

Percutaneous Repair for MR:

Follow-up and longer term outcomes

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Disclosure Information

The following relationships exist:

Grant support: Abbott, Atritech, BSC,
Edwards, St Jude, WL Gore
Consultant: Abbott, BSC, Coherex, Edwards, Intervale,
Diiachi Sankyo-Lilly, WL Gore
Speaker: Boston Scientific

*Off label use of products and investigational devices
will be discussed in this presentation*

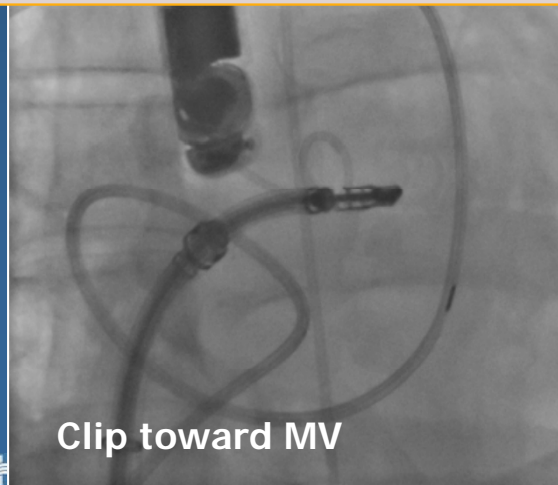
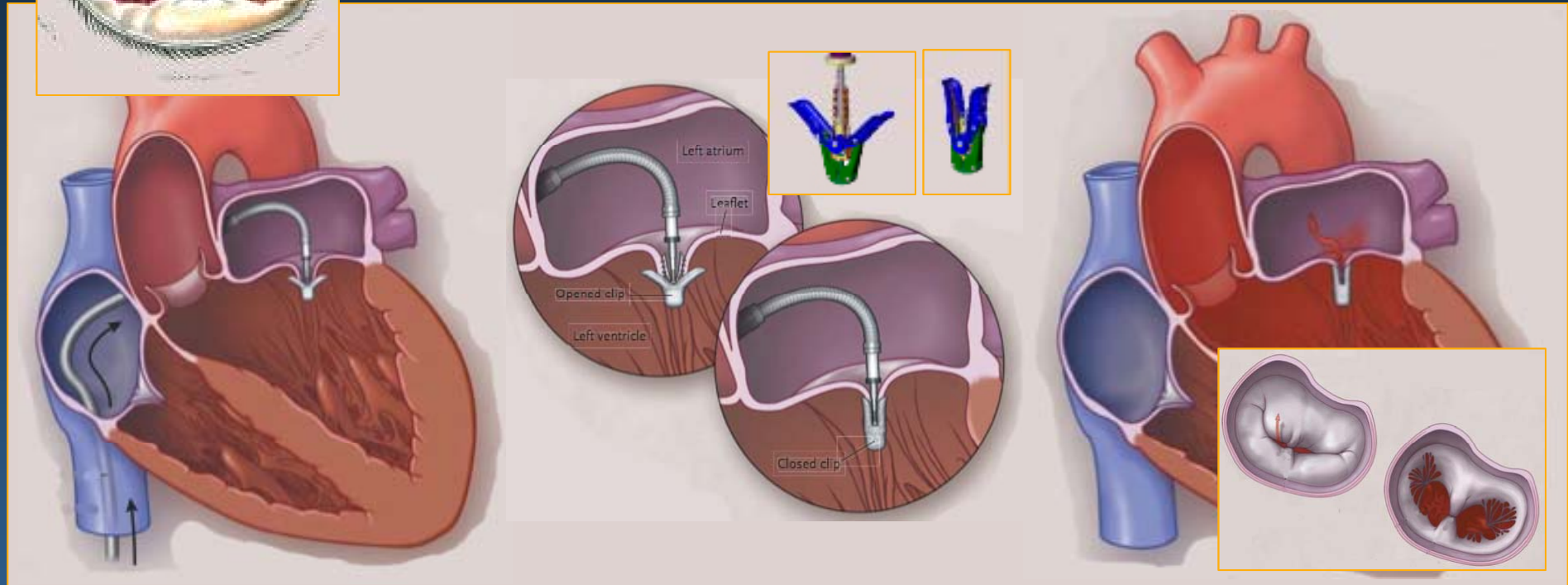
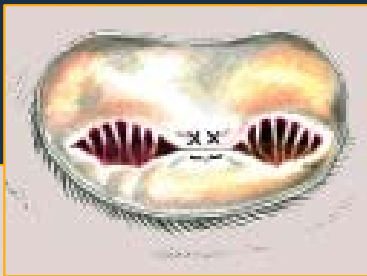
Clinical Experience

Study	Population	n
EVEREST I (Feasibility)*	Non-randomized	55
EVEREST II*	Pre-randomization	60
EVEREST II	High Risk Registry	78
EVEREST II (Pivotal)	Randomized patients (2:1 MitraClip to Surgery)	279 184 MitraClip 95 Surgery
REALISM (Continued Access)	High Risk & Non High Risk	561
European Experience		2,082
Total		3,200 MitraClip

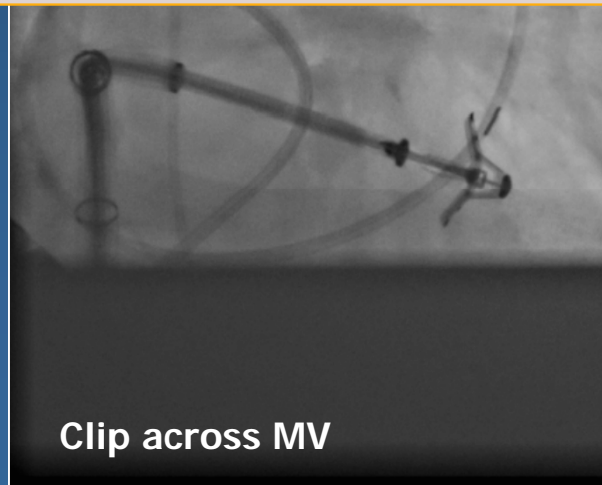
*Percutaneous Mitral Valve Repair Using the Edge-to-Edge Repair: Six months Results of the EVEREST Phase I Clinical trial, JACC 2005;46:2134-2140.
Percutaneous Mitral Repair with the MitraClip System: Safety and Midterm Durability in the Initial EVEREST Cohort, JACC 2009; 54:686-694.

Catheter-Based Mitral Valve Repair

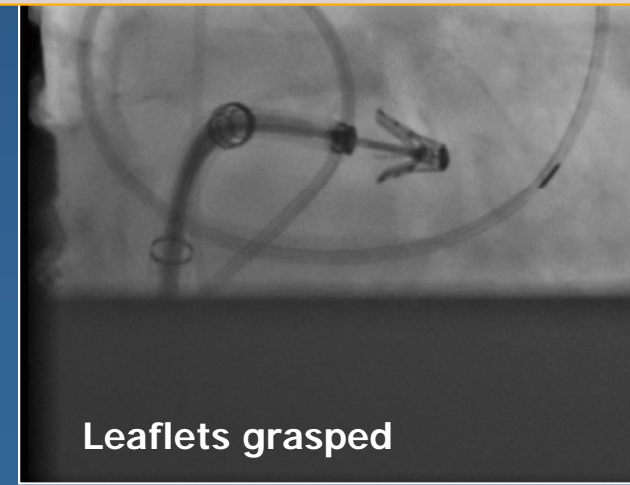
MitraClip System



Clip toward MV



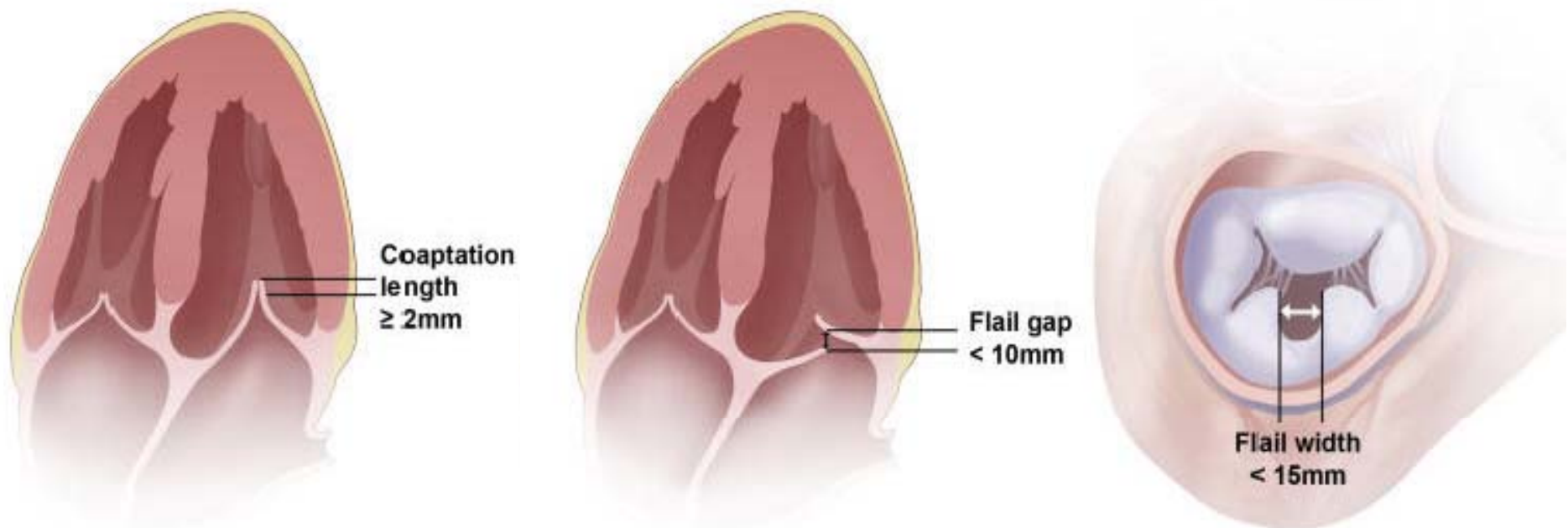
Clip across MV



Leaflets grasped

Anatomic Eligibility

Leaflet mal-coaptation resulting in MR



Non-rheumatic/endocarditic valve morphology; LVIDs $\leq 55\text{mm}$; MVA $\geq 4\text{cm}^2$

Feldman T, Kar S, Rinaldi M, Fail P, Hermiller J, Smalling R, Whitlow PL, Gray W, Low R, Herrmann HC, Lim S, Foster E, Glower D
Percutaneous Mitral Repair with the MitraClip System: Safety and Midterm Durability in the Initial EVEREST Cohort

J Am Coll Cardiol 54:686-694, 2009

EVEREST II Randomized Trial

KEY INCLUSION/EXCLUSION CRITERIA

Moderate-to-severe or severe (3 or 4+) MR

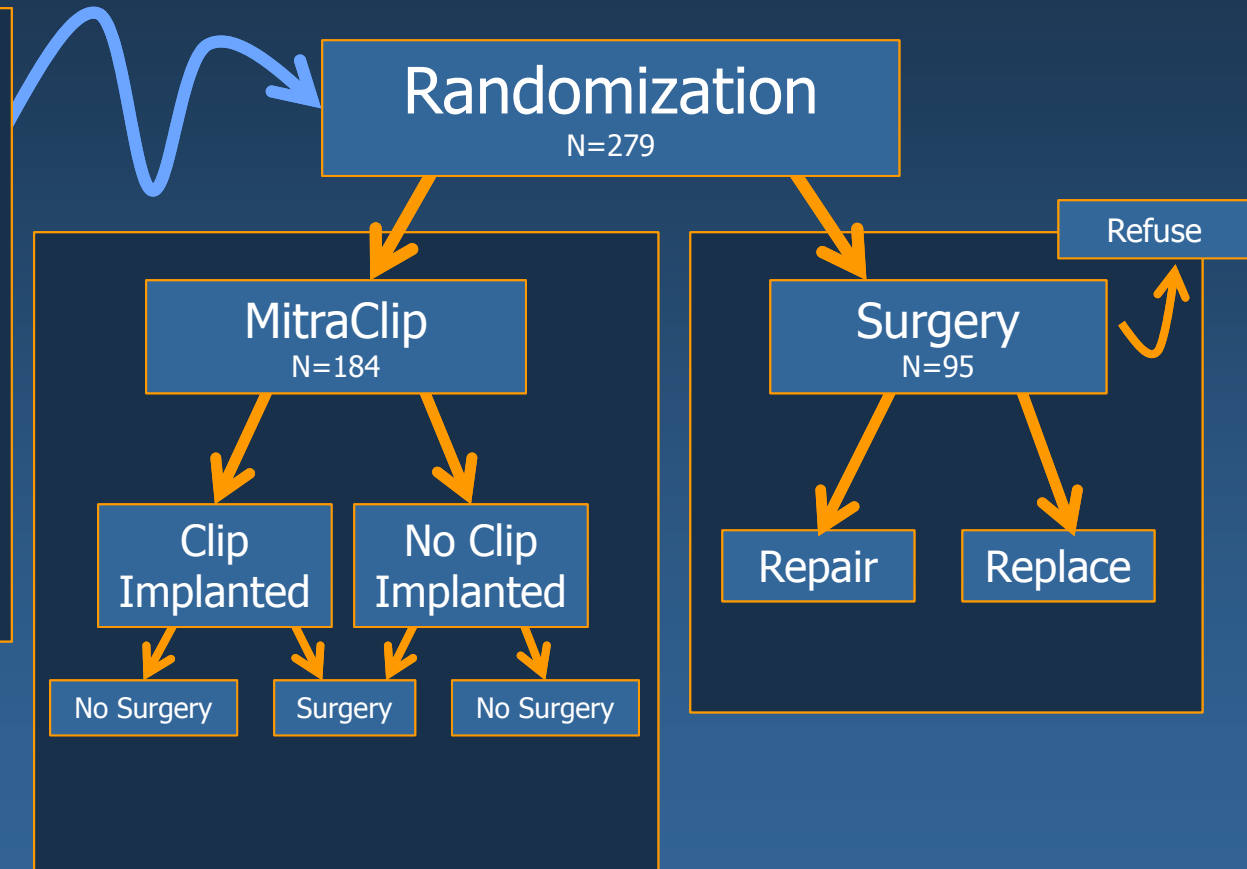
Symptomatic

Asymptomatic

LVEF < 60%

LVEDD > 40mm

ACC/AHA Guidelines
Circ. 114;450,2006



EVEREST II Randomized Clinical Trial

Demographic Comparison

	EVEREST II RCT n=279	2008 STS Database		Isolated 1 st Elective Operation for MR* High Volume Hospitals (>140/Yr)
		Repair	Replace	
Age yrs (mean)	68	60	61	59
≥65 yrs	58%	37%	45%	n/a
≥75 yrs	32%	n/a	n/a	0%
NYHA Class III or IV	50%	26%	45%	n/a
CHF	86%	41%	58%	n/a
Hypertension	75%	60%	67%	43%
Diabetes Mellitus	9%	13%	23%	6.5%
COPD / Chronic Lung Disease	15%	17%	29%	n/a
EF (mean)	60%	53%	55%	56%

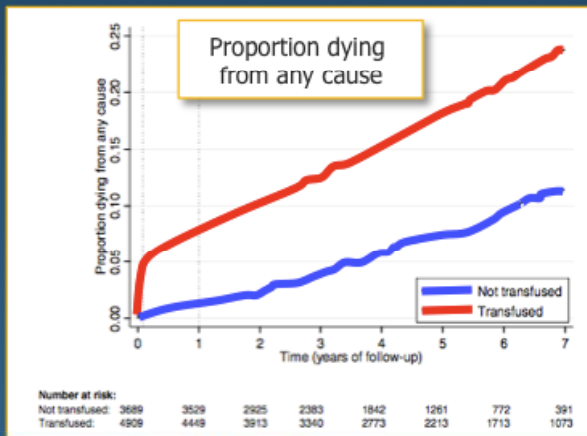
*Gammie JS et al Influence of Hospital Procedural Volume on Care Process and Mortality for Patients Undergoing Elective Surgery for Mitral Regurgitation. Circ 2007;115:881-887.

Safety Endpoint: 30 Day MAE

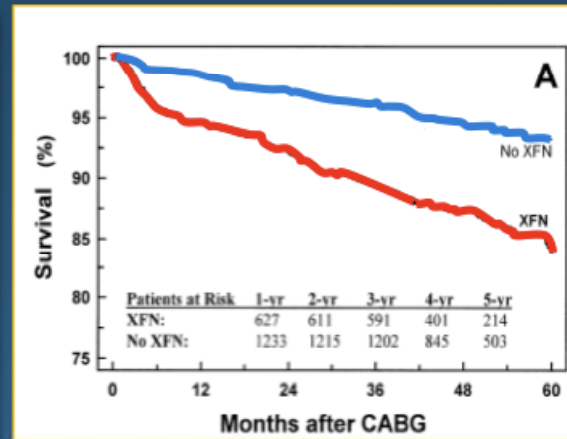
Intention to Treat

30 Day MAE	# (%) Patients experiencing event	
	Percutaneous (N=180)	Surgery (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	2 (1.1%)	0
Transfusions ≥ 2 units	24 (13.3%)	42 (44.7%)
TOTAL % of Patients with MAE	15.0%	47.9%
Difference (Percutaneous – Surgery) = -32.9%		
p<0.001; (95% CI: -20.7%, -45.0%)		

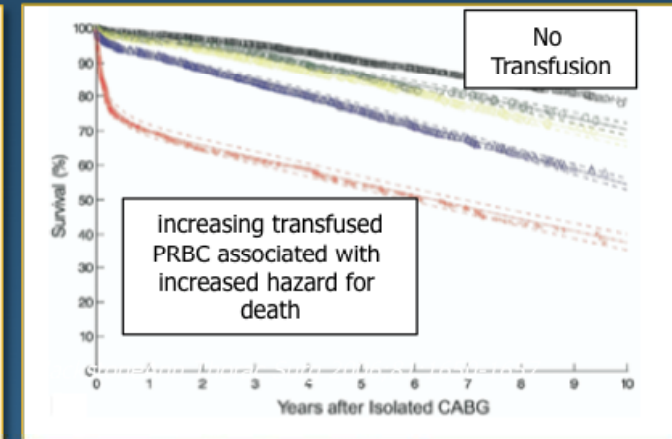
Increased morbidity & mortality with transfusion after cardiac surgery



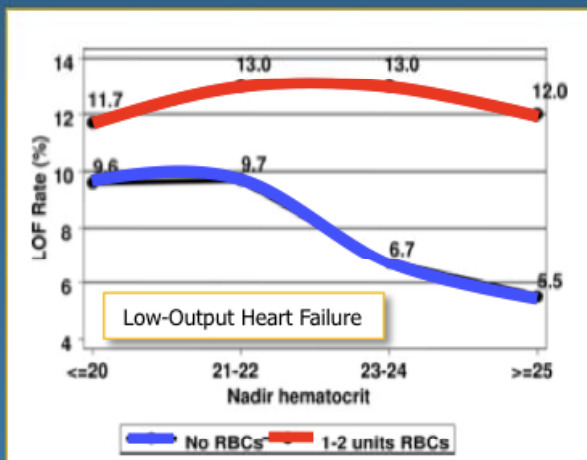
Circulation. 2007;116 :2544-2552



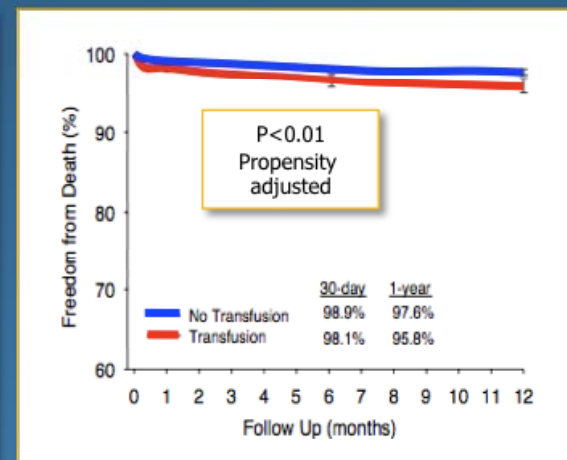
Ann Thorac Surg 2002;74:1180-1186



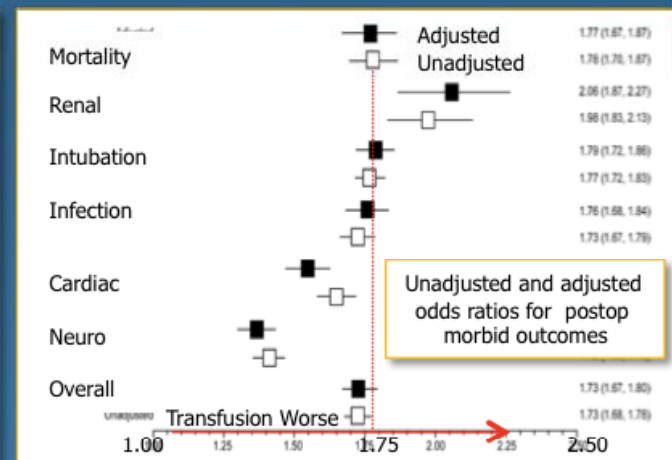
Ann Thorac Surg 2006;81:1650-1657



Circulation 2006;114:I-43-I-48

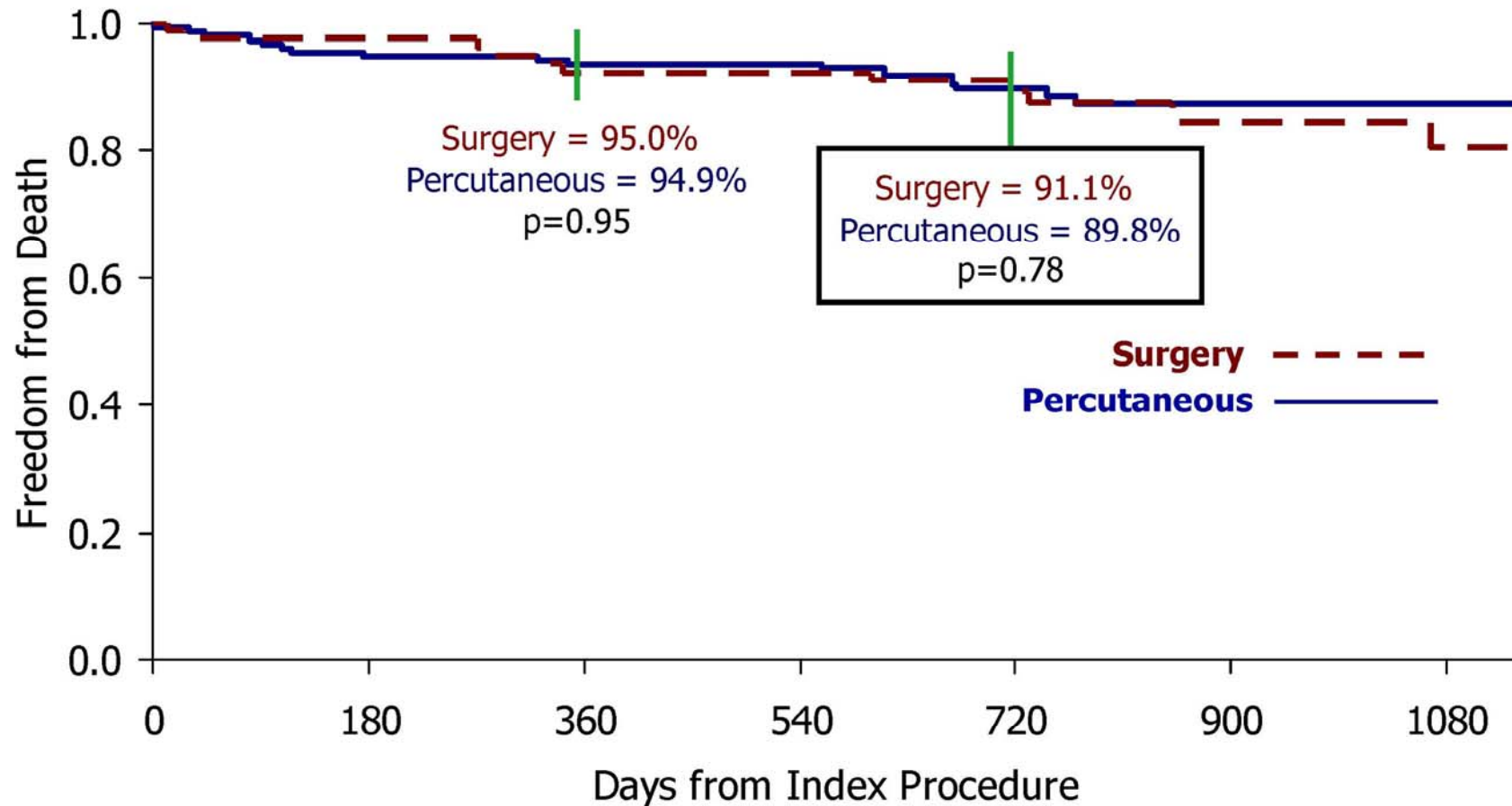


Eur J Cardio-thoracic Surg 27 (2005) 592-598



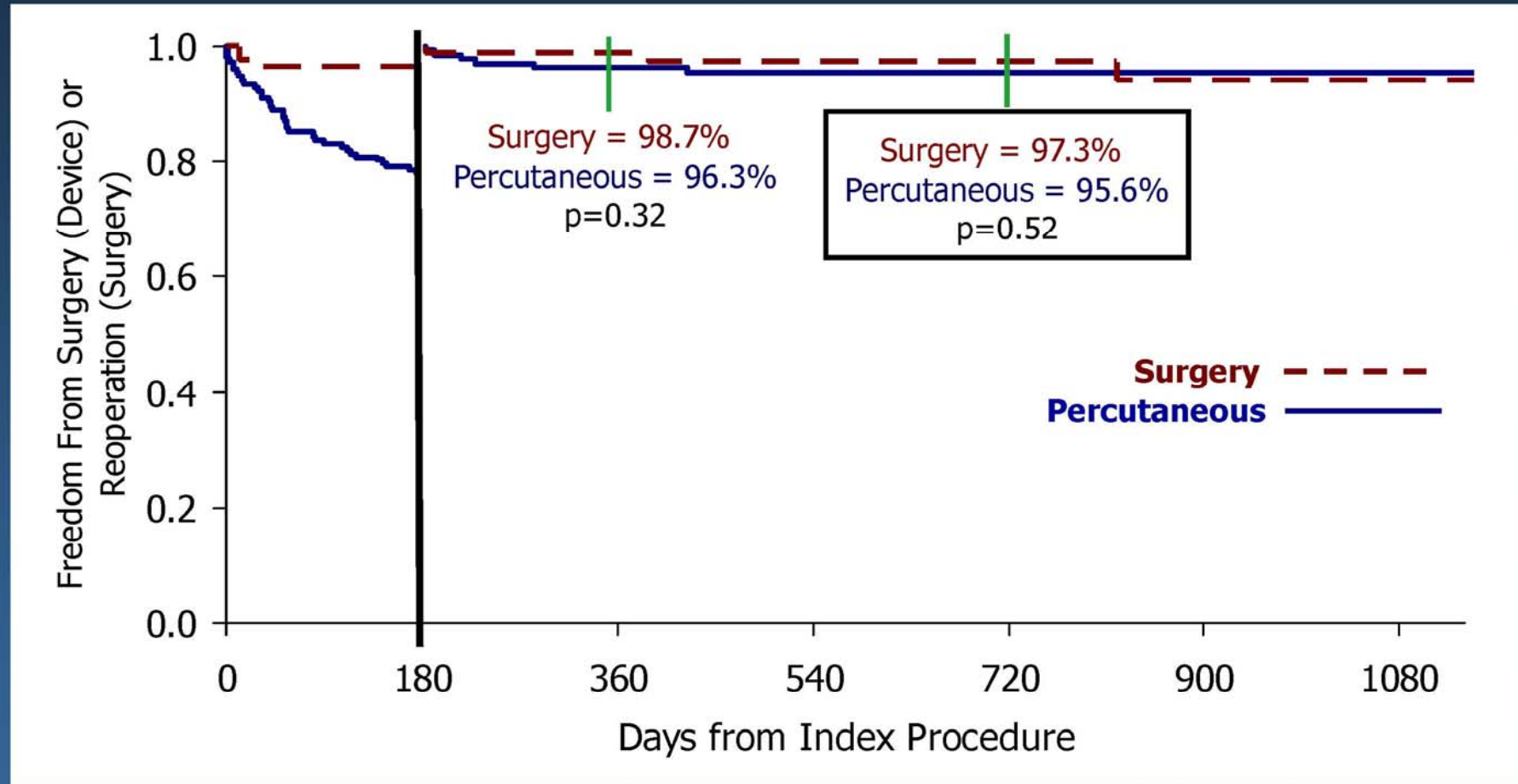
Crit Care Med 2006; 34:1608-1616

Kaplan-Meier Freedom from Death Intention to Treat



At Risk:	0 Days	6m	1yr	1.5yr	2yr	3yr
Percutaneous	184	166	163	153	133	52
Surgery	95	78	74	71	63	25

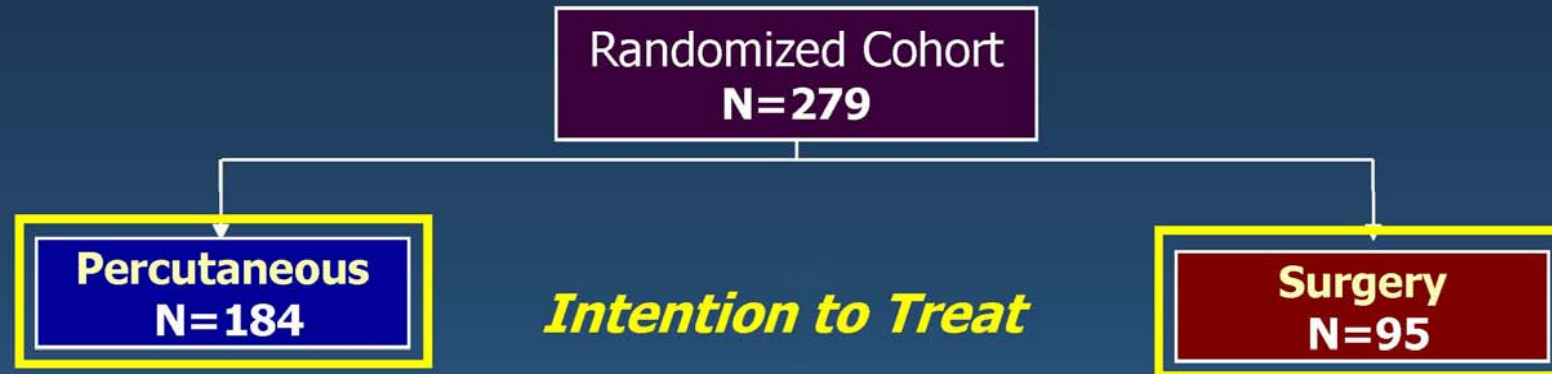
Landmark Analysis of Kaplan-Meier Freedom from MV Surgery (Percutaneous)/Re-operation (Surgery) Intention to Treat



At Risk:	0 Days	6m	1yr	1.5yr	2yr	3yr
Percutaneous	184	138	131	124	109	44
Surgery	95	77	72	69	61	24

Clinical Outcome Variables

Intention to Treat



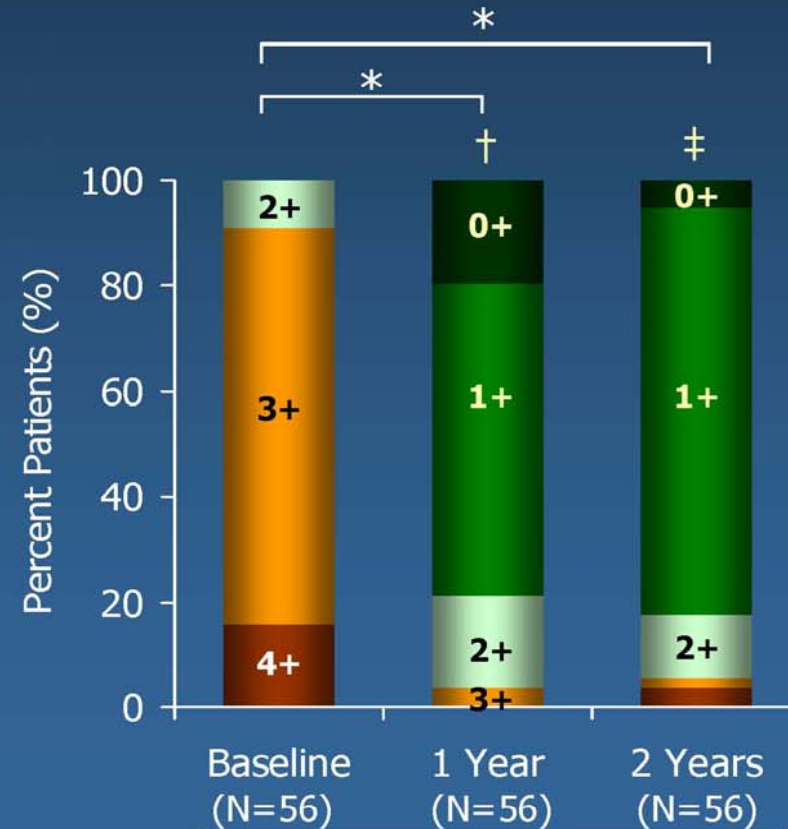
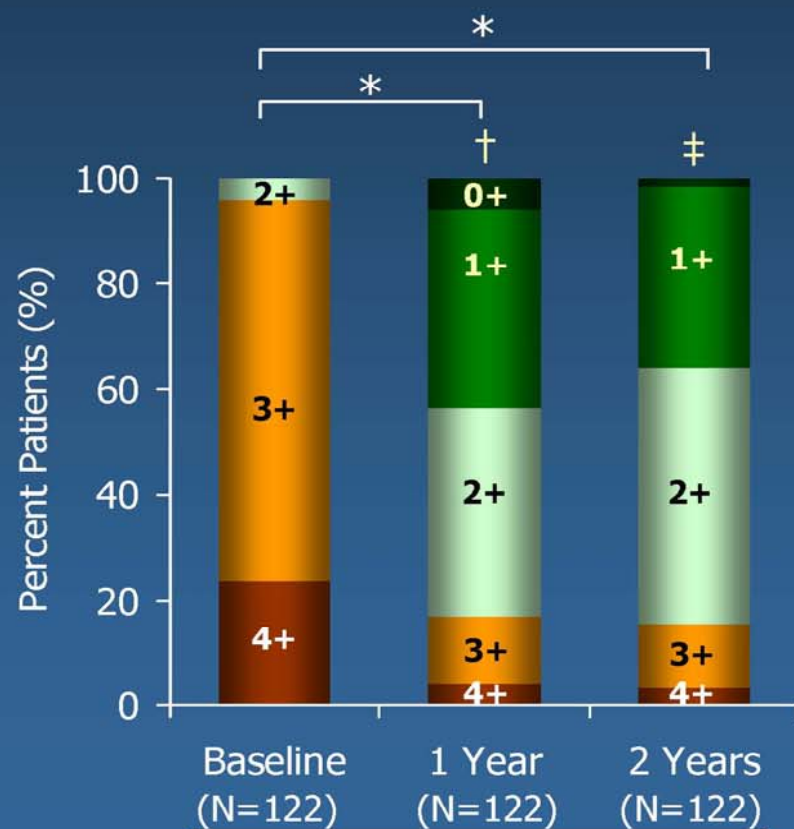
- Clinical outcome measures at 2 years include:
 - Mitral regurgitation grade
 - Left ventricular volumes
 - NYHA Functional Class

Mitral Regurgitation Grade

Baseline, 1 and 2 Years (matched)

Intention to Treat

- * Within group difference (p<0.05)
- † Between group difference at 1 year (p<0.05)
- ‡ Between group difference at 2 year (p<0.05)

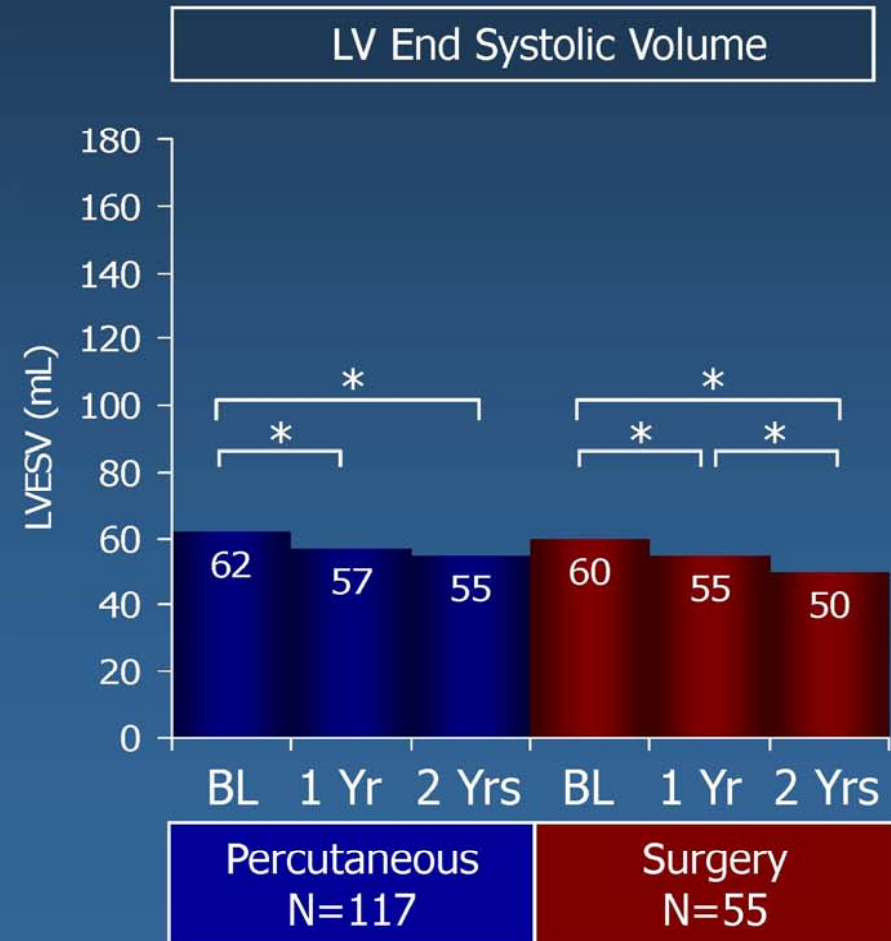
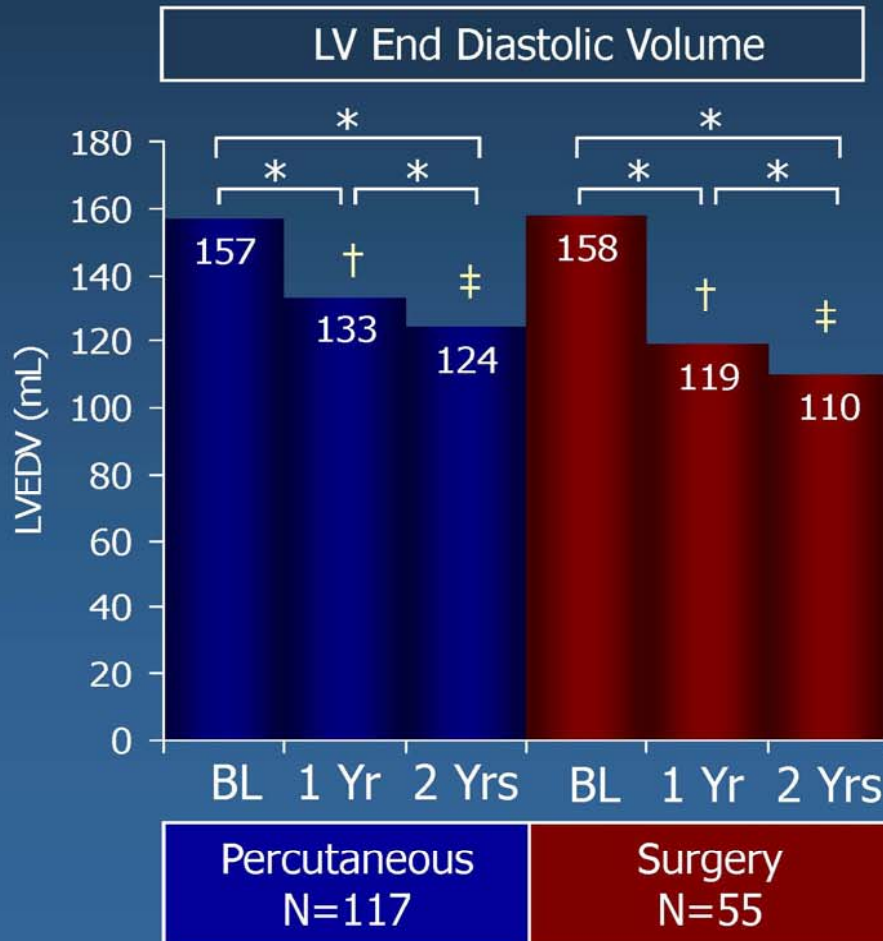


LV Volumes

Baseline, 1 and 2 Years (matched)

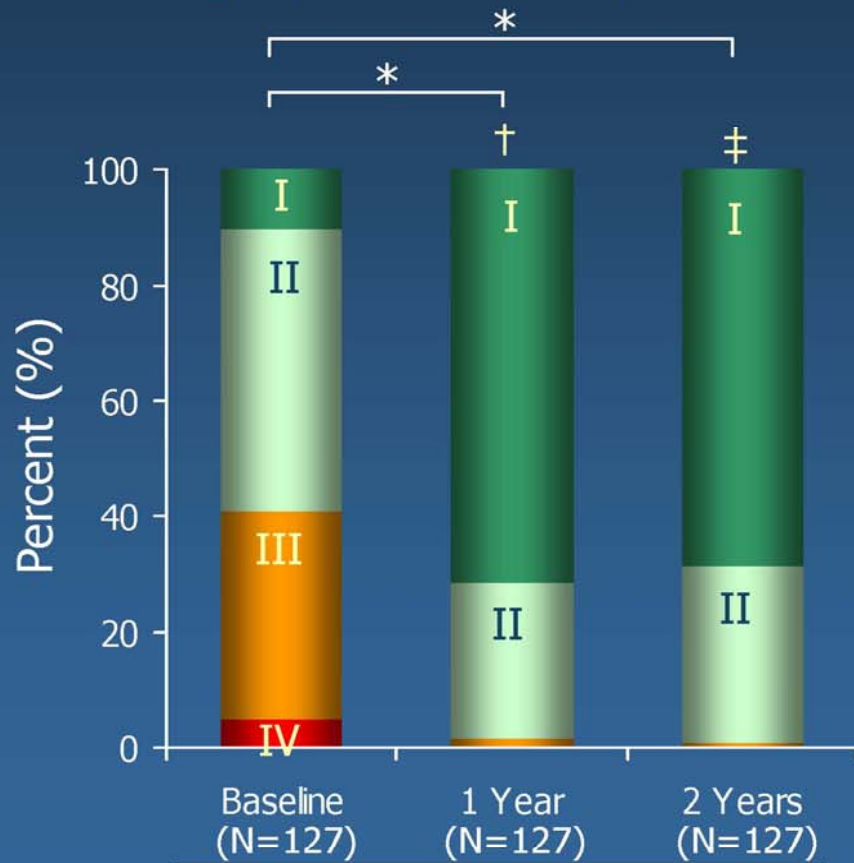
Intention to Treat

- * Within group difference (p<0.05)
- † Between group difference at 1 year (p<0.05)
- ‡ Between group difference at 2 year (p<0.05)

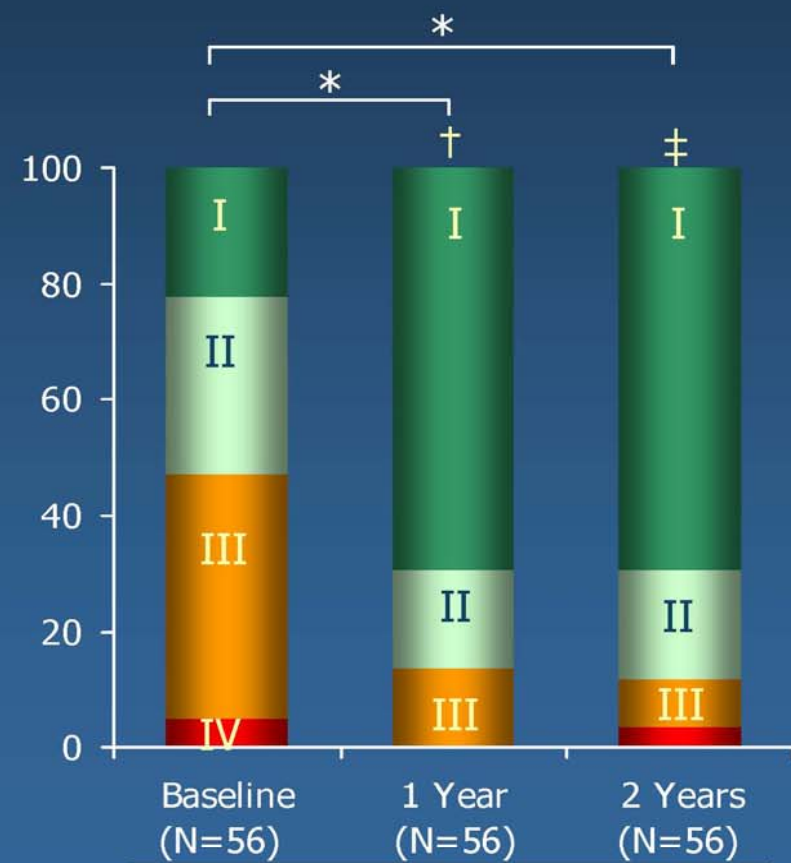


NYHA Functional Class At Baseline, 1 and 2 Years (matched) Intention to Treat

- * Within group difference (p<0.05)
- † Between group difference at 1 year (p<0.05)
- ‡ Between group difference at 2 year (p<0.05)



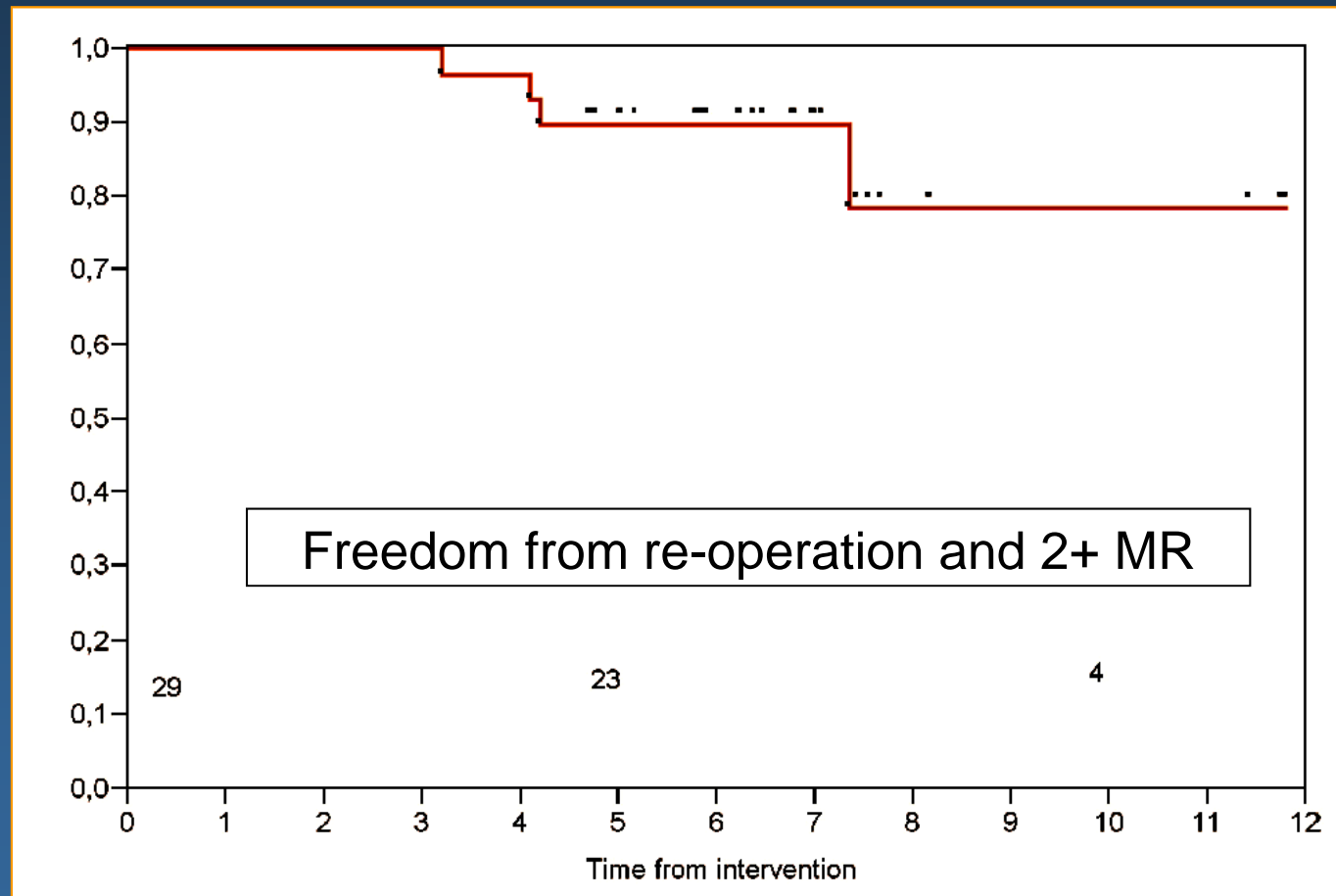
Percutaneous



Surgery

Surgical isolated edge-to-edge mitral repair without annuloplasty

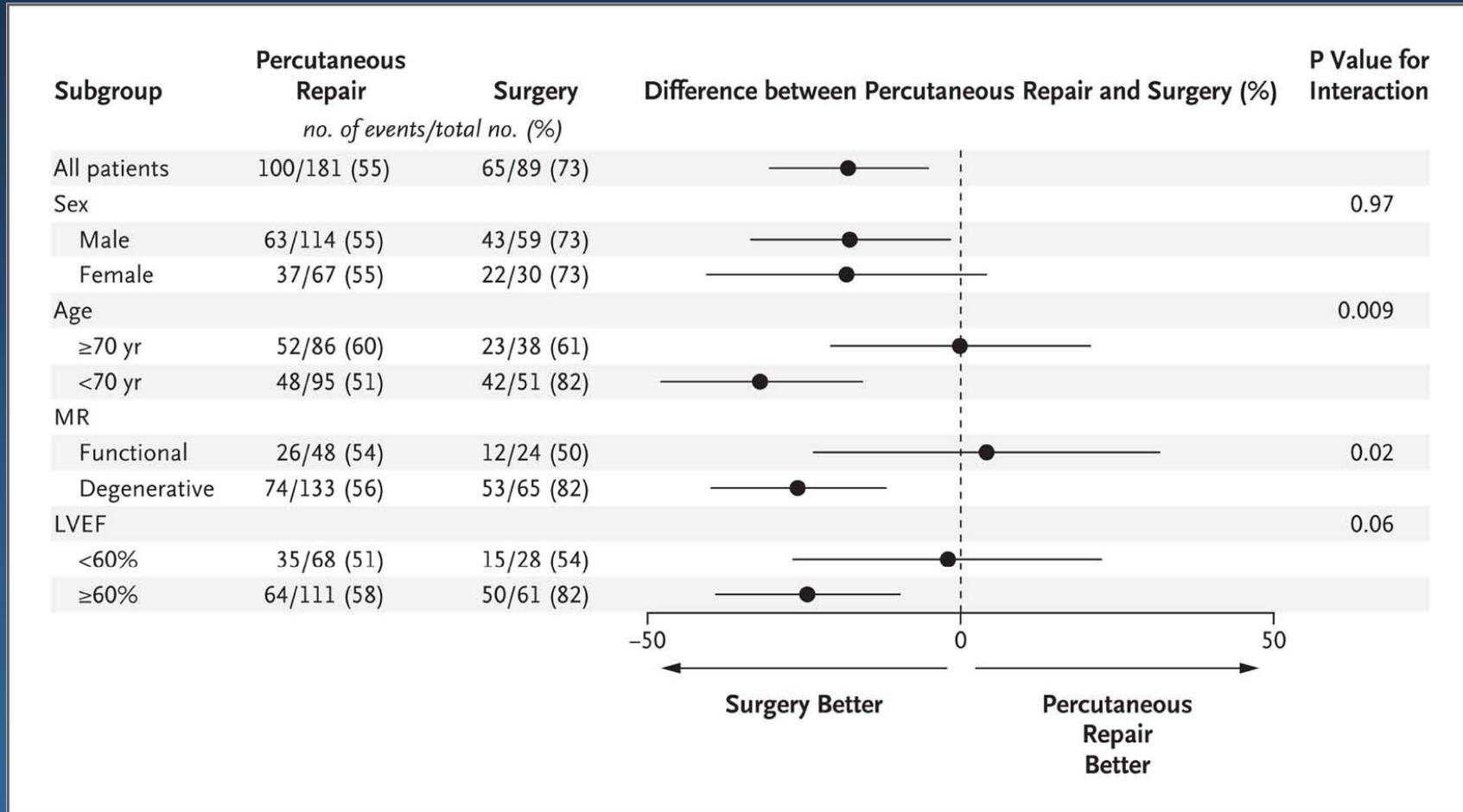
clinical proof of principle for an endovascular approach



Maisano F, Vigano G, Blasio A, Columbo A, Calabrese C, Alfieri O

Eurointervention 2:181-186, 2006

Endovascular Valve Edge-to-Edge REpair STUDY



Subgroup Analyses for the Primary End Point at 12 Months

Worldwide Experience Comparison

	Commercial	REALISM
Patients Treated	2082	561
Hospitals/Sites	98	38
Etiology: FMR/DMR/Mixed (%)	66%/28%/6%	58%/36%/6%
Average Device Time ¹ (hr)	1:45	1:46
Clip Implant Rate ¹ (%)	95%	94%
1 Clip/2 Clip/3 Clip/4 Clip ¹ (%)	68%/30%/2%/<1%	60%/40%
Site Reported MR Reduction ² (%)	98%	99%
Clip Embolization ^{2,3} (%)	0.1%	0%

¹Includes first-time procedures only – not 2nd Clip interventions

²Applies only to successful implants – does not include non-implants

³One possible embolization is under investigation, further details are pending

Data as of 4/10/2011

Acute outcomes of MitraClip therapy for mitral regurgitation in high-surgical-risk patients: emphasis on adverse valve morphology and severe left ventricular dysfunction

Olaf Franzen^{1*}, Stephan Baldus¹, Volker Rudolph¹, Sven Meyer¹, Malgorzata Knap¹, Dietmar Koschyk¹, Hendrik Treede², Achim Barmeyer¹, Joachim Schofer³, Angelika Costard-Jäckle¹, Michael Schlüter¹, Hermann Reichenspurner², and Thomas Meinertz¹

¹Department of General and Interventional Cardiology, University Heart Centre, Hamburg, Germany; ²Department of Thoracic and Cardiovascular Surgery, University Heart Centre, Hamburg, Germany; and ³Medical Care Centre Prof. Mathey, Prof. Schofer, Hamburg, Germany

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Table 2 Baseline patient characteristics

	All patients (n = 51)	EVEREST+ (n = 16)	EVEREST- (n = 35)	P (+ vs. -)
Age, years \pm SD	73 \pm 10	72 \pm 9	74 \pm 10	0.46
Male gender, n (%)	34 (67)	11 (69)	23 (66)	1.00
Logistic EuroSCORE \pm SD	28 \pm 22	18 \pm 17	33 \pm 23	0.027
STS score \pm SD	16 \pm 11	13 \pm 9	17 \pm 12	0.46
Ischaemic cardiomyopathy, n (%)	25 (49)	9 (56)	16 (46)	0.56
Dilated cardiomyopathy, n (%)	17 (33)	5 (31)	12 (34)	1.00
MR type, n (%)				
Functional	35 (69)	11 (69)	24 (69)	1.00
Organic	16 (31)	5 (31)	11 (31)	
MR severity, n (%)				
3+ (moderate-to-severe)	21 (41)	9 (56)	12 (34)	0.22
4+ (severe)	30 (59)	7 (44)	23 (66)	
NYHA functional class, n (%)				
II	1 (2)	1 (6)	0 (0)	0.29
III	24 (47)	8 (50)	16 (46)	
IV	26 (51)	7 (44)	19 (54)	
LVEF, % \pm SD	36 \pm 17	40 \pm 13	34 \pm 19	0.14
LVEDD, mm \pm SD	65 \pm 9	63 \pm 5	67 \pm 10	0.18
LVESD, mm \pm SD	54 \pm 10	52 \pm 5	55 \pm 12	0.26
LVEDV, mm ³ \pm SD	188 \pm 56	171 \pm 27	196 \pm 56	0.14
LVESV, mm ³ \pm SD	124 \pm 57	101 \pm 22	136 \pm 66	0.046
MVOA, cm ² \pm SD	4.6 \pm 1.0	4.8 \pm 0.9	4.4 \pm 1.0	0.16
Mean transmitral pressure gradient, mmHg \pm SD	1.9 \pm 1.5	1.4 \pm 1.2	2.1 \pm 1.6	0.14
Systolic pulmonary pressure, mmHg \pm SD	49 \pm 14	48 \pm 13	48 \pm 15	0.86

Evaluate Experience

- Similar results for both degenerative & functional MR
 - Decreased LV chamber size & septal-lateral dimensions
- Surgical option for repair preserved
 - Replacement in more complex valves
- Patients stable during procedure
- Unmet need for poor surgical candidates
 - Clinical adoption in FMR
- Randomized trial 2 year follow-up completed
 - Lesser efficacy at reducing MR
 - Superior safety & NYHA class
 - Excellent clinical outcomes to 3 years