Percutaneous Treatment of Mitral Insufficiency

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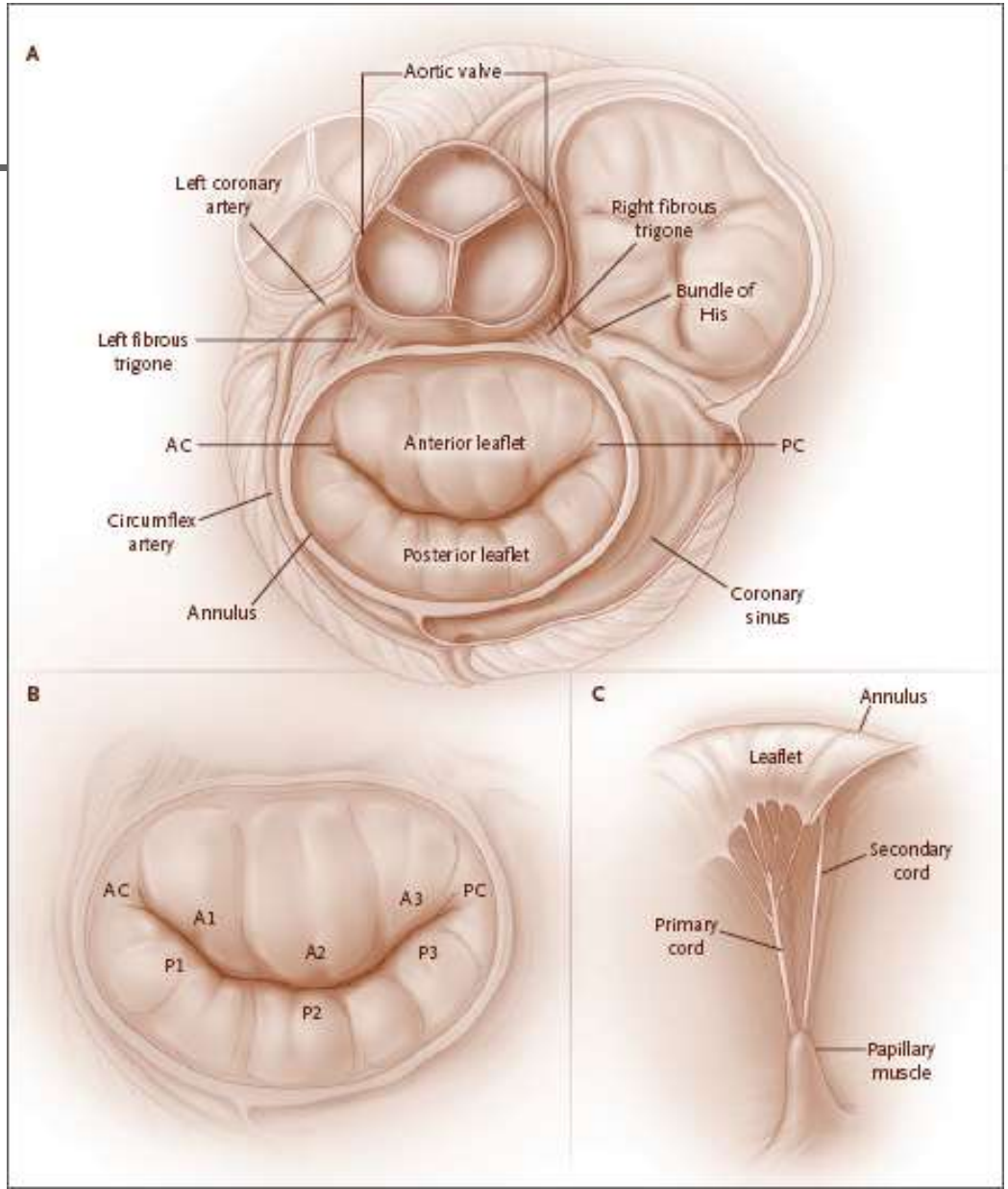
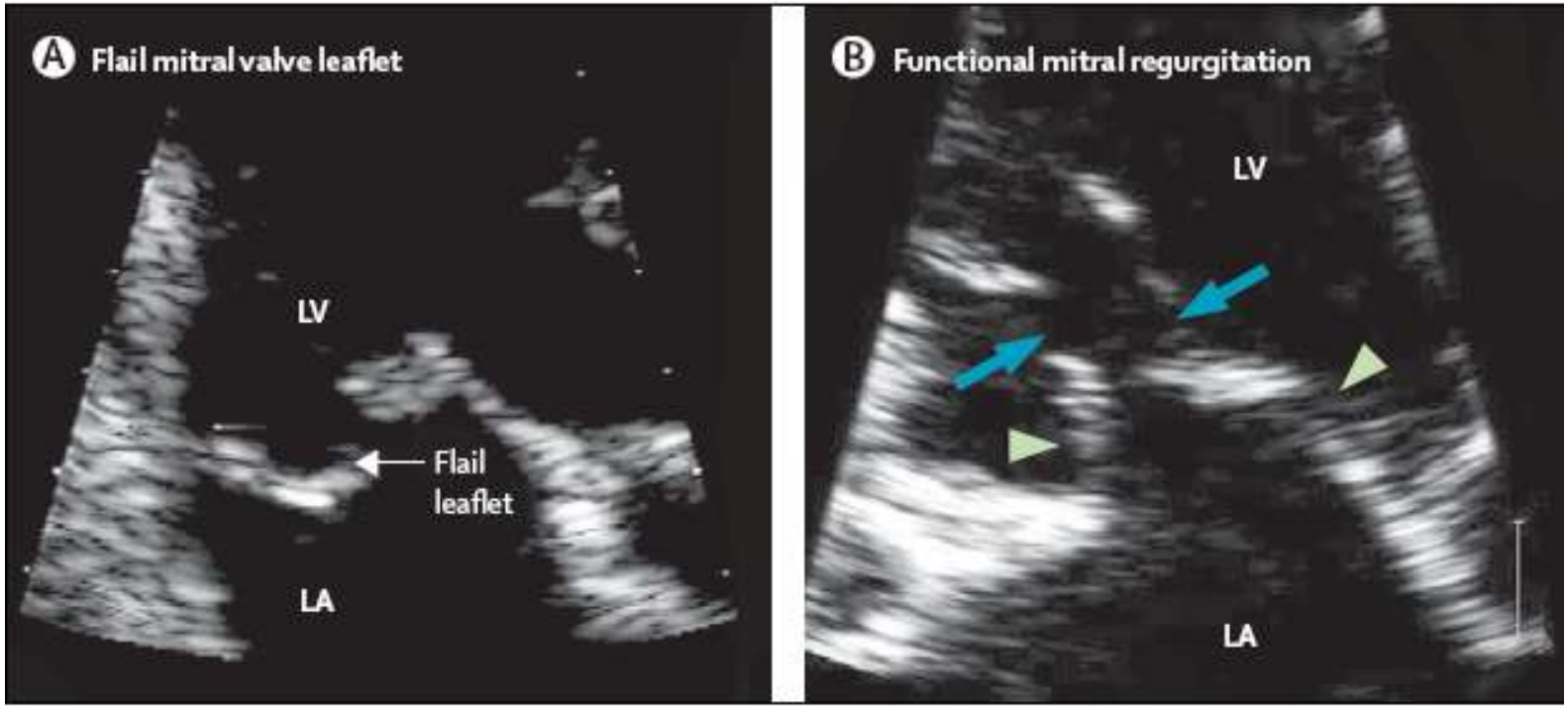
The Mitral Valve



Echocardiographic Appearance of the Two Anatomical Types of Mitral Regurgitation



Gradation of Mitral Regurgitation by Doppler Echocardiography

	Mild	Moderate	Severe
Specific signs	Small central jet <4 cm² or <10% of LA, vena contracta width <0·3 cm, no or minimum flow convergence	MR more than mild, without any criteria for severe MR	Vena contracta width ≥0·7 cm with large central MR jet (area >40% of LA) or with a wall-impinging jet of any size; large flow convergence; systolic reversal in pulmonary veins; prominent flail leaflet or ruptured papillary muscle
Supportive signs	Systolic dominant flow in pulmonary veins; A-wave dominant mitral inflow; low-density doppler MR signal; normal LV size	MR more than mild, but no criteria for severe MR	Dense, triangular doppler MR signal; E-wave dominant mitral inflow (>1·2 m/s); enlarged LV and LA, (particularly with normal LV function)
Quantitative variables			
RVol (mL per beat)	<30	30–44; 45–59	≥60
RF	<30%	30–39%; 40–49%	≥50%
ERO area (cm²)	<0·20	0·20–0·29; 0·30–0·39	≥0·40

Modified from Zoghbi and colleagues.[5] ERO=effective regurgitant orifice area. LA=left atrium. LV=left ventricle. MR=mitral regurgitation. RF=regurgitant fraction. RVol=regurgitant volume.

Table 2: **Gradation of mitral regurgitation by doppler echocardiography**

Mitral Regurgitation

Causes and Mechanisms of Mitral Regurgitation

	Organic			Functional
	Type I*	Type II†	Type IIIa‡	Type I*/Type IIIb‡
Non-ischaemic	Endocarditis (perforation); degenerative (annular calcification); congenital (cleft leaflet)	Degenerative (billowing/flail leaflets); endocarditis (ruptured chordae); traumatic (ruptured Chord/PM); rheumatic (acute RF)	Rheumatic (chronic RF); iatrogenic (radiation/drug); inflammatory (lupus/anticardiolipin, eosinophilic endocardial disease, endomyocardial fibrosis)	Cardiomyopathy; myocarditis; left-ventricular; dysfunction (any cause)
Ischaemic	..	Ruptured PM	..	Functional ischaemic

MR=mitral regurgitation. PM=papillary muscle. RF=rheumatic fever. *Mechanism involves normal leaflet movement. †Mechanism involves excessive valve movement. ‡Restricted valve movement, IIIa in diastole, IIIb in systole.

Echocardiographic Appearance of the Two Anatomical Types of Mitral Regurgitation

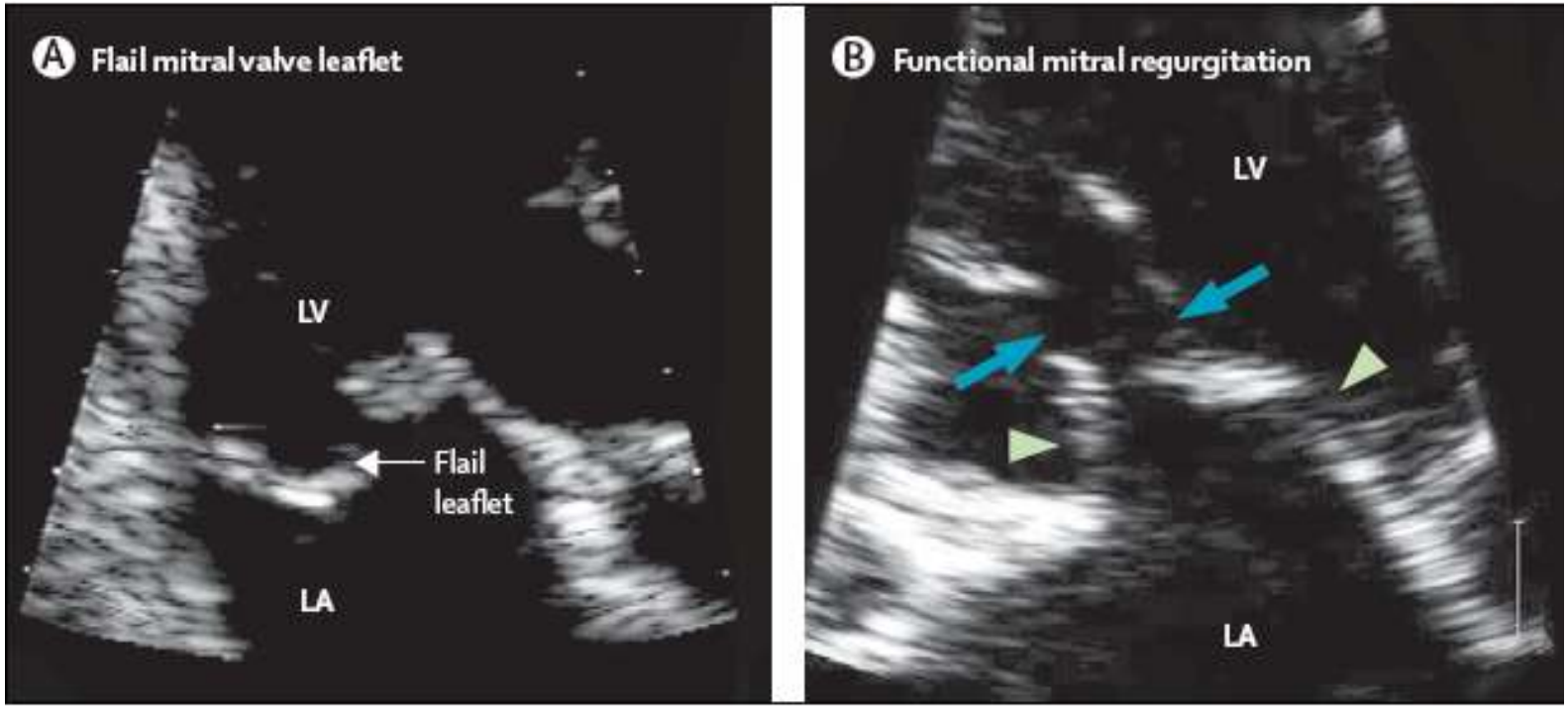


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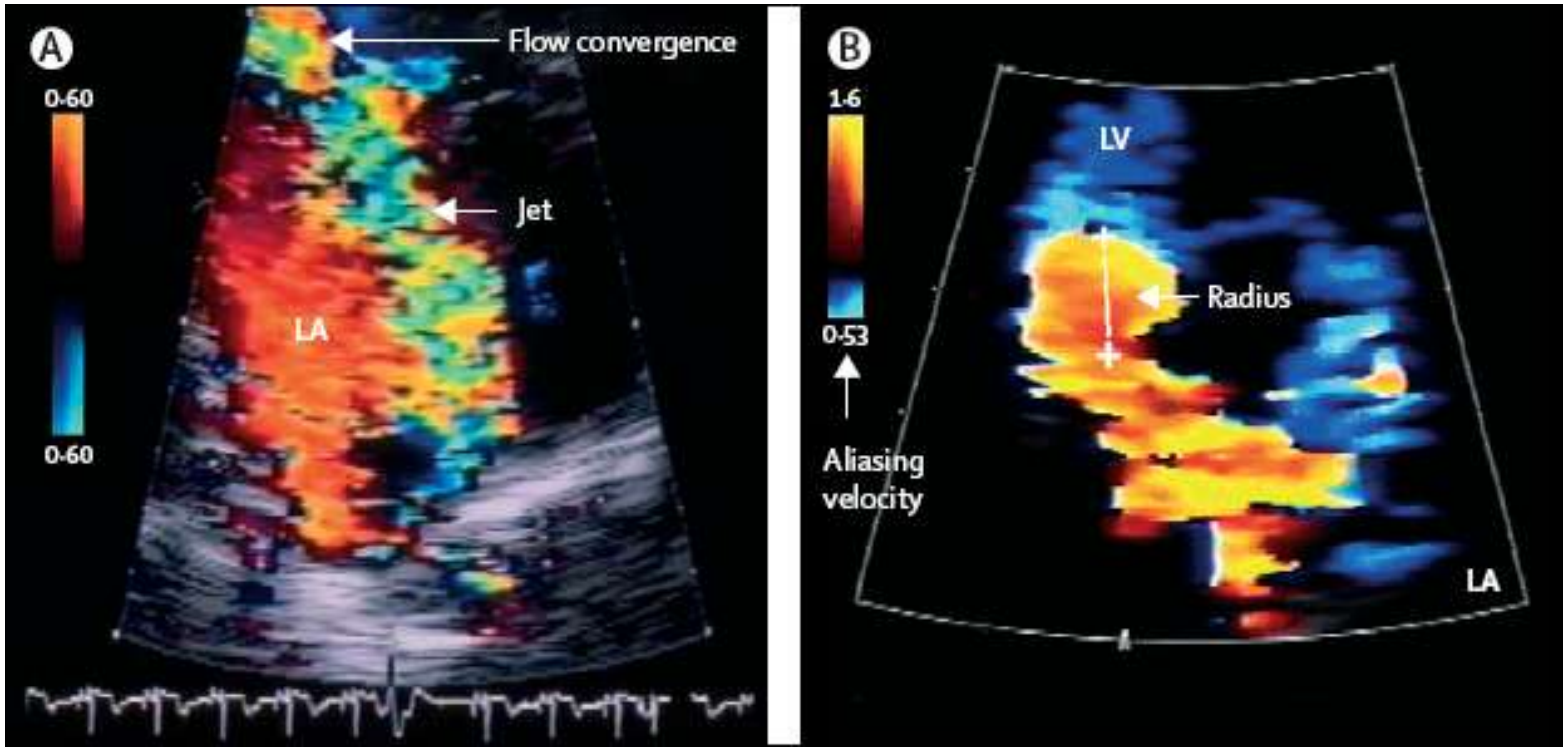
Table 2: **Gradation of mitral regurgitation by doppler echocardiography**

Use of Color-Flow Imaging for Assessment of Mitral Regurgitation



Vena Contracta

Proximal Isovelocity Surface Area (PISA)

Clinical Outcome of Organic Mitral Regurgitation Under Medical Management

	Number of patients	Symptoms	MR cause	MR severity	Age (years)	LV diameter (mm)	Study specifics	Yearly mortality	Yearly cardiac events	Relative risk (95% CI) with surgery
Enriquez-Sarano, et al[9]*†	129	0	Organic	Moderate (ERO area 20–39 mm²)	65	56	Quantitative; prospective	3%‡	8%	..
Rosenhek, et al[81]*	132	0	Degenerative	Moderate to severe	55	56	Referral centre; prospective	1%	6%	..
Avierinos, et al[83]*	153	0	MVP	Moderate to severe	60	58	Community based	6%	14%	..
Ling, et al[84]§	229	19%	Flail leaflets	Severe	66	64	Cause specific	6·3% overall; 4·1% without symptoms	10–11%	0·29 (0·15–0·56)
Grigioni, et al[67]§	360	19%	Degenerative in SR	Severe	65	60	Cause specific	6%	10–11%	..
Rosen, et al[80]§	31	0	Organic	Severe	52	65	Prospective with exercise	..	10%	..
Enriquez-Sarano, et al[9]§†	198	0	Organic	Severe (ERO area ≥40 mm²)	61	61	Quantitative; prospective	9%	15%	0·28 (0·14–0·55)

ERO=effective regurgitant orifice. LV=left ventricle. MR=mitral regurgitation. MVP=mitral valve prolapse. SR=sinus rhythm. *Data for patients with exclusively or mostly moderate MR (as shown by slight ventricular enlargement or quantitative measures), showing average yearly mortality of about 3%. †Mortality computed during the first 3 years of follow-up. ‡Part of the same study of 456 asymptomatic patients with quantified MR. §Data for patients with exclusively or mostly severe mitral regurgitation (as shown by substantial ventricular enlargement or quantitative measures), showing average yearly mortality of about 6%. Outcome after surgery was markedly improved, mortality decreased by about 70%.

Table 3: **Clinical outcome of organic mitral regurgitation under medical management**

Indications for Surgery in Chronic Mitral Regurgitation

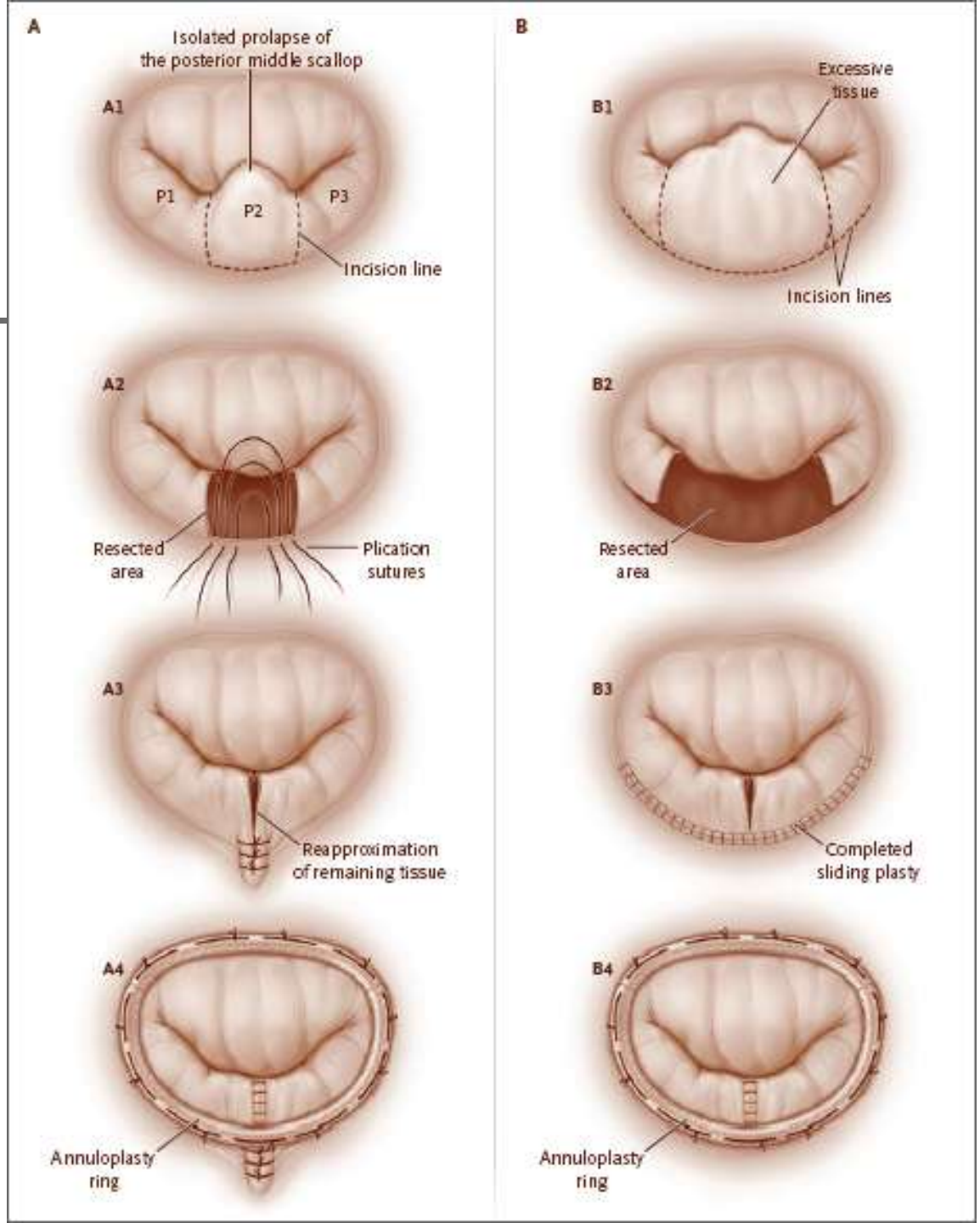
Table 8 Indications for surgery in severe chronic organic mitral regurgitation

	Class
Symptomatic patients with LVEF >30% and ESD <55 mm	IB
Asymptomatic patients with LV dysfunction (ESD >45 mm[a] and/or LVEF ≤60%)	IC
Asymptomatic patients with preserved LV function and atrial fibrillation or pulmonary hypertension (systolic pulmonary artery pressure >50 mmHg at rest)	IIaC
Patients with severe LV dysfunction (LVEF <30% and/or ESD >55 mm)[a] refractory to medical therapy with high likelihood of durable repair, and low comorbidity	**IIaC**
Asymptomatic patients with preserved LV function, high likelihood of durable repair, and low risk for surgery	**IIbB**
Patients with severe LV dysfunction (LVEF <30% and/or ESD >55 mm)[a] refractory to medical therapy with low likelihood of repair and low comorbidity	**IIbC**

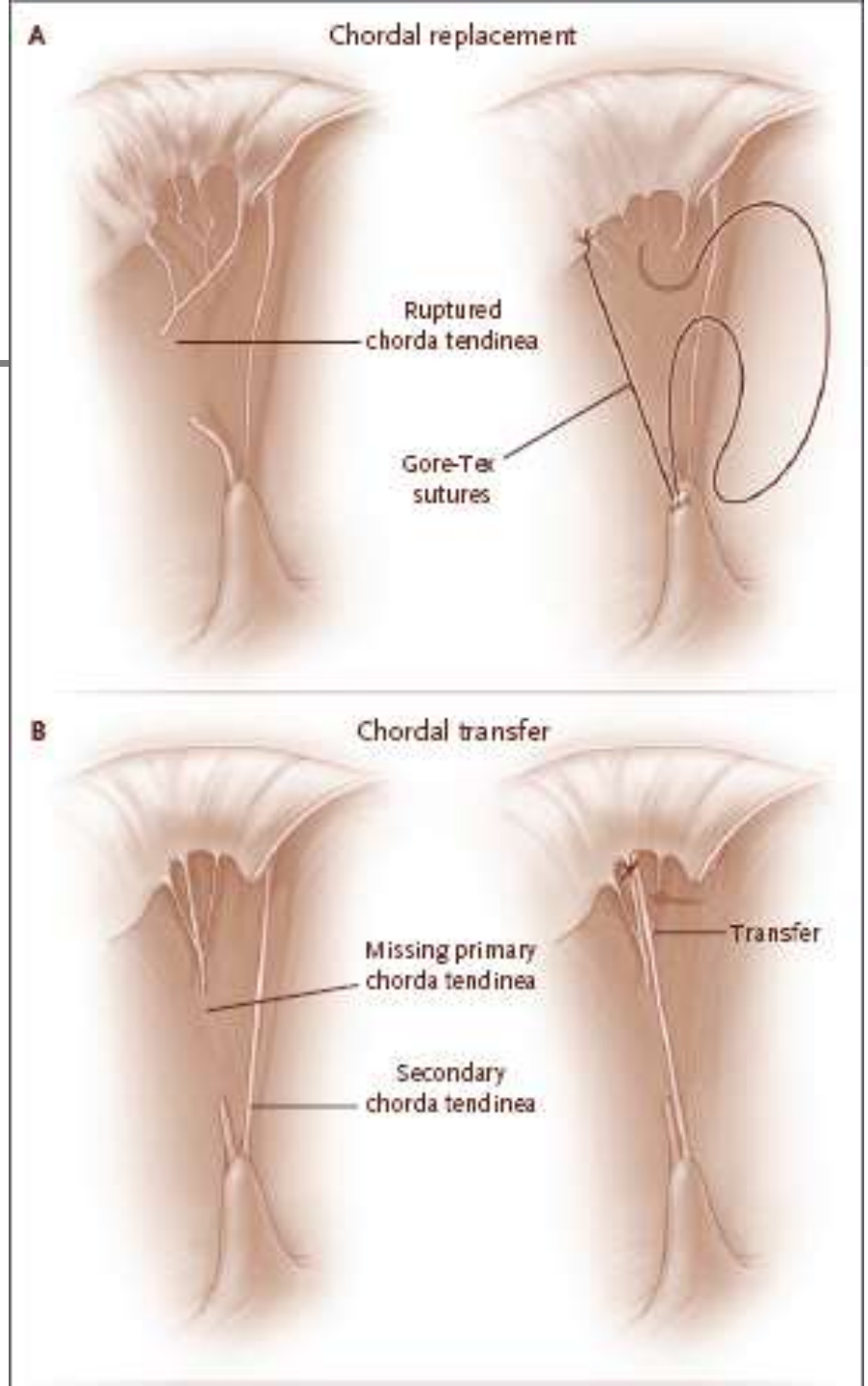
Table 9 Indications for surgery in chronic ischaemic mitral regurgitation

	Class
Patients with severe MR, LVEF >30% undergoing CABG	IC
Patients with moderate MR undergoing CABG if repair is feasible	IIaC
Symptomatic patients with severe MR, LVEF <30% and option for revascularization	IIaC
Patients with severe MR, LVEF >30%, no option for revascularization, refractory to medical therapy, and low comorbidity	**IIbC**

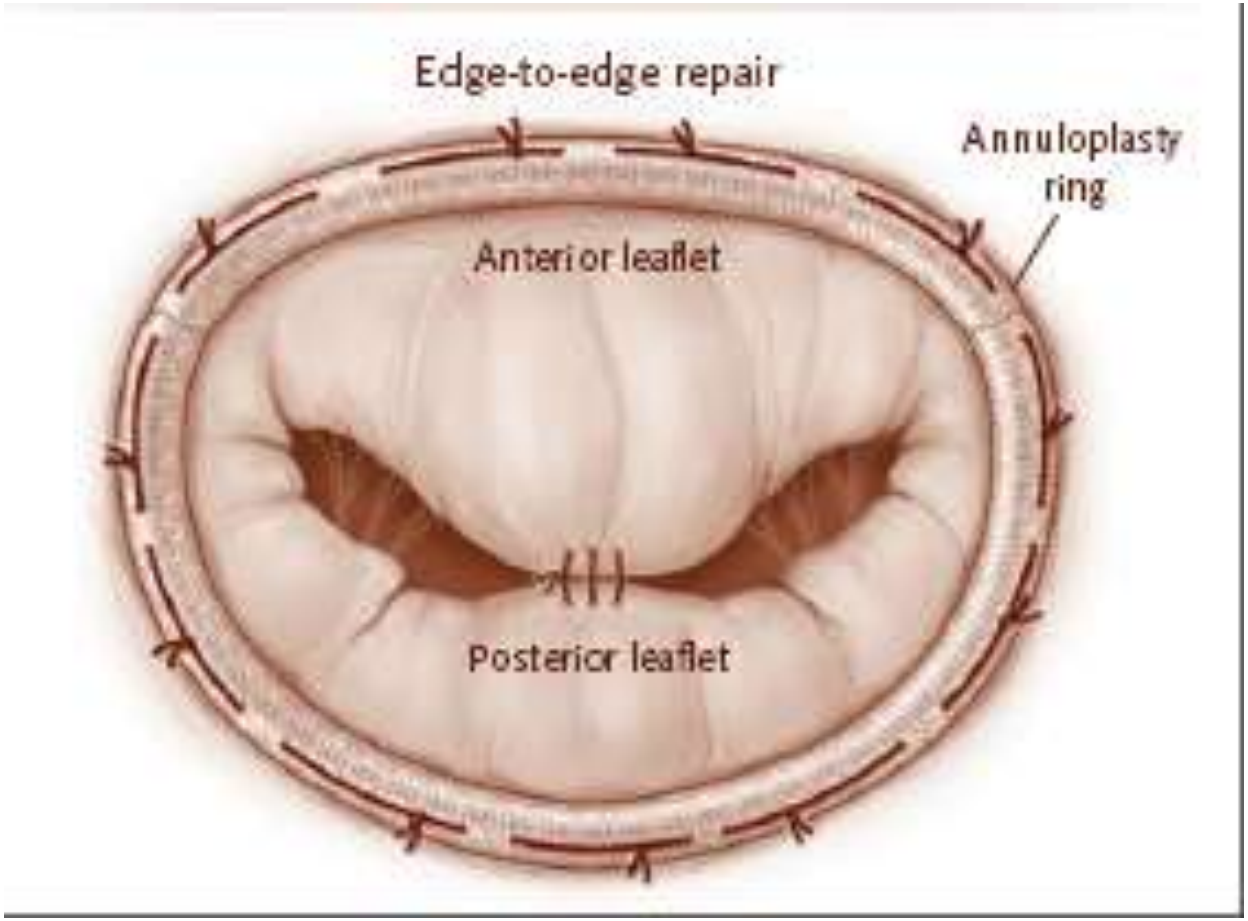
Mitral Valve Prolapse and Correction



Repair Techniques



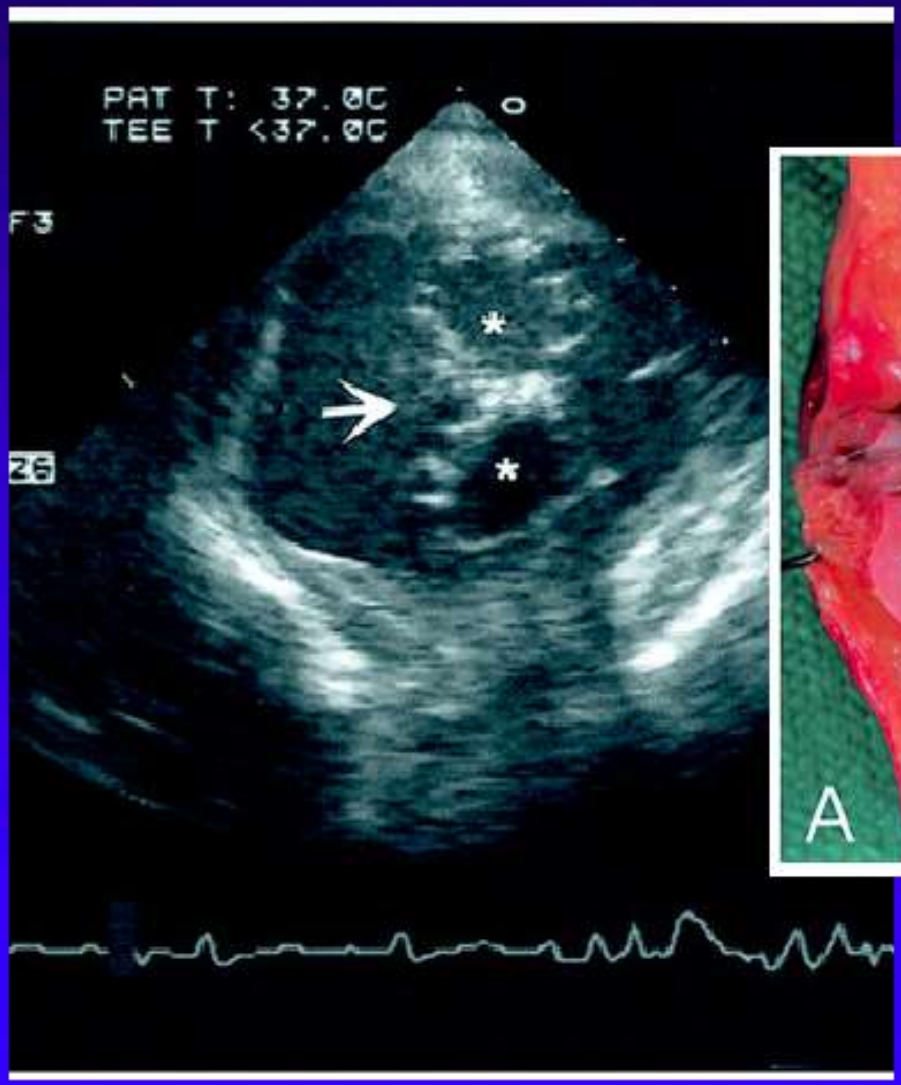
Edge–to-edge Repair

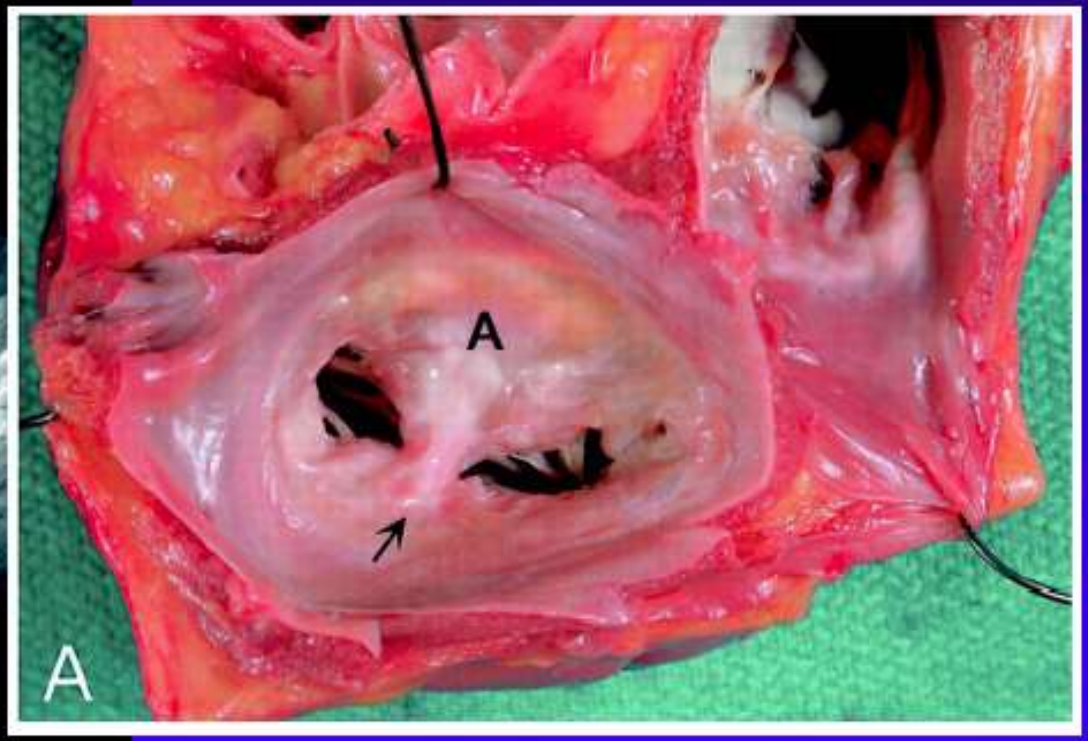


Images in Cardiovascular Medicine

Alfieri Mitral Valve Repair

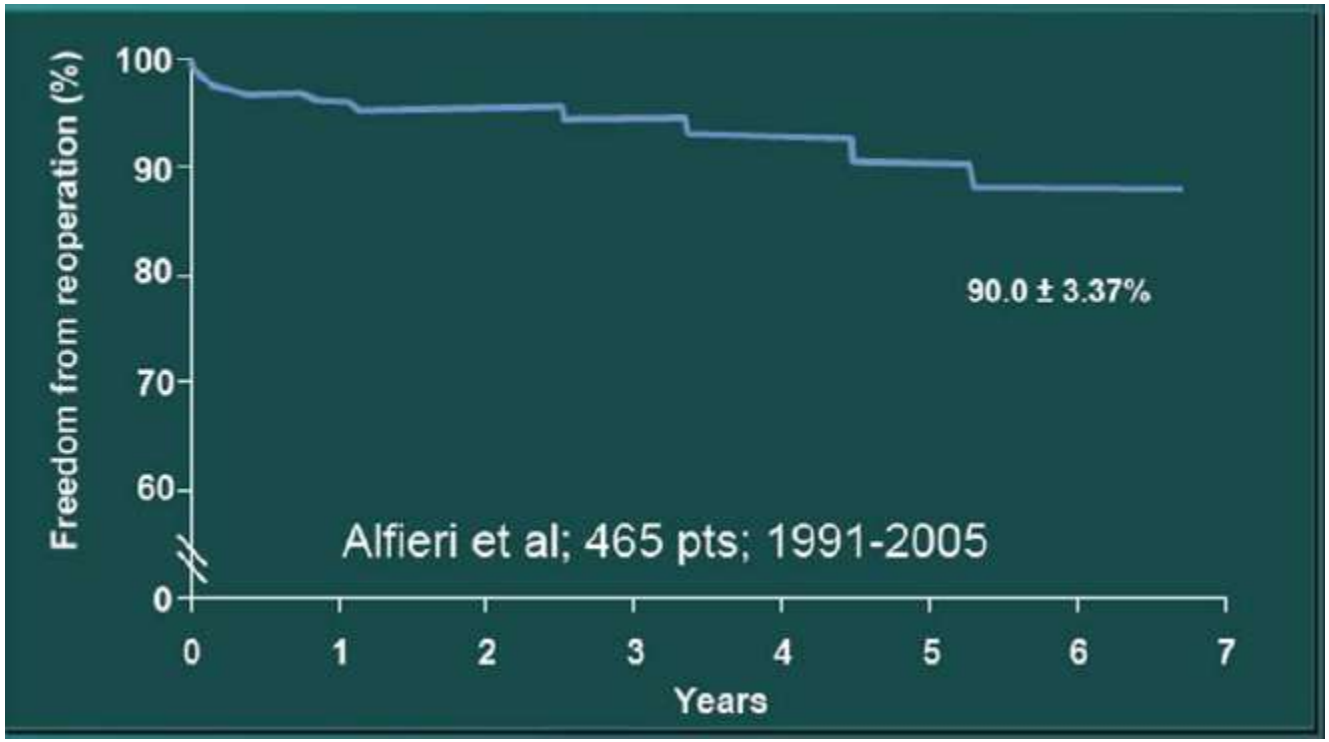
Clinical Outcome and Pathology





Circulation. 2002;106:e173

Alfieri technique. Long-term Follow-up



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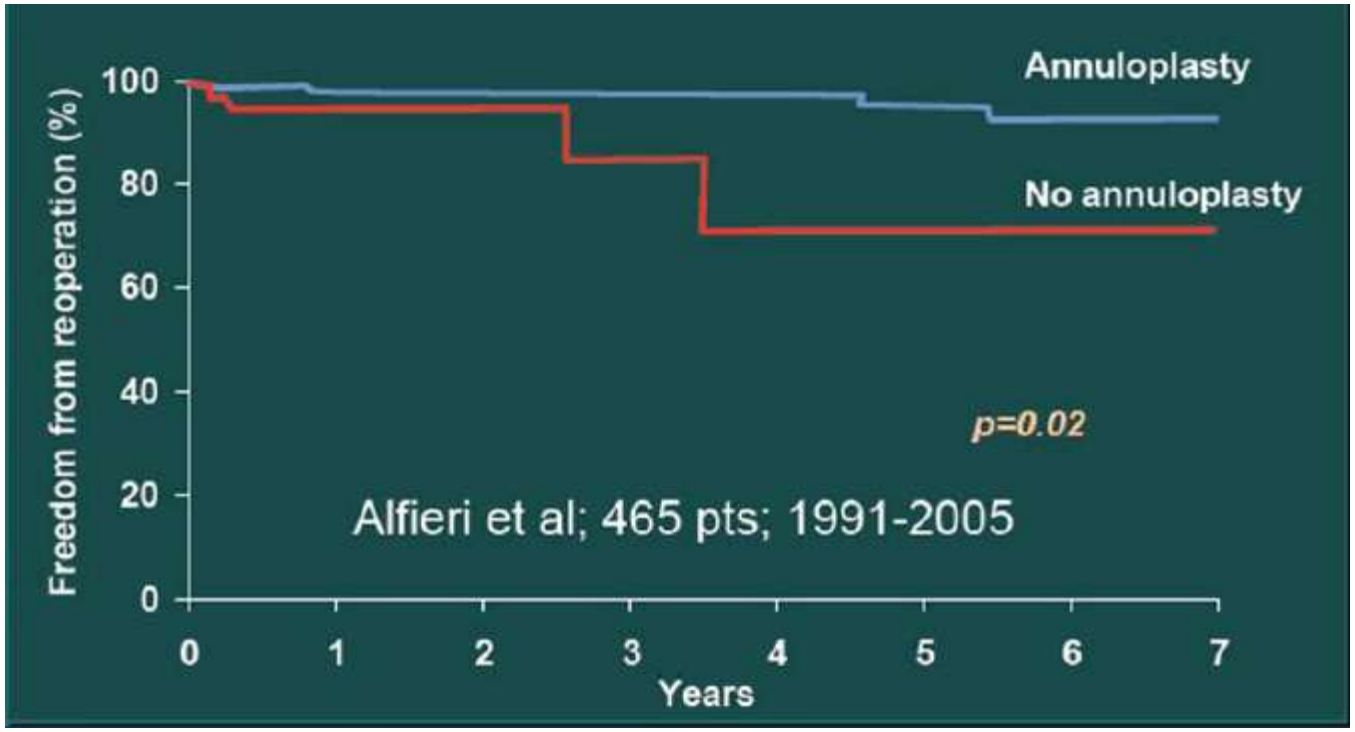
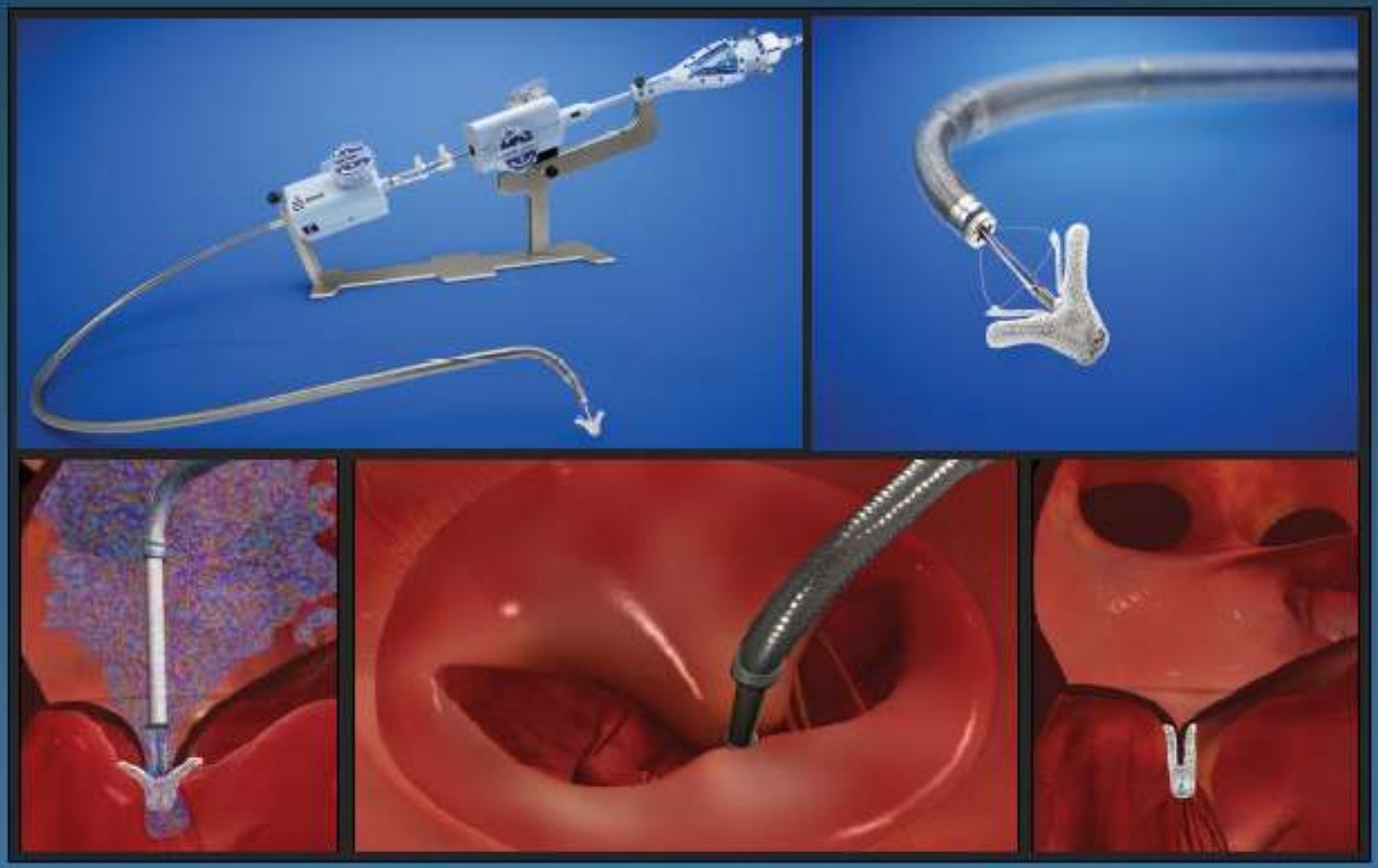


Techniques for Percutaneous Reduction of Mitral Insufficiency

- Edge-to-edge repair
- Coronary sinus annuloplasty
- Transventricular approach

Percutaneous Mitral Valve Repair
MitraClip® System



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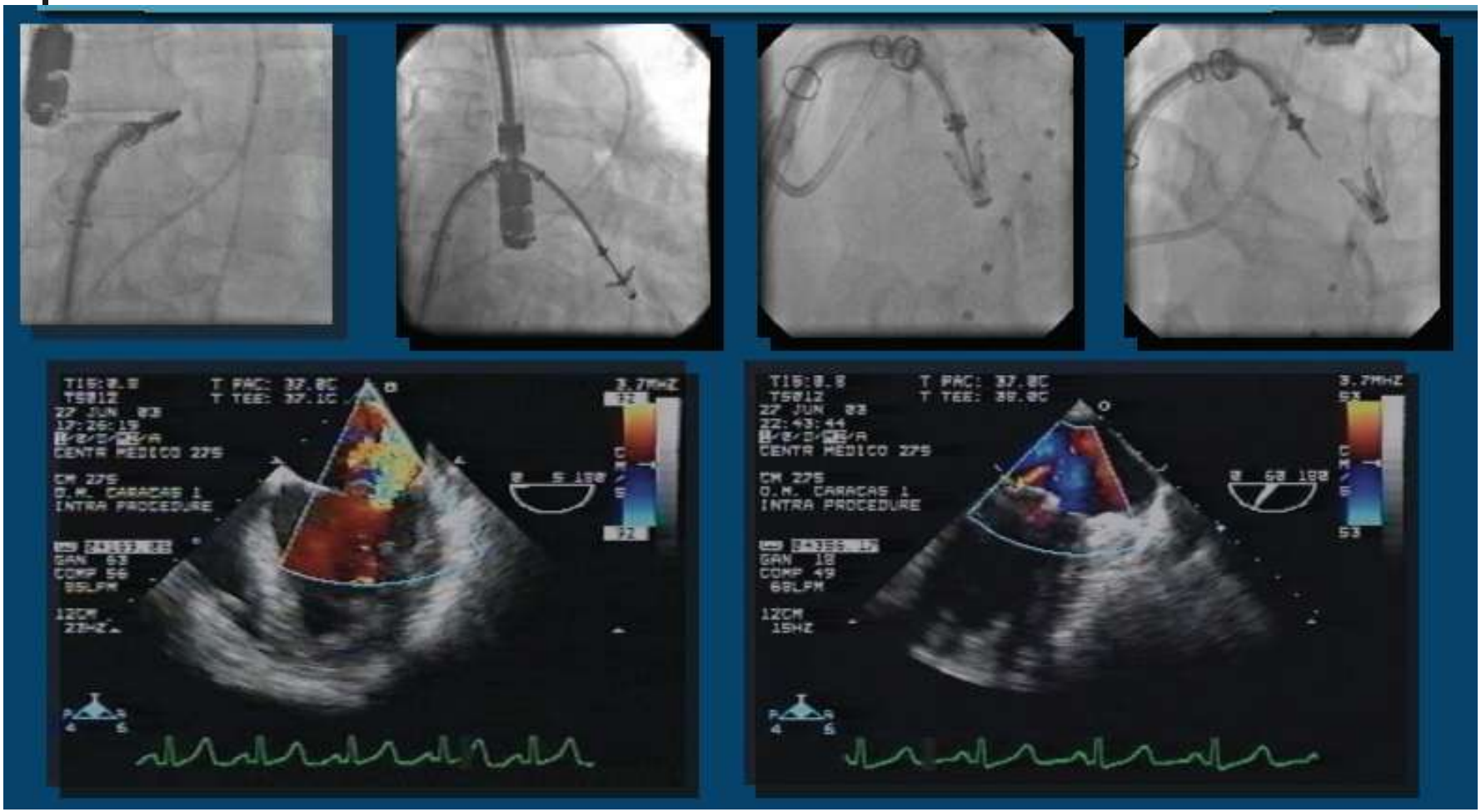
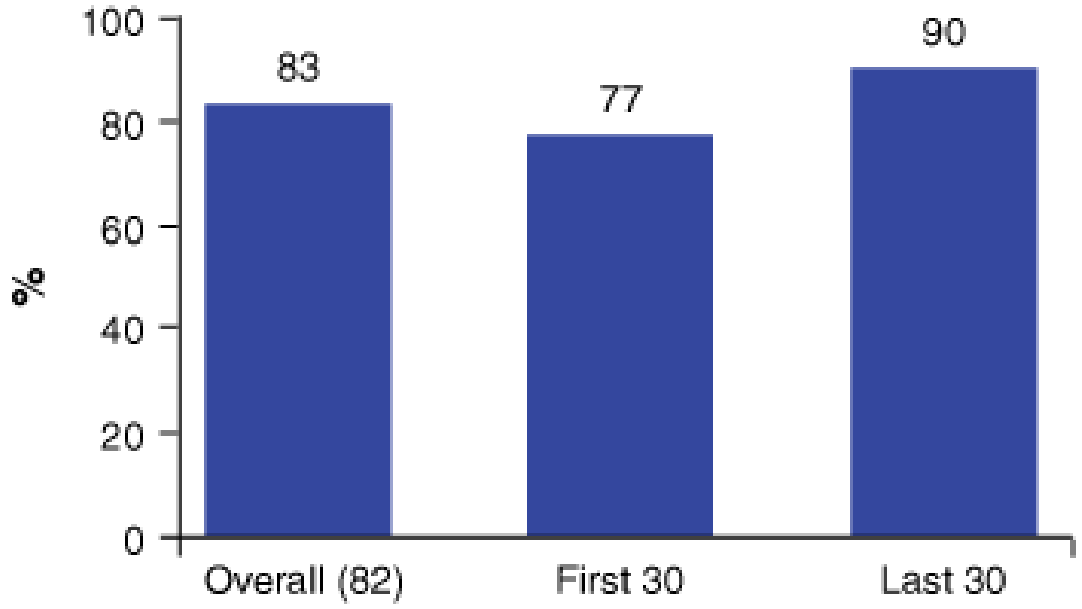
E-valve. First Case Performed



Evalve Clip Patients: Acute Procedural Success*
(n = 82)



*Defined as placement of one or more clips resulting in discharge mitral regurgitation severity of 2+ or less, as determined by core lab

Study Design

EVEREST II Randomized Controlled Trial (RCT)

279 Patients enrolled at 37 sites

Significant MR (3+ or 4+)
Specific Anatomical Criteria

↓

Randomized 2:1

Percutaneous Group
MitraClip System
N=184

Surgery Group
Surgical Repair or Replacement
N=95

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

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%)	

Primary Effectiveness Endpoint

- Effectiveness defined as freedom from death, MV surgery/re-operation or 3+ or 4+ MR
- Two analyses performed:
  1. Intention to Treat
     - Any mitral valve surgery following percutaneous repair was considered an "endpoint" event
  2. Comparison of Treatment Strategies
     - Mitral valve surgery following unsuccessful in-hospital percutaneous repair is not considered an "endpoint" event

Primary Effectiveness Analyses at 1 and 2 Years

Intention to Treat Analysis

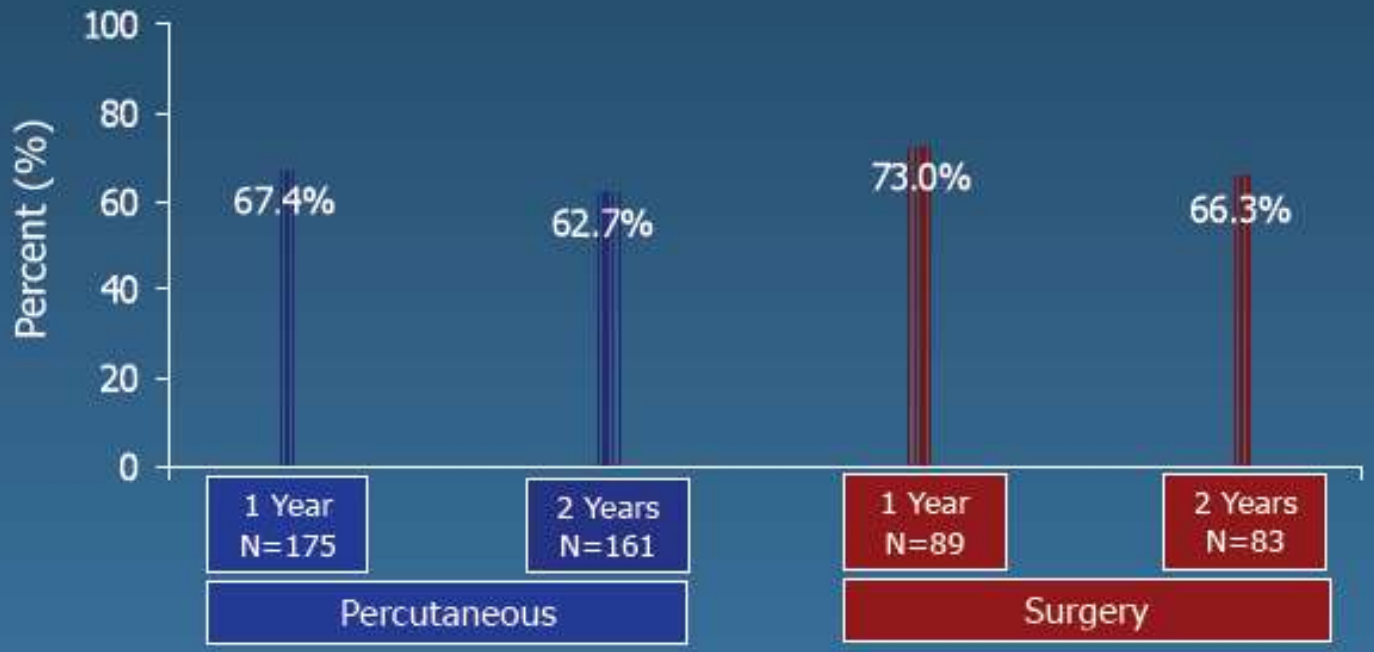
Primary Effectiveness:
Freedom from death, MV surgery/re-operation or 3+ or 4+ MR

Randomized not treated patients assigned MR 3+ or 4+ at 1 and 2 years
(Percutaneous N=6, Surgery N=15)

Primary Effectiveness Analyses at 1 and 2 Years

Comparison of Treatment Strategy Analysis

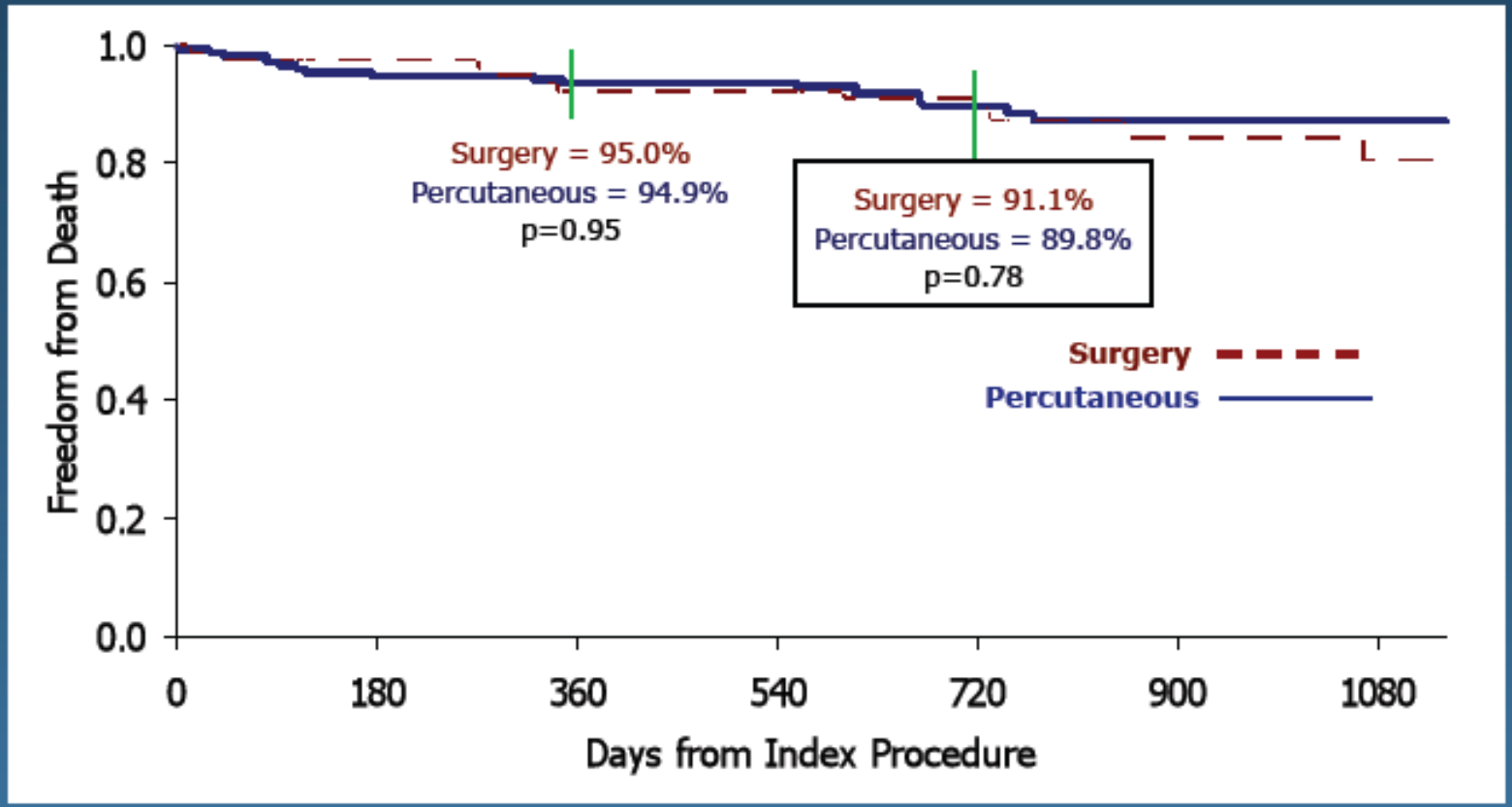
Primary Effectiveness:
Freedom from death, MV surgery/re-operation or 3+ or 4+ MR



Randomized not treated patients assigned MR 3+ or 4+ at 1 and 2 years
(Percutaneous N=6, Surgery N=15)

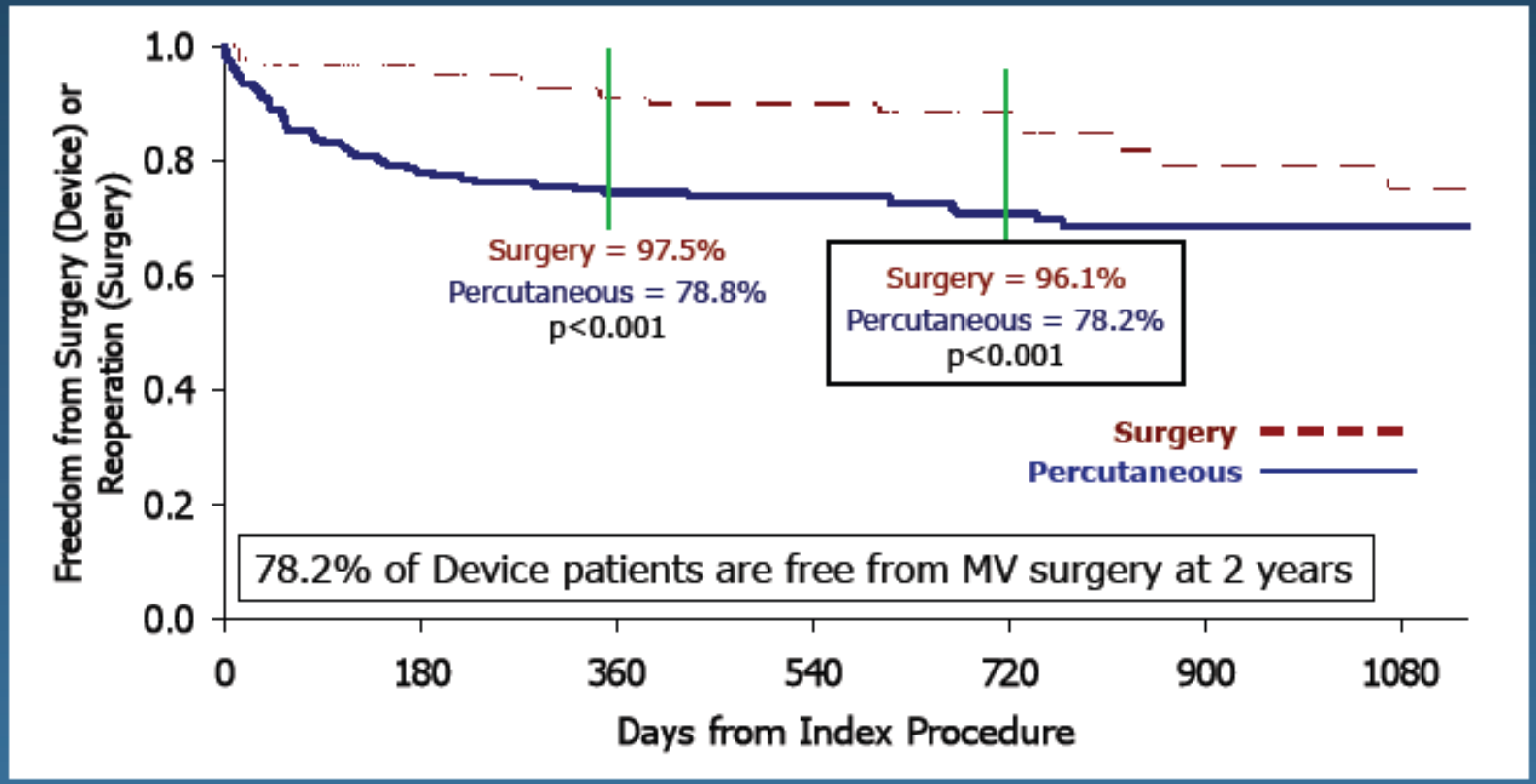
Kaplan-Meier Freedom from Death

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

Kaplan-Meier Freedom from MV Surgery (Device) or 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	69	24

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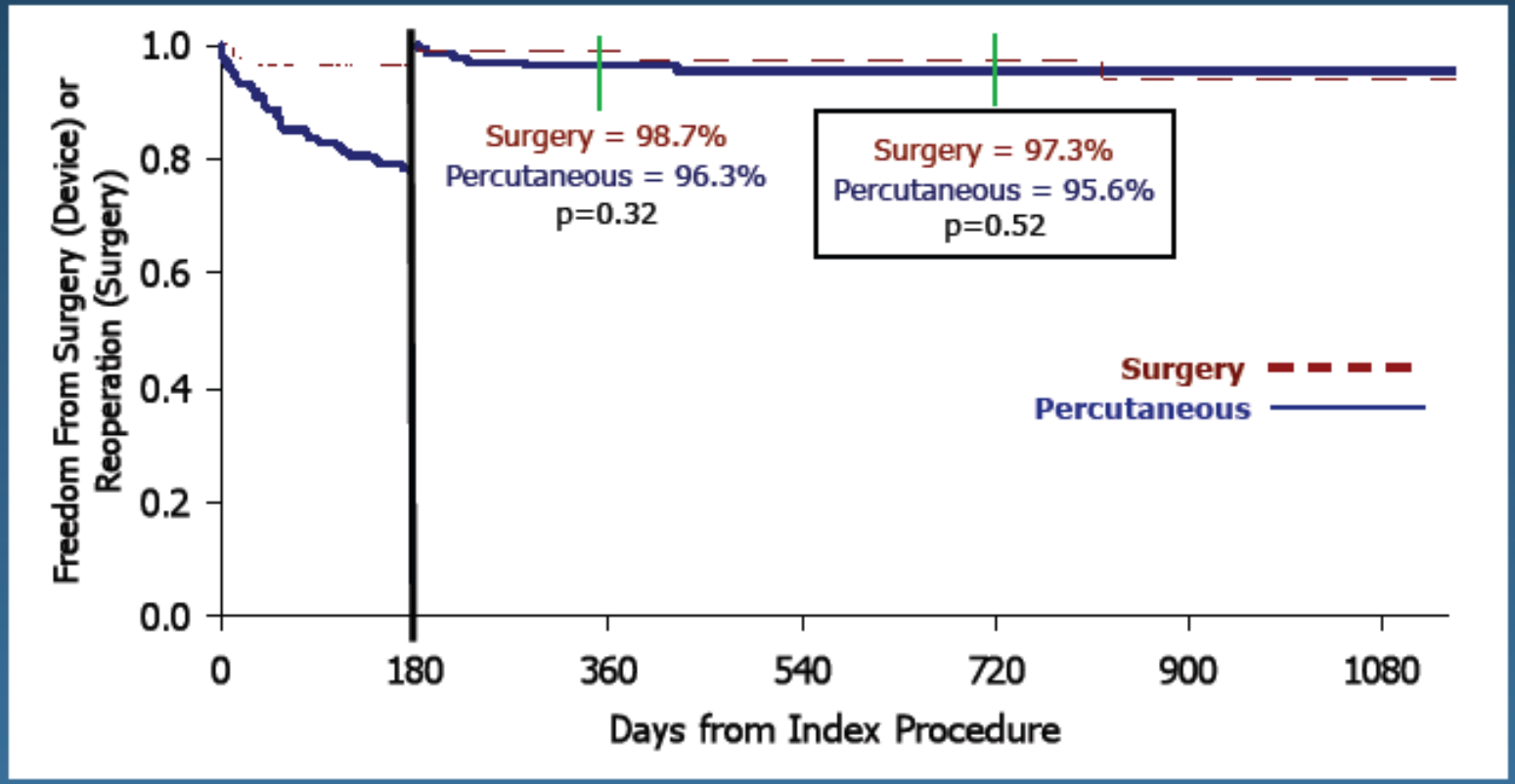
Landmark Analysis of Kaplan-Meier
Freedom from MV Surgery (Percutaneous)/Re-operation (Surgery)
Intention to Treat



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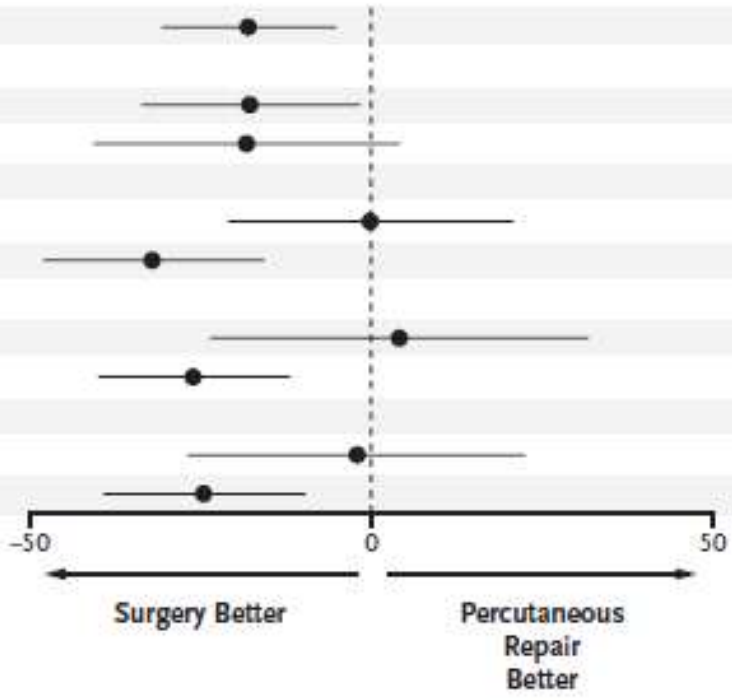
Subgroup Analysis for Primary End-Point at 12 Months

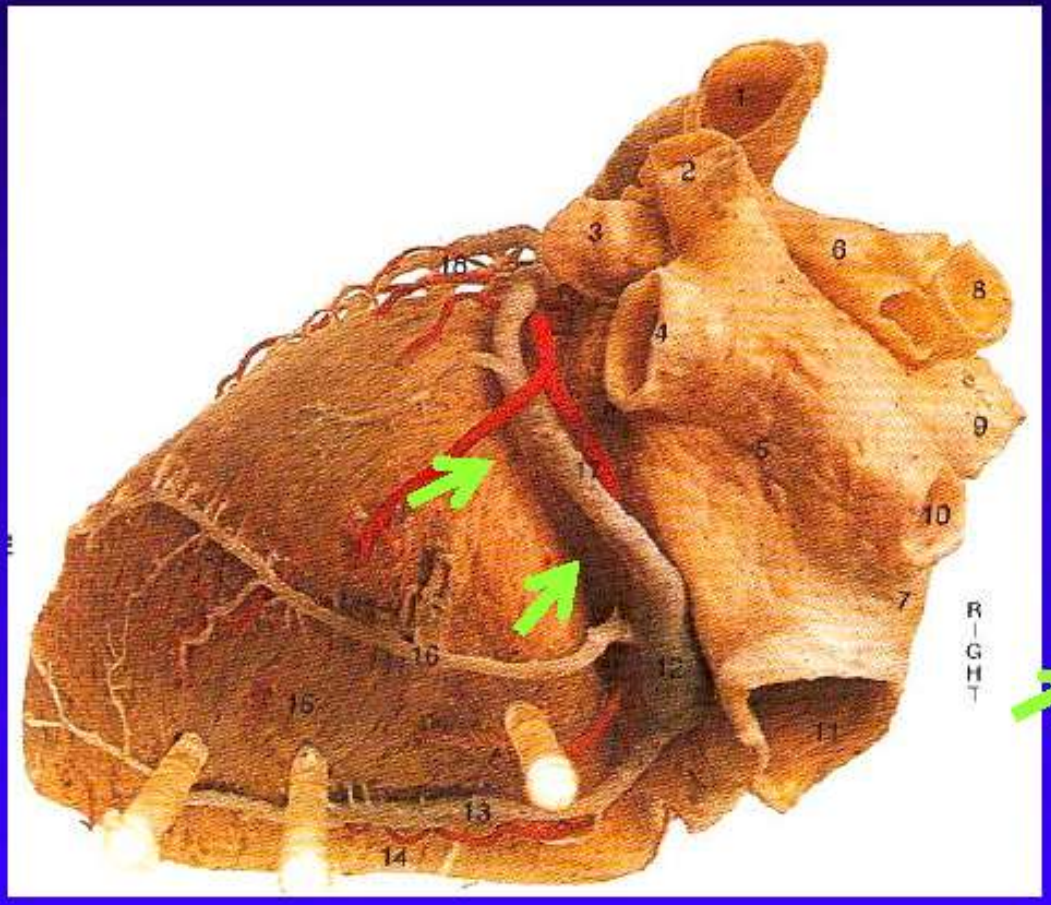
Subgroup	Percutaneous Repair	Surgery	P Value for Interaction
	no. of events/total no. (%)		
All patients	100/181 (55)	65/89 (73)	
Sex			0.97
Male	63/114 (55)	43/59 (73)	
Female	37/67 (55)	22/30 (73)	
Age			0.009
≥70 yr	52/86 (60)	23/38 (61)	
<70 yr	48/95 (51)	42/51 (82)	
MR			
Functional	26/48 (54)	12/24 (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)	

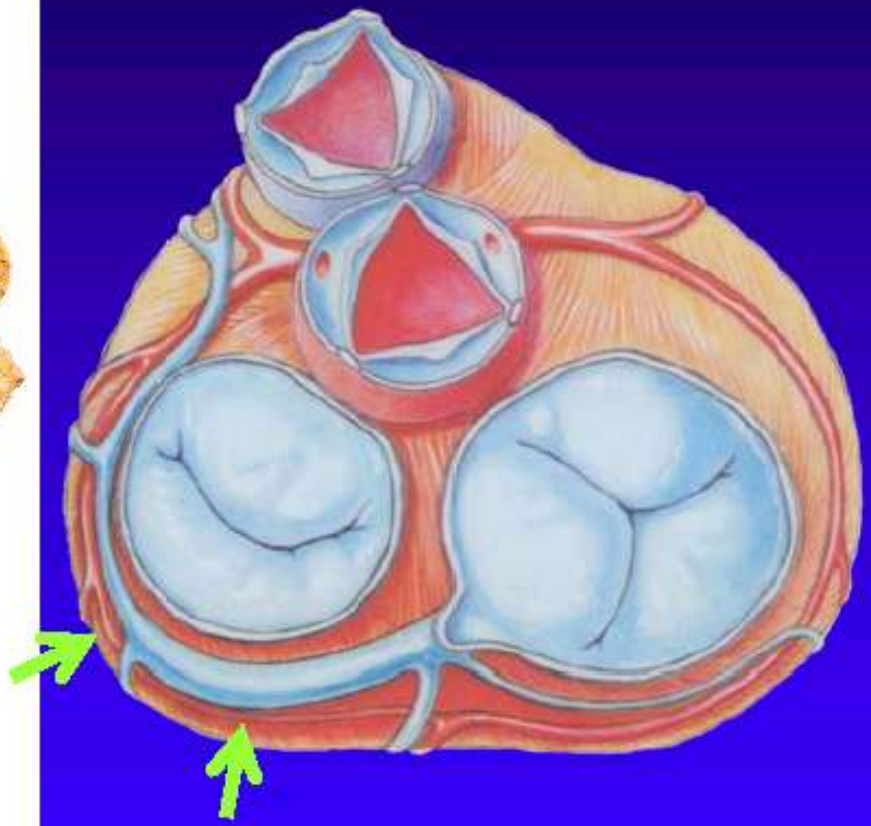


EVEREST II-Conclusions

- Percutaneous repair was less effective than surgery in reducing mitral regurgitation before hospital discharge
- However, at 12 and 24 months the rates of reduction were similar
- Percutaneous treatment was associated with increased safety

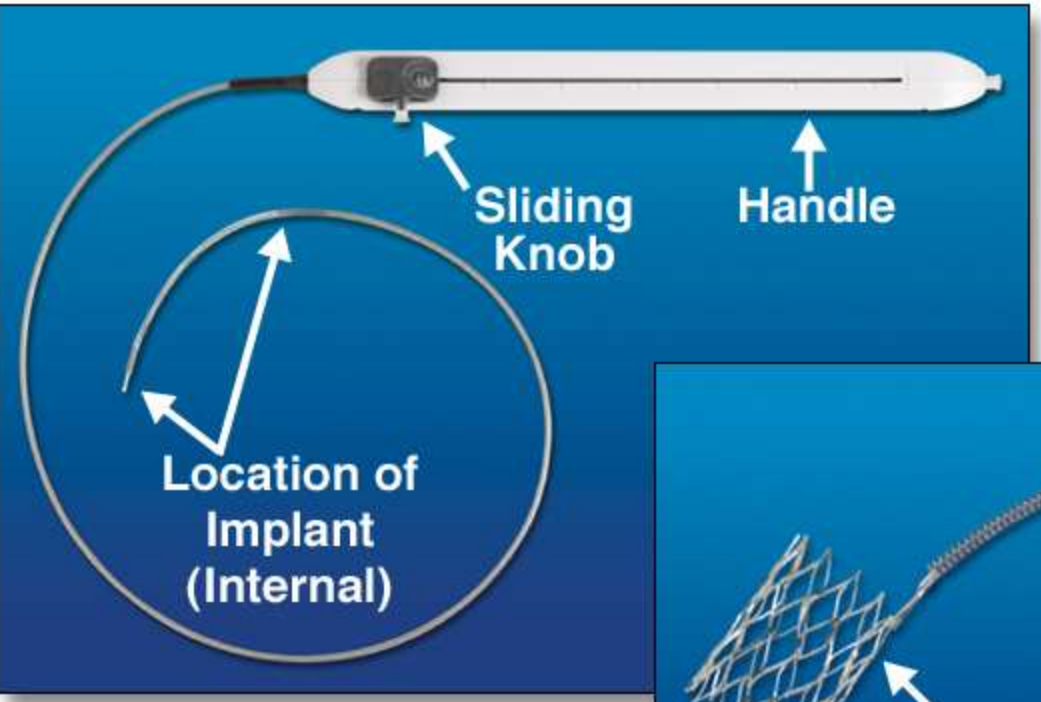
Relationship of Coronary Sinus to Mitral Valve



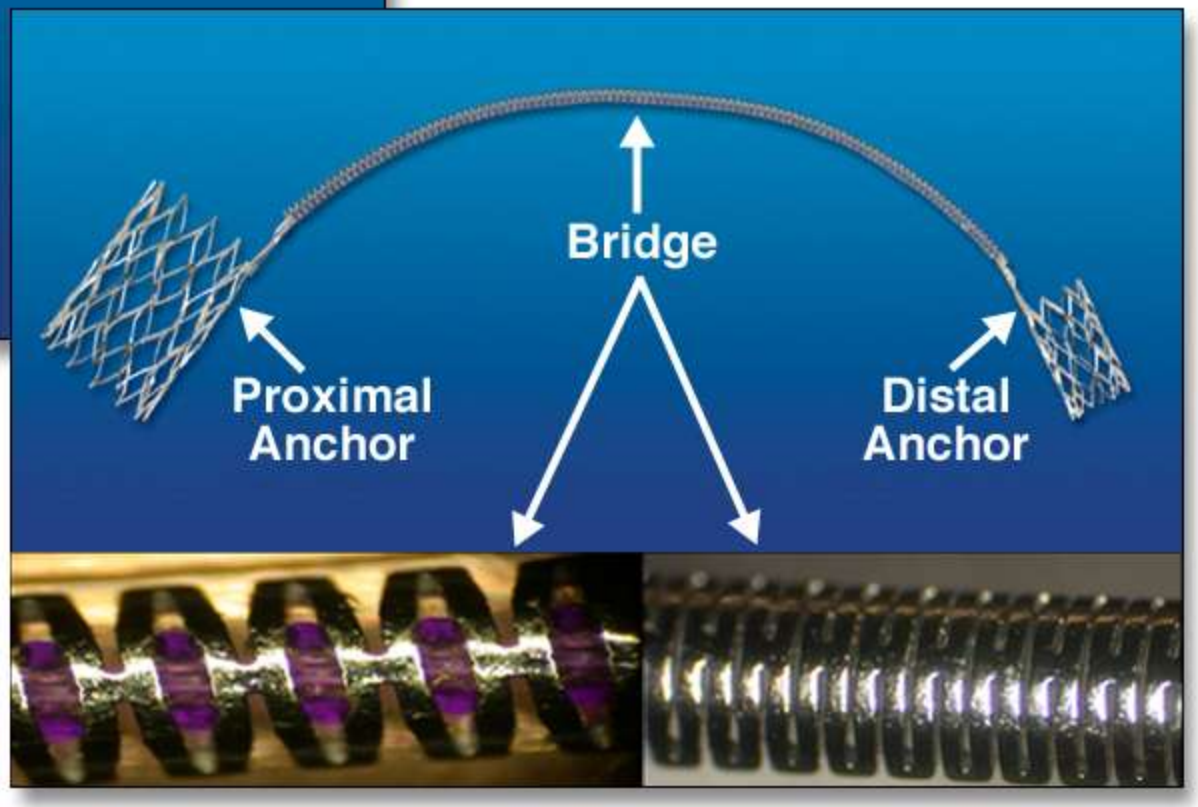


Coronary Sinus Parallels Mitral Valve Annulus

Edwards MONARC™ System



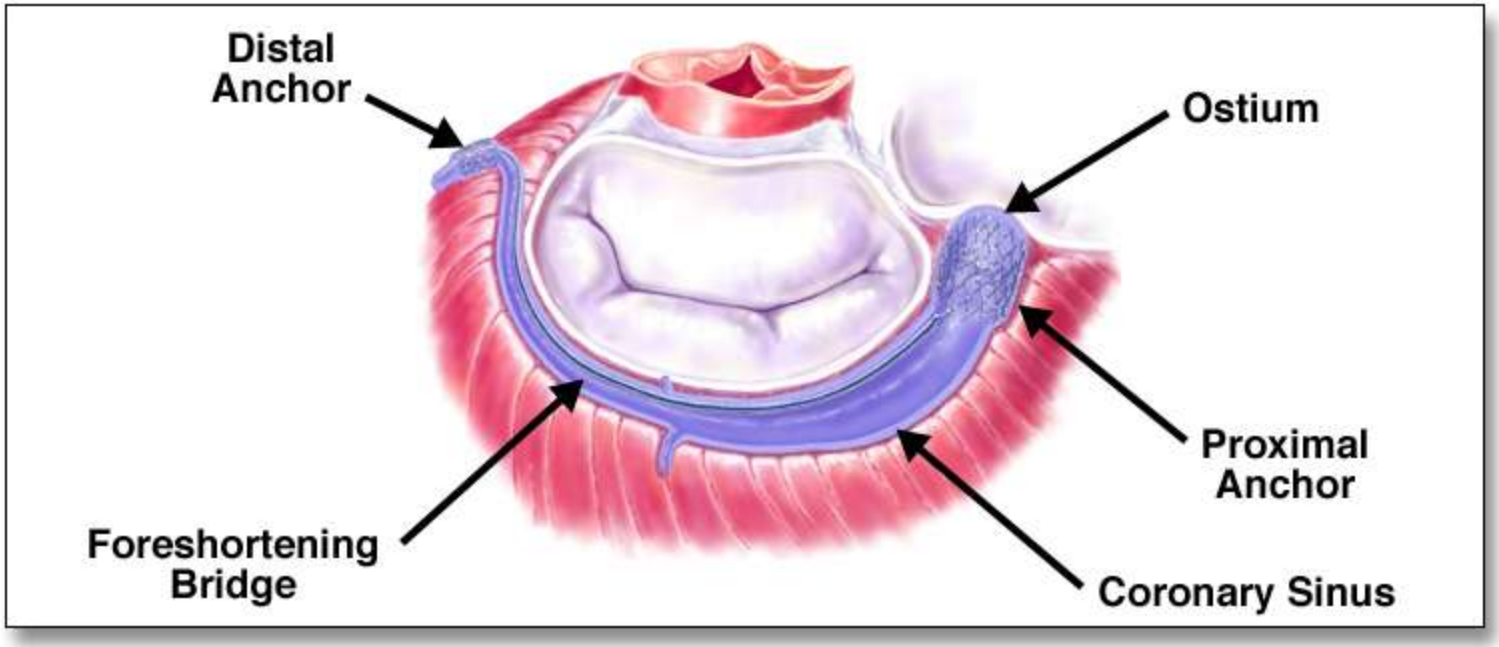
12F guiding catheter
9F delivery system

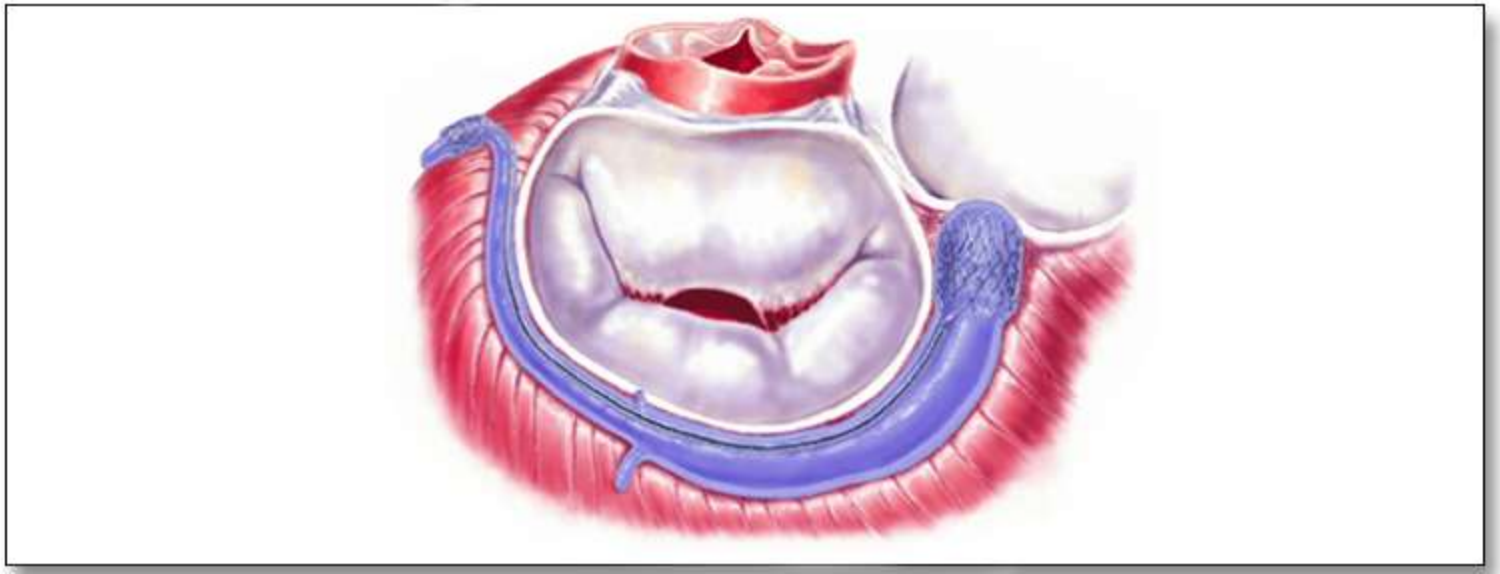


Elongated bridge at implant

Foreshortened state at ~6 weeks

The MONARC™ System Is Designed to Gradually Change the Geometry of the Heart

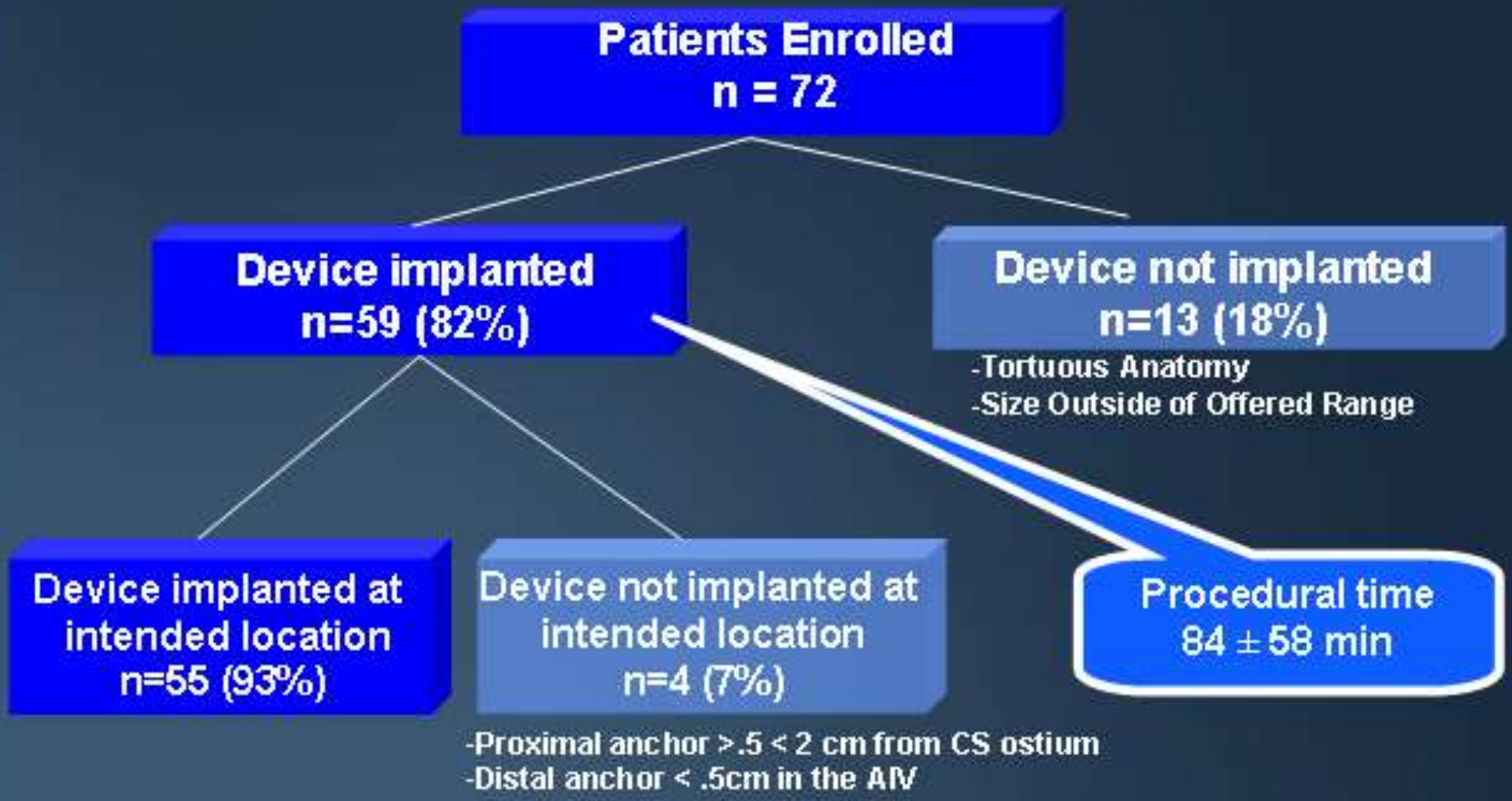




EVOLUTION Study Overview

- Prospective, multi-center feasibility study
- Primary objective of the study is to evaluate the acute safety (30d, 90d) of the MONARC system in treating functional mitral regurgitation in heart failure patients
- Secondary objective of the study is reduction in MR by at least one grade at 90 days

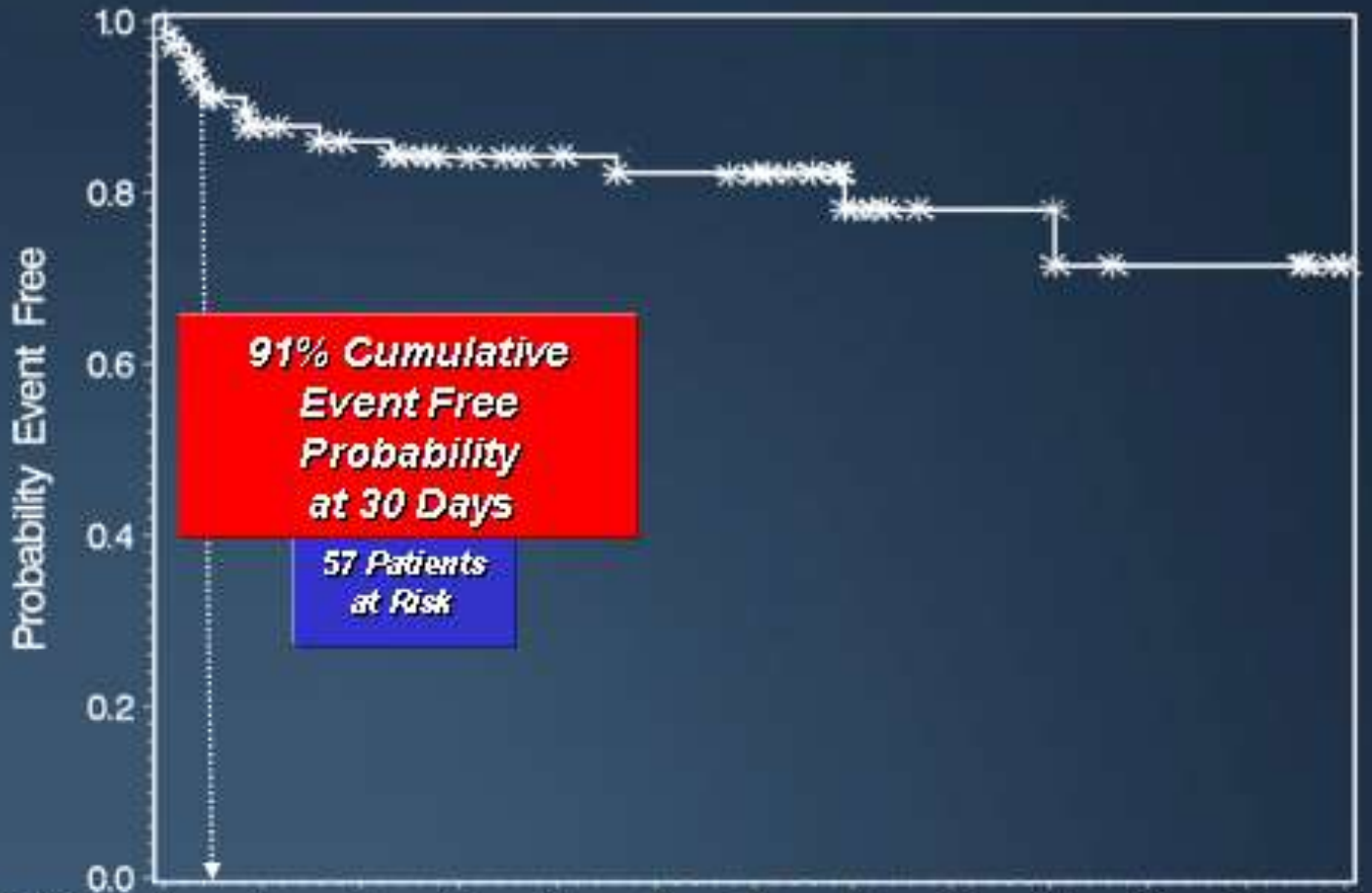
Procedural Success



20 YEARS OF INNOVATION TCT 2008

Primary Safety

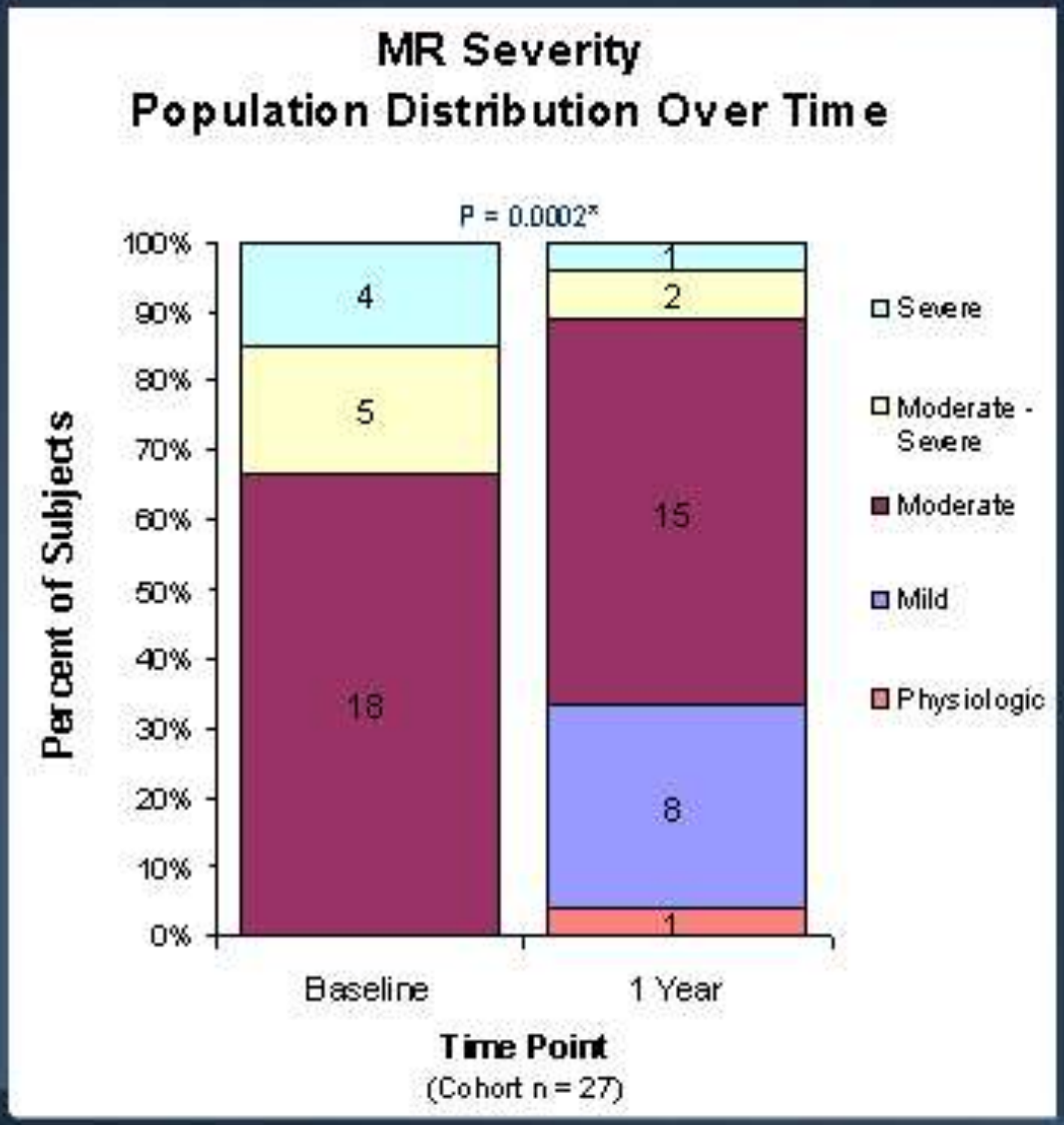
Death, Myocardial Infarction or Cardiac Tamponade



Months	0	2	4	6	8	10	12	14	16	18	20	22	24
N Pts @ risk	72	57	51	45			35						5
Cum Events	0	6	8	10			11						13
Probability		0.91	0.88	0.84			0.82						0.72

CARDIOVASCULAR RESEARCH FOUNDATION

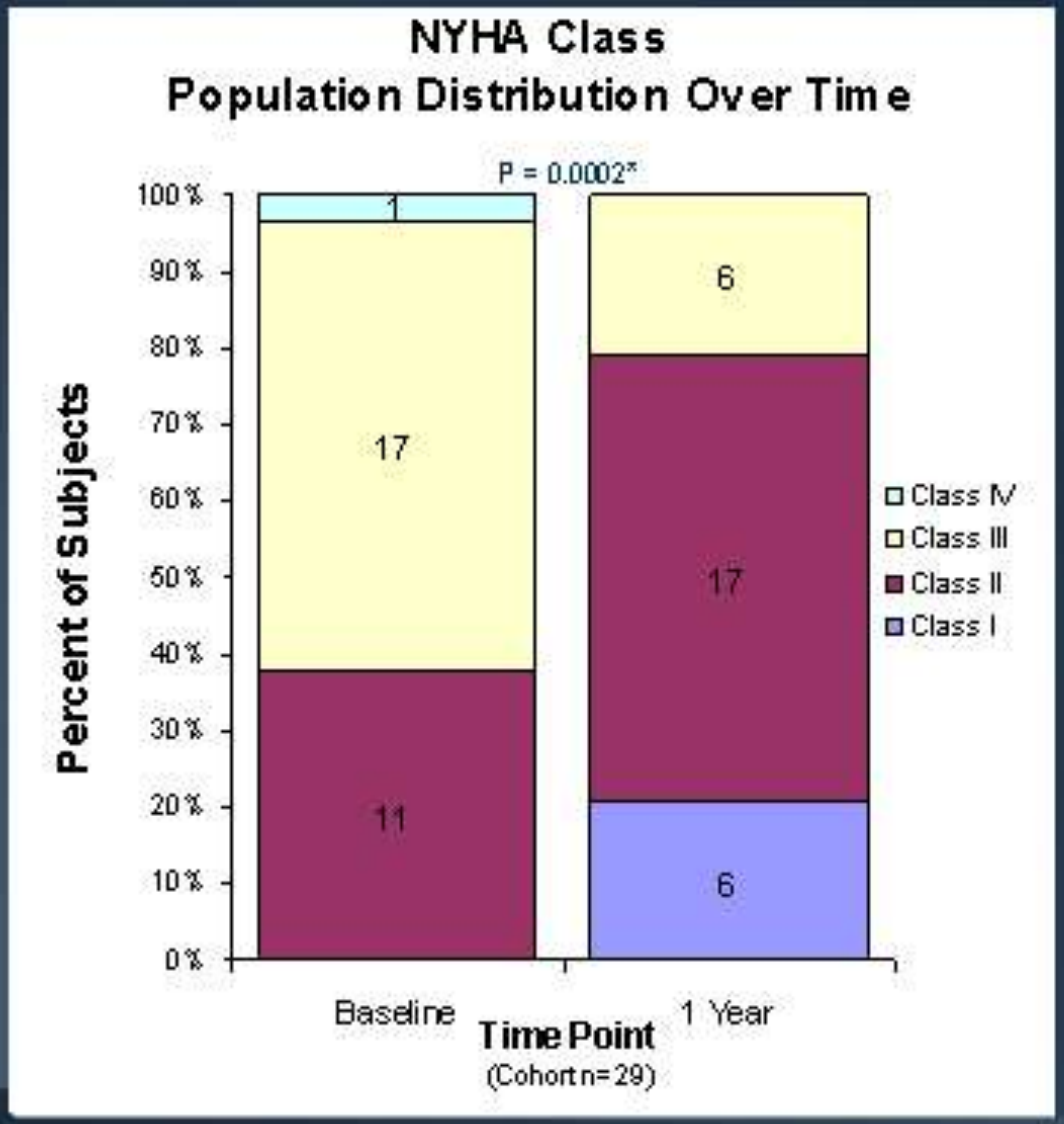
F.U. at 1year: MR Severity



	Baseline	1 Year
Mean	2.48	1.78
Median	2.00	2.00

* P-value calculated using Wilcoxon Signed Rank Test for non-parametric data

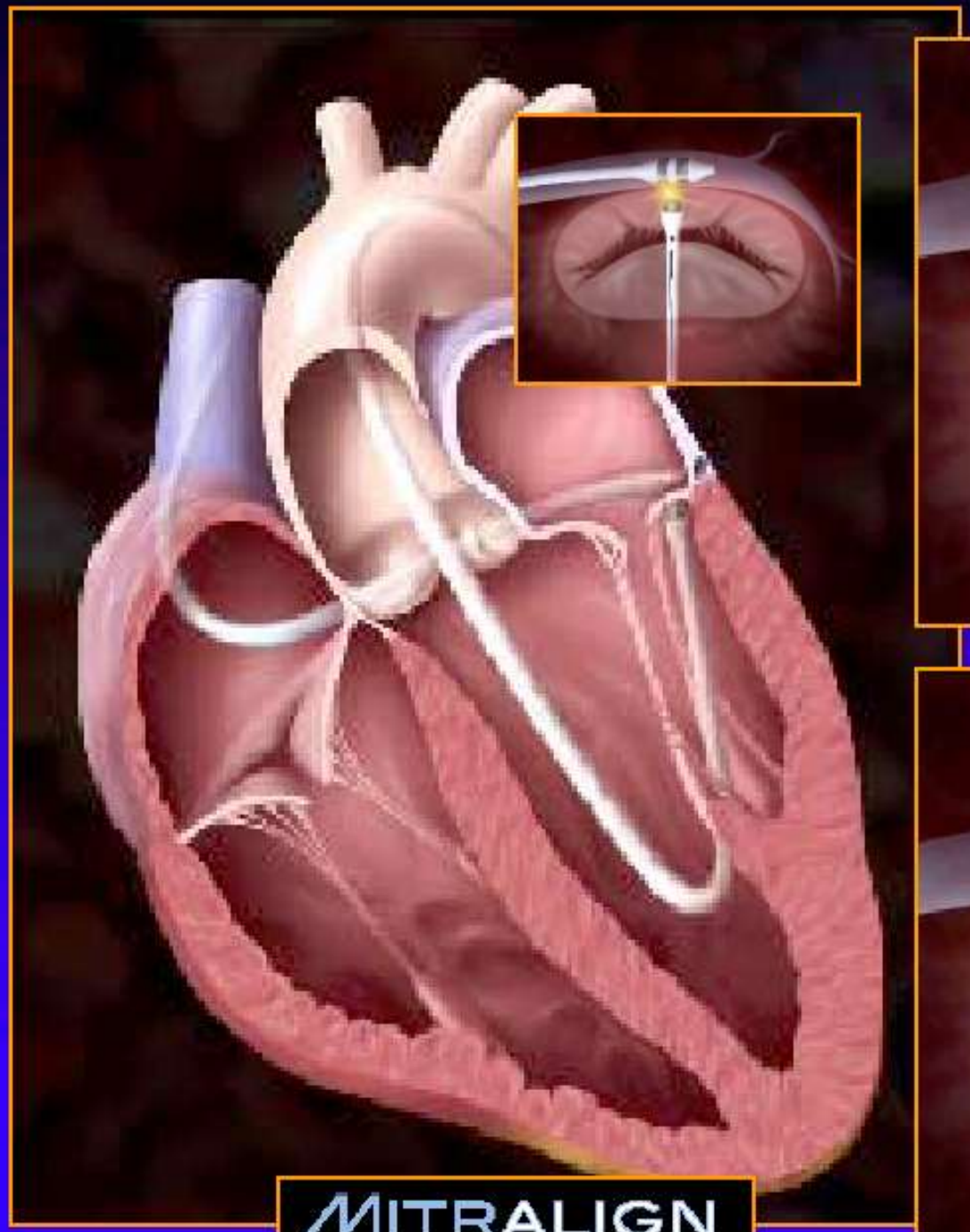
F.U. at 1year: NYHA Class

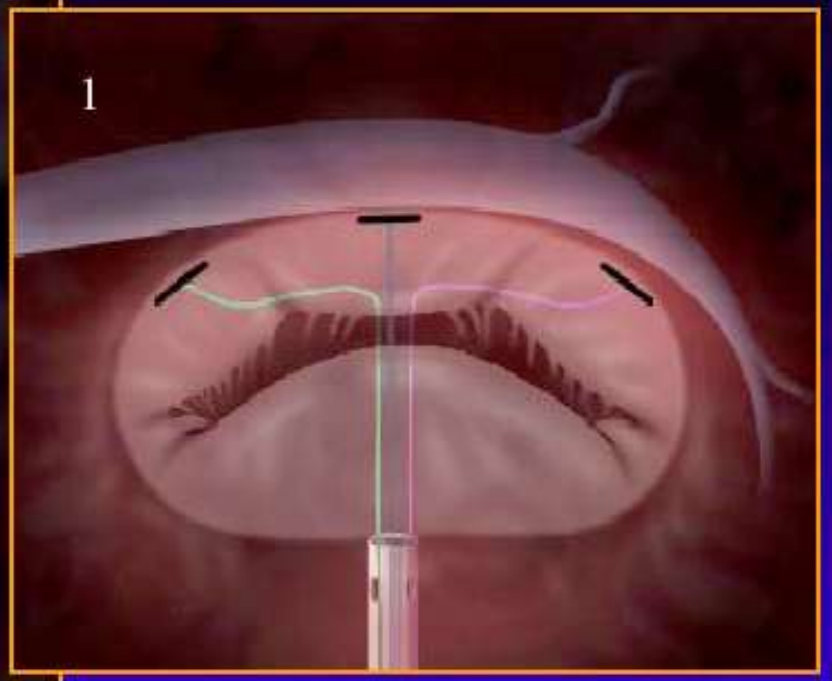


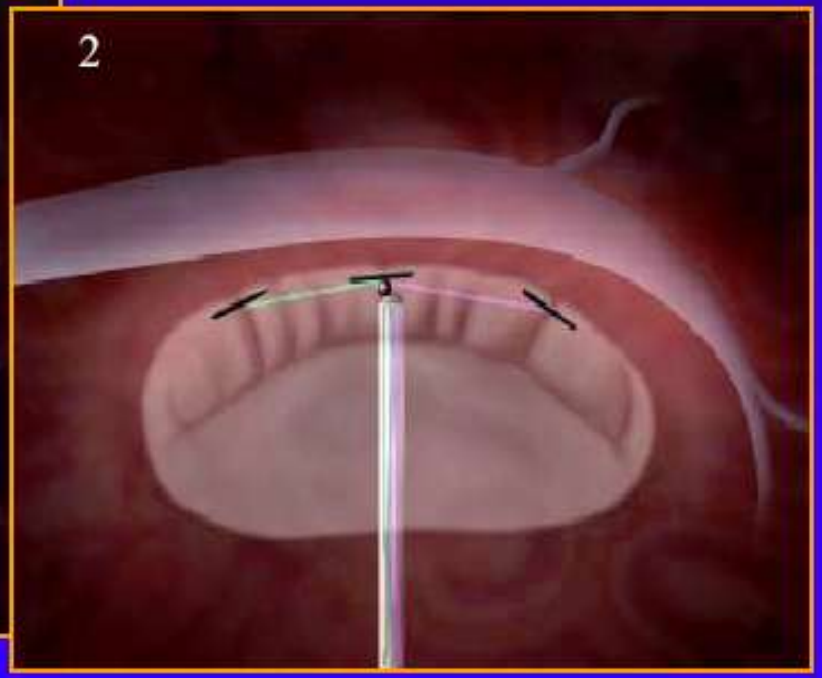
	Baseline	1 Year
Mean	2.66	2.00
Median	3.00	2.00

* P-value calculated using Wilcoxon Signed Rank Test for non-parametric data

- **EVOLUTION interim data with the MONARC system suggests:**
  - Feasibility of implantation in coronary sinus
  - At 12-months, 81% of patients are event-free
  - Encouraging 12-months results in terms of MR reduction and physiological parameters
  - EVOLUTION II will assess functional and clinical outcomes







MITRALIGN
Incorporated

External Left Ventricular Remodeling

Conclusions 1

1. The benefits of mitral valve surgery in patients with severe mitral regurgitation (MR) are variable and the indications for surgical therapy for MR in patients with diminished LV function are still not well established.

2. Mitral valve repair using a percutaneous edge-to-edge repair has been successfully performed utilizing a clip or a suture-based system. Preliminary outcomes with the Evalve clip have been favorable, with procedural success (reduction in MR to ≤2+) in 73%, and no procedural mortality. The EVEREST II trial has elucidated further the benefit of patients with severe MR randomized to the Evalve clip versus surgical valve repair.

Conclusions 2

3. Percutaneous coronary sinus annuloplasty is being actively investigated as an approach for treating MR. The coronary sinus has a variable anatomical relation to the mitral valve annulus and the circumflex artery, and the success and safety of the approach will be strongly influenced by patients' specific anatomy.

4. Other approaches to percutaneous treatment of MR include direct mitral annuloplasty via the LV route and transpericardial systems that achieve septal–lateral wall shortening. These systems are in various stages of development, and extensive human data are lacking

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Table 1. Necessary Components for the Successful Introduction of Transcatheter Heart Valve Therapy

1. Specialized heart centers with experienced multidisciplinary physicians and paramedical personnel
2. The professional multidisciplinary heart team
   a. Primary cardiologists
   b. Cardiac surgeons
   c. Interventional cardiologists
   d. Echocardiographers and imaging specialists
   e. Heart failure specialists
3. Proper procedure and facilities
   a. Modified conventional cardiac laboratory
   b. Hybrid operating room
4. Development of and participation in clinical databases and registries to evaluate practice patterns, treatment outcomes, and comparative effectiveness
5. Scientific literature—knowledge of and evaluation of evidence-based medical literature concerning patient selection, procedural performance, and complication management
6. Specific standardized protocols for management strategies, procedural performance, problem solving, and complication management
7. Appropriate ongoing personnel training