Secondary Mitral Valve Regurgitation in Heart Failure, Age 60 Years

From Medical Therapy to Surgical Repair to Transcatheter Intervention

The Interventionalist's View

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Prognostic Impact of FMR

1,256 pts. (mean age 67) with HF due to DCM (mean EF 32%):
27% no MR, 49% mild/mod FMR, and 24% severe FMR
Severe FMR defined as ERO > 0.2 cm2 or RV >30ml or VC >0.4cm
Survival free from HR hospitalization (median F/U 2.5yrs)

In a fully adjusted MV model, severe FMR was an independent predictor for:

Death or HF hospitalization
HR (95%CI) = 1.5 (1.2-1.9), P=0.001

Death
HR (95%CI) = 1.5 (1.1-2.1), P=0.009

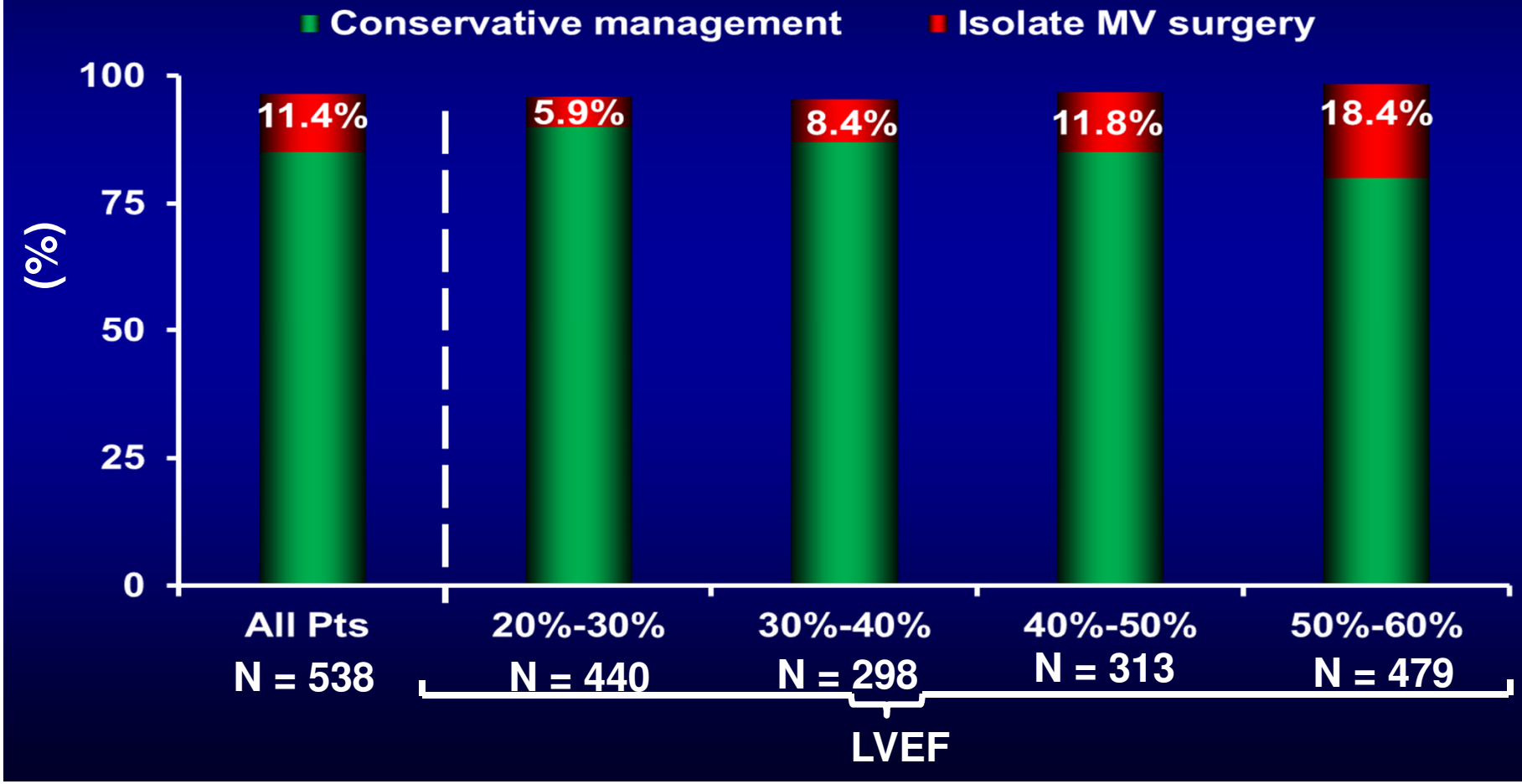
HF hospitalization
HR (95%CI) = 1.7 (1.2-2.5), P=0.004

Rossi A et al., Heart 2011;97:1675

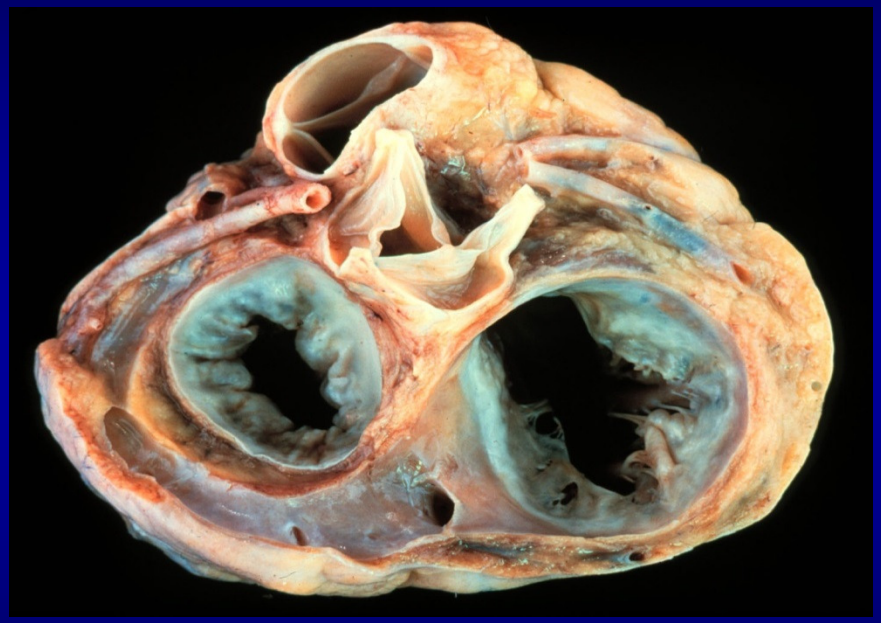
How are Patients with Isolated FMR Treated?

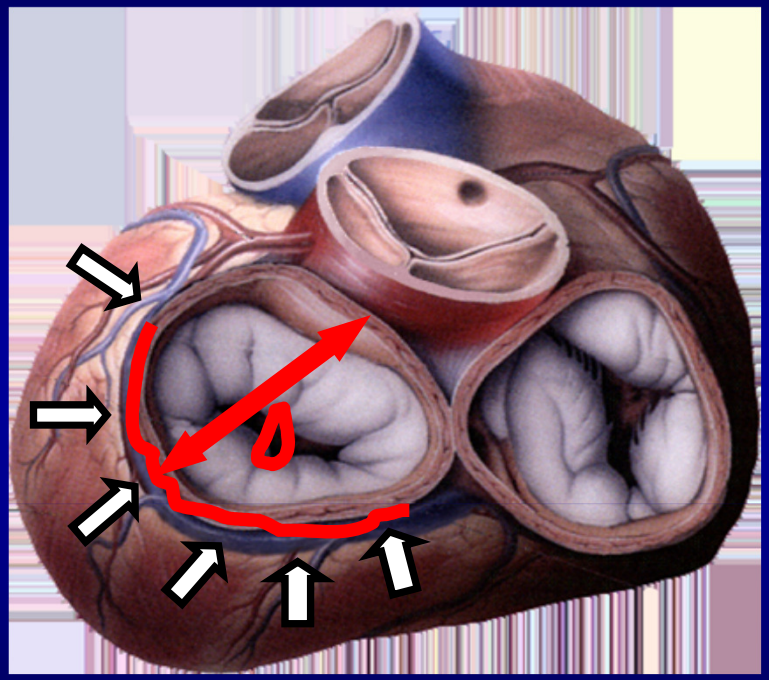
Duke Databank: 1,538 pts with echocardiographic 3+ - 4+ FMR And LVEF ≥ 20% between 2000 and 2010 not undergoing CABG

Management:



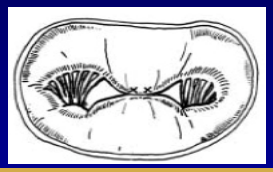
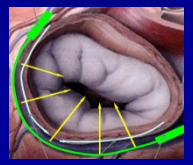
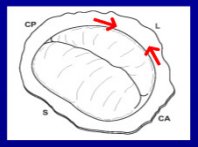
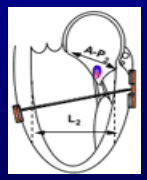
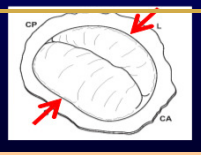
Percutaneous Mitral Valve Repair (pMVR) Requirements: Conducive Anatomy





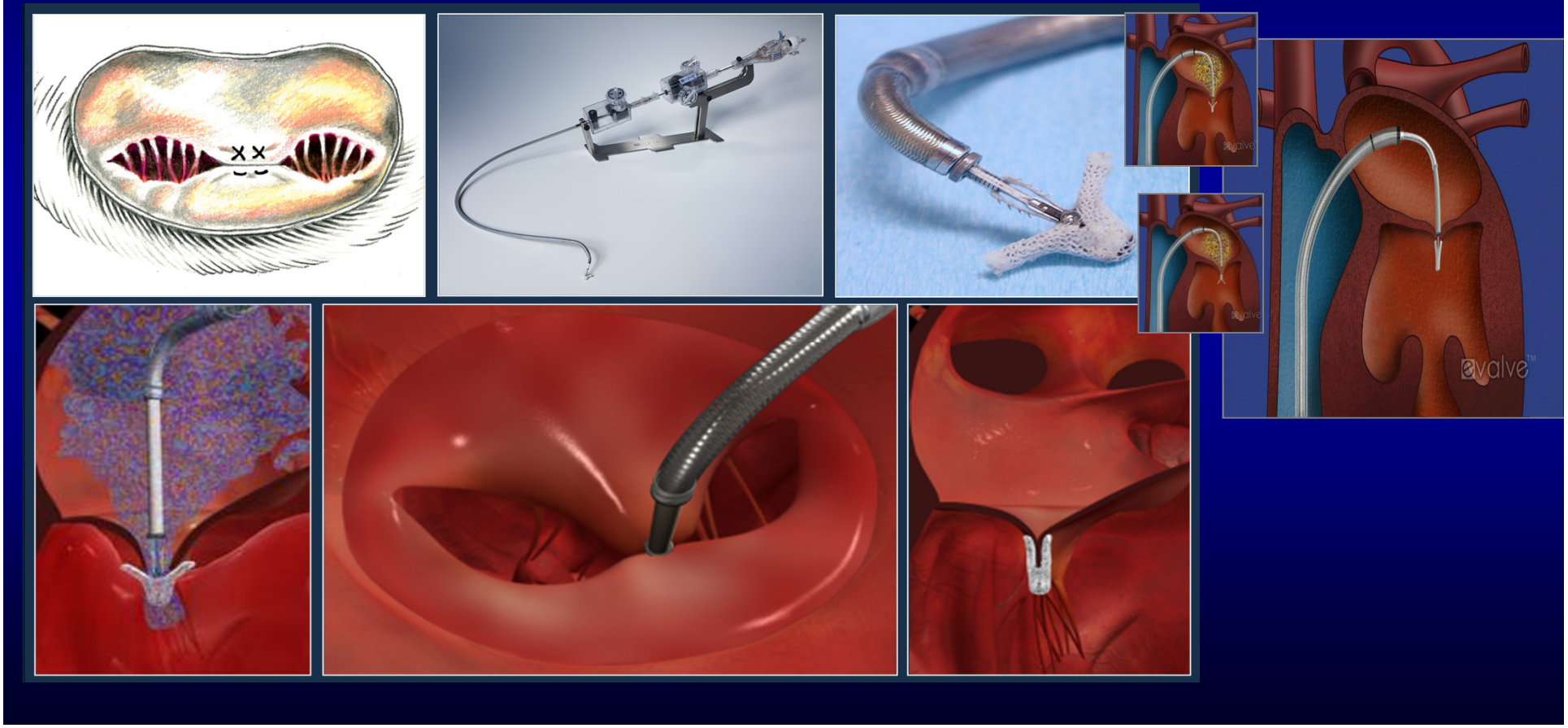
- Attractiveness of Coronary Sinus Approach
- Simple Clip the Mitral Leaflets
- Reducing Mitral Annular Dimensions/LV Cavity size

pMVR Technology Summary

Technology	Approach		Status
Bowtie • E Valve • Edwards	Leaflet Coupling		Clinical
Coronary Sinus • Edwards • Viaco • Cardiac Dimensions	Coronary Sinus Reshaping		Early Clinical
Annulus Plication • Mitralign • Guided Delivery Systems	Posterior Reshaping		Pre-Clinical
LV Shape Change • Myocor (Surgical/Endovascular)	External LA/LV		Clinical/ Pre-Clinical
• Ample Medical, Inc.	Internal Direct S-L		Pre-Clinical

EVEREST II (Endovascular Valve Edge-to-Edge E2E Repair) Study

Catheter-based Mitral Valve Repair – MitraClip System



MitraClip Concepts

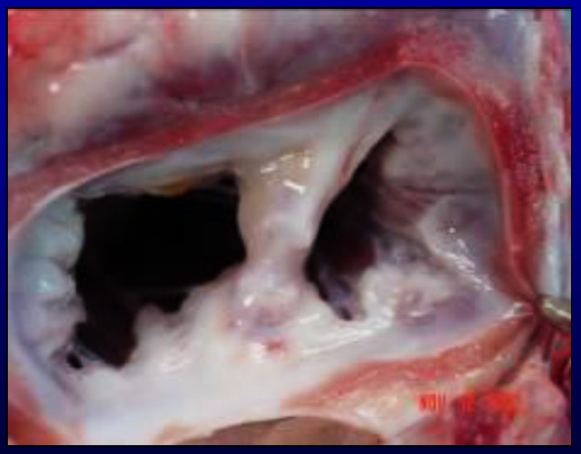
Facilitates proper leaflet coaptation

- Mechanical solution to a mechanical problem

Etiology

- Degenerative – Anchor flail and prolapsed leaflets (similar to chordal transfer/replacement)
- Functional – Coapt tethered leaflets to reduce time and force required to close valve

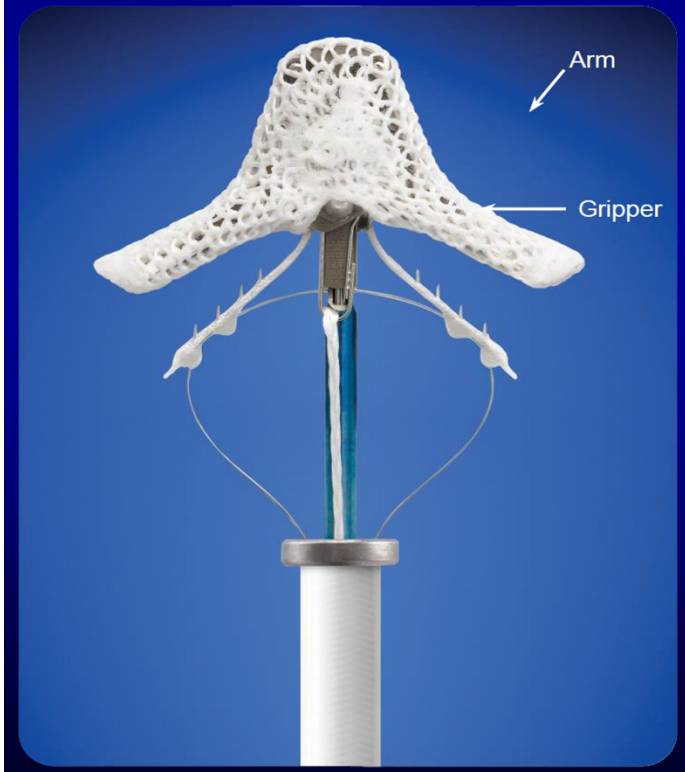
Creates tissue bridge



Porcine model, 6M

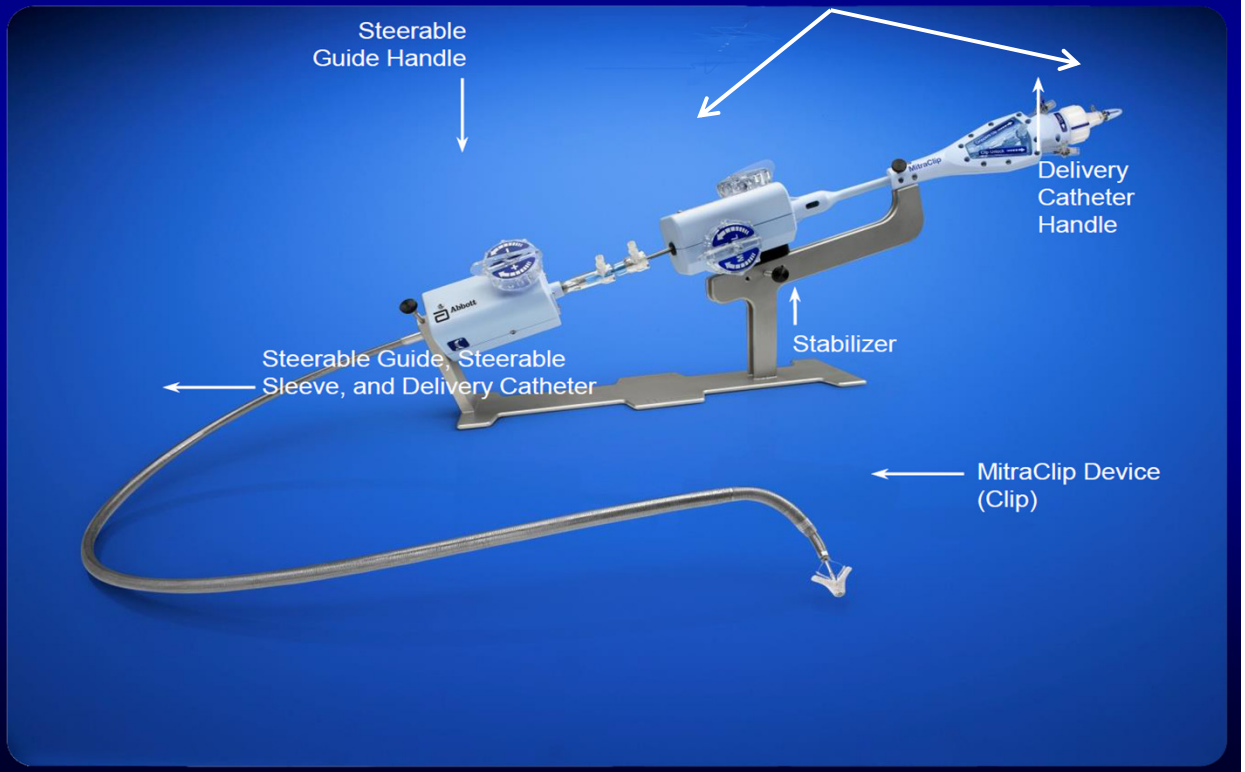
The MitraClip System

MitraClip Device (Clip)

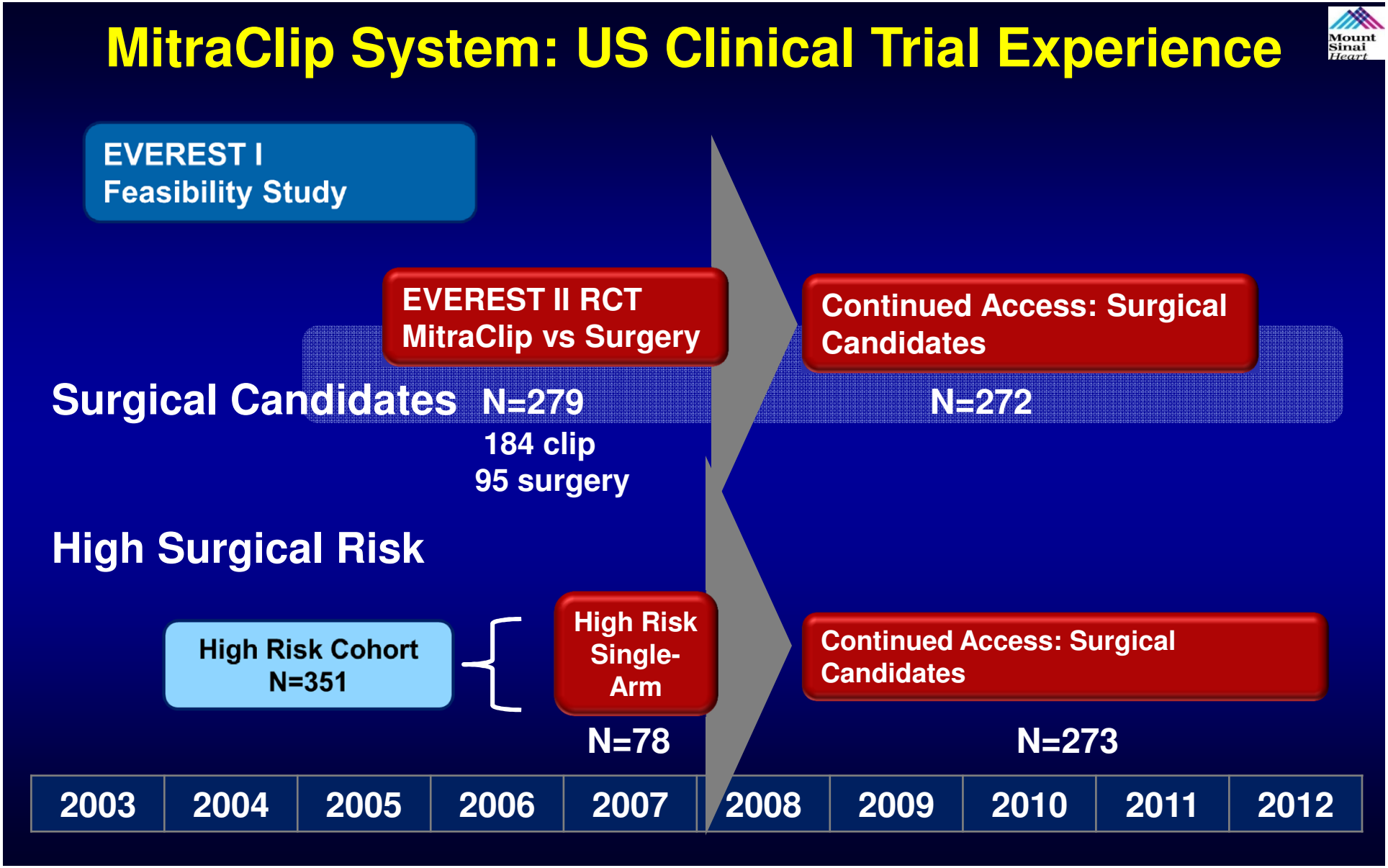


MitraClip System

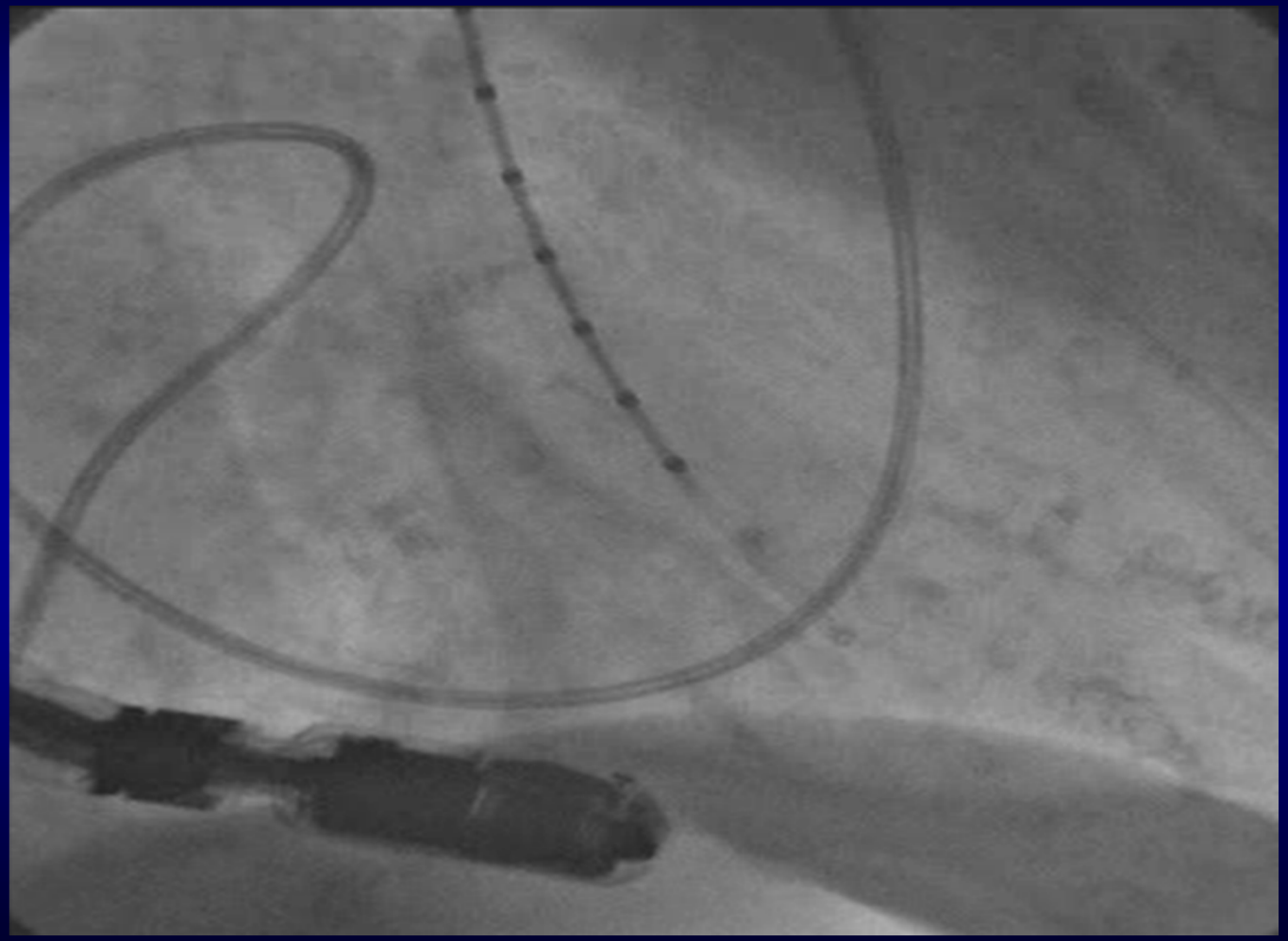
Clip Delivery System



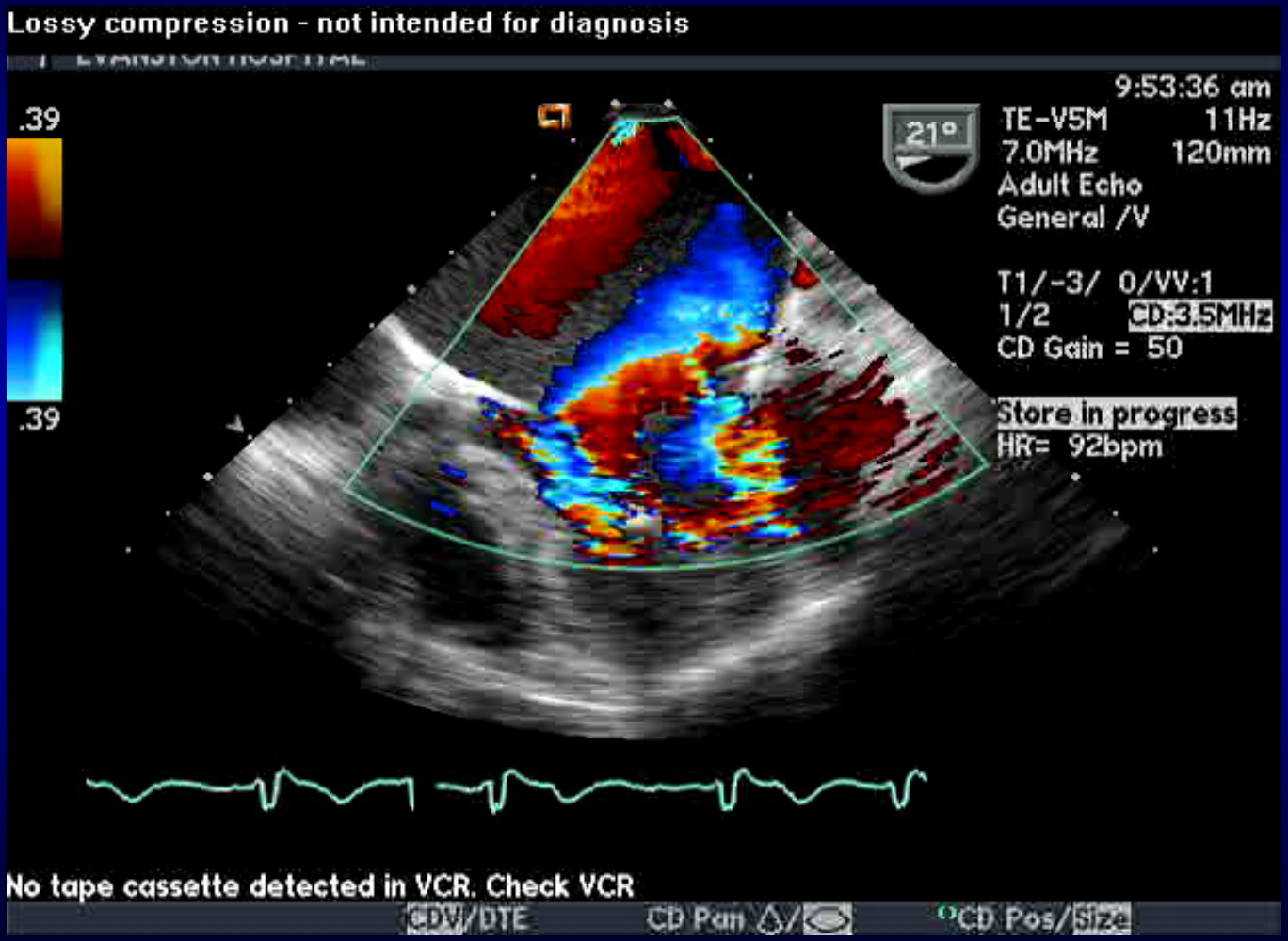
MitraClip System: US Clinical Trial Experience



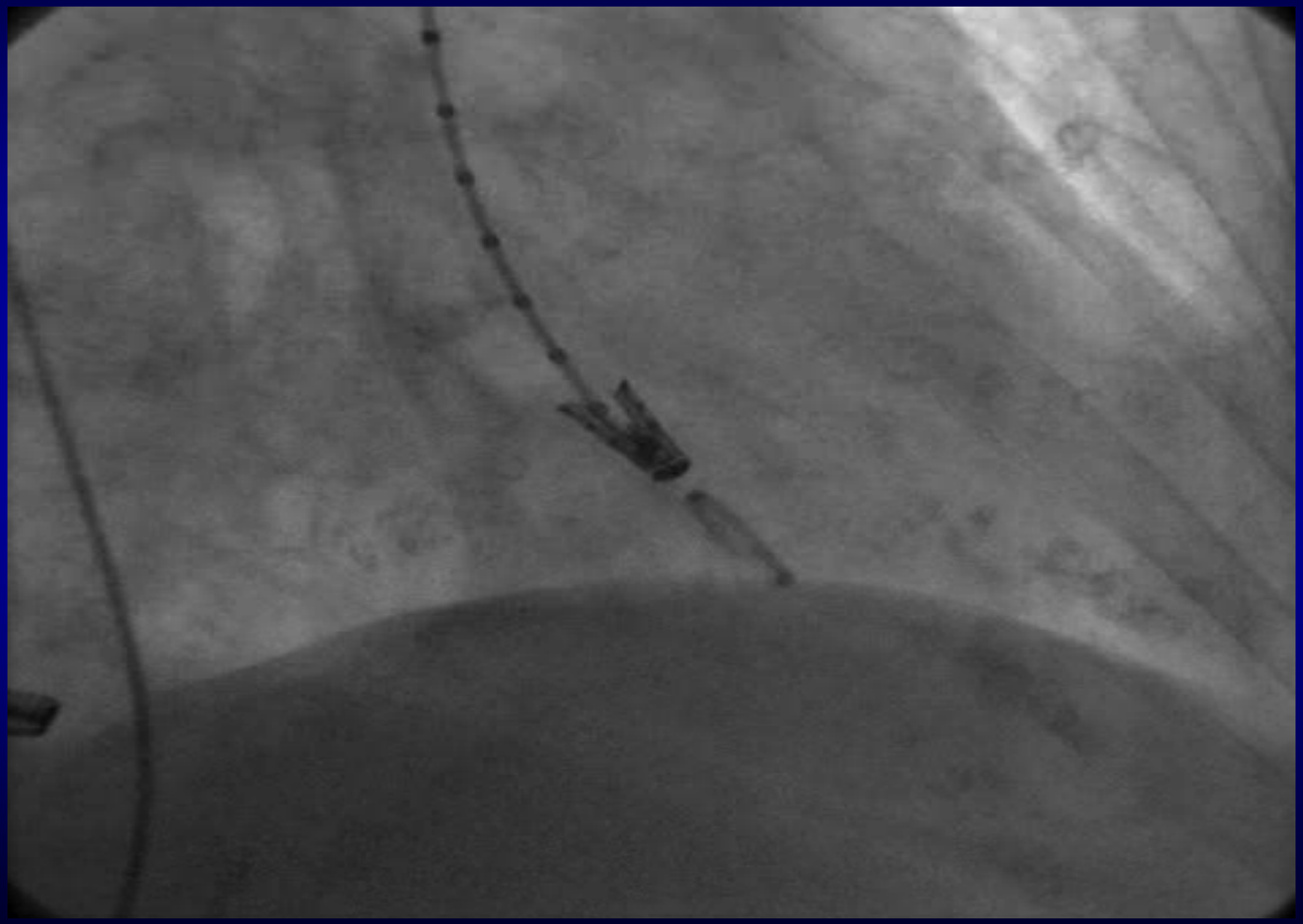
EValve Case: LV gram Pre MitraClip



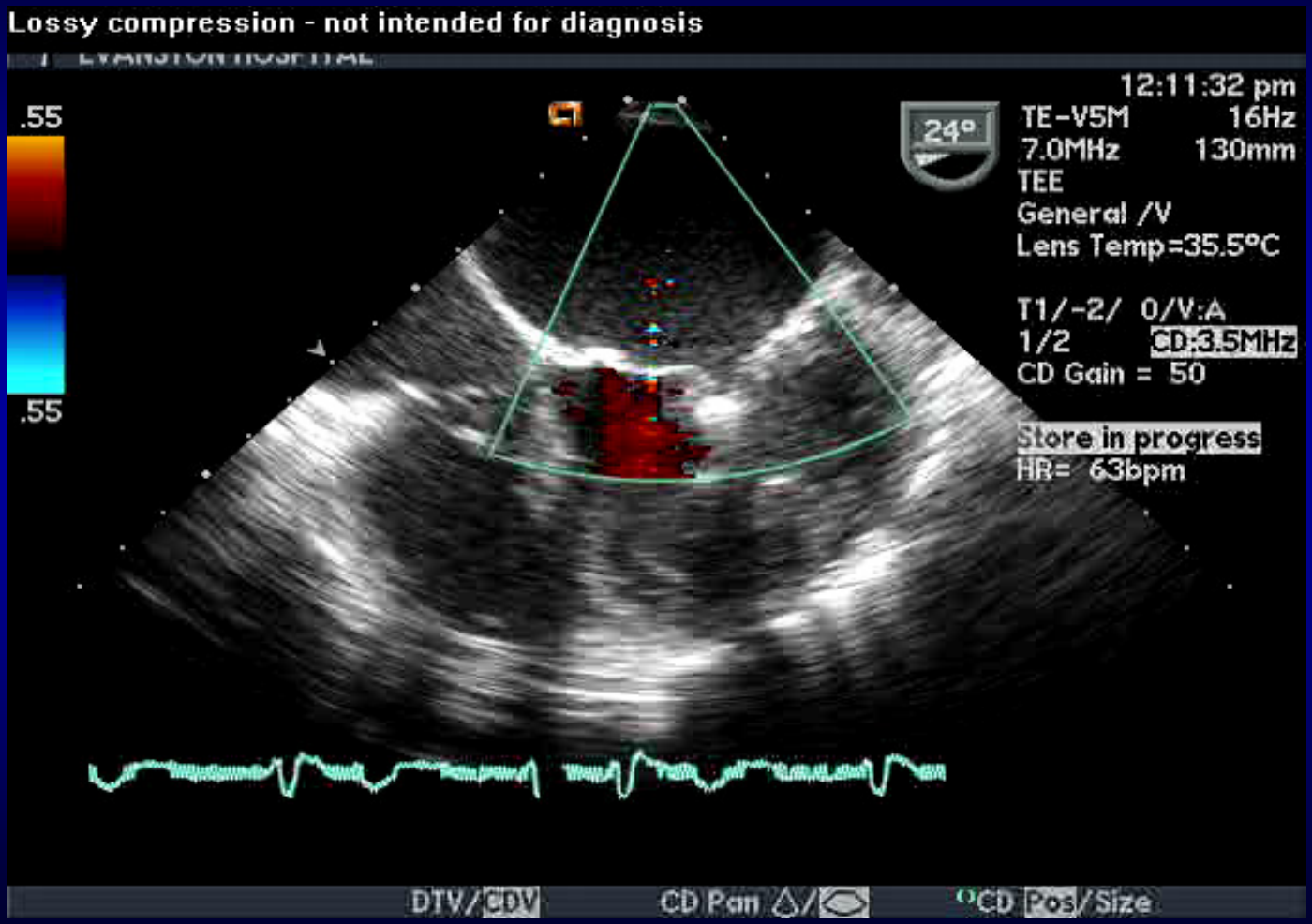
EValve Case: Echo Pre MitraClip



EValve Case: LV Gram Post MitraClip



EValve Case: Echo Post Clip



EVEREST II Randomized Clinical Trial Study Design

279 Patients Enrolled at 37 Sites

Significant MR (3+ - 4+)

Specific Anatomical Criteria

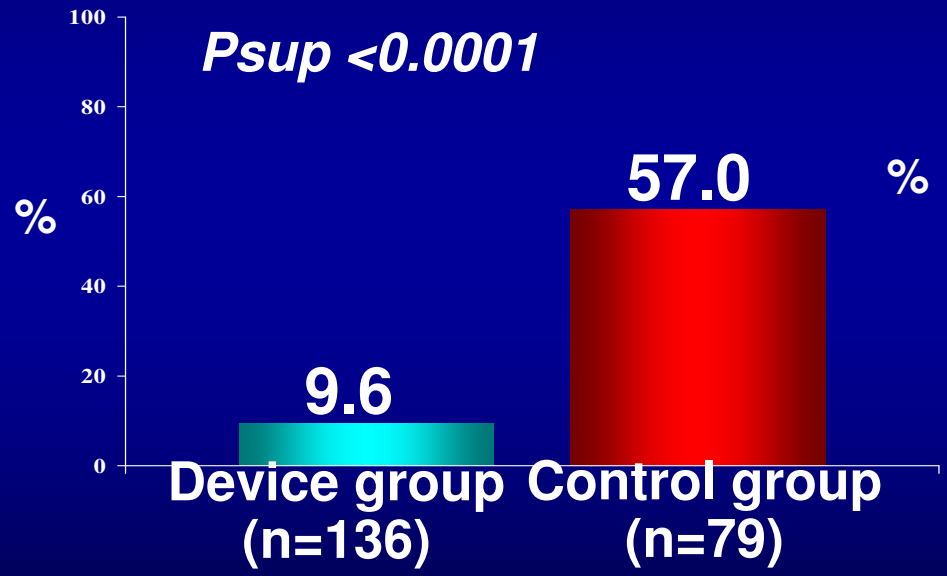
Randomized 2:1

Echocardiography Core Lab and Clinical Follow-Up:
Baseline, 30 days, 6 months, 1 year, 18 months, and annually through 5 years

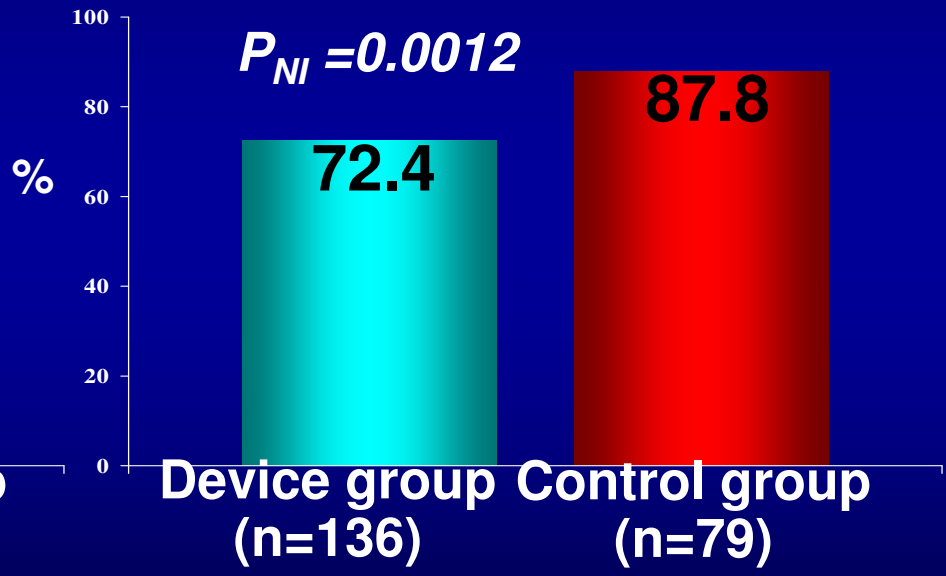
EVEREST II (Endovascular Valve Edge-to-Edge Repair) Study

Primary Endpoints Per Protocol Cohort

SAFETY
Major Adverse Events
30 days



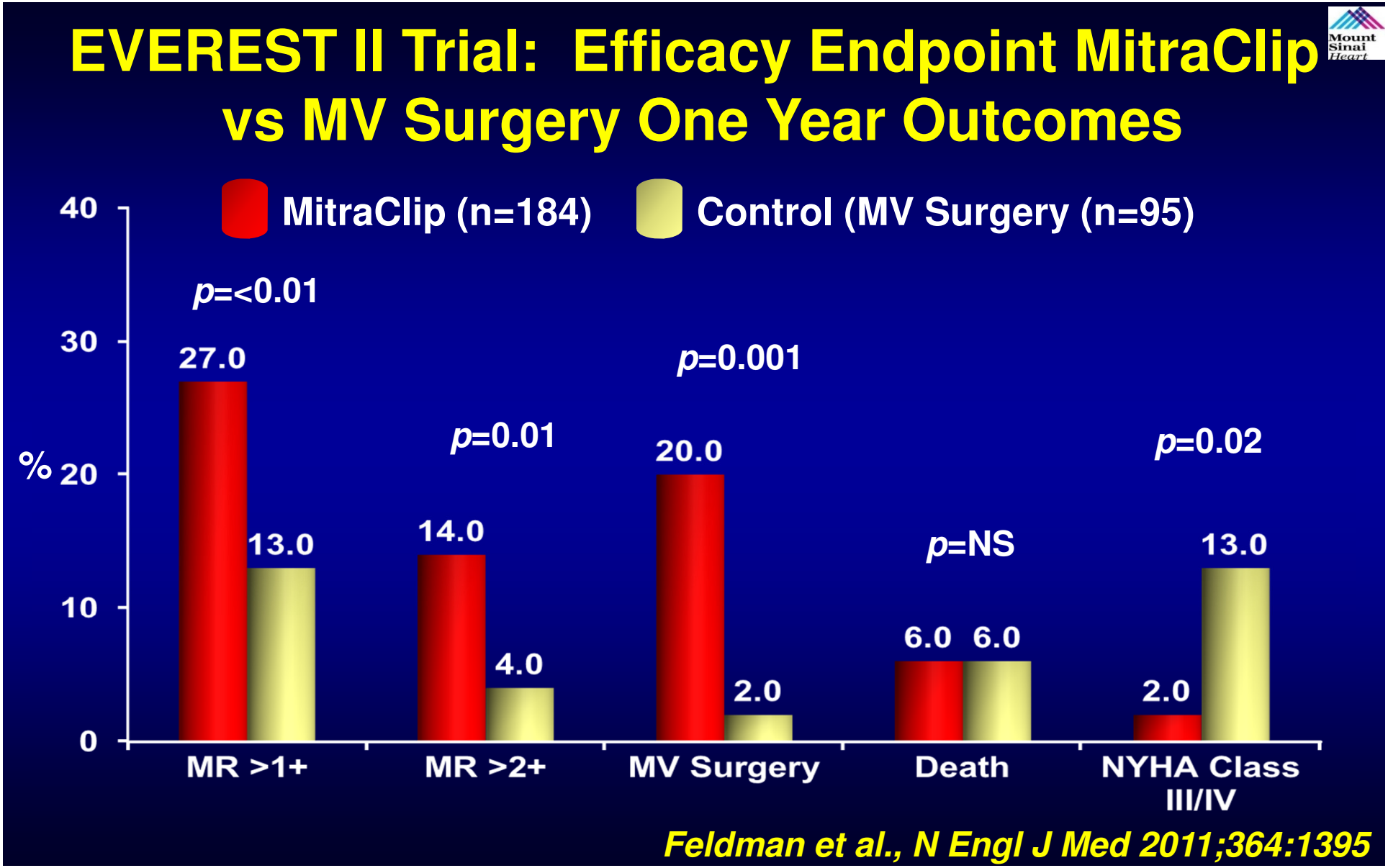
EFFECTIVENESS
Clinical Success Rate*
12 months



*Freedom from the combined outcome of death, MV surgery or re-operation for MV dysfunction, MR >2+ at 12 Month

Feldman et al. NEJM 2011;364:678

EVEREST II Trial: Efficacy Endpoint MitraClip vs MV Surgery One Year Outcomes



Feldman et al., N Engl J Med 2011;364:1395

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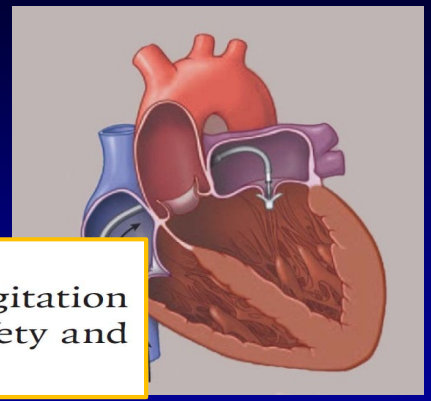
Percutaneous Repair or Surgery for Mitral Regurgitation

Ted Feldman, M.D., Elyse Foster, M.D., Donald D. 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.,



CONCLUSIONS

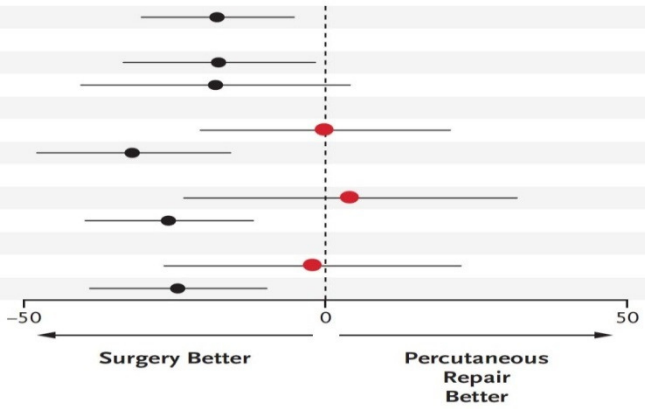
Although percutaneous repair was less effective at reducing mitral regurgitation than conventional surgery, the procedure was associated with superior safety and similar improvements in clinical outcomes.

edges of the mitral leaflets at the origin of the regurgitant jet.

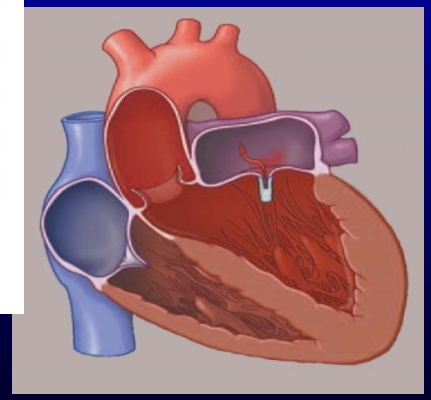
METHODS

We randomly assigned 279 patients with moderately severe or severe (grade 3+ or 4+)

Subgroup	Percutaneous Repair	Surgery	P Value for Interaction
	no. of events/total no. (%)		
All patients	100/181 (55)	65/89 (73)	
Sex			0.97
Male	63/114 (55)	43/59 (73)	
Female	37/67 (55)	22/30 (73)	
Age			0.009
≥70 yr	52/86 (60)	23/38 (61)	
<70 yr	48/95 (51)	42/51 (82)	
MR			
Functional	26/48 (54)	12/24 (50)	0.02
Degenerative	74/133 (56)	53/65 (82)	
LVEF			0.06
<60%	35/68 (51)	15/28 (54)	
≥60%	64/111 (58)	50/61 (82)	



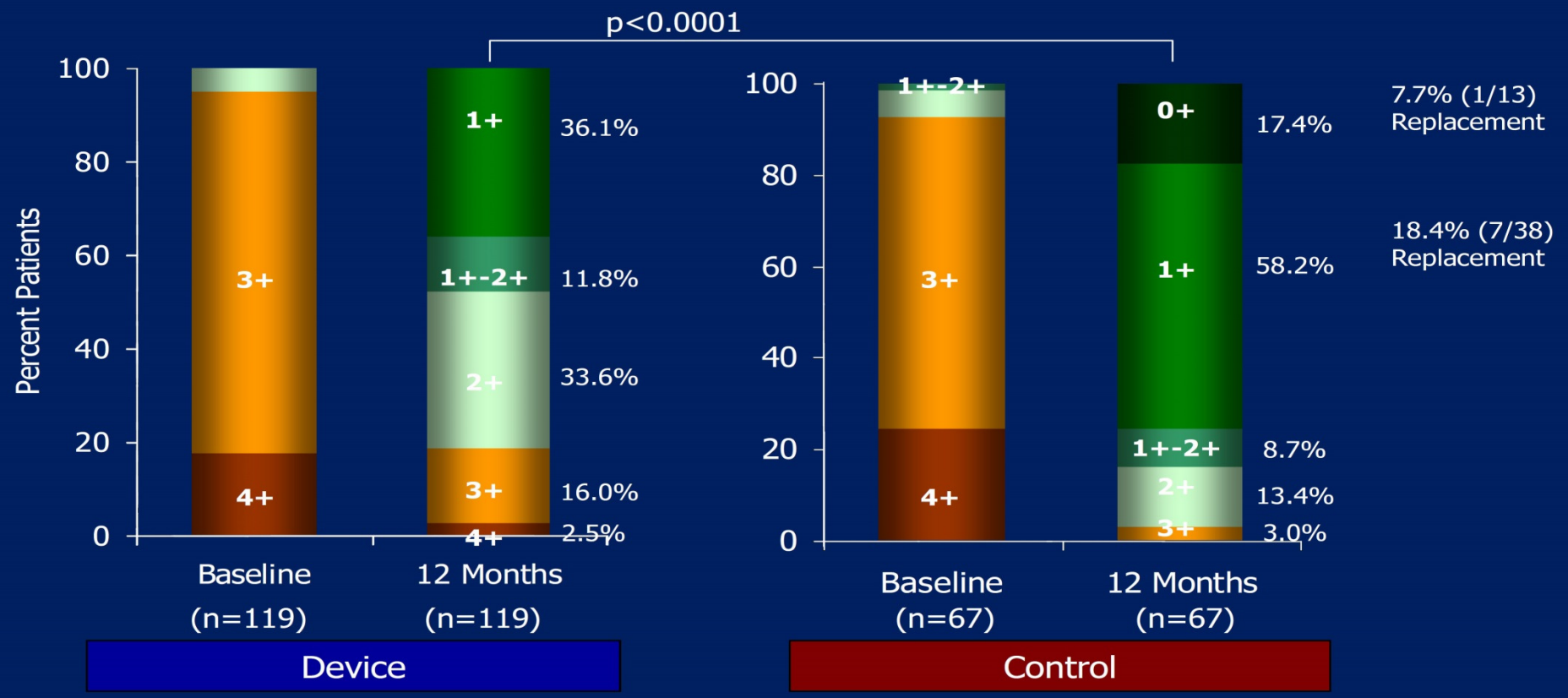
than conventional surgery, the procedure was associated with superior safety and similar improvements in clinical outcomes. (Funded by Abbott Vascular; EVEREST II ClinicalTrials.gov number, NCT00209274.)



Feldman et al. NEJM 2011:364;678

EVEREST II Trial: MR Reduction

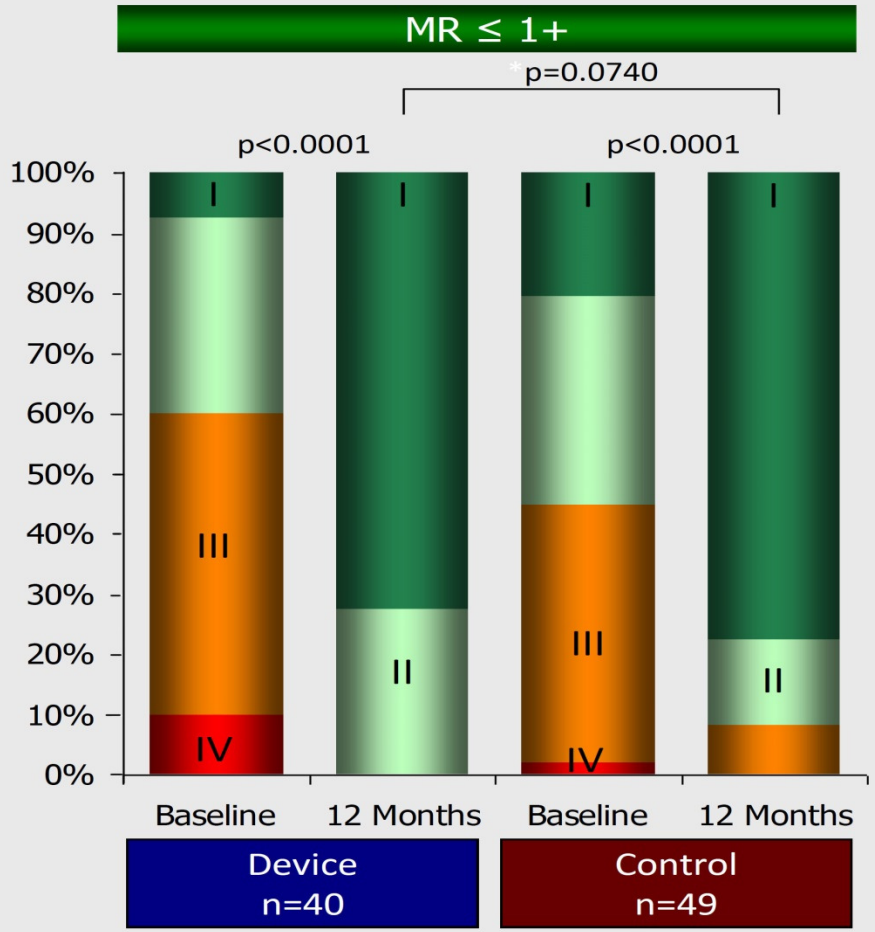
Baseline vs 12 Months, Per Protocol

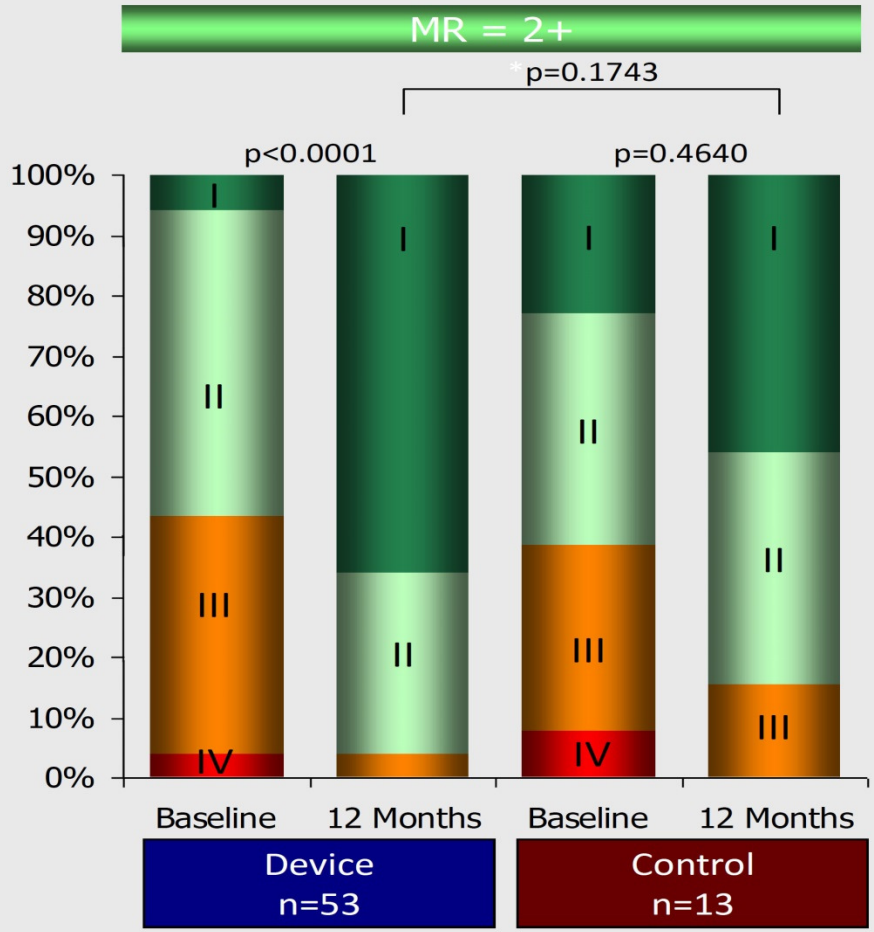


***p*-value compares the distribution of MR grade in device with the distribution of MR grade in control at 12 months (Fishers' Exact test)**

NYHA Functional Class

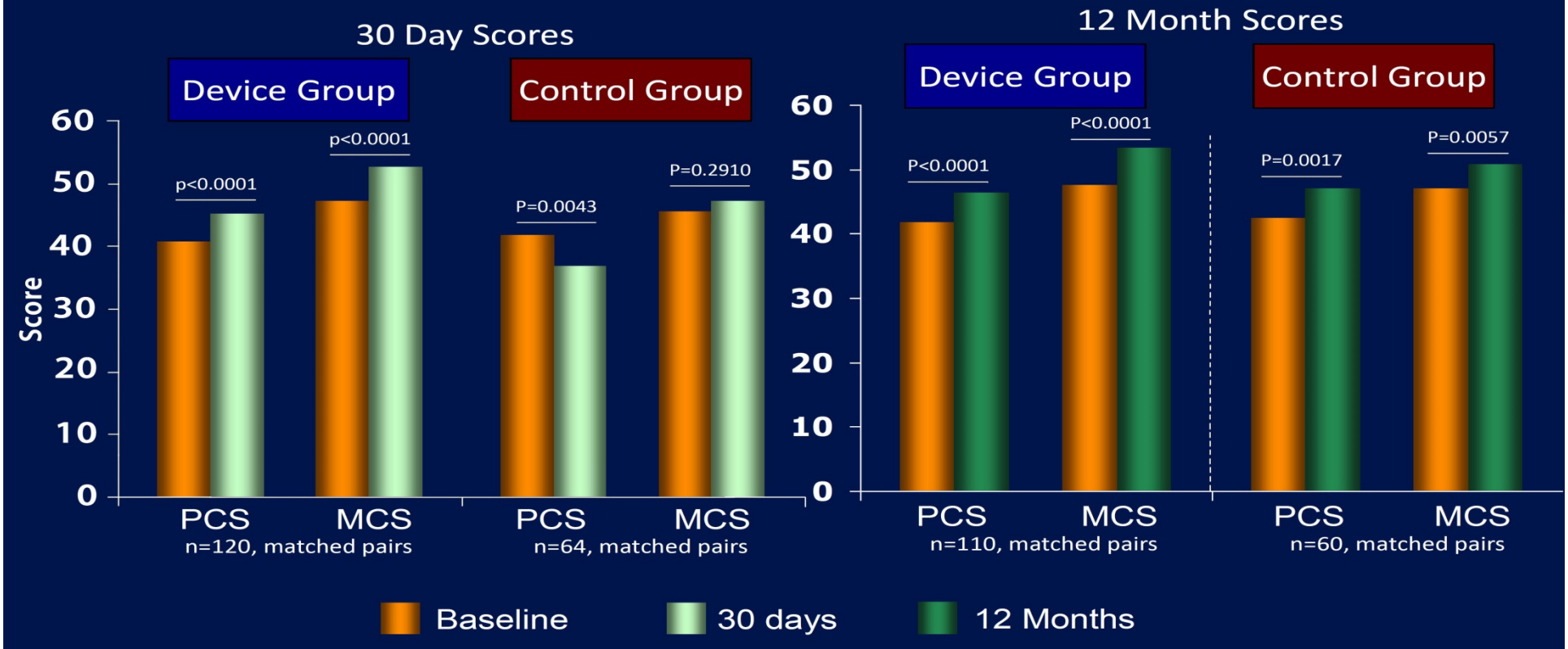
Baseline vs 12 Months, Per Protocol, Matched Cases





EVEREST II Trial: Quality of Life, SF-36

Per Protocol Cohort

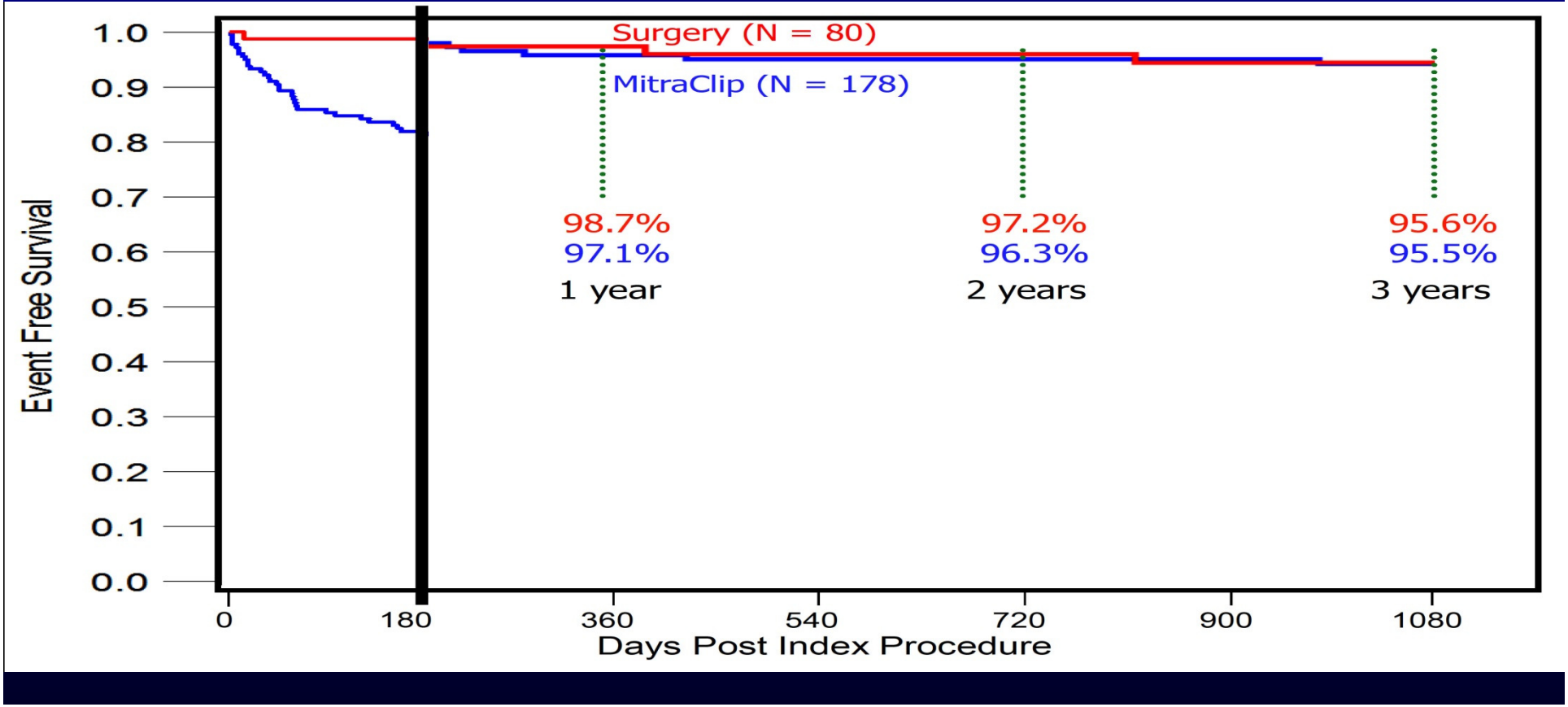


PSC = Physical Component Summary
MCS = Mental Component Summary

Hypothesis not pre-specified for statistical analysis

K-M Freedom From MV Surgery in MitraClip Group or Re-Operation in Surgery Group

All Treated Patients (n=258) – Landmark Analysis



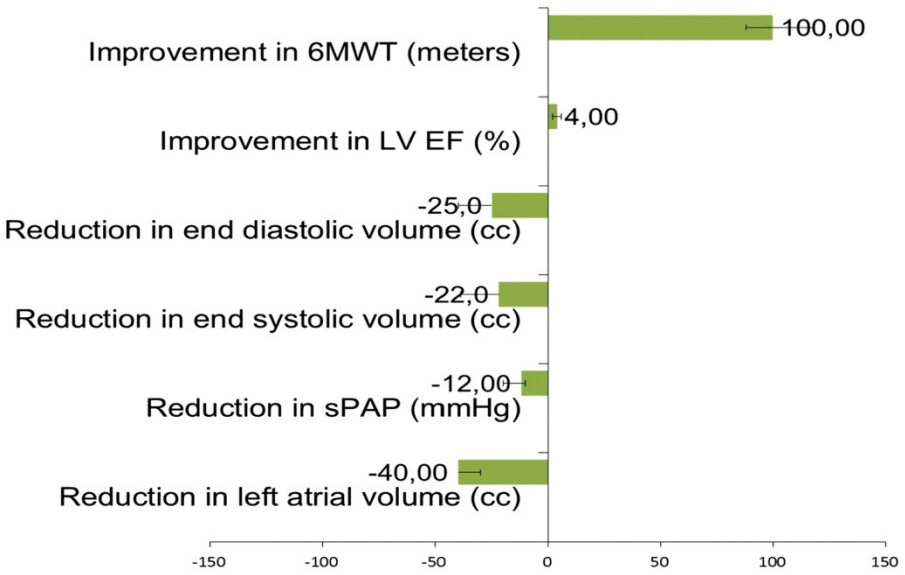
Long-Term Durability of Clinical Success

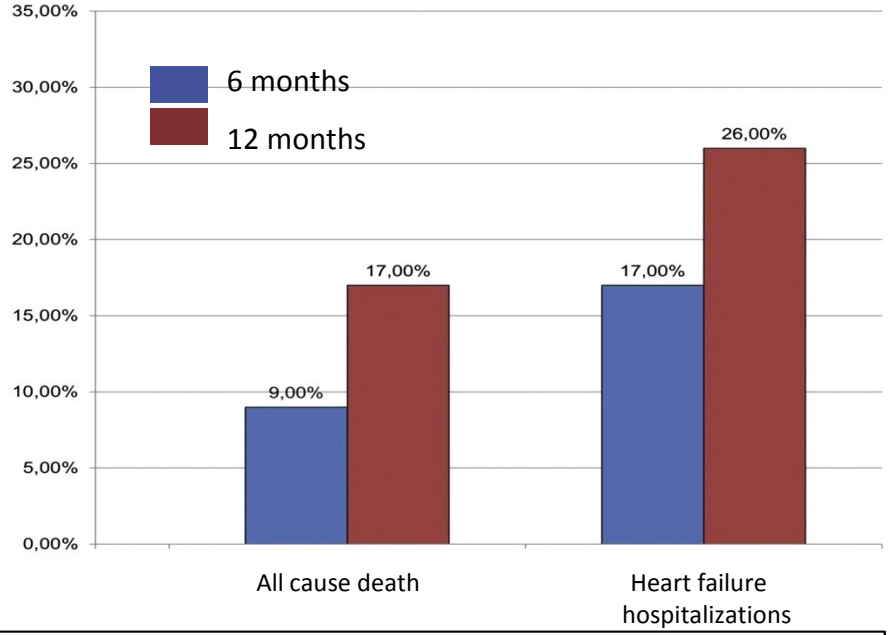
5-Year Outcomes in Patients Who Were Alive and Free From MR 3+/4+ and MV Surgery (or Re-Operation) at 1 Year

	EVEREST II RCT Clinical Success Groups	
Outcome	MitraClip (n=97)	Surgery (n=64)
Freedom From Death at 5 Years	87%	90%
Freedom from MV Surgery (or Re-Operation) at 5 Years	94%	95%
MR ≤ 2+ at 5 Years	86%	97%
MR ≤ 1+ at 5 Years	47%	92%
NYHA Class III/IV (%) Baseline → 5 Years	47% → 6%	40% → 3%
Mean Change in LVEDV From Baseline to 5 Years	- 27 ml	- 45 ml

Meta-Analysis of MitraClip in Functional MR

9 studies, 875 patients, STS median 12%,





significant improvement in functional class and remodeling, even with severely dilated hearts, although efficacy limited in atrial fibrillation

D'ascenzo F: Am JCardiol 116:325-331,2015

Surgical Recommendations for Treatment of FMR

Table 18. Summary of Recommendations for Chronic Severe Secondary MR

Recommendations	COR	LOE	References
MV surgery is reasonable for patients with chronic severe secondary MR (stages C and D) who are undergoing CABG or AVR	IIa	C	N/A
MV surgery may be considered for severely symptomatic patients (NYHA class III/IV) with chronic severe secondary MR (stage D)	IIb	B	(439,448–458)
MV repair may be considered for patients with chronic moderate secondary MR (stage B) who are undergoing other cardiac surgery	IIb	C	N/A

Table 13 Indications for mitral valve surgery in chronic secondary mitral regurgitation

	Class [a]	Level [b]
Surgery is indicated in patients with severe MR[c] undergoing CABG, and LVEF >30%.	I	C
Surgery should be considered in patients with moderate MR undergoing CABG.[d]	IIa	C
Surgery should be considered in symptomatic patients with severe MR, LVEF <30%, option for revascularization, and evidence of viability.	IIa	C
Surgery may be considered in patients with severe MR, LVEF >30%, who remain symptomatic despite optimal medical management (including CRT if indicated) and have low comorbidity, when revascularization is not indicated.	IIb	C

European Heart Journal (2012) 33, 2474

Evidence base
Therapy for MR

	Degenerative	Functional
Low Surgical Risk	✓ **Surgical Mitral Repair-registries** ✓ **EVEREST II**	✓ ? ✓ MVR
High Surgical Risk	✓ **Commercial MitraClip- TVT registry**	✓ **Global Practice-registries** ✓ **COAPT**

COAPT Trial: Clinical Outcomes Assessment of the MitraClip Percutaneous Therapy for High Surgical Risk

~420 patients enrolled at up to 75 US sites

Significant FMR >3+ core lab

High risk for mitral valve surgery – Local Heart Team

Specific valve anatomic criteria

Randomize 1:1

MitraClip

Control group
Standard of care

Saf
funct

Effec

Secondary MR with HF in 60 years old on MMT
- If high surgical risk: enrolled in the RCT
(COAPT in US, RESHAPE in OUS)
- If low surgical risk: MVR