

# Ischemic mitral regurgitation (IMR):

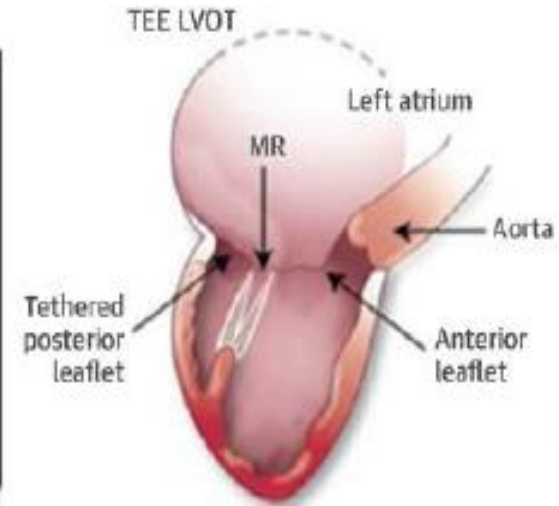
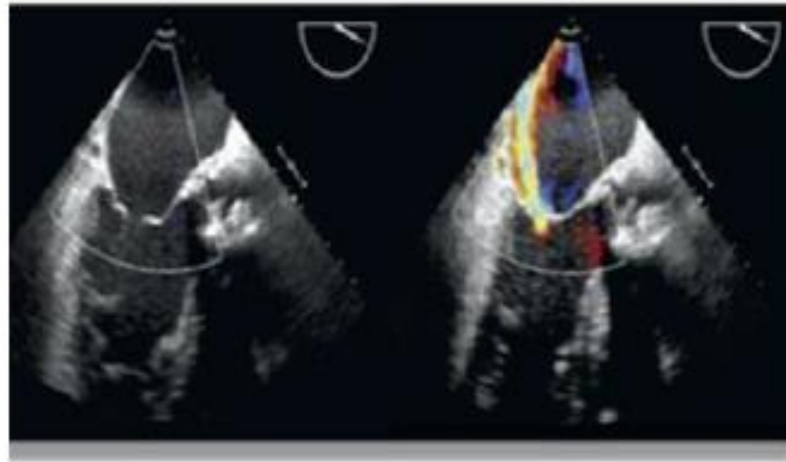
Is there any role of mitral valve clip ?

A nighttime photograph of a city skyline, likely Bangkok, with several illuminated skyscrapers and buildings. The lights are reflected in a body of water in the foreground. The sky is a deep orange and red from the setting or rising sun.

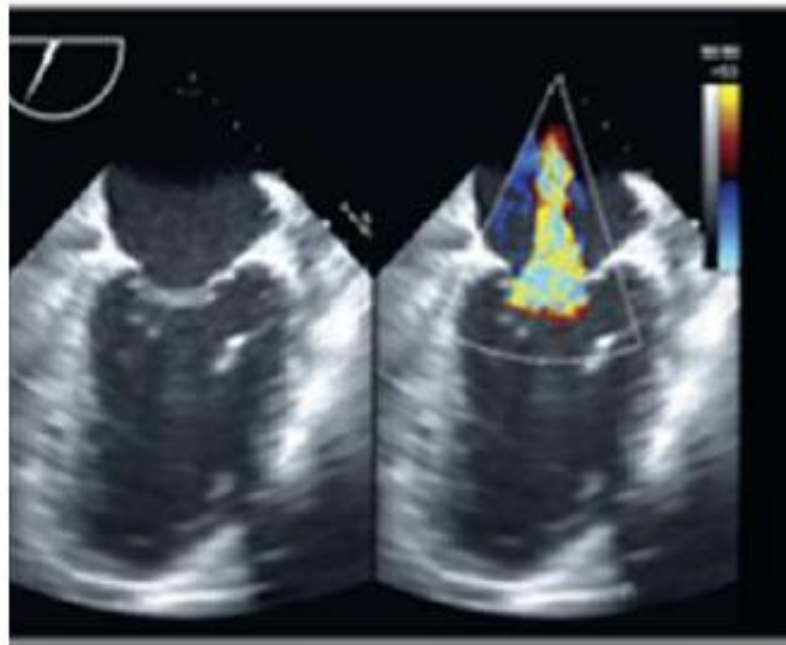
**Suphot Srimahachota**  
**Division of Cardiology**  
**Department of Medicine**  
**King Chulalongkorn Memorial Hospital**

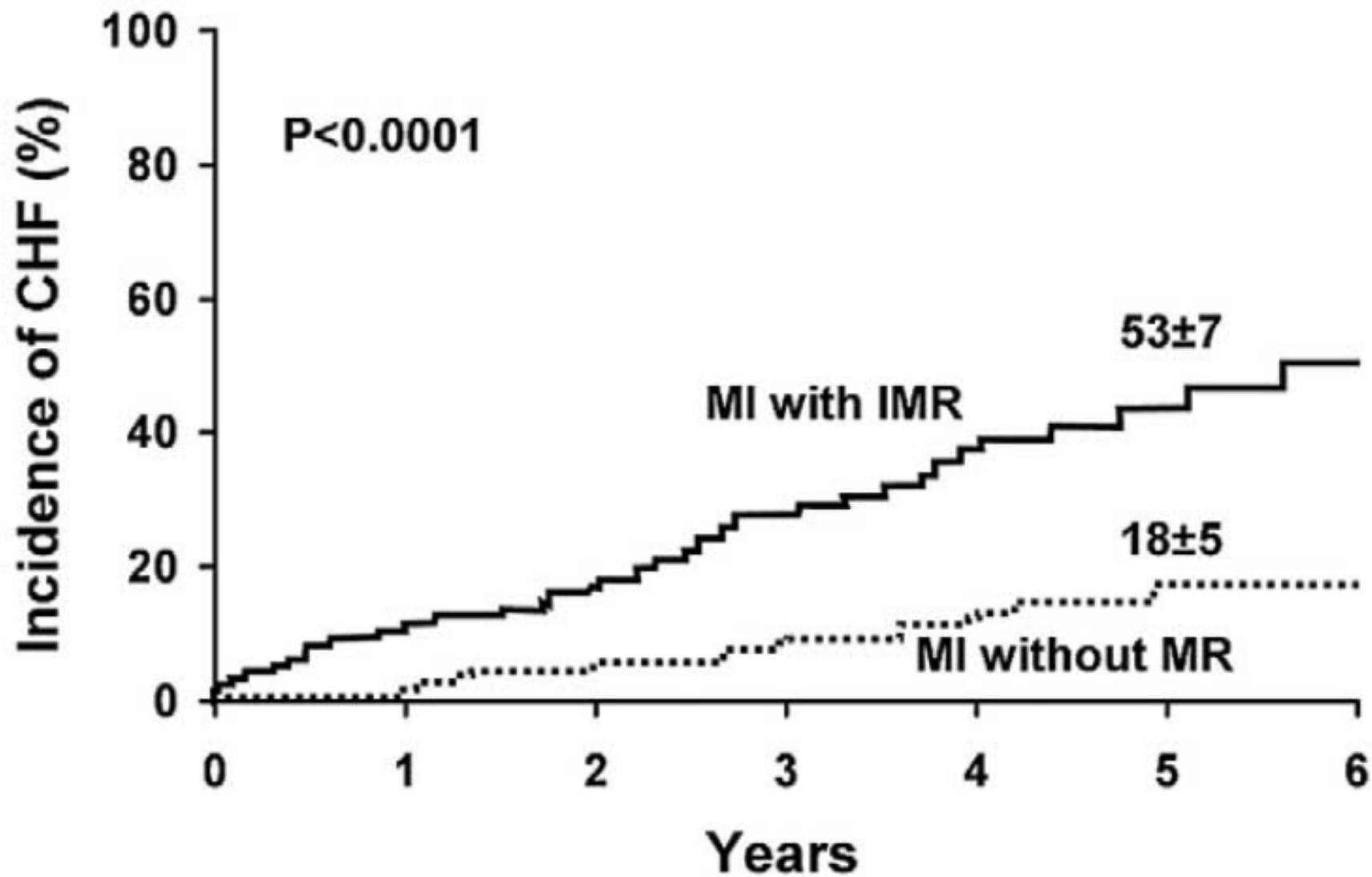
# Secondary (Functional) MR: **The disease is the LV!**

Ischemic  
cardiomyopathy



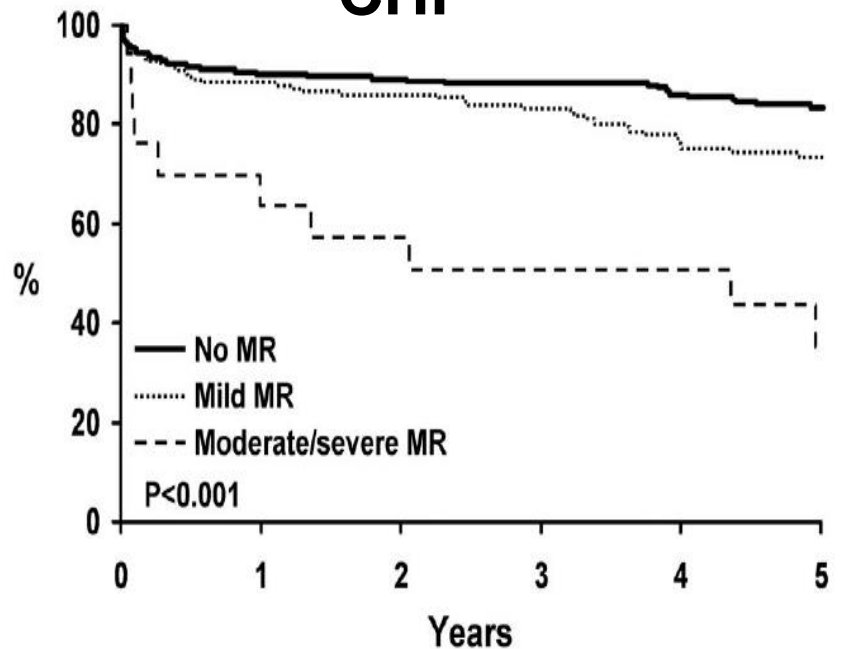
Idiopathic  
dilated  
cardiomyopathy





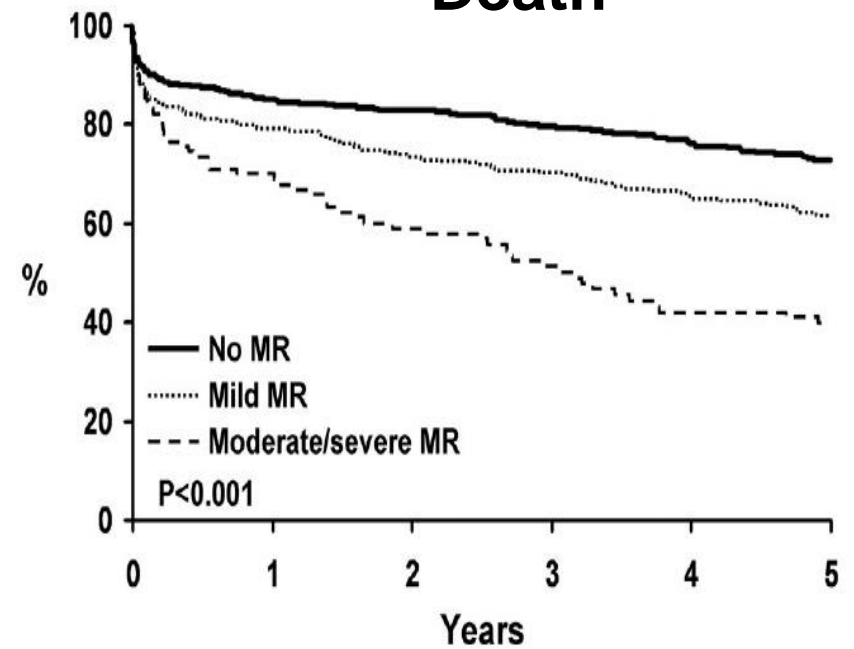
# CHF and death after MI according to MR

## CHF



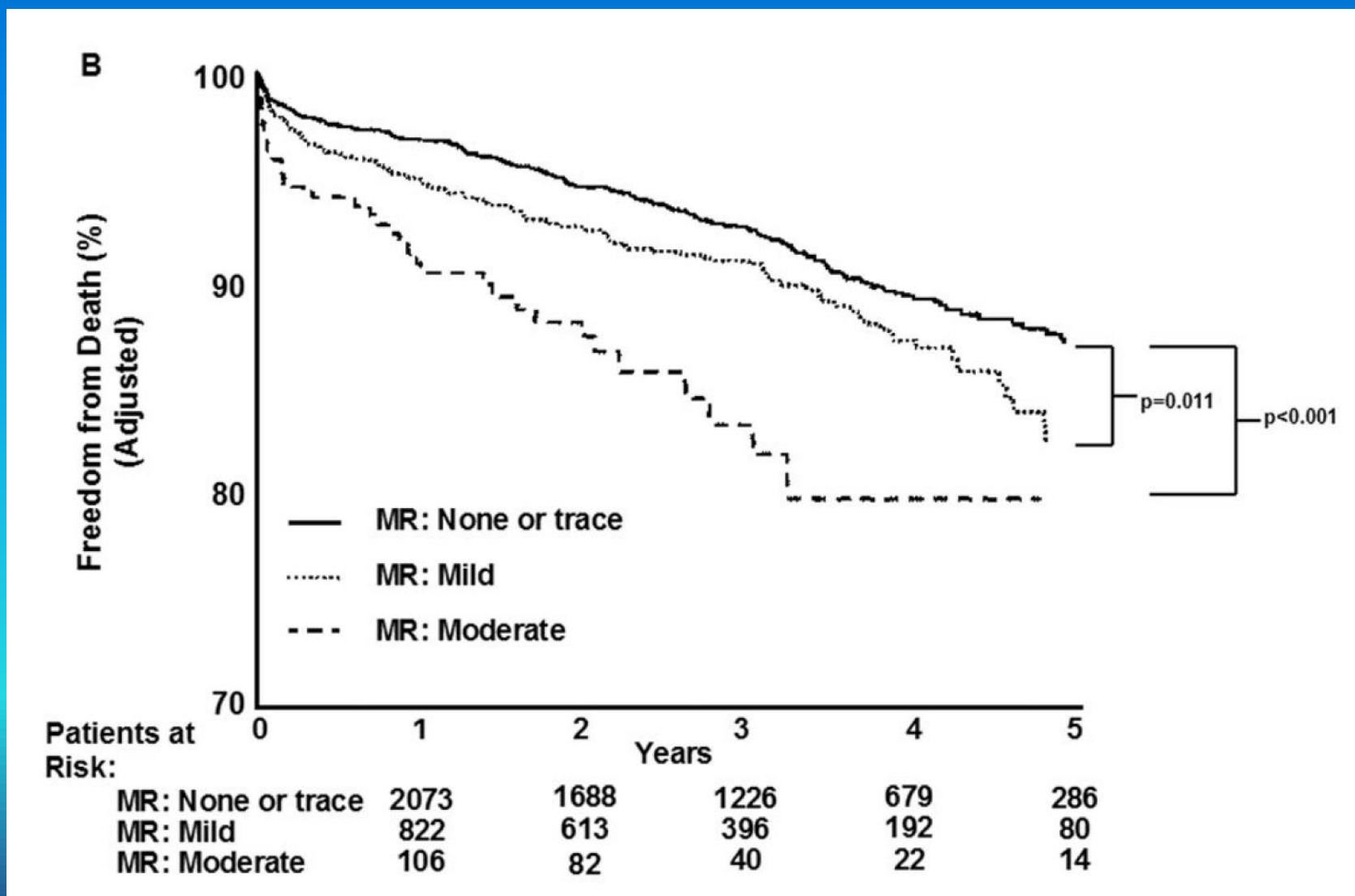
—	287	237	226	215	185	158
.....	175	138	131	116	88	74
---	20	10	9	8	7	4

## Death



—	386	327	311	289	254	222
.....	297	229	211	188	151	123
---	89	61	52	45	32	25

# Long-term outcome after CABG according to MR



# The vicious cycle of secondary MR

Global or regional LV dysfunction



LV dilatation

Improved prognosis?



Mitral leaflet tethering and MR

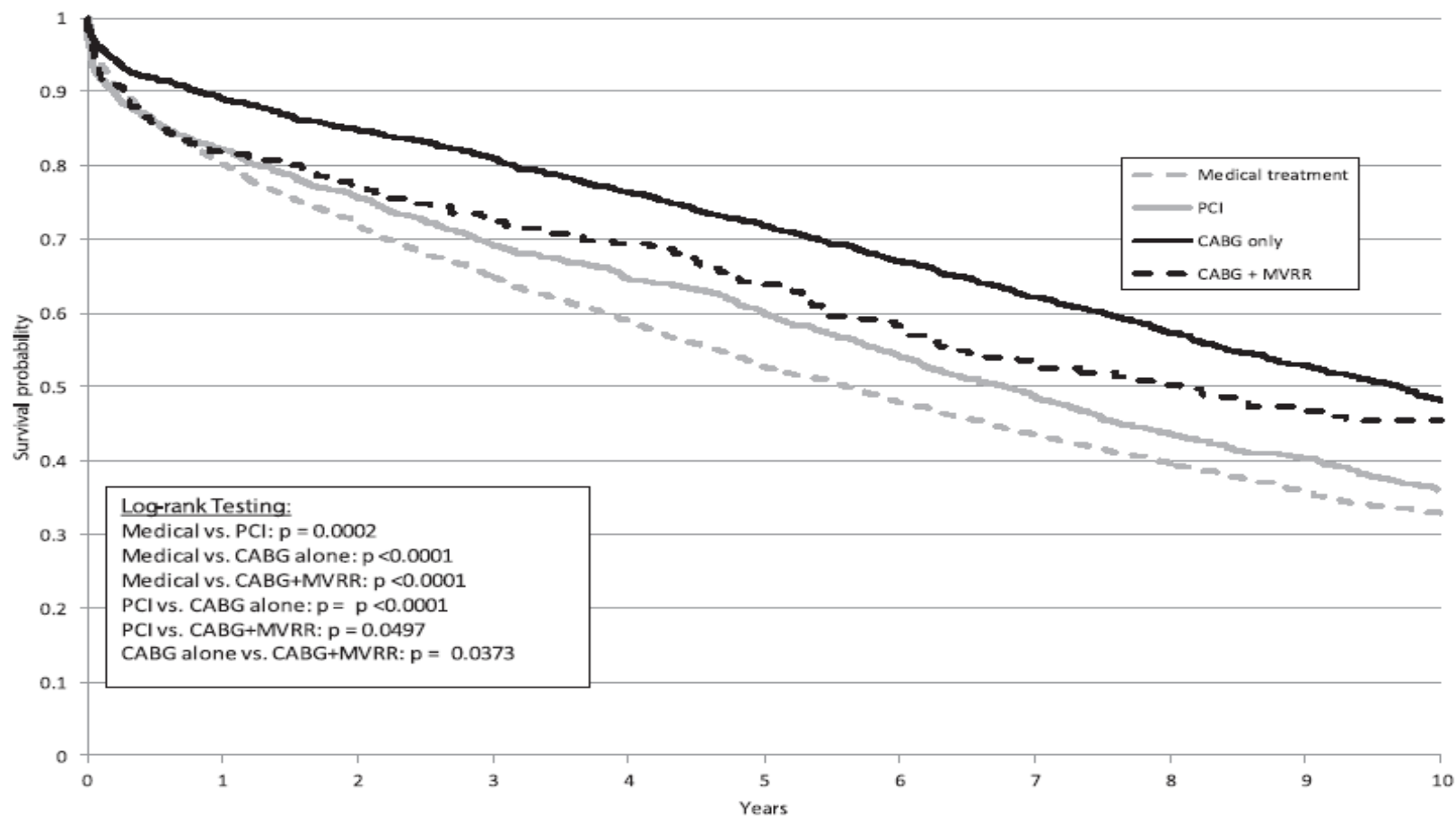


↑LV volume overload ↑dilatation



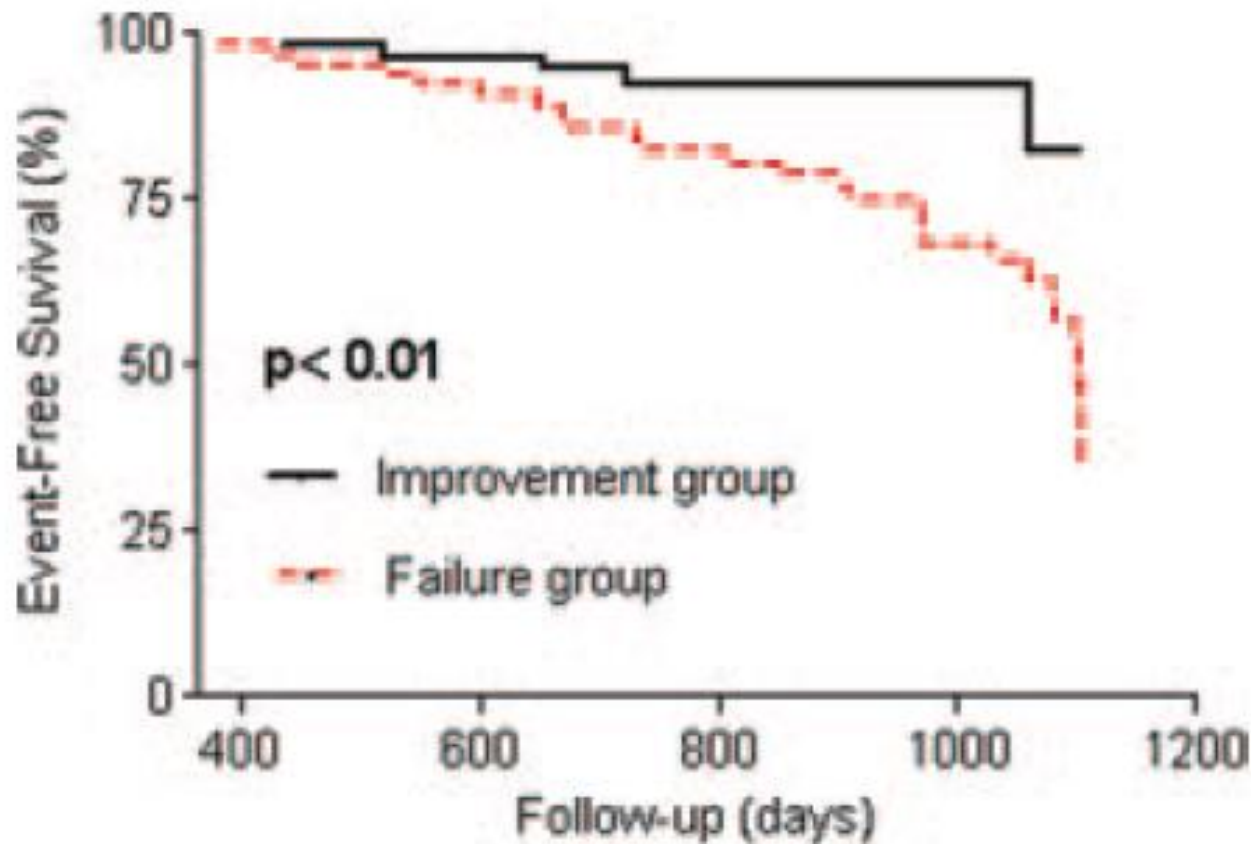
↑Mital leaflet tethering and ↑ MR





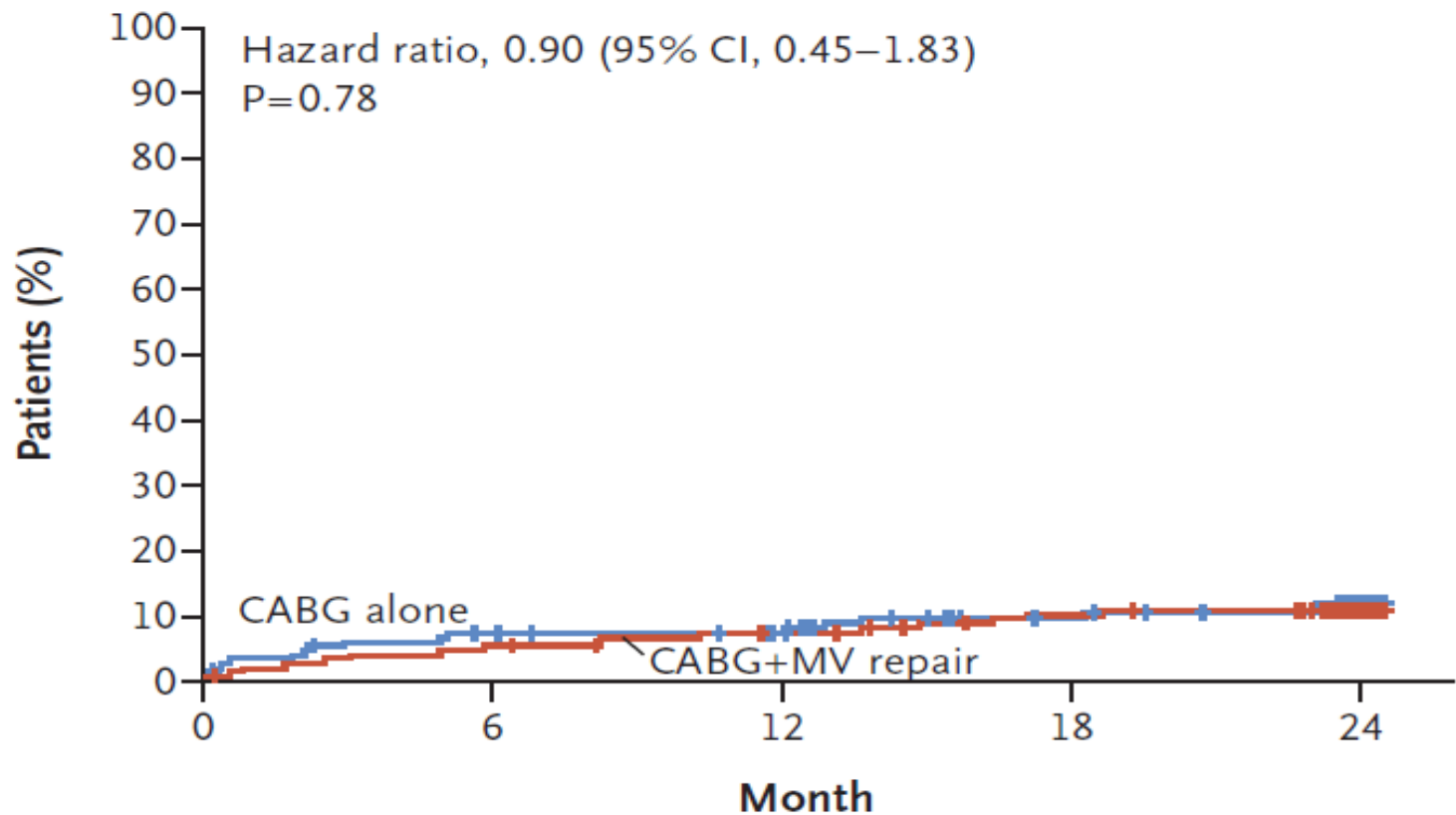
	Number at Risk					
Medical	1800	1198	877	633	461	332
PCI	1295	1038	858	677	486	352
CABG	1651	1402	1160	901	673	402
CABG+MVRR	243	181	144	103	72	48

# MV repair during CABG: Compared improvement vs failure group



# CABG alone vs CABG + MV repair

## A Death

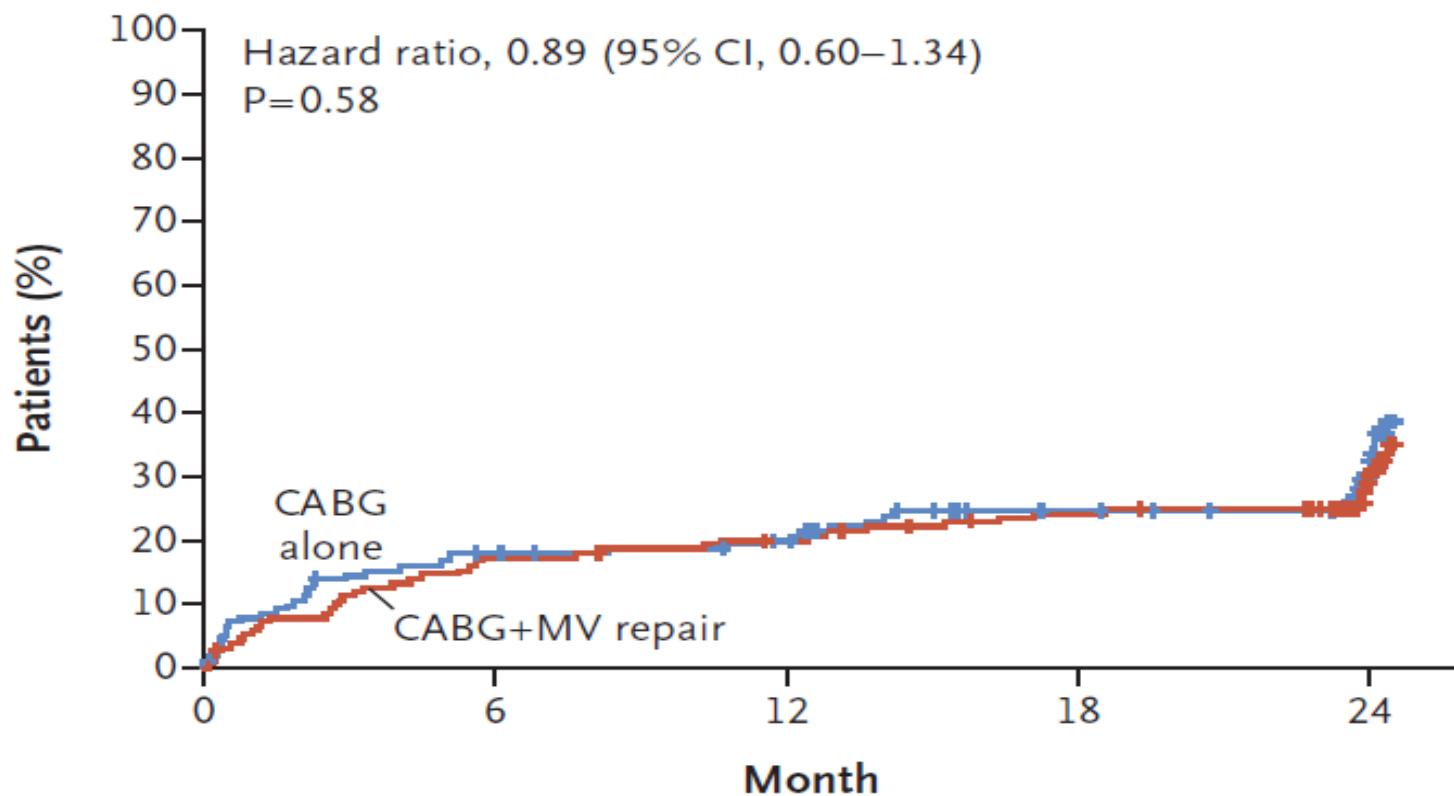


### No. at Risk

CABG alone	151	138	132	117	66
CABG+MV repair	150	142	136	126	80

# CABG alone vs CABG + MV repair

## B Major Adverse Cardiac or Cerebrovascular Event



### No. at Risk

CABG alone	151	121	113	96	53
CABG+MV repair	150	123	117	106	64

# Indications for mitral valve surgery in

## **CLASS IIa**

- 1. Mitral valve surgery is reasonable for patients with chronic severe secondary MR (stages C and D) who are undergoing CABG or AVR. (Level of Evidence: C)**

Transcatheter MV repair may be considered for severely symptomatic patients (NYHA class III/IV) with chronic severe primary MR (stage D) who have a reasonable life expectancy but a prohibitive surgical risk because of severe comorbidities

IIb

B

**secondary MR (stage D) who have persistent symptoms despite optimal GDMT for HF (224–235). (Level of Evidence: B)**

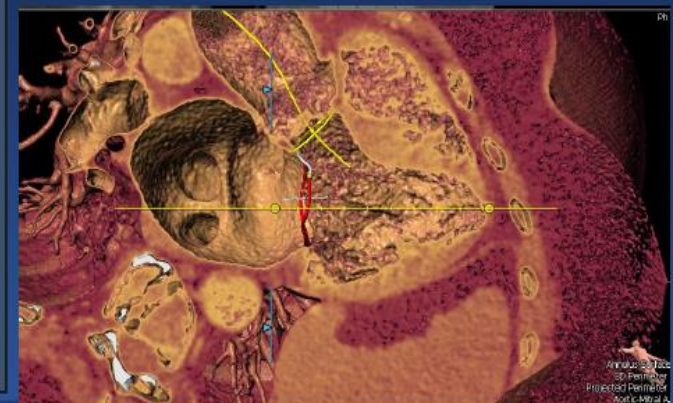
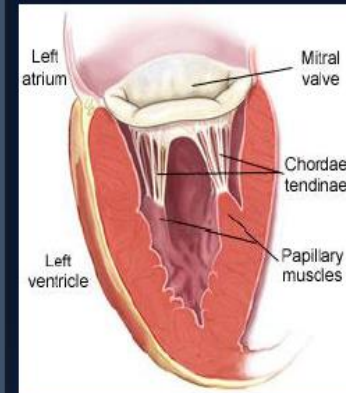
- 2. Mitral valve repair may be considered for patients with chronic moderate secondary MR (stage B) who are undergoing other cardiac surgery. (Level of Evidence: C)**

ACC/AHA guideline for VHD 2014

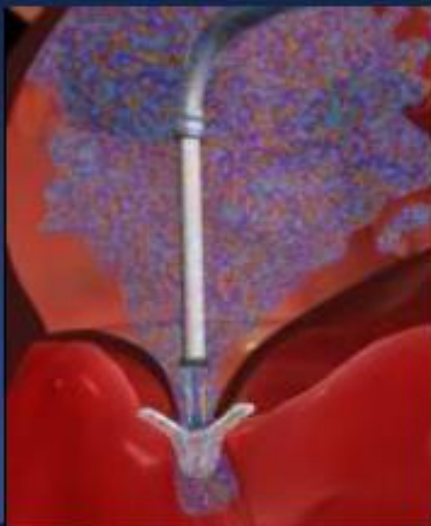
indicated) and have low comorbidity, when revascularization is not indicated.

# The Mitral Valve Complex is Complex!

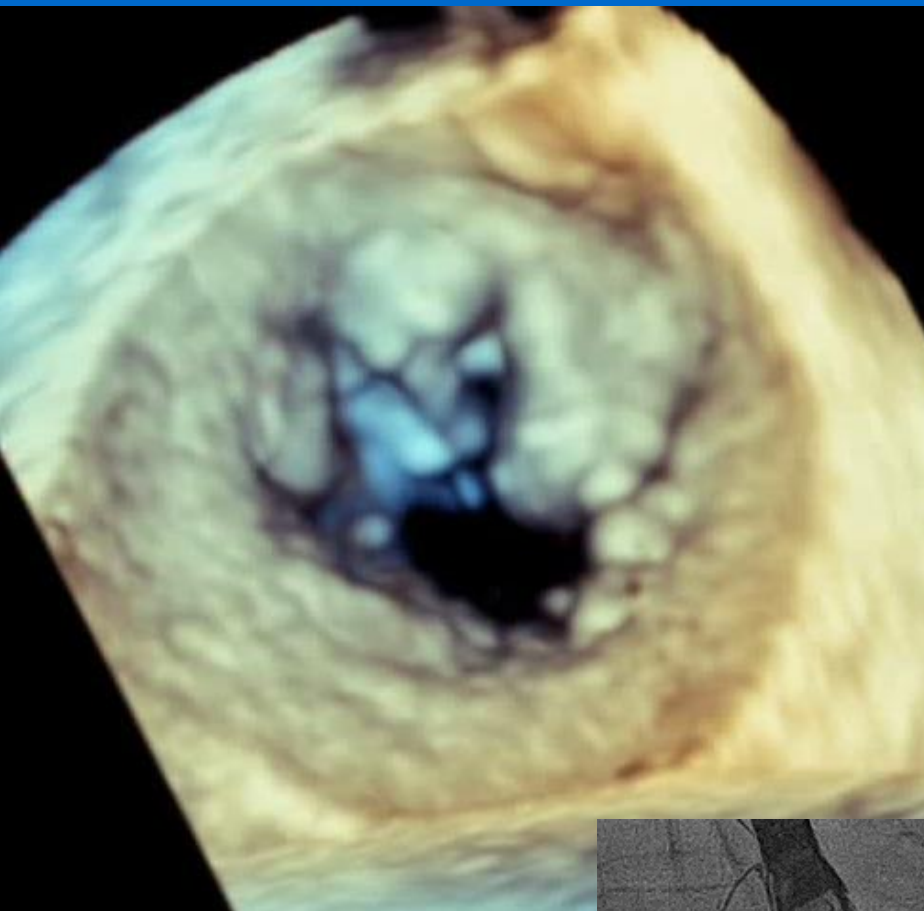
- It's not round nor "D" shaped – it's asymmetric
- It's not flat – it's saddle-shaped
- Its annulus is not rigid – it's "dynamic"
- It's not passive – it contracts, reducing valve area during systole
- It's a high pressure closure valve, not a high pressure opening valve
- It's got 24+ chords
- It's relatively easy to block aortic outflow
- It's easier to form thrombus on than the AV
- It has a much larger annulus than the AV
- Its annulus changes size as the heart fails
- MR is not one disease!



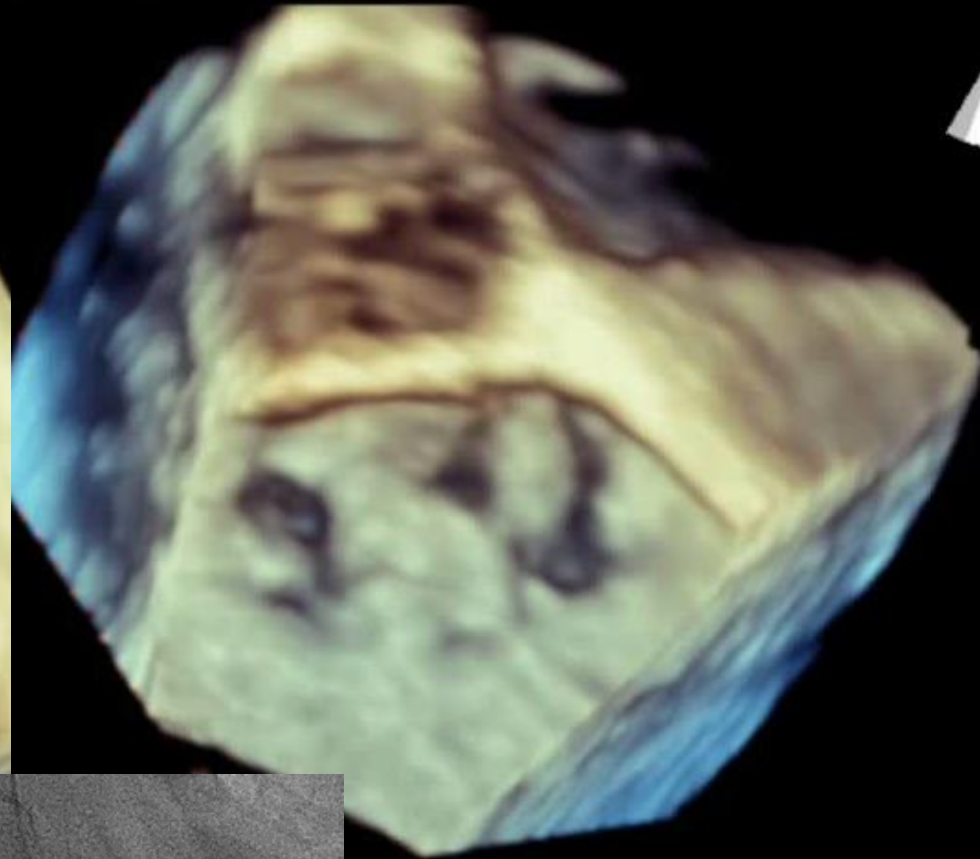
# MitraClip System and Implant



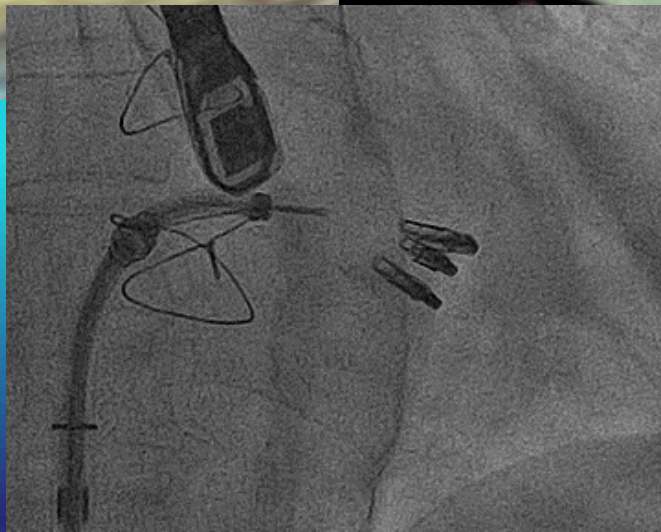
ITS HVRQ



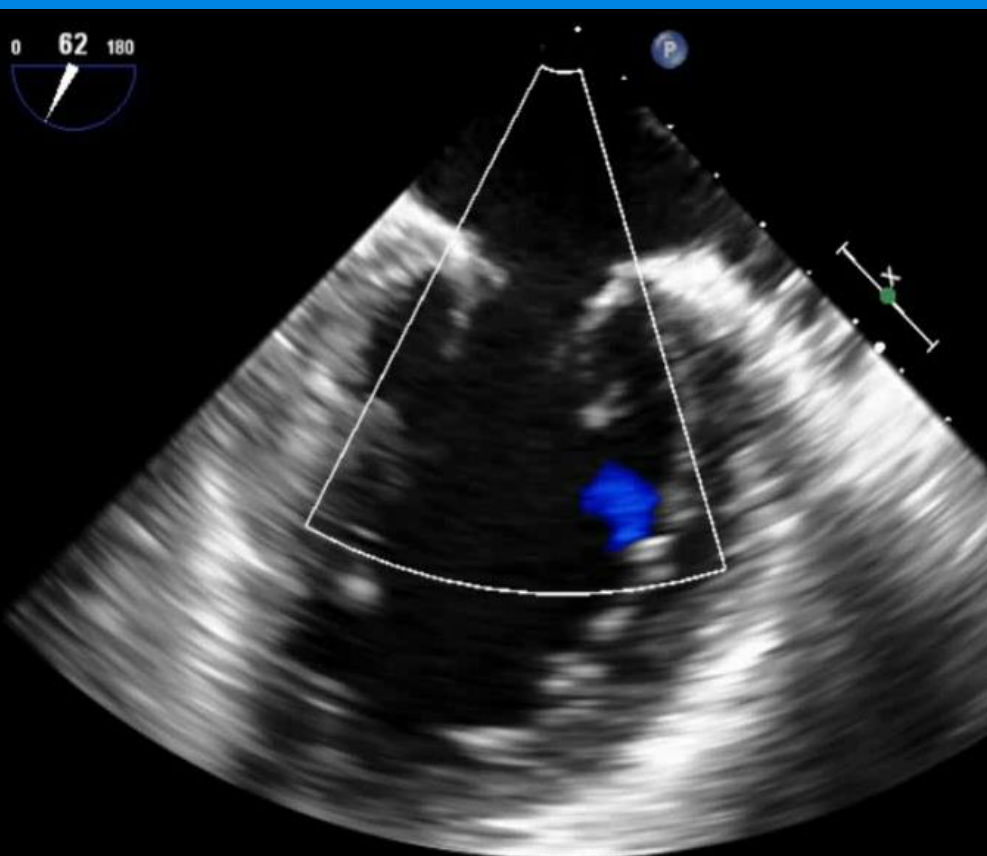
Pre



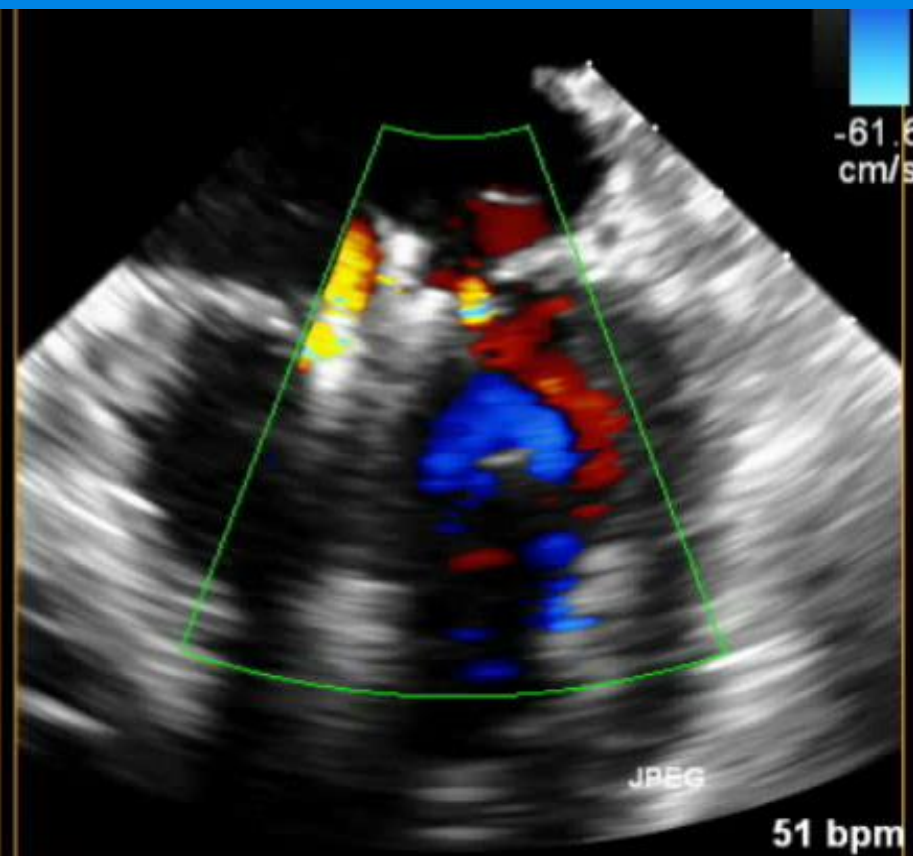
Post



# MitraClip implantation

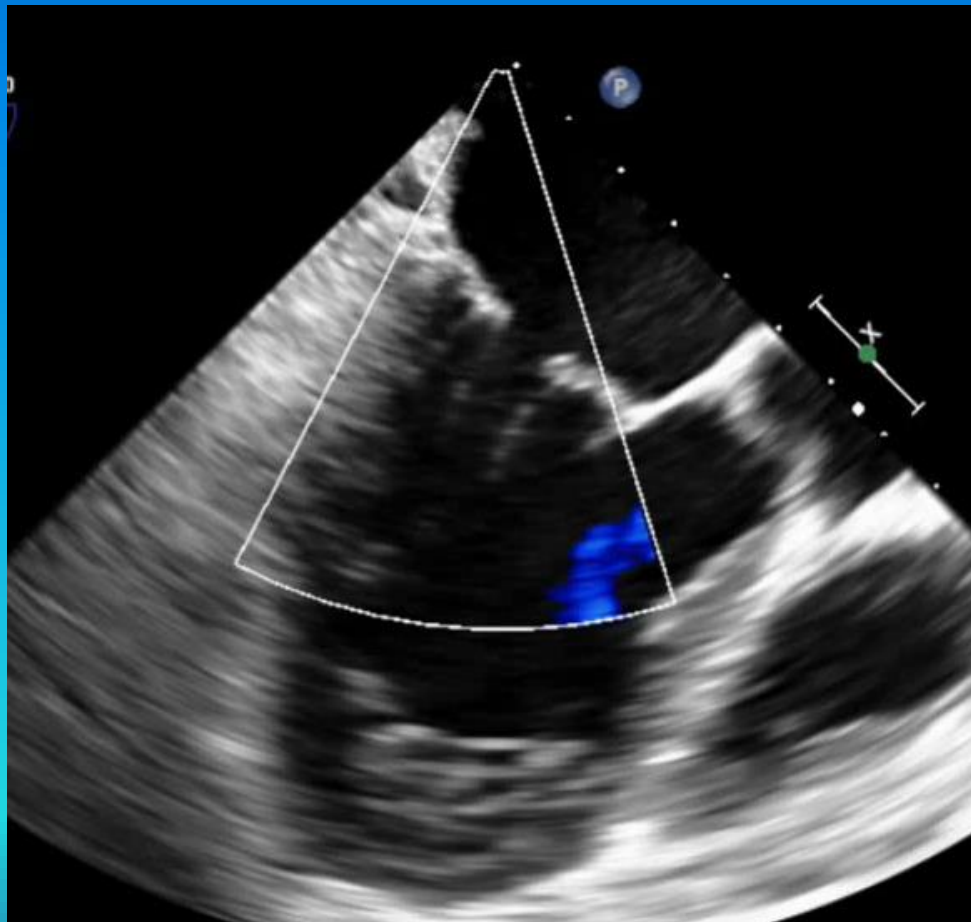


Pre

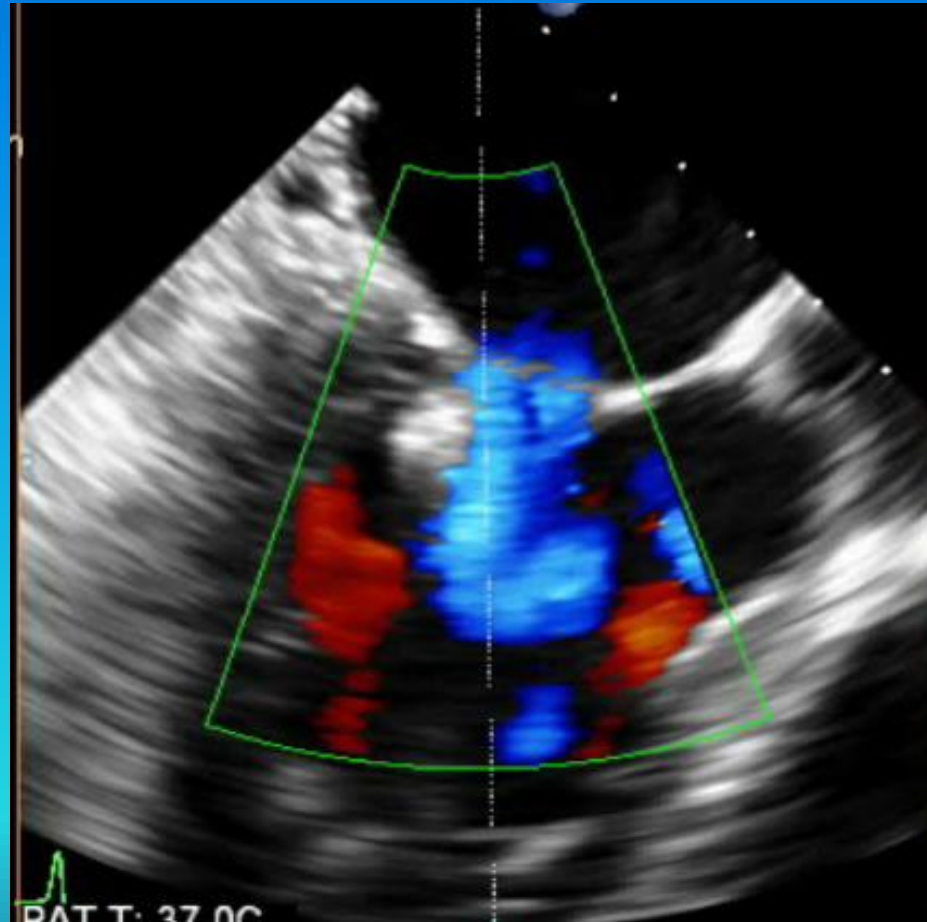


Post

# MitraClip implantation



Pre



Post

# EVEREST II Randomized Clinical Trial

279 patients enrolled at 37 sites

Severe MR (3+ or 4+)  
73% DMR, 27% FMR  
Specific anatomical criteria

↓  
Randomized 2:1

↙  
**Device Group**  
MitraClip System  
N=184

↘  
**Control Group**  
Surgical Repair or Replacement  
N=95

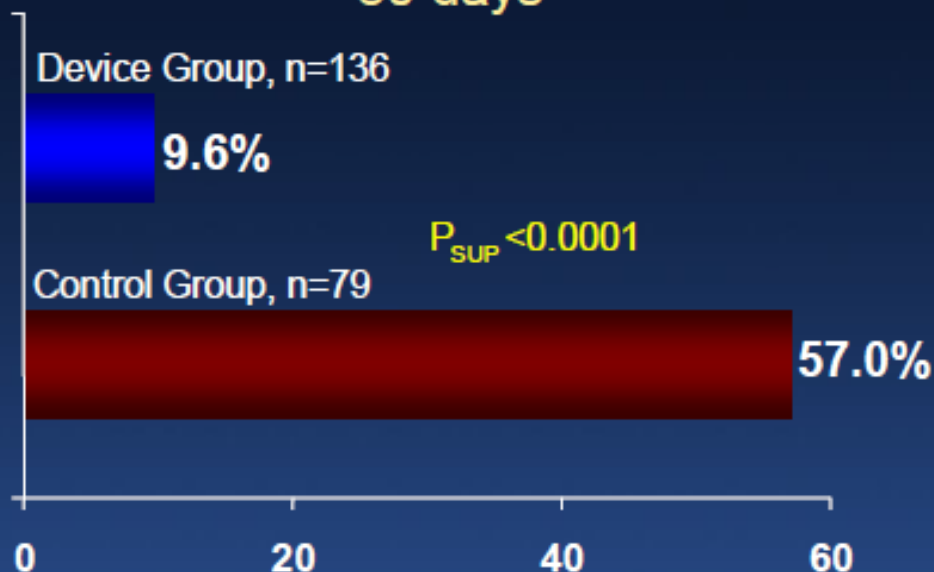
↓  
↓  
**Echocardiography Core Lab and Clinical Follow**  
Baseline, 30 days, 6 months, 1 year, 18 months, and  
annually through 5 years

# EVEREST II: 279 pts with 3+/4+ MR randomized 2:1 to MitraClip vs. Surgical Repair

## Primary Endpoints (per protocol cohort)

### Safety†

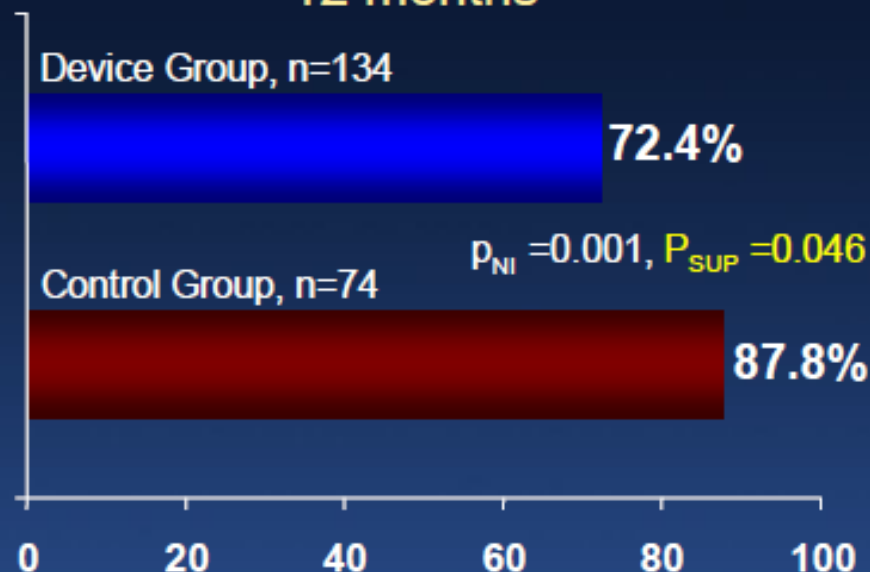
Major Adverse Events  
30 days



† Death, major stroke, reoperation of MV, urgent/emergent CV surgery, MI, renal failure, deep wound infection, sepsis, ventilation >48 hrs, new permanent AF, GI complication requiring surgery, transfusion  $\geq 2U$

### Effectiveness‡

Clinical Success Rate  
12 months



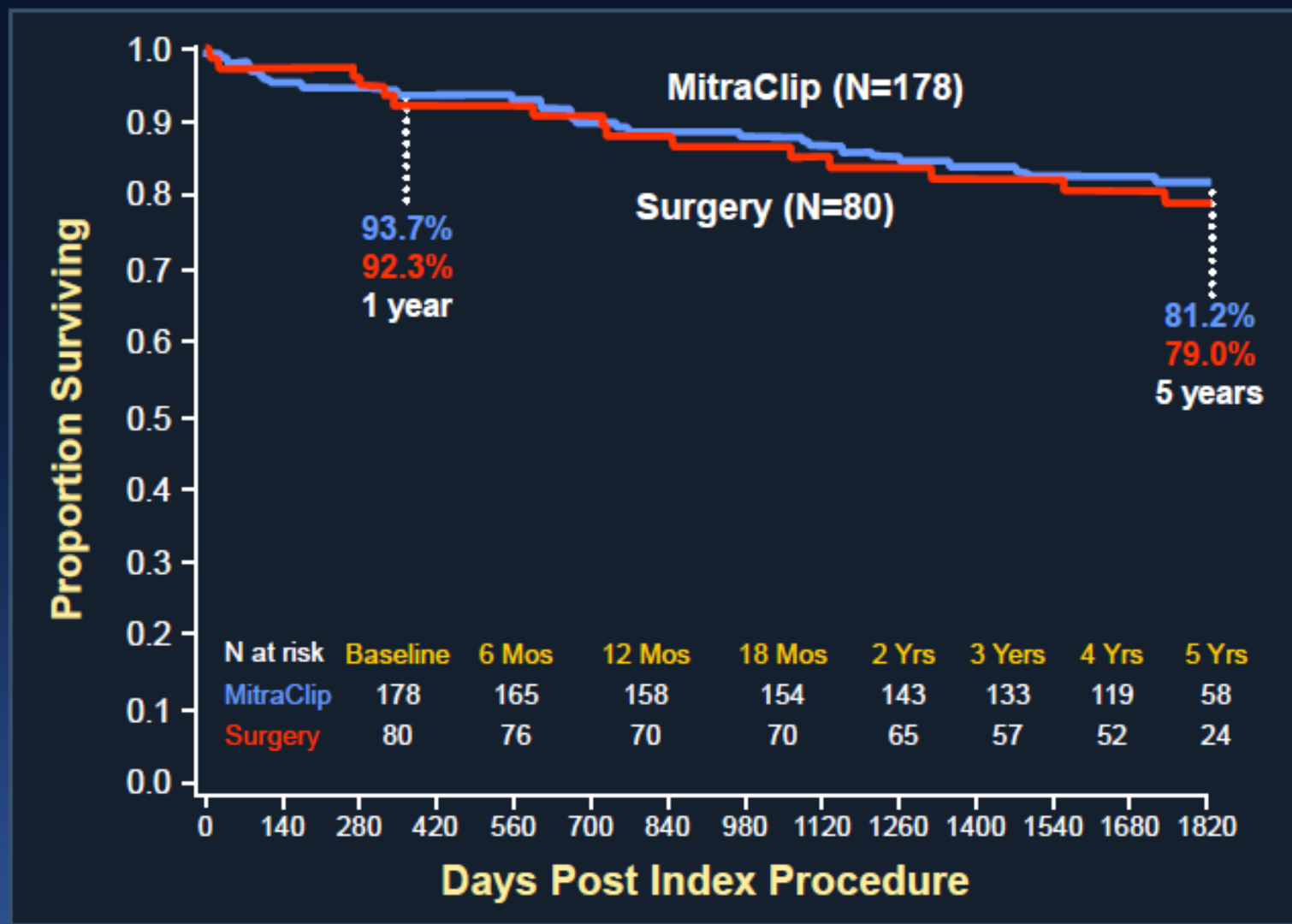
‡ Freedom from death, MV surgery or reoperation for MV dysfunction, or MR >2+ at 12 months

# EVEREST II: Efficacy at 5 Years\*

Primary endpoint	MitraClip (n=154)	Surgery (n=56)	<i>p</i> Value
Freedom from death, MV surgery or reoperation, and 3+ or 4+ MR	44.2%	64.3%	0.01
• Death	20.8%	26.8%	0.36
• MV surgery or reoperation	27.9%	8.9%	0.003
• 3+ or 4+ MR	12.3%	1.8%	0.02

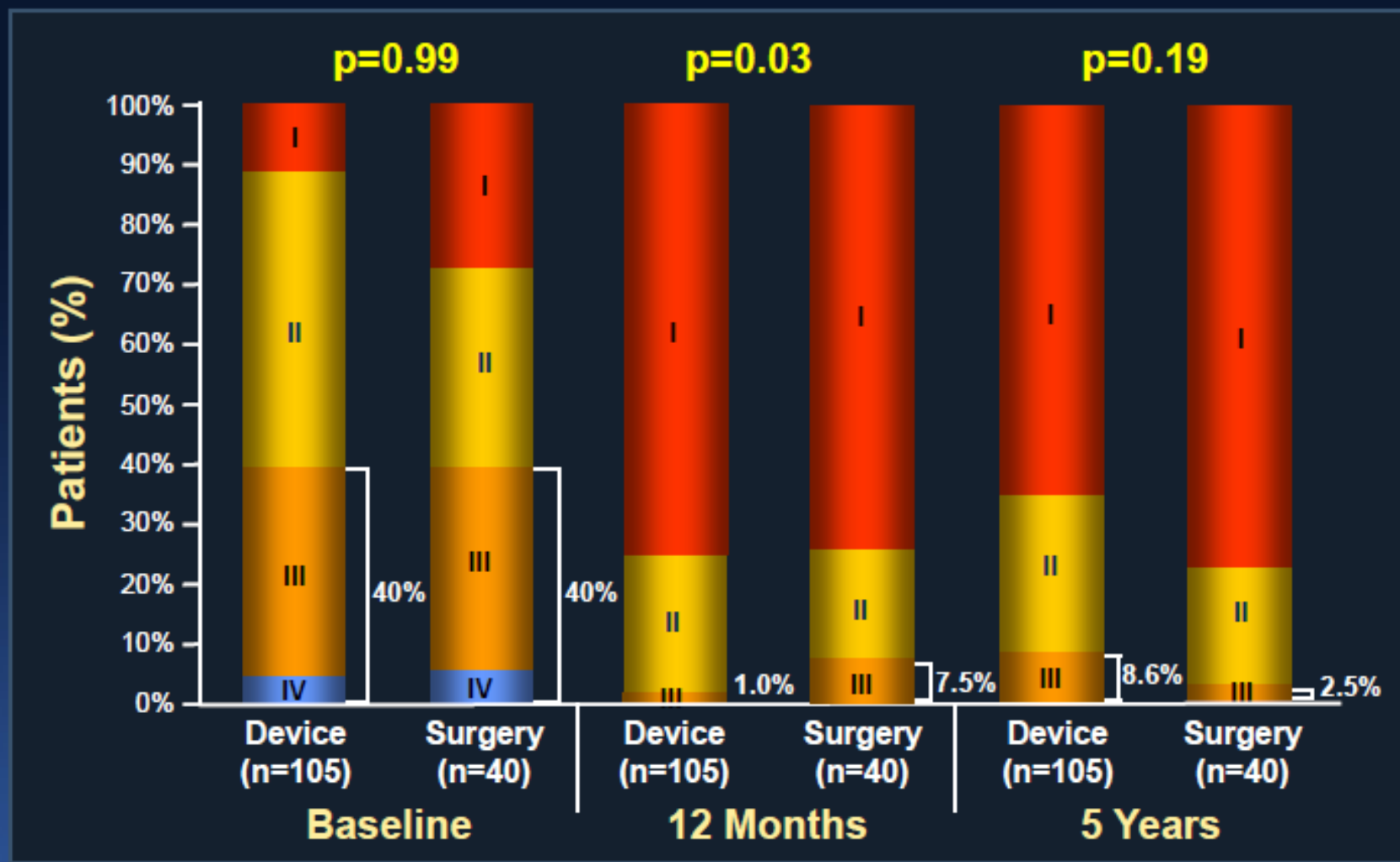
\*Includes pts that completed the 5-year visit and had MR grade available or died or had MV surgery before withdrawal from the study

# EVEREST II: Freedom From Mortality



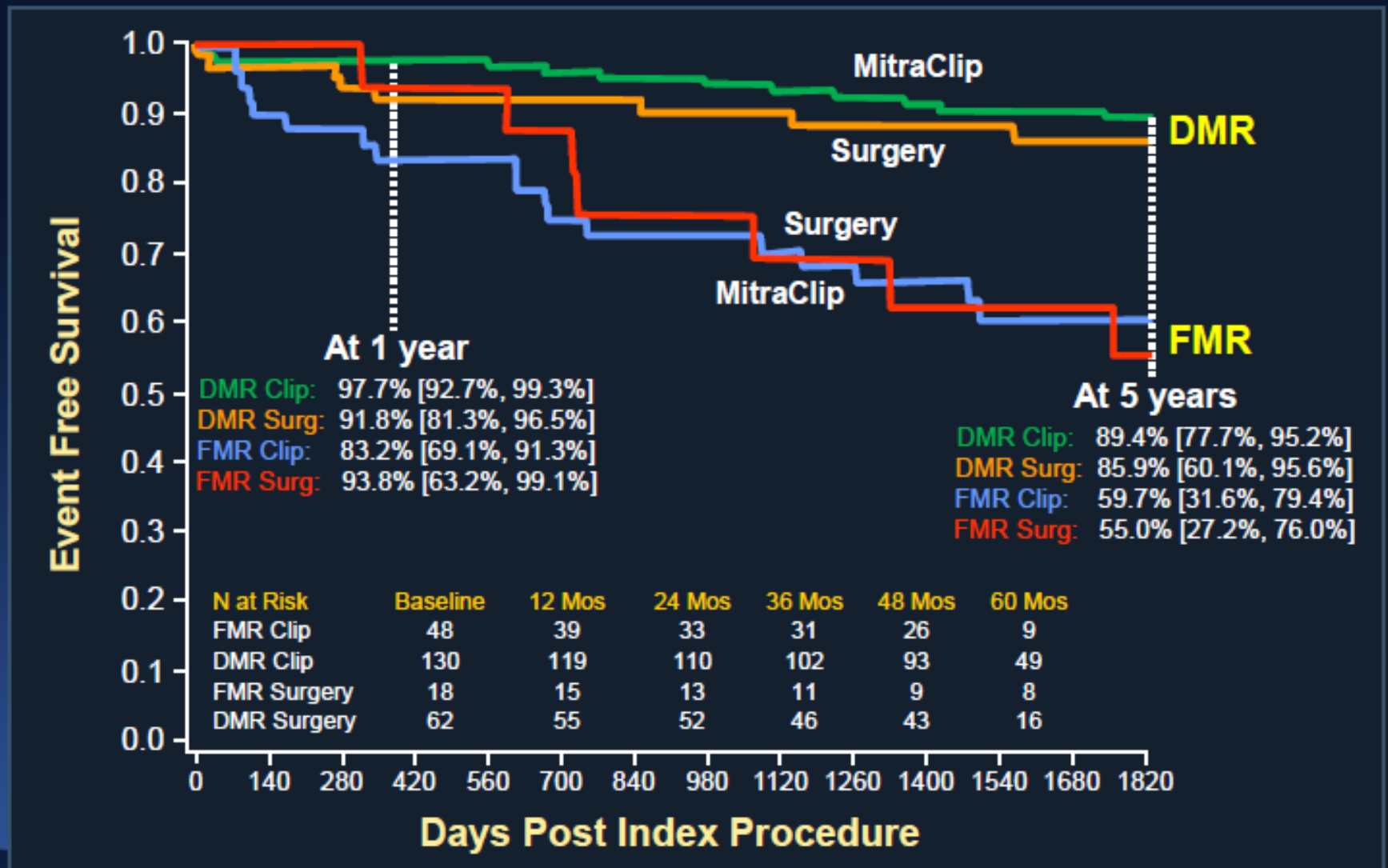
# EVEREST II: NYHA Class at 5 Years

145 surviving pts with serial assessment at bl, 1 year, 5 years



P values for NYHA I/II vs. III/IV

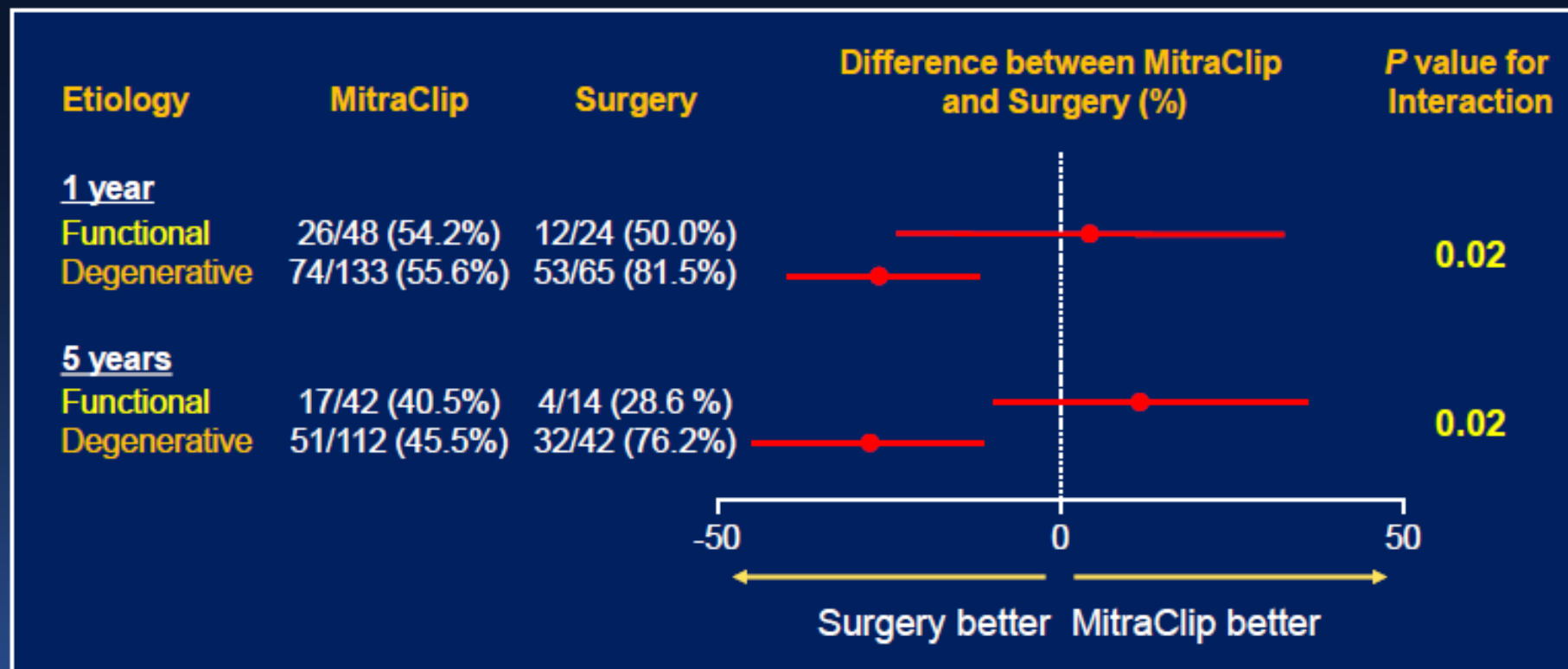
# EVEREST II: Freedom From Mortality and Reintervention



# EVEREST II: Primary EP at 1 and 5 Years

## - DMR (73%) vs. FMR (27%) -

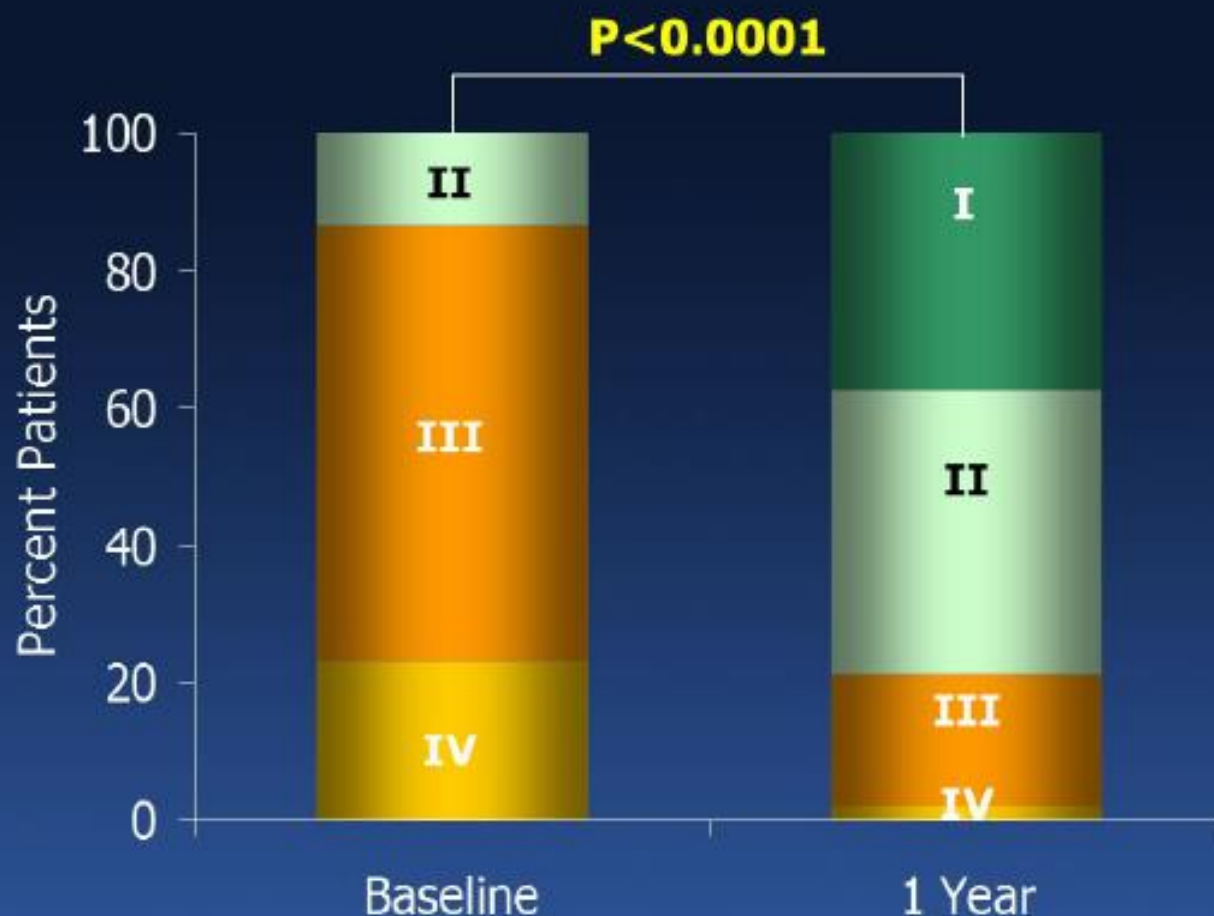
(Freedom from Death, MV Surgery, or 3+ or 4+ MR): ITT



# EVEREST II High Surgical Risk FMR Patients

## NYHA Functional Class

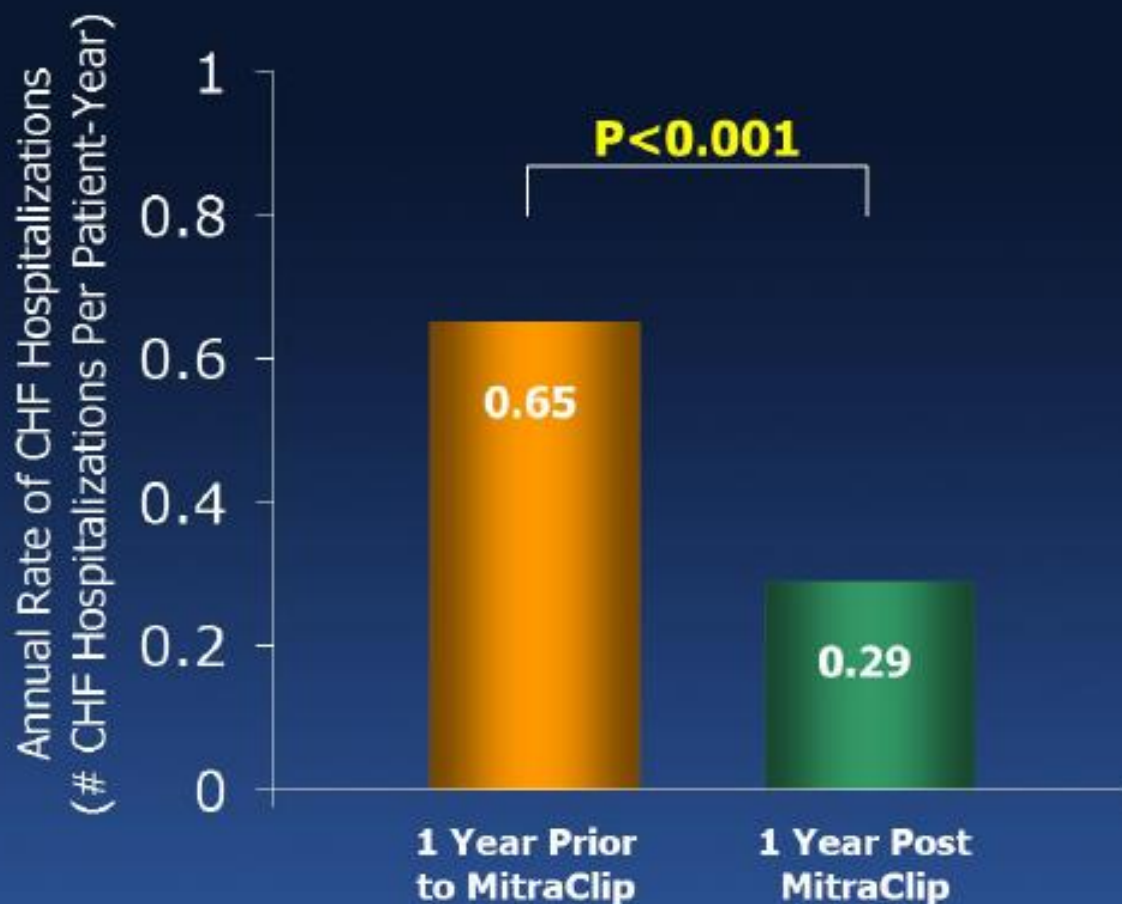
N = 104 Matched Cases, Site Assessed



# EVEREST II High Surgical Risk FMR Patients

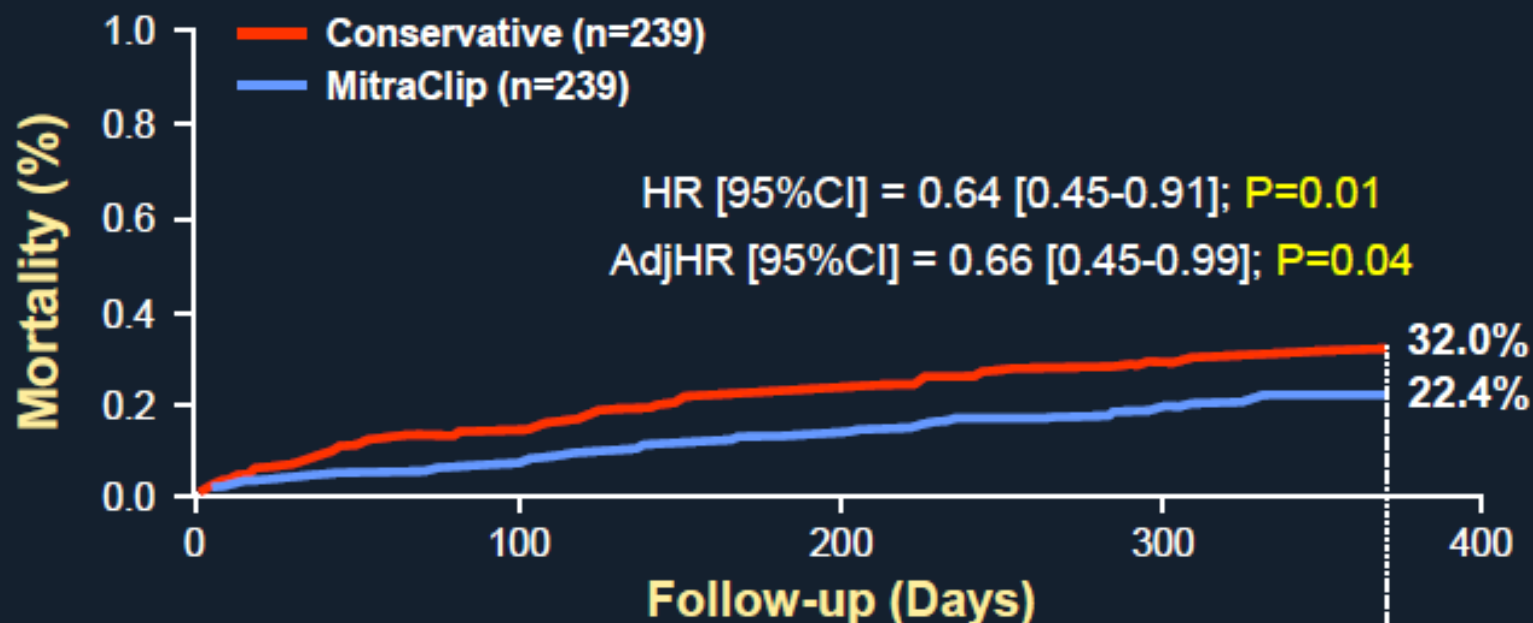
## Hospitalizations for CHF

N = 110 Matched Cases



# Comparison of MitraClip to Conservative Therapy in High-risk MR: **A Matched Registry Analysis**

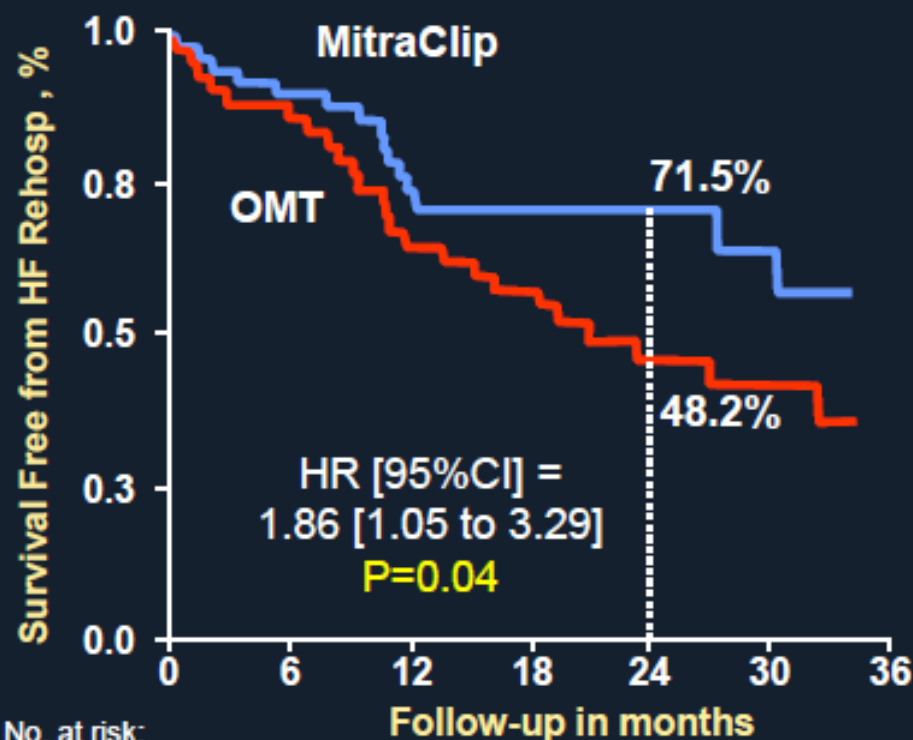
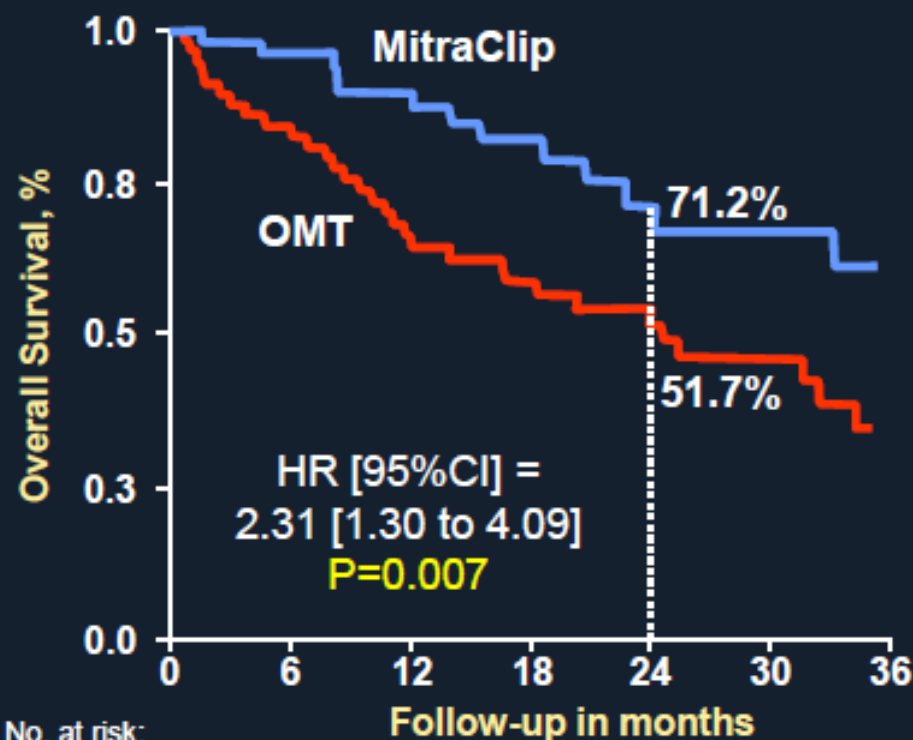
239 high risk MitraClip pts with 3+-4+ MR were propensity matched to 239 conservatively treated pts with 3+-4+ MR from the Duke Echo Lab Database  
87% FMR; mean age 74 yrs; mean LVEF 42%; mean STS score 12%



No. at risk:	Day 0	Day 30	Day 180	Day 365
MitraClip	239	226	202	175
Conservative	239	219	178	147

# Comparison of MitraClip to Conservative Therapy in FMR: **A Matched Registry Analysis**

60 high-risk MitraClip pts with 3+-4+ FMR were propensity matched to  
60 conservatively treated pts with 3+-4+ FMR from a single center in Italy  
Mean age 75 yrs; mean LVEF 34% (52% ICM); median FU 515 days



# MitraClip RCT in functional MR

	<b>COAPT</b>	<b>RESHAPE-HF-2</b>
N patients, sites	555 pts @ 85 NA sites	380 pts @ 50 EU sites
Control arm	GDMT ± CRT	GDMT ± CRT
FMR grade	≥3+ (EROA ≥30 mm <sup>2</sup> and/or Rvol >45 mL by ECL)	≥3+ (EROA ≥30 mm <sup>2</sup> and/or Rvol >45 mL by ECL)
NYHA class	II, III, or ambulatory IV	III or ambulatory IV
Other inclusion criteria	HF hosp within 12 months or BNP ≥300 pg/ml or nT-proBNP ≥1500 pg/ml within 12 months; MV surgery is not local standard of care	HF hosp within 12 months or BNP ≥350 pg/ml or nT-proBNP ≥1400 pg/ml within 90 days; not eligible for MV surgery
LVEF	≥20% - ≤50%	≥15% - ≤40%
LV volumes	LVESD ≤70 mm	LVEDD ≥55 mm
Primary efficacy endpoint	Recurrent HF hospitalization at 12 months	Death or recurrent HF hospitalization at 12 months
Primary safety endpoint	SLDA, device embolizations, endocarditis/MS/device-related complications requiring non-elective CV surgery, LVAD, OHT	All-cause mortality, stroke, MI, new renal replacement therapy, non-elective CV surgery for device related complications
Total follow-up	5 years	1 year
PIs	GW Stone, M Mack	P Ponikowski, S Anker

# MitraClip RCT in functional MR

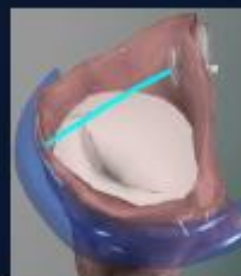
	MITRA-FR	MATTERHORN
N patients, sites	288 pts @ 22 French sites	210 pts @ 15 EU sites
Control arm	GDMT ± CRT	MV Surgery
FMR grade	Severe (EROA >20 mm <sup>2</sup> + Rvol >30 mL) by ECL	≥3+
NYHA class	II - IV	≥III
Other inclusion criteria	HF hosp within 12 months; not eligible for MV surgery	-
LVEF	≥15% - ≤40%	≥20% - ≤45%
LV volumes	-	-
Primary efficacy endpoint	Death or recurrent HF hospitalization at 12 months	Death, HF rehosp, reintervention, assist device implantation or stroke at 12 months
Primary safety endpoint	-	Major adverse events at 30 days
Total follow-up	2 years	1 year
PIs	JF Obadia	J Hausleiter

# MitraClip RCT in functional MR

	<b>EVOLVE-HF</b>
N patients, sites	168 patients @ 15 global sites
Design	2x2 assignment to MitraClip vs. control, and CRT on vs. off (all pts receive CRT-D with defibrillator function on) - <b>blinded</b>
FMR grade	Severe (3-4+) by ECL
NYHA class	II - IVa
Other inclusion criteria	Patient on GDMT but without CRT; Class IIa indication for CRT (LBBB with QRS 120-149 ms or RBBB with QRS >150 ms); 6MWD >0 - <450 m
LVEF	>15% - ≤35%
LV volumes	-
Primary efficacy endpoint	Improvement in 6 minute walk test from baseline to 6 months
Primary safety endpoint	-
Total follow-up	12 months
PI	A. Asgar

# A Sampling of Mitral Annuloplasty Devices

\* CE mark



	Cardiac Dimensions Carillon *	MVRx ARTO	Mitralign TAMR *
<b>Mechanism</b>	Coronary sinus mediated posterior annulus cinching	A-P shortening via coronary sinus - LA band	Retrograde aortic pledget-mediated annular plication
<b>N pts treated</b>	~400 (113 in studies)	14	71 (51 with 2 <sup>nd</sup> gen)



	Valtech Cardioband *	GDS Accucinch	Millipede IRIS
<b>Mechanism</b>	LA semi-rigid posterior partial annuloplasty band with anchor cinching	LV postero-basal annuloventriculoplasty via anchor cinching	Complete circumferential semi-rigid direct annuloplasty ring
<b>N pts treated</b>	~100	39 (6 versions)	9

# Transcatheter MVR

## *What are the Challenges ?*

### Anatomical





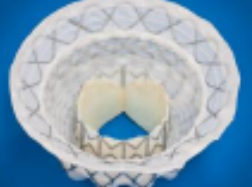
- Large, assymmetric, saddle-shaped annulus
- Lack of leaflet calcification
- $\pm$  MAC (frequently assymmetric)
- Subvalvar apparatus
- Dynamic implant environment








### Technical

- Large size – folding, access/closure issues
- Orientation
- Fixation
- Ability to retrieve/ reposition
- LVOT obstruction
- Loss of native subvalvular apparatus
- SAM
- Device thrombosis
- PVL (hemolysis)
- Invasiveness

# TMVR Device Features – Human Implants

Device	Edwards CardiAQ	Neovasc Tiara	Edwards Fortis	Abbott Tendyne	Medtronic Intrepid
					
Access	TA / TF	TA	TA	TA	TA
Nitinol frame	+	+	+	+	+
Pericardial leaflet tissue type	Bovine	Bovine	Bovine	Porcine	Bovine
Trileaflet valve	+	+	+	+	+
Symmetric leaflets	+	-	+	+	+
Implant shape	Circular	D-shaped	Circular	D-shaped	Circular
Seal	Pericardial	Synthetic	Synthetic	Synthetic	Synthetic
Atrial flange	-	+	+	+	+
Apical tether	-	-	-	+	-
Barbs/Tines	+	-	-	-	+
Clips/Tabs/Paddles	+	+	+	-	-

# TMVR Device Features – Human Implants

Device	Edwards CardiAQ	Neovasc Tiara	Edwards Fortis	Abbott Tendyne	Medtronic Intrepid
					
Fixation required					
Posterior leaflet	-	-	+	-	-
Posterior ridge	-	+	-	-	-
Anterior leaflet	-	-	+	-	-
Recapture/retrieval	-	-	-	Retrievable	Retrievable
Suitable for	soon				
FMR / DMR	+ / +/-	+ / +	+ / -	+ / +	+ / +
Sheath size	36 Fr	32 Fr	42 Fr	32 Fr	35 Fr
N patients treated	14	17	23	37	17
Procedural success	9/11 (82%)	14 (82%)	10/13 (77%)	26/28 (93%)	15 (88%)
Early mortality	6/12 (50%)	3 (18%)	5/13 (39%)	1/23 (4%)	4 (24%)

# Transcatheter MVR

More than 33 in development!

## Potential advantages (vs. repair)

1. Applicable to primary and secondary MR, regardless of anatomy or pathology
2. Ease of implantation
3. Reliable elimination of MR
4. Greater durability

# Conclusion

- **Functional MR is one of poor indicator for developing adverse outcomes.**
- **MitraClip is only one established and widespread use in EU and US.**
- **It seem to have clinical benefit and comparable with surgical MV repair for functional MR.**
- **However, RCT to compare with OMT is needed.**
- **New MV repair techniques or devices and percutaneous MVR are under development and seem to have promising.**

A photograph of a city skyline at dusk, with several tall buildings illuminated by their own lights. The sky is a mix of orange and blue. In the foreground, there is a body of water that reflects the city lights and the sky. Some tree branches are visible in the upper left corner.

*Thank you for your attention*