



SABATO 2 MARZO

TRATTAMENTO DELL'INSUFFICIENZA MITRALICA CON LA MITRACLIP

A FAVORE

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Milanese - MI*

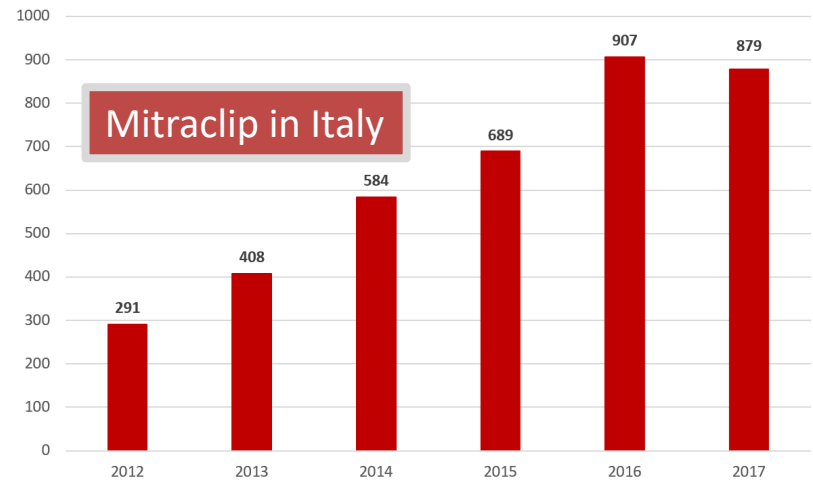
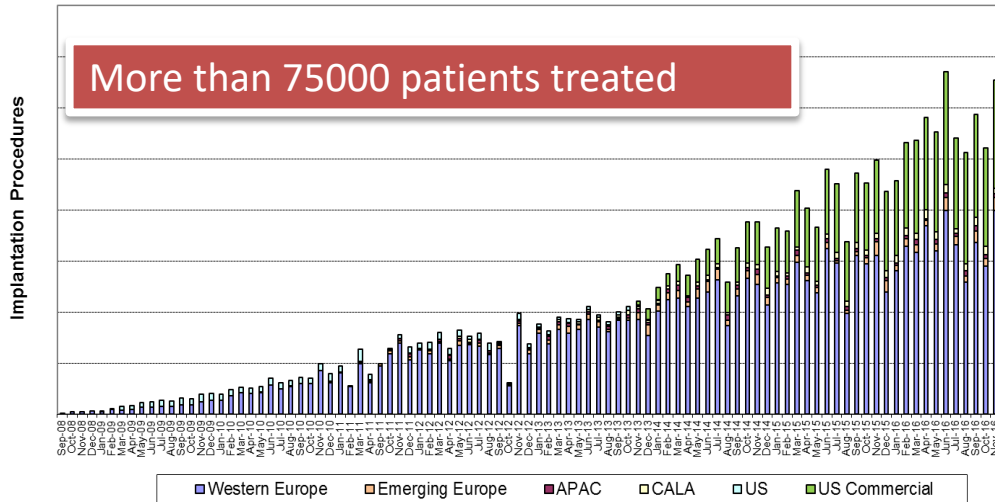




Worldwide MitraClip diffusion



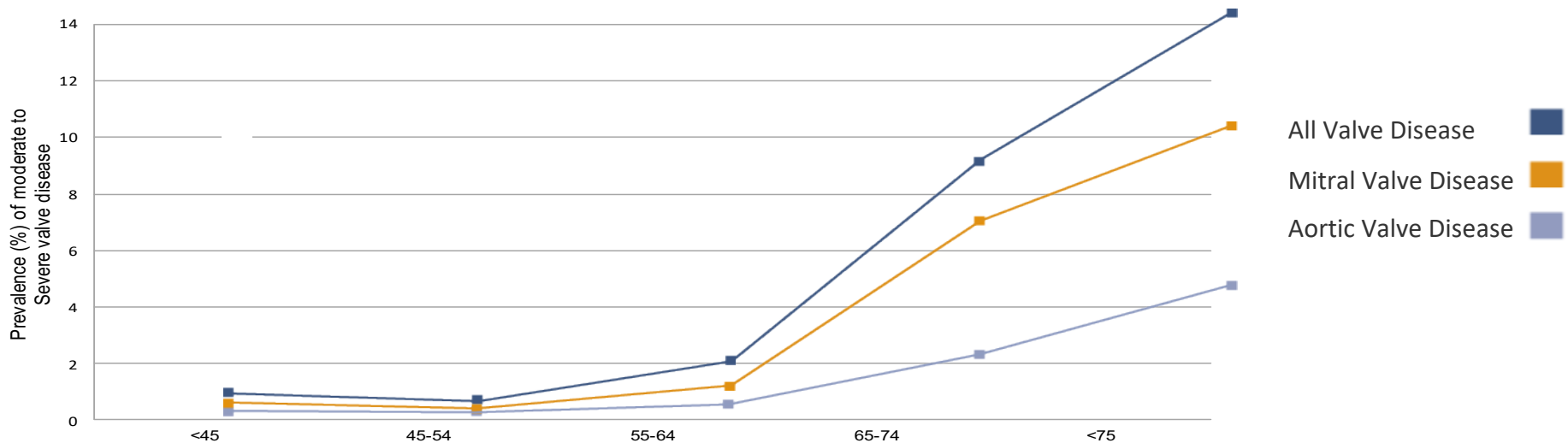
Global MitraClip Experience





A Disease that Increases with Age ^{1,2}

MR affects approximately **1 in 10 people** after the age of 75

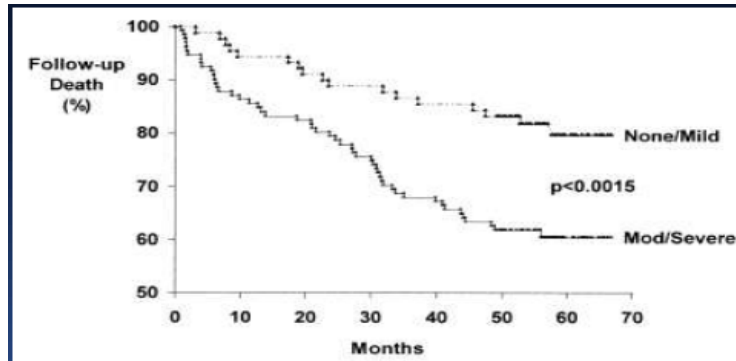


¹ Heart Disease and Stroke Statistics 2010 Update: A Report From the American Heart Association. *Circulation*. 2010;121:e46-e215

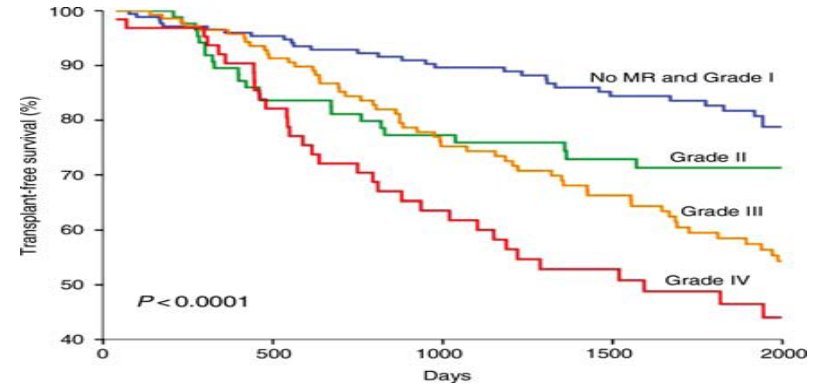
² Nkomo et al. Burden of Valvular Heart Diseases: A Population-based Study, *Lancet*, 2006; 368: 1005-11

Independent Predictor of death

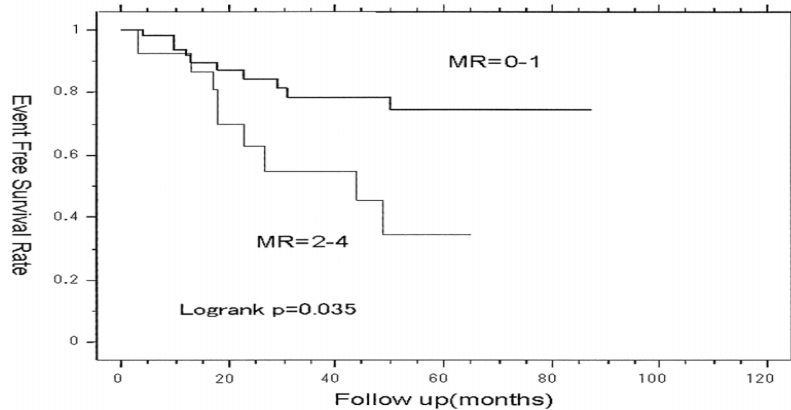
Robbins, Am J Cardiol 2003



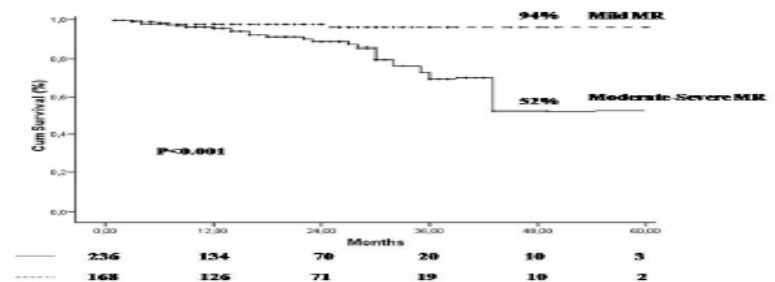
Bursi, European J Heart failure 2010



Eisuke Amiya, Circ J 2006



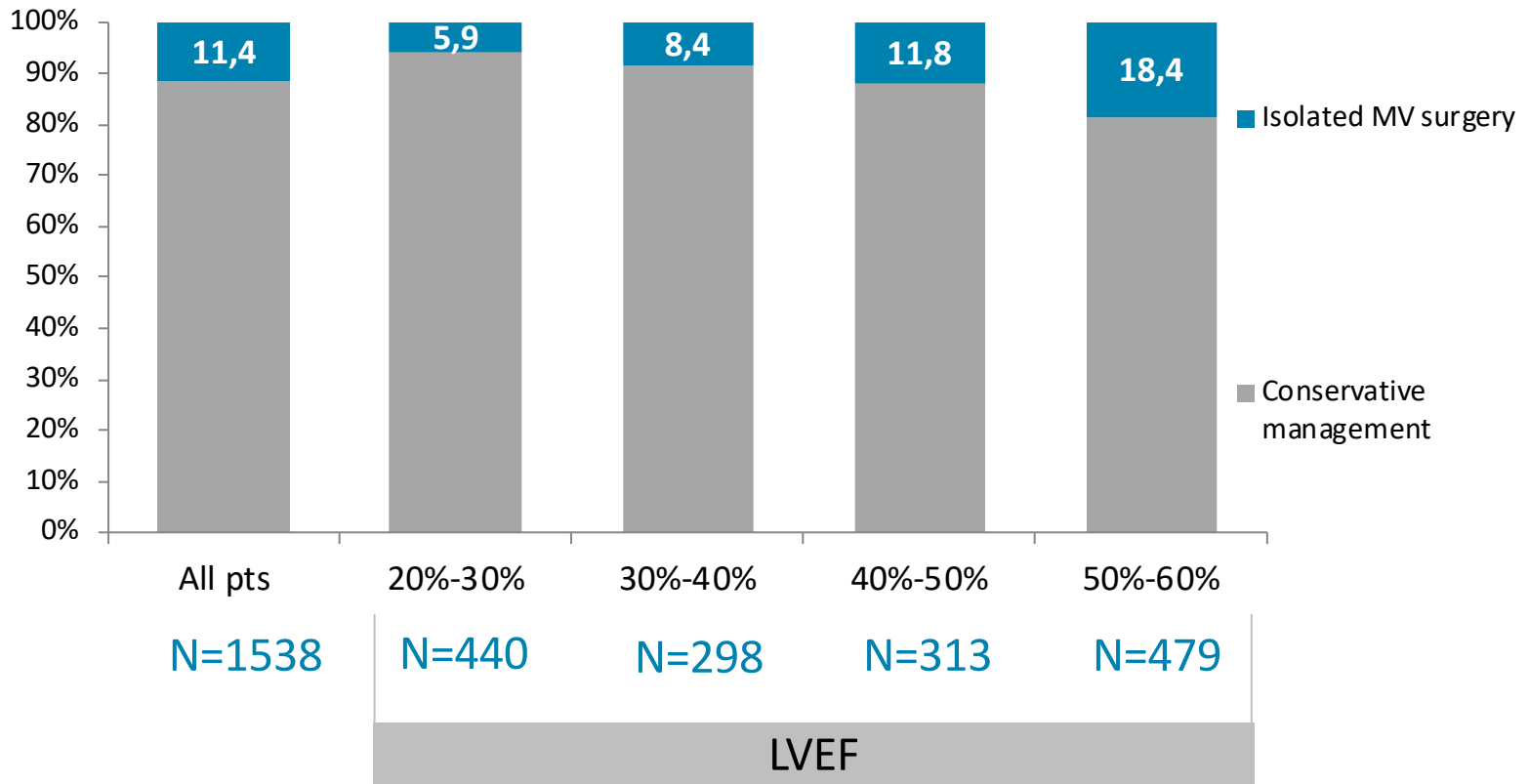
Agricola, Eur J Heart Fail. 2009



Class I A indication of surgery for severe MR
Repair preferred to surgery



How are patients with isolated FMR treated?†



† **Duke Databank:** 1,538 pts with echocardiographic 3+ to 4+ FMR and LVEF \geq 20% between 2000 and 2010 not undergoing CABG



TRAMI Registry (Elderly)

Acute Results

	Age <76 years n=420	Age ≥76 years n=430	<i>p</i> -value
Procedural success,* n (%)	375/394 (95.2)	382/401 (95.3)	0.96
Intraprocedural complications	27/397 (6.8)	29/405 (7.2)	0.84
Death	0	0	NA
Total procedure time, min	112.6±56.9	105.8±57.4	0.22
Radiation time, min	27.8±16.8	26.4±16.7	0.38
No. of clips	1.5±0.6	1.4±0.6	0.19

* Procedure completed with clip successfully placed and MR non-severe.



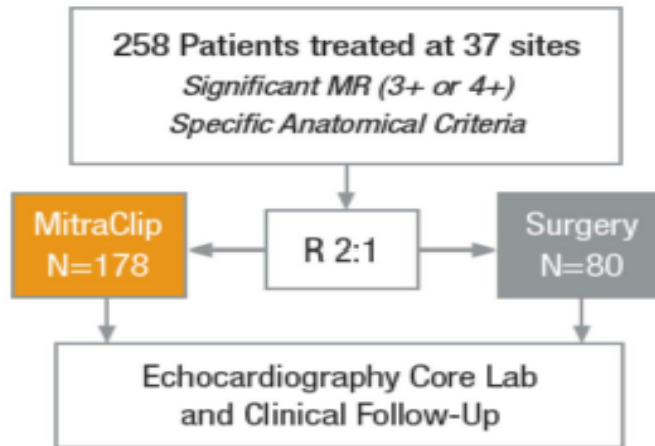
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The NEW ENGLAND JOURNAL of MEDICINE

Percutaneous Repair or Surgery for Mitral Regurgitation

Ted Feldman, M.D., Elyse Foster, M.D., Donald G. 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., for the EVEREST II Investigators*

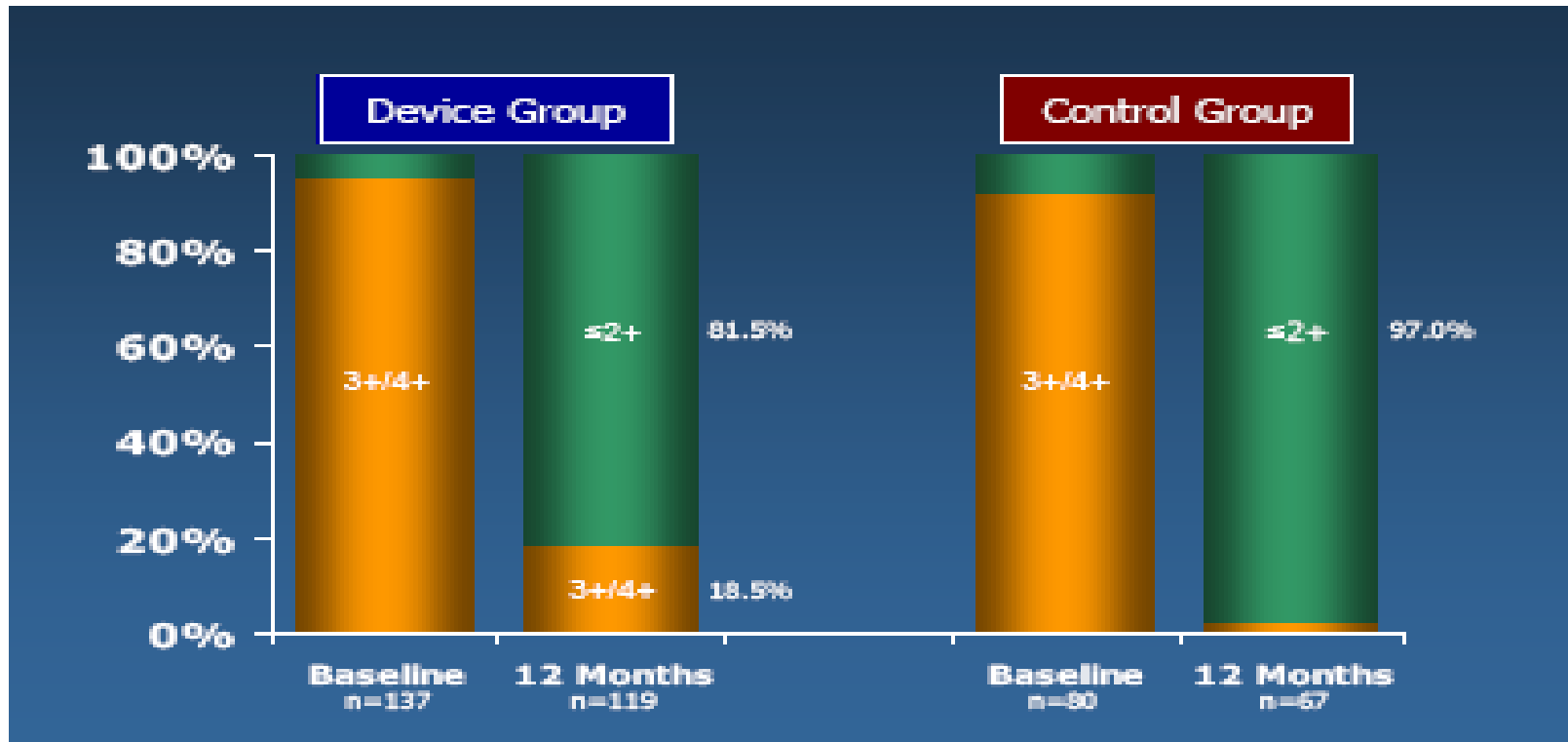
EVEREST II TRIAL RCT



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

Patient Demographics	MitraClip Therapy (n=184)	Surgery (n=95)	P-value
Age (mean)	67 years	68 years	0.32
Male	63%	66%	0.60
History of CHF	91%	78%	0.005
Degenerative MR Etiology	73%	73%	0.81
Functional MR Etiology	27%	27%	0.81
Mean Ejection Fraction	60%	61%	0.65
Previous Cardiovascular Surgery	22%	19%	0.54
NYHA Functional Class III/IV	51%	47%	0.61
Atrial Fibrillation	34%	39%	0.42

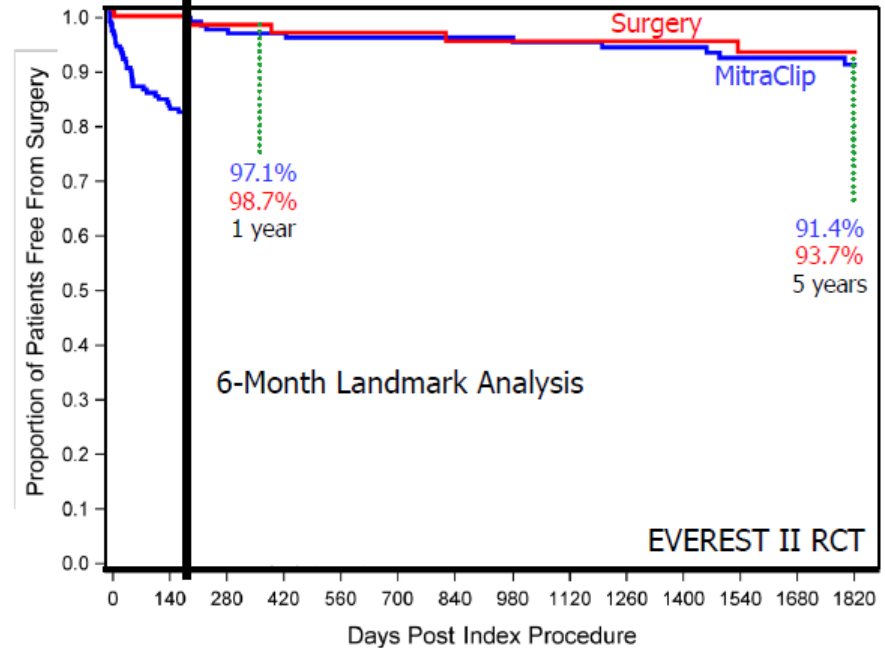
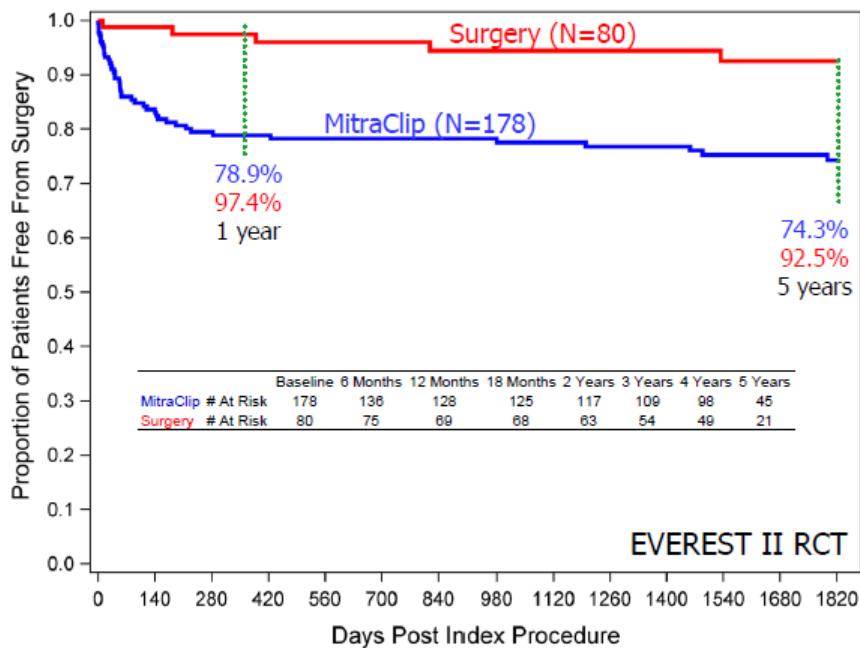
12 months MR Reduction





EVEREST II RCT 5-year Results

- Long term event free survival comparable to surgery *initial efficacy difference

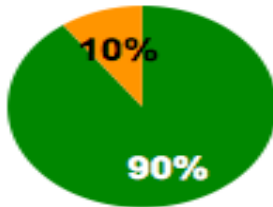
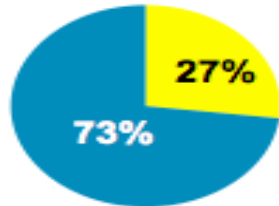




Changing demographics

EVEREST II

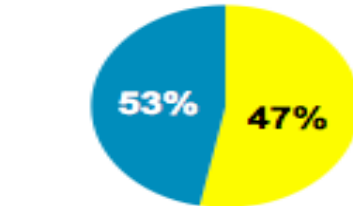
(Randomized Controlled Trial)



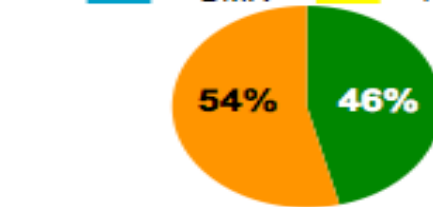
- 178 patients
- Implant rate – 89%

REALISM

(Continued Access Registry)



■ = DMR¹ ■ = FMR¹

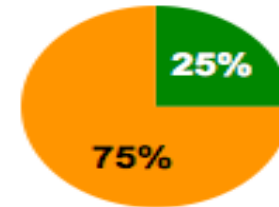
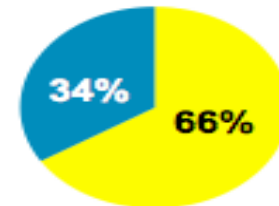


■ = Standard Risk² ■ = High Risk²

- 571 patients
- Implant rate – 94%

Commercial

(Europe, Canada, Asia, Australia)



- 2,472 patients
- Implant rate – 95%

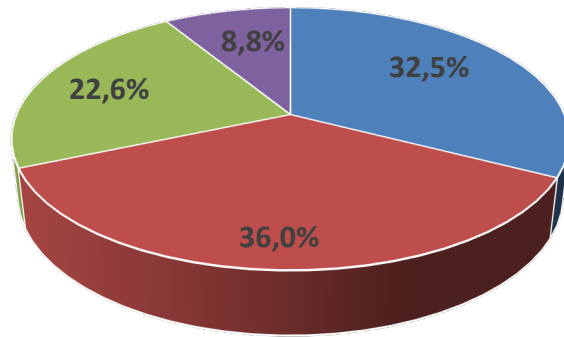


GIOTE registry of transcatheter treatment of mitral valve regurgitation (GIOTTO): epidemiology and acute results.

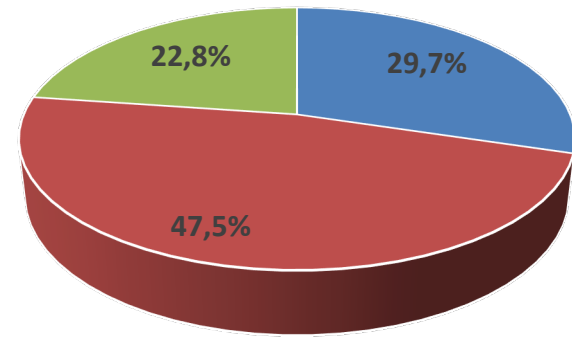
Co PI: Francesco Bedogni

Corrado Tamburino

Etiology



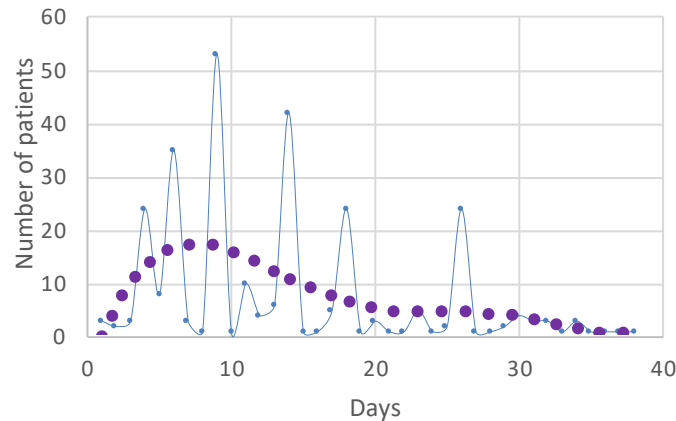
Ejection fraction



■ Ischemic FMR ■ Idiopathic FMR ■ Degenerative MR ■ Mixed MR

■ < 30 % ■ 30 - 50 % ■ > 50 %

Hospitalization for HF (last year)





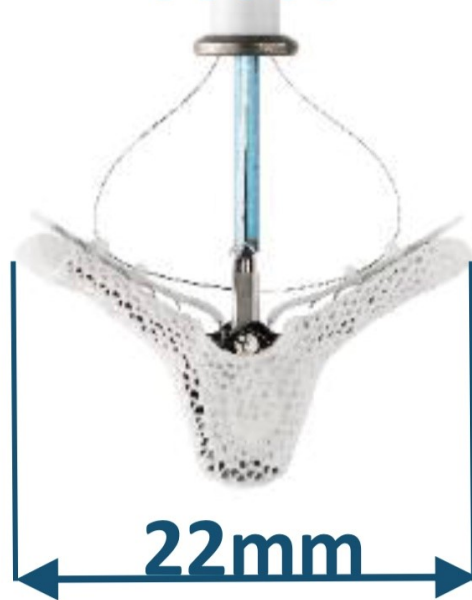
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New Mitraclips

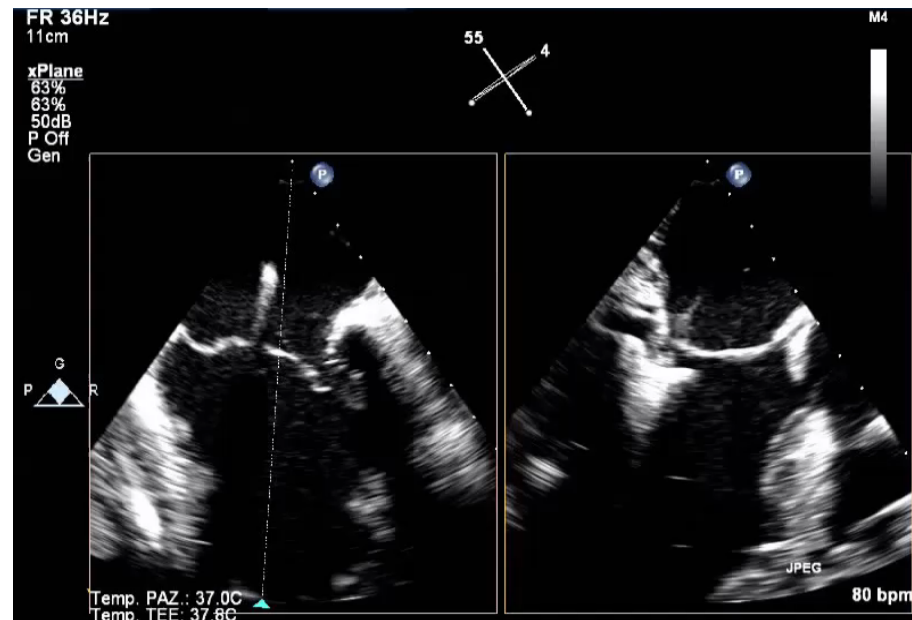
NTR



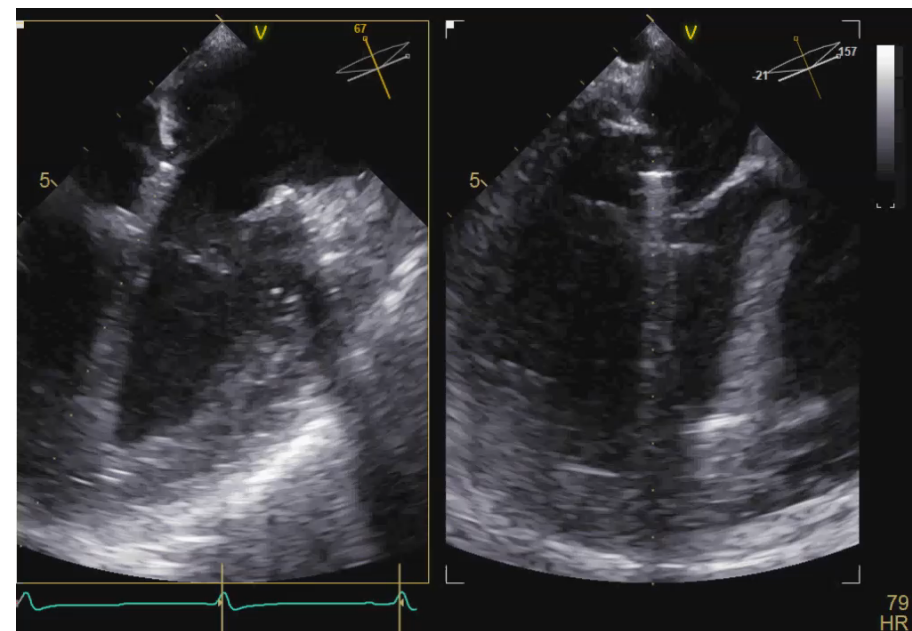
XTR



Old clip

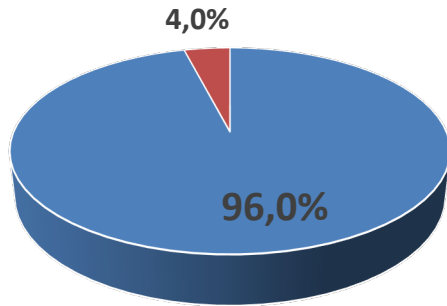


New XTR



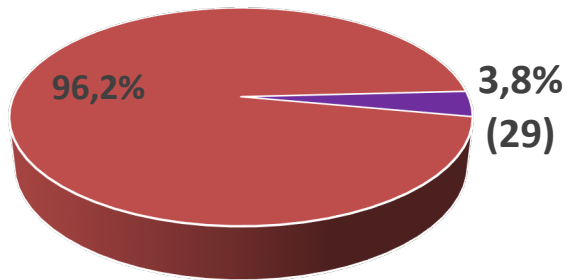
Giotto Results

Procedural Success MR<2+



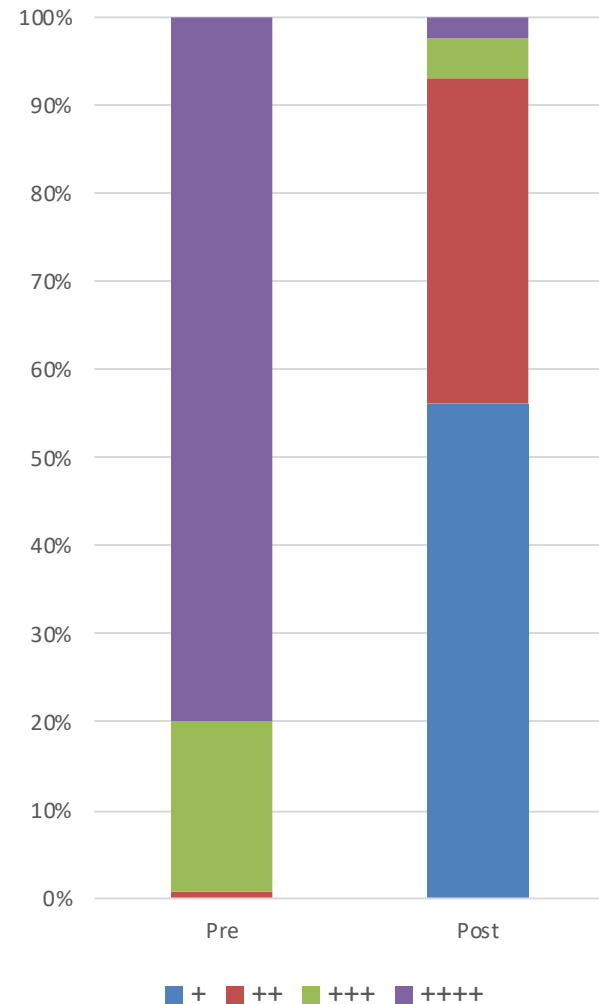
■ Yes ■ No

Intraprocedural complications



■ Yes ■ No

MR reduction



Meta-Analysis of the Usefulness of Mitraclip in Patients With Functional Mitral Regurgitation

Fabrizio D'ascenzo, et al. (Am J Cardiol 2015;116:325–331)

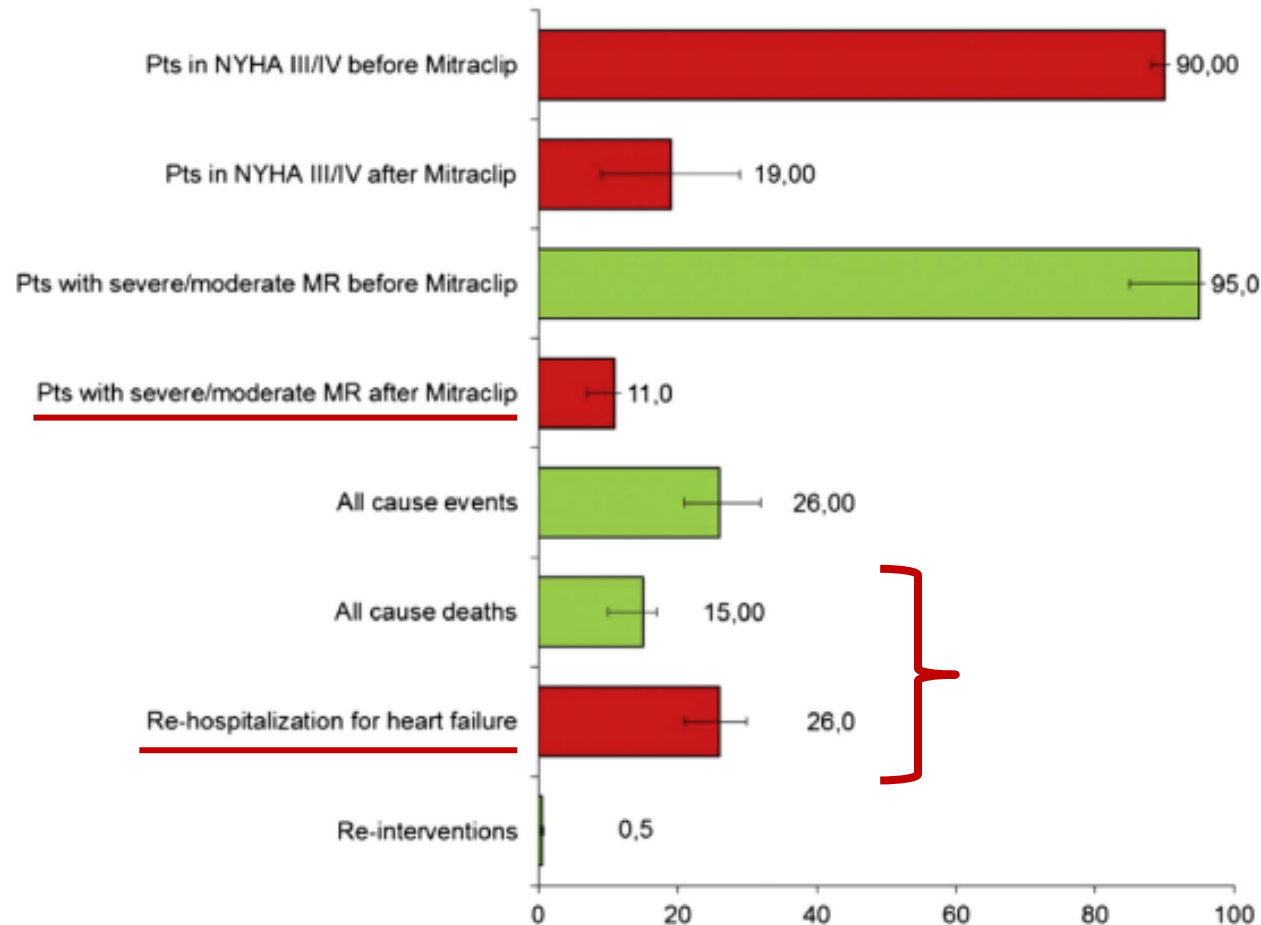
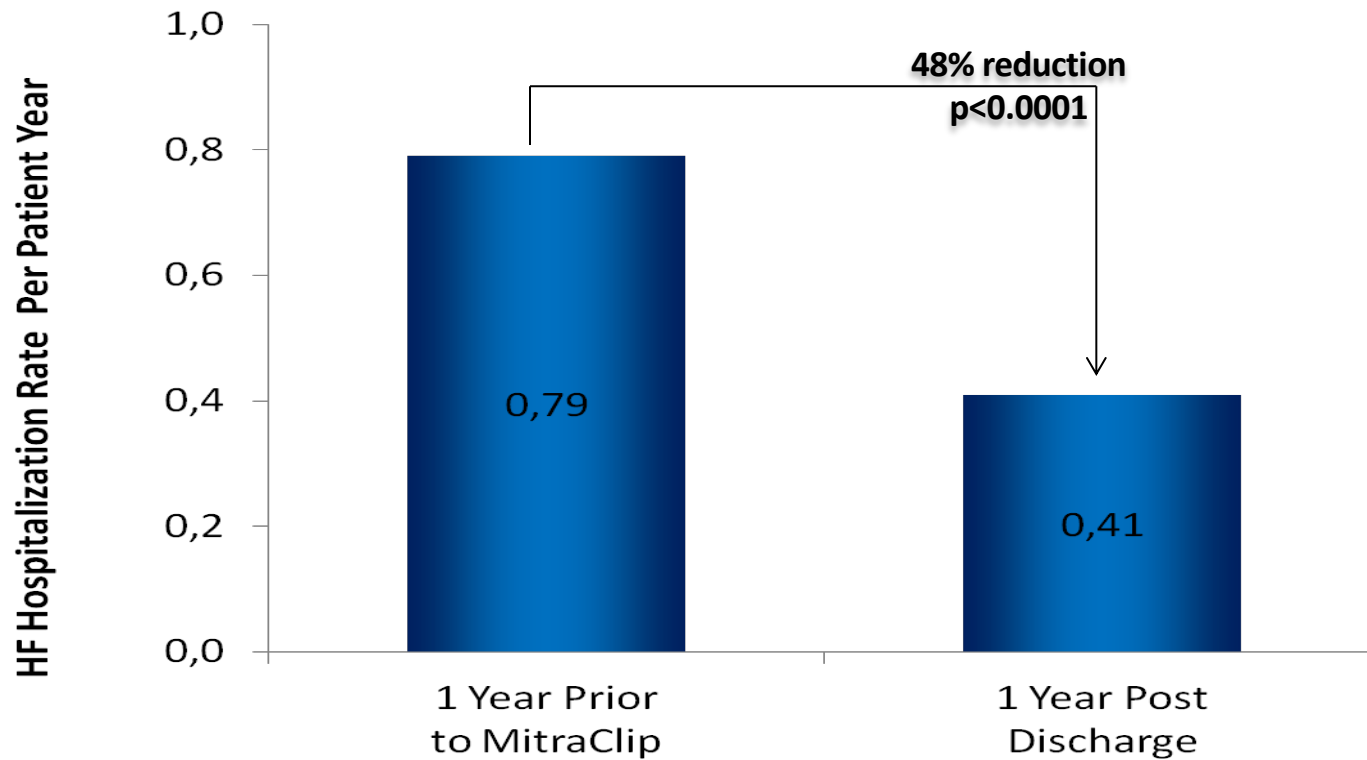


Figure 2. Adverse clinical events at follow-up of 9 months (6 to 12).

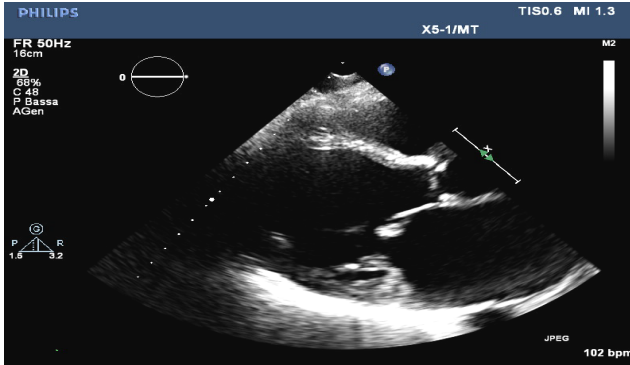
Hospitalizations for Heart Failure



All treated

72 y/o patient
long history atrial fibrillation
Two hospitalisations for heart failure

Basal



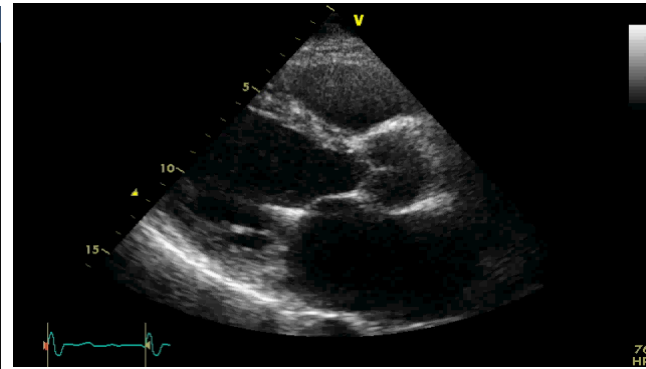
LVEF = 33%;
LVEDD = 71mm;
LVESD = 62mm;
Severe MR;

PAPs: 57mmHg

Pro-BNP: 5283

Therapy:
Diuretic High dose

4 years after 2 clips

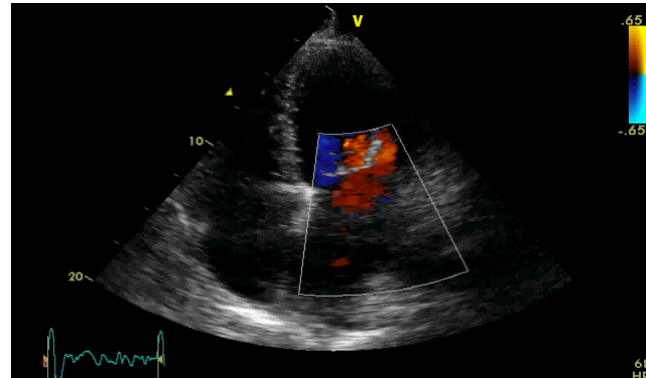
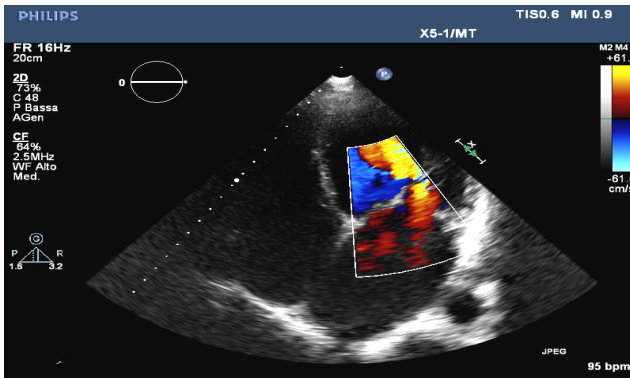


LVEF = 55%;
LVEDD = 65mm;
LVESD = 50mm;
Mild MR;

PAPs: 35mmHg

Pro-BNP: 842

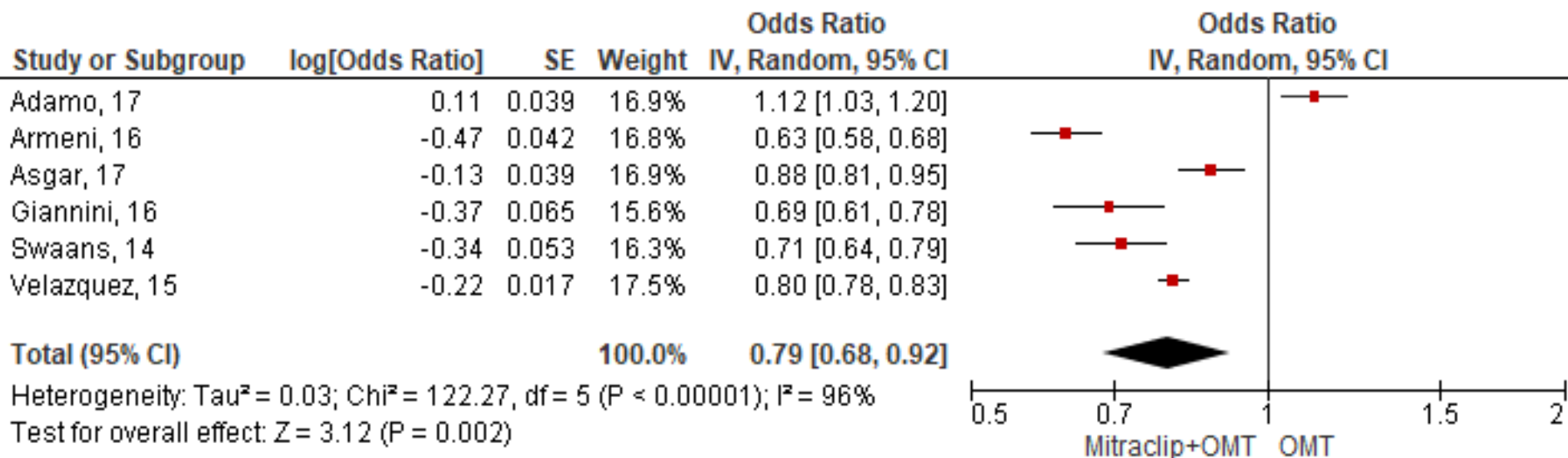
Therapy:
50mg Furosenide





A meta-analysis of MitraClip combined with medical therapy versus medical therapy alone for treatment of mitral regurgitation in heart failure patients

Death from any cause



Randomized trials Mitraclip vs OMT in FMR on survival

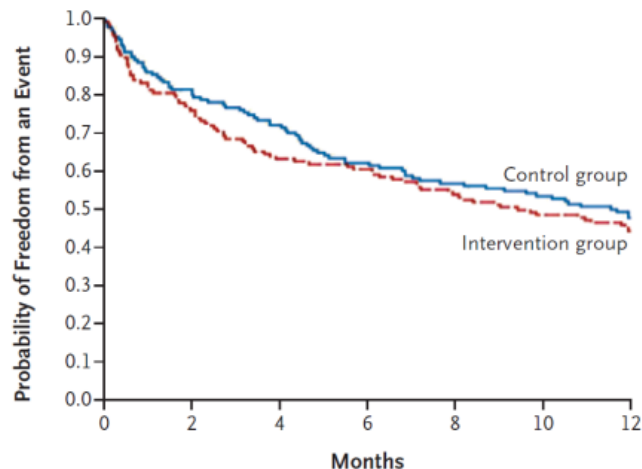
	MITRA-FR	COAPT	RESHAPE-HF-2
N patients	290+ pts @ 22 sites	614 pts @ 85 NA sites	380 pts @ 50 EU sites
Control arm	GDMT ± CRT	GDMT ± CRT	GDMT ± CRT
FMR grade	Severe (EROA >20mm ² & Rvol >30mL)	≥3+ (EROA ≥30mm ² & Rvol >45mL)	≥3+ (EROA ≥30mm ² &/or Rvol >45mL-ECL)
NYHA class	II, III, or ambulatory IV	II, III, or ambulatory IV	III or ambulatory IV
Other inclusion	HF hosp within 12 mos; <i>ineligible for MV surgery</i>	HF hosp within 12 mos; BNP ≥300 pg/ml or nT-proBNP ≥1500 pg/ml <90 days; <i>MV surgery</i>	HF hosp <12 mos or BNP ≥350 pg/ml or nT-proBNP ≥1400 pg/ml <90 days; <i>ineligible for MV surgery</i>
LVEF	≤40%	≤50%	≥15% - ≤40%
LV volumes	-	≤70 mm	LVEDD ≥55 mm
Efficacy endpoint	Death or HF hosp at 12 mos	HF hosp or hospitalization 12 months	Death or HF hosp 12 mos
Safety endpoint	-	SLD, stroke, 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
Duration Follow-up	2 years	5 years	1 year

ESC August 2018

TCT September 2018

Percutaneous Repair or Medical Treatment for Secondary Mitral Regurgitation

J.-F. Obadia, D. Messika-Zeitoun, G. Leurent, B. Lung, G. Bonnet, N. Piriou, T. Lefèvre, C. Piot, F. Rouleau, D. Carrié, M. Nejari, P. Ohlmann, F. Leclercq, C. Saint Etienne, E. Teiger, L. Leroux, N. Karam, N. Michel, M. Gilard, E. Donal, J.-N. Trochu, B. Cormier, X. Armoiry, F. Boutitie, D. Maucort-Boulch, C. Banel, G. Samson, P. Guerin, A. Vahanian, and N. Mewton, for the MITRA-FR Investigators[†]



No. at Risk							
Control group	152	123	109	94	86	80	73
Intervention group	151	114	95	91	81	73	67

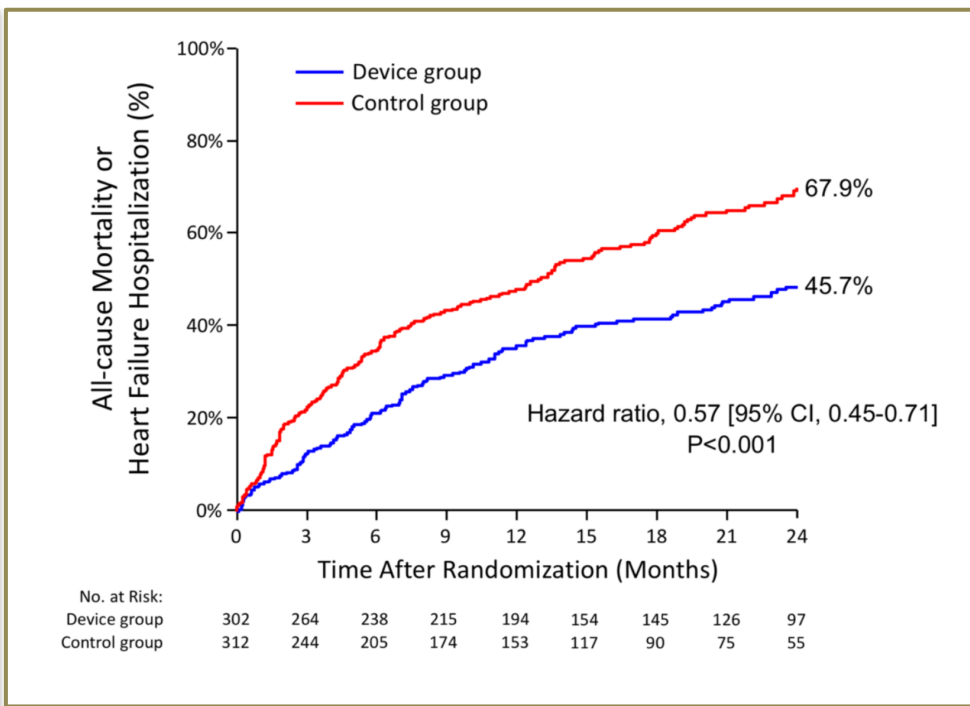
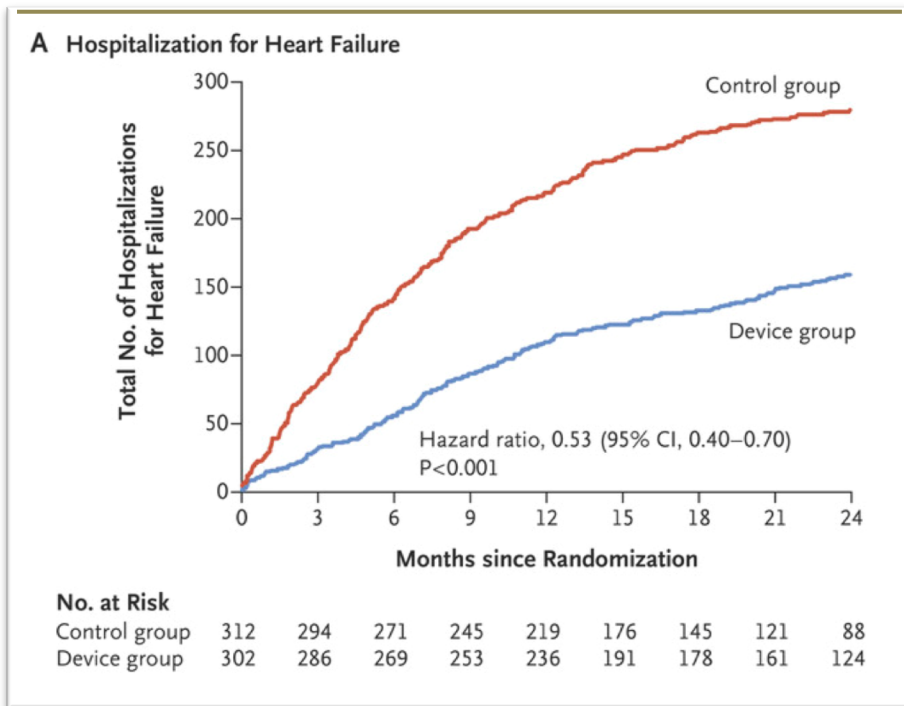
Table 3. Primary Outcome and Secondary Efficacy Outcomes at 12 Months (Intention-to-Treat Population).

Outcome	Intervention Group (N = 152)	Control Group (N = 152)	Hazard Ratio or Odds Ratio (95% CI)*	P Value†
Composite primary outcome: death from any cause or unplanned hospitalization for heart failure at 12 months — no. (%)	83 (54.6)	78 (51.3)	1.16 (0.73–1.84)	0.53
Secondary outcomes‡				
Death from any cause	37 (24.3)	34 (22.4)	1.11 (0.69–1.77)	
Cardiovascular death	33 (21.7)	31 (20.4)	1.09 (0.67–1.78)	
Unplanned hospitalization for heart failure	74 (48.7)	72 (47.4)	1.13 (0.81–1.56)	
Major adverse cardiovascular events§	86 (56.6)	78 (51.3)	1.22 (0.89–1.66)	

Transcatheter Mitral-Valve Repair in Patients with Heart Failure

G.W. Stone, J.A. Lindenfeld, W.T. Abraham, S. Kar, D.S. Lim, J.M. Mishell,
B. Whisenant, P.A. Grayburn, M. Rinaldi, S.R. Kapadia, V. Rajagopal,
I.J. Sarembock, A. Brieke, S.O. Marx, D.J. Cohen, N.J. Weissman,
and M.J. Mack, for the COAPT Investigators*

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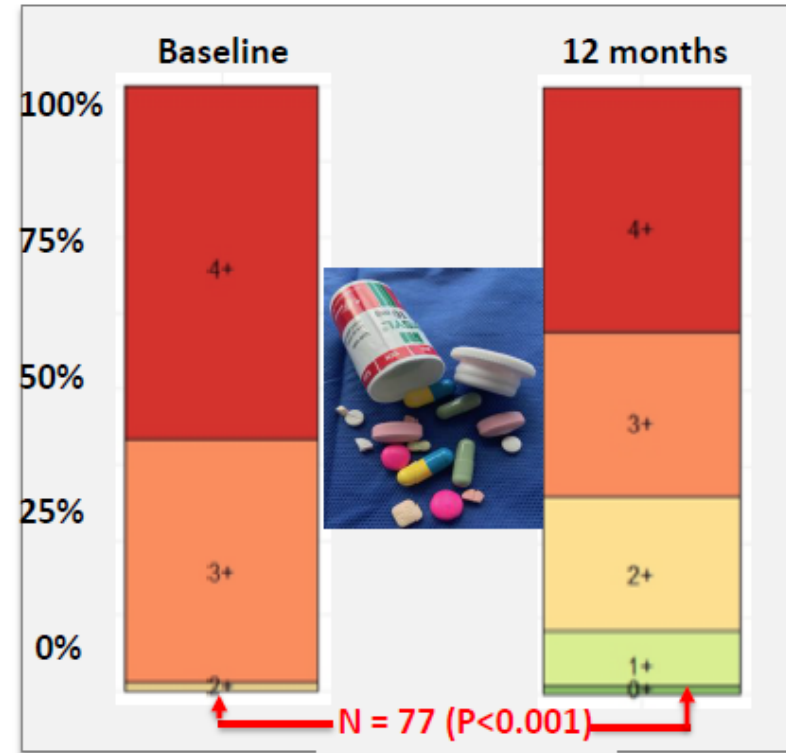
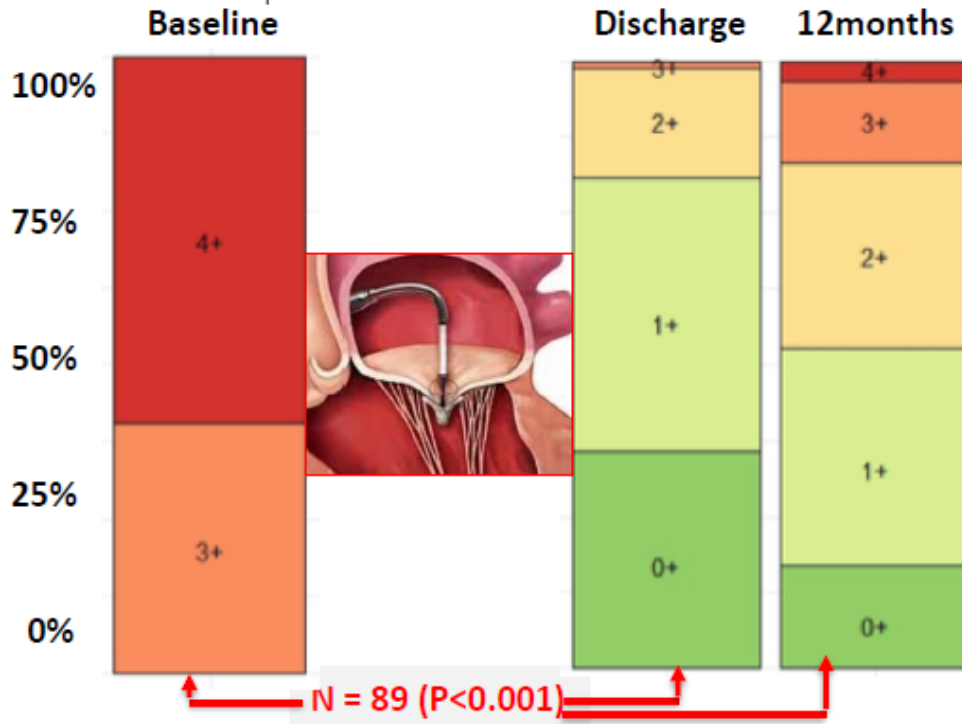


Differences between COAPT and MITRA FR: Study design

VARIABLE	COAPT (N=614)	MITRA FR (N=304)
Fundings	ABBOTT	French Ministry of Health and Research National Program and Abbott Vascular
Primary Endpoint	Effectiveness EP: Hospitalizations for HF within 24 months of follow-up Safety EP: freedom from device-related complications at 12 months of follow -up	Composite of death from any cause or unplanned hospitalization for HF at 12 months
Eligibility Committee	Not appropriate by local heart team assessment and central eligibility committee	Not appropriate by local heart team assessment
Time to Mitral repair after randomization	14 days	21 days
Crossover	Not allowed	Allowed
Medical Therapy	GMTD	OMT (no informations about MT Changes during the study period)



MR grade evolution in both groups (paired data)

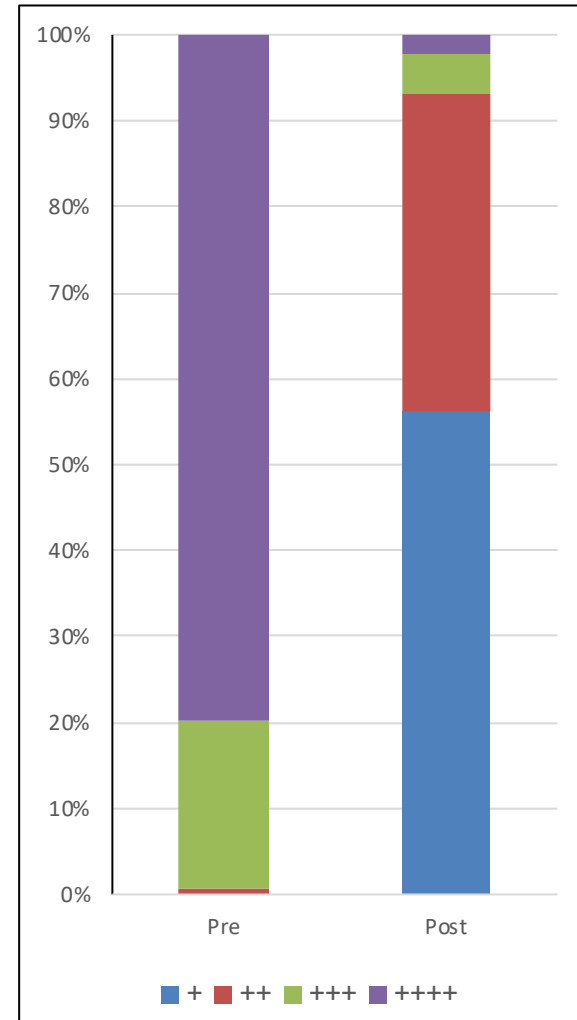
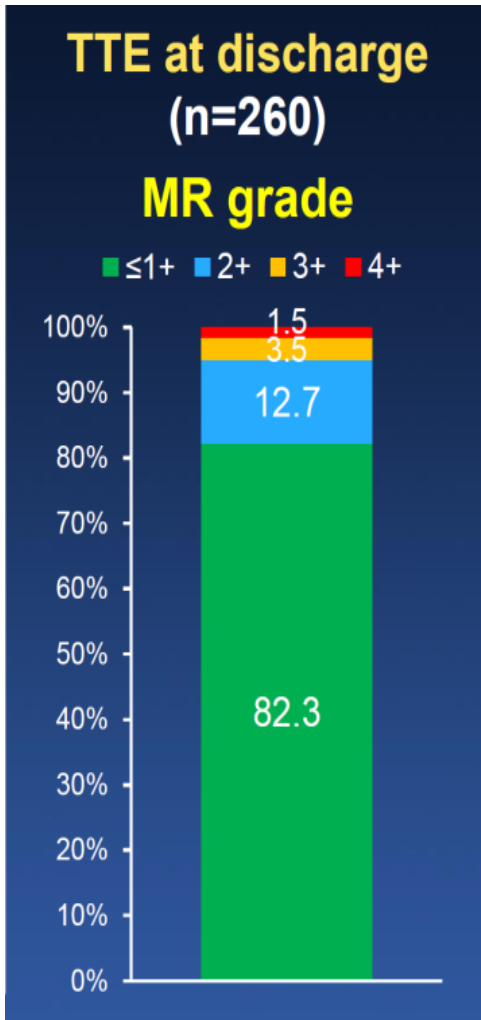


P < 0.001

Success Rate MR <2+

COAPT 95%
Compl. 3.4%

GIOTTO 94%
Compl. 3.8 %





Mitra FR Procedural results

Intention to treat analysis

Table 2. Periprocedural Complications and Prespecified Serious Adverse Events (Intention-to-Treat Population).*

Variable	Intervention Group (N=152)	Control Group (N=152)
Periprocedural complications during device implantation — no./total no. (%) [†]	21/144 (14.6)	NA
Device-implantation failure	6/144 (4.2) [‡]	NA
Hemorrhage resulting in transfusion or vascular complication resulting in surgical intervention	5/144 (3.5)	NA
Atrial septum lesion or atrial septal defect	4/144 (2.8)	NA
Cardiogenic shock resulting in intravenous inotropic support	4/144 (2.8)	NA
Cardiac embolism, including gas embolism and stroke	2/144 (1.4)	NA
Tamponade	2/144 (1.4)	NA
Urgent conversion to heart surgery	0	NA
Prespecified serious adverse events at 1 year — no. (%)		
All serious adverse events	125 (82.2)	121 (79.6)
Heart transplantation or mechanical cardiac assistance	6 (3.9)	9 (5.9)
Ischemic or hemorrhagic stroke [§]	7 (4.6)	1 (0.7)
Myocardial infarction	0	2 (1.3)
Need for renal-replacement therapy	5 (3.3)	1 (0.7)
Severe hemorrhage [¶]	11 (7.2)	6 (3.9)
Infections	28 (18.4)	27 (17.8)

152 patients Mitraclip
 8 pts excluded
 6 failures
 91% Technical success

**Reduction MR <2+
 113 pts (74.3%)**

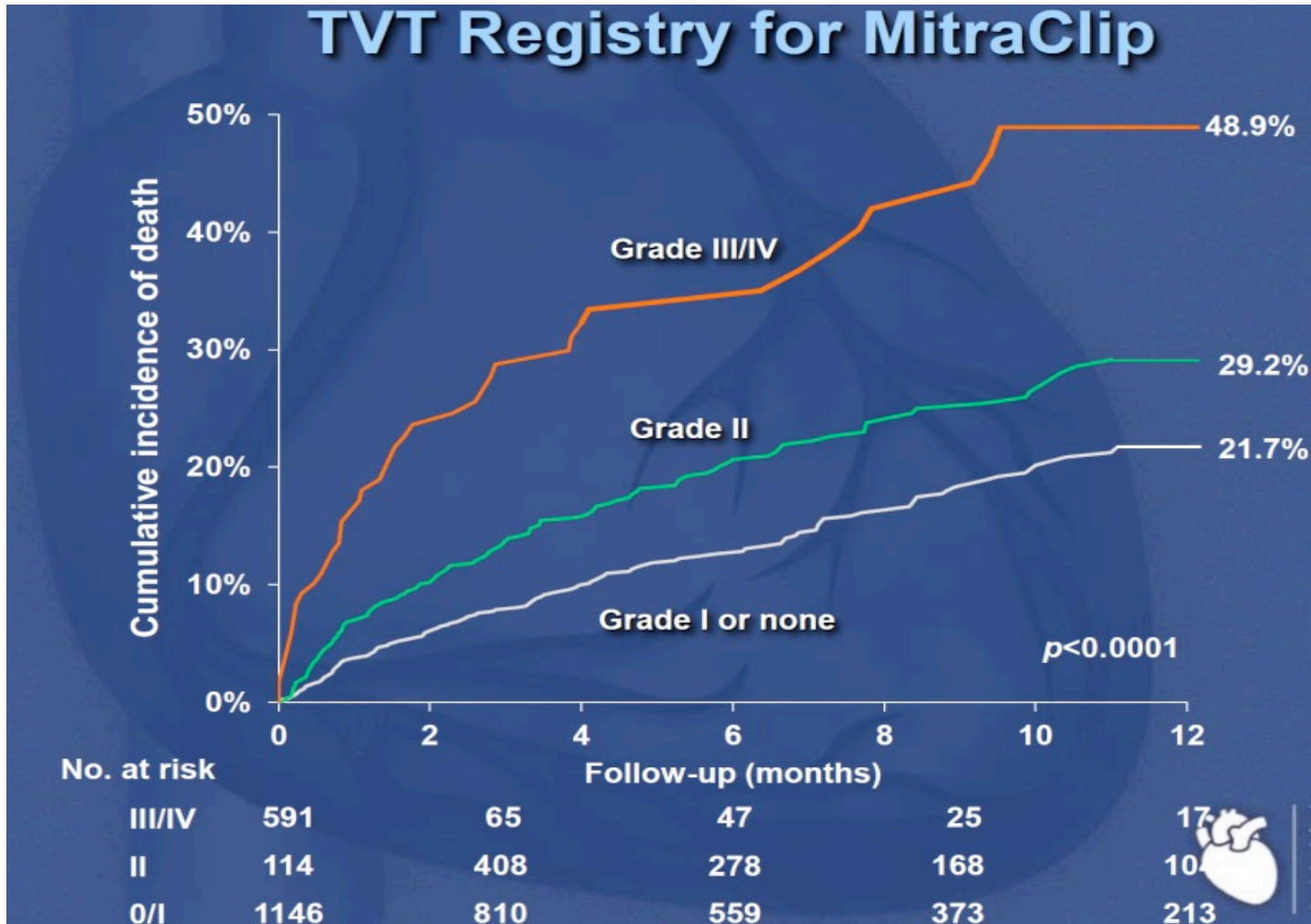
37 centri, 40 mesi di arruolamento (2013/12 <-> 2017/03),
 152 pazienti = 1,23 pz per centro all'anno



Successo procedurale centri GIOTTO

	Centri che svolgono più di 25 procedure	Centri che svolgono meno di 25 procedure	p
Procedure totali	569	552	-
Successo procedurale MR finale <2+	552 (97,0%)	518 (93,8%)	0,01
Complicanze procedurali	25 (4,4%)	16 (2,9%)	0,19

Post Procedural MR and Survival





Why so Different? Basal Characteristics

GIOTTO
vs.
Mitra.FR and
COAPT

Caratteristica	GIOTTO (n= 732)	Mitra.FR (n= 152) Percutaneous repair group	COAPT (n=302) Percutaneous repair group
NT-proBNP (pg/mL, mediana, IQR)	1136 [370,5 – 3362]	3407 [1948 – 6790]	-
NT-proBNP (pg/mL, media, DS)	2235 ± 2730	-	5174 ± 6567
ICD	375 (51,2%)	90 (59,2%)	91 (30,1%)
Frazione di eiezione (%)	32,5 ± 9,9	33,3 ± 6,5	31,3 ± 9,1
LVEDV (mL/m ² ,media, DS)	90 ± 56	135 ± 35	101 ± 34*
EROA (mm ²)	-	31 ± 10	41 ± 15
IM 2+	8 (1,1%)	-	-
IM 3+	168 (22,9%)	-	148 (49,0%)
IM 4+	556 (76,0%)	-	154 (51,0%)

Key Exclusion Criteria

1. ACC/AHA stage D HF, hemodynamic instability or cardiogenic shock
2. Untreated clinically significant CAD requiring revascularization
3. COPD requiring continuous home oxygen or chronic oral steroid use
4. Severe pulmonary hypertension or moderate or severe right ventricular dysfunction
5. Aortic or tricuspid valve disease requiring surgery or transcatheter intervention
6. Mitral valve orifice area $<4.0 \text{ cm}^2$ by site-assessed TTE
7. Life expectancy <12 months due to non-cardiac conditions



Predictors of combined events post Mitraclip

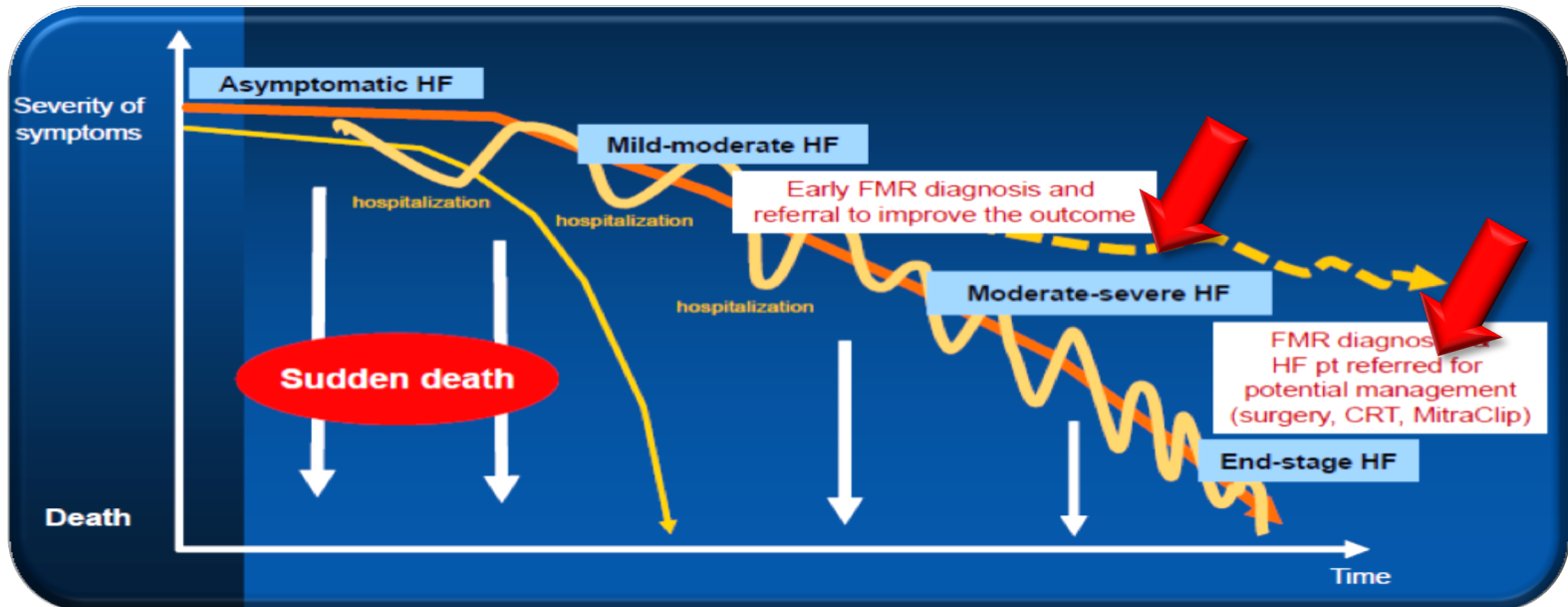
Table 4 Predictors of the combined event (primary endpoint: combination of all-cause mortality, left ventricular assist device implantation, mitral valve surgery, unsuccessful implantation) in univariate and multivariate analysis (Cox model)

Parameter	Univariate analysis		Multivariate analysis: optimized model	
	HR (95% CI)	P-value	HR (95% CI)	P-value
NT-proBNP >10 000 pg/mL	4.6 (2.6–8.2)	<0.001	3.5 (1.9–6.7)	<0.001
Age >80 years	1.8 (1.0–3.3)	0.046	2.2 (1.2–4.2)	0.008
Serum creatinine >150 mmol/L	2.4 (1.4–4.3)	0.002		
NYHA class IV	2.1(1.2–3.7)	0.008	1.7(1.0–3.2)	0.049
TAPSE < 15 mm	3.2 (1.8–5.6)	<0.001	1.9(1.0–3.6)	0.038
TR grade >2 +	2.0 (1.0–4.0)	0.052		

When refer to PMVR...

Piotr Ponikowski, MD, PhD, FESC

Medical University, Centre for Heart Disease Clinical Military Hospita HFA Athens 2014



... Indications , Results and Timing
are crucial!