

MITRACLIP

Pour qui et comment ?

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CHU Nantes. FR

MITRACLIP : for who ?

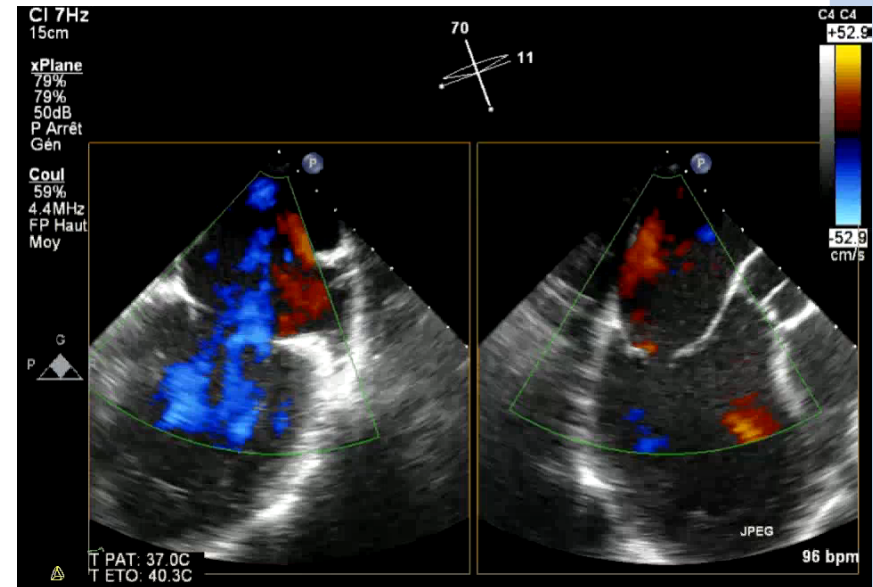
- MR
 - Secondary MR
 - Primitive MR
 - Rescue



Eugénie sur la plage de Biarritz

Quid de l'IM secondaire ?

- Quand corriger ?
- Comment corriger



IM fonctionnelle : Quand corriger ?

- Traitement cardiopathie +/- plastie mitrale
- STICH

Indications for mitral valve surgery in chronic secondary mitral regurgitation

Revascularisation possible

Revascularisation impossible

ou non indiquée

	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

	Class ^a	Level ^b
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

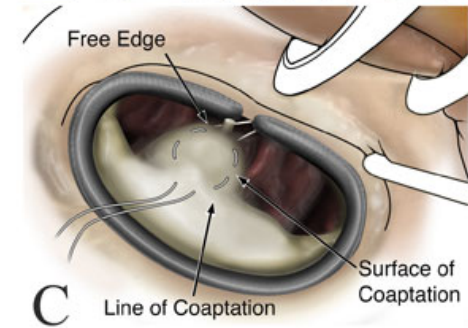
- Pronostic moindre / IM organiques
- Population différente

Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC), European Association for Cardio-Thoracic Surgery (EACTS), Vahanian A, Alfieri O, Andreotti F, Antunes MJ, et al. Guidelines on the management of valvular heart disease (version 2012). Eur Heart J. oct 2012;33(19):2451-2496.

Deja MA, Grayburn PA, Sun B, Rao V, She L, Krejca M, et al. Influence of mitral regurgitation repair on survival in the surgical treatment for ischemic heart failure trial. Circulation. 29 mai 2012;125(21):2639-2648. **STICH**

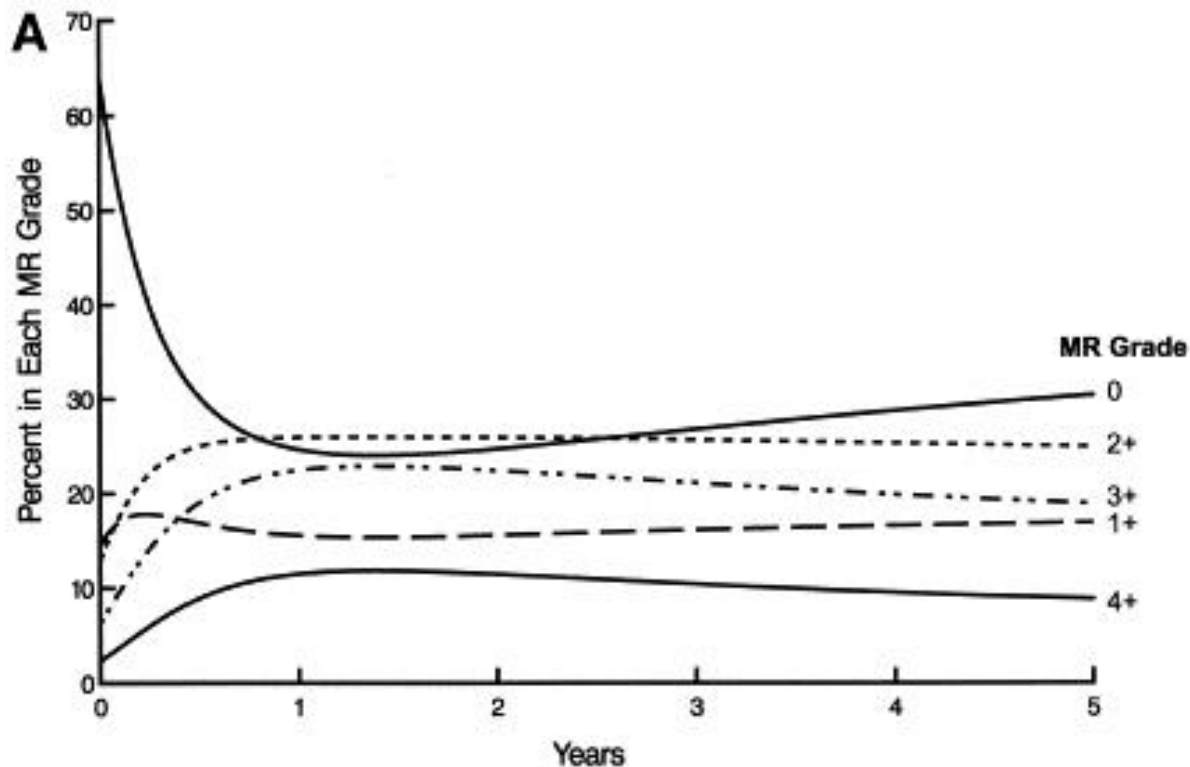
Mitral regurgitation

- Surgery



Quid de l'IM secondaire ?

- Récidives fréquentes de l'IM malgré l'annuloplastie (>20%)



Mc Gee et al. J Thorac Cardiovasc Surg 2004;128: 916-24.

Quid de l'IM secondaire ?

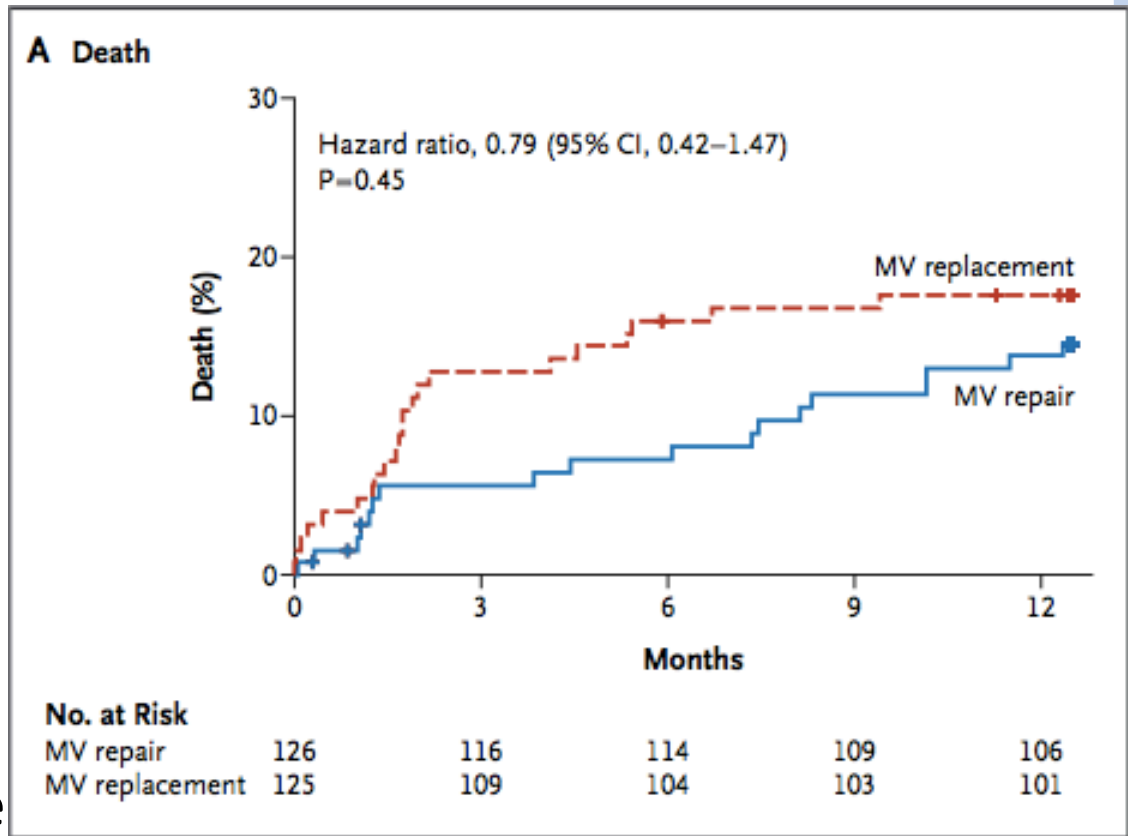
- La chirurgie

- FE 40%

Acker et al.

NEJM 2014; 370: 23-32

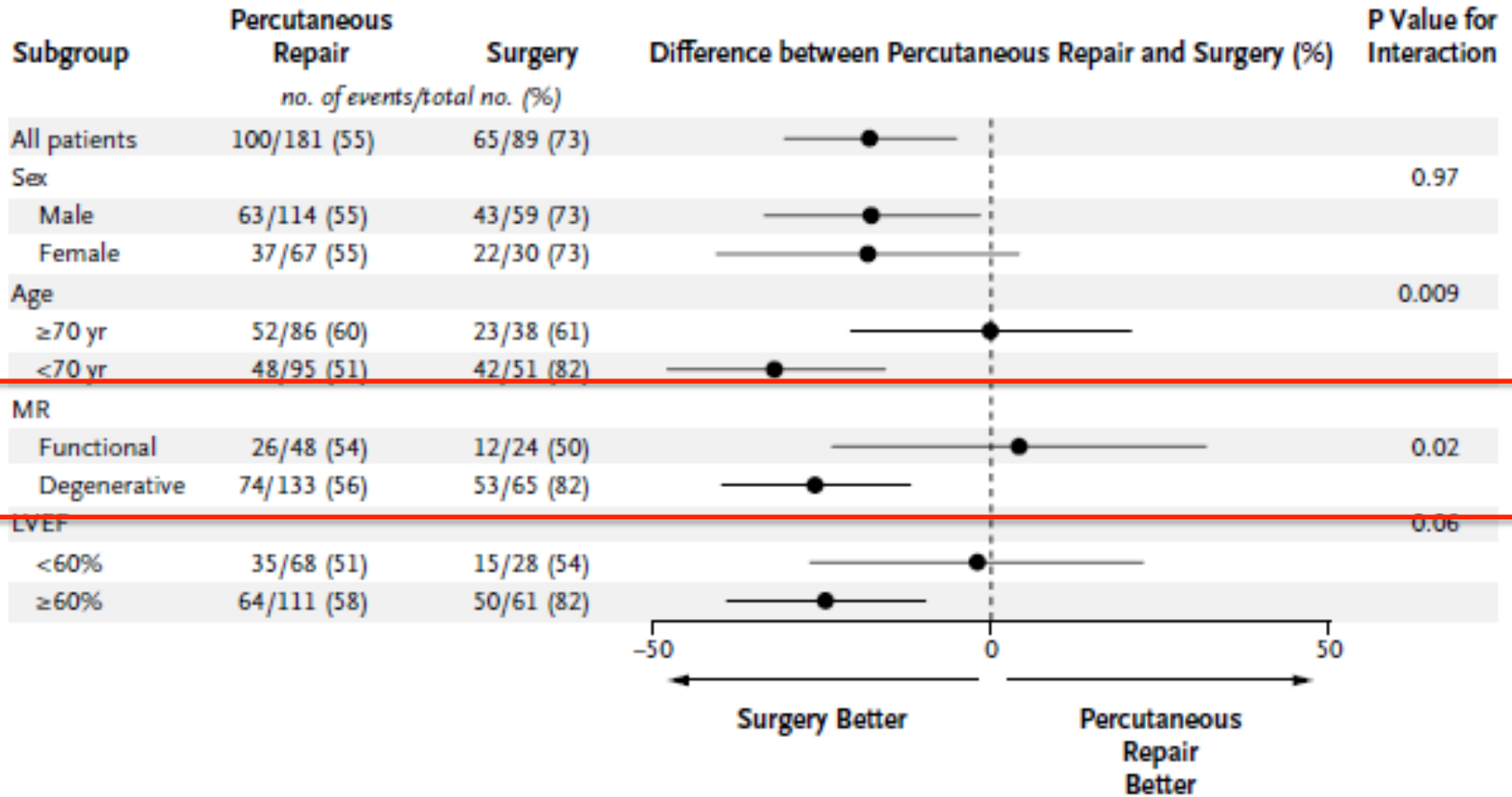
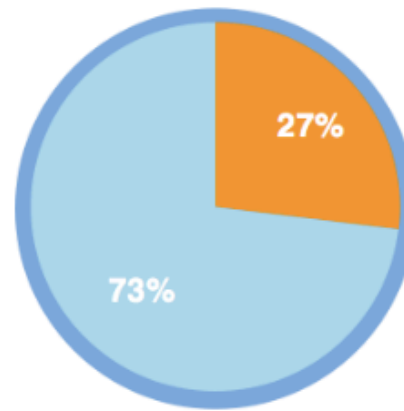
- Pas d'avantage de
 - Etude marseillaise...



Quid de l'IM secondaire ?

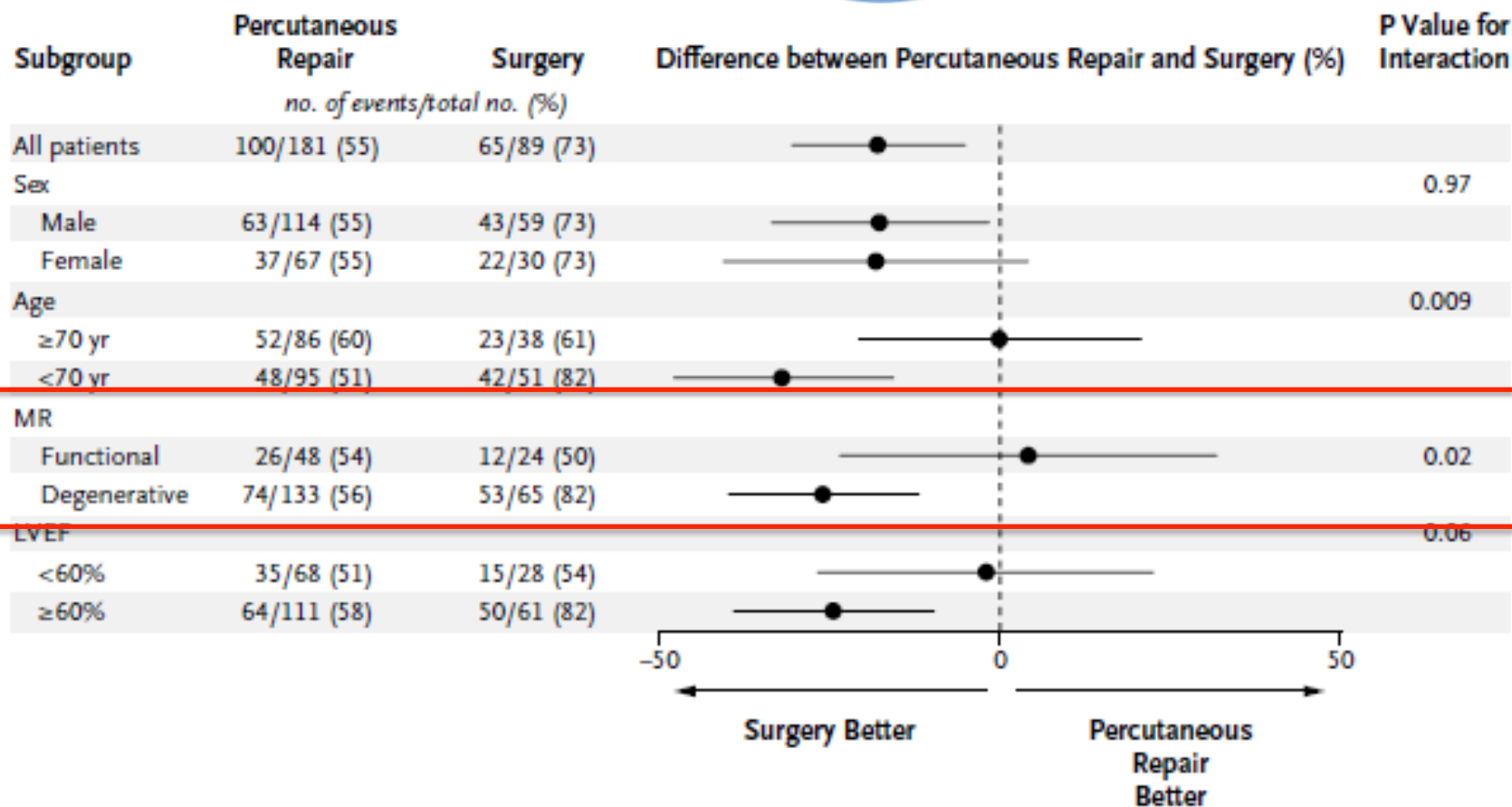
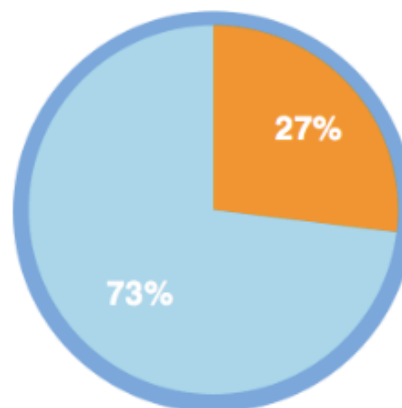
- Pour résumer : Chirurgie de l'IM secondaire
 - Les indications isolées sont rares
 - Indiquées si revascularisations avec FE>30%...
 - Le geste est à risque
 - Les récurrences d'IM sur plastie sont fréquentes
 - Probablement pas d'effet sur la survie
 - C'est pas la révolution !....

• EVEREST II

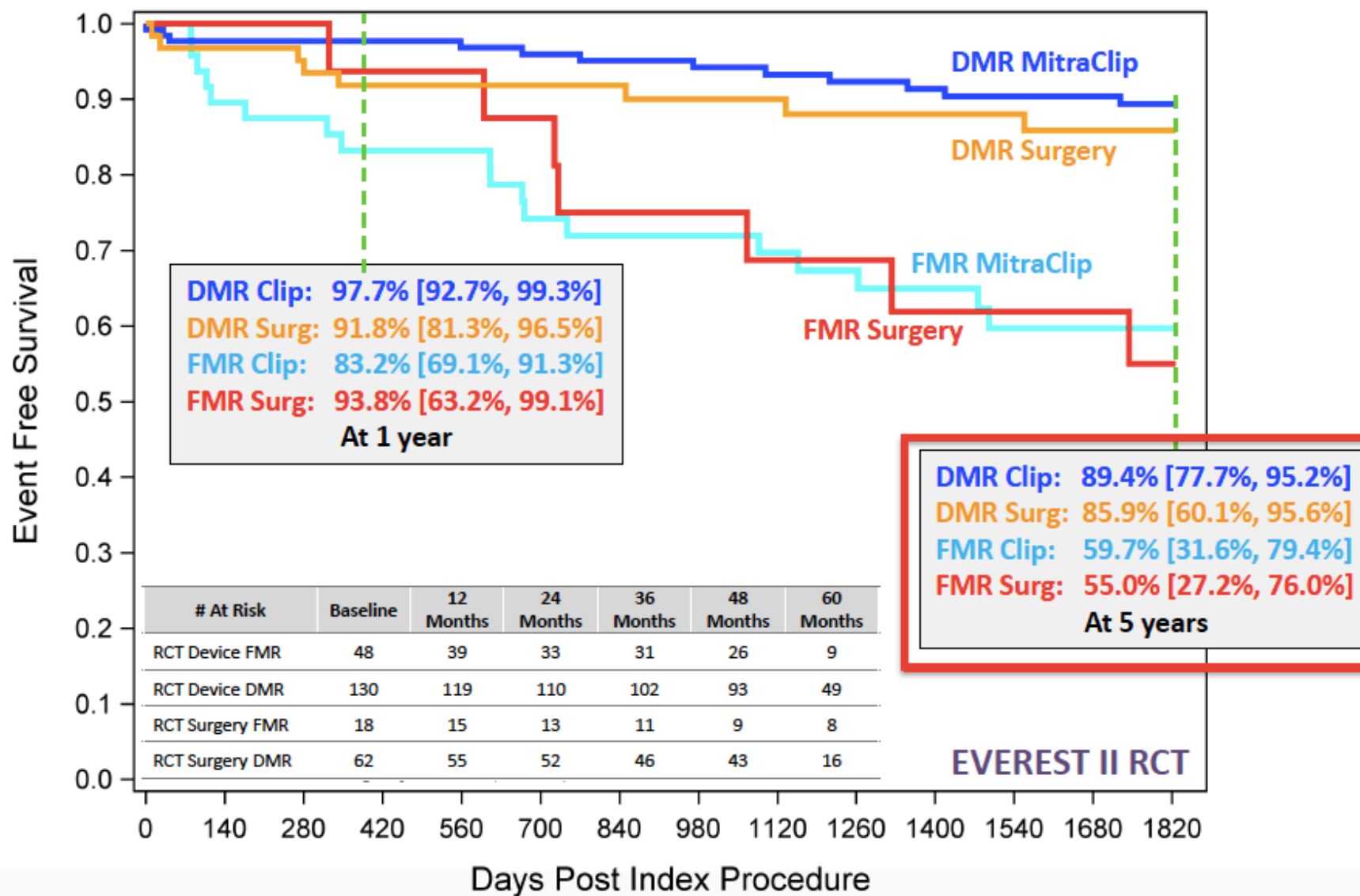




• EVEREST II



Freedom From Mortality in MitraClip and MV Surgery Groups Comparable Within Etiologies



Percutaneous treatment of secondary MR

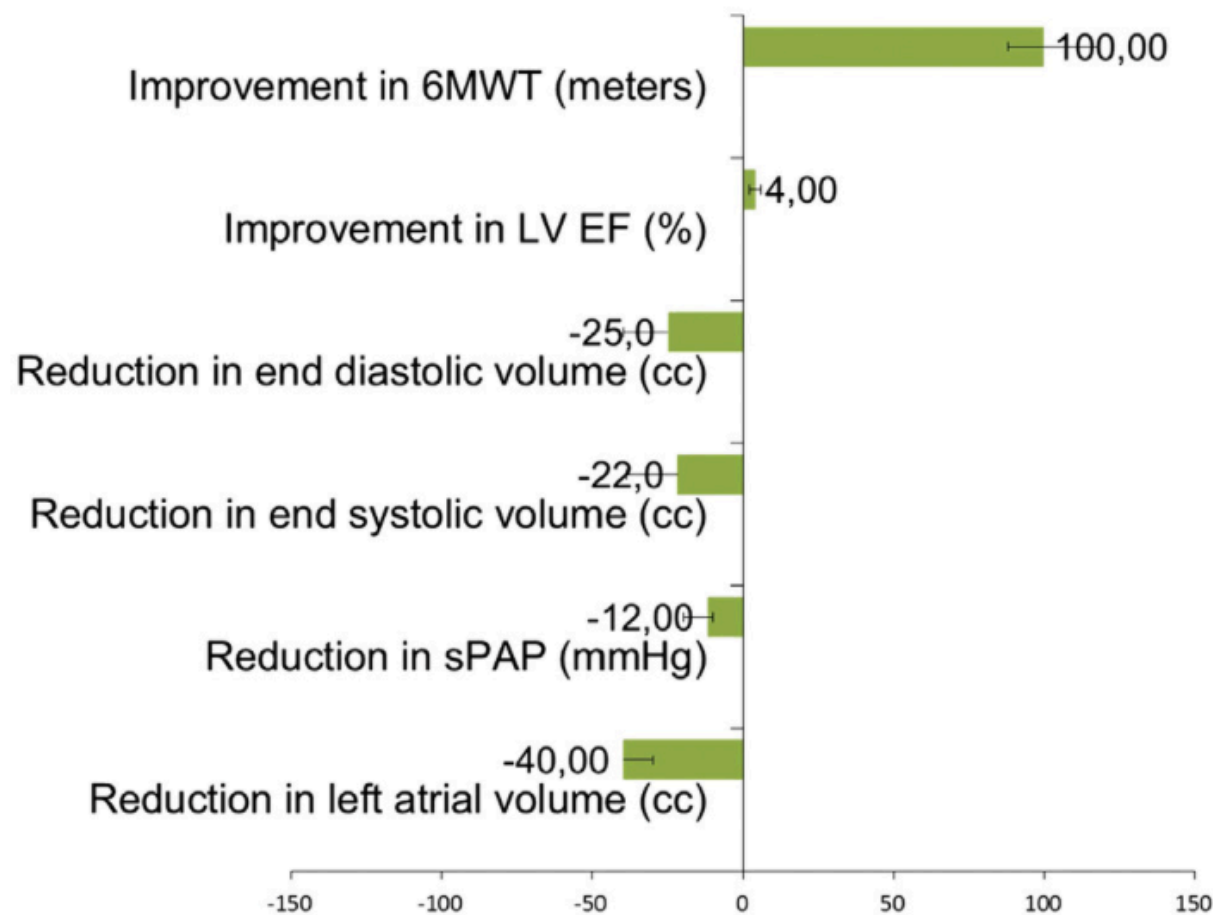
Why ?

	FMR (n = 264)				DMR (n = 85)			
	Pre-Clip	Post-Clip	Δ	p Value	Pre-Clip	Post-Clip	Δ	p Value
LVEDV, ml	171.1 ± 90.2	167.0 ± 90.8	4.1	0.212	118.9 ± 57.9	113.1 ± 54.3	5.8	0.265
LVESV, ml	116.3 ± 71.3	114.8 ± 78.4	1.5	0.634	54.0 ± 32.4	56.5 ± 33.4	-2.5	0.313
LA volume, ml	122.5 ± 59.7	113.4 ± 57.9	9.1	0.029	114.1 ± 85.4	99.3 ± 63.2	14.8	0.040
LVEF, %	37.1 ± 13.6	37.0 ± 13.5	0.1	0.792	59.9 ± 9.3	55.5 ± 9.6	4.4	<0.001
Degree of MR, %				<0.001				<0.001
None/mild	1.0	71.9			0	72.1		
Moderate	14.3	26.1			9.8	26.2		
Severe	84.7	2.0			90.2	1.6		
MR quantification								
EROA, cm ²	0.42 ± 0.15	—	—		0.46 ± 0.18	—	—	
VC, mm	7.5 ± 2.7	—	—		7.6 ± 2.9	—	—	
RV, ml	51.1 ± 27.7	—	—		62.7 ± 21.3	—	—	
Mean TMG, mm Hg	1.9 ± 1.3	3.4 ± 2.1	-1.5	<0.001	2.3 ± 1.3	3.6 ± 1.6	-1.3	0.003
SPAP, mm Hg	44.2 ± 13.2	39.2 ± 11.2	5	<0.001	53.5 ± 16.9	43.4 ± 12.2	10.2	0.001

Nickenig et al. , JACC 2014; 64:875-84

Percutaneous treatment of secondary MR

Why ?

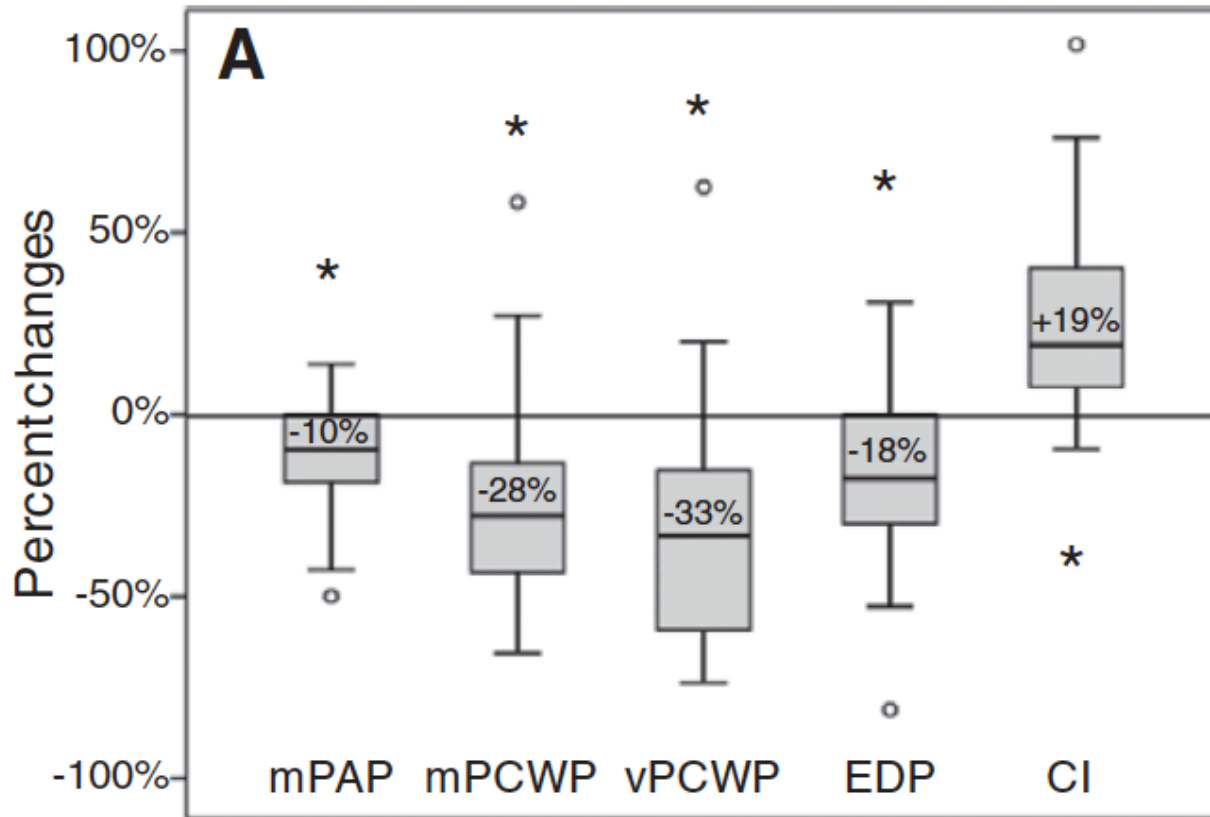


FMR :
Median follow-up
of 9 months (6 to 12)

Figure 4. Change of functional and echocardiographic data at follow-up.

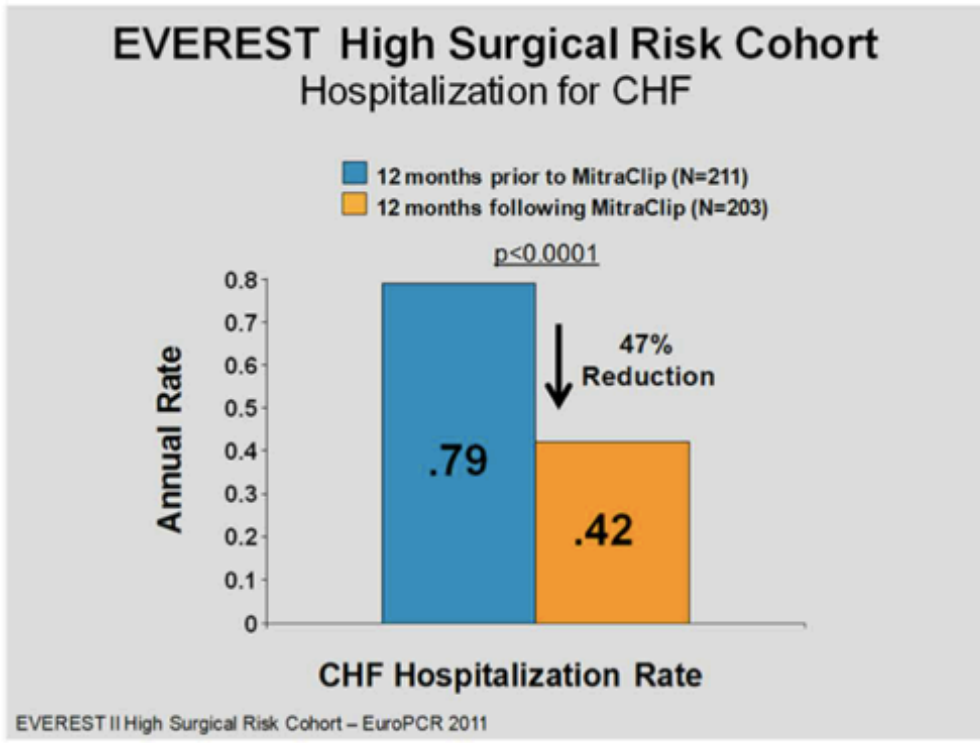
Percutaneous treatment of secondary MR

Why ?



The EVEREST II High Risk Registry (STS>12)

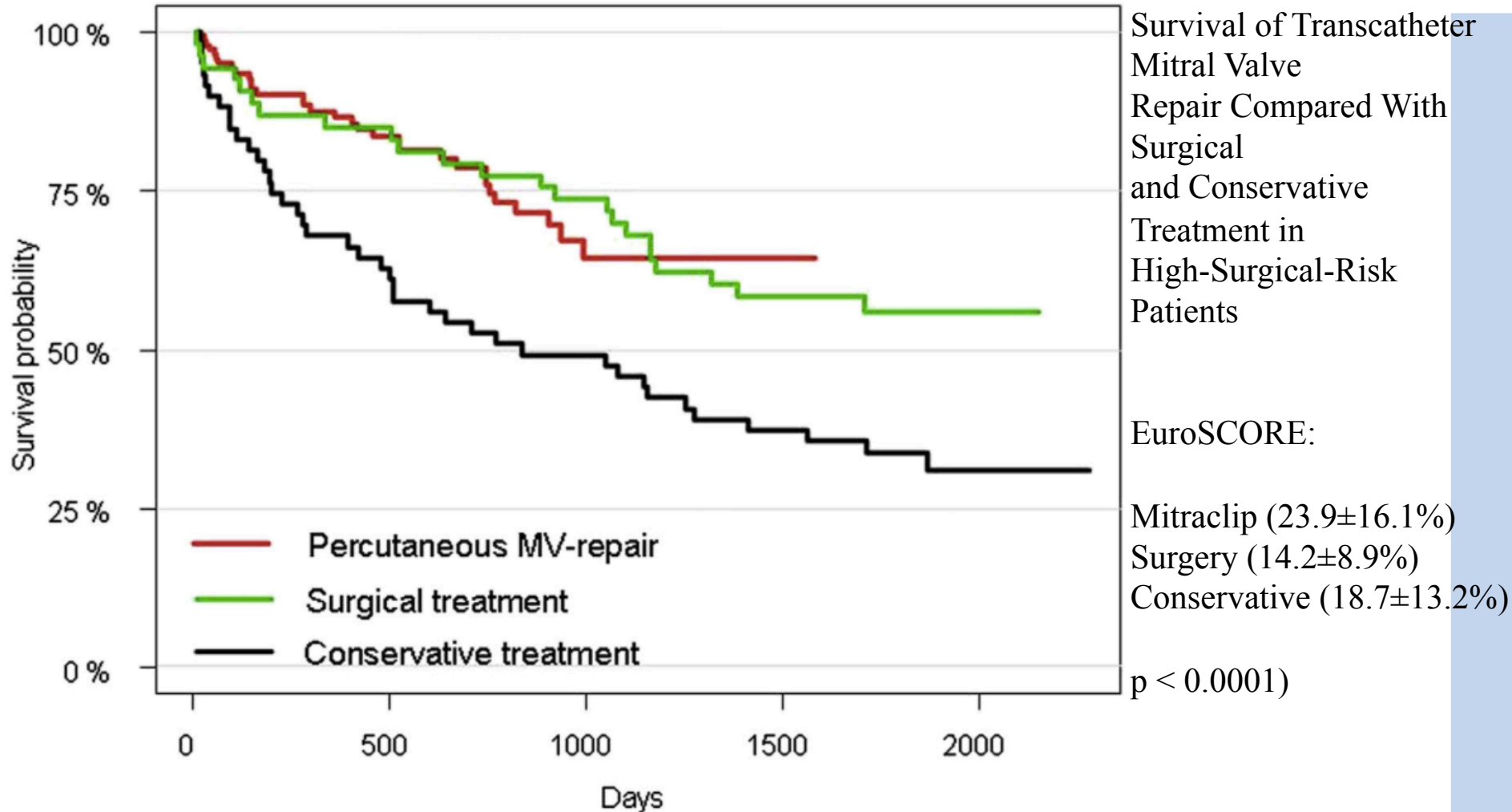
Demographics and Comorbidities	High Risk Cohort (N=211)
Age (years)	76 ± 10
≥ 75 years, (%)	57
Predicted Mortality †, (%)	15
Prior Cardiac Surgery, (%)	58
History Myocardial Infarction, (%)	49
Prior Stroke, (%)	14
COPD/Chronic Lung Disease, (%)	30
Moderate to Severe Renal Failure, (%)	31
History Atrial Fibrillation, (%)	64
Diabetes Mellitus, (%)	40
Ejection Fraction < 30%, (%)	9
LV ESD (mm)	4.2
NYHA Class III or IV, (%)	86
Etiology—Functional MR, (%)	71



†Based on STS ≥ 12% or an assigned mortality 12% for pre-specified co-morbidities

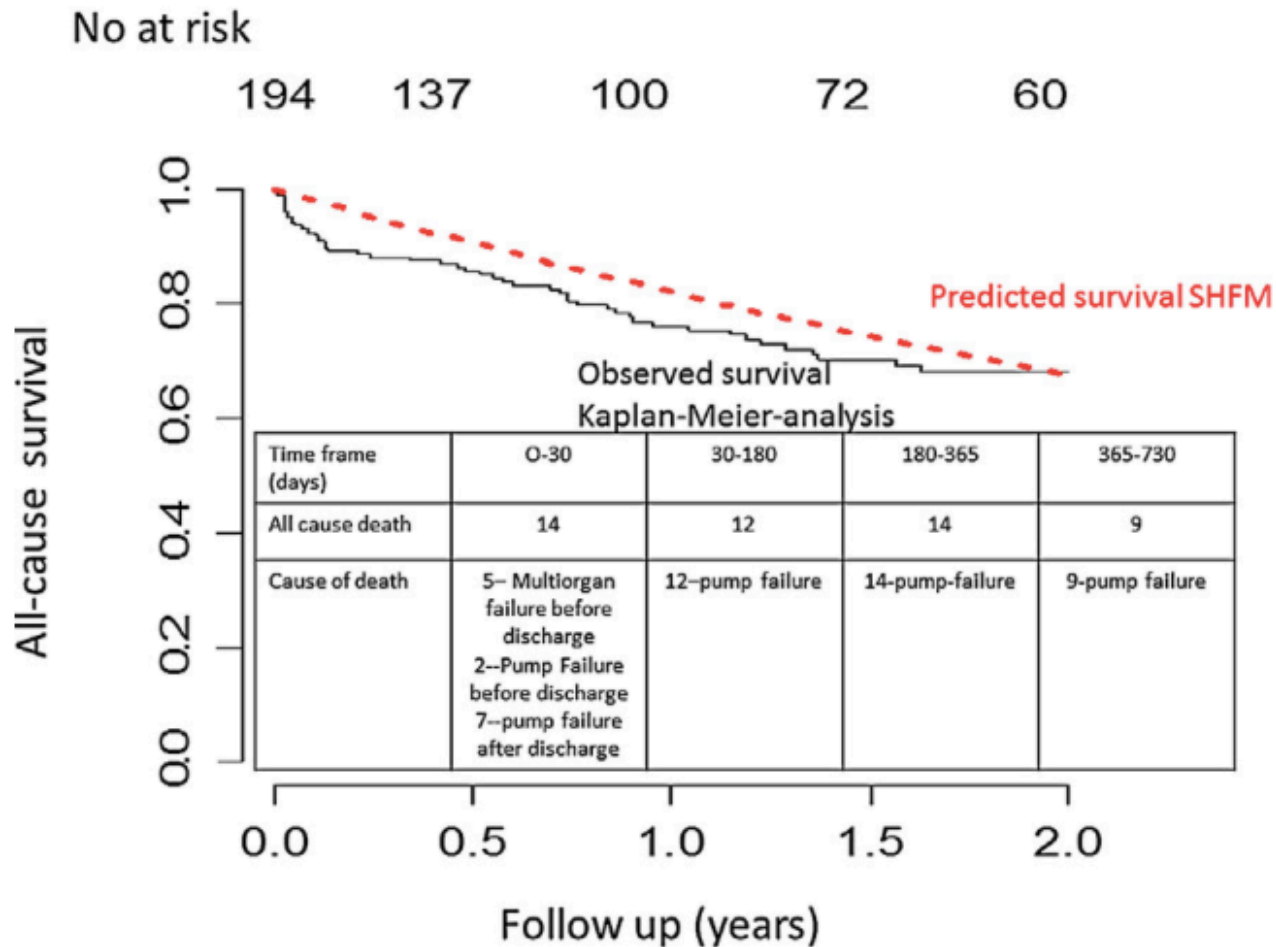
Percutaneous treatment of secondary MR

Why ?



Swaans et al. , JACC intervention 2014; 7:875-81

Retrospective study (194 patients): Observed mortality vs predicted by Heart failure model (Seattle HF model)



Schau et al. Journal of Cardiology 2015.

Percutaneous treatment of secondary MR

Who ?

- Inoperable or at high surgical risk +++
- Severe LV dysfunction +++
 - ! ntProBNP > 10 000 ?
 - LVESV > 110 ml
 - Ischemic etiology
 - NYHA 4
 - Tricuspid insufficiency > 2
 - TAPSE < 15 mm
 - Comorbidities
- Patients non-responders to cardiac resynchronization therapy (CRT) ?

Percutaneous Mitral Valve Repair (PMVR)

- EF > 30% and revascularisation : which one ? Angioplasty or surgery ?

Management of Valvular Heart Disease

Guidelines on the management of valvular heart disease (version 2012)

The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Authors/Task Force Members: Alec Vahanian (Chairperson) (France)*, Ottavio Alfieri (Chairperson)* (Italy), Felicità Andreotti (Italy), Manuel J. Antunes (Portugal), Gonzalo Barón-Esquivias (Spain), Helmut Baumgartner (Germany), Michael Andrew Borger (Germany), Thierry P. Carrel (Switzerland), Michele De Bonis (Italy), Arturo Evangelista (Spain), Volker Falk (Switzerland), Bernard Jung (France), Patrizio Lancellotti (Belgium), Luc Pierard (Belgium), Susanna Price (UK), Hans-Joachim Schäfers (Germany), Gerhard Schuler (Germany), Janina Stepinska (Poland), Karl Swedberg (Sweden), Johanna Takkenberg (The Netherlands), Ulrich Otto Von Oppell (UK), Stephan Windecker (Switzerland), Jose Luis Zamorano (Spain), Marian Zembala (Poland)

Indication for primary MR

Scenario	Recommendation Class	Level of Evidence
Class IIb: Indications for percutaneous mitral repair	IIb	C
Class IIa: Indications for percutaneous mitral repair	IIa	C
Class I: Indications for percutaneous mitral repair	I	C

“Percutaneous edge-to-edge procedure may be considered in patients with symptomatic severe primary MR who fulfill the echo criteria of eligibility, are judged inoperable or at high surgical risk by a ‘heart team’, and have a life expectancy greater than 1 year (recommendation class IIb, level of evidence C).” *page 21*

Indication for secondary MR

Scenario	Recommendation Class	Level of Evidence
Class IIb: Indications for percutaneous mitral repair	IIb	C
Class IIa: Indications for percutaneous mitral repair	IIa	C
Class I: Indications for percutaneous mitral repair	I	C

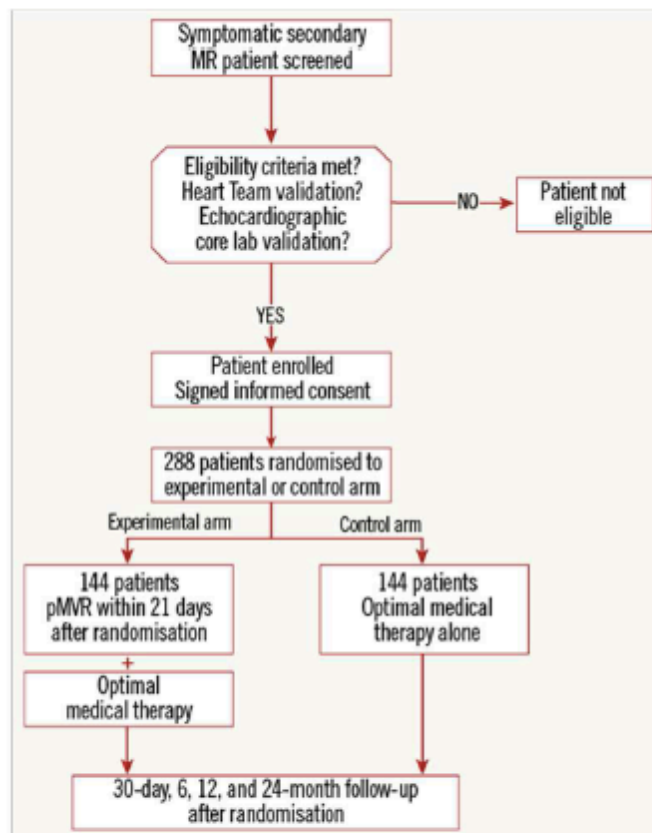
“The percutaneous mitral clip procedure may be considered in patients with symptomatic severe secondary MR despite optimal medical therapy (including CRT if indicated), who fulfill the echo criteria of eligibility, are judged inoperable or at high surgical risk by a team of cardiologists and cardiac surgeons, and who have a life expectancy greater than 1 year (recommendation class IIb, level of evidence C).” *page 25*

The MITRA-FR study: design and rationale of a randomised study of percutaneous mitral valve repair compared with optimal medical management alone for severe secondary mitral regurgitation

Jean-François Obadia^{1,2*}, MD, PhD; Xavier Armoiry^{3,4}, PharmD, PhD; Bernard Jung⁵, MD, PhD; Thierry Lefèvre⁶, MD; Nathan Mewton⁷, MD, PhD; David Messika-Zeitoun⁵, MD, PhD; Bertrand Cormier⁶, MD; Julien Berthiller³, MSc; Delphine Maucort-Boulch⁸, MD, PhD; Florent Boutitie⁸, PhD; Bernadette Vaz⁷, PharmD, MSc; Jean-Noël Trochu⁹, MD, PhD; Alec Vahanian⁵, MD, PhD

EuroIntervention

2015 Mar;10(11):1354-60



MITRACLIP : for who ?

- MR
 - Secondary MR
 - Primitive MR
 - Rescue



Napoléon III. Empereur des Français (1852-1870).

The NEW ENGLAND JOURNAL *of* MEDICINE

Percutaneous Repair or Surgery for Mitral Regurgitation

Ted Feldman, M.D., Elyse Foster, M.D., Don 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., M.Sc.,
for the EVEREST II Investigators*

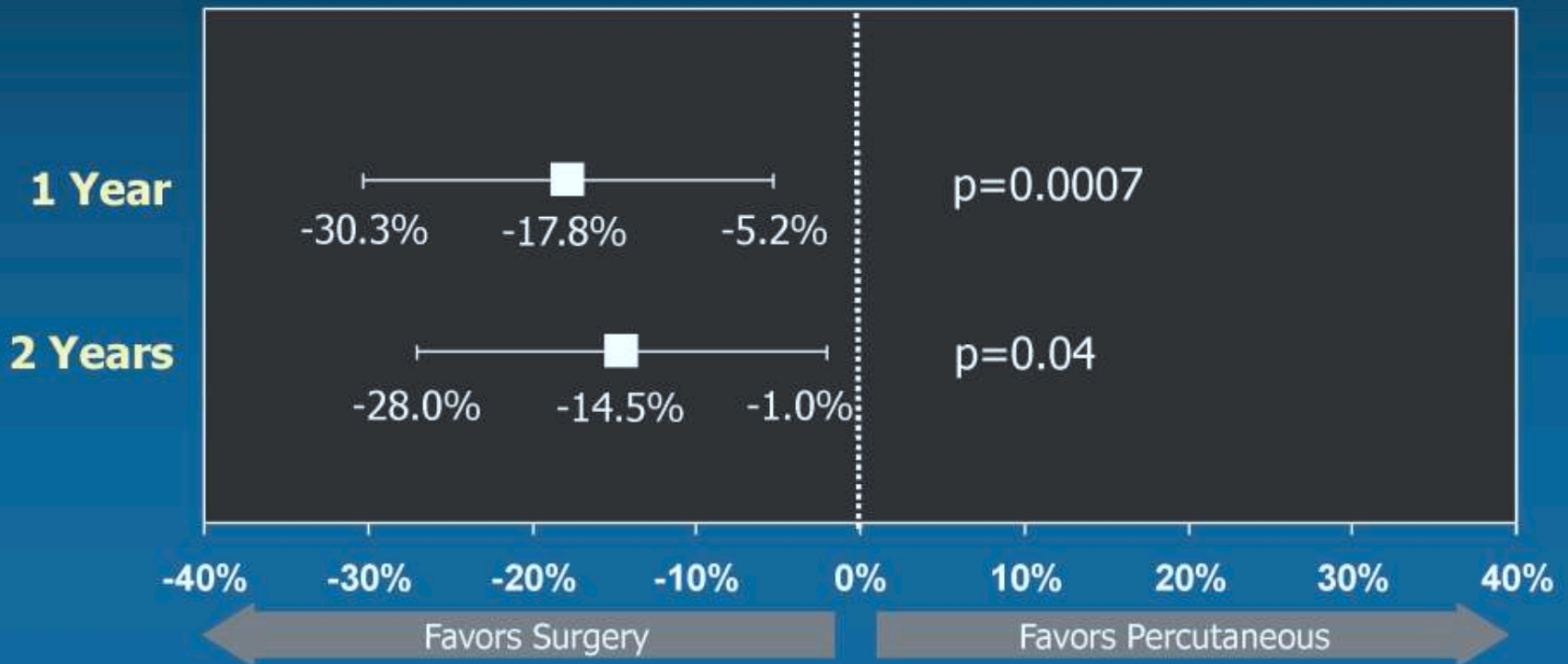
Feldman et al. , NEJM 2011; 364:1395-406

Primary Effectiveness Analyses at 1 and 2 Years

EVEREST DEUX
LA CHIRURGIE FAIT MIEUX !!!!!!!

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

Difference: Percutaneous – Surgery (% , 95% CI)



Superiority of surgery compare to Mitraclip

The incredible study...

EVEREST II Randomized Clinical Trial Study Design

279 Patients enrolled at 37 sites

Significant MR (3+-4+)
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-Up:
Baseline, 30 days, 6 months, 1 year, 18 months, and
annually through 5 years

Baseline Demographics & Co-morbidities

Intention to Treat

Patient Demographics	Percutaneous % N=184	Surgery % N=95	P-value
Degenerative MR Etiology	73	73	0.81
Anterior leaflet involvement (prolapse or flail)	31	26	-
Posterior leaflet involvement only (prolapse or flail)	39	45	-
Neither prolapse nor flail (thickened leaflets)	3	2	-
Functional MR Etiology	27	27	0.81
NYHA Functional Class III/IV	51	47	0.61
MR Severity: 3+ to 4+	96	93	0.48
Mean Ejection Fraction (%)	60	61	0.65
Mean LVIDs (cm)	3.7	3.5	0.16

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 \geq 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

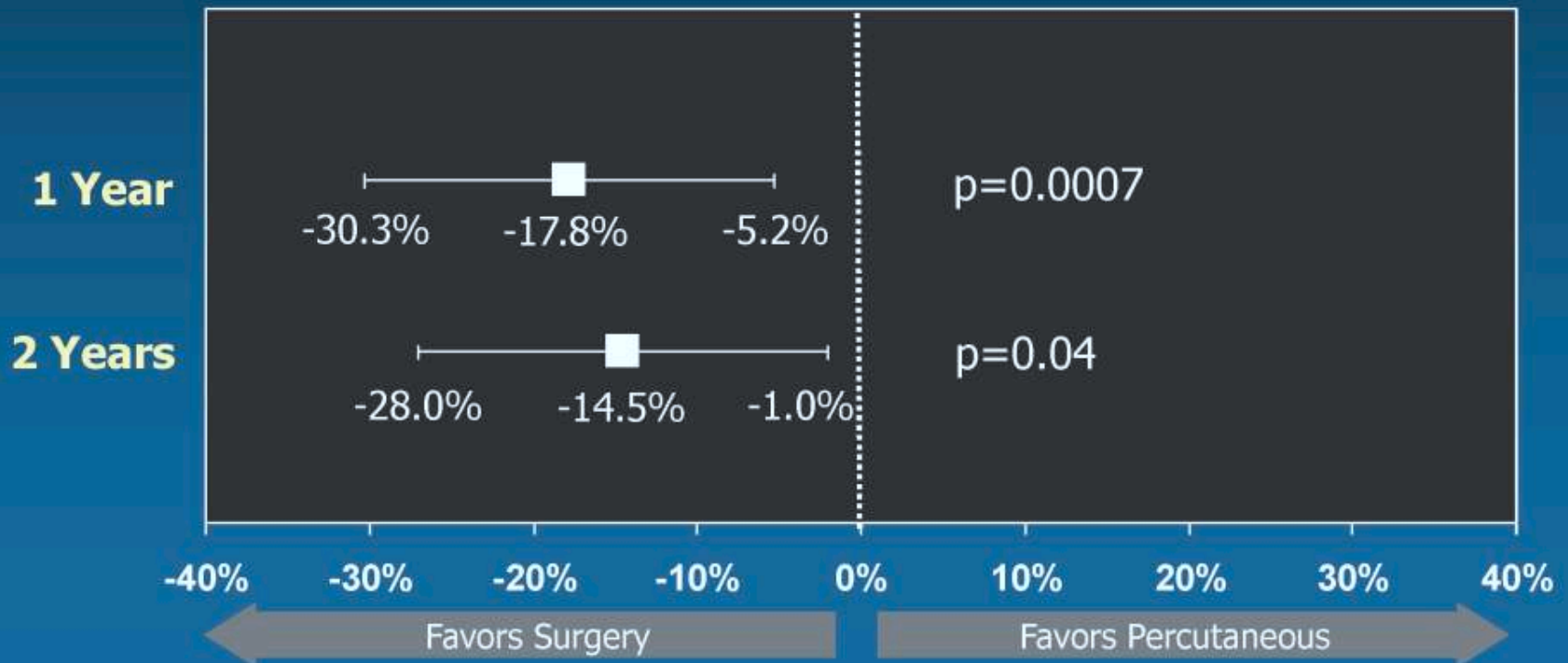
Primary Effectiveness Analyses at 1 and 2 Years Difference Between Percutaneous & Surgery

Intention to Treat Analysis

Primary Effectiveness:

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

Difference: Percutaneous – Surgery (% , 95% CI)

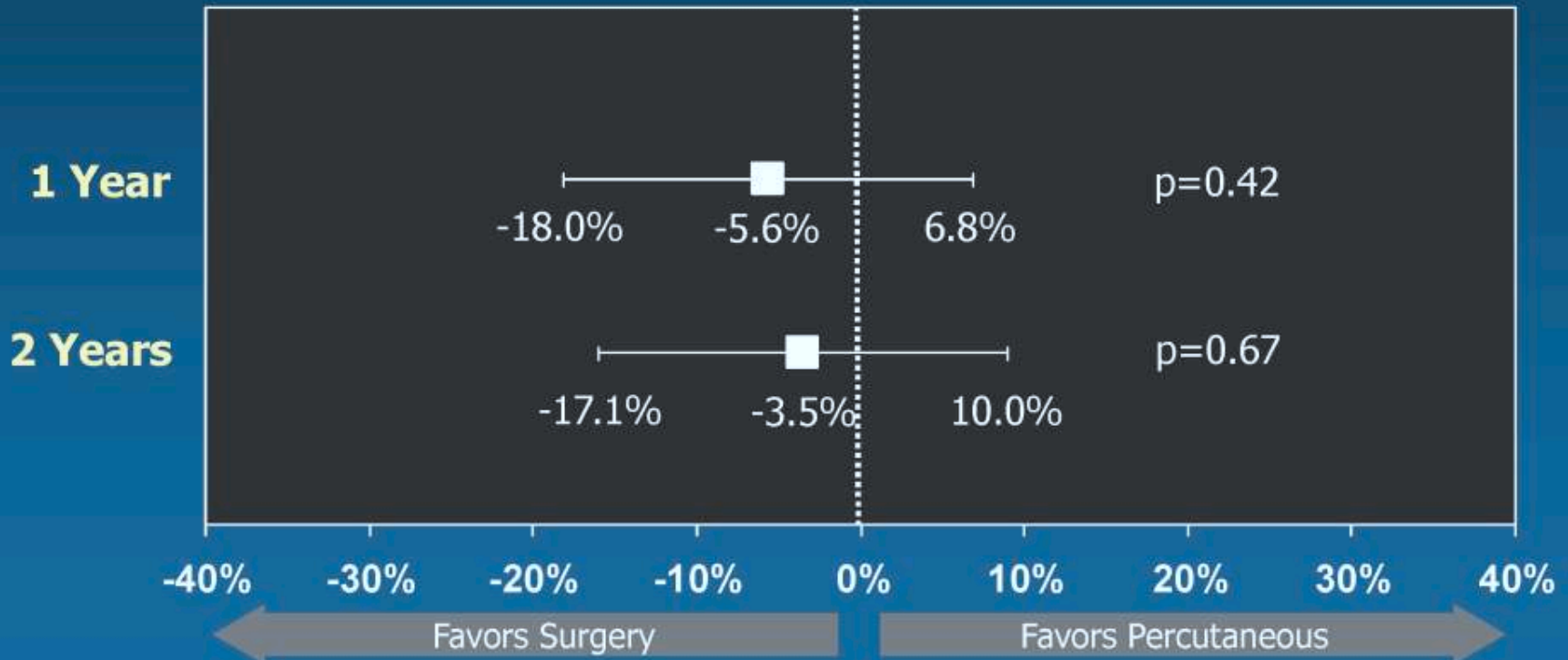


Superiority of surgery compare to Mitraclip

Primary Effectiveness Analyses at 1 and 2 Years Difference Between Percutaneous & Surgery Comparison of Treatment Strategies Analysis

Primary Effectiveness:
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Difference: Percutaneous – Surgery (% , 95% CI)



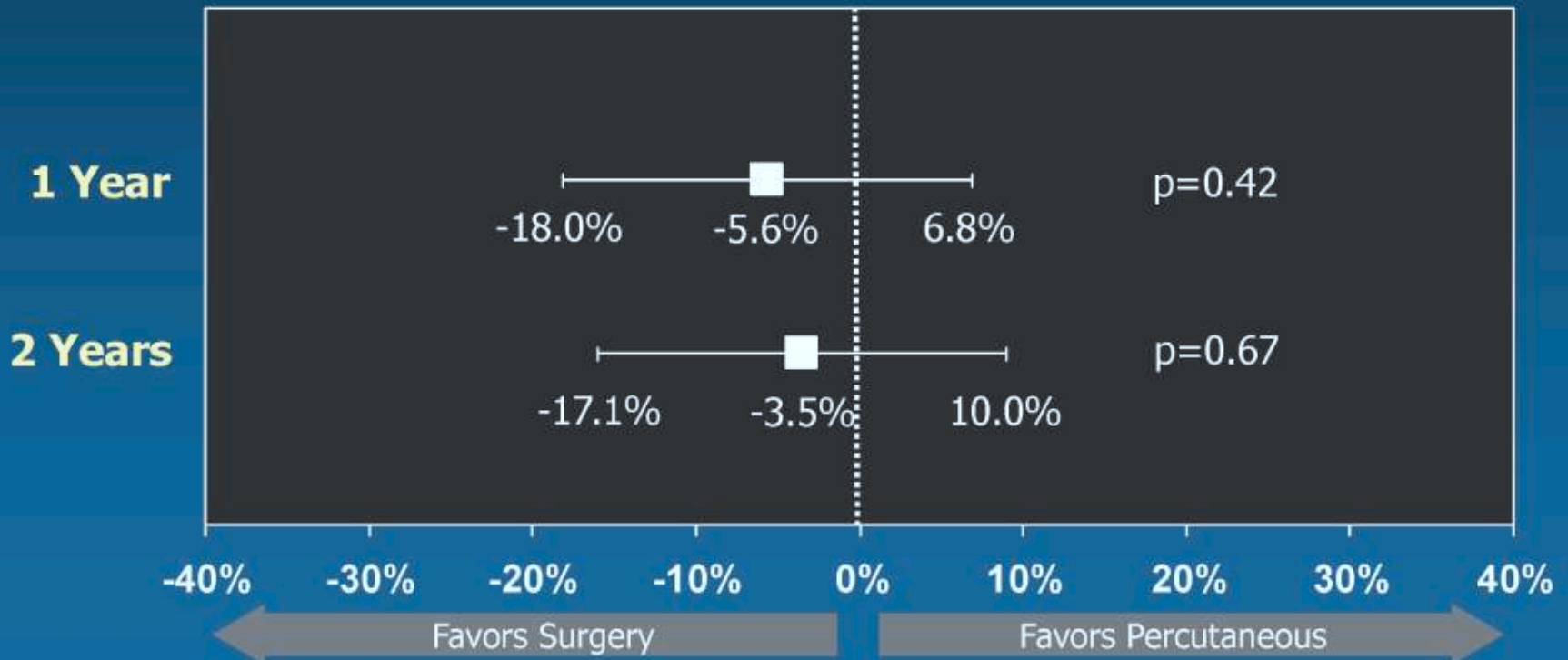
Equivalence between surgery and Mitraclip



Primary Effectiveness Analyses at 1 and 2 Years Difference Between Percutaneous & Surgery Comparison of Treatment Strategies Analysis

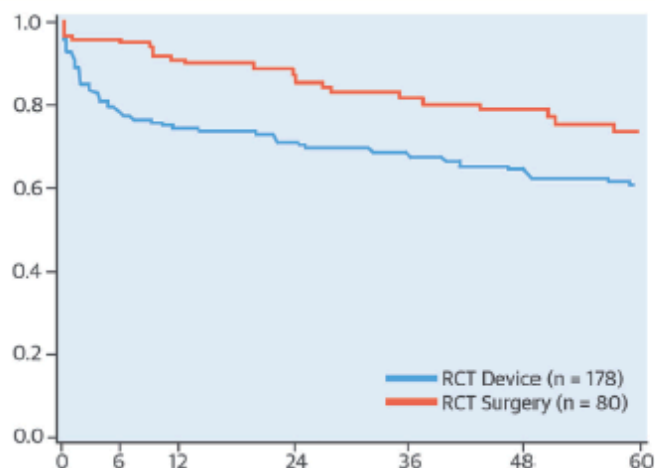
Primary Effectiveness:
Freedom from death, MV surgery/re-operation or 3+ or 4+ MR

Difference: Percutaneous – Surgery (% , 95% CI)



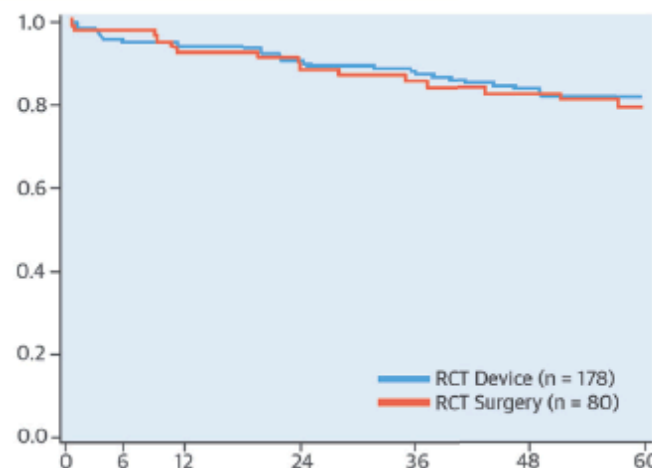
Equivalence between surgery and Mitraclip

A. Freedom From Death, MV Surgery or Reoperation



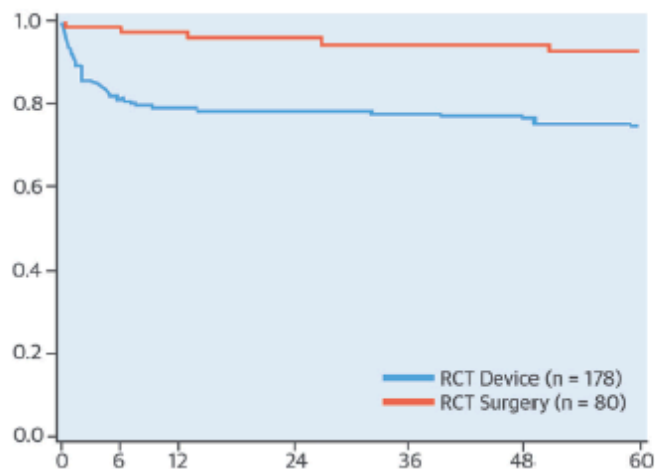
Patients At Risk	Months						
	0	6	12	24	36	48	60
Device Group	178	136	128	117	109	98	45
Control Group	80	75	69	63	54	49	21

B. Freedom From Death



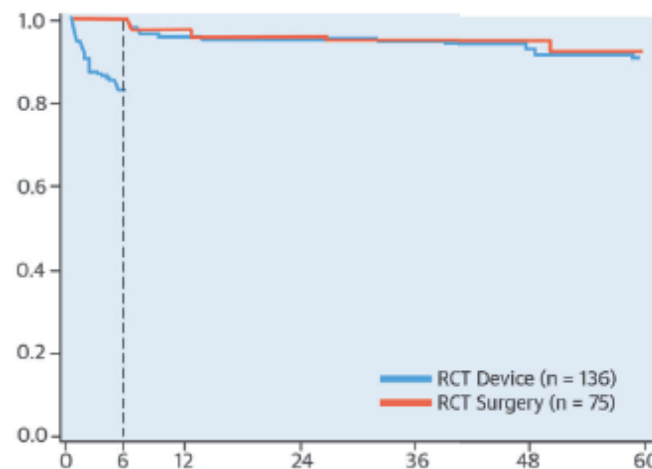
Patients At Risk	Months						
	0	6	12	24	36	48	60
Device Group	178	165	158	143	133	119	58
Control Group	80	76	70	65	57	52	24

C. Freedom From MV Surgery or Reoperation



Patients At Risk	Months						
	0	6	12	24	36	48	60
Device Group	178	136	128	117	109	98	45
Control Group	80	75	69	63	54	49	21

D. Landmark Analysis of Freedom From MV Surgery or Reoperation Beyond 6 Months



Patients At Risk	Months						
	0	6	12	24	36	48	60
Device Group	178	136	128	117	109	98	45
Control Group	80	75	69	63	54	49	21

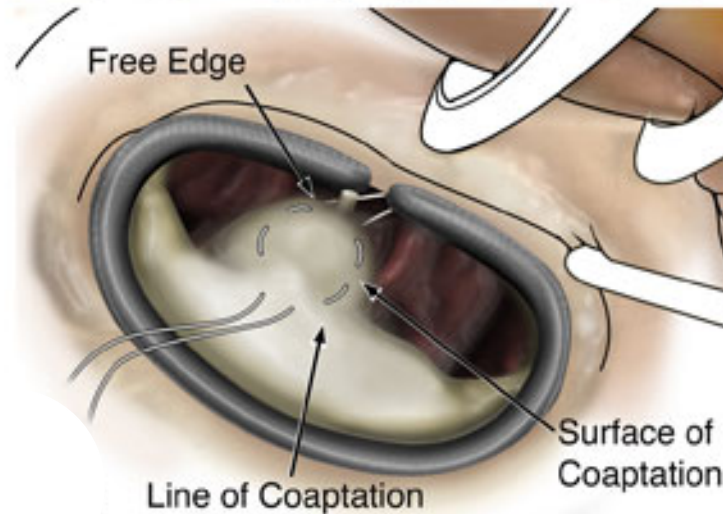
Feldman
JACC
2015

HAS

- Patients avec **insuffisance mitrale sévère, d'origine dégénérative, symptomatique malgré une prise en charge médicale optimale, non éligibles à la chirurgie** et répondant aux critères échocardiographiques d'éligibilité.
- Tous ces critères et en particulier la contre-indication chirurgicale doivent être validés par une équipe multidisciplinaire ad hoc.
- Les patients ayant une espérance de vie inférieure à un an compte tenu de facteurs extracardiaques (comorbidités) ne sont pas éligibles à la technique (non indication).
- **ASA 2**

Comment ?

- Alfieri ?



Fucci C, Sandrelli L, Pardini A, et al: Improved results with mitral valve repair using new surgical techniques. *Eur J Cardiothorac Surg* 1995;9:621-627.
Alfieri O, Ozkan J: Spotlight: Ottavio Alfieri MD, FETCS, FESC. *Circulation* 2010;122:F19-F21.

Mitraclip

- Mitraclip = Alfieri ?

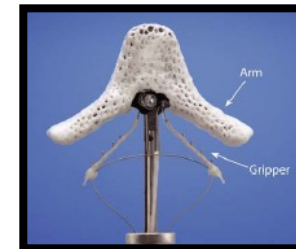


- Equation :

- Edge to edge à l'aveugle + anneau + sternotomie + CEC (Alfieri)

- Vs

- Edge to edge guidée – anneau – sternotomie - CEC (Mitraclip)



Alfieri

- Alfieri ?

Alfieri and colleagues¹ recommend implanting an annuloplasty ring at the time of EtE repair. Animal studies have found that peak stitch tension occurs in diastole, at the maximum annulus diameter, hence the durability of the EtE stitch without annuloplasty has been questioned.^{4,6} However, there has been no long-term patient follow-up to suggest that repair fails if an annuloplasty ring has not been used.

In all three of our cases, the patients were elderly, frail, and required complex surgery to other parts of the heart. Each had a severely calcified mitral annulus

Fucci C, Sandrelli L, Pardini A, et al: Improved results with mitral valve repair using new surgical techniques. Eur J Cardiothorac Surg 1995;9:621-627.
Alfieri O, Ozkan J: Spotlight: Ottavio Alfieri MD, FETCS, FESC. Circulation 2010;122:F19-F21.

Ca ne marche pas ?

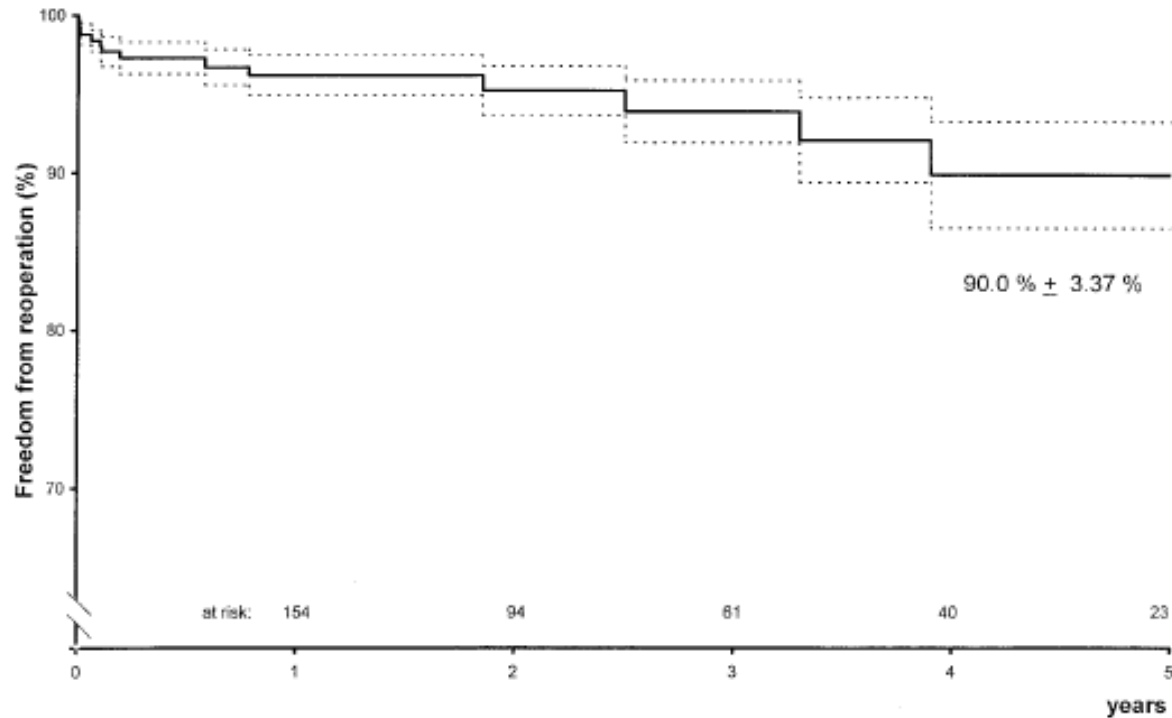


Figure 2. Overall freedom from reoperation. *Dotted lines* depict SE estimates for the mean actuarial freedom from the reoperation curve.

Ca ne marche pas sans annuloplastie ?

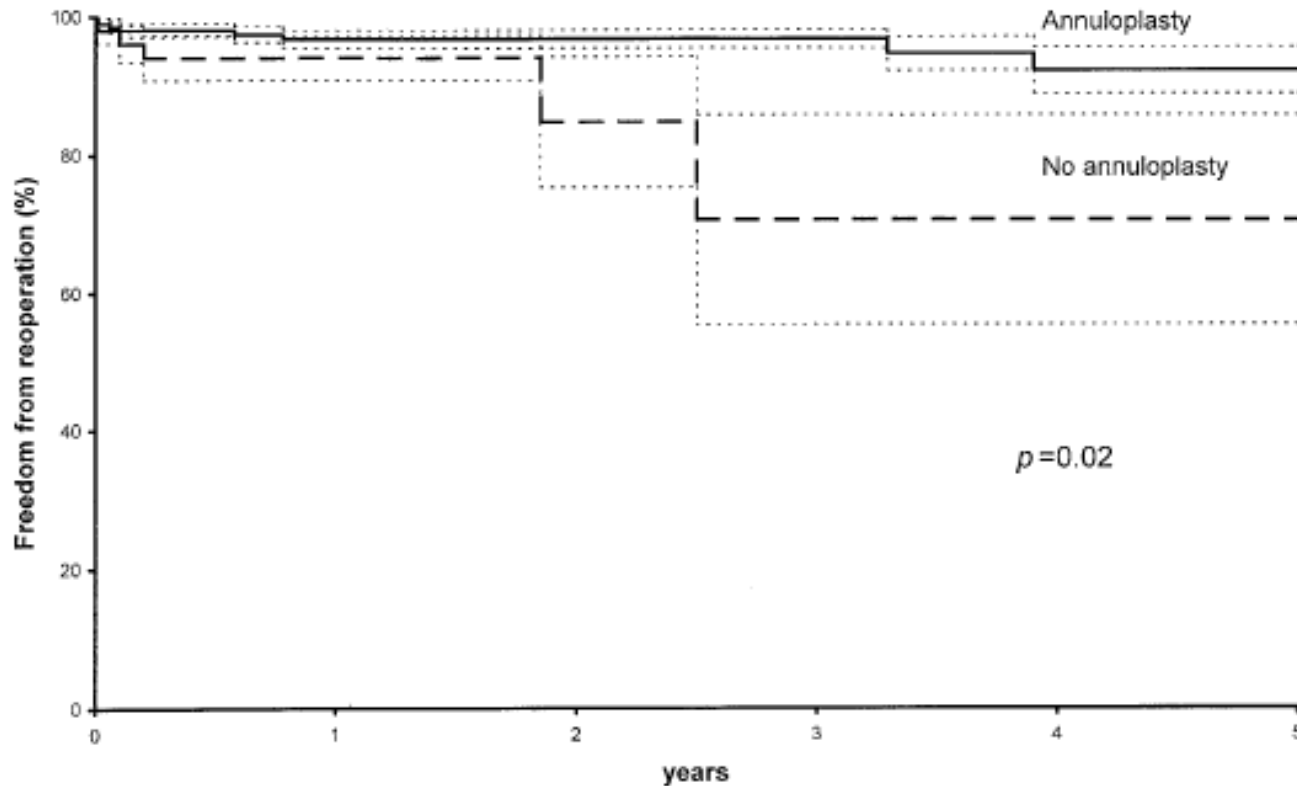
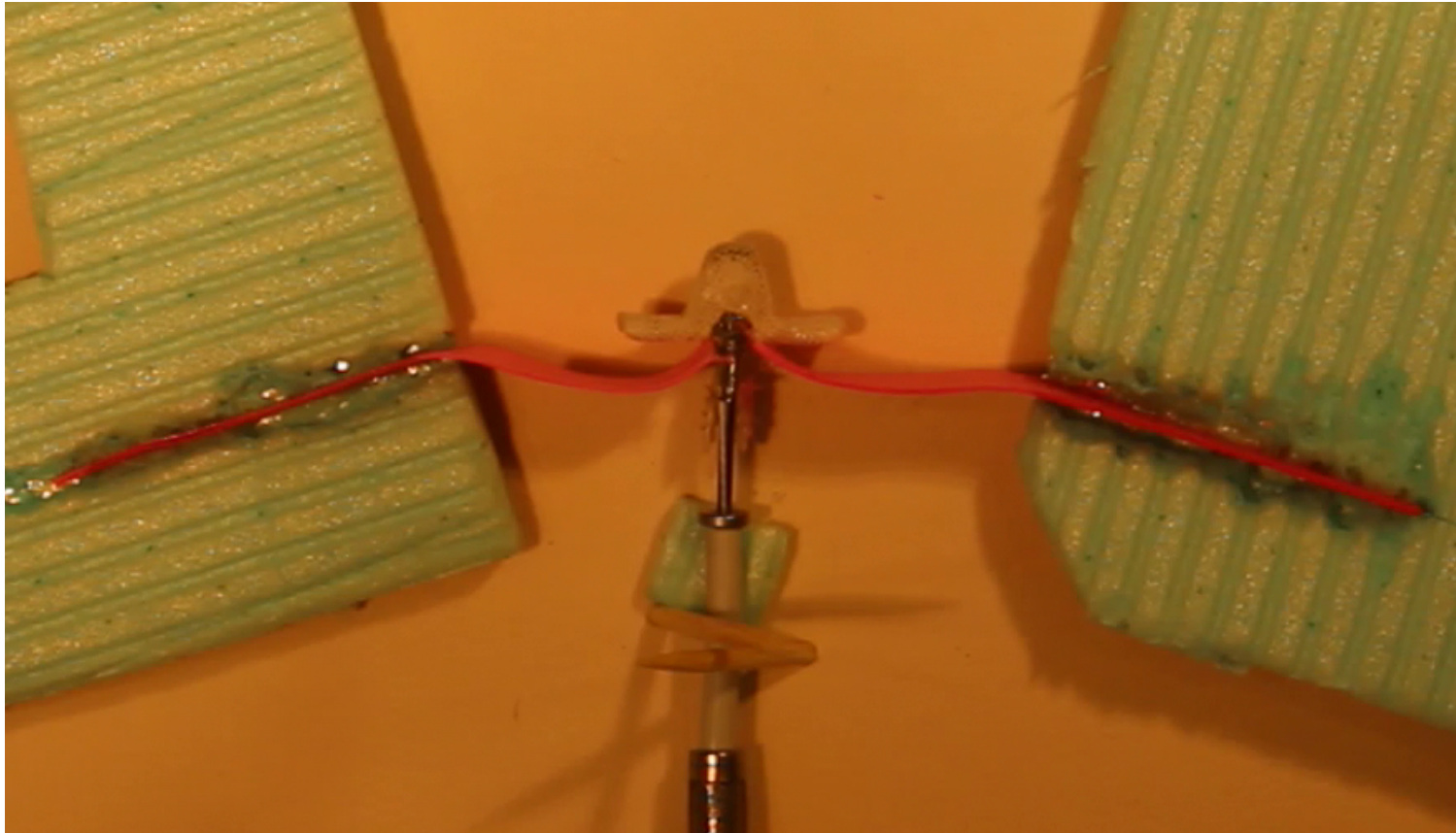


Figure 4. Freedom from reoperation in patients who received an annuloplasty procedure versus those who did not. Dotted lines depict SE estimates for the actuarial curves.



Just a regurgitant orifice closure ?



1. Capture of the two leaflets
2. Traction of the leaflets :
3. Creation of a bridge
4. Restriction of the antero-posterior annulus diameter

Is it just an experimental finding ?

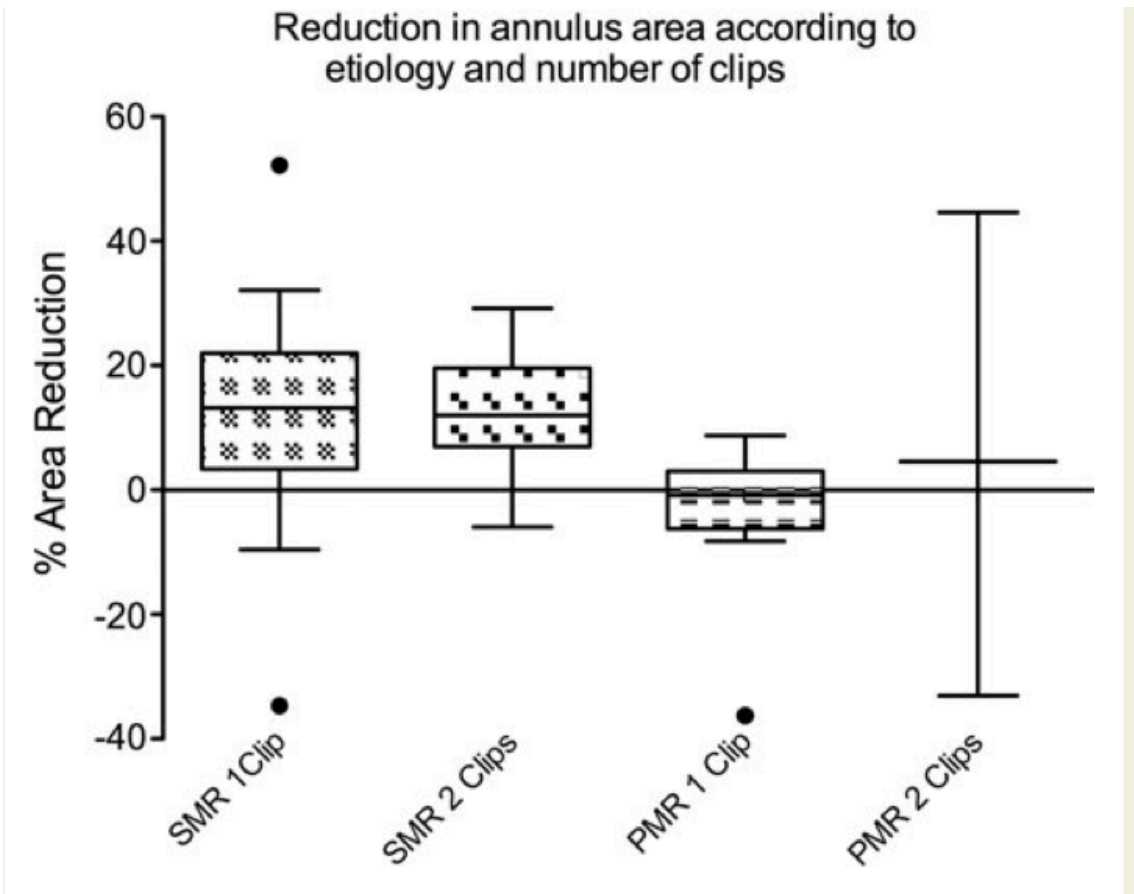
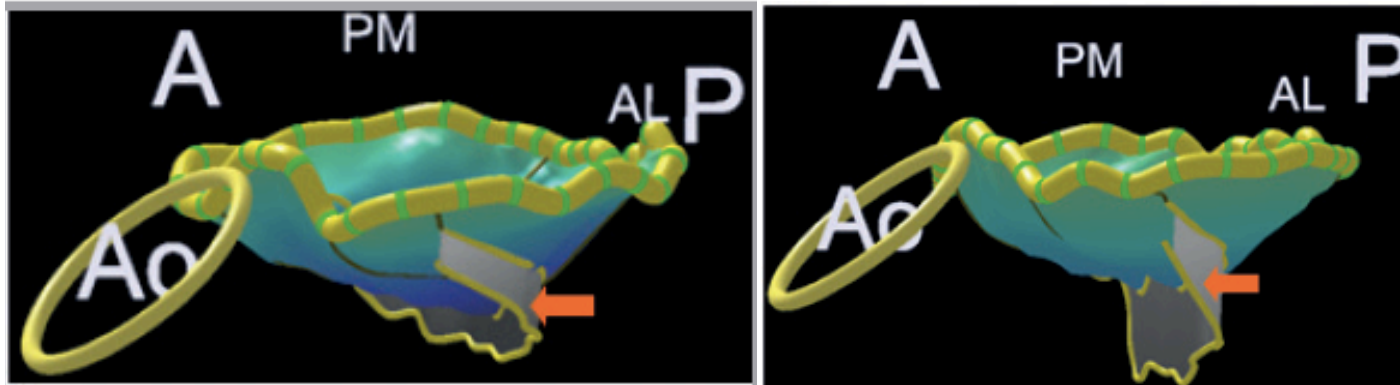
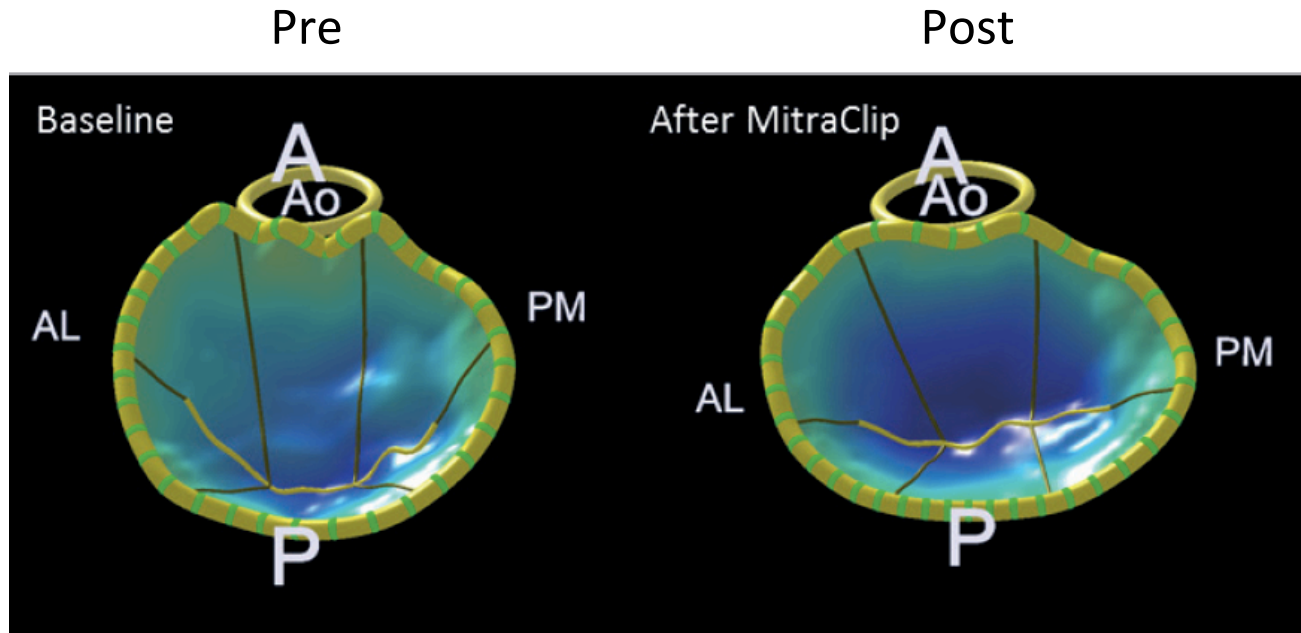


Figure 4 Relative reduction of mitral annulus area with 1 and 2 clips given as boxplot (Tukey Method)



1. Restriction of the antero posterior diameter
2. Increase in coaptation length and coaptation area (A2 P2)
 Responsible for MR reduction

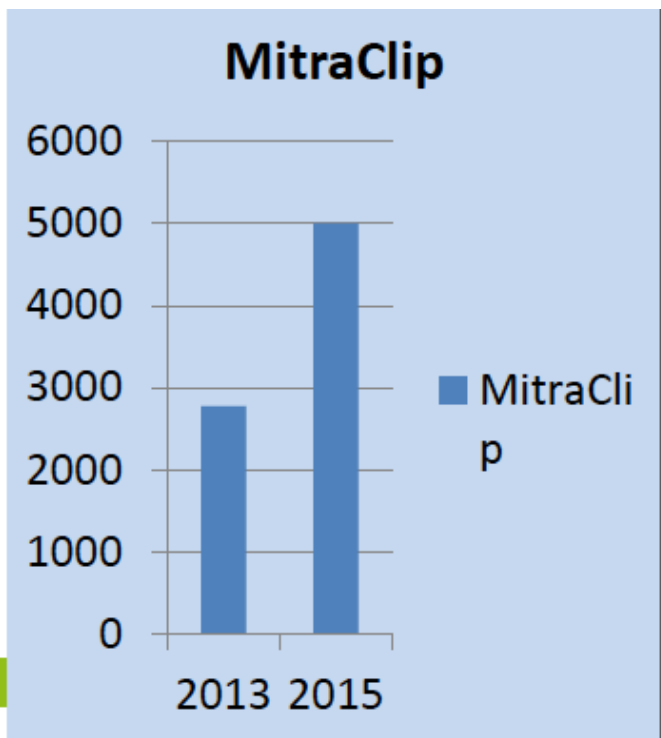
Chirurgie ou Percutané



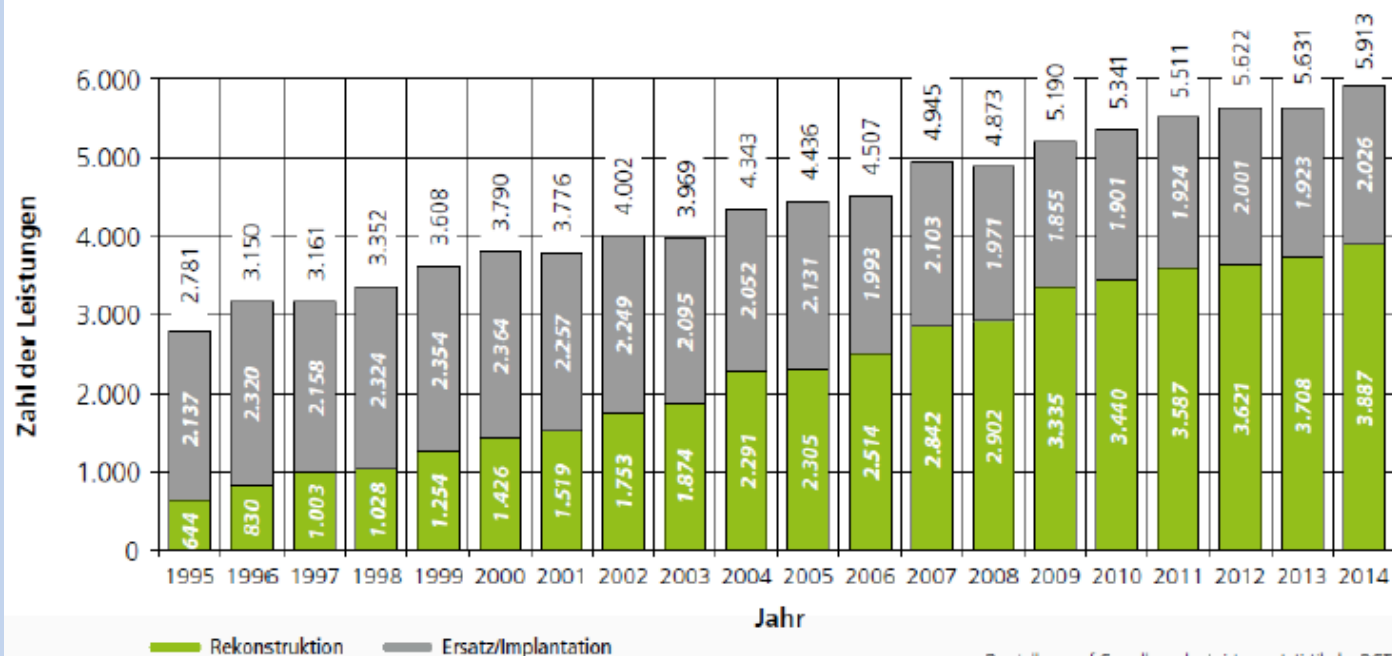
Chirurgie ou Percutané

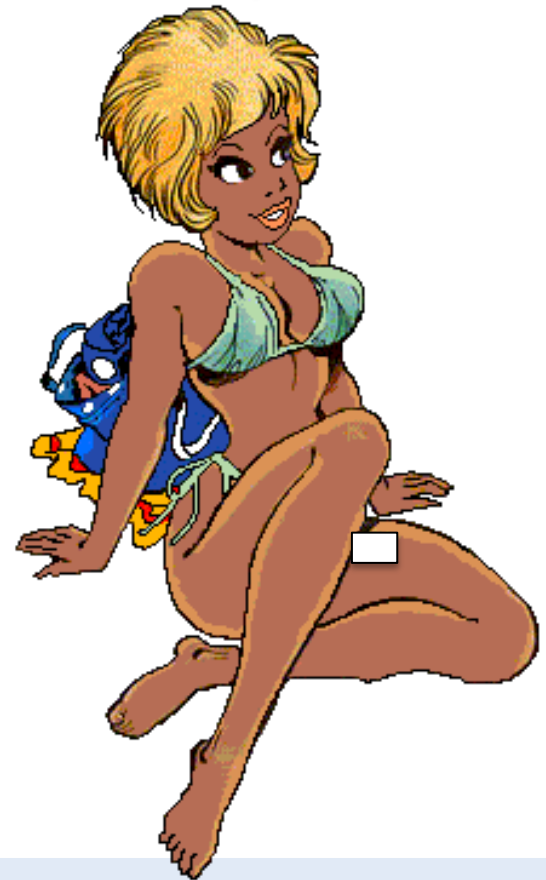
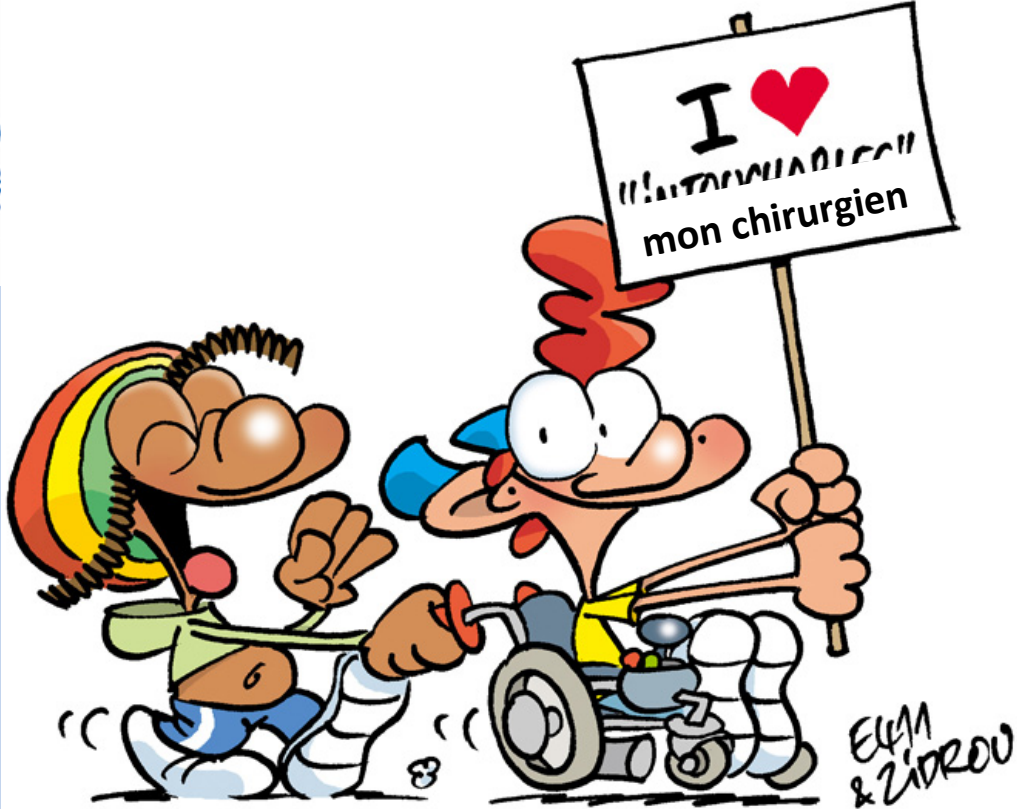


2015 German Heart Report: Treatment of TMVR with MitraClip passed surgical volume



Entwicklung der isolierten Mitralklappenchirurgie nach Operationsverfahren





Merci pour votre attention