



Montreal

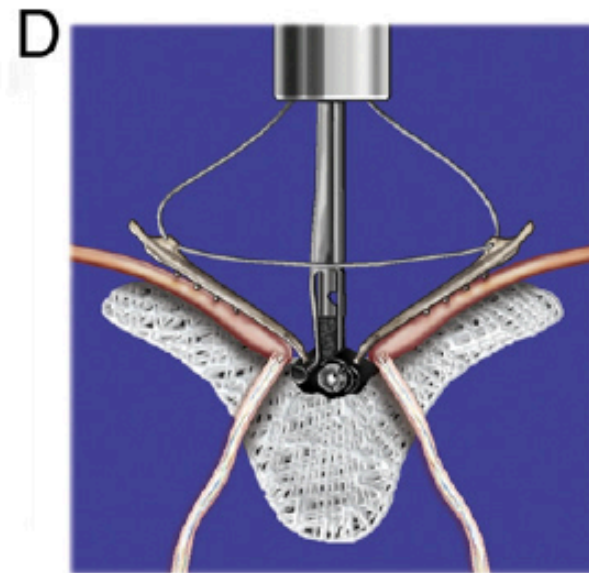
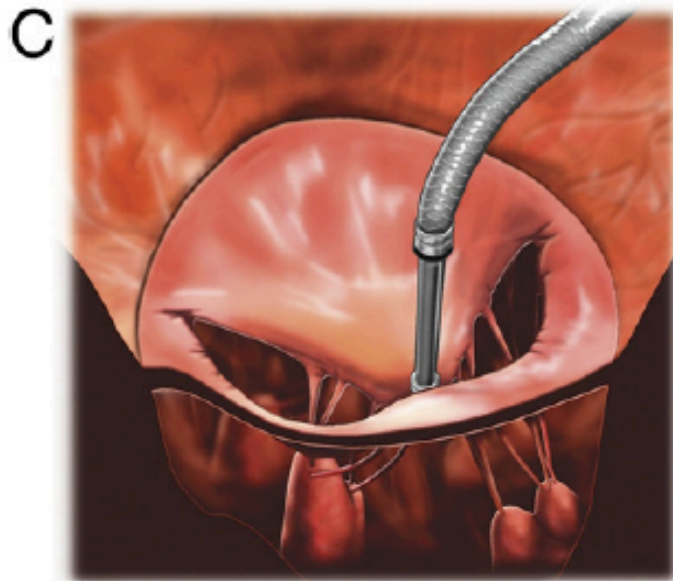
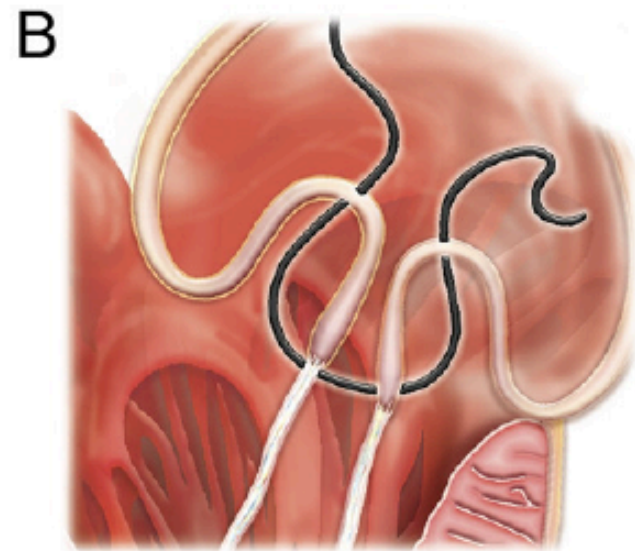
Transcatheter Mitral Valve Landscape



Munich

Approach	Commercial	In Development	Abandoned
Edge-to-Edge Repair			
Direct Annuloplasty		 	
Indirect Annuloplasty			
Chordal Repair			
Ventricular Remodeling		 	
Enhanced coaptation		 	
MV Replacement		 	

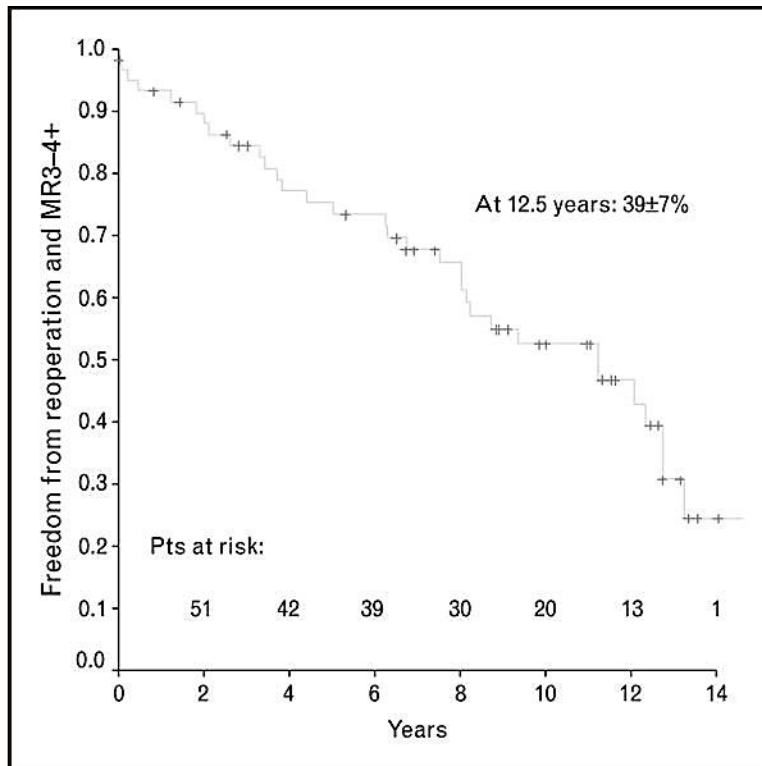
MitraClip



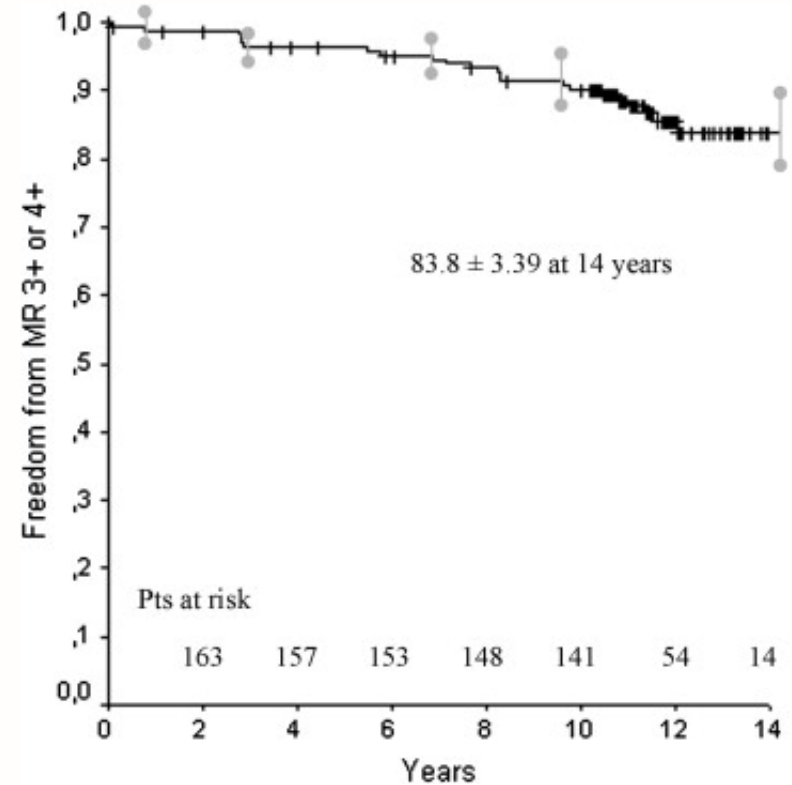
(Maisano. J Am Coll Cardiol 2011;58: 2174–82)

Edge-to-edge surgical mitral valve repair what if the annuloplasty ring is missed ?

Without annuloplasty

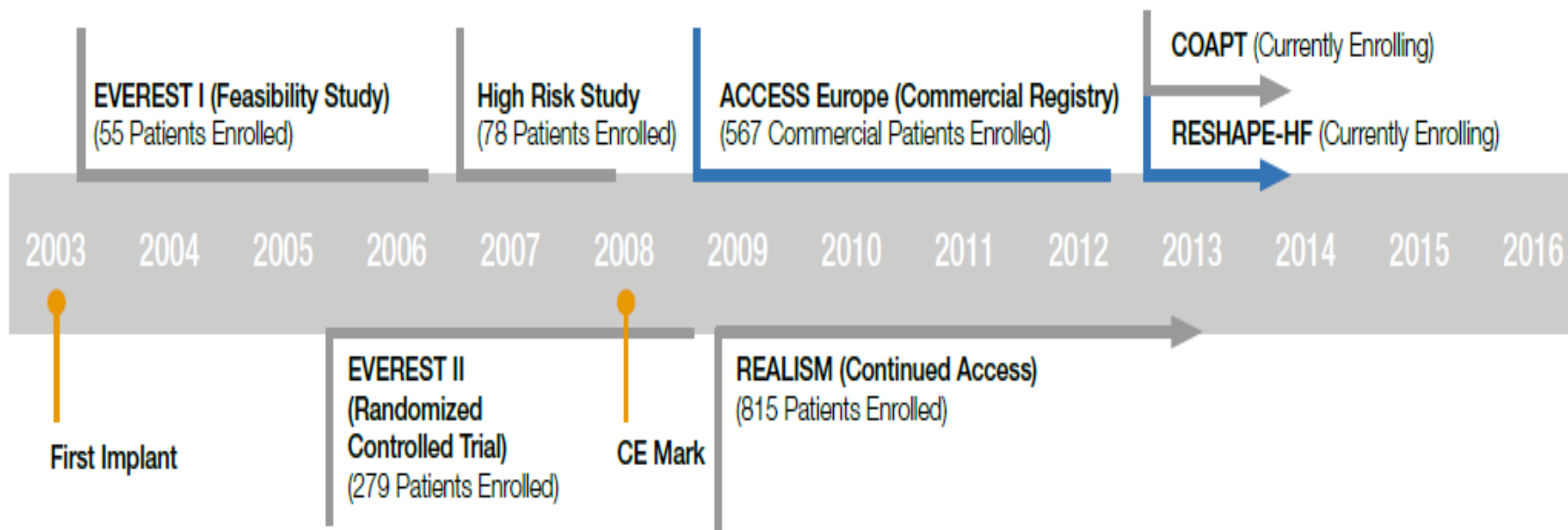
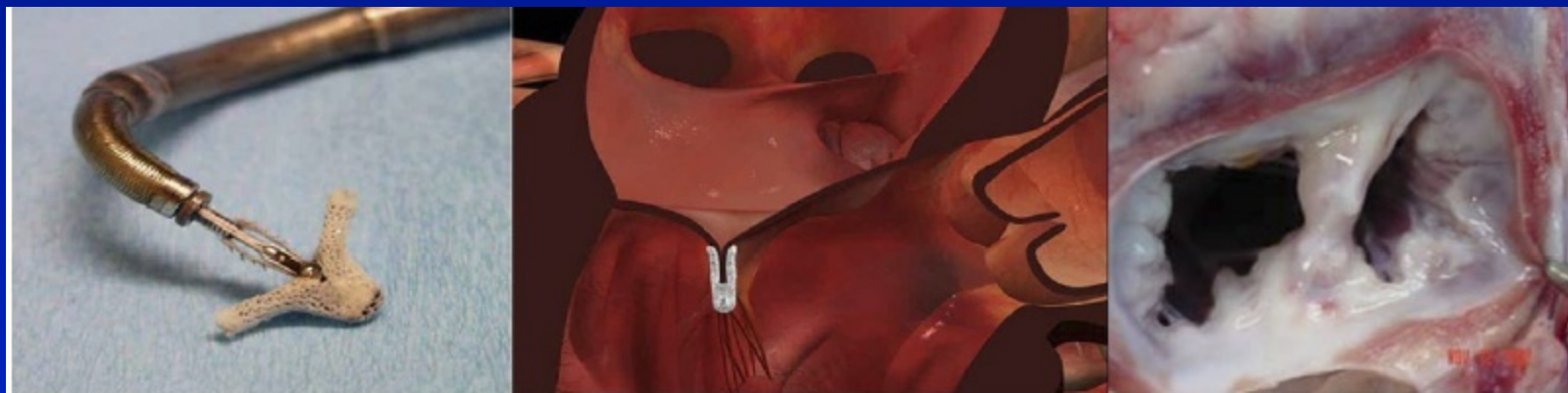


With annuloplasty



(De Bonis *Curr Op Cardiol.* 2014 30:155-160 - *J Thorac Cardiovasc Surg* 2012;144:1019-1026)

Worldwide Clinical Experience



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

Key Inclusion/Exclusion Criteria

EVEREST II RCT

Inclusion

- Candidate for MV Surgery
- Moderate to severe (3+) or severe (4+) MR
 - Symptomatic
 - $>25\%$ EF & LVESD $\leq 55\text{mm}$
 - Asymptomatic with one or more of the following
 - LVEF 25-60%
 - LVESD $\geq 40\text{mm}$
 - Pulmonary hypertension
 - Atrial fibrillation

ACC/AHA Guidelines
JACC 52:e1-e142, 2008

Exclusion

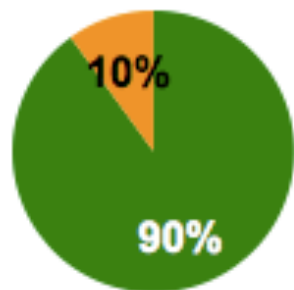
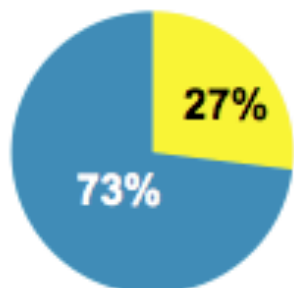
- AMI within 12 weeks
- Need for other cardiac surgery
- Renal insufficiency
 - Creatinine $>2.5\text{mg/dl}$
- Endocarditis
- Rheumatic heart disease
- MV anatomical exclusions
 - Mitral valve area $<4.0\text{cm}^2$
 - Leaflet flail width ($\geq 15\text{mm}$) and gap ($\geq 10\text{mm}$)
 - Leaflet tethering/coaptation depth ($>11\text{mm}$) and length ($<2\text{mm}$)

(Feldman T, N Engl J Med 2011;364:1395 – 1406)

MitraClip indication

EVEREST II

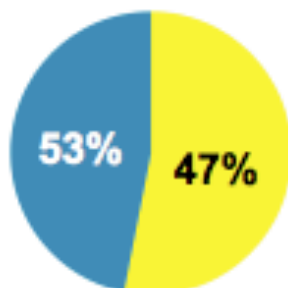
(Randomized Controlled Trial)



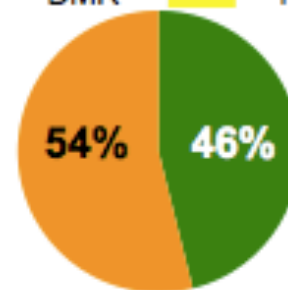
- 178 patients
- Implant rate – 89%

REALISM

(Continued Access Registry)



■ = DMR¹ ■ = FMR¹

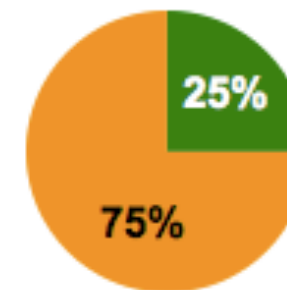
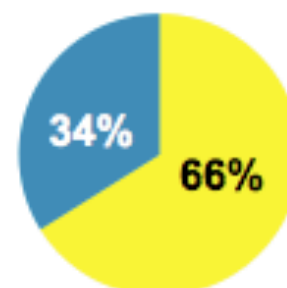


■ = Standard Risk² ■ = High Risk²

- 571 patients
- Implant rate – 94%

Commercial

(Europe, Canada, Asia, Australia)



- 2,472 patients
- Implant rate – 95%

Safety Endpoint: 30 Day MAE

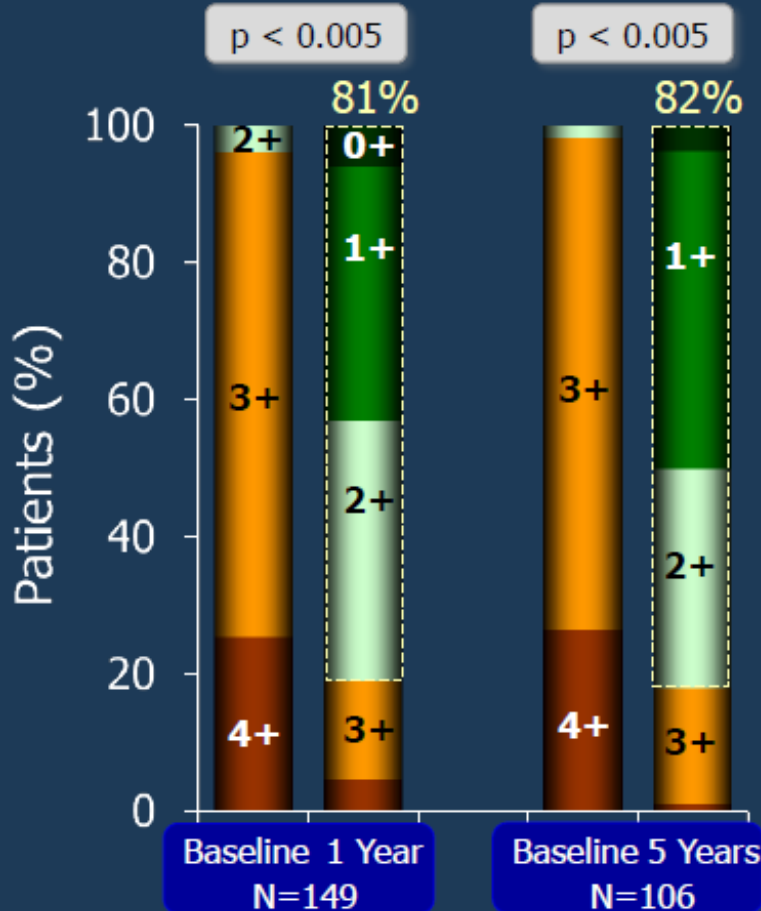
Intention to Treat

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%)	

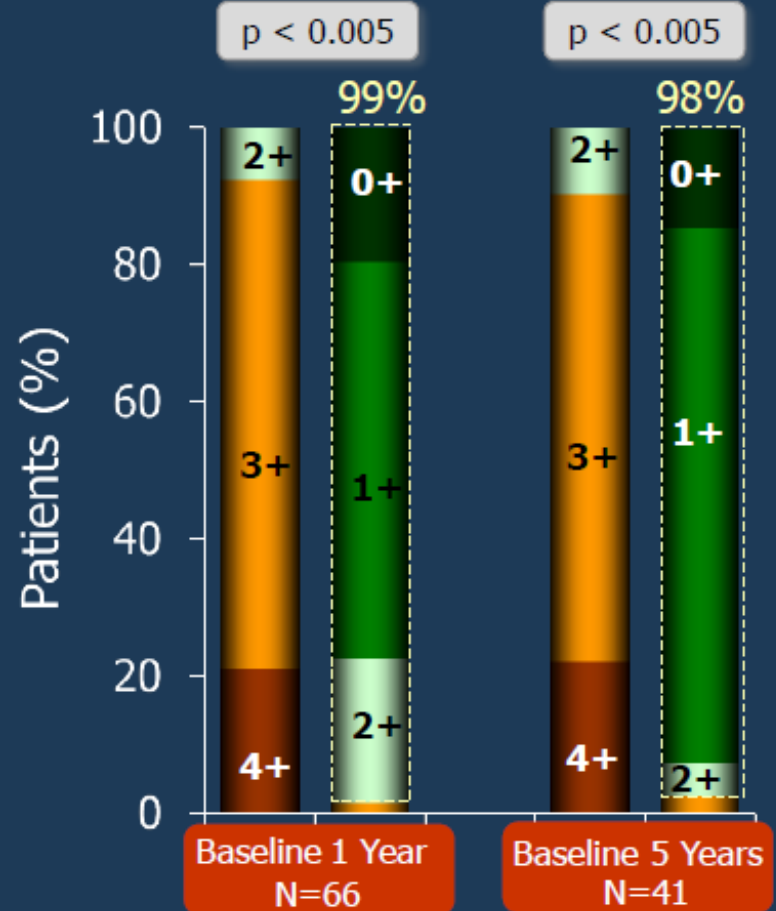
Mitral Regurgitation Grade

EVEREST II RCT All Treated Patients (N=258)

MitraClip (N=178)
MR ≤ 2+ at 1 and 5 Years



Surgery (N=80)
MR ≤ 2+ at 1 and 5 Years



Reduction in LV Volumes at 1 and 5 Years

LVEDV (ml) at 1 Year

N=144
p<0.0001

-25.3

N=65
p<0.0001

-40.2

LVEDV (ml) at 5 Years

N=105
p<0.0001

-30.1

N=40
p<0.0001

-42.9

EII RCT

- MitraClip
- Surgery

LVESV (ml) at 1 Year

N=144
p<0.0001

-5.5

N=65
p=0.05

-5.1

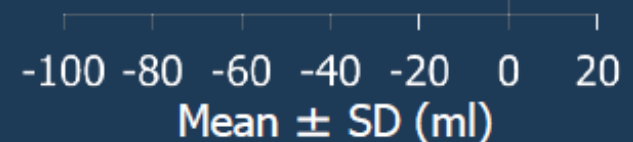
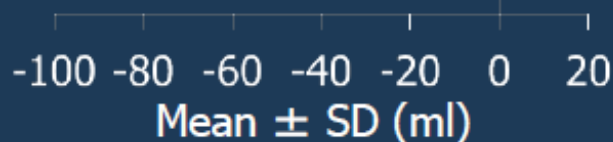
LVESV (ml) at 5 Years

N=105
p<0.01

-5.3

N=40
p<0.01

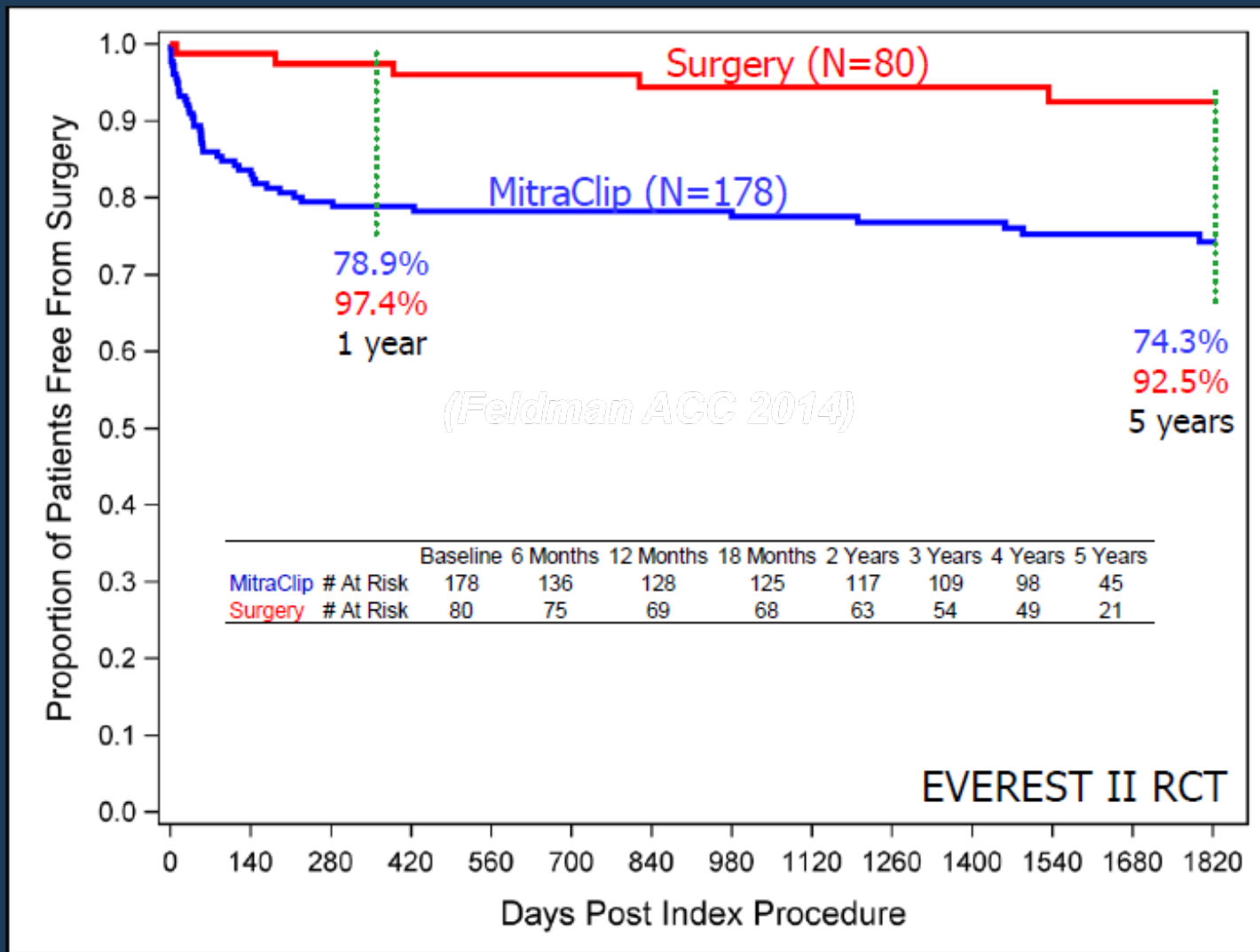
-8.2



(Feldman ACC 2014)

N = survivors with paired data; p-values baseline vs 1 & 5 years, for descriptive purposes only

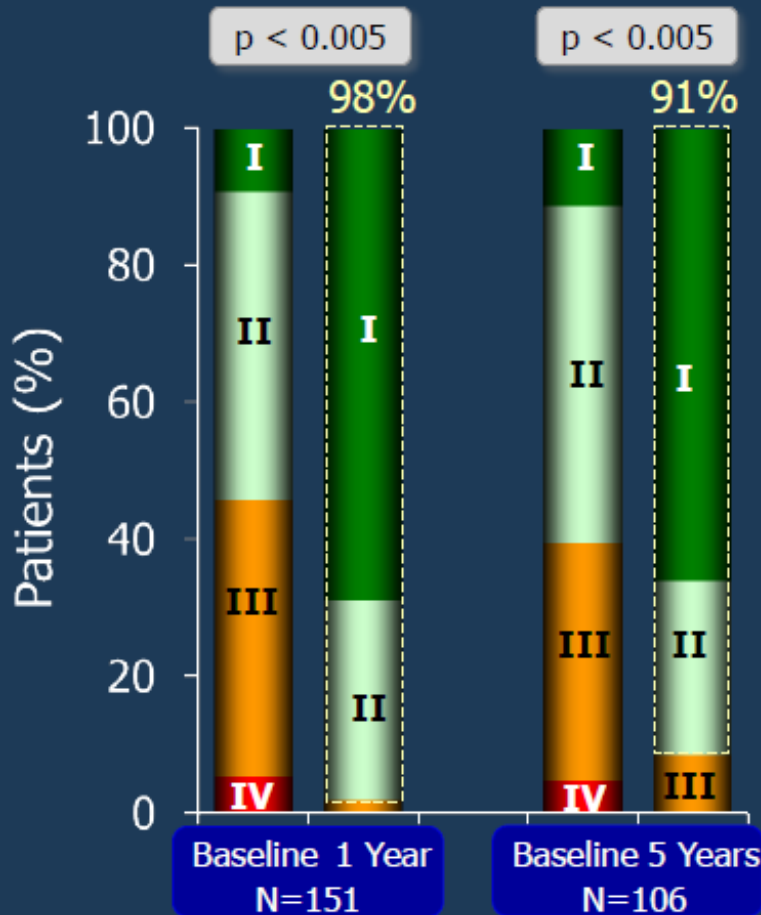
Kaplan-Meier Freedom From MV Surgery in MitraClip Group or Re-operation in Surgery Group



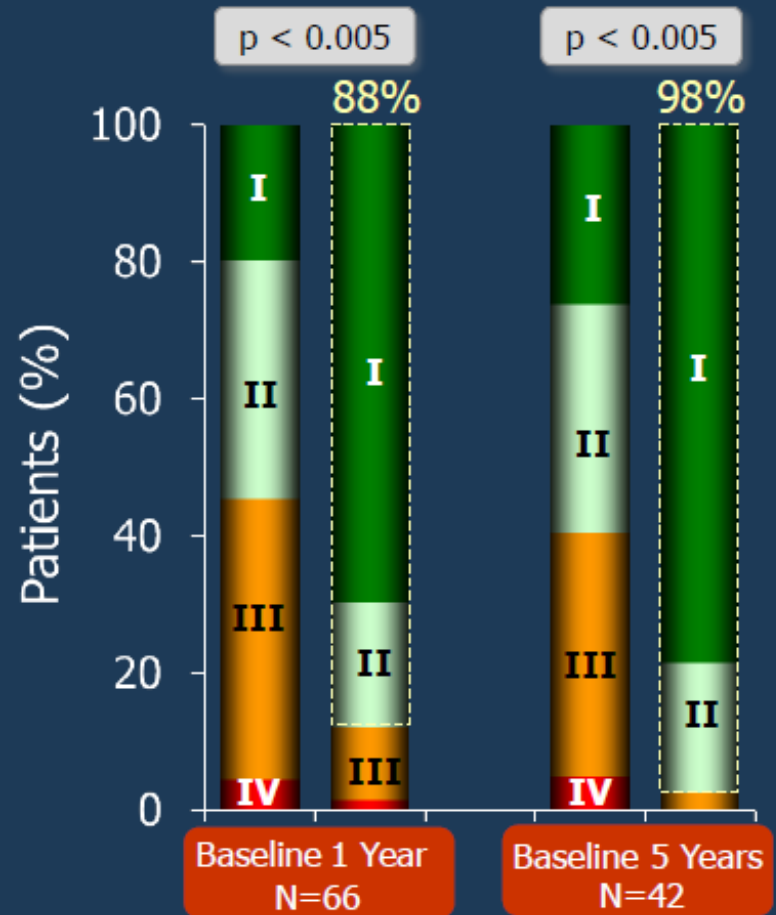
NYHA Functional Class

EVEREST II RCT All Treated Patients (N=258)

MitraClip (N=178)
NYHA I/II at 1 and 5 Years



Surgery (N=80)
NYHA I/II at 1 and 5 Years



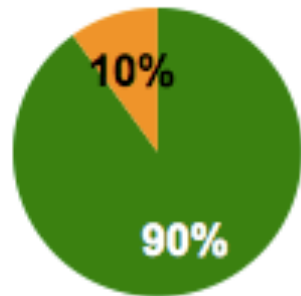
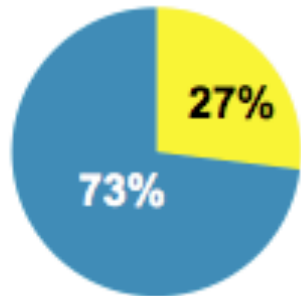
(Feldman ACC 2014)

N = survivors with paired data; p-values for descriptive purposes only

Temporal Changes in MitraClip Indication

EVEREST II

(Randomized Controlled Trial)



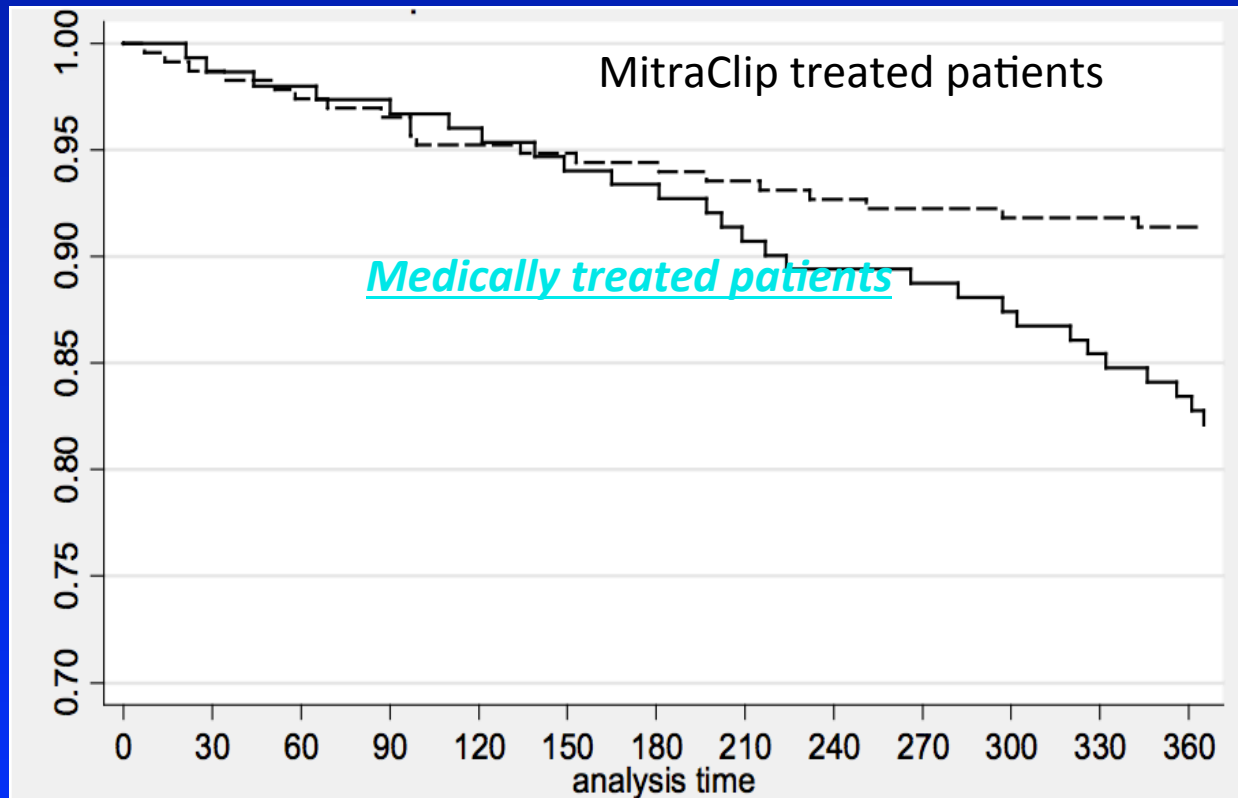
Treating Centers	563
Patients (clinical and commercial)	Over 25,000
Implant Rate ¹	96%
Functional MR ²	65%
Degenerative MR ^{2,3}	21%
Mixed	14%

Registries on MitraClip

	Age (yrs)	DMR	MR ≤2	In-hospital death
• STS/ACC TVT (US)	83	86%	93%	2.3%
• SENTINEL (EU)	74	28%	95%	2.9%
• ACCESS (EU)	74	23%	91%	
• TRAMI (DE)	75	29%	95%	2.9%
• MitraSwiss (CH)	77	38%	85%	4.0%
• France (FR)	73	23%	88%	3.3%
• GRASP (IT)	72	24%	100%	
• Netherlands (NL)	73	18%	93%	
• MARS (Asia)	71	46%	94%	4.2%
• EVEREST I	71	79%	74%	0.9%
• EVEREST II RCT	67	51%	77%	1.1%
• EVEREST II HRS	76	30%	86%	2.6%

Survival of MitraClip vs Controls

(IN-HF registry 32 centres from ANMCO database) Heart failure patients with $MR_{\geq 3+}$. Propensity-matched analysis



(Source: CERGAS Dr Tarricone)

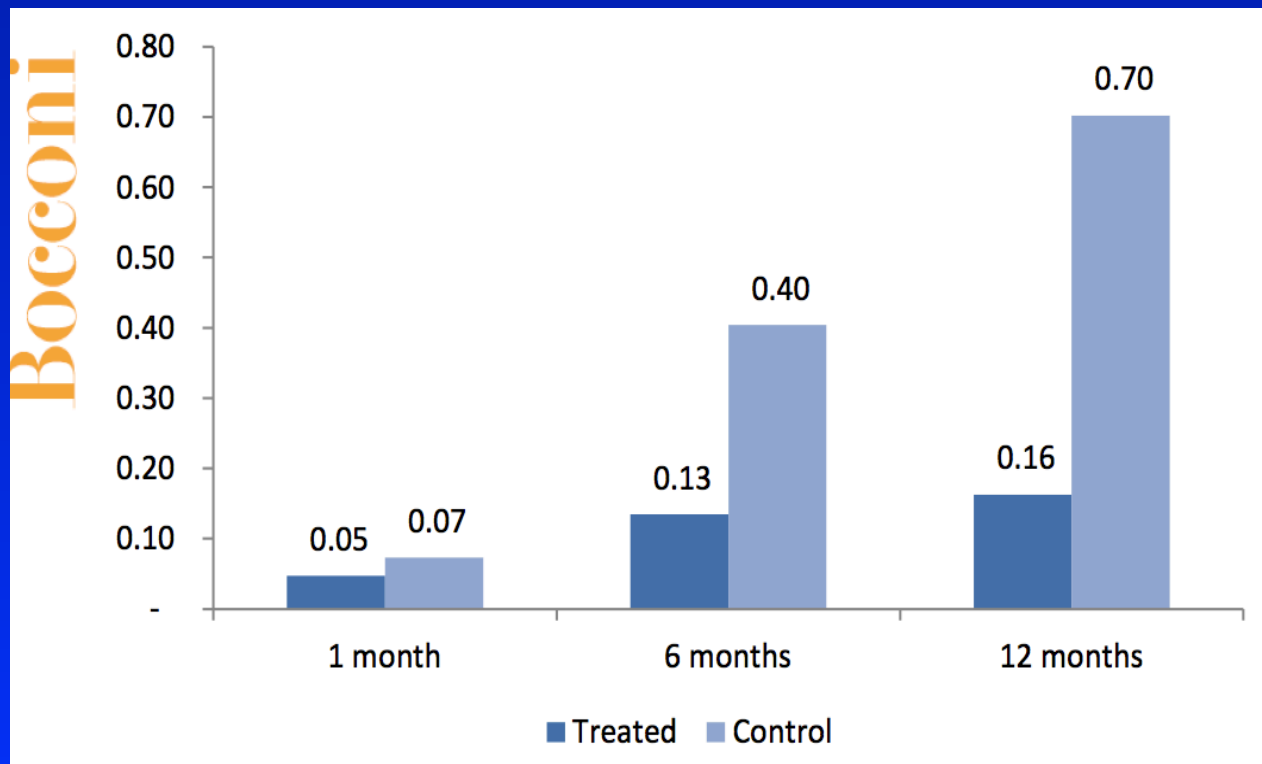
Predictors of 1-Yr Mortality

	Multivariable analysis (Cox regression model)	
	HR (95% CI)	P
Age >75 years	1.29 (0.90–1.87)	0.16
Female gender	1.13 (0.78–1.64)	0.53
NYHA IV	1.62 (1.10–2.40)	0.02
Anaemia	2.44 (1.16–5.12)	0.02
Previous aortic valve intervention	2.12(1.32–3.41)	0.002
Creatinine \geq 1.5 mg/dL	1.77 (1.24–2.54)	0.002
Peripheral artery disease	2.12 (1.41–3.20)	0.0003
LVEF <30%	1.58 (1.10–2.31)	0.01
<u>Severe tricuspid regurgitation</u>	1.84 (1.23–2.77)	0.003
Procedural failure ^a	4.36 (2.37–8.02)	<0.0001

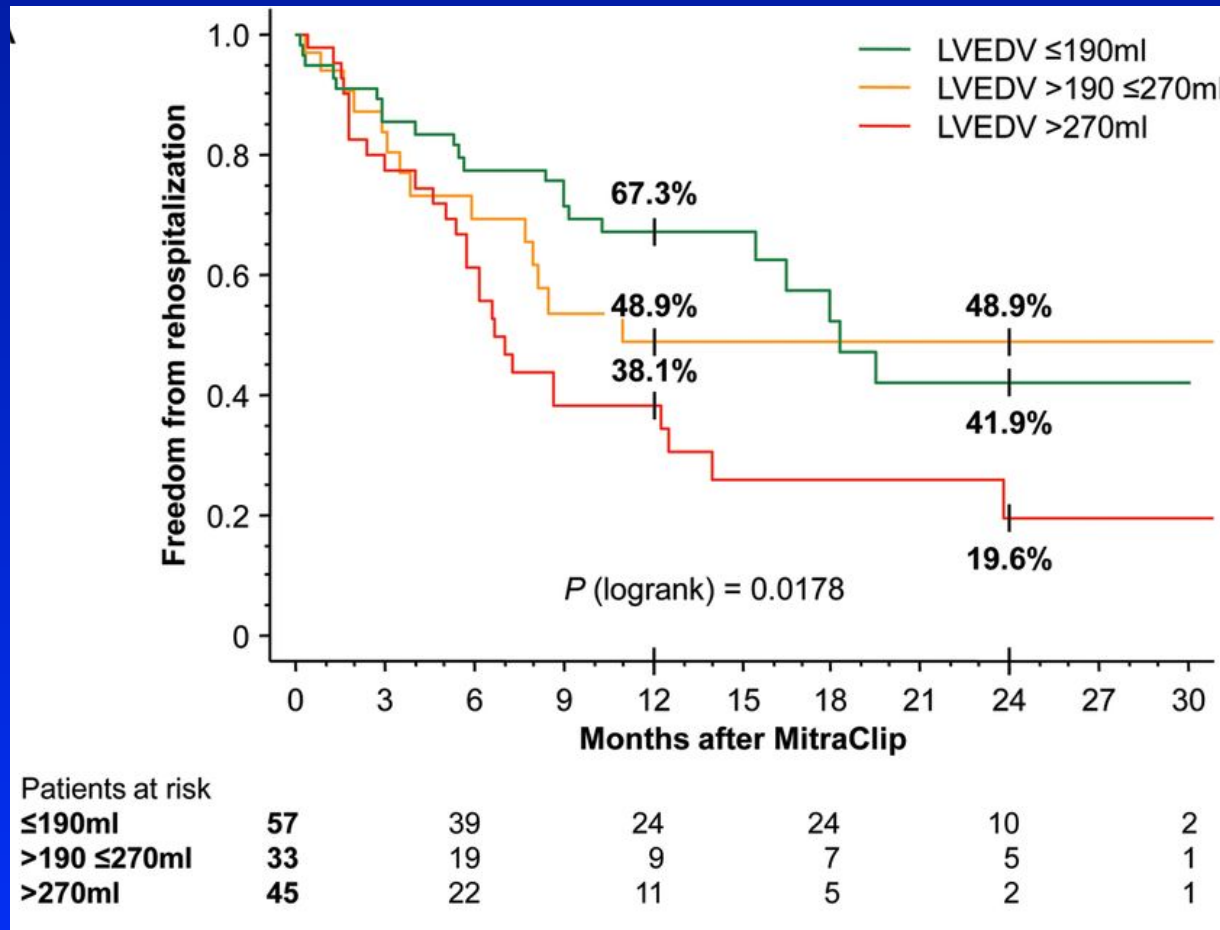
Need for Rehospitalization

Propensity-matched cohorts of MitraClip vs Control heart failure patients with $FMR \geq 3+$

- Treated patients: 232 patients enrolled in 2 centres (Milano, Catania).
- Untreated patients were extracted from the in-hf database from ANMCO.

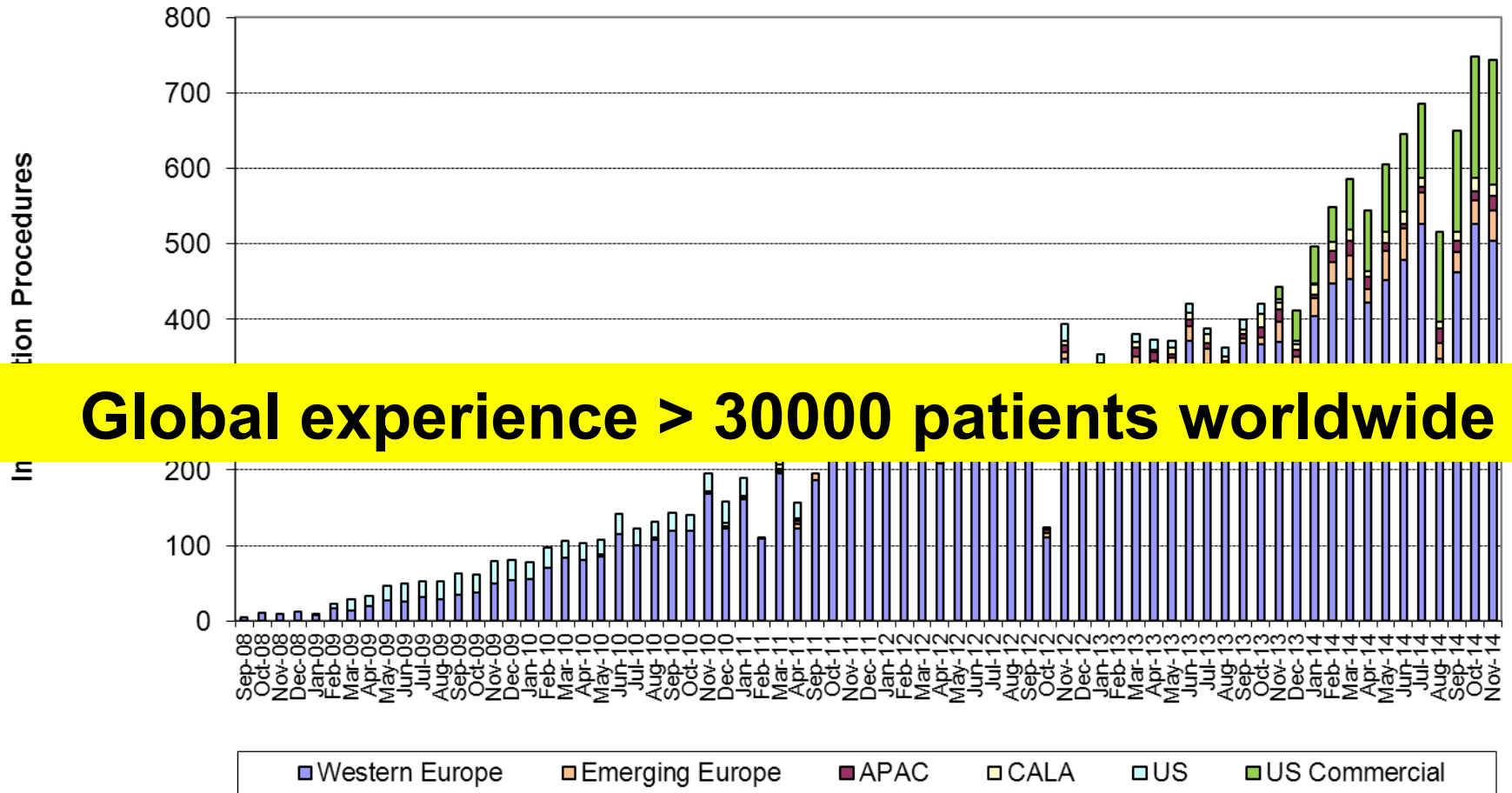


Timing of Intervention is Key



(Rudolph V et al. Eur J Heart Fail 2013;15:796-807)

World Wide Experience MitraClip Procedures



ESC/ EACTS Guidelines for the Management of Valvular Heart Disease

« The percutaneous MitraClip procedure may be considered in symptomatic patients with severe *primary or secondary* MR despite optimal medical therapy, who fulfil the echo criteria of eligibility, are judged inoperable or at high risk for surgery by a heart team, and who have a life expectancy greater than one year »

(Recommendation class IIb, level of Evidence C)

European Heart Journal 2012 - doi:10.1093/eurheartj/ehs109 &
European Journal of Cardio-Thoracic Surgery 2012 - doi:
10.1093/ejcts/ezs455).



ACC/AHA Recommendations for chronic primary MR

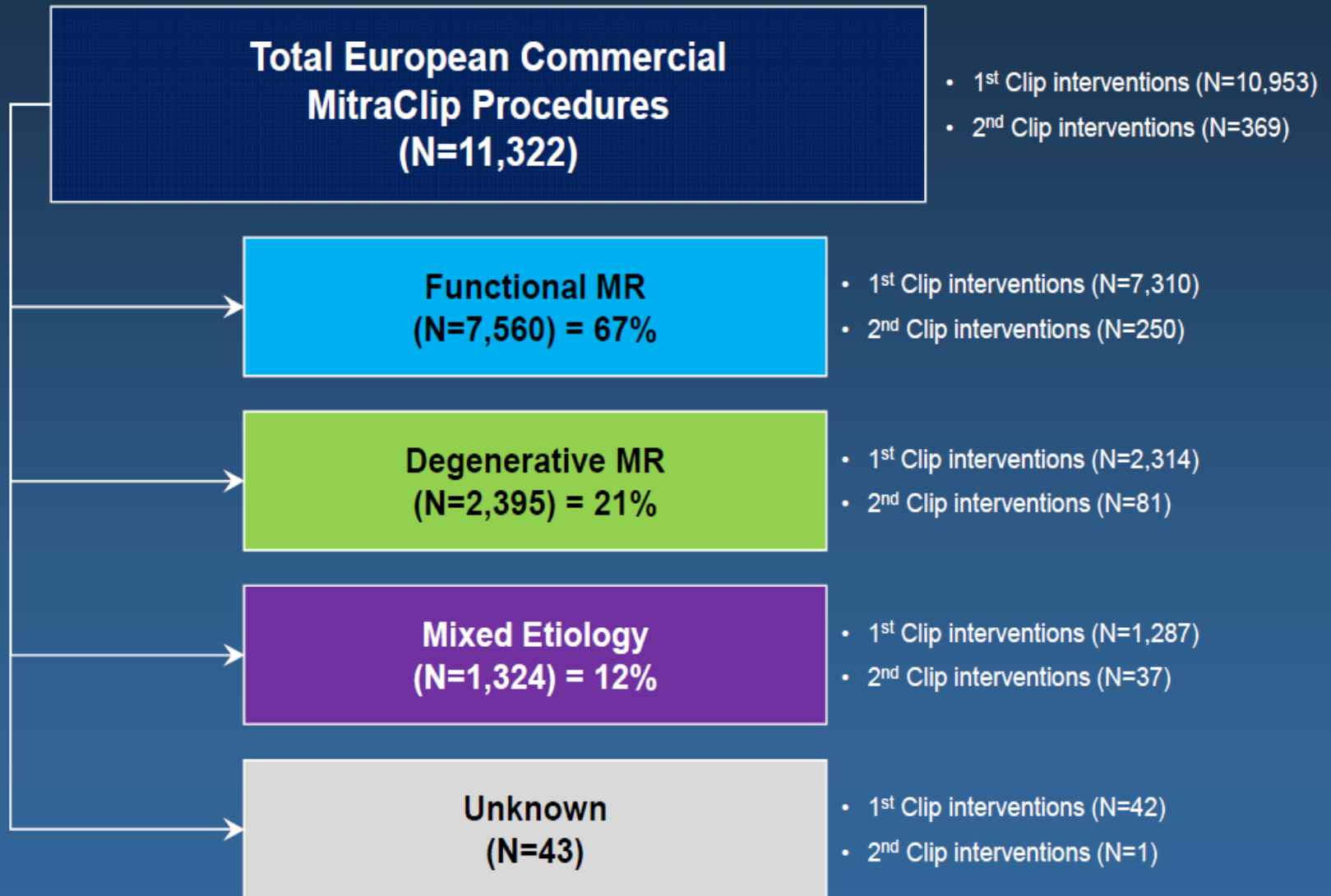
Recommendations	COR	LOE
Transcatheter mitral valve repair may be considered for severely symptomatic patients with <i>chronic severe primary MR</i> who have a reasonable life expectancy but a prohibitive surgical risk because of severe comorbidities	IIb	B

(Nishimura et al. J Am Coll Cardiol 2014 In Press. DOI: 10.1016/j.jacc.2014.02.537)

Les Autres Techniques

PMVR in TRAMI: 99,5% MitraClip **0,5% Annuloplasty**

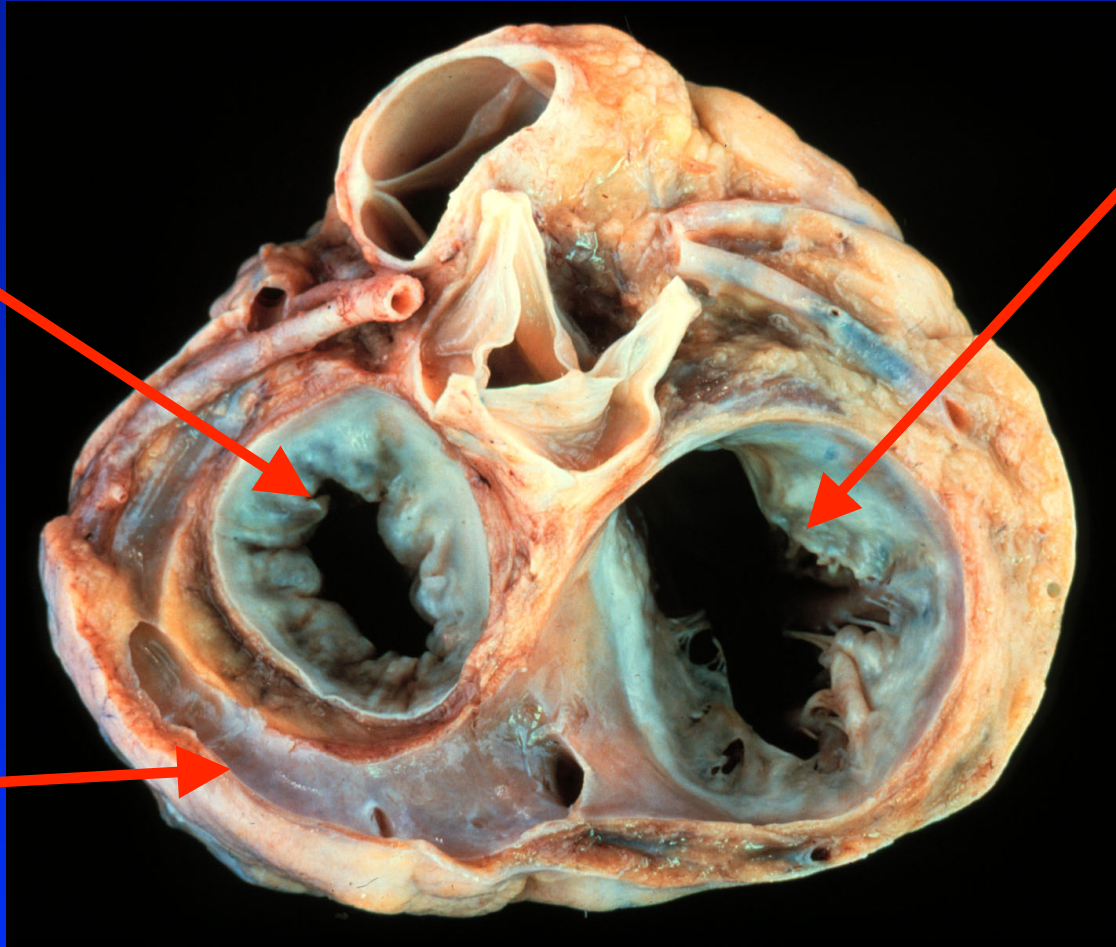
Total MC Experience 13,500 cases in registries and commercial use



Percutaneous Coronary Sinus Annuloplasty

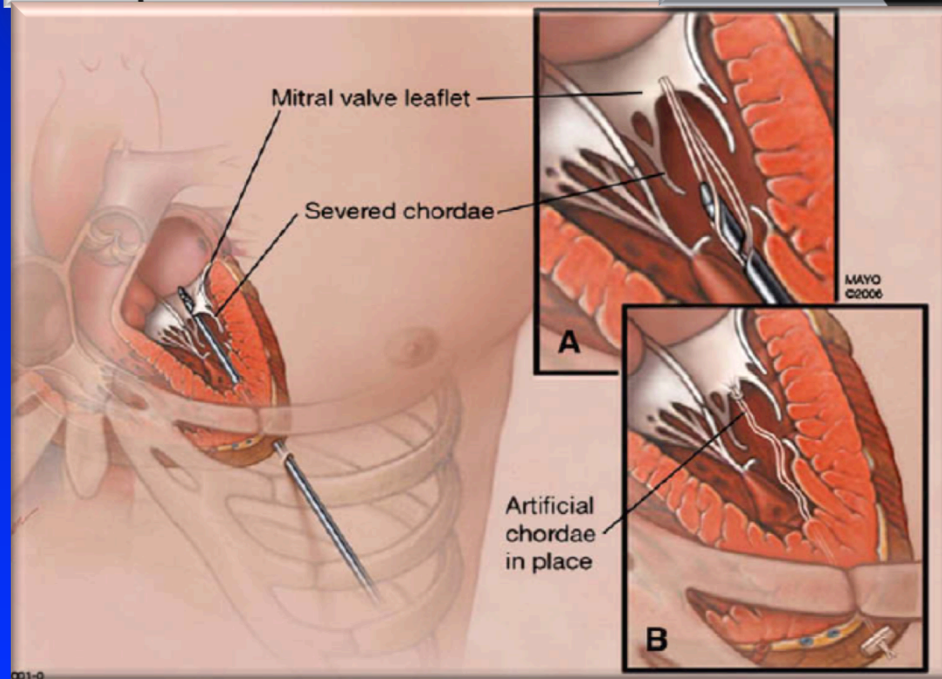
Mitral valve

Tricuspid
valve

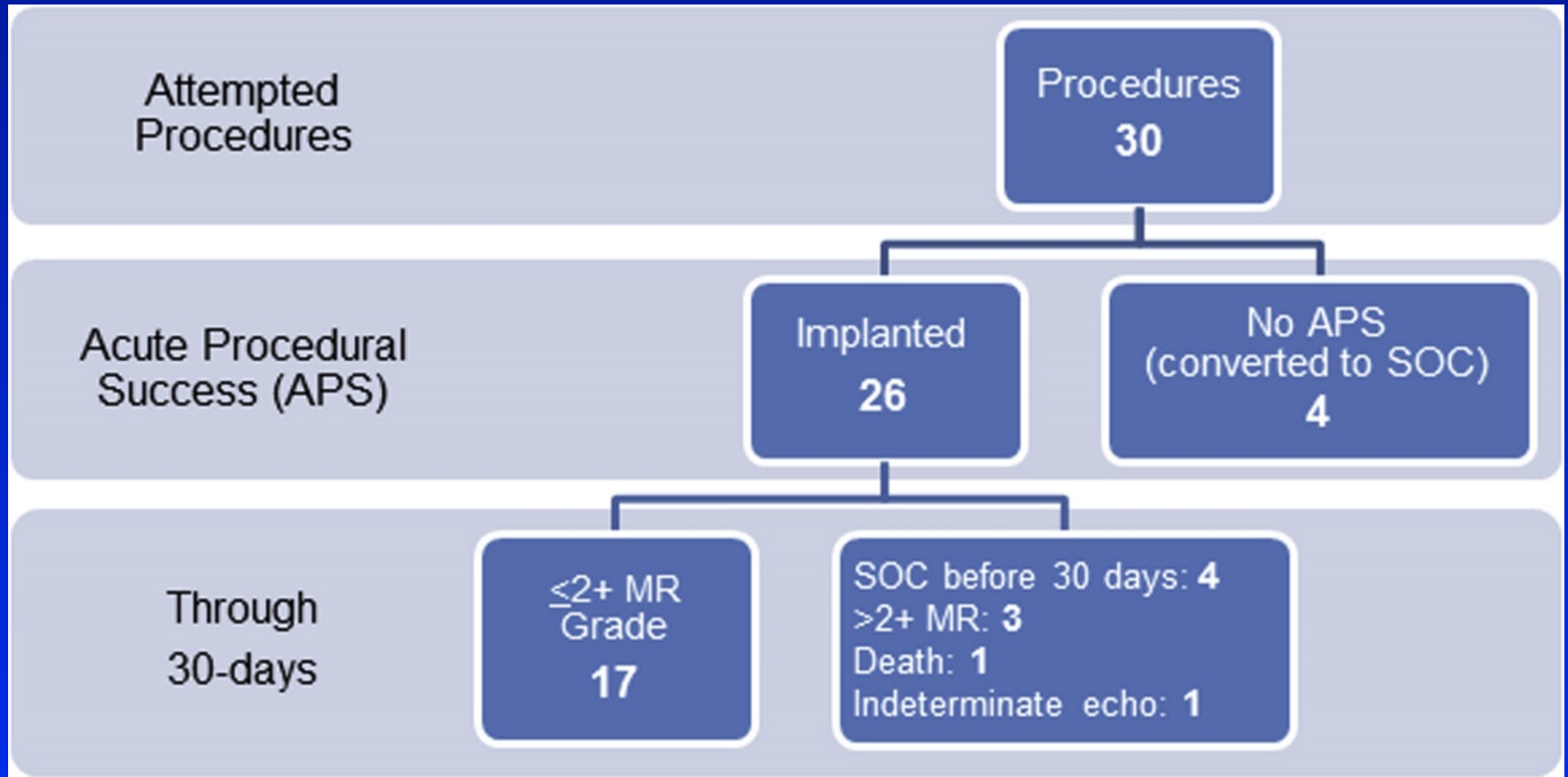


Coronary
sinus

Chordal Implants



The TACT Study



(Seeburger. J Am Coll Cardiol 2014;63:914–9)

Patient Stratification in Padova

Ideal
(Type A)

Adequate
(Type B)

Challenging
(Type C)

Central P2

→ towards P1/P3 Pericommissural

Eccentric Jet

+Central jet component

Good Coapt.

Marginal Coapt.

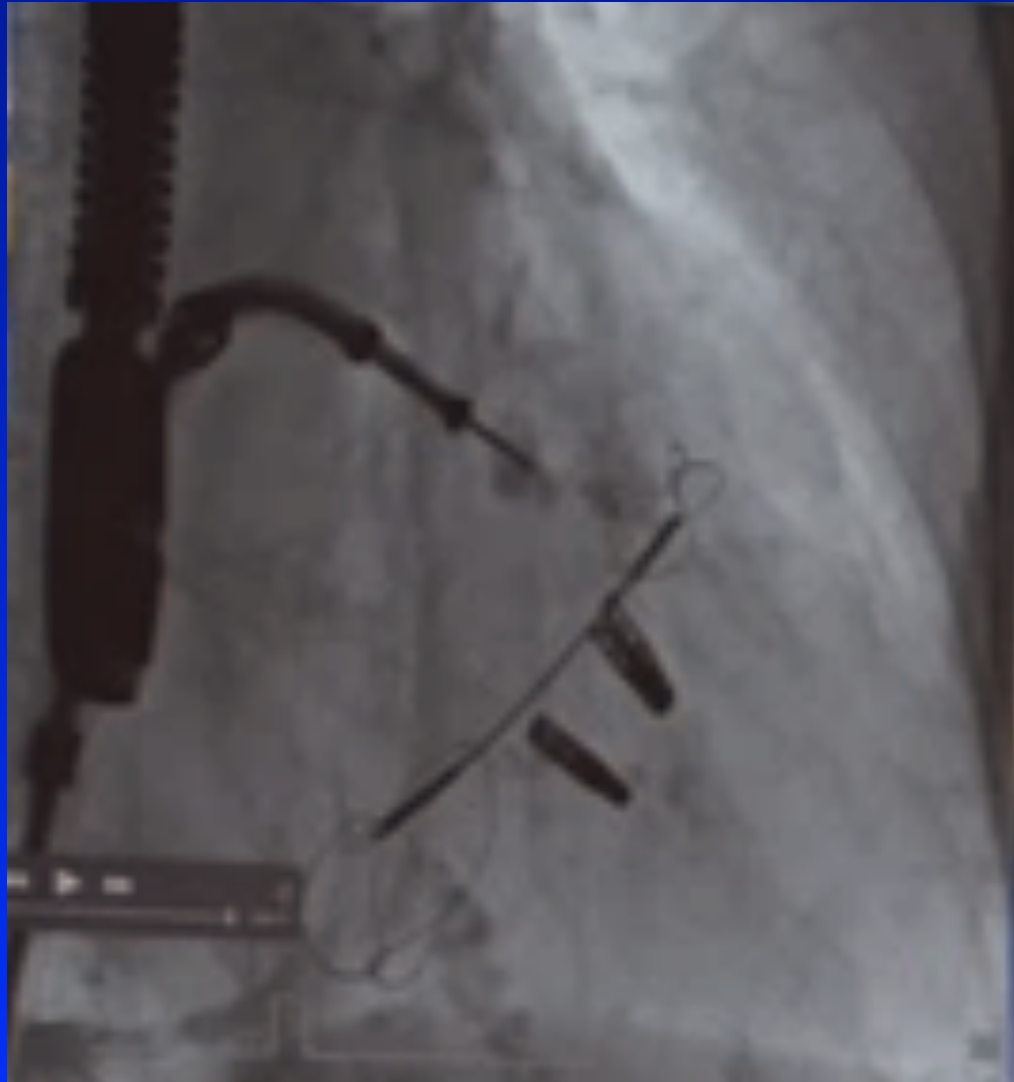
No LV Dilatation

LV Dilatation

No Tethering

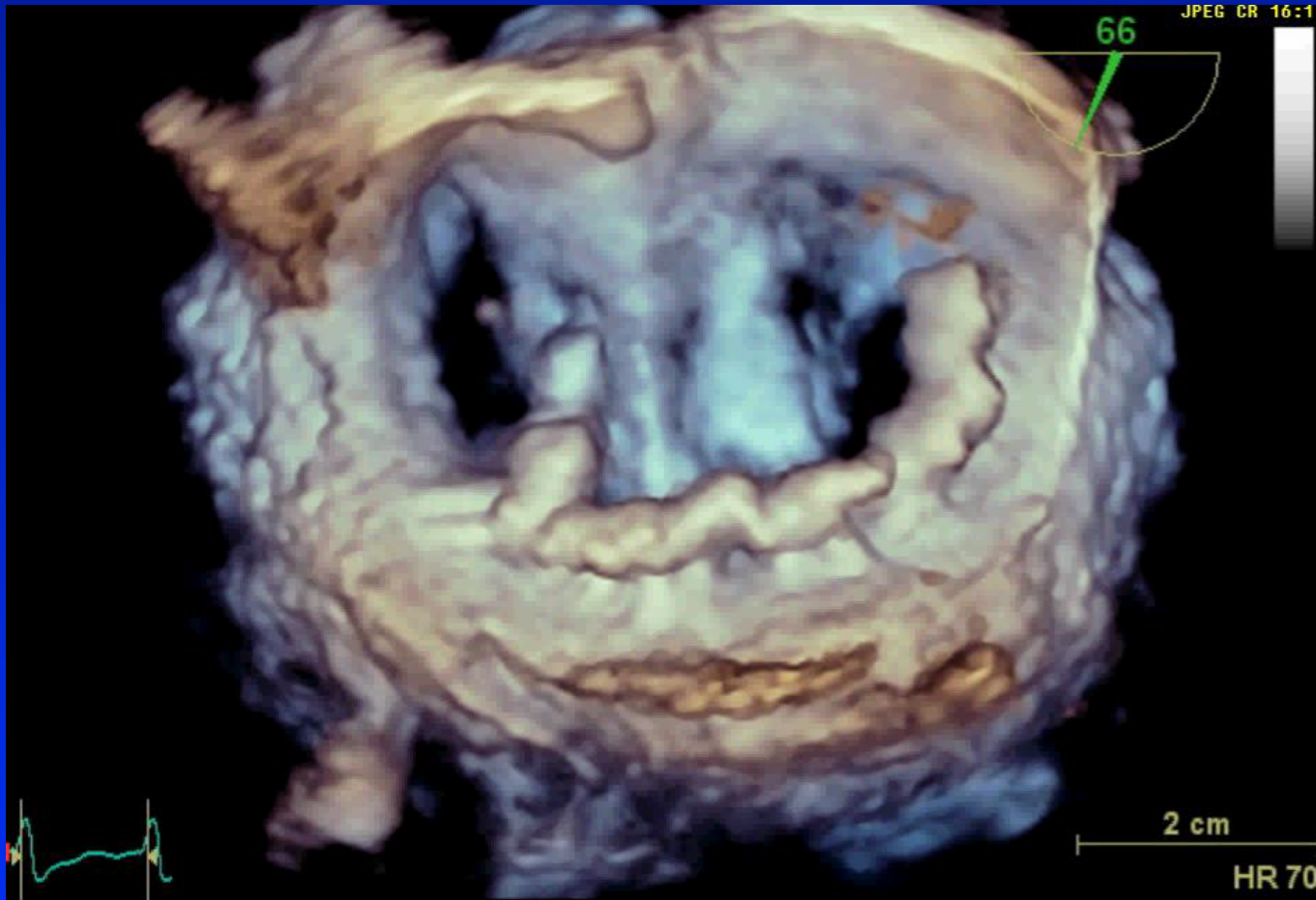
Leaflet Tethering

Coronary Sinus Annuloplasty + Mitraclip



(Courtesy G Nickenig)

MitraClip after Annuloplasty Failure



(Courtesy of KH Kuck)

Transcatheter Mitral Valve Implantation in Native valves (n<100)

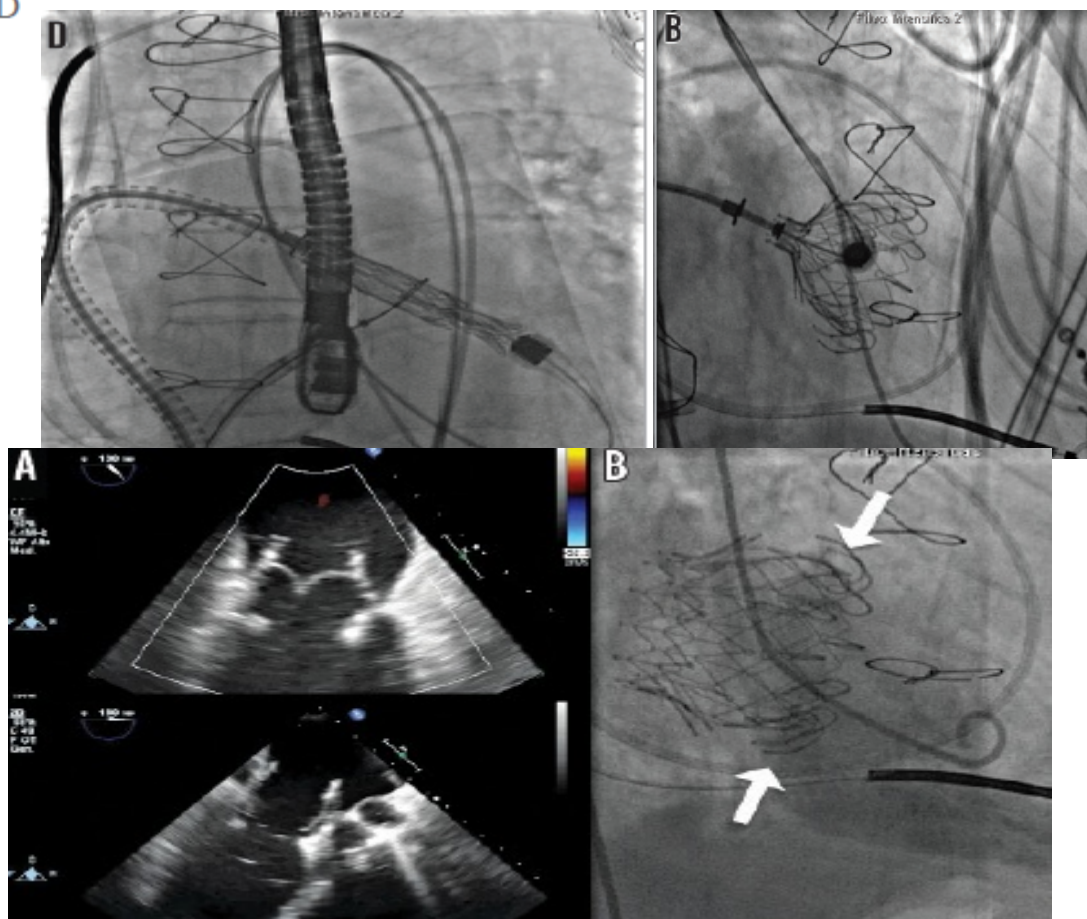
Challenges

- Positioning
- Fixation
- Paravalvular leaks
- Valve gradient and LV outflow track obstruction
- Thrombosis
- Durability
- Feasibility of reintervention
-



Percutaneous transfemoral-transseptal implantation of a second-generation CardiAQ™ mitral valve bioprosthesis: first procedure description and 30-day follow-up

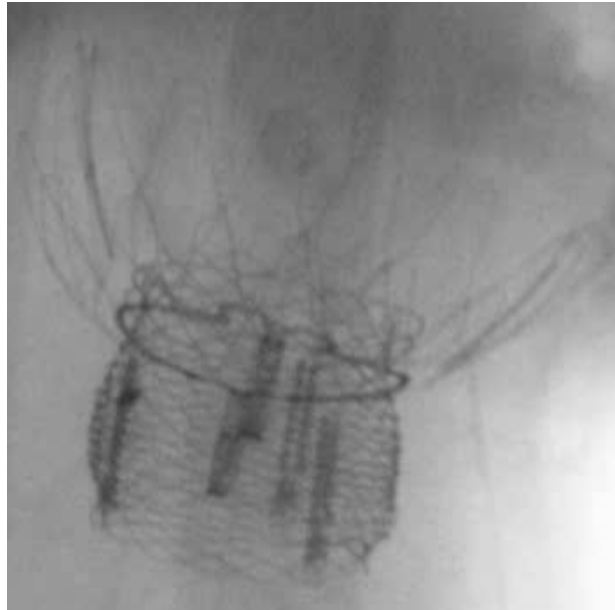
Gian Paolo Ussia^{1*}, MD; Arshad Quadri², MD; Valeria Cammalleri¹, MD; Pasquale De Vico³, MD; Saverio Muscoli¹, MD; Massimo Marchei¹, MD; Giovanni Ruvolo⁴, MD; Lars Sondergaard⁵, MD, MDSc; Francesco Romeo¹, MD



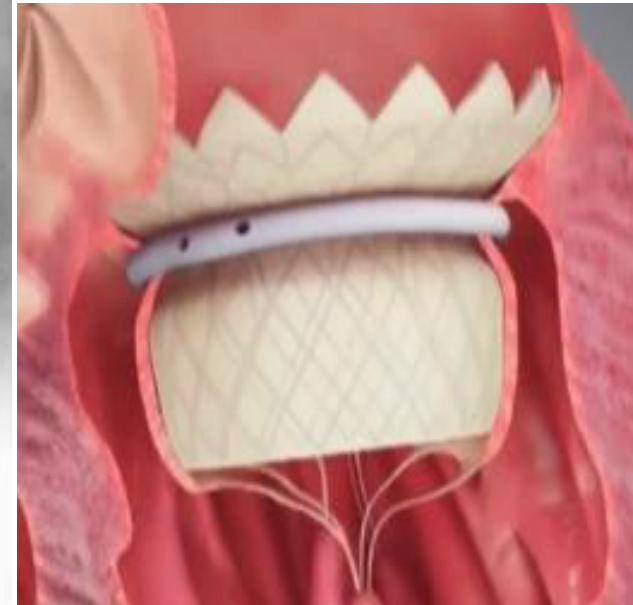
Valve in a « Docking Device »



(Courtesy of R Lange)



(Courtesy of M Butchbinder)



(Courtesy of E Grube)

Valve in Valve International Registry



Patients undergoing procedures in 94 sites in Europe, North-America, Australia, New Zealand, South Africa, South America and the Middle-East
(n=1,671)

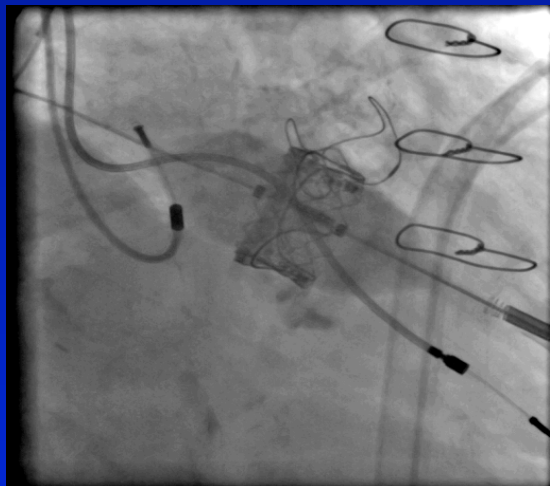
Aortic Valve in Valve
(n= 1,074)

Tricuspid Valve in Valve /
Valve in Ring (n=156)

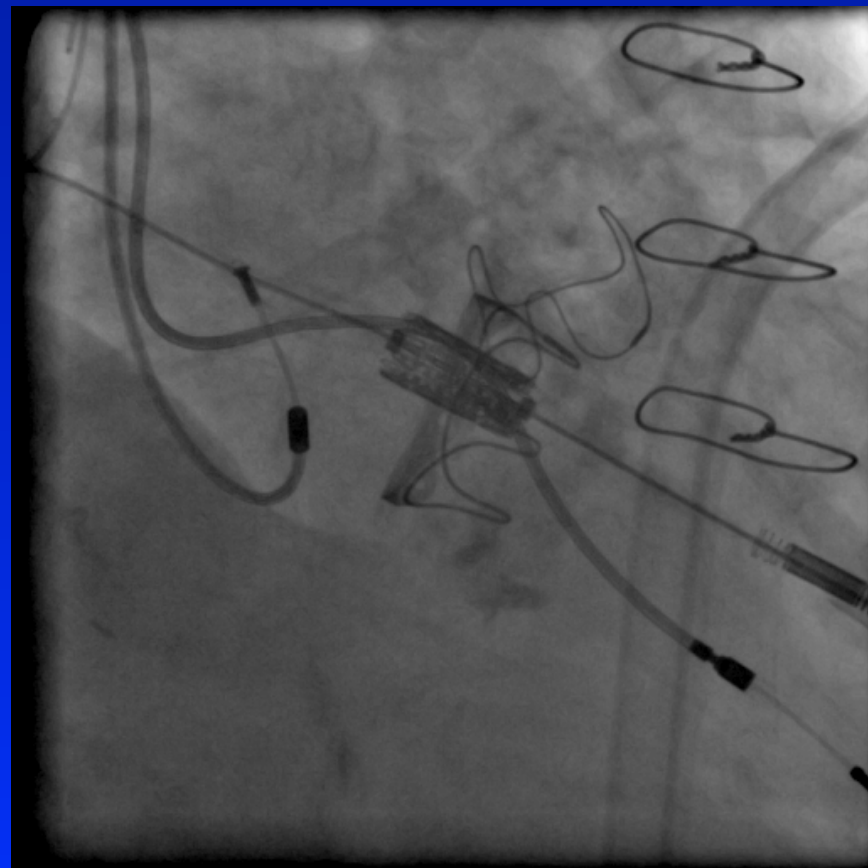
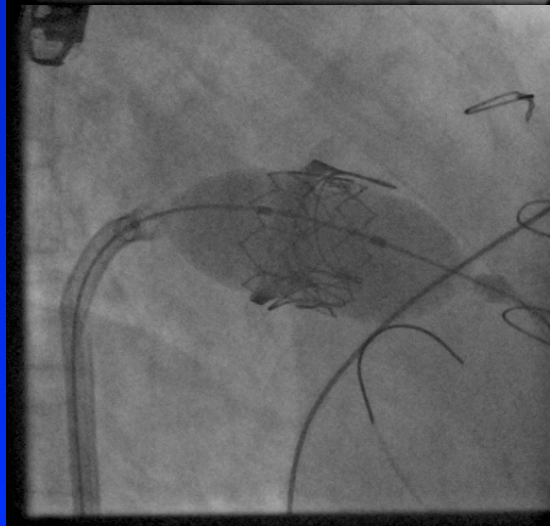
Transcatheter Mitral implants in failed valves post
surgery
(n=437)

Transcatheter « Valve in Valve » for Mitral Bioprosthesis Failure

Transapical



Transseptal

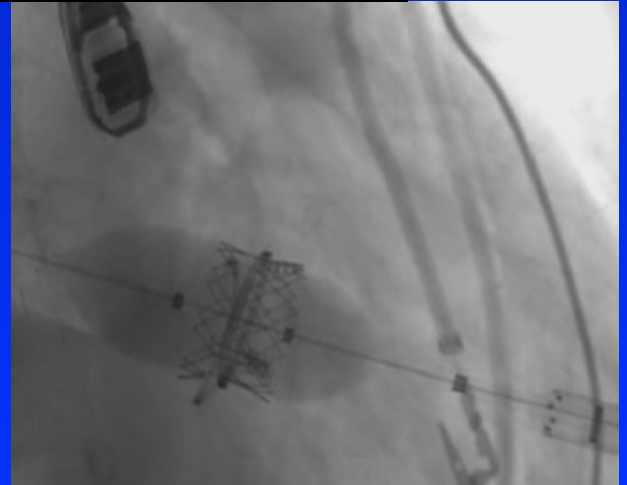


Transcatheter « Valve in a Ring »

Transseptal



Transapical



Aims and population

Redo mitral surgery: high risk or contraindicated

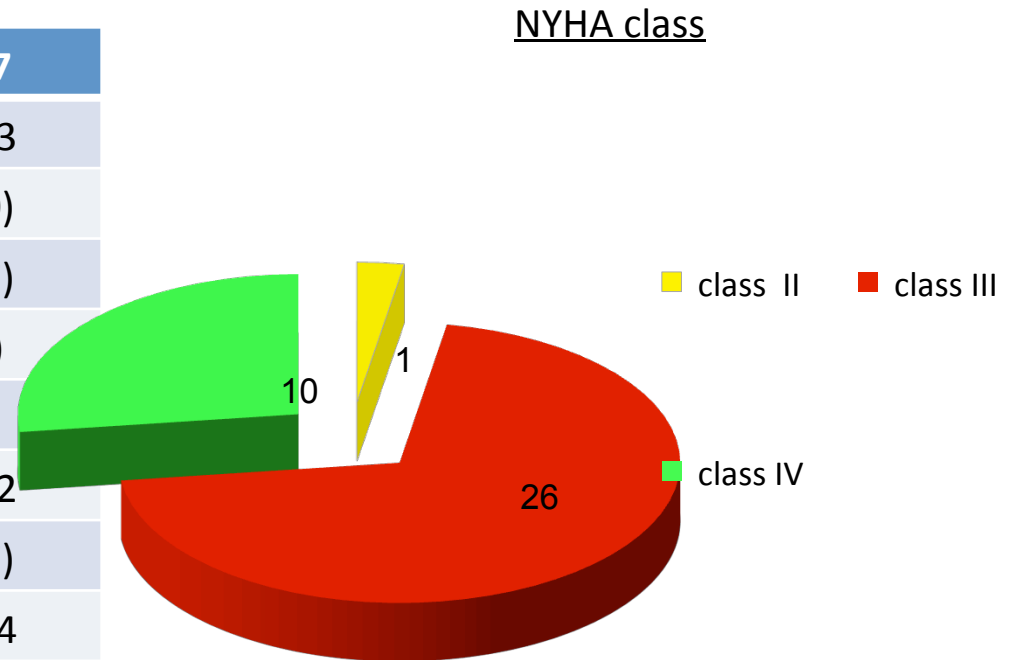


Heart Team

Transcatheter Heart Valve (THV) implantation in degenerated bioprosthesis (MVIVI) / ring annuloplasty (MVIRI) may be considered.

Bichat hospital: 37 patients between 2011-2015

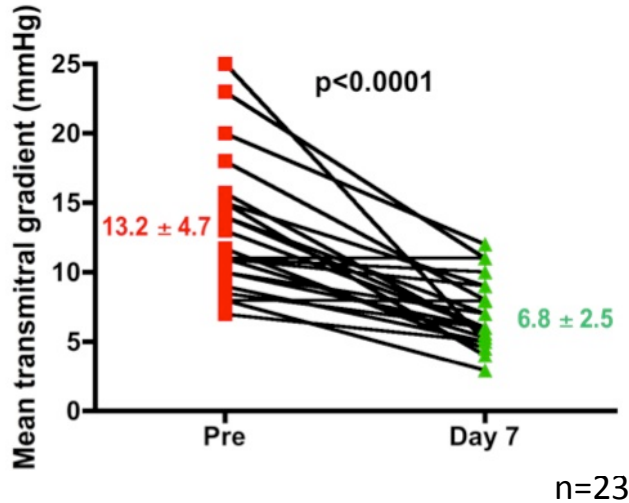
Variables	n= 37
Age (yrs)	61 ± 23
Male Sex	11 (30)
Chronic Lung Disease	10 (27)
≥2 previous cardiac surgeries	8 (22)
Delay since last surgery (yrs)	9 ± 5
LVEF (%)	56 ± 12
Atrial fibrillation	21 (57)
Systolic PAP (mmHg)	56 ± 14
Euroscore I (%)	30 ± 24
Euroscore II (%)	15 ± 16



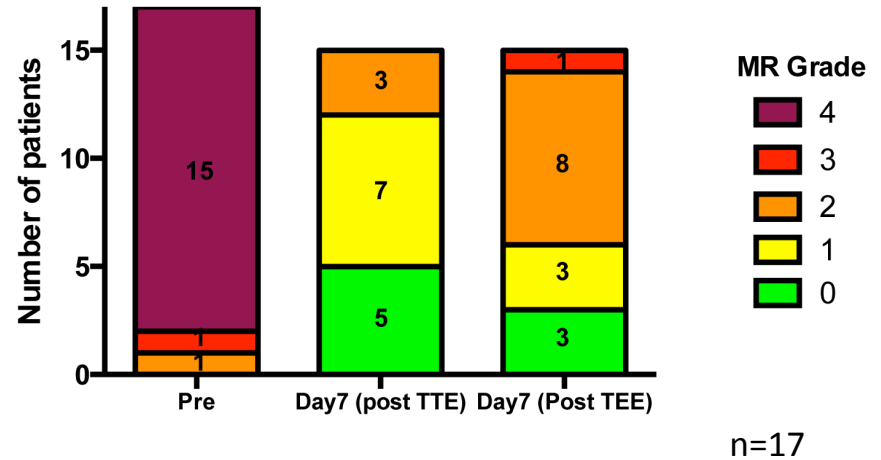
3 rescue procedures under ECMO

Immediate and 30-day Results

For stenotic degeneration, mean mitral gradient significantly decreased



MR grades improved among patients with regurgitation failure



30-day events

30-day survival = 92% /

30-day event-free survival = 84%

Procedural success (VARC-2) = 30/37 (81%)

Failures:

1 death (IVC rupture during rescue procedure),

1 paraprosthetic leak 3/4,

1 conversion to surgery (aorta perforation)

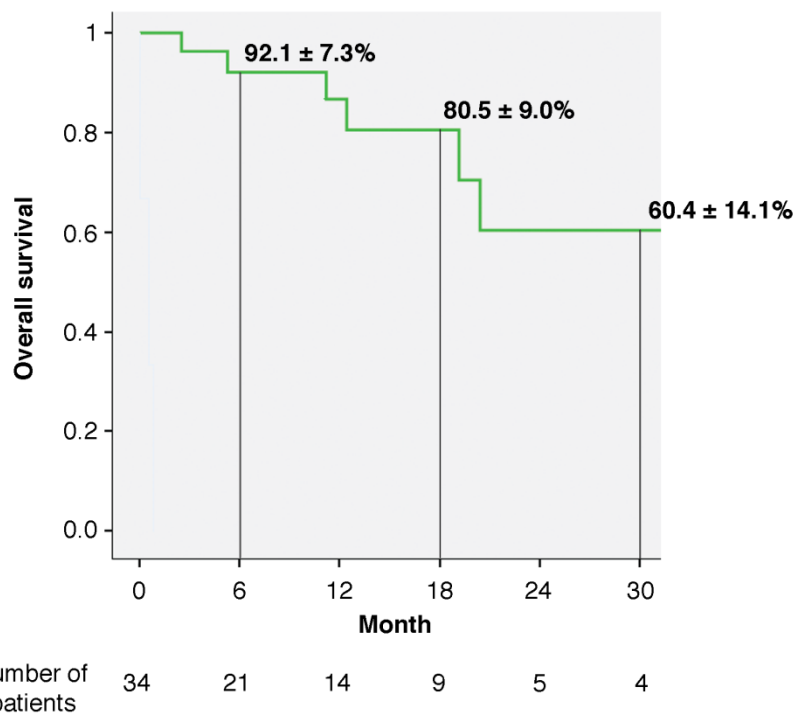
4 implantations of a 2nd prosthesis

Mid-term (30 months) results

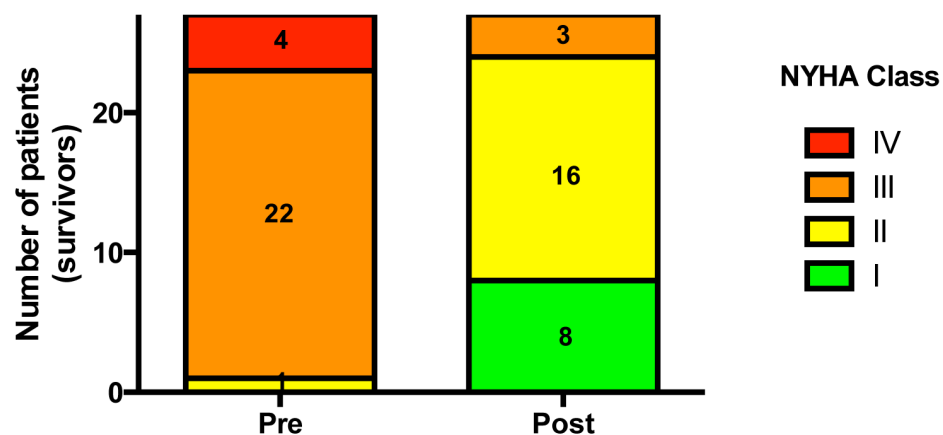
Among the patients discharged alive, 7 died during a mean follow-up of 30 months (6 from cardiac cause).

At last follow-up, 89% of survivors were in NYHA class I or II.

Overall 30-months survival



Sustained good functional results

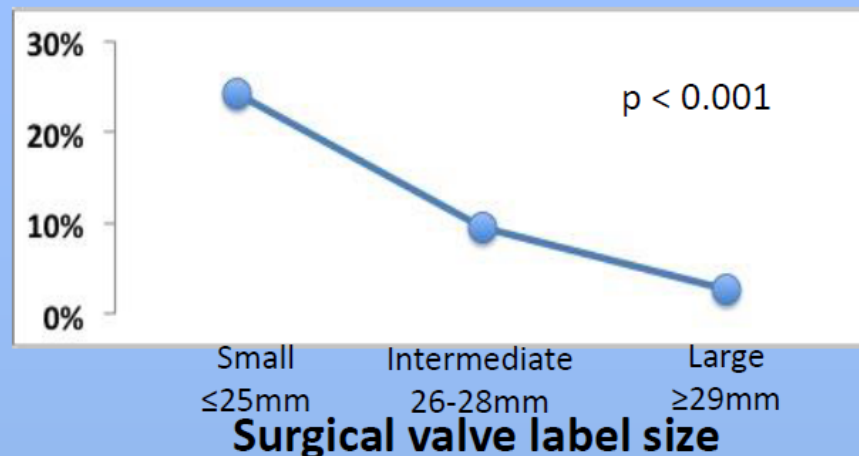


Residual stenosis

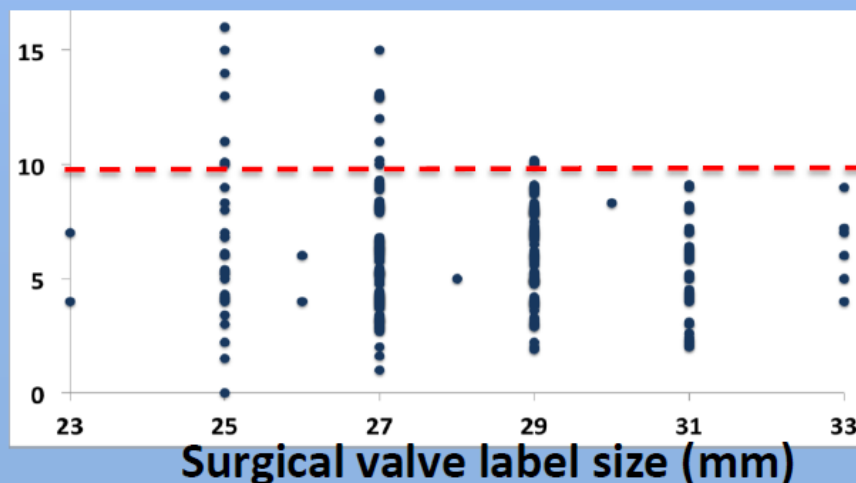


Multivariate analysis for elevated gradients:
the main independent predictor is having **small surgical valve size**:
Odds Ratio 3.7 (CI 1.79-7.69, $p < 0.001$)

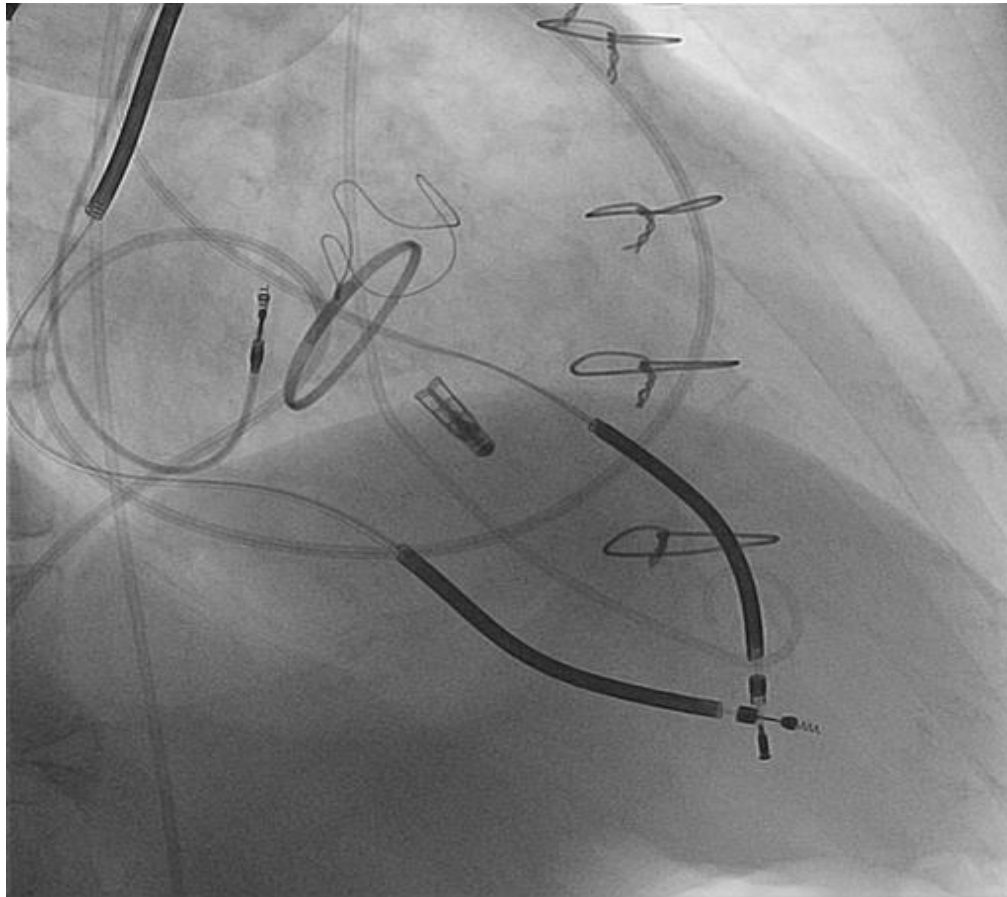
Rate of elevated gradient after mitral valve-in-valve (mean ≥ 10 mmHg)



Post procedural mean gradient (mmHg)



MitraClip after Annuloplasty Failure



(Courtesy of KH Kuck)

Le Futur

Heart Valve Centres of Excellence

- « The optimal care of patients with complex heart valve disease is best performed in centres that can provide all available options for diagnosis and management, including the expertise for complex aortic or mitral valve repair, aortic surgery, and transcatheter therapies. »
- This has led to the development of Heart valve Centres of Excellence

(Nishimura et al. J Am Coll Cardiol 2014;63:e57–e185)

The « Heart Team »

CARDIOLOGISTS (General, HF, EP, Interventionists)

SURGEONS

Anesthesiologists

**Treatment of
Valve disease**

**Other specialists:
Geriatricians**

Imaging specialists (Echo, CT, MRI)

Patient Selection for Percutaneous Mitral Valve Intervention

The « Heart Team »

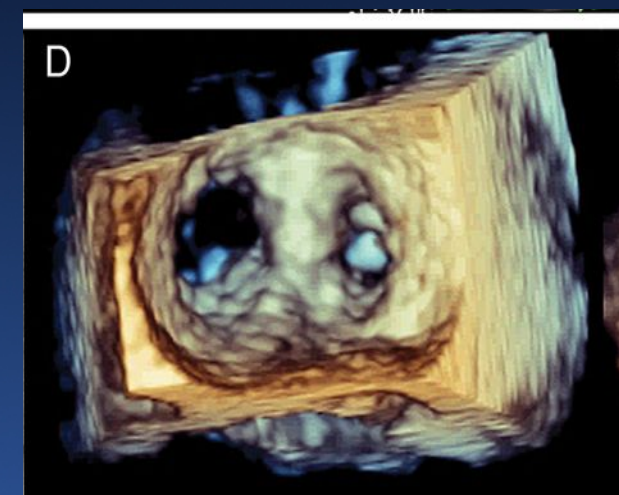
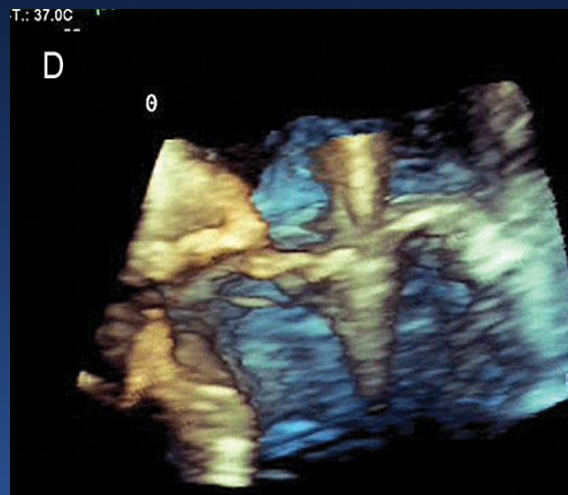
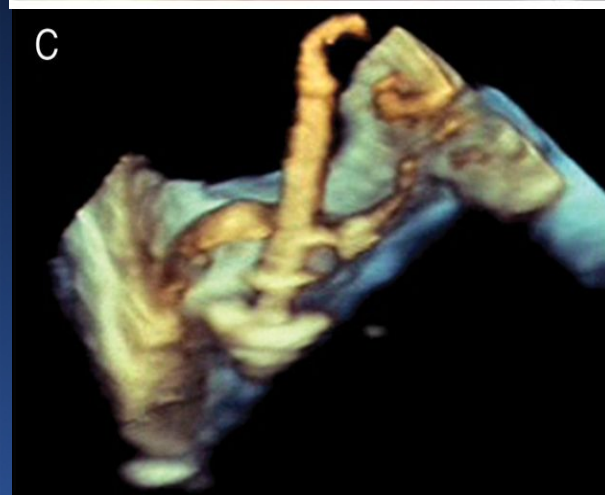
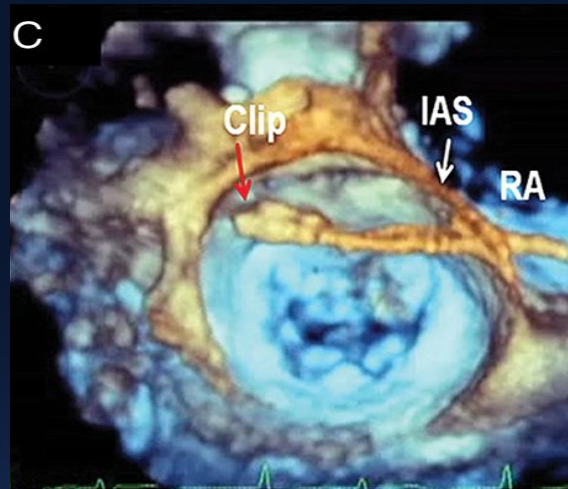
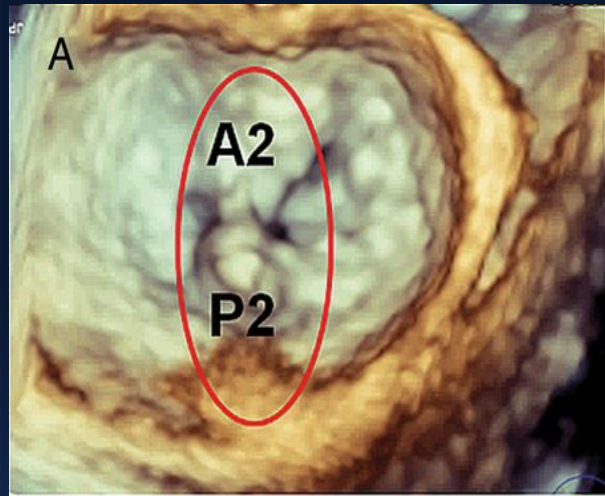
Medical Rx

PMVR

Surgery
(Repair, Replacement, LVAD,
Transplantation)

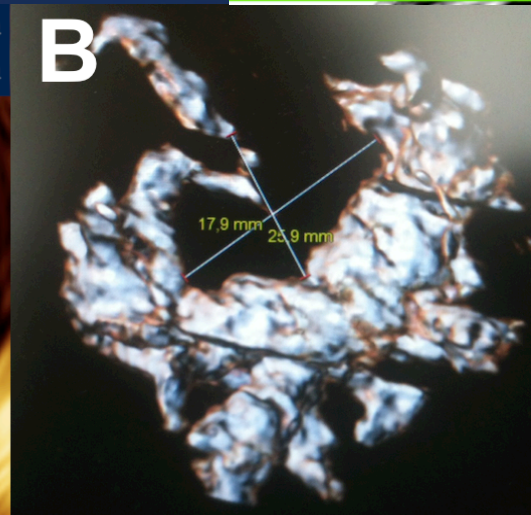
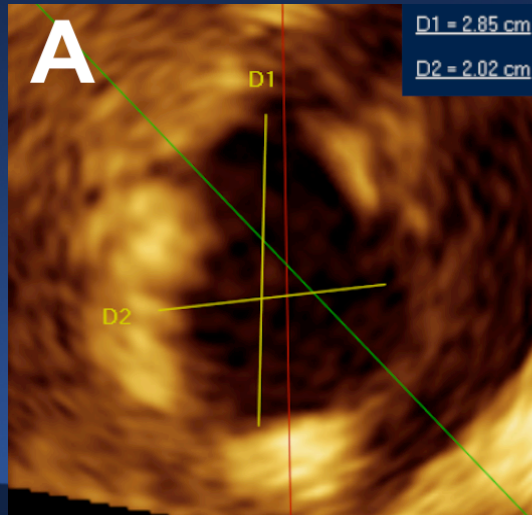
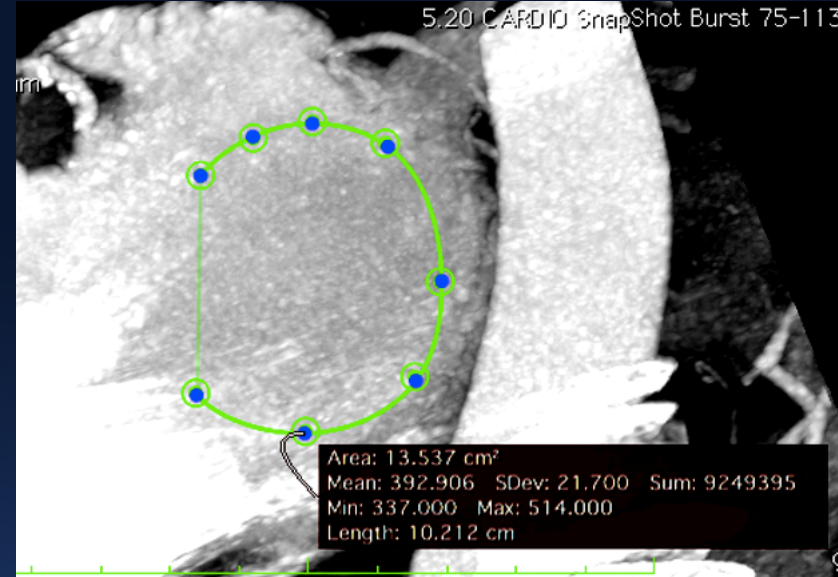
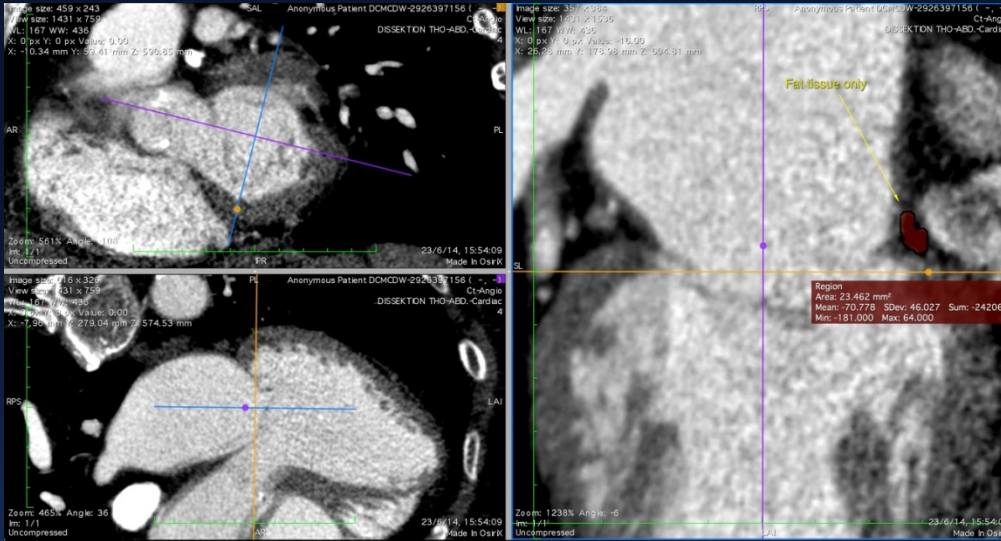
« Futility > Utility »
because of extra cardiac
factors

Echocardiography is Key

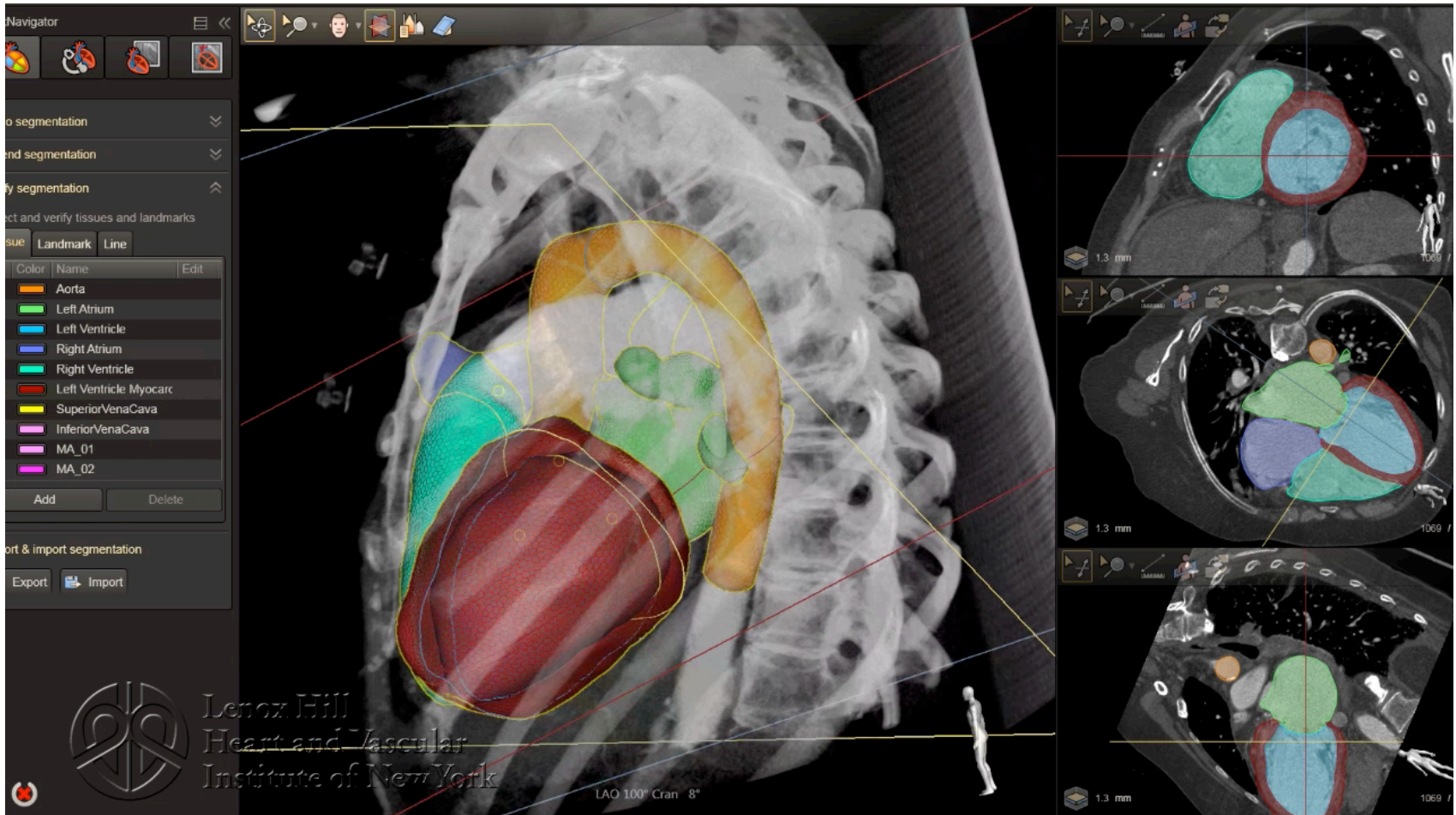


(Wunderlich NC, *Eur Heart J Cardiovasc Imag* 2013;14:935-949)

CT for Procedural Planning



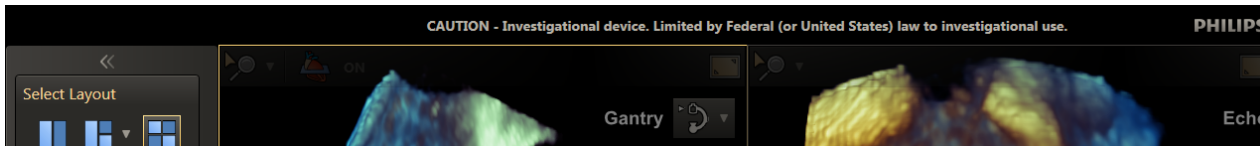
Multimodality Imaging for Preprocedural Planning



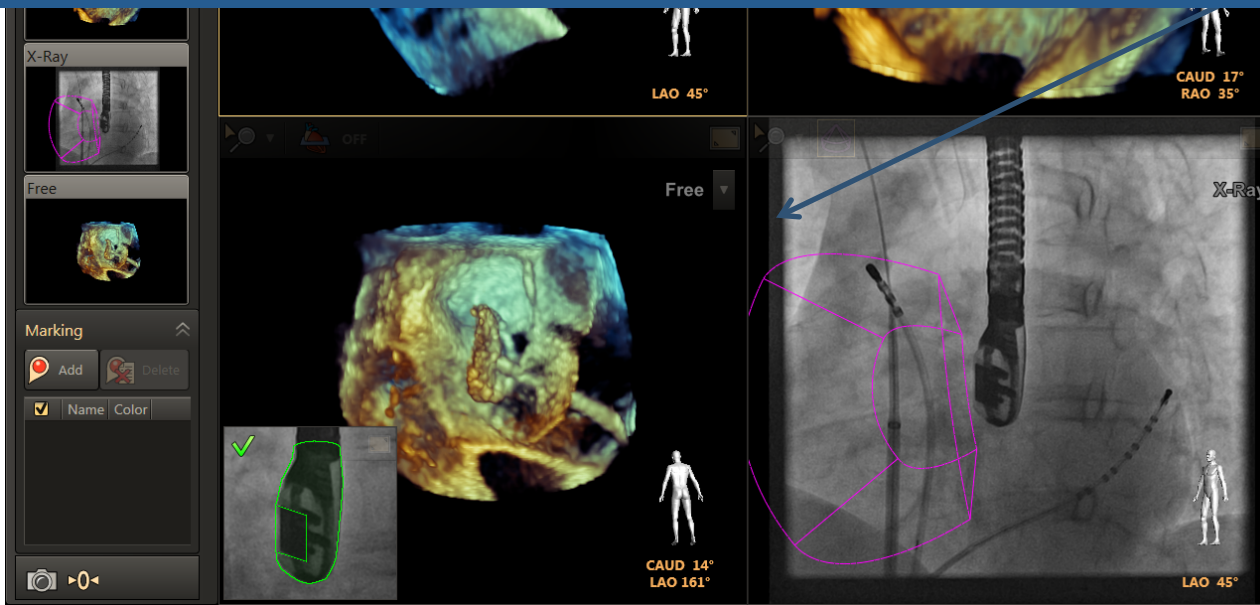
(Courtesy of C. Ruiz)

Multimodality Imaging for Procedural Guidance

Linked Live 3DTEE and fluoroscopic images



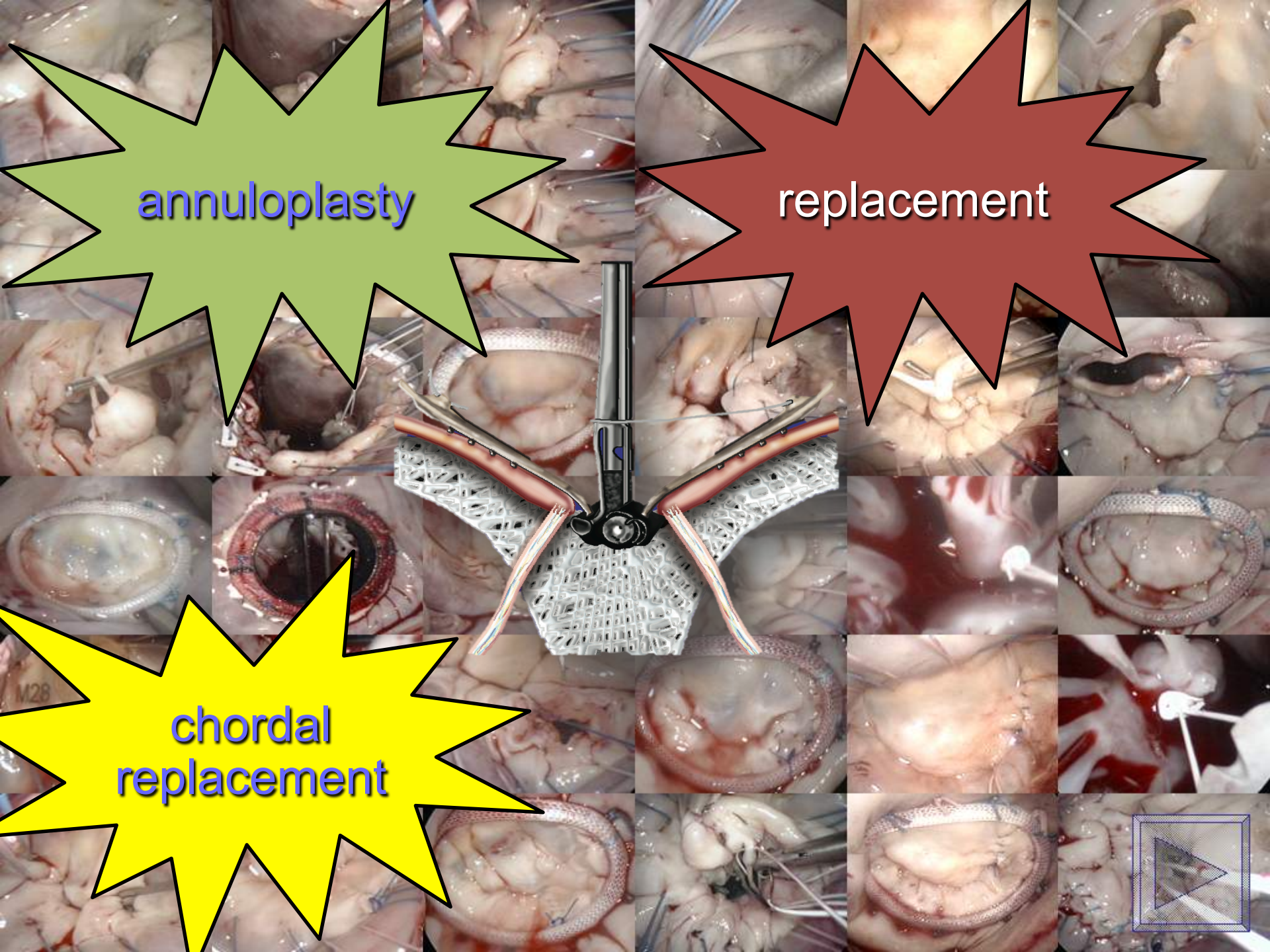
Extended imaging training for Interventionists



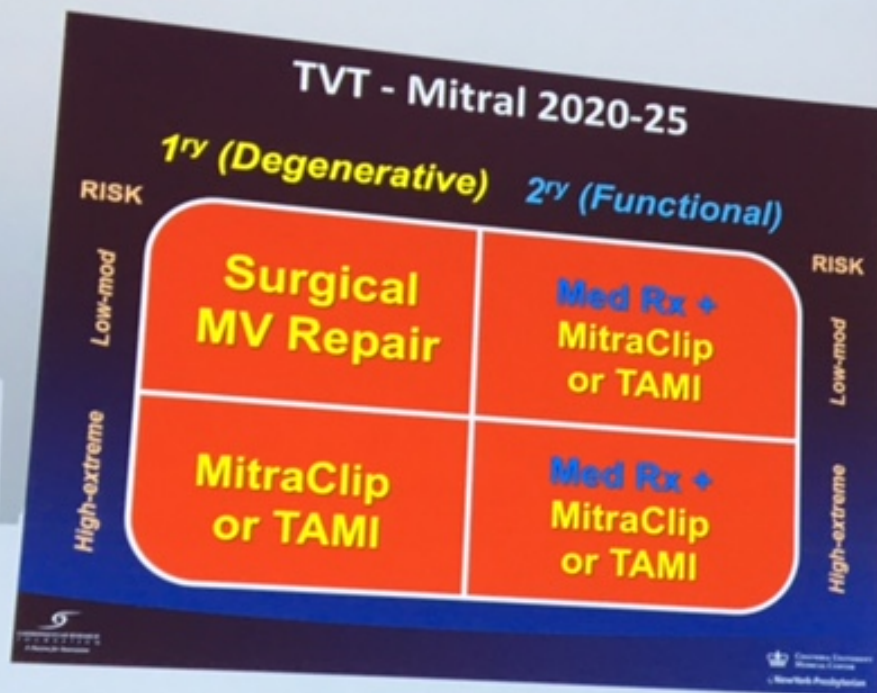
annuloplasty

replacement

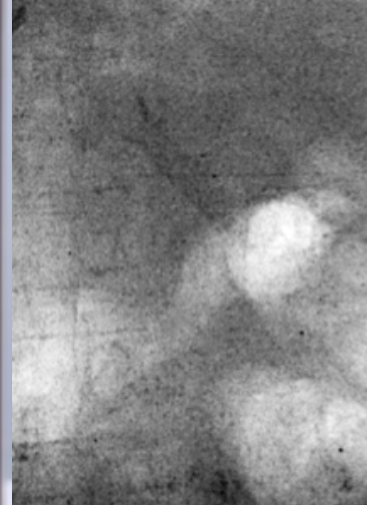
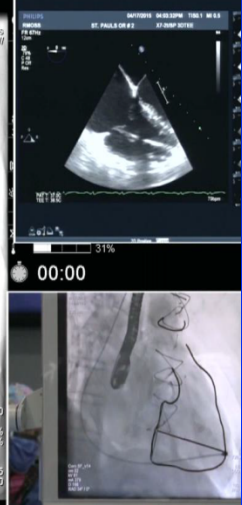
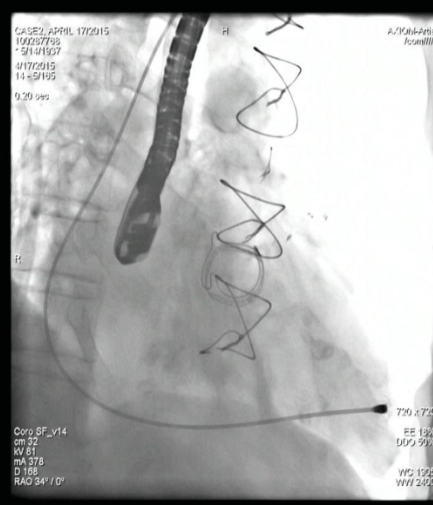
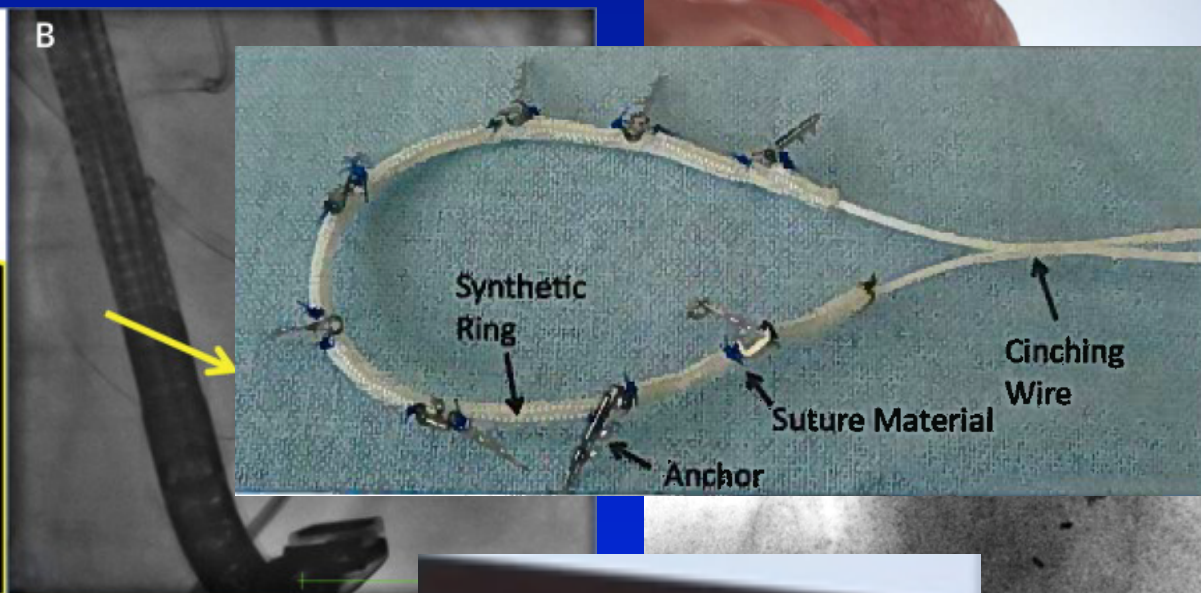
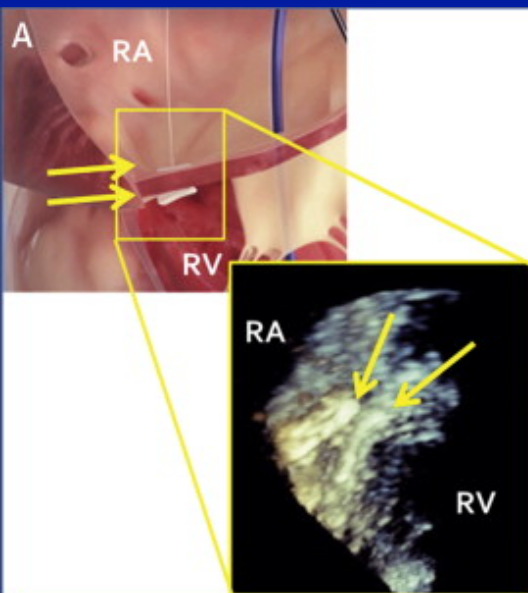
chordal
replacement



M
VE



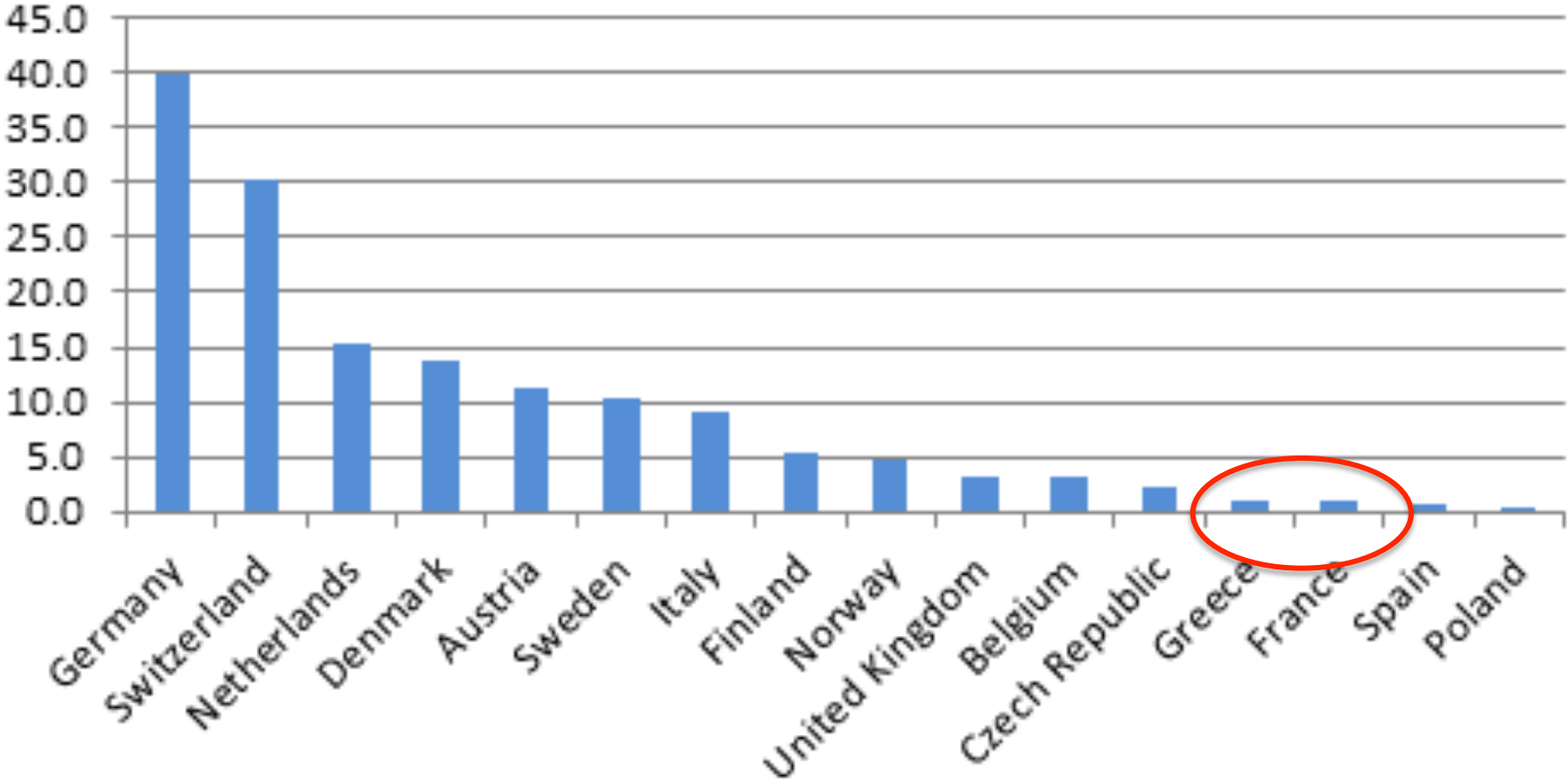
Percutaneous Tricuspid Valve Repair



When you do not Know : Randomize !

	COAPT	MITRA-FR
N patients, sites	430 @ 75 US sites	288 @ 22 French sites
Control arm	GDMT ± CRT	GDMT ± CRT
FMR grade	≥3+ (EROA ≥30 mm ² and/or Rvol >45 mL by ECL)	Severe (EROA >20 mm ² + Rvol >30 mL) by ECL
NYHA class	II, III, or ambulatory IV	II - 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; not eligible for MV surgery
LVEF	≥20% - ≤50%	≥15% - ≤40%
LV volumes	LVEDD ≤70 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	-
Total follow-up	5 years	2 years
PIs	GW Stone, M Mack	JF Obadia

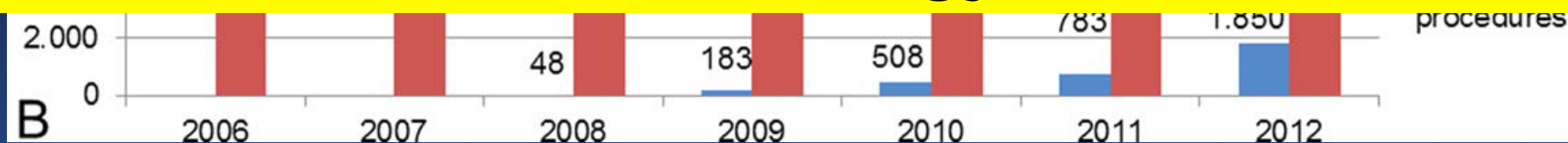
Variation in MitraClip Utilization/ Health Policy and Reimbursement



Evolution of Mitral valve Procedures in Germany in the Advent of Endovascular Treatment Options



A larger number of patients with MR will be treated by less invasive surgery or interventional cardiology



(Conradi L .Catheterization and cardiovascular Interventions 2015)



« The duty of any valvular surgeon today is no longer to correct a mitral valve regurgitation, but to correct a mitral valve regurgitation for the rest of the patient's life »

A .Carpentier



Merci

