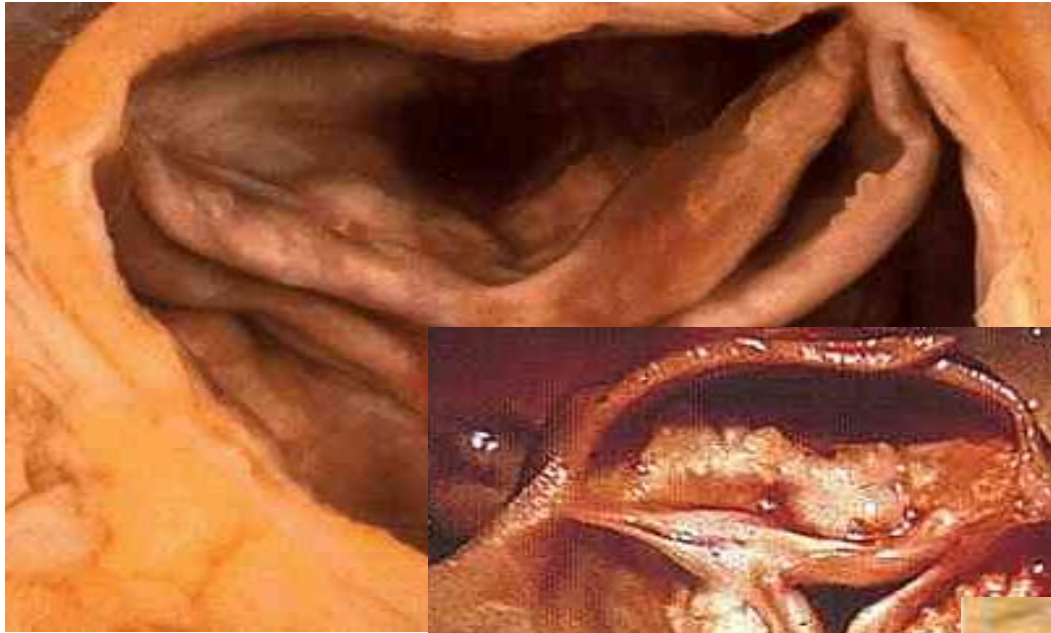


# **Valvular Intervention**

# Outline

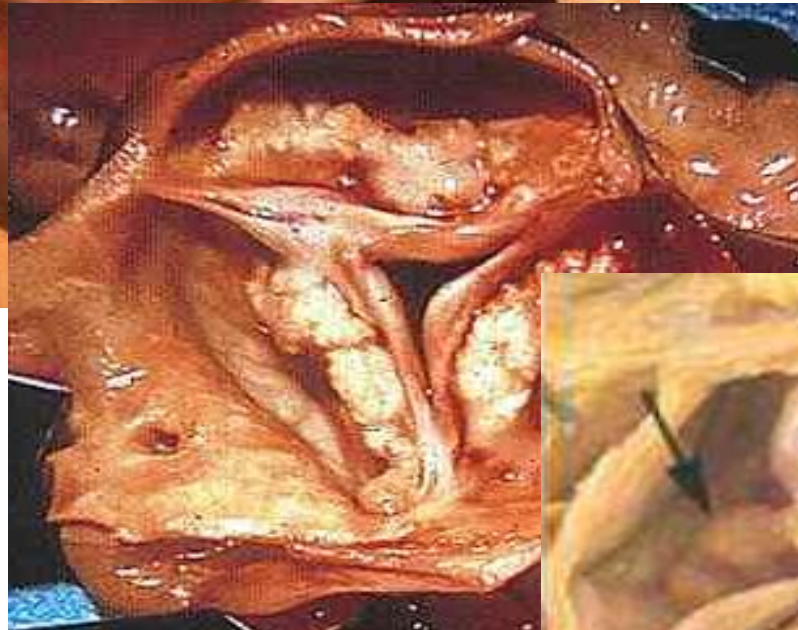
- **Introduction**
- **Aortic Stenosis**
- **Mitral Regurgitation**
- **Conclusion**

# Calcific Aortic Stenosis



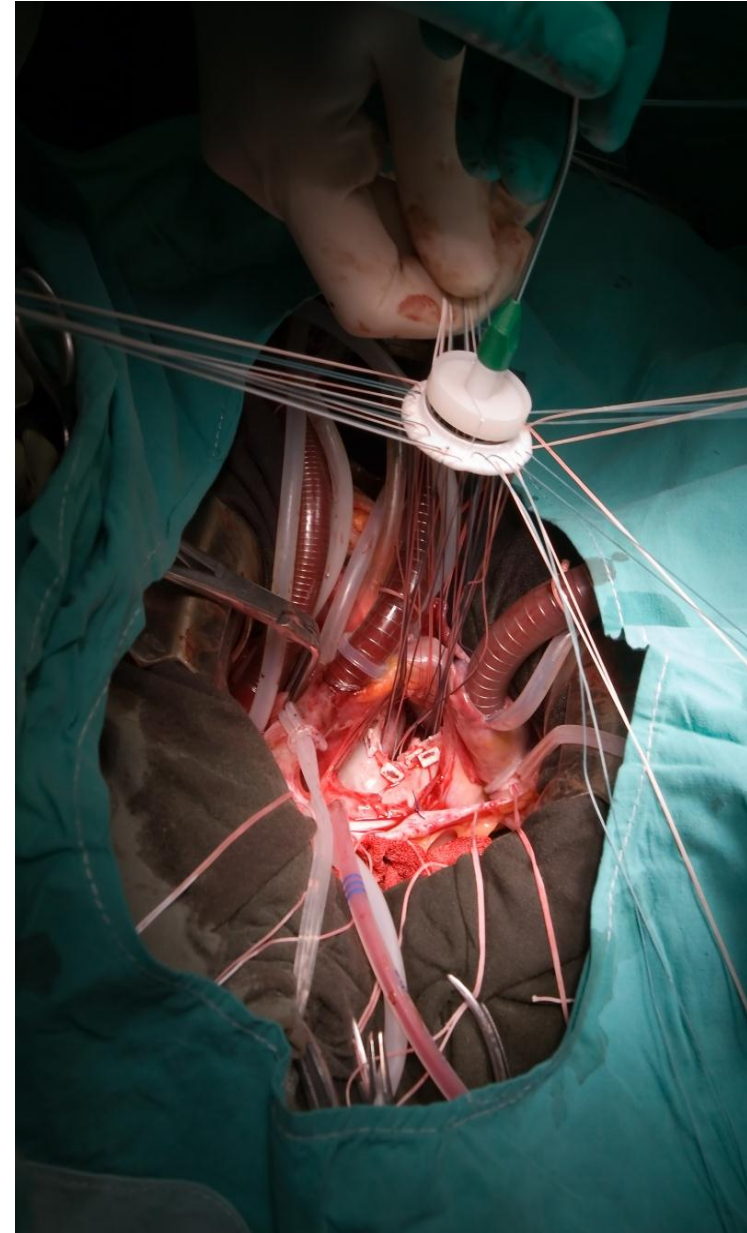
**Deformed  
Eccentric  
Calcified  
Nodular  
Rigid**

**HOSTILE  
TARGET**



- difficult to displace
- prone to fragmentation and embolization

# Aortic Valve Replacement in the Gold Standard For Aortic Stenosis



# Don't Mess With the Guidelines – or the Surgeons

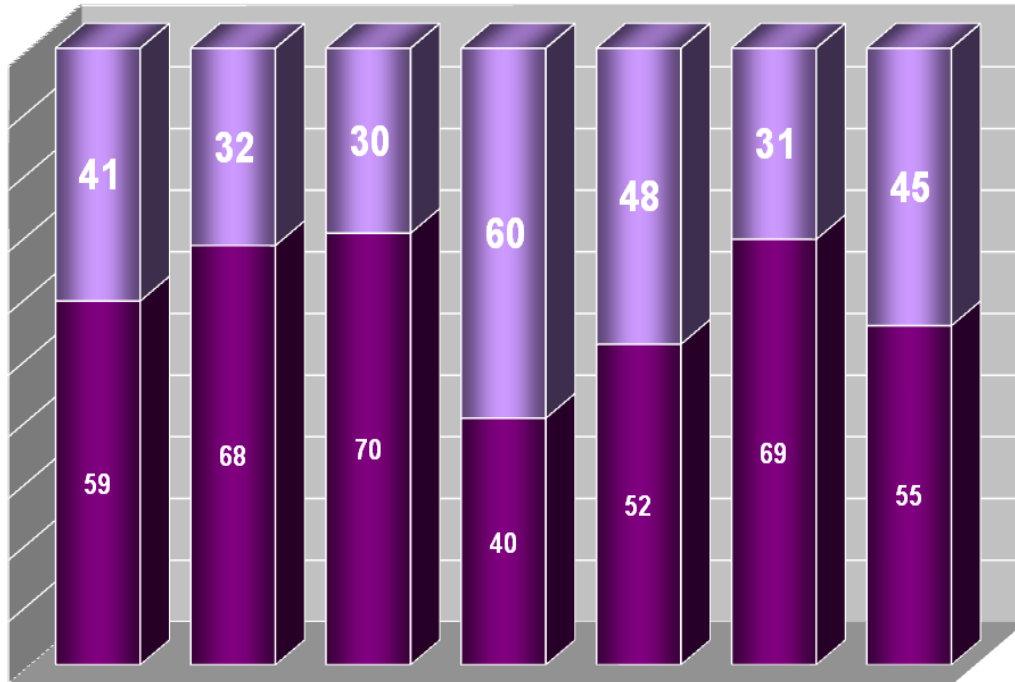


Are all patients with  
symptomatic aortic stenosis  
now being treated with  
definitive surgical aortic valve  
replacement?

# And, 30-60% of AS Patients Go Untreated...

## Severe Symptomatic Aortic Stenosis

Percent of Cardiology Patients Treated



**Under-treatment especially prevalent among patients managed by *Primary Care* physicians**

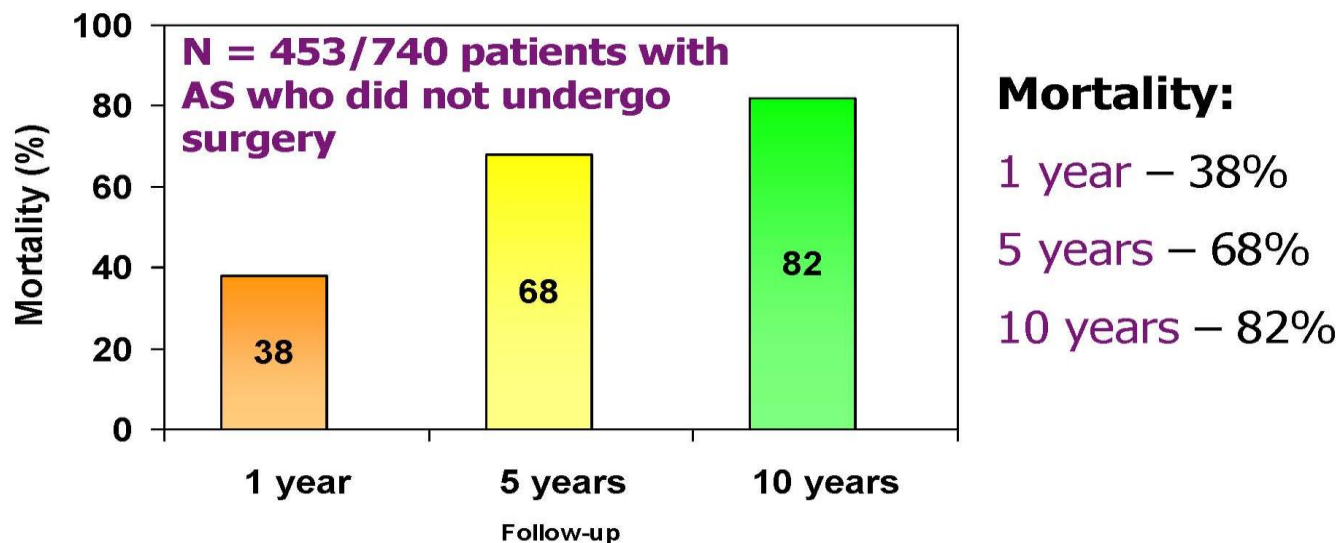


1. Bouma B J et al. Heart 1999;82:143-148
2. Iung B et al European Heart Journal 2003;24:1231-1243 (\*includes both Aortic Stenosis and Mitral Regurgitation patients)
3. Pellikka, Sarano et al Circulation 2005
4. Charlson E et al. J Heart Valve Dis 2006;15:312-321

Source: Patrick Serruys, EuroPCR 2008

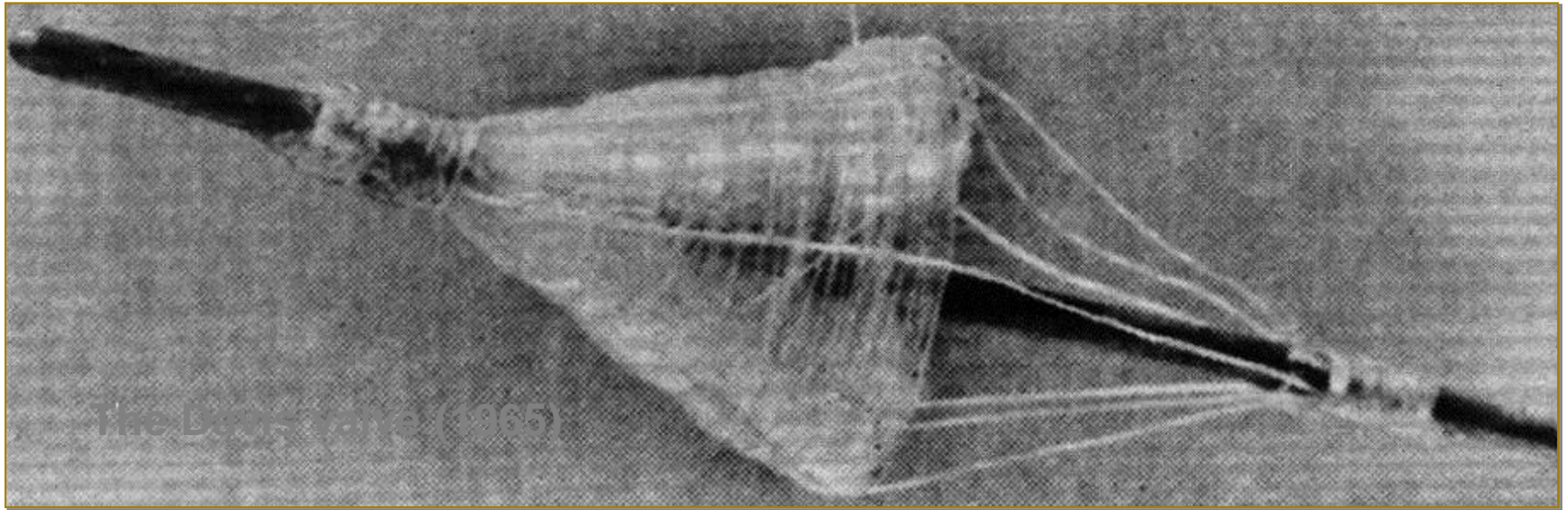
# Untreated, AS Patients Have Poor Prognosis

## Mortality of the Nonsurgically Treated Patients with Severe AS

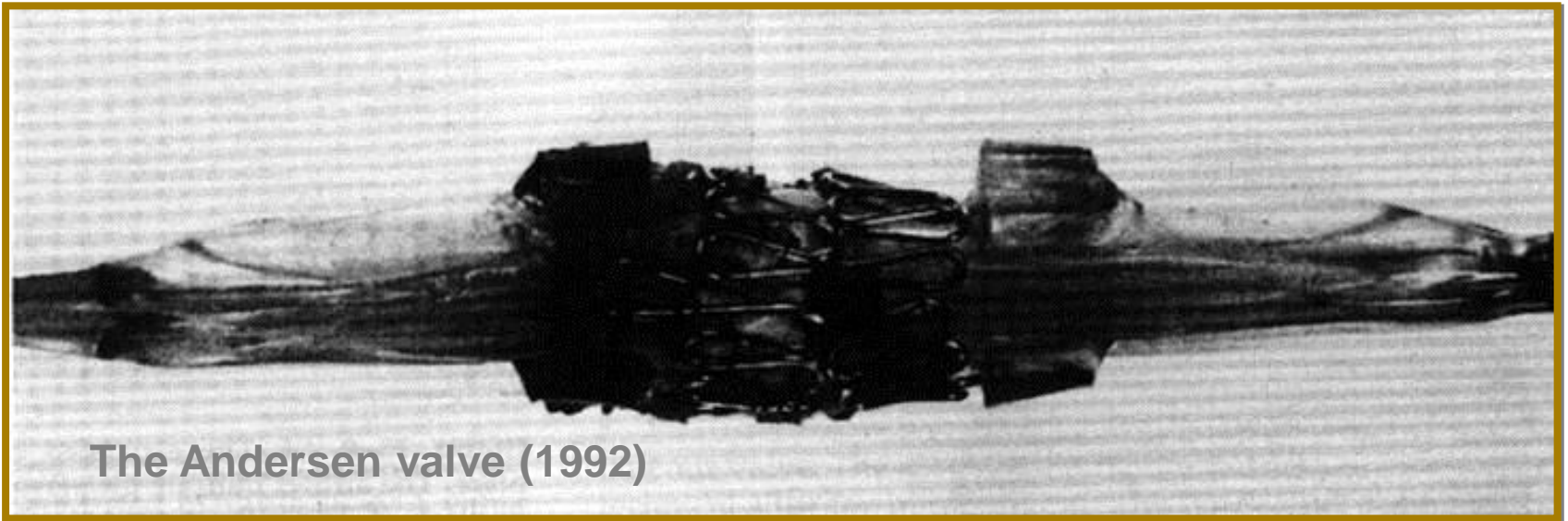


**SAFE TO ASSUME THAT THE PROGNOSIS HAS CHANGED LITTLE FROM THAT OFFERED FROM ROSS AND BRAUNWALD 40 YEARS AGO (Ross J, Braunwald E. Aortic stenosis. Circulation.1968; 38 [Suppl 5]:61-7)**

# Early Catheter-Based AV Designs



The Debus valve (1965)



The Andersen valve (1992)

The clinical development of percutaneous heart valve technology

A position statement of the Society of Thoracic Surgeons (STS), the American Association for Thoracic Surgery (AATS), and the Society for Cardiovascular

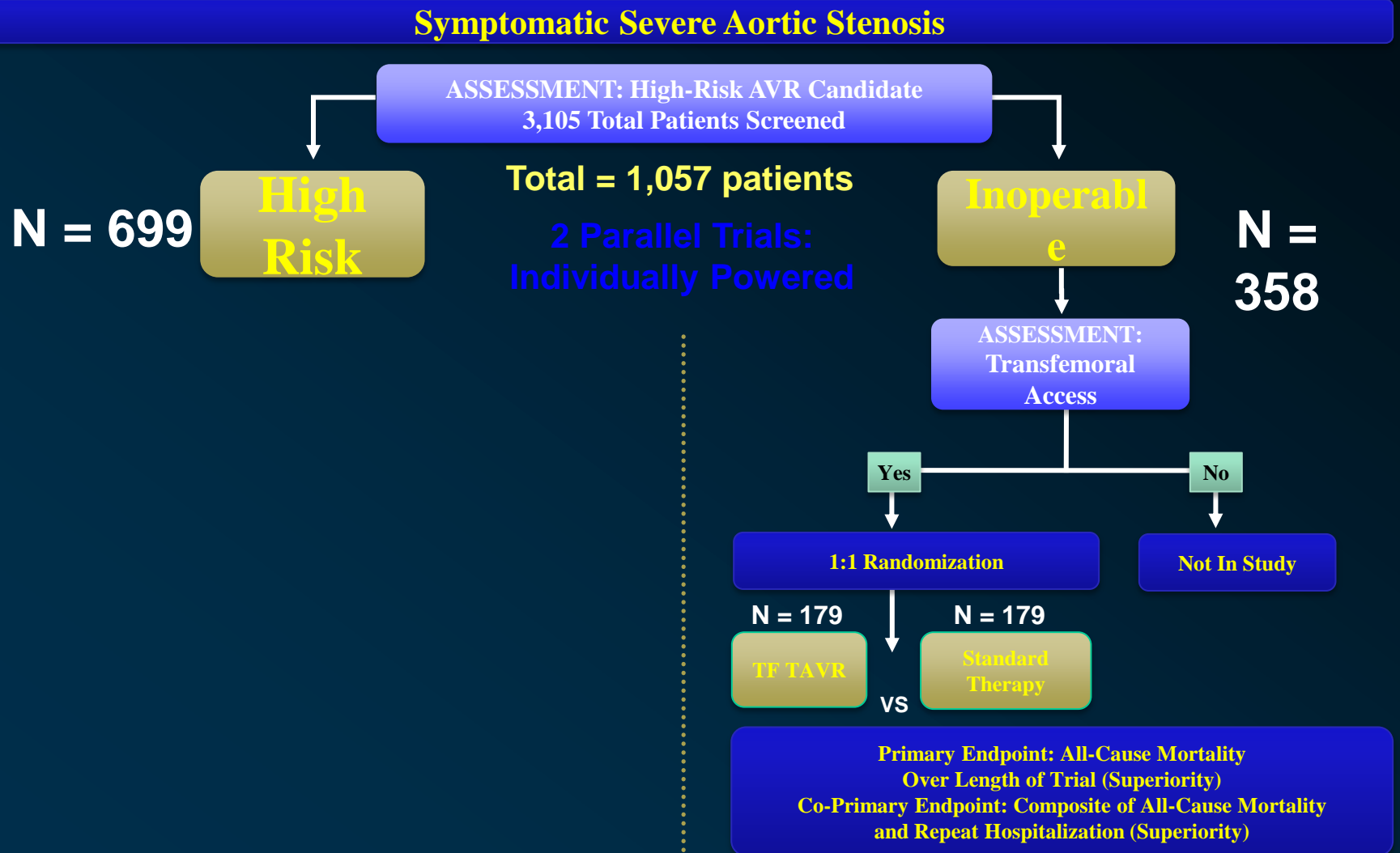
**STS-AATS-SCAI**  
Position

# Collaboration Between Multiple Subspecialties Is In the Best Interest of the Patient

# The Current Cath Lab – Hybrid OR



# PARTNER Study Design



# Inoperable PARTNER Cohort Primary Endpoint: All-Cause Mortality

## *The* NEW ENGLAND JOURNAL *of* MEDICINE

### Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D.,  
Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D.,  
Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D.,  
Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela C. Douglas, M.D.,  
John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D.,  
and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators\*

MONTHS

#### Numbers at Risk

TAVI	179	138	122	67	26
Standard Rx	179	121	83	41	12

# PARTNER Study Design

## Symptomatic Severe Aortic Stenosis

ASSESSMENT: High-Risk AVR Candidate  
3,105 Total Patients Screened

N = 699

**High Risk**

Total = 1,057 patients

2 Parallel Trials:  
Individually Powered

**Inoperable**

N = 358

ASSESSMENT:  
Transfemoral  
Access

Yes

No

**Transfemoral (TF)**

**Transapical (TA)**

1:1 Randomization

1:1 Randomization

N = 244

N = 248

N = 104

N = 103

**TF TAVR**

**AVR**

VS

**TA TAVR**

**AVR**

VS

Primary Endpoint: All-Cause Mortality at 1 yr  
(Non-inferiority)

ASSESSMENT:  
Transfemoral  
Access

Yes

No

1:1 Randomization

Not In Study

N = 179

N = 179

**TF TAVR**

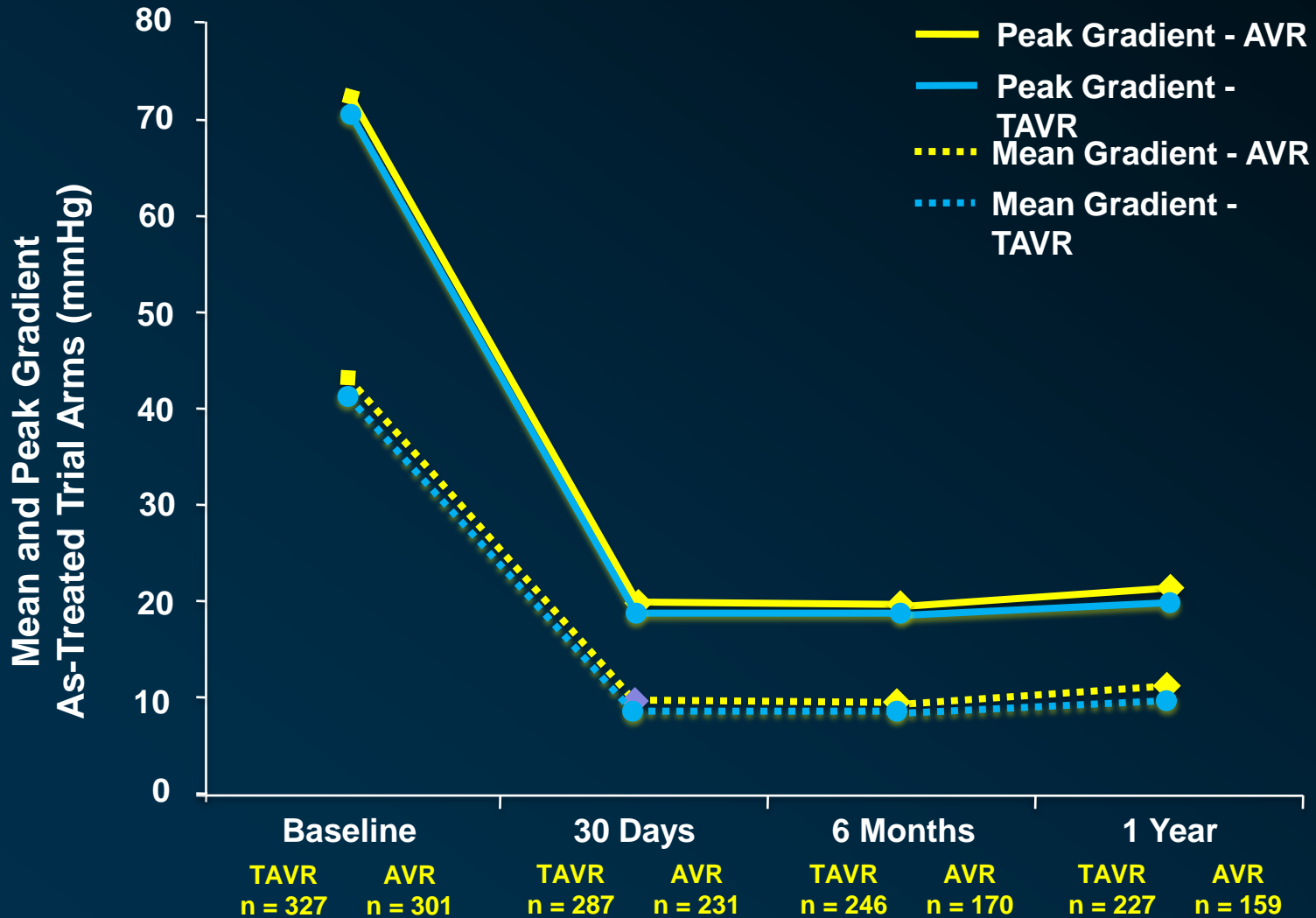
**Standard Therapy**

VS

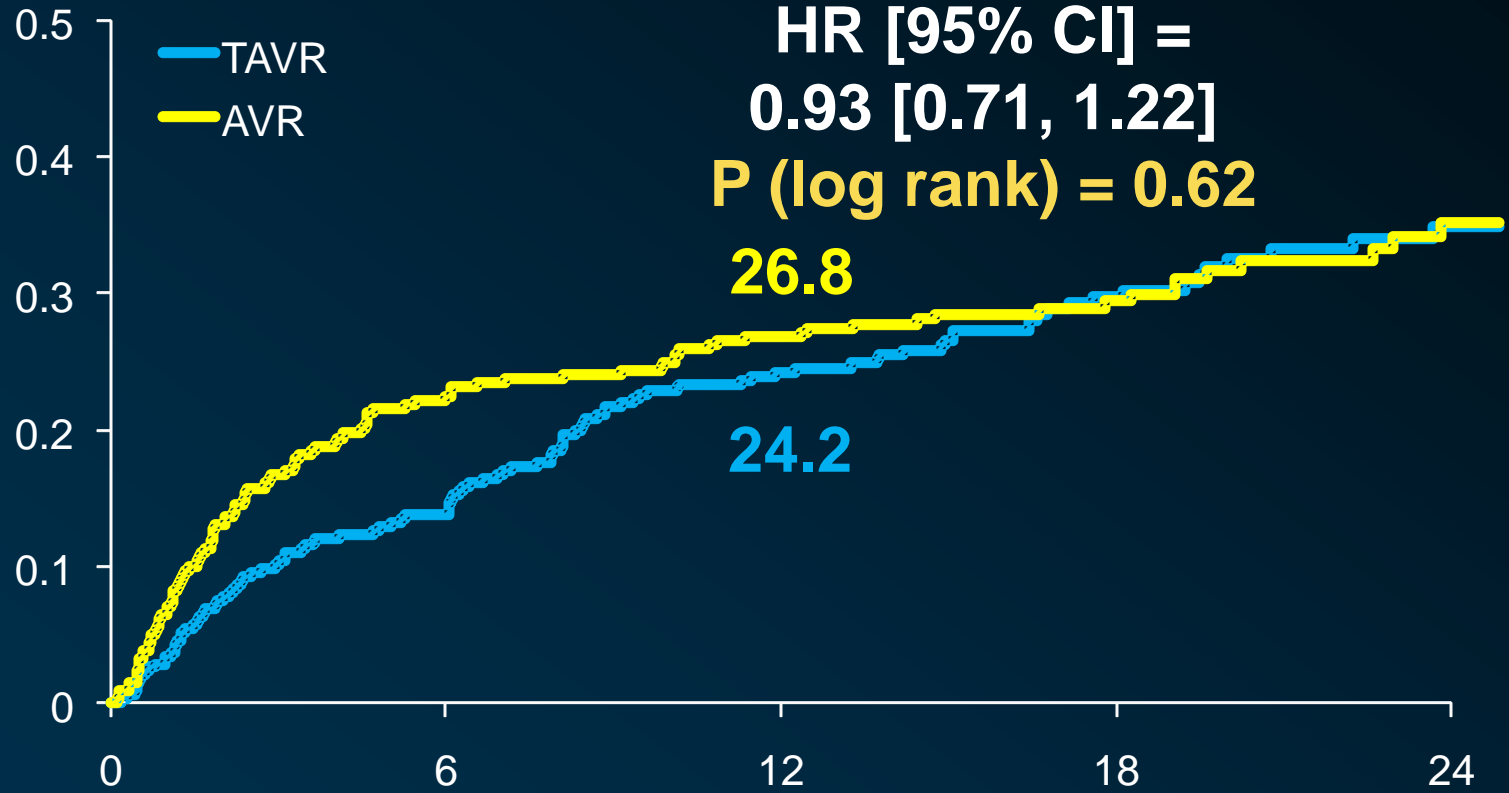
Primary Endpoint: All-Cause Mortality  
Over Length of Trial (Superiority)  
Co-Primary Endpoint: Composite of All-Cause Mortality  
and Repeat Hospitalization (Superiority)

# Echo Findings

## Aortic Valve Gradients



# Primary Endpoint: All-Cause Mortality at 1 Year



	No. at Risk				
	0	6	12	18	24
TAVR	348	298	260	147	67
AVR	351	252	236	139	65

# Mitral Valve Repair

---



*September 1983*

*The Journal of* **THORACIC AND  
CARDIOVASCULAR SURGERY**

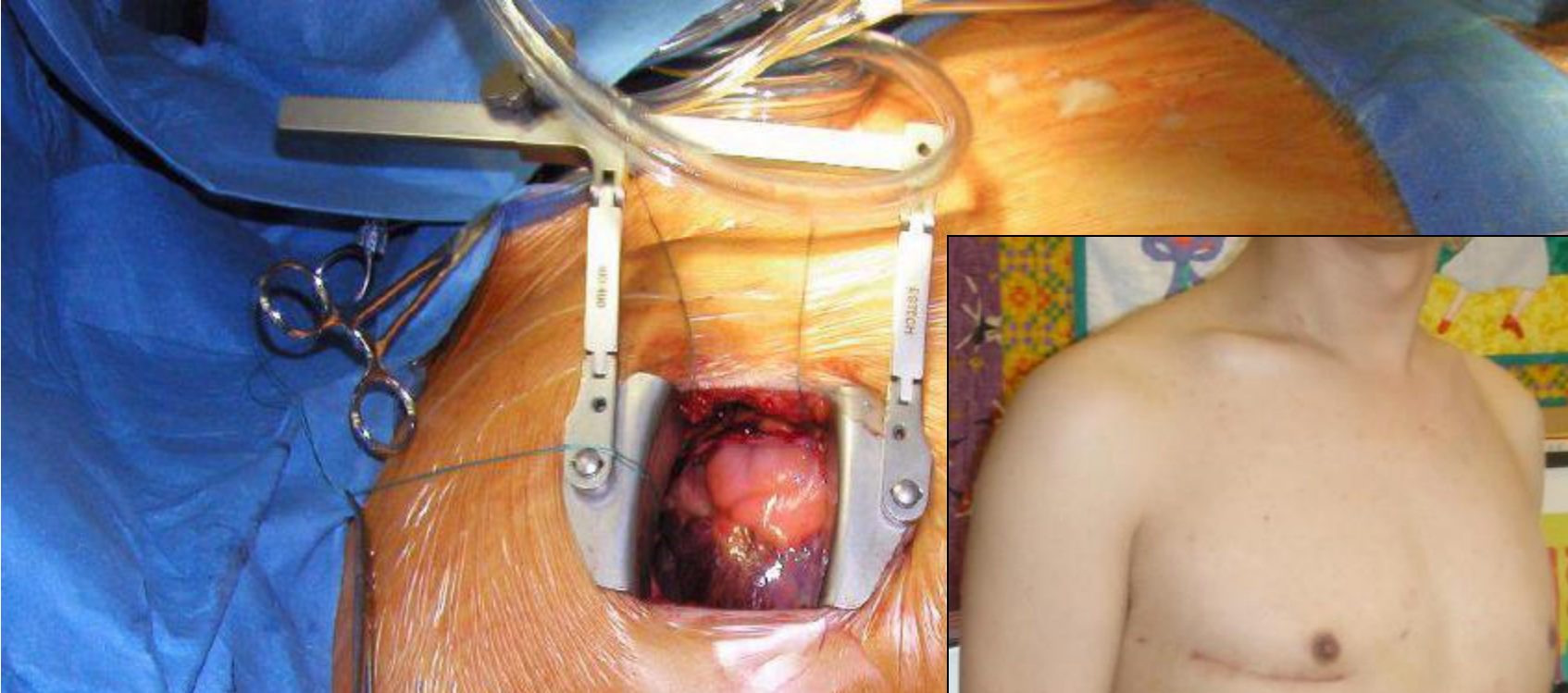
J THORAC CARDIOVASC SURG 86:323-337, 1983

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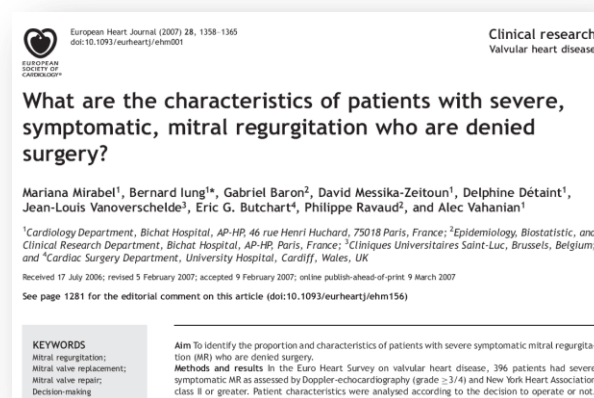
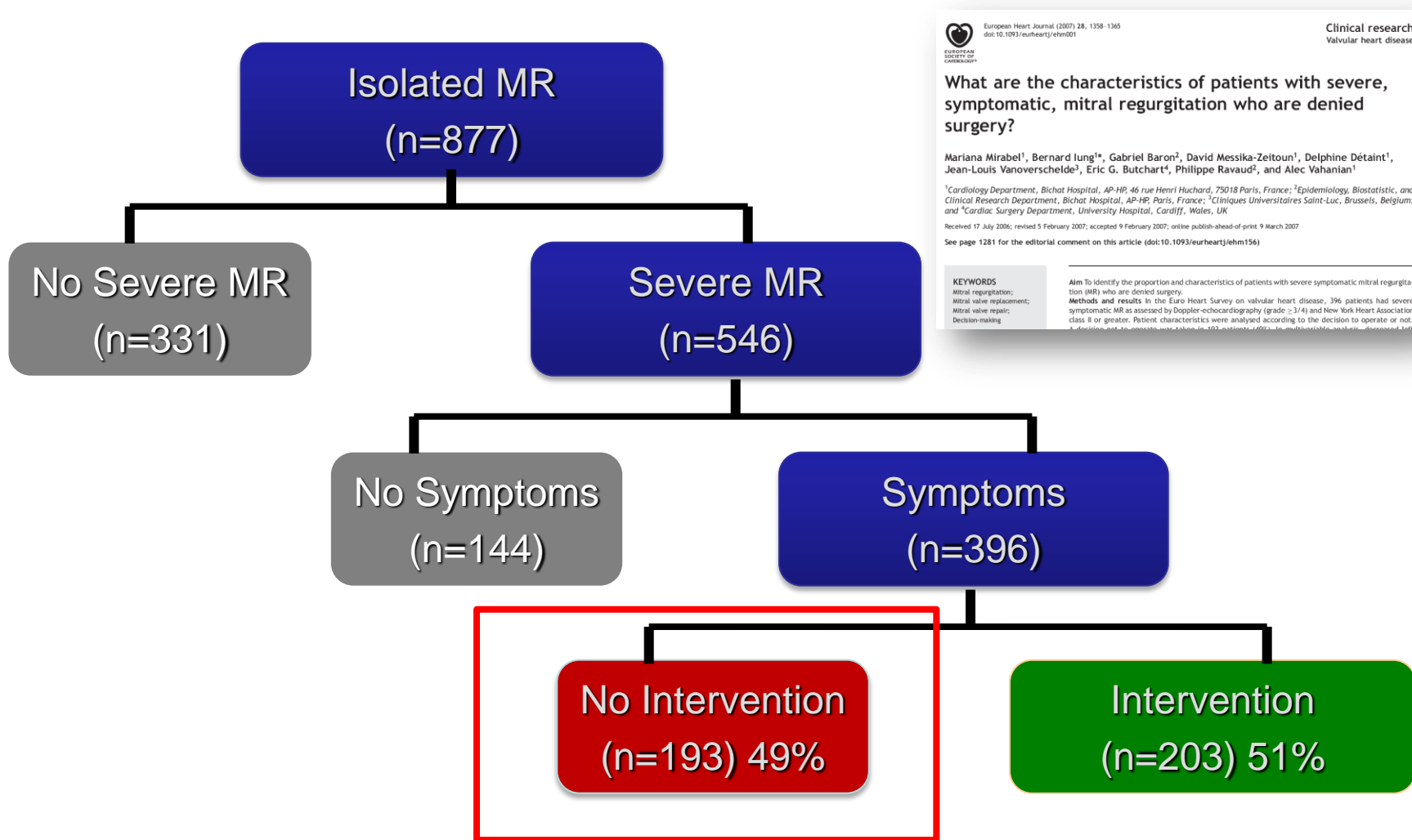
*Honored Guest's Address*

Cardiac valve surgery—the “French correction”

Alain Carpentier, M.D., *Paris, France*

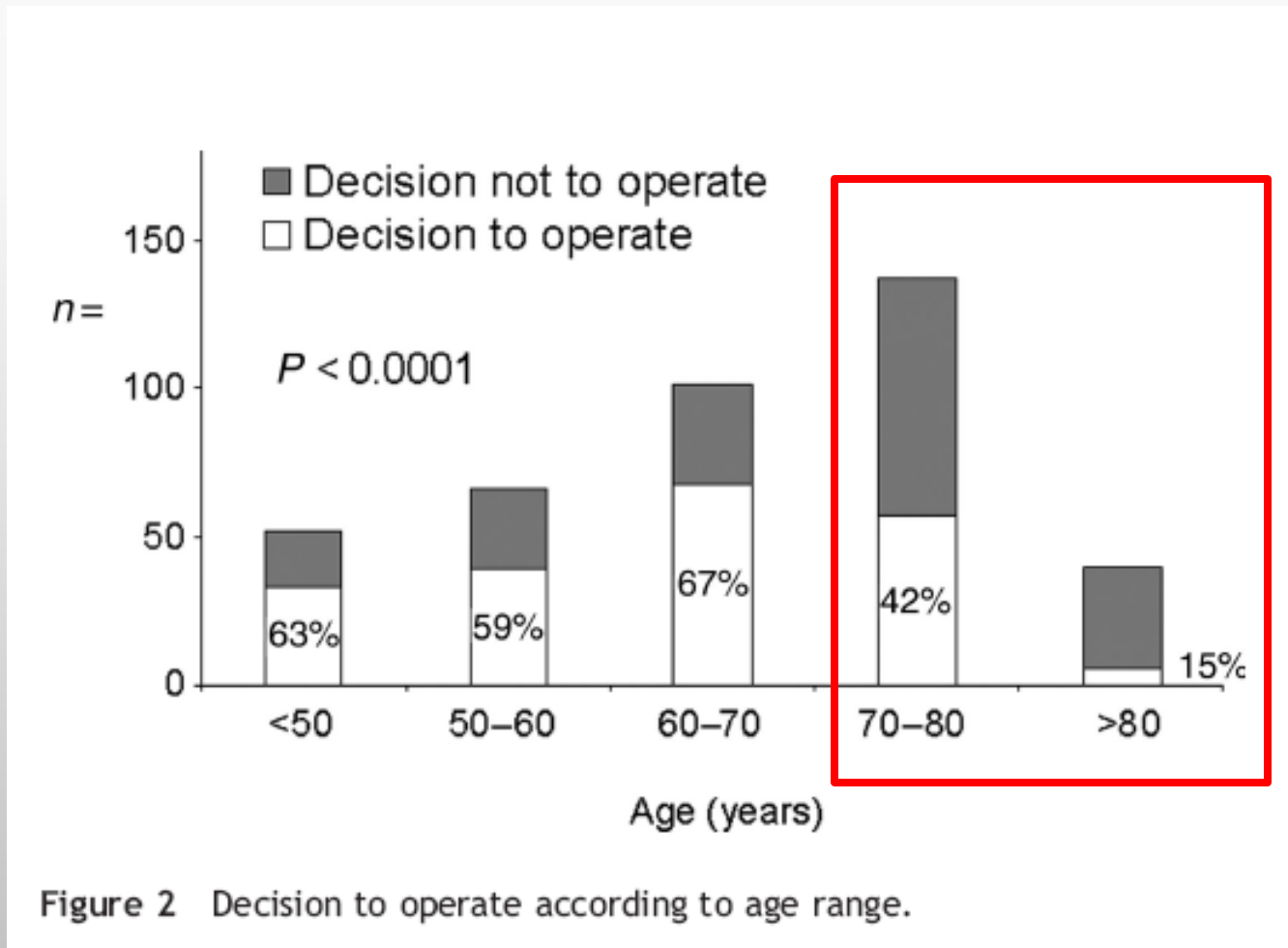


# Euro Heart Survey: Surgery for Functional Mitral Regurgitation Not an Option



# Euro Heart Survey: Surgery is often denied in the older patients

2/3 of symptomatic MR patients >70 are denied surgery

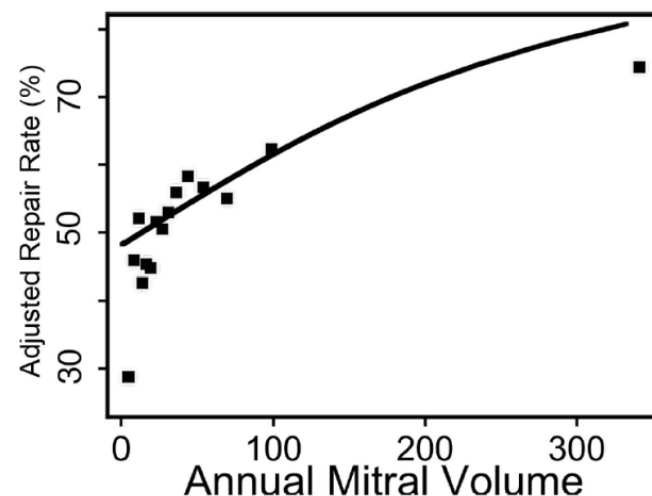


# Surgical Gold Standard

13 614 patients elective surgery for isolate MR - 2000 and 2003 in 575 North American centers participating in the Society of Thoracic Surgeons – Avg Number Mitral Surgeries = 5 in US National Cardiac Database

TABLE 2. Frequency of Adverse Outcomes by Category of Hospital Volume

	Hospital Mitral Volume (Procedures/Year)				P*
	1-35	36-70	71-140	>140	
Operative mortality	3.08	2.31	2.02	1.11	<0.0001
Reoperation	8.19	8.65	8.85	6.59	0.8894
Renal failure	2.85	2.82	1.96	1.90	0.0264
Prolonged mechanical ventilation (>24 h)	7.19	5.98	6.05	4.01	0.0026
Stroke	1.12	1.55	1.41	1.22	0.7434
Mortality plus major morbidity	15.61	15.12	14.30	11.31	0.0364

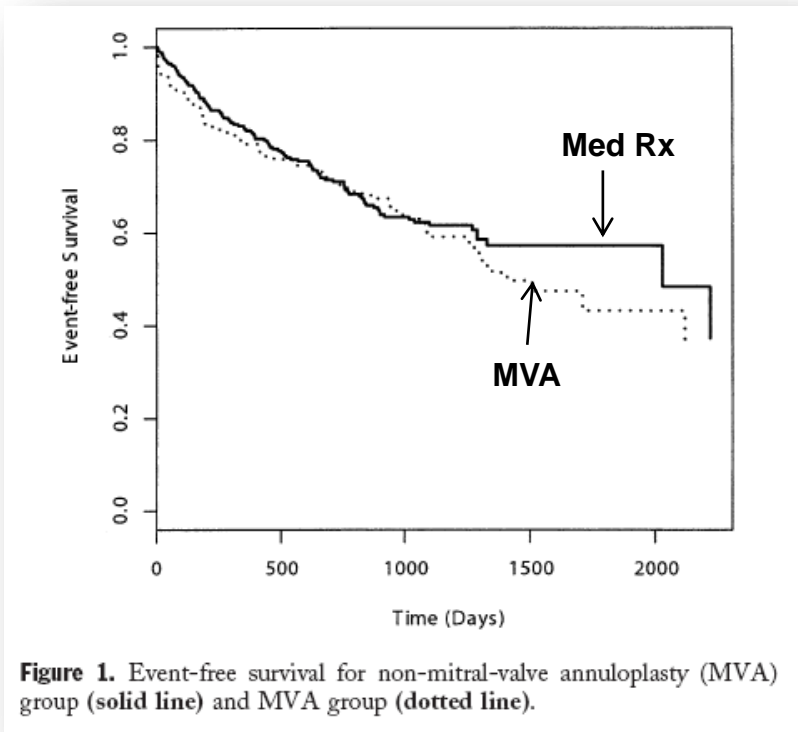


**Gammie JS, et al *Circulation*. 2007;115:881-887.**

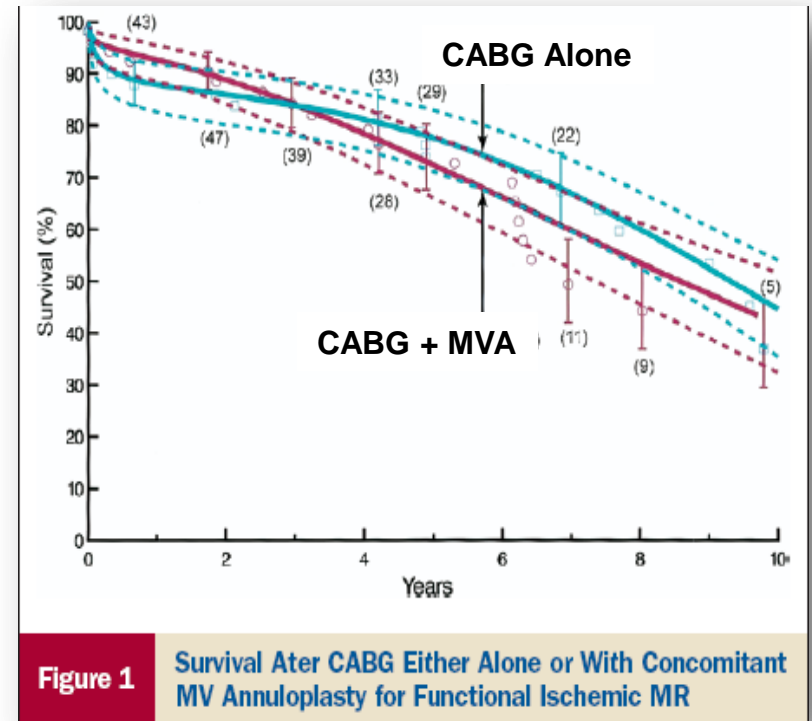
# Survival after undersized MVA

## Surgical vs Medical Rx in DCM-MR

## CABG alone vs CABG+MVA in IMR



Wu A, et al, J Am Coll Cardiol  
2005;45:381-7



Mihalijevic T, et al. J Am Coll  
Cardiol 2007;49:2191-201

# 20-30% 1 year recurrence of MR after annuloplasty in FMR

- Early
  - Insufficient annular reduction
  - Increased tethering
  - Distortion
- Late
  - Ongoing remodeling
  - Insufficient valve reserve
  - Leaflet degeneration

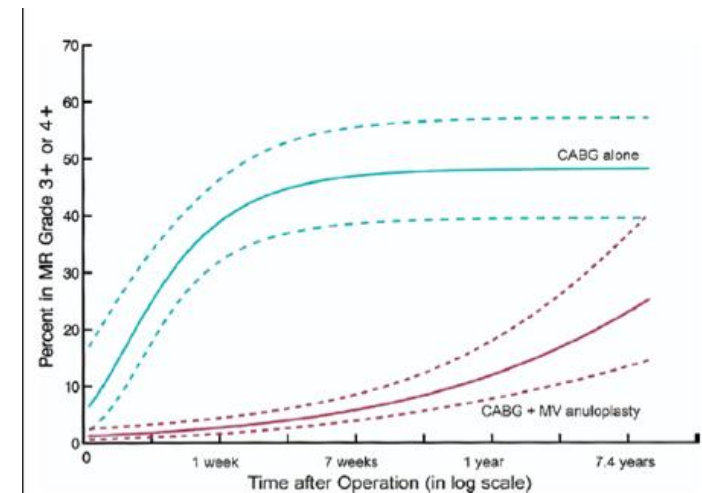
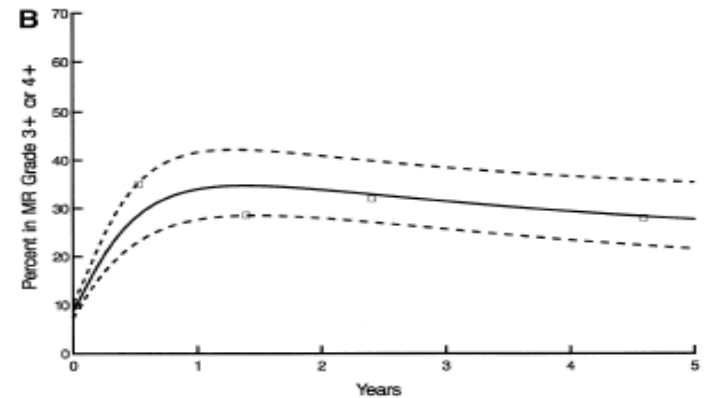


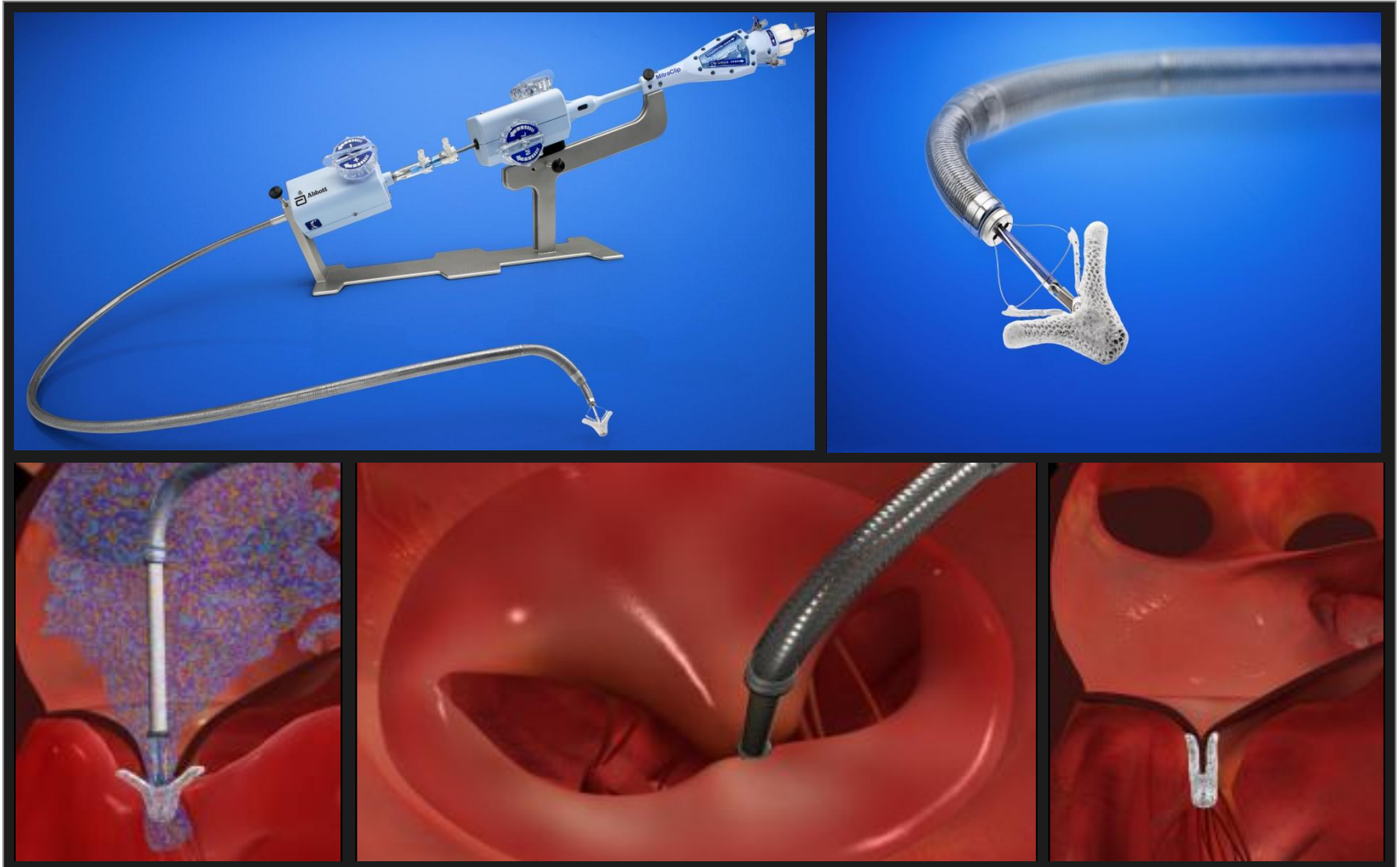
Figure 2 Proportion of Patients in MR Grades 3+ or 4+

McGee, et al, *JTCVS*, 2004;128:916-24

Mihaljevic T et al. *J Am Coll Cardiol* 2007;49:2191-201

# Percutaneous Mitral-Valve Repair

## MitraClip System



*The* NEW ENGLAND  
JOURNAL *of* MEDICINE

Percutaneous Repair or Surgery for Mitral Regurgitation

Ted Feldman, M.D., Elyse Foster, M.D., Donald G. Glower, M.D., Saibal Kar, M.D., Michael J. Rinaldi, M.D., Peter S. Fail, M.D., Richard W. Smalling, M.D., Ph.D., Robert Siegel, M.D., Geoffrey A. Rose, M.D., Eric Engeron, M.D., Catalin Loghin, M.D., Alfredo Trento, M.D., Eric R. Skipper, M.D., Tommy Fudge, M.D., George V. Letsou, M.D., Joseph M. Massaro, Ph.D., and Laura Mauri, M.D., for the EVEREST II Investigators\*

Feldman T, et al. This article (10.1056/NEJMoa1009355) was published on April 4, 2011, at NEJM.org.

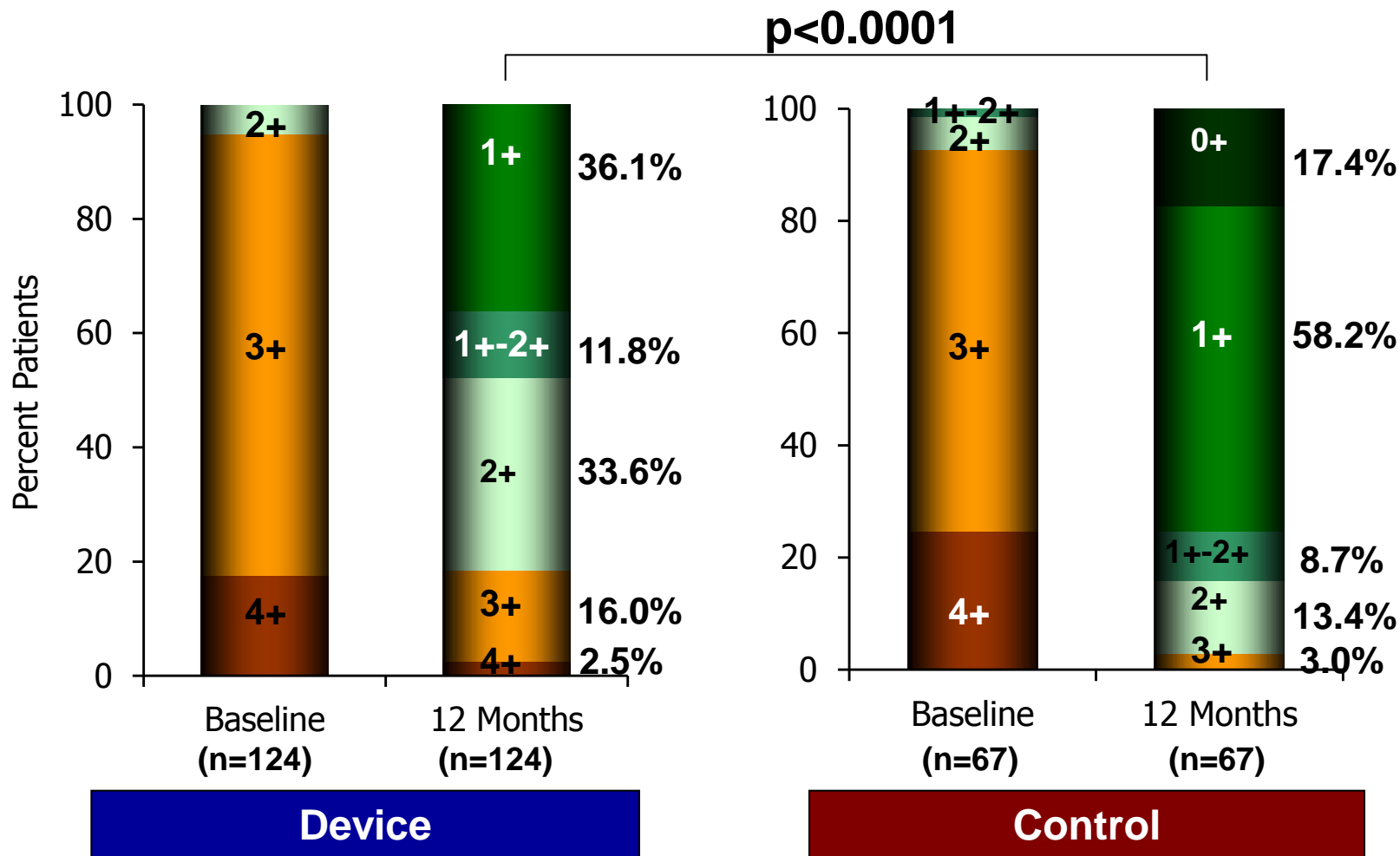
# EVERST II Randomized Trial

- At 12 months freedom from death, mitral valve surgery and 3+/4+ MR were 55% in MitraClip and 73% in the surgical arm respectively (p=0.0007)
- 20% in MitraClip arm and 2.2% in the control group had mitral surgery
- No difference in mortality – 2 years - 11%
- Greater reduction in MR in surgical group (p<0.001)
- Similar improvements in favorable LV remodeling, functional status and QOL

# MR Reduction

Baseline to 12 Months, Per Protocol

*Surgery more often achieves lower degree of residual MR*



**p-value compares the distribution of MR grade in device with the distribution of MR grade in control at 12 months (Fishers' Exact test)**  
*Feldman T, et al. NEJM 2011*

# EVEREST II RCT: Primary Safety Endpoint

## Intention to Treat Strategy

30 Day MAE, non-hierarchical	# Patients experiencing event	
	Device Group (n=180)	Control Group (n=94)
Death	2 (1.1%)	2 (2.1%)
Major Stroke	2 (1.1%)	2 (2.1%)
Re-operation of Mitral Valve	0	1 (1.1%)
Urgent / Emergent CV Surgery	4 (2.2%)	4 (4.3%)
Myocardial Infarction	0	0
Renal Failure	1 (0.6%)	0
Deep Wound Infection	0	0
Ventilation >48 hrs	0	4 (4.3%)
New Onset Permanent Atrial Fib	2 (1.1%)	0
Septicemia	0	0
GI Complication Requiring Surgery		
Transfusions $\geq 2$ units		
TOTAL % of Patients with MAE		

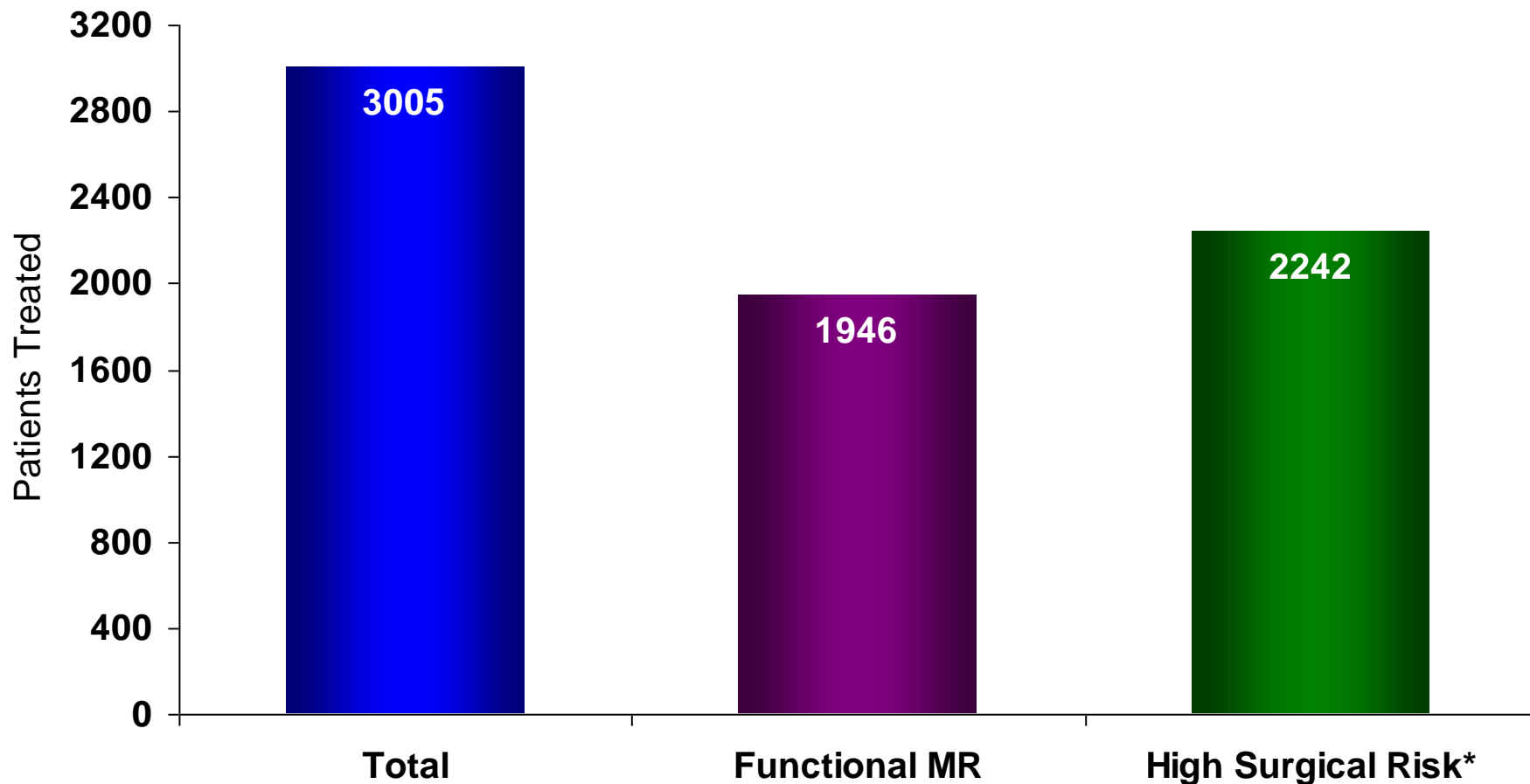
**Exclude Transfusions:  
5% vs 10% (p=0.23)**

$p_{sup} < 0.0001$ ; 2% margin  
(95% CI 20.7%, 45%)



# MitraClip Therapy

## Worldwide Clinical Experience: Total Patients



Estimates of worldwide clinical experience as of March 31, 2011

\* High Surgical Risk estimate based on: logistic EuroSCORE  $\geq$  20%; or STS calculated or surgeon estimated mortality  $\geq$  12% or pre-specified co-morbidities

# Functional MR Patients Treated with the MitraClip Device in Clinical Studies Worldwide

EVEREST Clinical Trials	
EVEREST I	9
EVEREST II Roll-in	19
EVEREST II Randomized	48
EVEREST II High Risk*	46
REALISM	360
European Experience	
ACCESS-EU Registry	400
<b>TOTAL FMR Patients</b>	<b>882</b>

**N=122  
Presented**

\* High risk defined by predicted surgical mortality  $\geq 12\%$  using STS risk calculator or surgeon estimate (based on pre-specified comorbidities)

# EVEREST Functional MR, Treated Patients

Patient Demographics	Patients N=122
NYHA Functional Class III/IV	78%
MR Severity: 3+ to 4+	95%
Mean Ejection Fraction (%)	48.2 ± 10.2
Mean LVIDs (cm)	4.5 ± 0.9

# 30 Day Major Adverse Events

EVEREST Functional MR, Treated Patients

30 Day MAE	Patients Experiencing Event N=122 # (%)
Death	4 (3.3%)
Major Stroke	1 (0.8%)
Re-operation of Mitral-Valve	0
Urgent / Emergent CV Surgery	2 (1.6%)
Myocardial Infarction	2 (1.6%)
Renal Failure	3 (2.5%)
Deep Wound Infection	0
Ventilation >48 hrs	2 (1.6%)
New Onset Permanent Atrial Fib	1 (0.8%)
Septicemia	0
GI Complication Requiring Surgery	0
Transfusions $\geq$ 2 Units	20 (16.4%)
<b>Total</b>	<b>21.3%</b>
<b>Total Excluding Transfusions</b>	<b>8.2%</b>

# 30 Day MAE Stratified by Risk Status

EVEREST Functional MR, Treated Patients

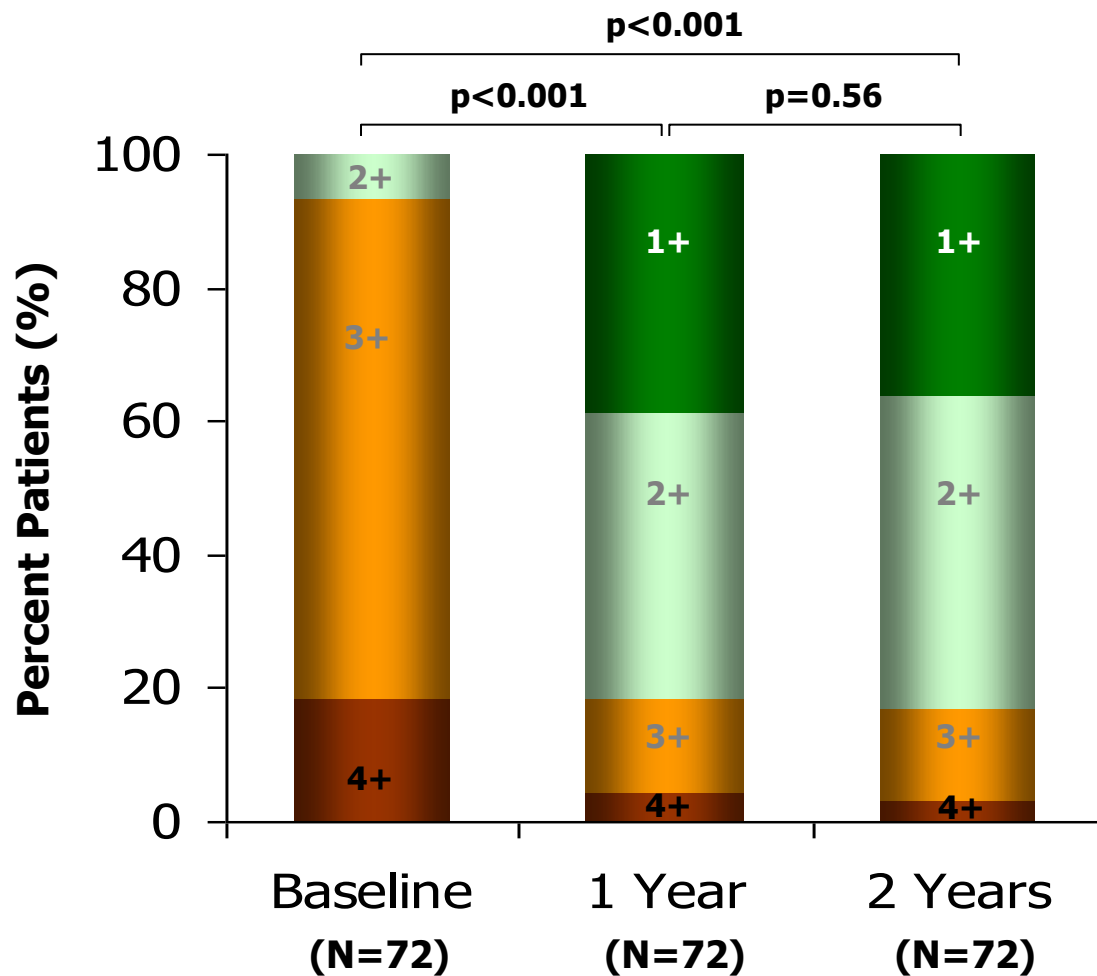
30 Day MAE	Non-High Risk	High Risk*
	FMR Patients N=76 # (%)	FMR Patients N=46 # (%)
Death	0	4 (8.7%)
Major Stroke	0	1 (2.2%)
Re-operation of Mitral-Valve	0	0
Urgent / Emergent CV Surgery	2 (2.6%)	0
Myocardial Infarction	0	2 (4.3%)
Renal Failure	1 (1.3%)	2 (4.3%)
Deep Wound Infection	0	0
Ventilation >48 hrs	0	2 (4.3%)
New Onset Permanent Atrial Fib	1 (1.3%)	0
Septicemia	0	0
GI Complication Requiring Surgery	0	0
Transfusions ≥ 2 Units	12 (15.8%)	8 (17.4%)
<b>Total</b>	<b>17.1%</b>	<b>28.3%</b>
<b>Total Excluding Transfusions</b>	<b>3.9%</b>	<b>15.2%</b>

\* 17% predicted surgical operative mortality rate, based on STS calculator or surgeon estimate

# Mitral Regurgitation Grade

Baseline, 1 and 2 Years (matched)

EVEREST Functional MR, Treated Patients



# Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION



**Mitral Repair versus Replacement for Ischemic Mitral Regurgitation:  
Comparison of Short-Term and Long-Term Survival**

Julien Magne, Nicolas Girerd, Mario Sénéchal, Patrick Mathieu, François Dagenais,  
Jean G. Dumesnil, Éric Charbonneau, Pierre Voisine and Philippe Pibarot

*Circulation* 2009;120:S104-S111

DOI: 10.1161/CIRCULATIONAHA.108.843995

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX  
72514

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ISSN: 1524-4539

**Conclusion**—As opposed to what has been reported in patients with organic MR, the results of this study suggest that MVRp is not superior to MVR with regard to operative and overall mortality in patients with ischemic MR. These findings provide support for the realization of a randomized trial comparing these 2 treatment modalities. (***Circulation*. 2009;120[suppl 1]:S104–S111.**)