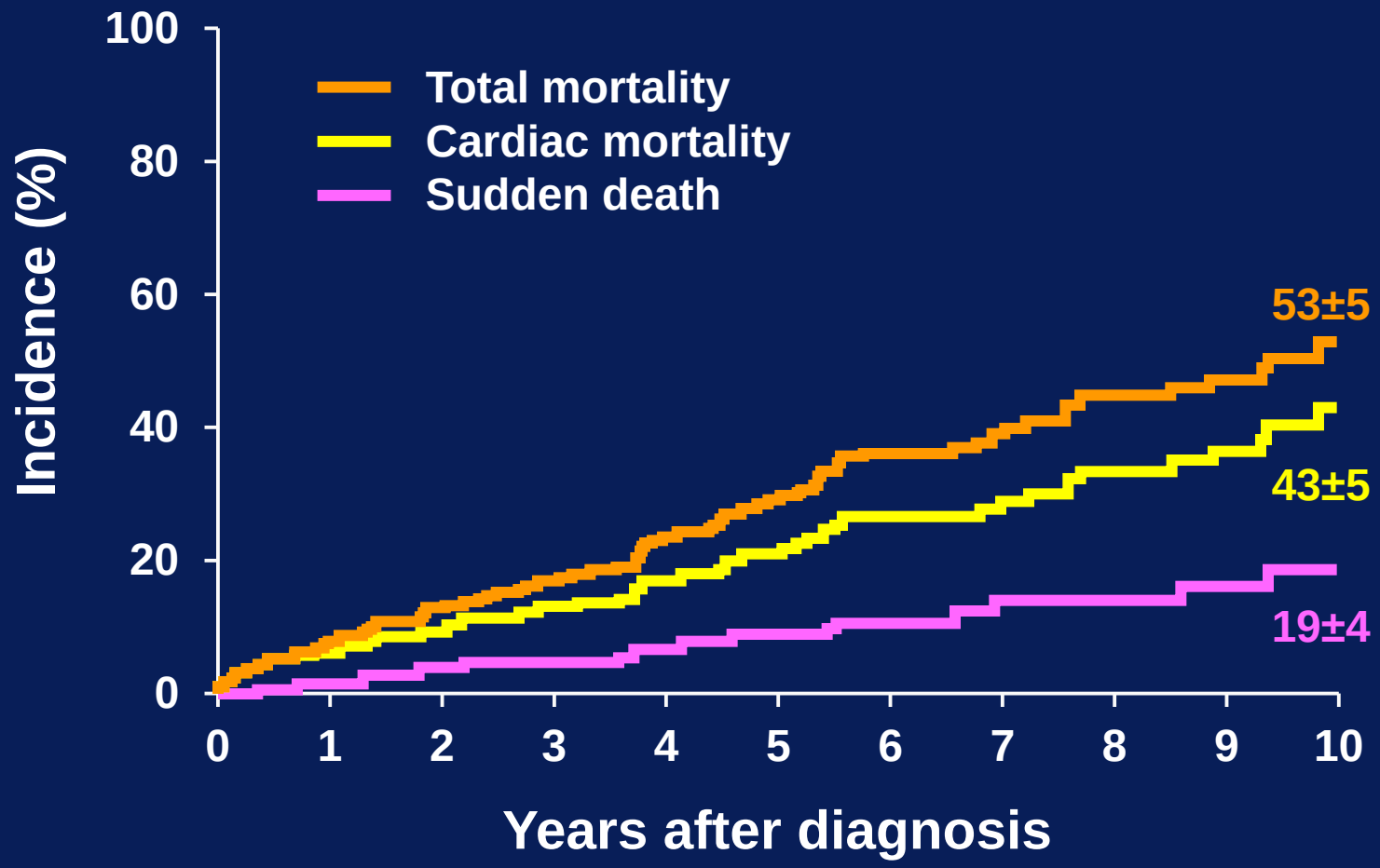
… of the ultimate end-point

Sudden Death in Severe MR Due to Flail Leaflet

- 348 Patients with flail MV leaflet
- Mean age: 67 ± 12 yrs; 48 ± 41 mo. F/U
- Under medical therapy: 99 deaths
  Sudden death: 25 patients (7.2%)
- Sudden death multivariate predictors :
  - NYHA functional class
  - LVEF (mean initial EF 63 ± 10%)
  - Atrial fibrillation

Grigioni F, et al. JACC 1999; 34:2078

Sudden Death in Severe MR Due to Flail Leaflet



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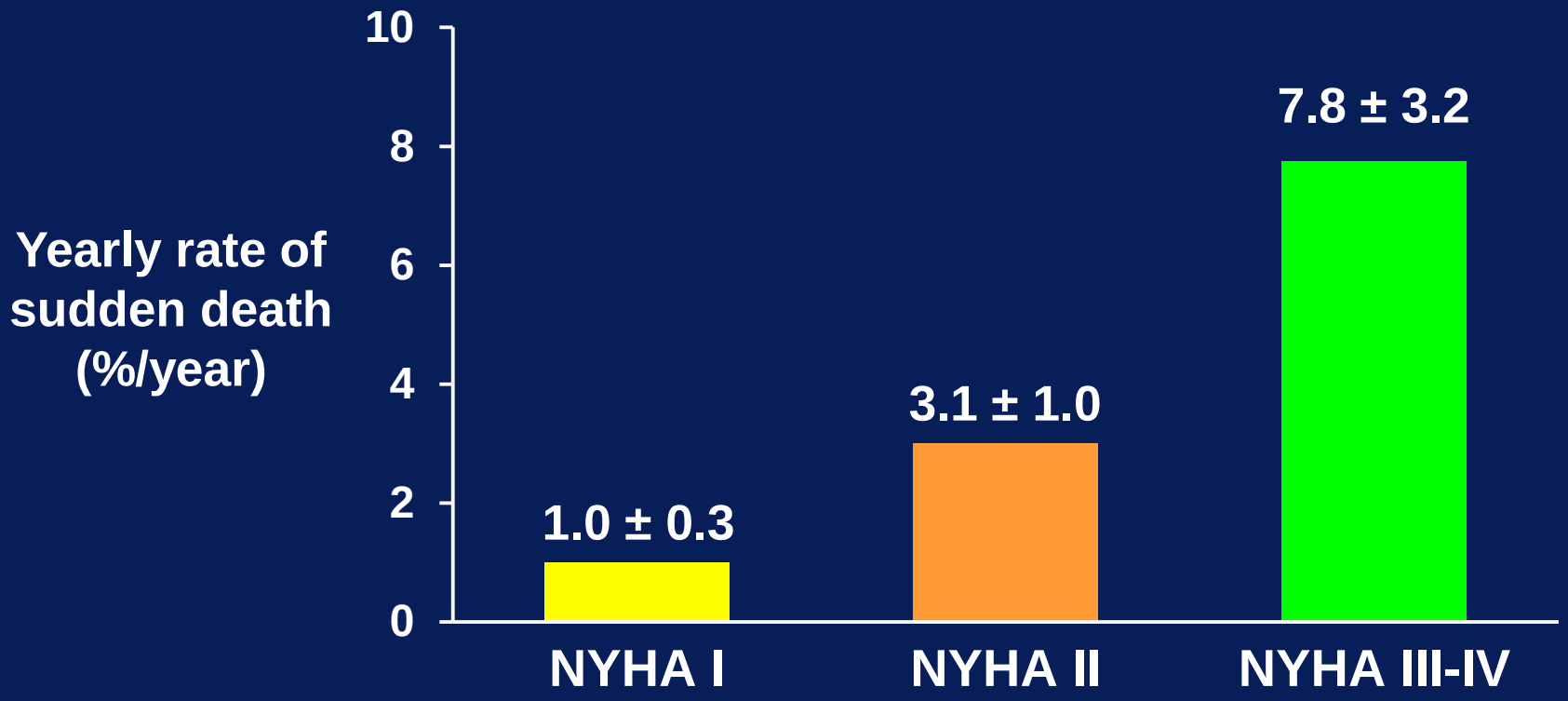
Grigioni F, et al. JACC 1999; 34:2078

Sudden Death in Severe MR Due to Flail Leaflet:
Relation to NYHA Functional Class



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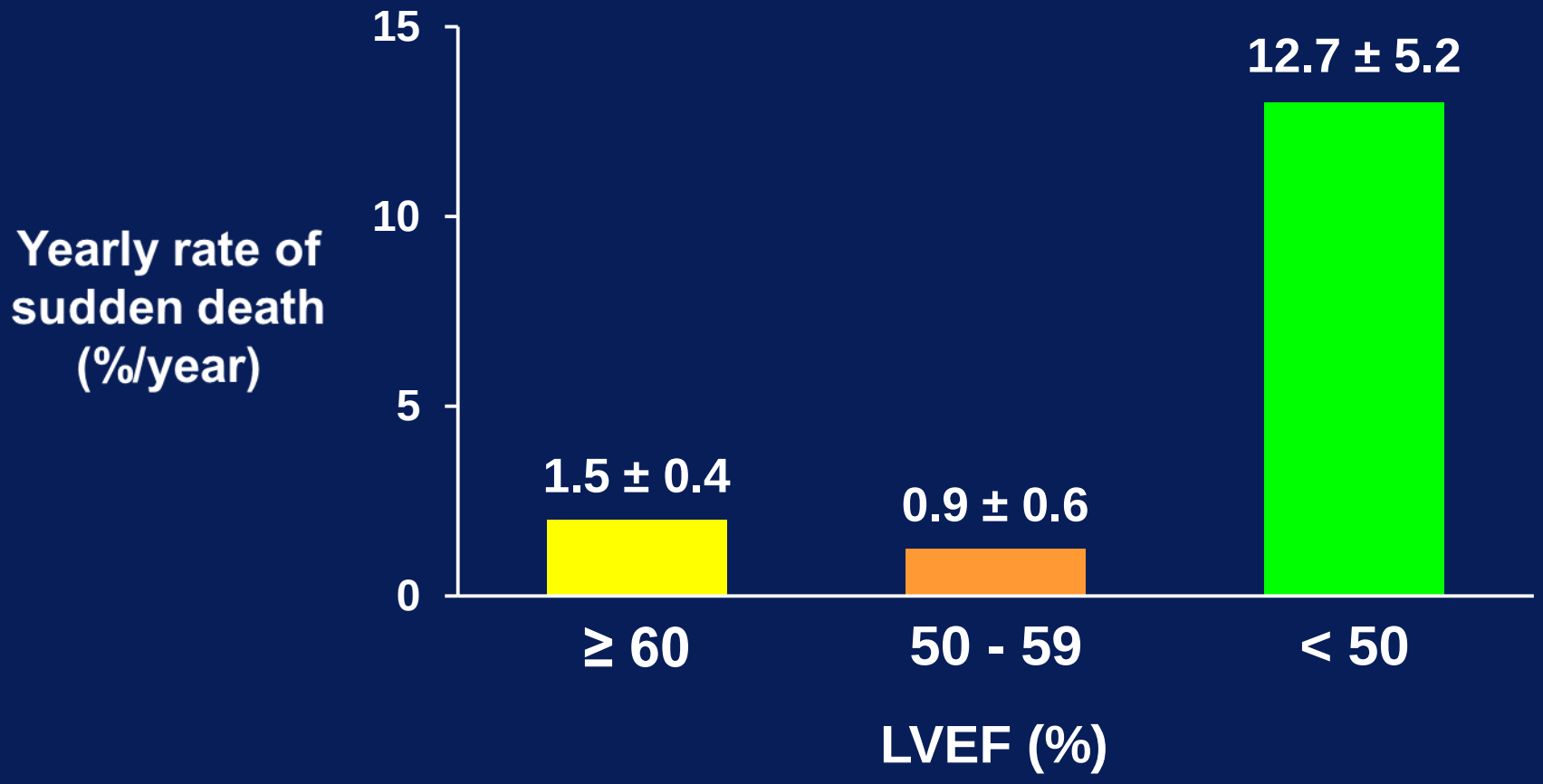
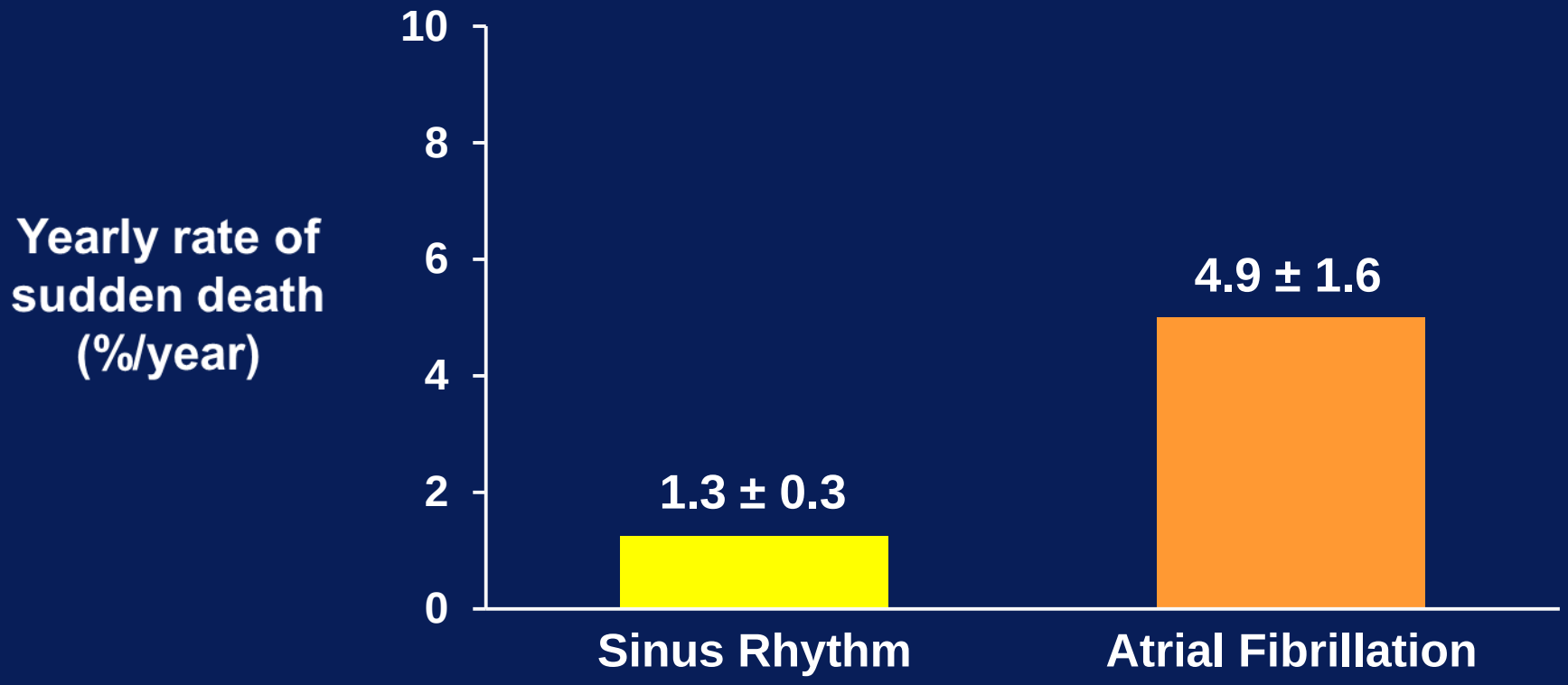
Grigioni F, et al. JACC 1999; 34:2078

Sudden Death in Severe MR Due to Flail Leaflet:
Relation to LVEF



Grigioni F, et al. JACC 1999; 34:2078

Sudden Death in Severe MR Due to Flail Leaflet:
Sinus Rhythm vs. Atrial Fibrillation



Grigioni F, et al. JACC 1999; 34:2078

Sudden Death in Severe MR Due to Flail Mitral Leaflet

In patients NYHA Class I-II, in sinus rhythm, LVEF ≥ 60%, and no history of CAD:

Rate of sudden death = 0.8% / yr

Grigioni F, et al. JACC 1999; 34:2078

If There Are No Randomized Controlled Trials . . .

. . . Perform a Meta - Analysis

Early Surgical Intervention vs. Watchful Waiting for Asymptomatic MR
A Meta-Analysis

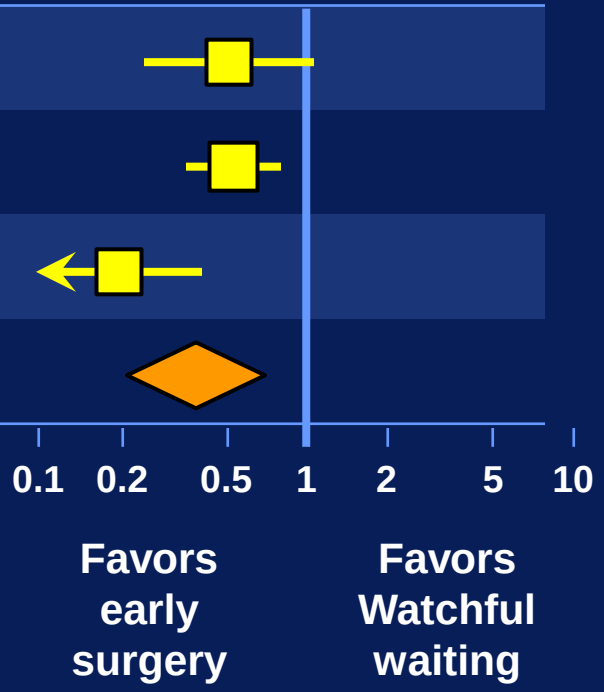
- Observational studies; tertiary referral
- Asymptomatic patients without Class I Guideline triggers for surgery
- All primary (degenerative) MR etiology
- All included a watching waiting cohort

Goldstone AB, et al. Ann Cardiothorac Surg 2015; 4: 220

Timing of Surgical Intervention for Asymptomatic MR (No Class I Trigger)

All Cause Mortality (1,823 Patients)

Study	HR	Lower limit	Upper limit	Z	P
Kang (2014)	0.509	0.241	1.076	-1.769	0.077
Suri (2103)	0.520	0.346	0.781	-3.149	0.002
Montant (2009)	0.190	0.093	0.388	-4.566	0.000
	0.38	0.206	0.708	-3.057	0.002



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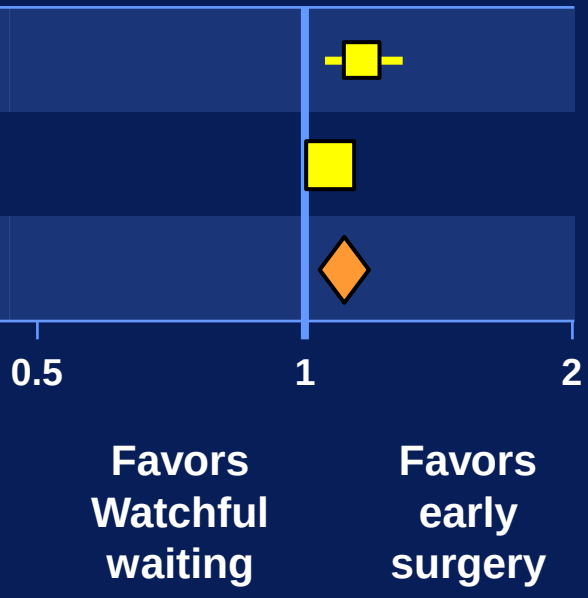
Timing of Surgical Intervention for Asymptomatic MR (No Class I Trigger)

Mitral Repair Rate (1,631 Patients)

Study	HR	Lower limit	Upper limit	Z	P
Kang (2014)	1.155	1.047	1.273	2.879	0.004
Suri (2013)	1.069	1.019	1.122	2.718	0.007
	1.10	1.022	1.179	2.559	0.010



Goldstone AB, et al. Ann Cardiothorac Surg 2015; 4: 220

A Stitch in Time . . .

. . . Saves Nine

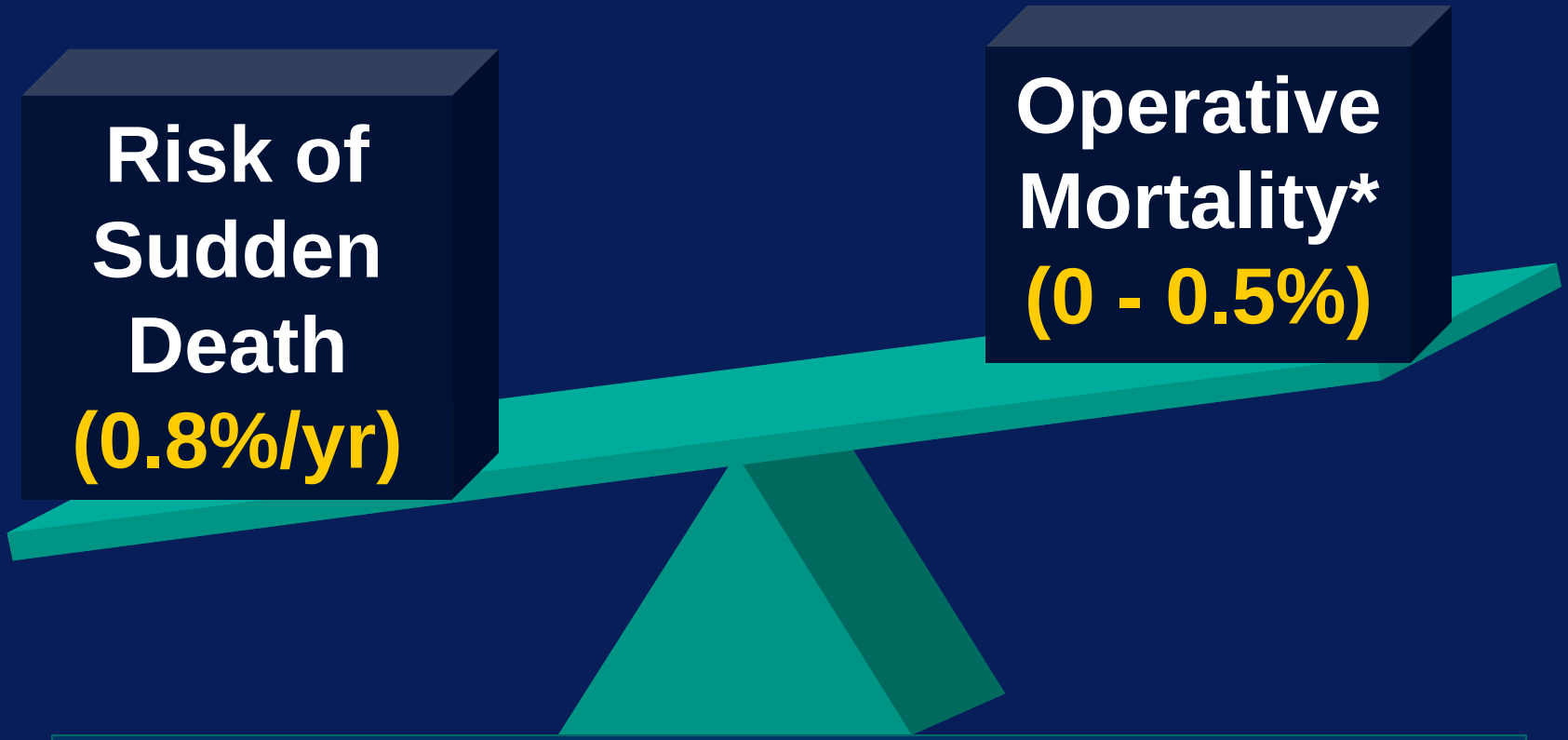
Surgery for MR: The Importance of Experience and Volume

STS Database (13,614 MV operations)

	Hospital Mitral Procedures / Year			
	≤ 35	36-70	71-140	> 140
Operative Mortality	3.1%	2.3%	2.0%	1.1%
MV Repair Rate	48%	55%	65%	78%

Gammie JS, et al. Circulation 2007; 115: 881

Elective Mitral Repair For Severe MR vs. Risk of Sudden Death



* High volume, tertiary referral surgical centers

Grigioni F, et al. JACC 1999; 34:2078

DeBonis M, et al Eur Heart J 2013;34;13

Kang DH et al. Circulation 2009; 119:797

Suri RM et al. JAMA 2013; 310:609

Yazdchi F, et al. Ann Thorac Surg 2015; 99:1992

Are we delaying surgery too long….

. . . with the current guideline triggers to intervention?

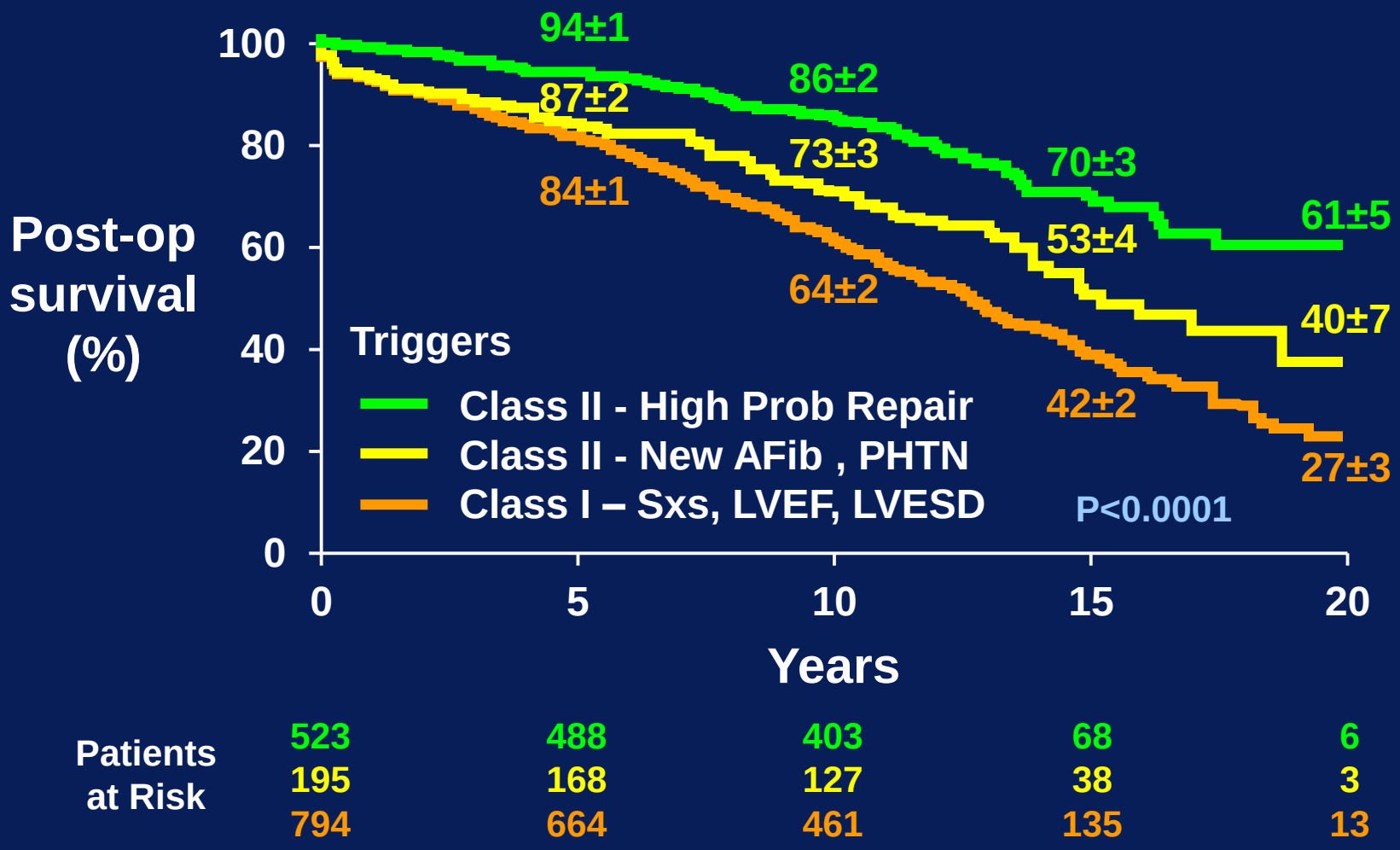
Current (2014) Guideline Indications Triggering Surgery for Severe MR
Is There an Outcome Penalty?

1,512 Patients: Surgery for Primary MR

Class I Triggers:	**Cardiac Symptoms, LVEF < 60%, or LVESD > 40 mm (n = 794)**
Class II Triggers:	**Clinical complications: New AFib, or pulmonary HTN (n = 195)**
Class II Triggers:	**Early Asymptomatic: Gr 4/4 MR, High probability of MV Repair only (n = 523)**

Sarano ME, et al. J Thorac Cardiovasc Surg 2015; 150: 50
Nishimura RA, CM Otto, et al. JACC 2014; 63: e57

Guideline Indication Triggers for Surgery in Severe MR: Impact on Post-Op Survival



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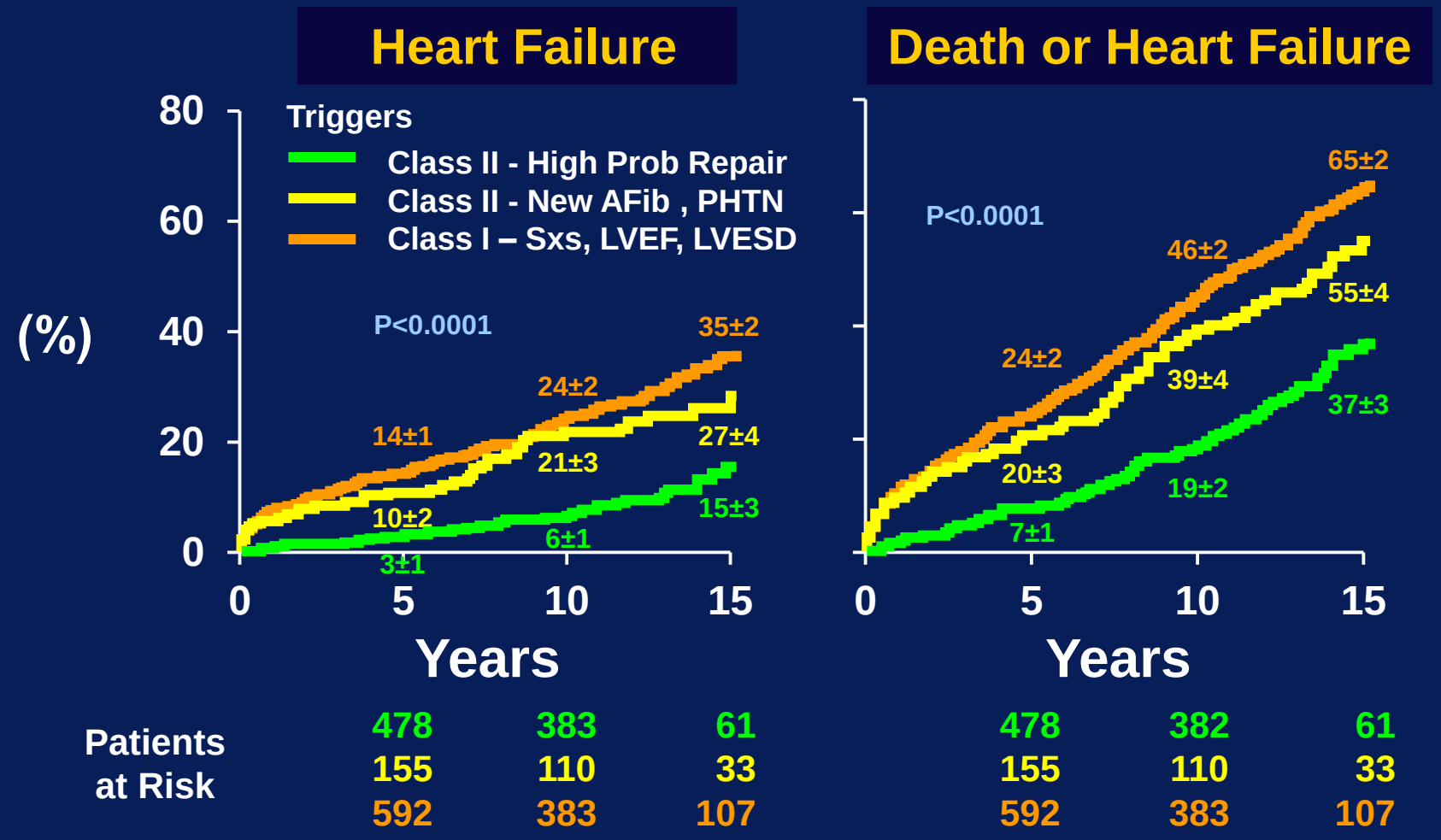
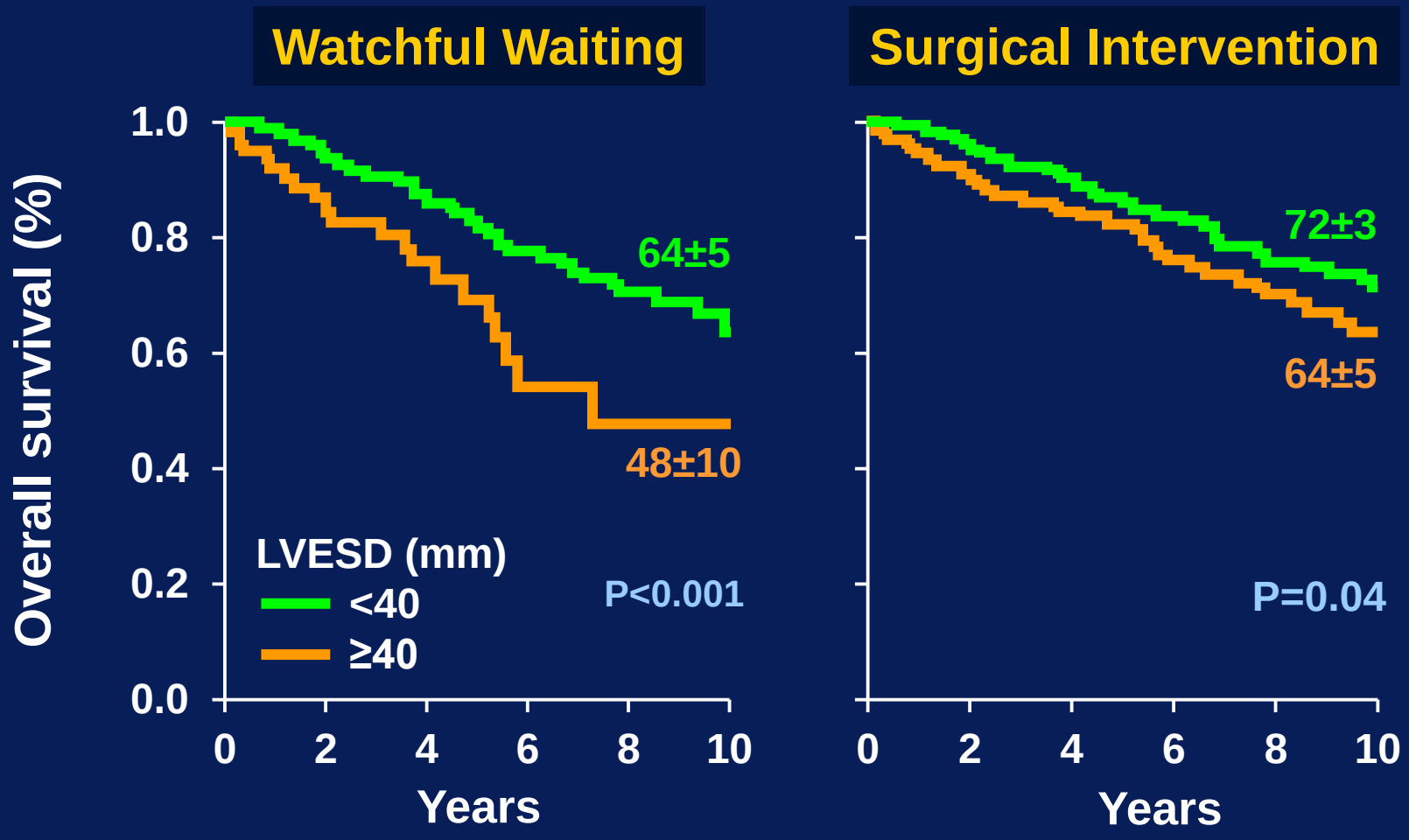
Guideline Indication Triggers for Surgery in Severe MR: Impact on Outcome



Sarano ME, et al. J Thorac Cardiovasc Surg 2015; 150: 50

Left Ventricular End-Systolic Dimension (LVESD) in Severe MR

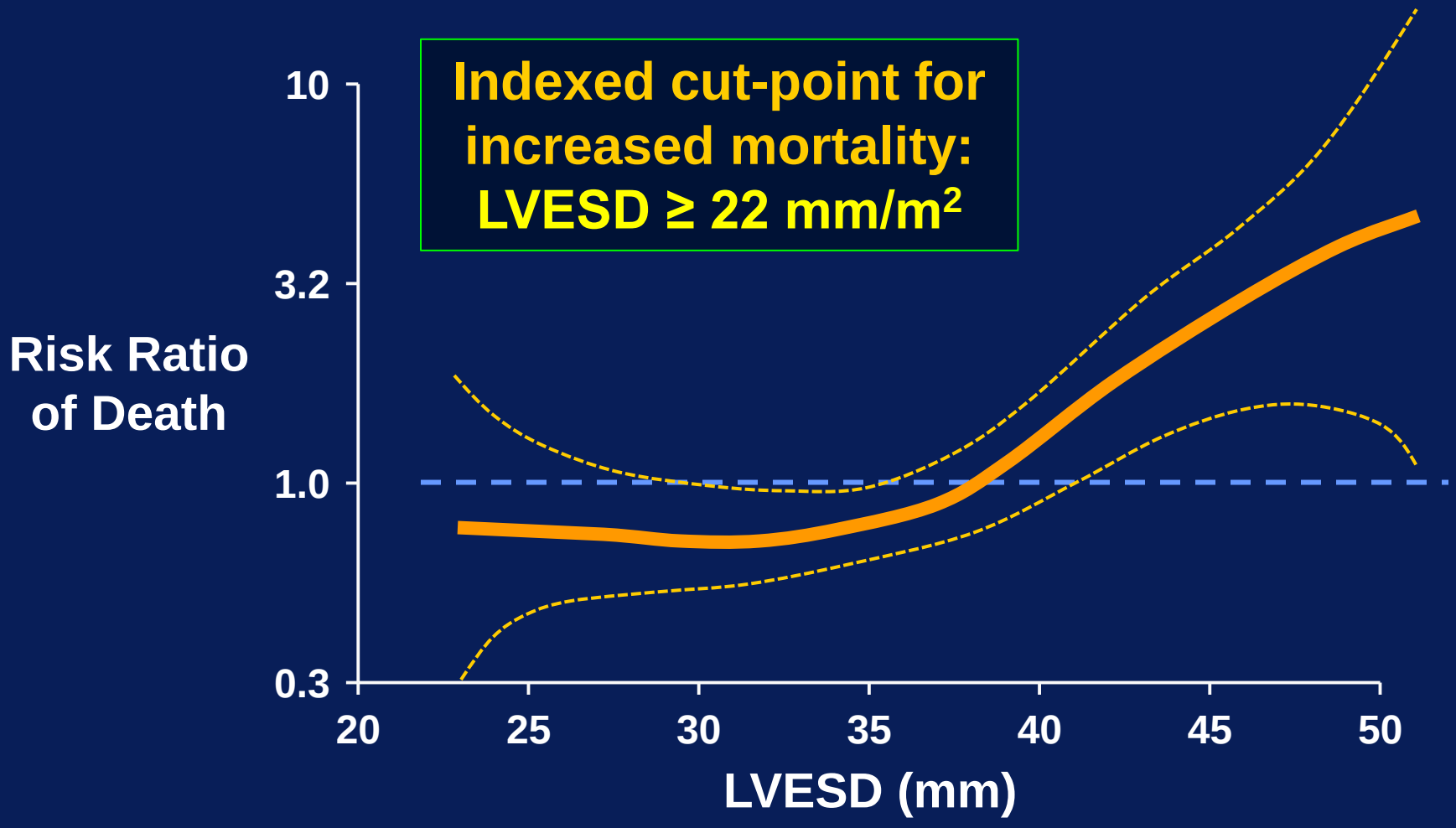
MIDA Database: 739 Patients with Flail Lealflet



Tribouilloy et al: JACC 2009; 54:1961

Left Ventricular End-Systolic Dimension (LVESD) in Severe MR

Risk of Mortality With Watchful Waiting



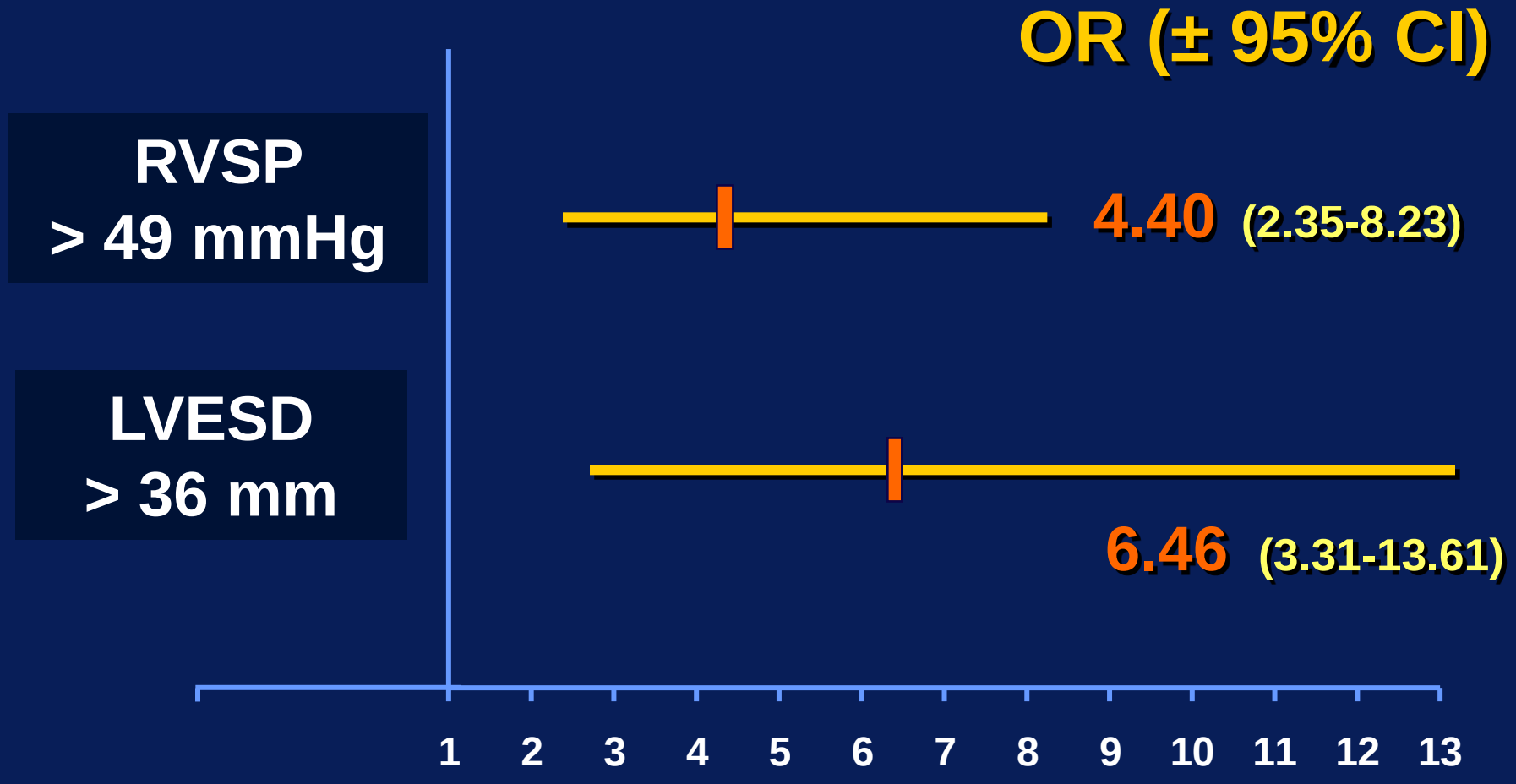
Tribouilloy et al: JACC 2009; 54:1961

Severe MR: The Fallacy of "Normal" Preoperative LV Function

	Post-Op LV Ejection Fraction ≥ 50% (n = 1,391)	Post-Op LV Ejection Fraction < 50% (n = 314)	
LVEF (%)			
Pre-Op	66.8 ± 4.8	65.3 ± 4.0	
Post-Op	59.2 ± 5.8	41.8 ± 6.2	p<0.001
LVESD (mm)			
Pre-Op	34.2 ± 4.6	37.7 ± 4.4	p<0.001
Post-Op	33.4 ± 5.1	41.9 ± 5.4	p<0.001

Quintana E, et al. J Thorac Cardiovasc Surg 2014; 148; 2752

Severe MR: Predictors of Early Postoperative LVEF < 40% *



* Post-Operative Death HR = 1.74 (1.03-2.92)

Quintana E, et al. J Thorac Cardiovasc Surg 2014; 148; 2752

Severe Primary Mitral Regurgitation: The Case for Early Surgical Intervention
Conclusions

- Unoperated severe MR has serious clinical consequences, even if asymptomatic
- Clinical symptom status is often unreliable
- Stress testing discriminates elusive functional status and prognosticates
- Early surgical intervention improves outcome
- Selection of surgical center and surgeon is critical
- Current ACC/AHA guideline triggers to surgery may delay intervention, resulting in suboptimal outcome
- Why wait for the inevitable, and increase patient risk?