Indications, evidence and future perspectives for secondary mitral regurgitation treatment

Claudio Moretti
Cardiologia Universitaria
Città della Salute edella Scienza di Torino

PubMed.gov
US National Library of Medicine
National Institutes of Health

PubMed

functional mitral regurgitation

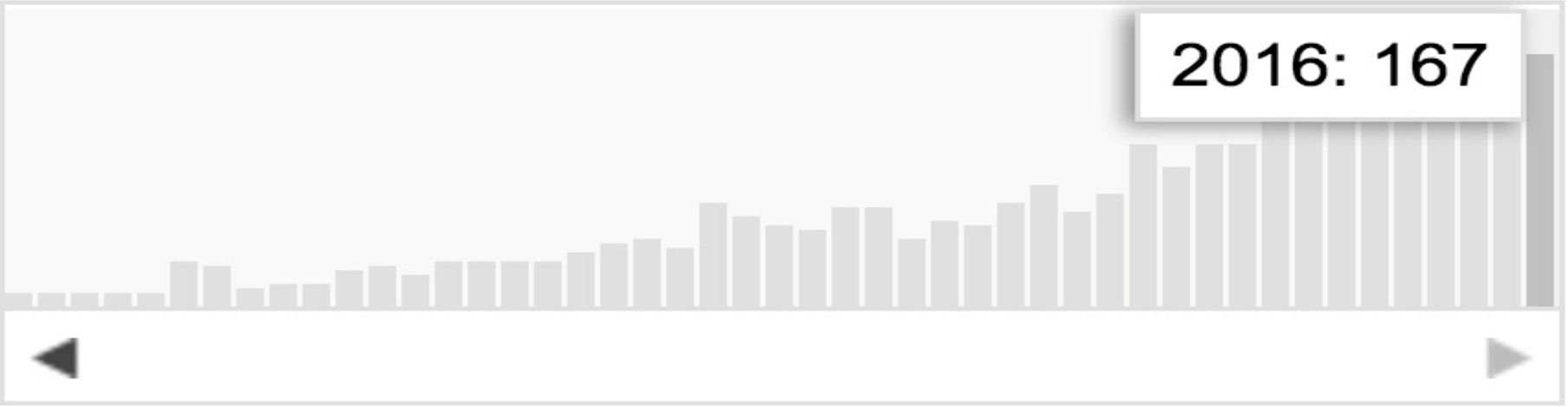
Create RSS Create alert Advanced

Search results

Items: 1 to 20 of 3109

<< First < Prev Page 1 of 156 Next > Last >>

Results by year



Download CSV

FUNCTIONAL MITRAL REGURGITATION
WHAT WE CAN AGREE ON

- FMR is primarily a disorder of the LV
- FMR is common
- FMR predicts increased mortality in a graded fashion
- Medical therapy is often effective

Functional mitral regurgitation: are we treating the real target?

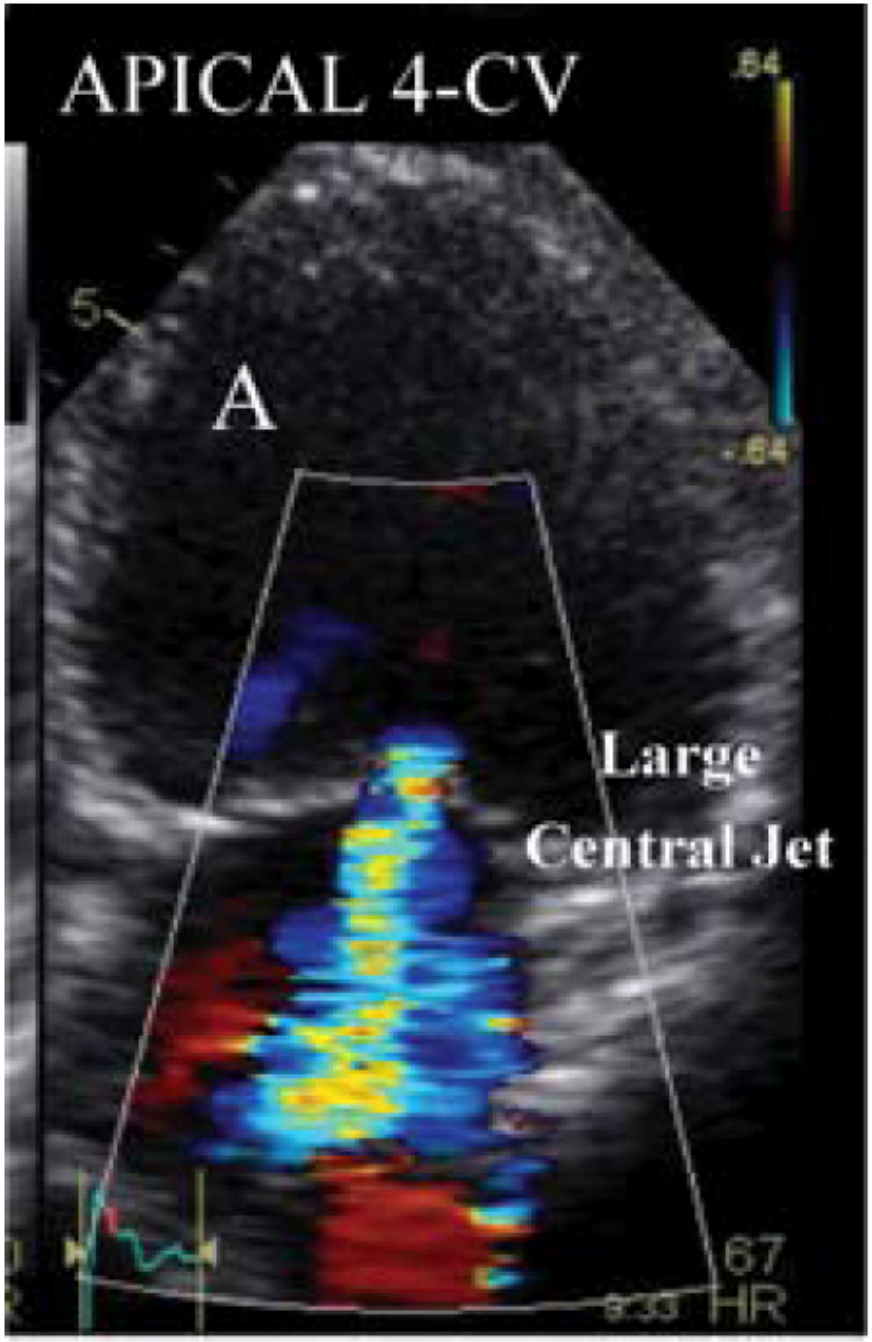
Giovanni Benfari[a], Rajesh Dandale[a], Andrea Rossi[a], Francesco Onorati[b], Giacomo Mugnai[a], Flavio Ribichini[a], Pier L. Temporelli[c] and Corrado Vassanelli[a]

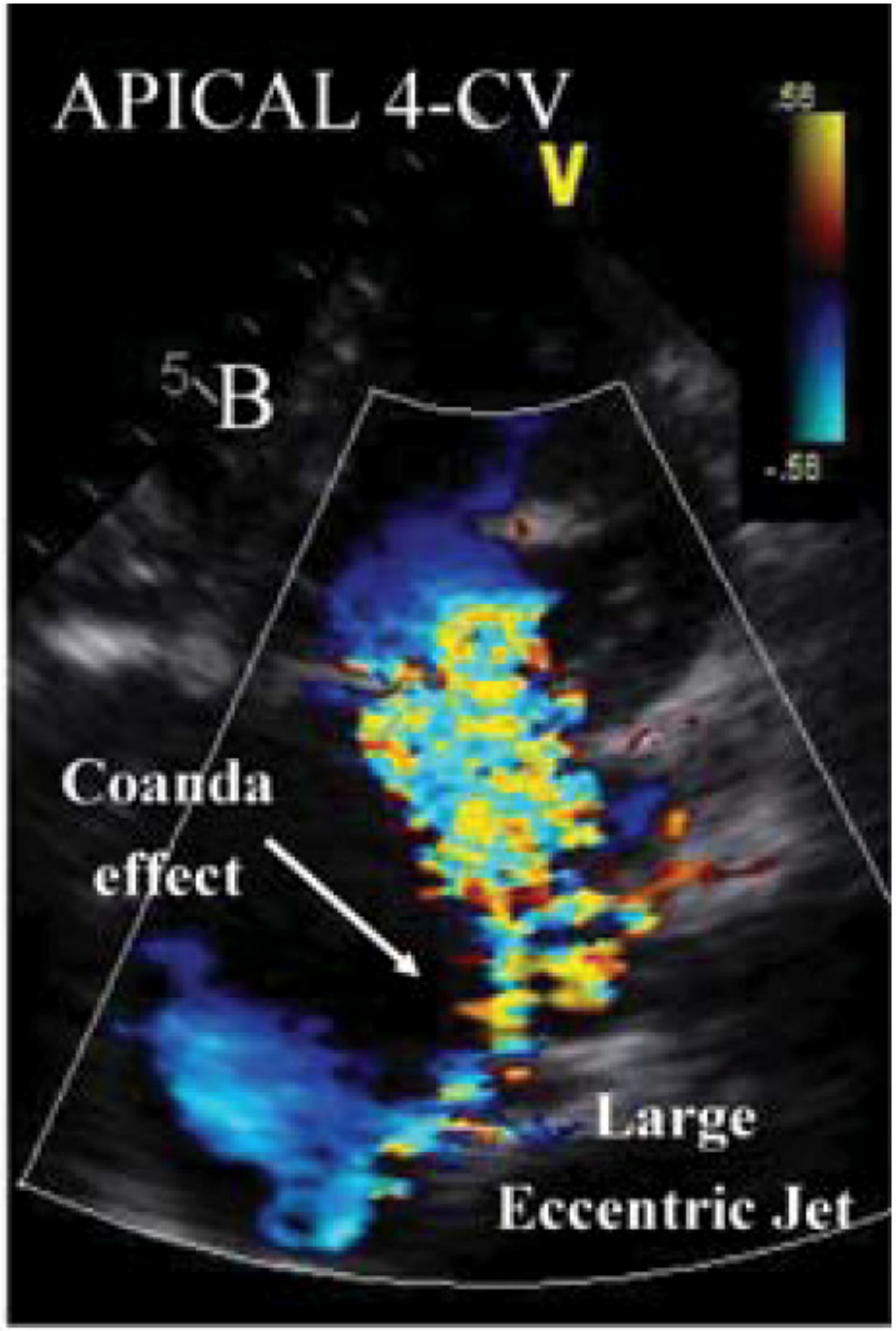
Table 1 Overview on the different prognostic relevance of functional mitral regurgitation as reported by literature

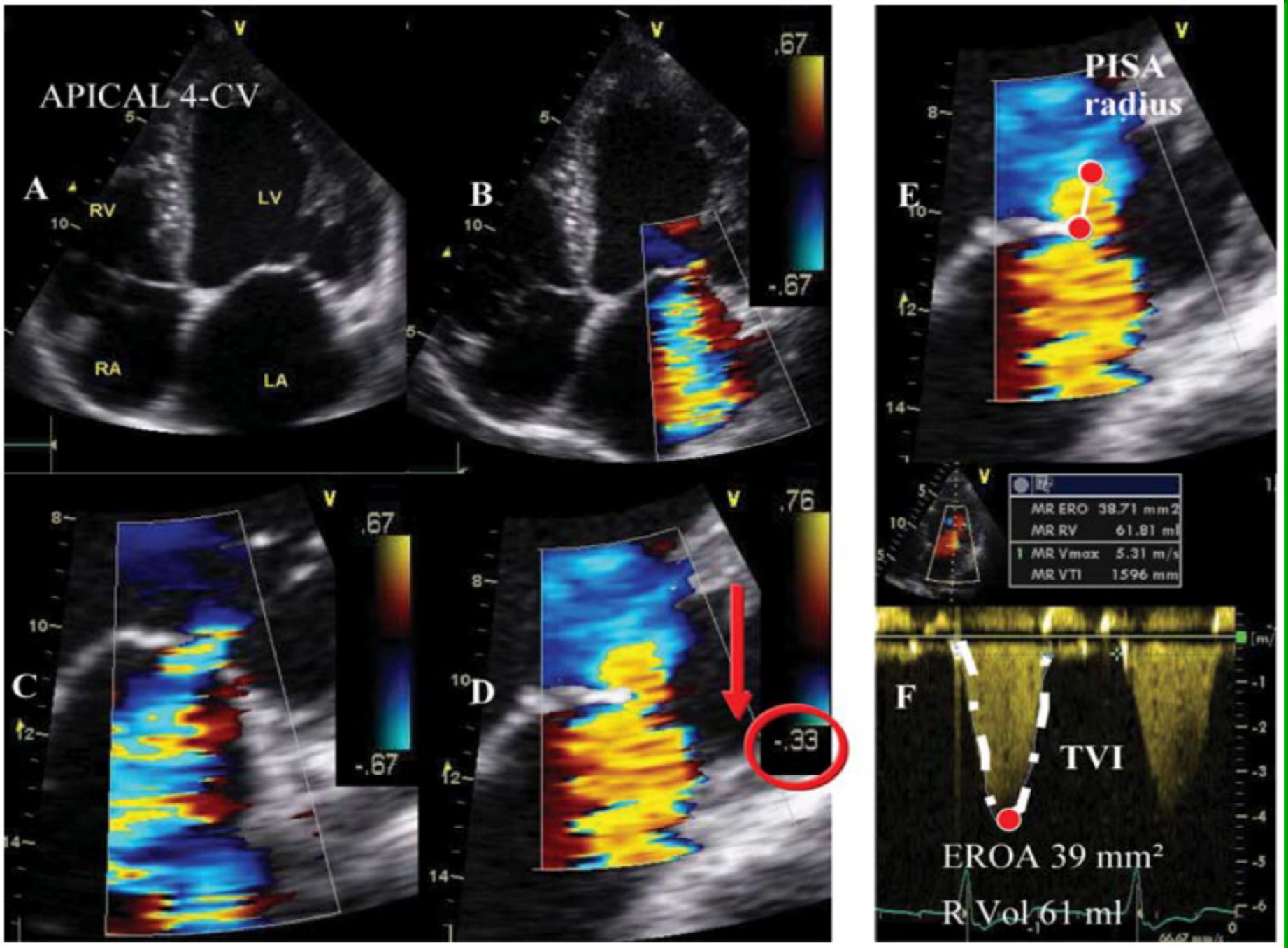
References	Patients (*n*)	Female (%)	Mean FU (days)	Age (years)	EF (%)	F-MR evaluation	F-MR-adjusted HR
Rossi *et al.*[19]	1256	22	985	67±11	32±8	PISA, VC	1.5 (1.1–2.1) *P*=0.009
Grigioni *et al.*[14]	303	27	1825	71±10	33±13	PISA	2.23 (1.31–3.7) *P*=0.003
Bruch *et al.*[24]	370	22	790	59±13	31±10	PISA, VC, Jet area	2.4 (1.4–4.1) *P*=0.001
Koelling *et al.*[25]	1421	32	365	63±14	20±5	Jet area	1.84 (1.42–2.38) *P*=0.006
Merlo *et al.*[26]	242	70	3300	43±13	31±10	Jet area	1.7 (1.02–2.83) *P*=0.04
Robbins *et al.*[20]	221	38	1470	64±15	27±9	Jet area	NS
Giannuzzi *et al.*[18]	508	11	870	59±9	26±5	Jet area	NS
Temporelli *et al.*[21]	144	18	780	57±9	22±6	Jet area	NS
Dini *et al.*[22]	207	29	660	71 (34–86)	32±8	Jet area	NS
Rihal *et al.*[23]	102	36	1050	61±14	23±8	Jet area	NS

EF, ejection fraction; F-MR, functional mitral regurgitation; FU, follow-up; HR, hazard ratio; PISA, proximal isovelocity surface area; VC, vena contracta.

J Cardiovasc Med 2016, 17:767–773


APICAL 4-CV
A
Large
Central Jet
67
HR


APICAL 4-CV
V
B
Coanda
effect
Large
Eccentric Jet


APICAL 4-CV
A
RV
LV
RA
LA
B
.67
-.67
C
.67
-.67
D
.76
-.33
E
PISA
radius
MR ERO 38.71 mm2
MR RV 61.81 ml
MR Vmax 5.31 m/s
MR VTI 1596 mm
F
TVI
EROA 39 mm²
R Vol 61 ml

Independent prognostic value of functional mitral regurgitation in patients with heart failure. A quantitative analysis of 1256 patients with ischaemic and non-ischaemic dilated cardiomyopathy

Andrea Rossi,[1] Frank L Dini,[2] Pompilio Faggiano,[3] Eustachio Agricola,[4] Mariantonietta Cicoira,[1] Silvia Frattini,[3] Anca Simioniuc,[2] Mariangela Gullace,[4] Stefano Ghio,[5] Maurice Enriquez-Sarano,[6] Pier Luigi Temporelli[7]

Table 1 Clinical and functional parameters of patients divided according to severity of functional mitral regurgitation (FMR)

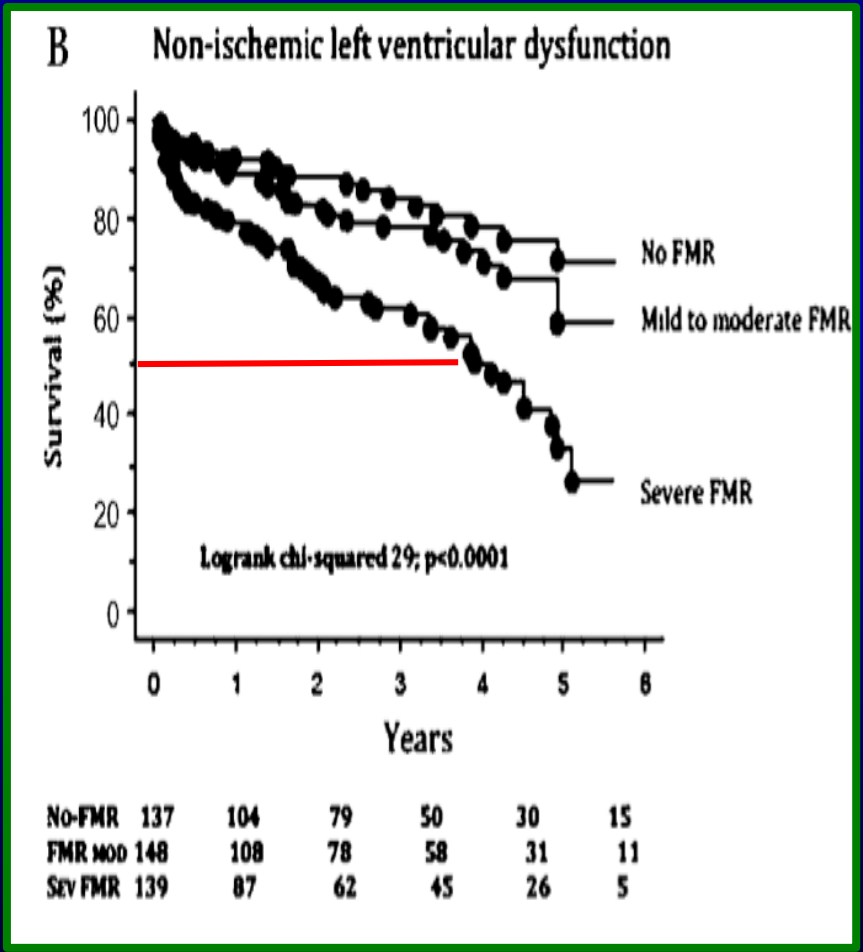
Parameters	No FMR	Mild to moderate FMR	Severe FMR	p Value
Age (years)	65±11	68±10	69±11	<0.0001
Female (%)	22	22	20	0.8
NYHA class	2.2±0.7	2.2±0.8	2.5±0.9	<0.0001
Ischaemic aetiology	51%	73%	49%	<0.0001
LVD (mm)	61±7	63±8	66±9	<0.0001
LVS (mm)	51±8	53±10	57±15	0.01
PWT (mm)	11±2	10±2	10±2	<0.0001
LVEF (%)	34±8	33±8	29±8	<0.0001
RMP (%)	20	30	62	<0.0001
DTE (ms)	177±53	174±69	140±73	<0.0001

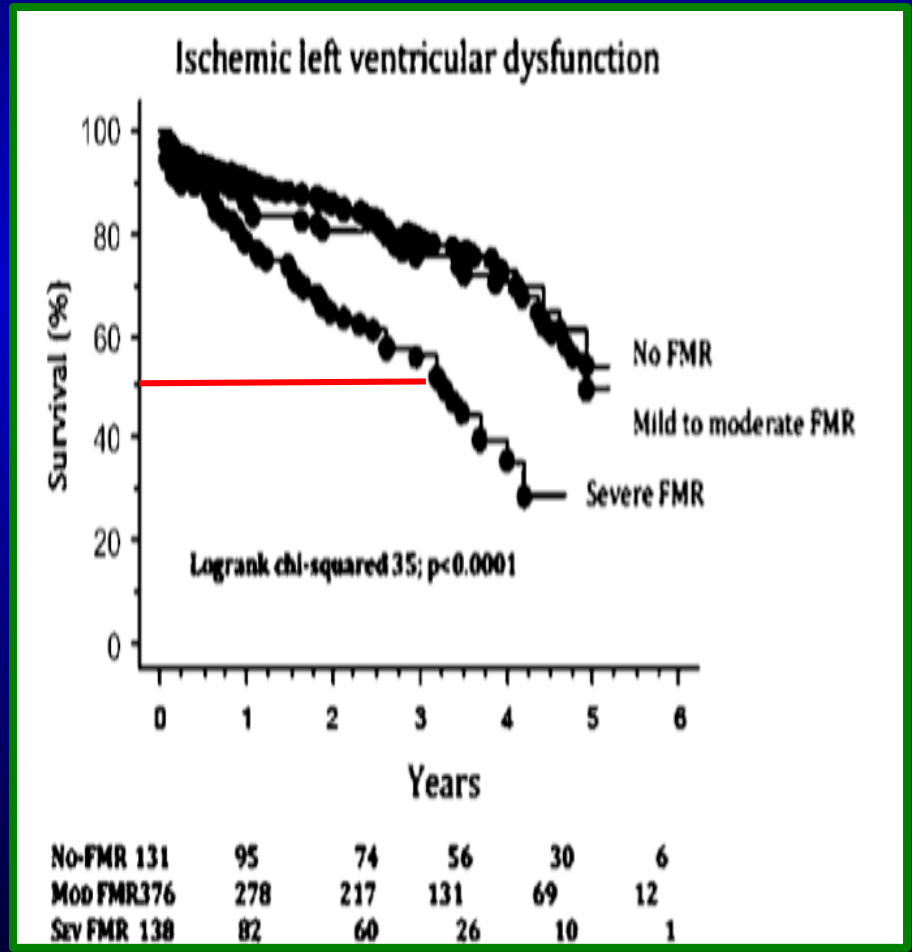
DTE, E-wave deceleration time; LVD, left ventricular diastolic diameter; LVEF, left ventricular ejection fraction; LVS, left ventricular systolic diameter; NYHA, N
PWT, posterior wall thickness; RMP, restrictive mitral filling pa

Heart 2011;**97**:1675–1680.

Independent prognostic value of functional mitral regurgitation in patients with heart failure. A quantitative analysis of 1256 patients with ischaemic and non-ischaemic dilated cardiomyopathy

Andrea Rossi,[1] Frank L Dini,[2] Pompilio Faggiano,[3] Eustachio Agricola,[4] Mariantonietta Cicoira,[1] Silvia Frattini,[3] Anca Simioniuc,[2] Mariangela Gullace,[4] Stefano Ghio,[5] Maurice Enriquez-Sarano,[6] Pier Luigi Temporelli[7]





Independent prognostic value of functional mitral regurgitation in patients with heart failure. A quantitative analysis of 1256 patients with ischaemic and non-ischaemic dilated cardiomyopathy

Andrea Rossi,[1] Frank L Dini,[2] Pompilio Faggiano,[3] Eustachio Agricola,[4] Mariantonietta Cicoira,[1] Silvia Frattini,[3] Anca Simioniuc,[2] Mariangela Gullace,[4] Stefano Ghio,[5] Maurice Enriquez-Sarano,[6] Pier Luigi Temporelli[7]

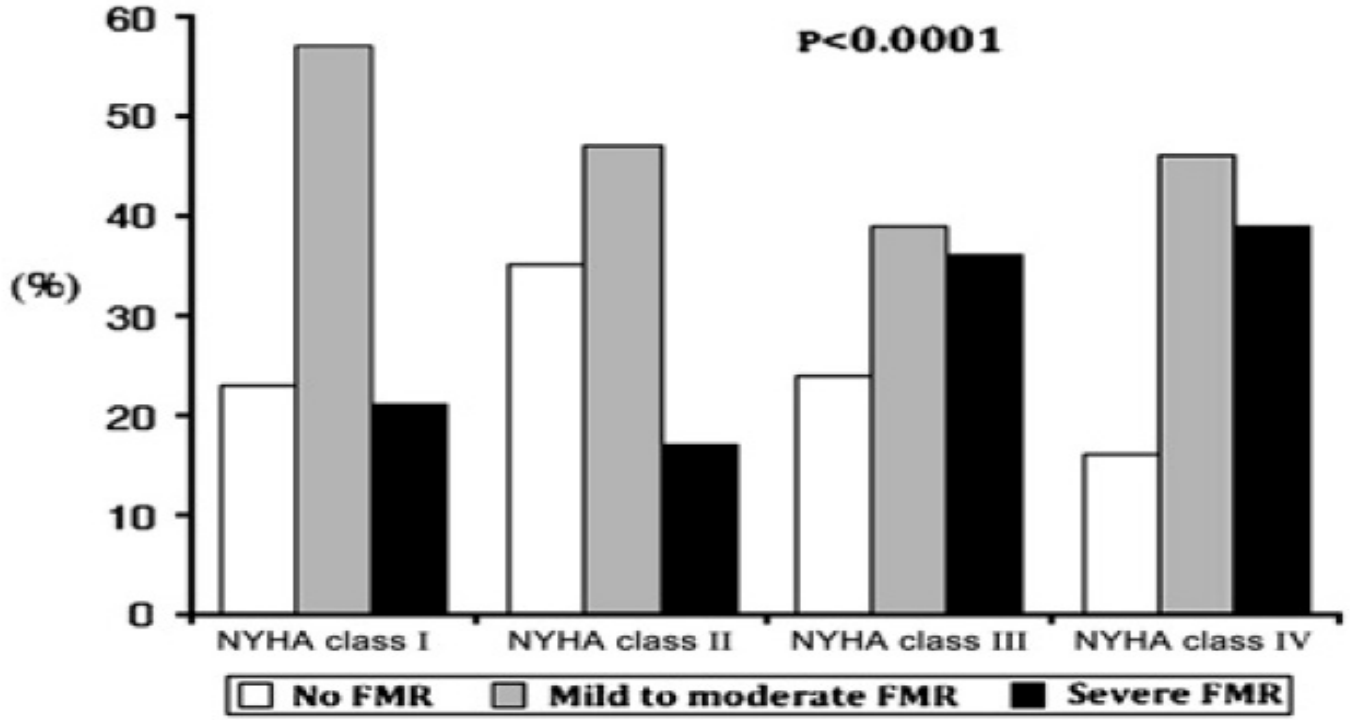
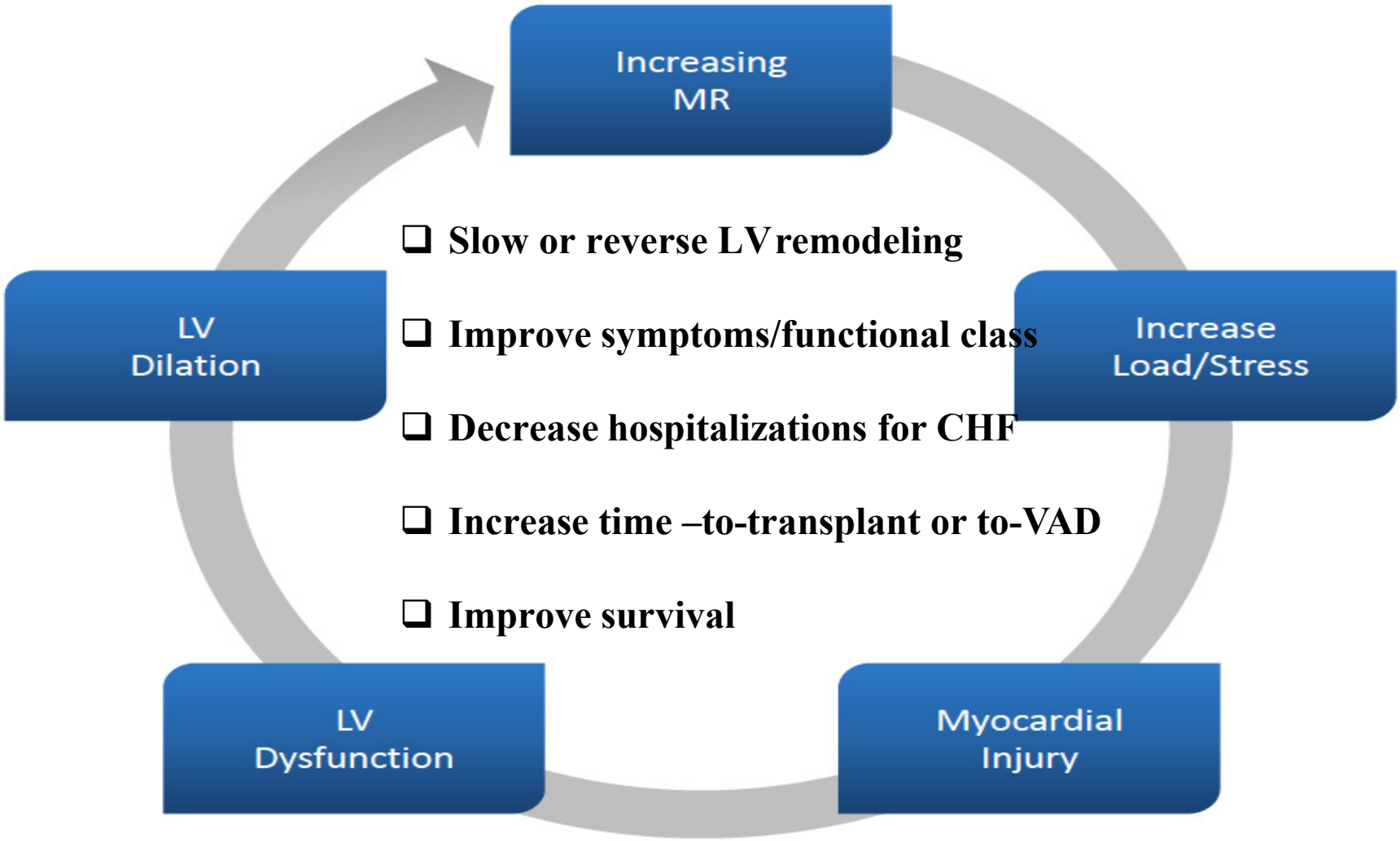


Figure 1 Prevalence of functional mitral regurgitation (FMR) according New York Heart Association class.

FUNCTIONAL MITRAL REGURGITATION
GOALS OF TREATMENT



- ❑ **Slow or reverse LV remodeling**
- ❑ **Improve symptoms/functional class**
- ❑ **Decrease hospitalizations for CHF**
- ❑ **Increase time –to-transplant or to-VAD**
- ❑ **Improve survival**

FUNCTIONAL MITRAL REGURGITATION THERAPEUTIC OPTIONS

After GDMT & Resynchronization when appropriate

- **PCI / CABG ?**
- **UNDERSIZED SURGICAL ANNULOPLASTY ?**
- **MITRAL VALVE REPLACEMENT ?**
- **PERCUTANEOUS TECHNIQUE ?**

SMMART-HF trial (Effectiveness of Surgical Mitral Valve Repair Versus Medical Treatment for People With Significant Mitral Regurgitation and Non-ischemic Congestive Heart Failure)

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

Effectiveness of Surgical Mitral Valve Repair Versus Medical Treatment for People With Significant Mitral Regurgitation and Non-ischemic Congestive Heart Failure (SMMART-HF)

This study has been terminated.

(Unable to recruit sufficient numbers of patients.)

Sponsor:
Duke University

Collaborators:
National Heart, Lung, and Blood Institute (NHLBI)
Heart Failure Clinical Research Network

Information provided by (Responsible Party):
Duke University

ClinicalTrials.gov Identifier:
NCT00608140

First received: January 24, 2008
Last updated: July 9, 2014
Last verified: July 2013
History of Changes

	1 Medical Therapy Plus Surgical Repair	2 Medical Therapy Only	Total
Number of Participants [units: participants]	1	1	2
Age [units: participants]			
<=18 years	0	0	0
Between 18 and 65 years	0	1	1
>=65 years	1	0	1
Age [1] [units: years] Mean (Standard Deviation)	65.5	63	64.25 (1.49)
Gender [units: participants]			
Female	0	1	1
Male	1	0	1
Region of Enrollment [units: participants]			
United States	1	1	2

FMR: RESULTS OF SURGERY

Trichon 2003 (R_adj)
2757 pts
PCI – 31%
CABG -42%
CABG+MV surgery (-42%)
NO BENEFIT of MV_S
vs CABG)
Angio!!

Bolling 2005 (R)
Annuloplasty
126 pts / EF 23%
NO BENEFIT

Castleberry 2014 (R)
4989 pts / EF 45%
NO BENEFIT of MV_S
vs CABG
Echo

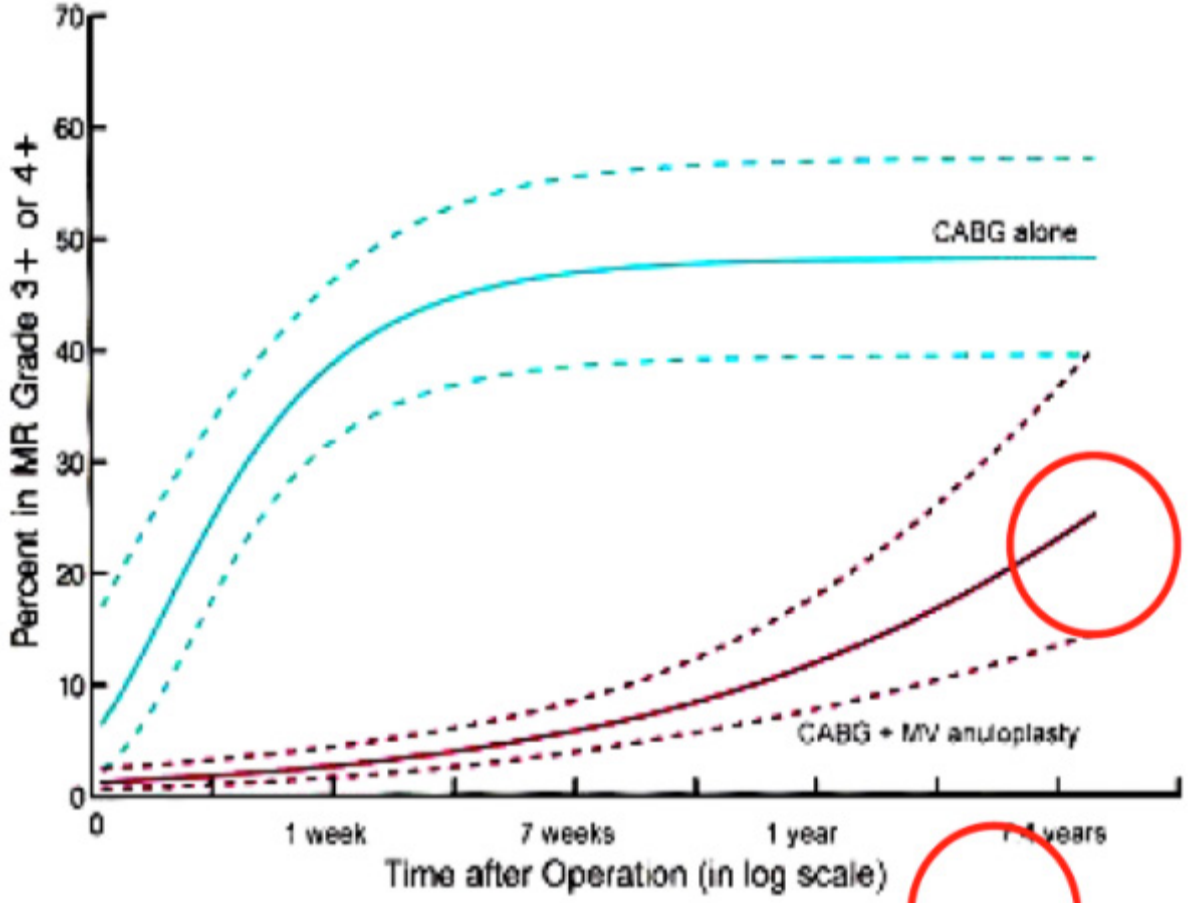
RIME 2012 (RCT)
73pts / EF >30%
CABG+MVR better
(MV02)

CTSN 2012 (RCT)
301pts / EF >40%
NO BENEFIT of MV_S
vs CABG
(LV remod.)

FUNCTIONAL MITRAL REGURGITATION
WHAT WE CAN AGREE ON

- Surgery can reduce FMR acutely
- Some pts get clear improvement in HF symptoms after surgery
- NO mortality benefit has been shown to result from surgery

Recurrence of Severe MR after CABG ± Annuloplasty



- Recurrent severe MR lower with annuloplasty, but still 20% at 5 years

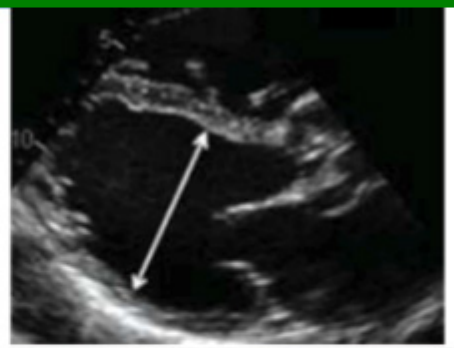
Mihaljevic et al, JACC 2007;49:2191

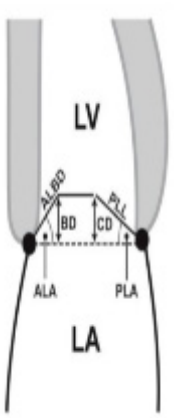
Predictors of Recurrent MR After MVA

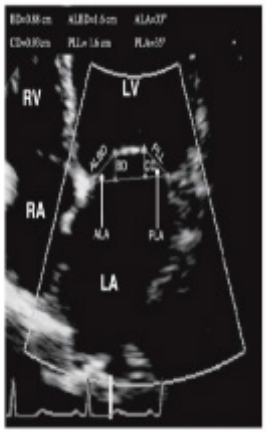
No or Mild annular dilatation
Coaptation depth >1 cm
Posterior leaflet angle >45°
Distal anterior leaflet angle >25°

Advanced LV remodelling

- LVEDD > 65 mm
- Systolic sphericity index > 0.7
- End systolic interpapillary muscle distance >20 mm
- LVESV ≥ 145 ml (or ≥ 100 ml/m2)







The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Mitral-Valve Repair versus Replacement for Severe Ischemic Mitral Regurgitation

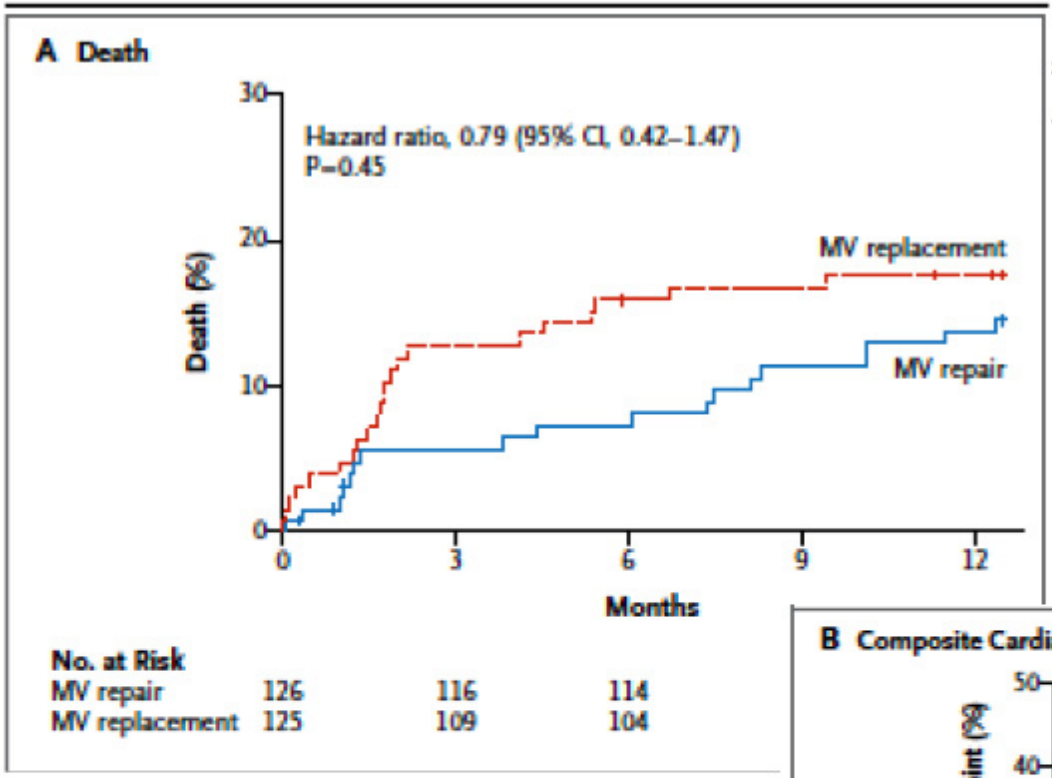
Michael A. Acker, M.D., Michael K. Parides, Ph.D., Louis P. Perrault, M.D., Alan J. Moskowitz, M.D., Annetine C. Gelijns, Ph.D., Pierre Voisine, M.D., Peter K. Smith, M.D., Judy W. Hung, M.D., Eugene H. Blackstone, M.D., John D. Puskas, M.D., Michael Argenziano, M.D., James S. Gammie, M.D., Michael Mack, M.D., Deborah D. Ascheim, M.D., Emilia Bagiella, Ph.D., Ellen G. Moquete, R.N., T. Bruce Ferguson, M.D., Keith A. Horvath, M.D., Nancy L. Geller, Ph.D., Marissa A. Miller, D.V.M., Y. Joseph Woo, M.D., David A. D'Alessandro, M.D., Gorav Ailawadi, M.D., Francois Dagenais, M.D., Timothy J. Gardner, M.D., Patrick T. O'Gara, M.D., Robert E. Michler, M.D., and Irving L. Kron, M.D., for the CTSN*

November 18, 2013, at NEJM.org.

CONCLUSIONS

We observed no significant difference in left ventricular reverse remodeling or survival at 12 months between patients who underwent mitral-valve repair and those who underwent mitral-valve replacement. Replacement provided a more durable correction of mitral regurgitation, but there was no significant between-group difference in clinical outcomes. (Funded by the National Institutes of Health and the Canadian Institutes of Health; ClinicalTrials.gov number, NCT00807040.)

The NEW ENGLAND JOURNAL of MEDICINE

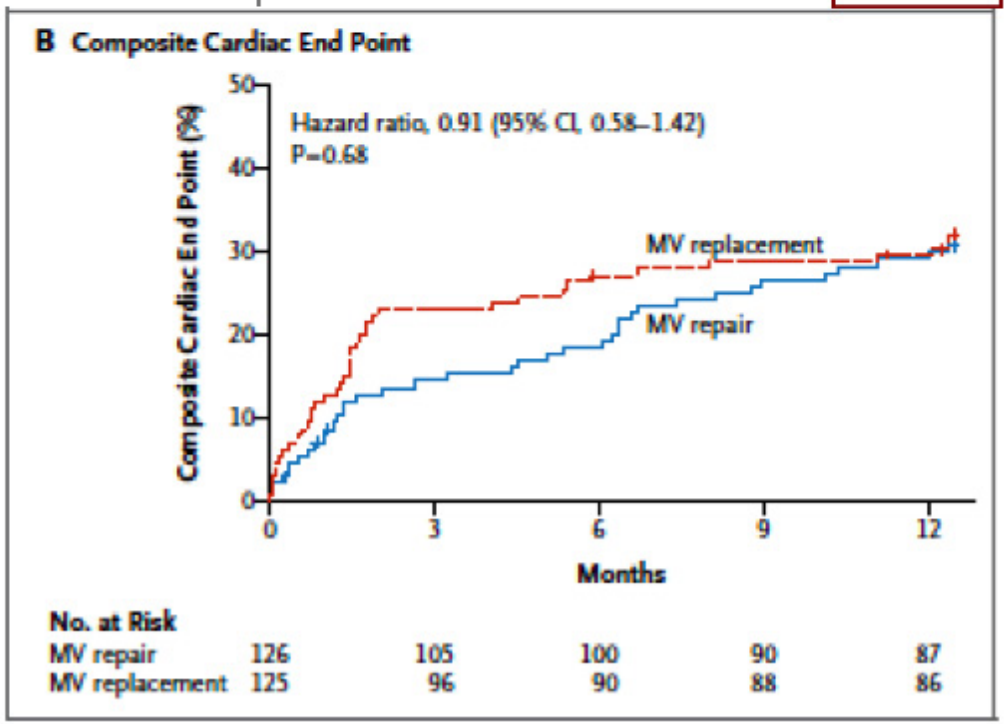


ORIGINAL ARTICLE

Mitral-Valve Repair versus Replacement for Severe Ischemic Mitral Regurgitation

Michael A. Acker, M.D., Michael K. Parides, Ph.D., Louis P. Perrault, M.D., Alan J. Moskowitz, M.D., Annetine C. Gelijns, Ph.D., Pierre Voisine, M.D., Peter K. Smith, M.D., Judy W. Hung, M.D., Eugene H. Blackstone, M.D., John D. Puskas, M.D., Michael Argenziano, M.D., James S. Gammie, M.D., Michael Mack, M.D., Deborah D. Ascheim, M.D., Emilia Bagiella, Ph.D., Ellen G. Moquete, R.N., T. Bruce Ferguson, M.D., Keith A. Horvath, M.D., Nancy L. Geller, Ph.D., Marissa A. Miller, D.V.M., Y. Joseph Woo, M.D., David A. D'Alessandro, M.D., Gorav Ailawadi, M.D., Francois Dagenais, M.D., Timothy J. Gardner, M.D., Patrick T. O'Gara, M.D., Robert E. Michler, M.D., and Irving L. Kron, M.D., for the CTSN*

N=251



30-d deaths 2 vs 5

<u>12-m mod-to-severe MR 32,6 vs 2,3 %</u>

12-m NO difference in MACE

SURGERY: results

are these our benchmarks ?

	EACTS (2010)	STS (2010)	UK (2004–2008)	Germany (2009)
Aortic valve replacement, no CABG (%)	2.9 (40 662)	3.7 (25 515)	2.8 (17 636)	2.9 (11 981)
Aortic valve replacement + CABG (%)	5.5 (24 890)	4.5 (18 227)	5.3 (12 491)	6.1 (9113)
Mitral valve repair, no CABG (%)	2.1 (3231)	1.6 (7293)	2 (3283)	2 (3335)
Mitral valve replacement, no CABG (%)	4.3 (6838)	6.0 (5448)	6.1 (3614)	7.8 (1855)
Mitral valve repair/replacement +CABG (%)	6.8/11.4 (2515/1612)	4.6/11.1 (4721/2427)	8.3/11.1 (2021/1337)	6.5/14.5 (1785/837)

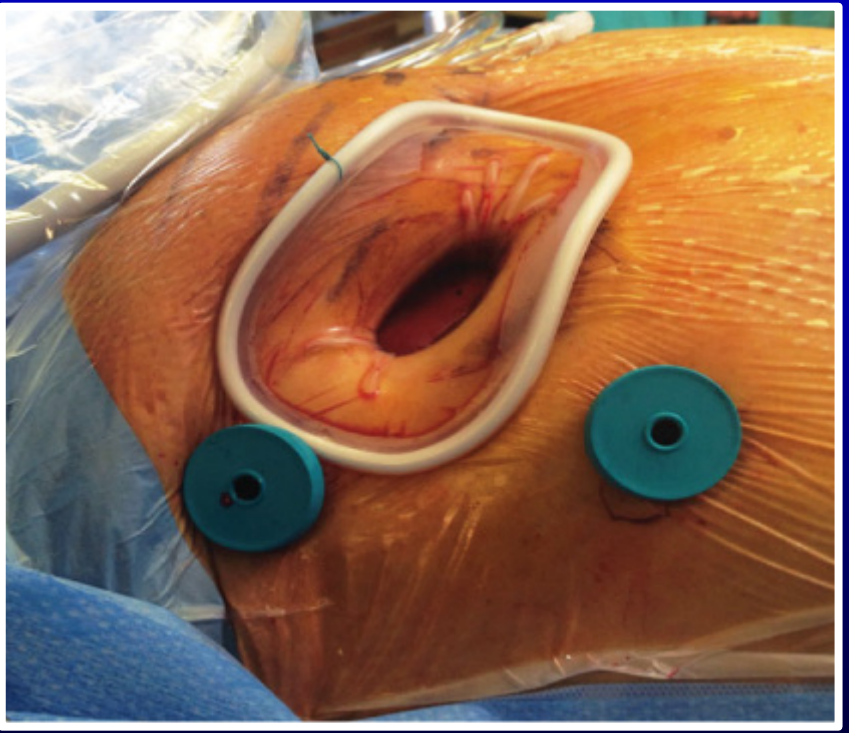
Guidelines on the management of valvular heart disease (version 2012)

SEVERE PRIMARY MITRAL REGURGITATION
SURGERY IS A NEVER ENDING STORY…

Minimally invasive MV surgical approach
Right mini thoracotomy / lower ministernotomy

LESS SURGICAL TRAUMA
LESS BLEEDING
LESS STERNAL WOUND INFECTION
LESS POST-OP PAIN
BETTER RESPIRATORY FUNCTION
BETTER COSMESIS
FASTER RECOVERY

with the same quality, safety, efficacy.



Mitral valve pathology in severely impaired left ventricles can be successfully managed using a right-sided minimally invasive surgical approach†

Jens Garbade*, Joerg Seeburger, Denis R. Merk, Bettina Pfannmüller, Marcel Vollroth, Markus J. Barten, Michael A. Borger and Friedrich-Wilhelm Mohr

Department of Cardiac Surgery, Heart Center, University of Leipzig, Leipzig, Germany

European Journal of Cardio-Thoracic Surgery 44 (2013)

Table 1: Baseline clinical characteristics in patients undergoing Mini-MV with an LVEF < 30%

Variable	Mini-MV *n* = 177 patients
Study period	1999–2010
Demographics	
Age (years)	67 ± 11
Sex (male)	110 (63%)
Weight (kg)	75.3 ± 13.3
BMI	25.8 ± 3.6
LVEF (%)	23.9 ± 5.8
LVEDD (mm)	69 ± 11
NYHA class	3.1 ± 0.8
Comorbidities	
Previous cardiac surgery	32 (18.3%)
Primary ICM	22 (12.4%)
Primary DCM	155 (87.6%)
COPD	9 (5.4%)
Renal insufficiency	45 (25%)
Stroke	2 (1.1%)
Hypertention	35 (19.8%)
Diabetes	51 (28.8%)
EuroSCORE (%)	14.7 ± 13.6
Indication for surgery	
MV insufficiency	172 (97.2%)
MV stenosis/insufficiency	5 (2.8%)
Concomitant indications	
TV insufficiency	27 (15.4%)
Atrial fibrillation	61 (34.5%)
ASD/PFO	10 (5.6%)

Mitral valve pathology in severely impaired left ventricles can be successfully managed using a right-sided minimally invasive surgical approach†

Jens Garbade*, Joerg Seeburger, Denis R. Merk, Bettina Pfannmüller, Marcel Vollroth, Markus J. Barten, Michael A. Borger and Friedrich-Wilhelm Mohr

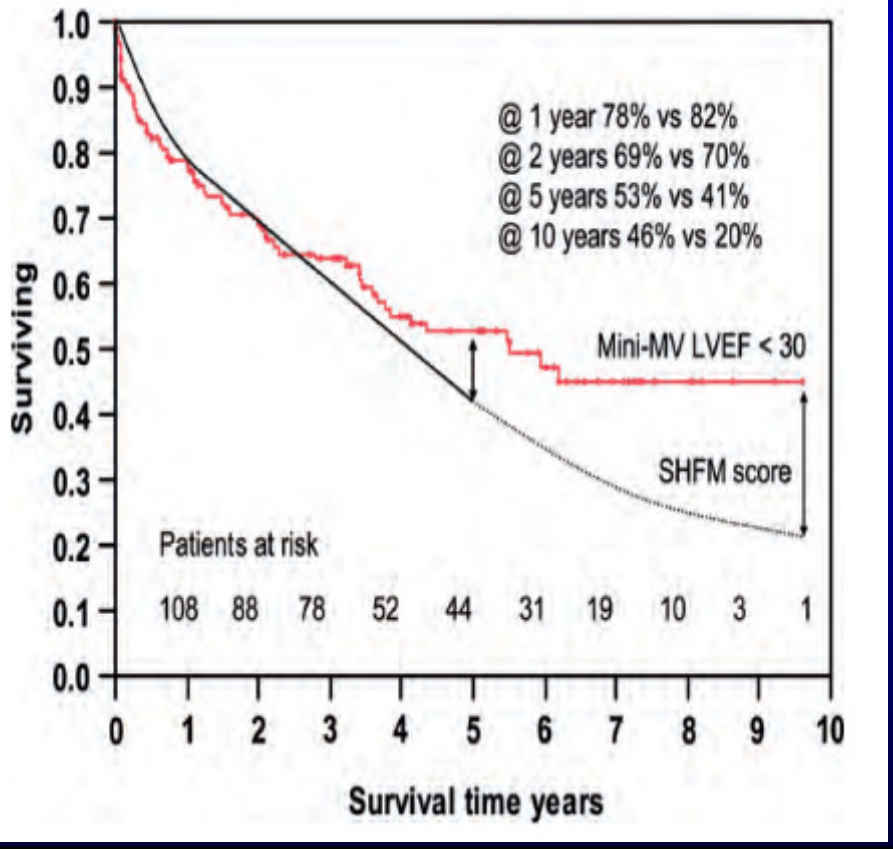
Department of Cardiac Surgery, Heart Center, University of Leipzig, Leipzig, Germany

European Journal of Cardio-Thoracic Surgery 44 (2013)

Table 4: Outcomes, complications and reinterventions in patients undergoing Mini-MV with LVEF < 30%

Variable	Mini-MV $n = 177$
Early postoperative course	
30-day mortality	14 (7.9%)
Inotropic support	132 (74%)
Low cardiac output syndrome requiring mechanical circulatory support	15 (8.5%)
IABP	9 (5%)
ECMO	6 (3.8%)
Bleeding, requiring surgery within 24 h	12 (6.9%)
Sepsis	14 (7.9%)
Acute renal failure/haemodialysis	12 (6.7%)
Respiratory failure	7 (4.0%)
CVE (transient or persistent)	4 (2.7%)
Intensive care time > 24 h	129 (72.8%)
Hospital stay (days)	17 ± 12
Long-term follow-up	
Heart transplantation	10 (5.7%) 3–47 months after Mini-MV
LVAD implantation	3 (1.7%) 4–8 months after Mini-MV
Reoperation on MV during the follow-up	7 (4.0%)

IABP: intra-aortic ballon pump; ECMO: extracorporeal membrane oxygenation; CVE: cerebrovascular event; LVAD: left ventricular assist device.



Indications for mitral valve surgery in secondary mitral regurgitation

	Class	Level
Surgery is indicated in patients with severe MR undergoing CABG, and LVEF > 30%.	I	C
Surgery should be considered in patients with moderate MR undergoing CABG (Exercise echo is recommended to identify dyspnea, increase in severity of MR and in SPAP).	IIa	C
Surgery should be considered in symptomatic patients with severe MR, LVEF < 30%, option for revascularization, and evidence of viability.	IIa	C
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

Management and outcomes in patients with moderate or severe functional mitral regurgitation and severe left ventricular dysfunction

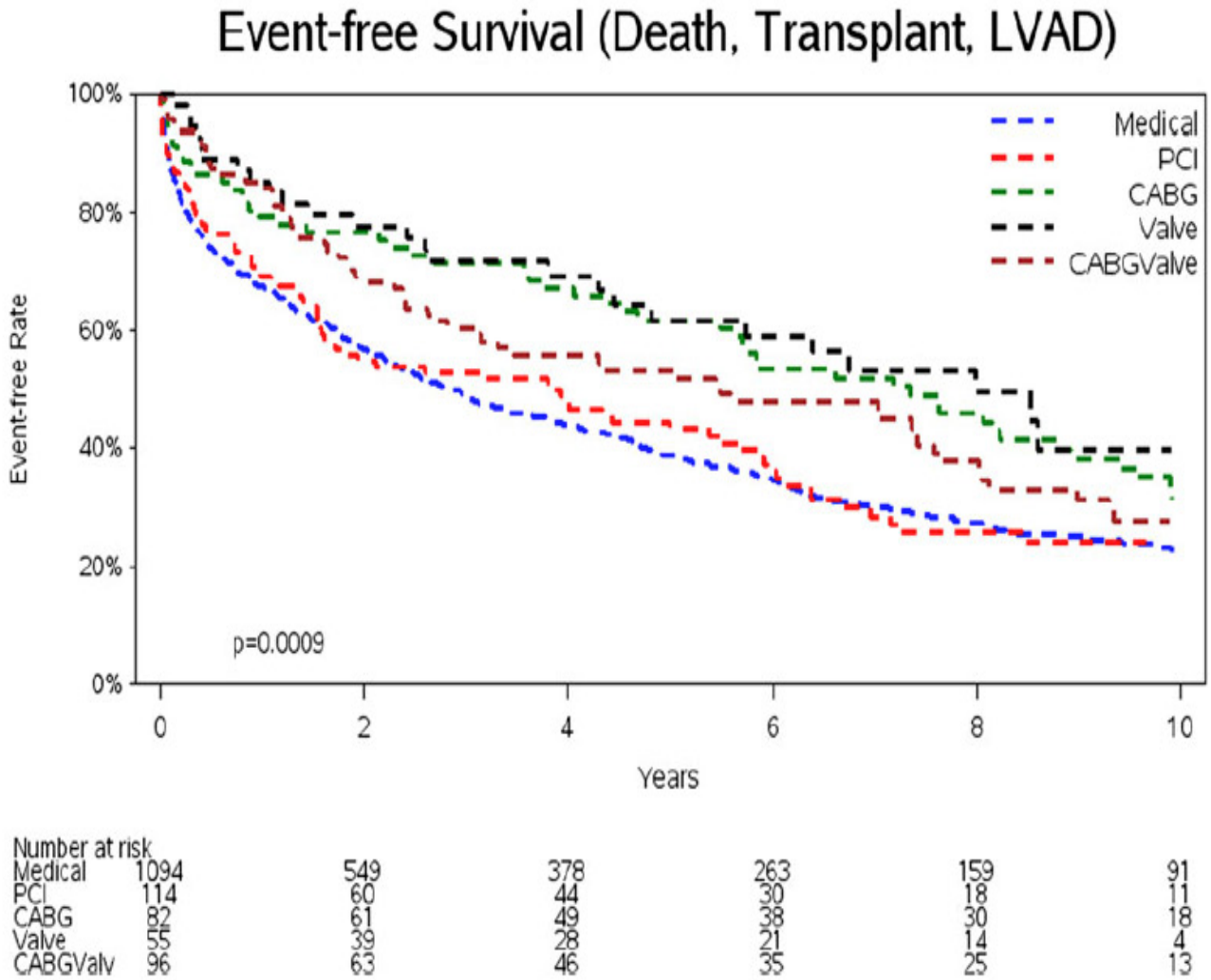
Samad Z, et al. European H J 2015

Table I Patients with moderate or severe functional MR and severe LV dysfunction stratified by treatment strategies

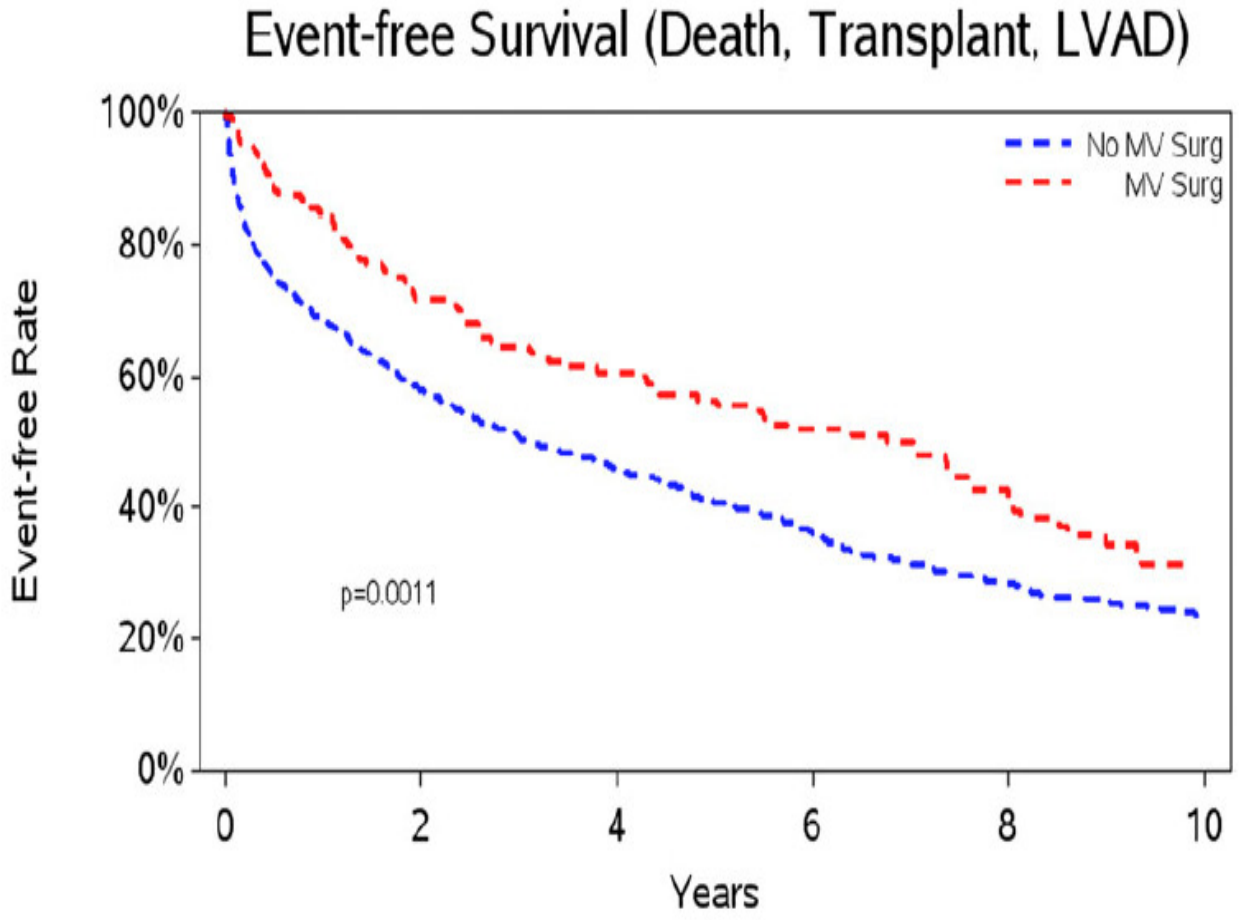
Characteristic	Medical (*n* = 1094)	PCI (*n* = 114)	CABG surgery (*n* = 82)	MV surgery (*n* = 55)	CABG + MV surgery (*n* = 96)	*P*-value
MR severity						<0.001
Moderate	764 (70%)	95 (83%)	73 (89%)	24 (44%)	54 (56%)	
Severe	330 (30%)	19 (17%)	9 (11%)	31 (56%)	42 (44%)	
EF, median, %	20	25	25	25	25	<0.001
LVIDd, median, cm	6.2	5.9	5.9	6.5	6.0	<0.001
LVIDs, median, cm	5.5	5.0	4.9	5.6	5.1	<0.001
Estimated RVSP, median, mmHg,	47 (39, 55)	46 (40, 55)	43 (36, 50)	45 (35, 56)	48 (40, 60)	0.071
Age, median, years	62	69	68	60	68	<0.001
Female	428 (39%)	45 (40%)	27 (33%)	24 (44%)	41 (43%)	0.679
Caucasian	616 (58%)	81 (71%)	57 (73%)	29 (54%)	65 (69%)	0.001
History of revascularization	293 (27%)	54 (47%)			17 (18%)	<0.001
Hypertension	637 (58%)	82 (72%)			63 (66%)	0.006
Diabetes	299 (27%)	40 (35%)			29 (30%)	0.042
Significant CAD	456 (55%)	114 (96%			96 (100%)	<0.001
NYHA III/IV	935 (86%)	87 (77%)			72 (76%)	<0.001
Renal disease	36 (3%)	6 (5%)			4 (4%)	0.730
COPD	83 (8%)	13 (11%)			3 (3%)	0.260
History of cerebrovascular disease	117 (11%)	14 (12%)			8 (8%)	0.800
History of PVD	87 (8%)	13 (11%)			17 (18%)	0.016
Atrial fibrillation	476 (44%)	56 (49%)	36 (44%)	30 (55%)	60 (63%)	0.004
History of ICD/BiV	61 (6%)	3 (3%)	0 (0%)	2 (4%)	3 (3%)	0.092

DUKE Databank
1995-2010
1441 pts /Fup 4,7yrs
EF<30% or
LVESD > 55 mm

Unadjusted K-M event free survival across treatment groups



K-M event free survival stratified by MV surgery



Number at risk						
No MV Surg	1290	670	471	331	207	120
MV Surg	151	102	74	56	39	17

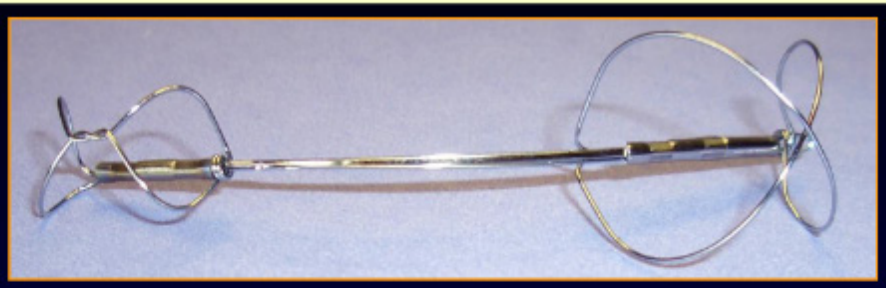
Take home messages_1

- The majority of pts are managed medically
- This strategy is associated with poor survival
- Pts selected for MV surgery have higher event-free-survival
- Surgical repair has a high recurrence rate

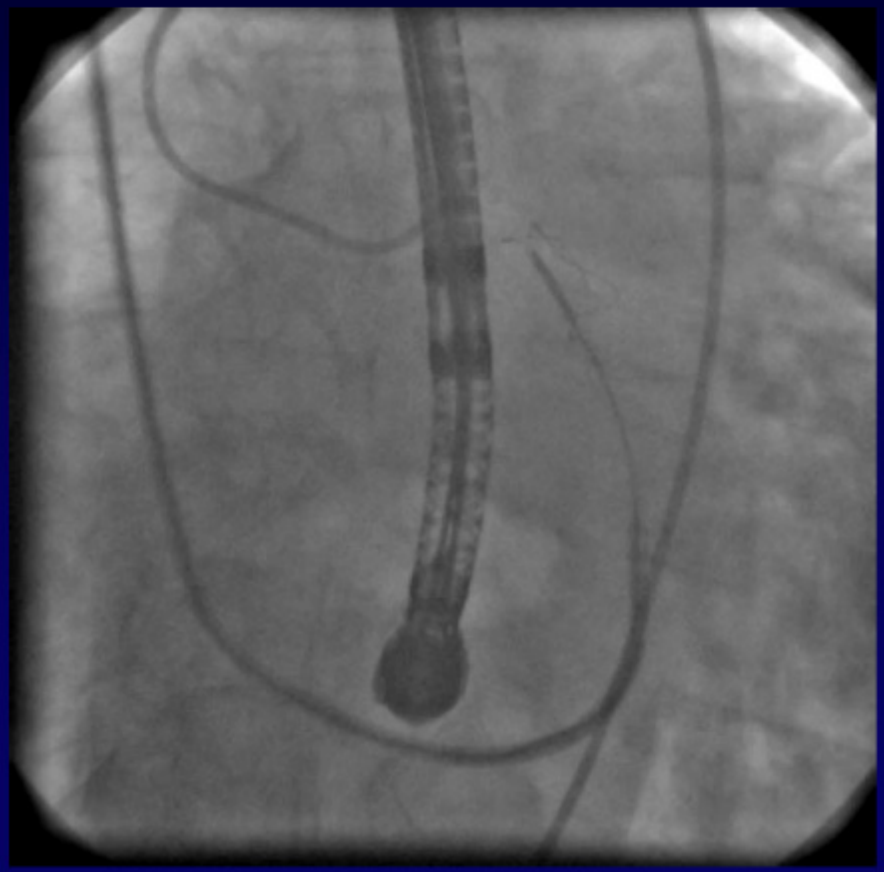
Can a less invasive therapy than surgery improve symptoms better than Medical TX ?

ANATOMIC TARGET	DEVICE NAME	MANUFACTURER	STATUS
LEAFLET / CHORDAL	MitraClip	Abbott Vascular (IL)	CE Mark, FDA approved
	NeoChord	NeoChord (MN)	Phase 1 (OUS)
	Mitra-Spacer	Cardiosolutions (MA)	Phase 1 (OUS)
	MitraFlex	TransCardiac Ther (GA)	Preclinical
	Middle Peak Medical	Middle Peak Med (CA)	Preclinical
	V-Chordal	Valtech (Israel)	Preclinical
INDIRECT ANNULOPLASTY	Carillon XE2	Cardiac Dimensions (CA)	CE Mark
	Kardium MR	Kardium (Canada)	Preclinical
	Cerclage	NHLBI (MD)	Preclinical
DIRECT/LV ANNULOPLASTY	Perc Annulo System	Mitralign (MA)	Phase 1 (OUS)
	Accucinch	GDS (CA)	Phase 1 (OUS)
	Boa RF	QuantumCor (CA)	Preclinical
	Cardioband	Valtech (Israel)	Phase 1 (OUS)
	Tasra	MitraSpan (MA)	Preclinical
	Millipede	Millipede (TX)	Preclinical
HYBRID SURGICAL	Adjustable Ring	St Jude Med (MN)	CE Mark
	enCor Dynaplasty	MiCardia (CA)	CE Mark
	Cardinal	Valtech (Israel)	CE Mark, Phase 1 (US)
LV REMODELING	Basal annuloplasty	Mardil (MN)	Phase 1
	Tendyne	Tendyne (MD)	Preclinical
	Parachute	CardioKinetix (CA)	CE Mark, Phase III (US)

Cardiac Dimensions CARILLON Device



- Implantable device
  - Permanently placed into the coronary sinus
  - Reduces annulus by traction
  - Restores valve leaflet closure
- Status
  - 3 European Trials for safety and efficacy resulted in CE Mark (Amadeus, TITAN, TITAN II)
  - 2 Novel trials (Reduce FMR and Clinch) now enrolling



CARILLON Studies – 30-Day Safety

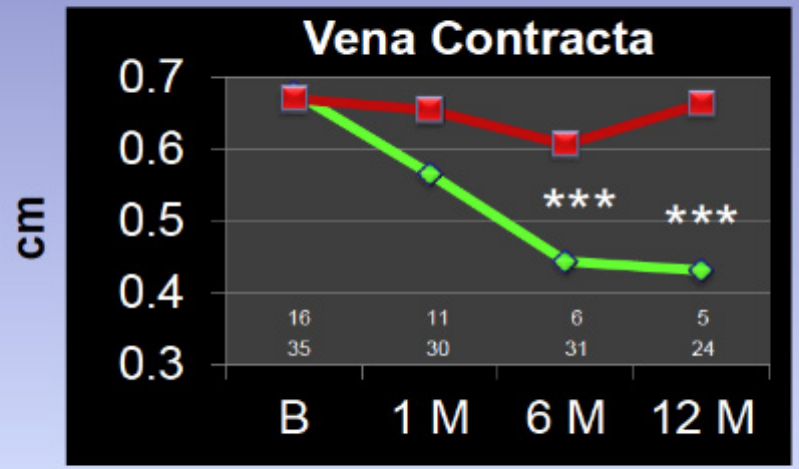
Event	AMADEUS (final data) MAE Incidence (intent-to treat population)		TITAN (final data) MAE Incidence (intent-to treat population)		TITAN II (final data) MAE Incidence (intent-to treat population)	
	30-Day Rate	Device Related	30-Day Rate	Device Related	30-Day Rate	Device Related
Death	2.2% (1/46)	0%	2.8% (1/36)	0%	2.8% (1/36)	0%
MI	6.5% (3/46)	0%	0.0% (0/36)	0%	0.0% (0/36)	0%
Cardiac Perforation	6.5% (3/46)	0%	0.0% (0/36)	0%	0.0% (0/36)	0%
Device Embolization	0.0% (0/53)	0%	0.0% (0/36)	0%	0.0% (0/36)	0%
Surgery or PCI Related to the Device	0.0% (0/53)	0%	0.0% (0/36)	0%	0.0% (0/36)	0%
MAE Rate	13.0%	0%	2.8%	0%	2.8%	0%

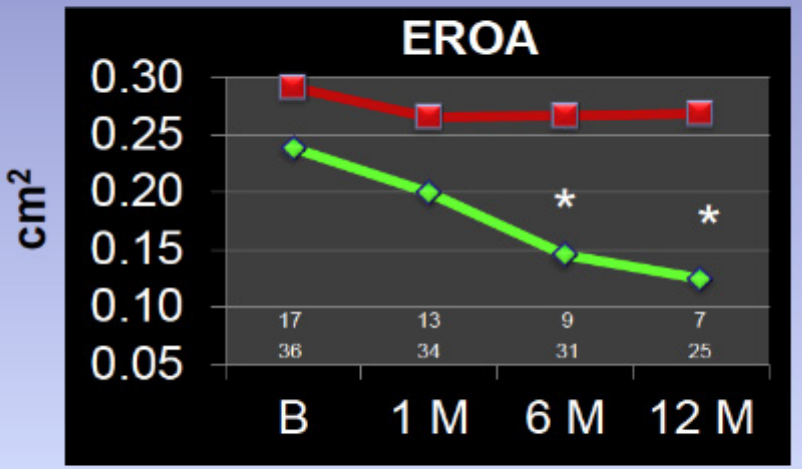
MitraClip 30 DAY Mortality
in HRR: 7.7%
In Franzen: 6%
TRAMI registry: 5.7%

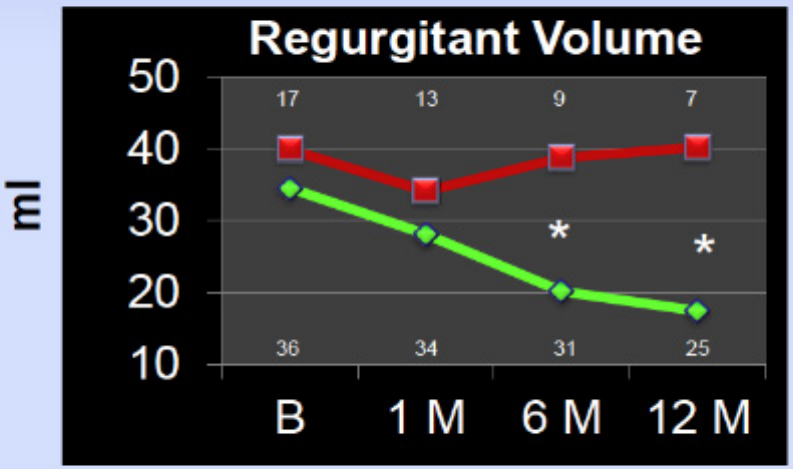
Schofer J, Siminiak T, Haude M, et al. Circulation, 2009; 120: 326-333.
Siminiak T, Wu JC, Haude M,, et.al, *Eur J HF*, May 2012.

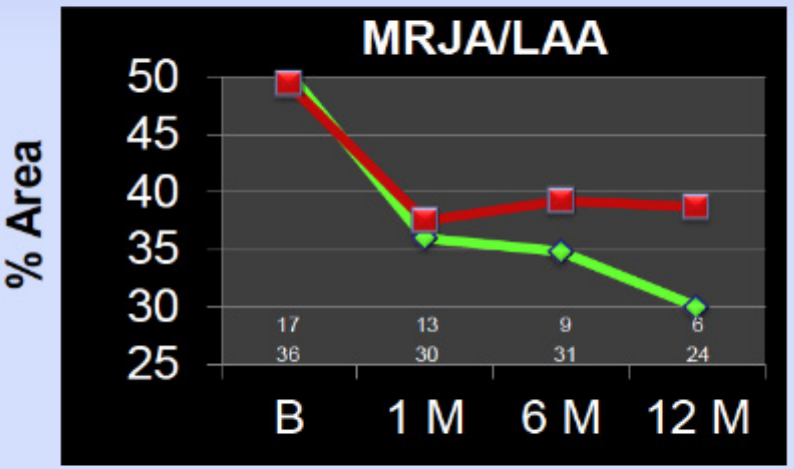
Slide courtesy of S. Goldberg, MD

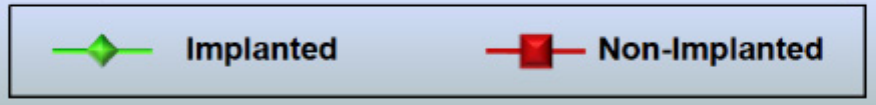
TITAN – MR Results







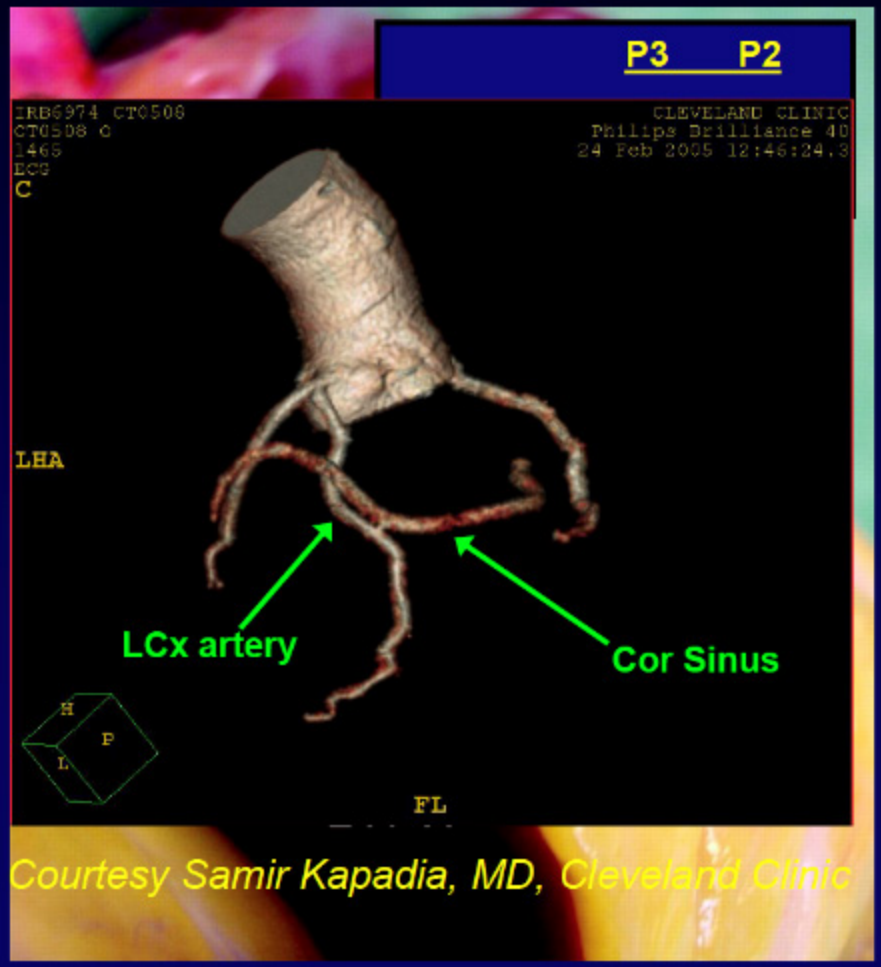




*p<0.05, **p<0.01, ***p<0.001
Between groups comparison of absolute differences from baseline

Issues and Problems

- CS approach to perc annuloplasty
  - CS not truly co-planar with annulus (just above)
    - Will that help to restore normal saddle shape or prevent annular movement
    - Role of individual variability in cor sinus anatomy
    - Influence of MAC
  - Can pinch LCx artery (just below)
  - Unknowns
    - Long-term benefit of partial circumference ring
    - Risks of erosion, perforation, thrombosis
    - How to assess functional MR quantitatively and account for its dynamic nature

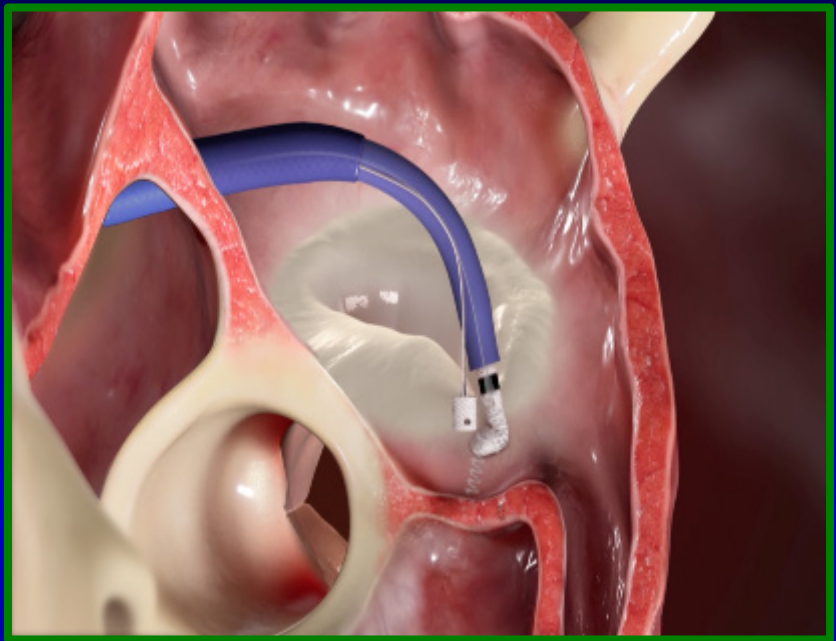


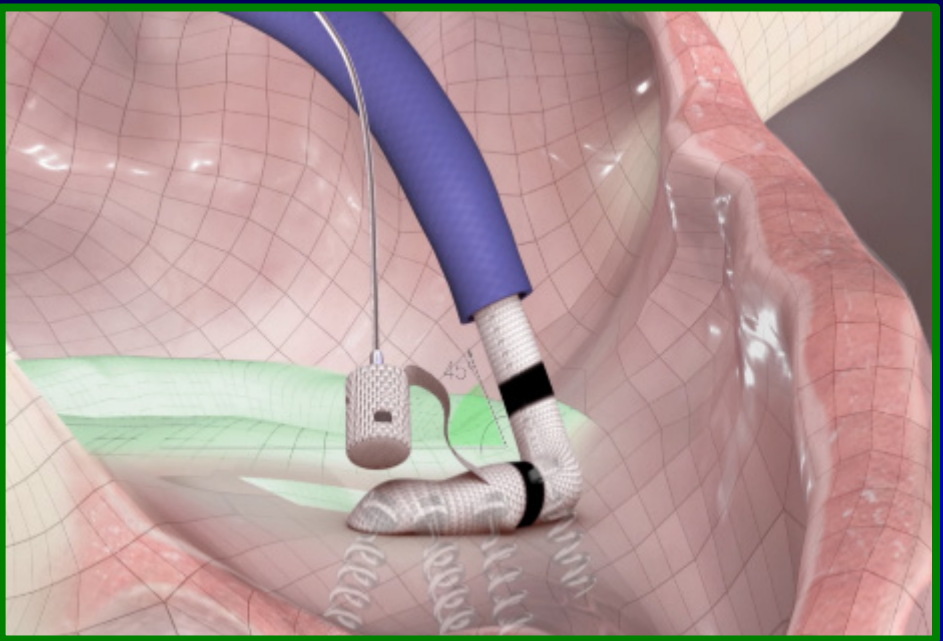
Maselli et al, Circ 2006;114:377-380

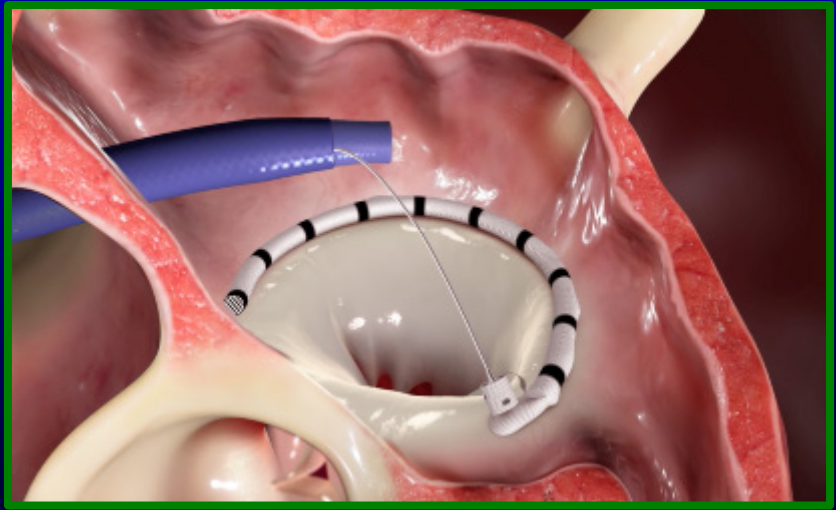
Table 1. Characteristics of the ideal patient with FMR for Carillon implantation.

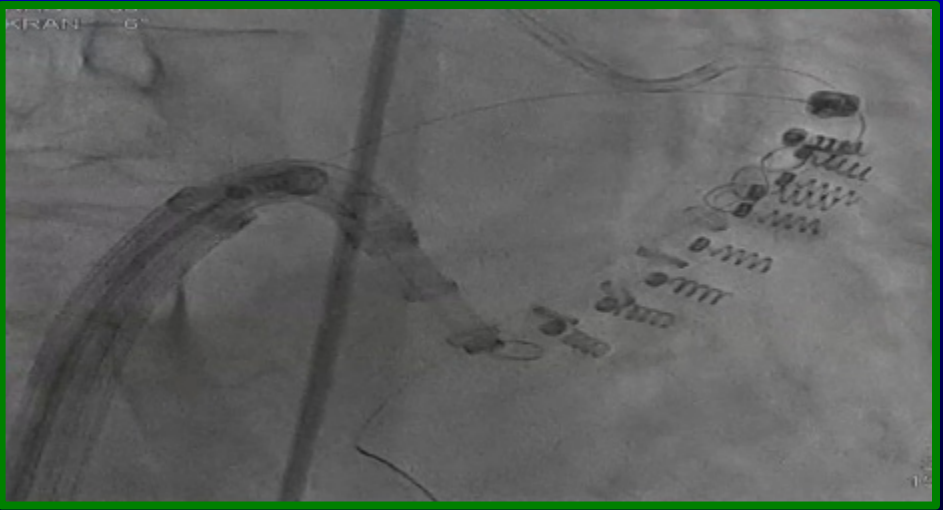
Characteristics	Recommendation/Ideal scenario	Rationale
Age	Younger age	With age and/or prior surgery, fibrosis and calcification of the mitral annulus are more likely to allow less plication with the Carillon device.
Aetiology	Ischaemic or non-ischaemic	Non-ischaemic is more likely to be seen in younger patients with fewer comorbidities. Especially for ischaemic patients, consider improvement of comorbidities if suitable.
Pathology	No annular calcification No obvious leaflet pathology	The extent of mitral annulus calcification reduces the ability to plicate tissue. Full ring calcification is regarded as an exclusion for the Carillon device. Leaflet prolapse should not be treated with mitral annuloplasty. Significant disease of the mitral leaflets or the chordae resulting in MR should not be treated with the Carillon device.
Comorbidities	Minimal	Severe renal insufficiency is the most important comorbidity. In any case, contrast use should be limited as much as possible and patients should be prepared with careful fluid administration.
Arterial anatomy	Occluded LCx and bypassed LCx Dominant RCA	No compromise of flow due to the Carillon device. Patients with a dominant RCA and small LCx are less prone to show compromise of the LCx with the Carillon device.
Venous anatomy	"Typical" anatomy in which CS/GCV parallels the posterior leaflet from P1–P3	Consider performing arteriogram with venous follow-through (ideally in LAO caudal and RAO caudal projections) with a second LCA injection when CS is opacified as a screening procedure to visualise the arteriovenous anatomy.
MR pathology	Pure functional MR	Primary MR is unlikely to benefit from mitral annuloplasty alone.
MR grade	2+ - 3+ Moderate – moderately severe	In patients with massive left atrium enlargement and severe 4+ FMR, the likelihood of dramatic efficacy may be reduced.
NYHA class	(II), III	NYHA IV patients are at higher risk. Patients with 2+ FMR and NYHA (II) to III are, by definition, presenting with limited symptoms and are candidates for treatment. Since the Carillon responder will improve by one NYHA class within three to six months, best clinical results will be achieved in NYHA classes II and III.

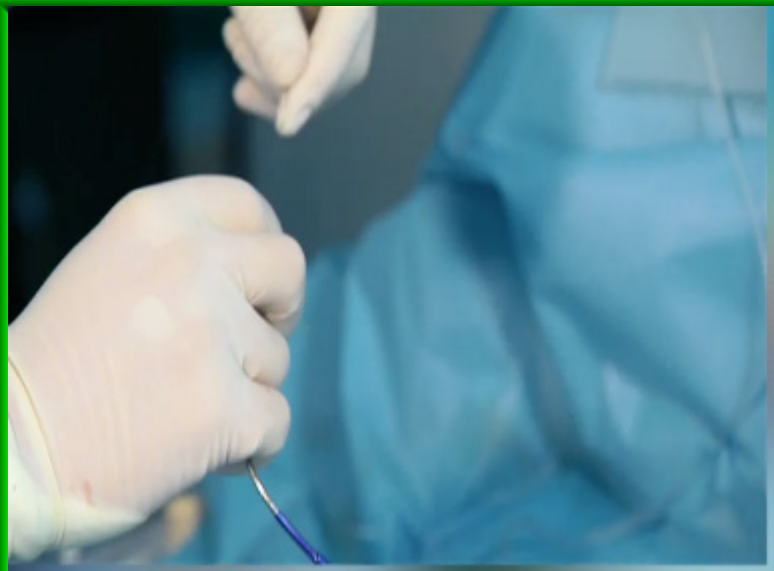
CARDIOBAND

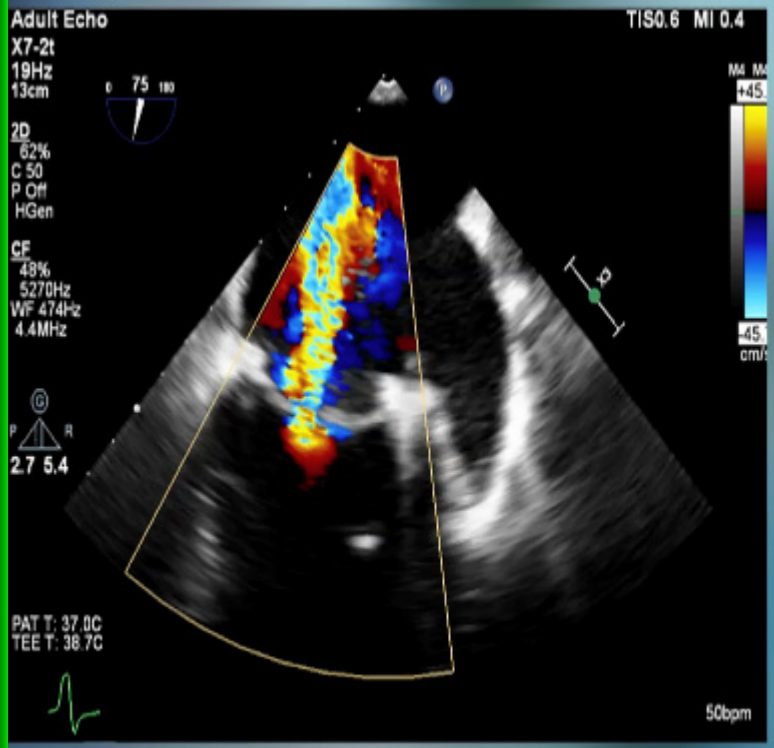


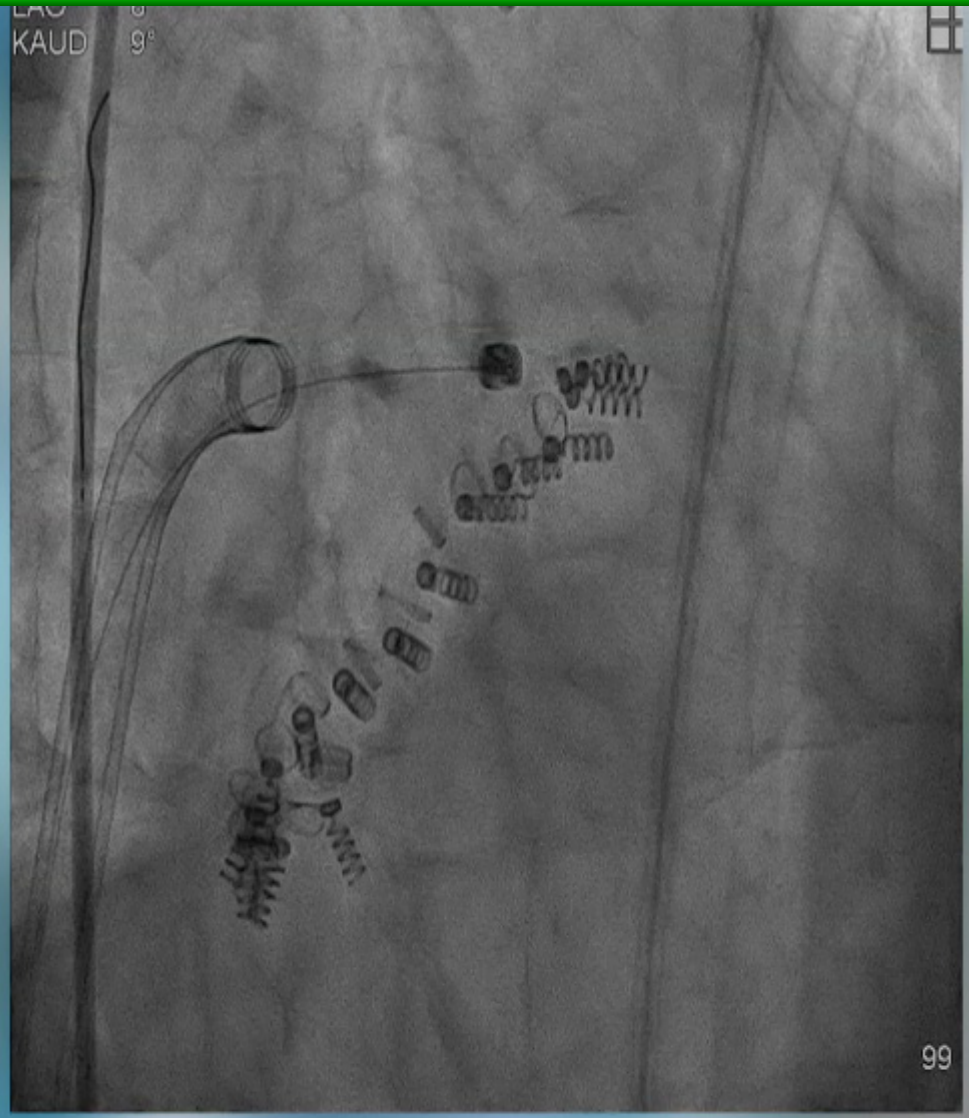


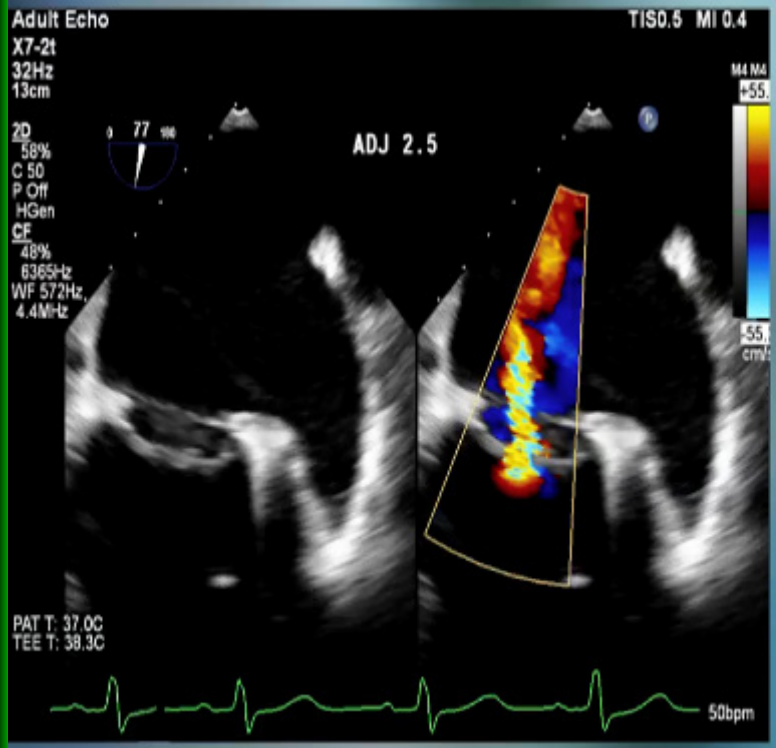


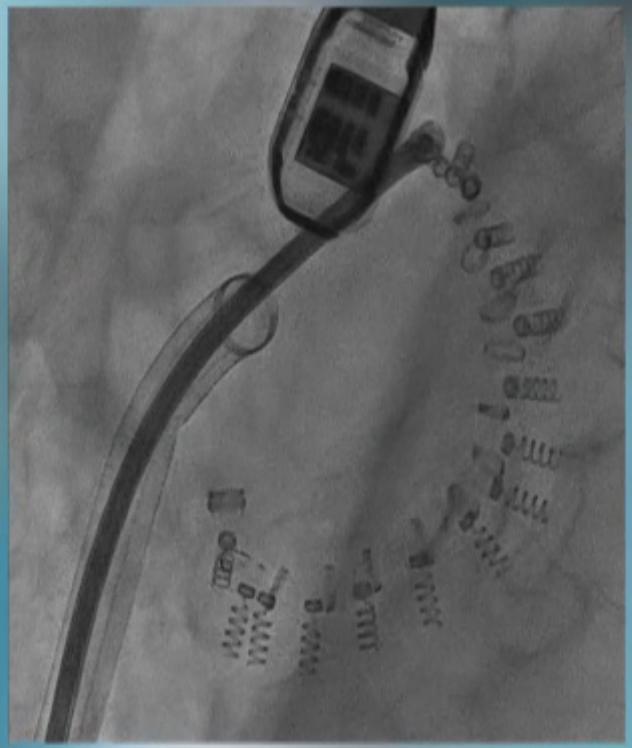




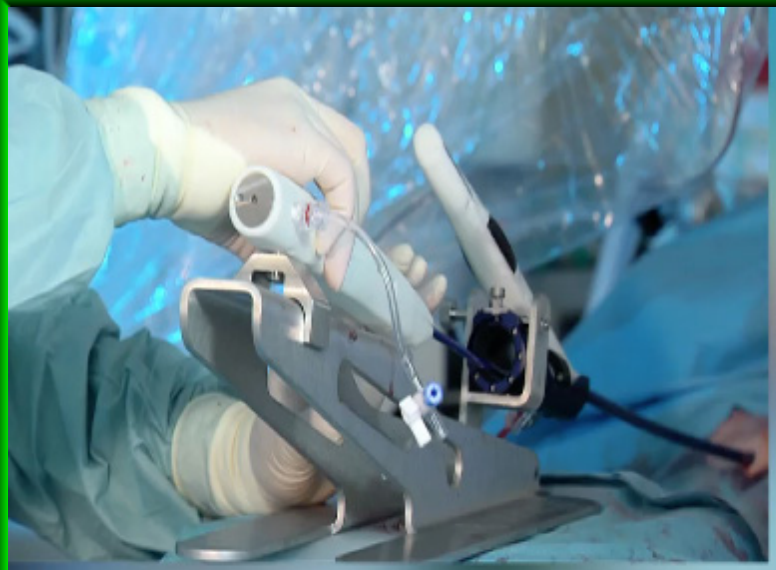

Adult Echo
TIS0.6 MI 0.4
X7-2t
19Hz
13cm
2D
62%
C 50
P Off
HGen
CF
48%
5270Hz
WF 474Hz
4.4MHz
2.7 5.4
PAT T: 37.0C
TEE T: 36.7C
50bpm

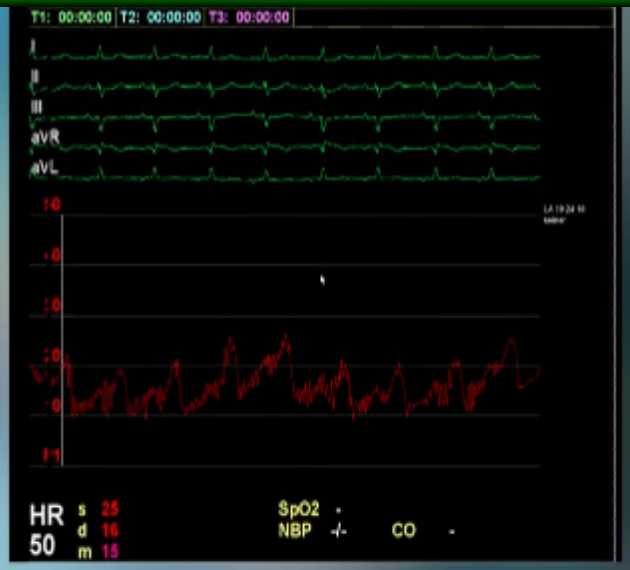

KAUD 9°
99

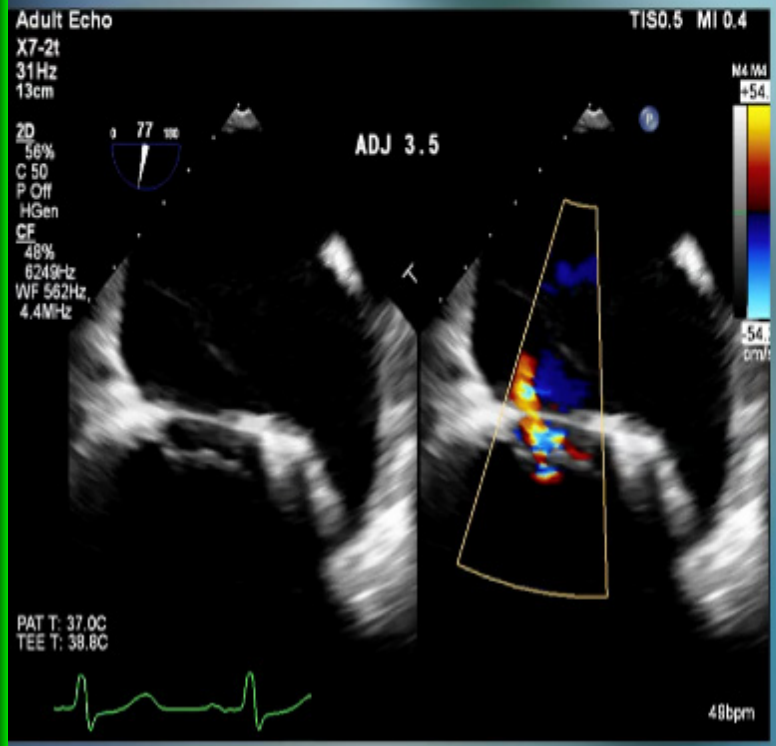


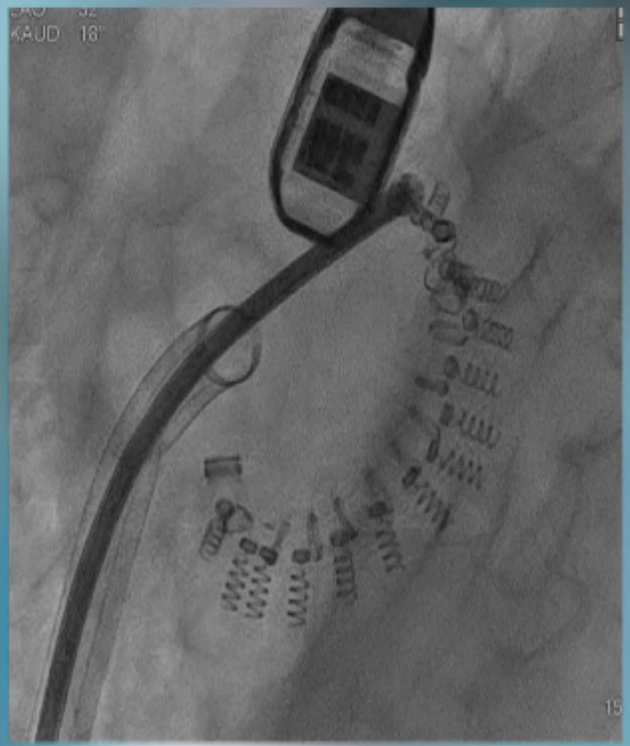


CONTRACTION TO
15% ORIGINAL SIZE



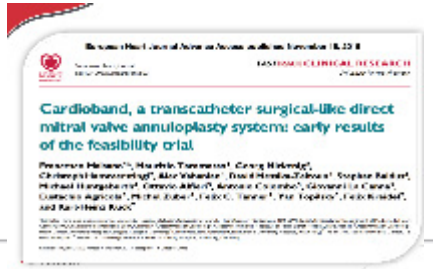






CONTRACTION TO
30% ORIGINAL SIZE

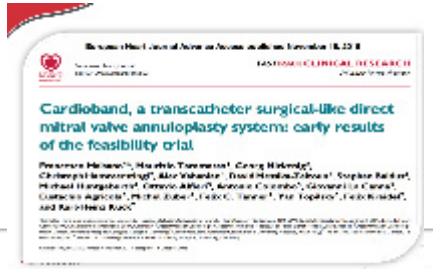
Study Demographics (N=50)


Cardioband, a transcatheter surgical-like direct mitral valve annuloplasty system: early results of the feasibility trial

Variable	No. (%) or Mean
Age (years)	71 ± 8
Gender	Male 39 Female 11
Euroscore II (%)	7.5
Baseline NYHA Class of III or IV (%)	84
Ischemic Non Ischemic	31 19
LVEDD (mm) Avg±SD	61 ± 6
EF (%) Avg±SD	33 ± 11
Prev CABG COPD Moderate to Severe Renal Failure Severe Pulmonary Hypertension Afib	16 (32%) 11 (22%) 38 (76%) 12(24%) 39 (78%)

Valtech

Reported Major Safety Events at 30 Days


Cardioband, a transcatheter surgical-like direct mitral valve annuloplasty system: early results of the feasibility trial

30 Day Events*	Patients Experiencing Event, # (%) All Patients N=50
Death	2 (4%)
Hemorrhagic Stroke**	1 (2%)
Need for elective Mitral Operation**	1 (2%)
Ischemic attack	1 (2%)
Major Bleeding Complications	1 (2%)
Renal Failure	2 (4%)
Myocardial Infarction	0 (0%)
Respiratory Failure	0 (0%)
Cardiac Tamponade	1 (2%)

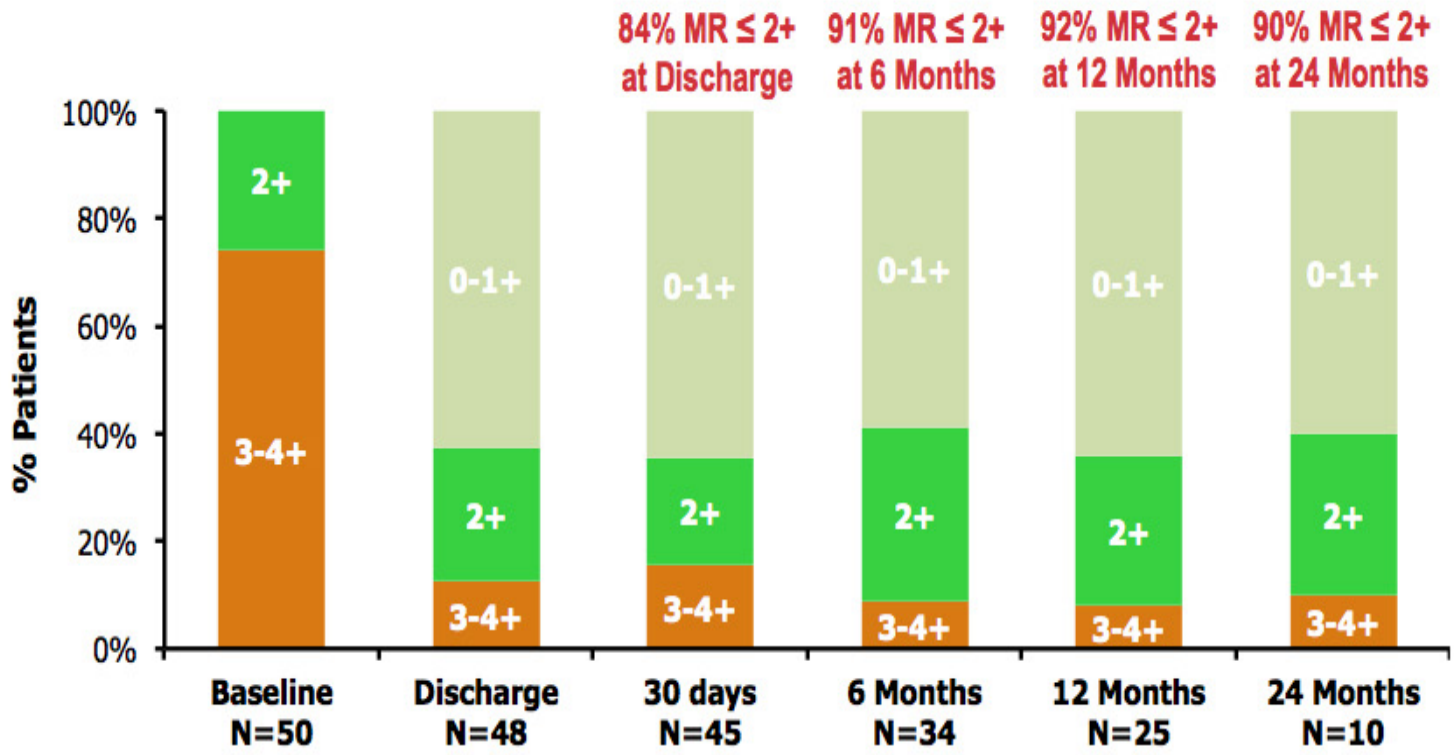
* VARC Guidelines (European Heart Journal, 2012, 33:2403-2414)

** Part of the Death case

One additional death case per ITT - compassionate

Valtech

90% patients with MR≤2+ At 24 Months By Core Lab*

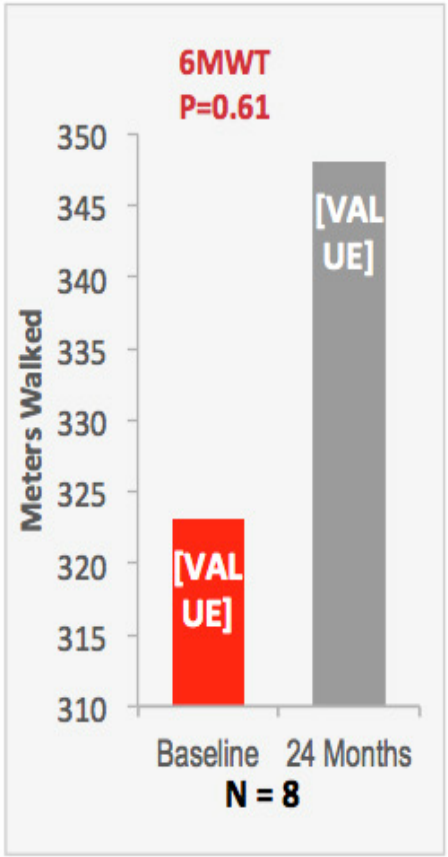


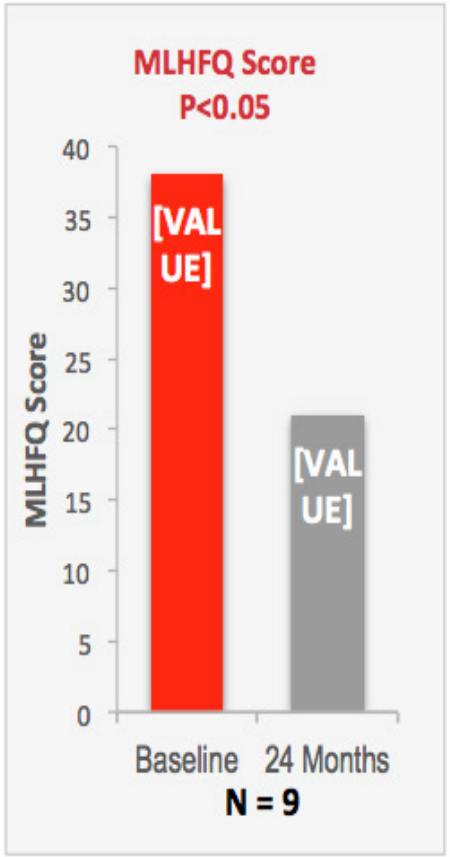
Valtech

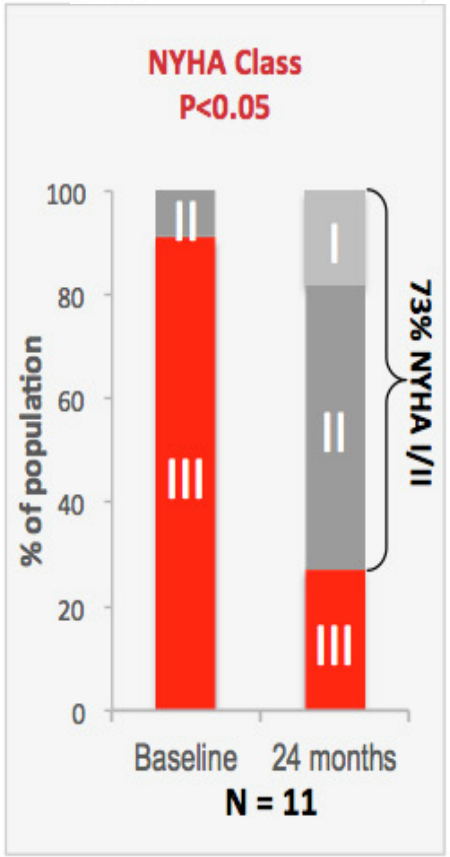
*Dr. Paul Grayburn – Baylor University

Functional Improvement at 24 Months


Cardioband, a transcatheter surgical-like direct mitral valve annuloplasty system: early results of the feasibility trial



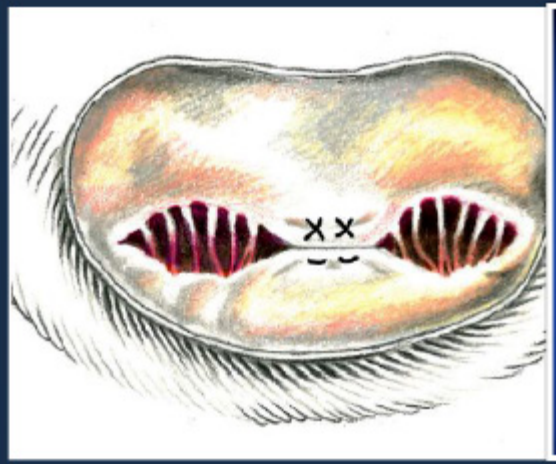


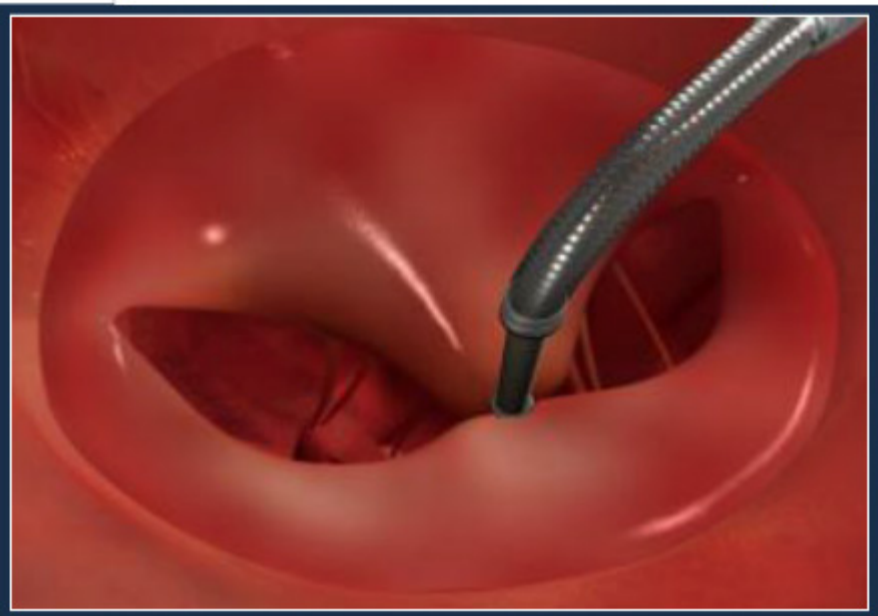


Valtech

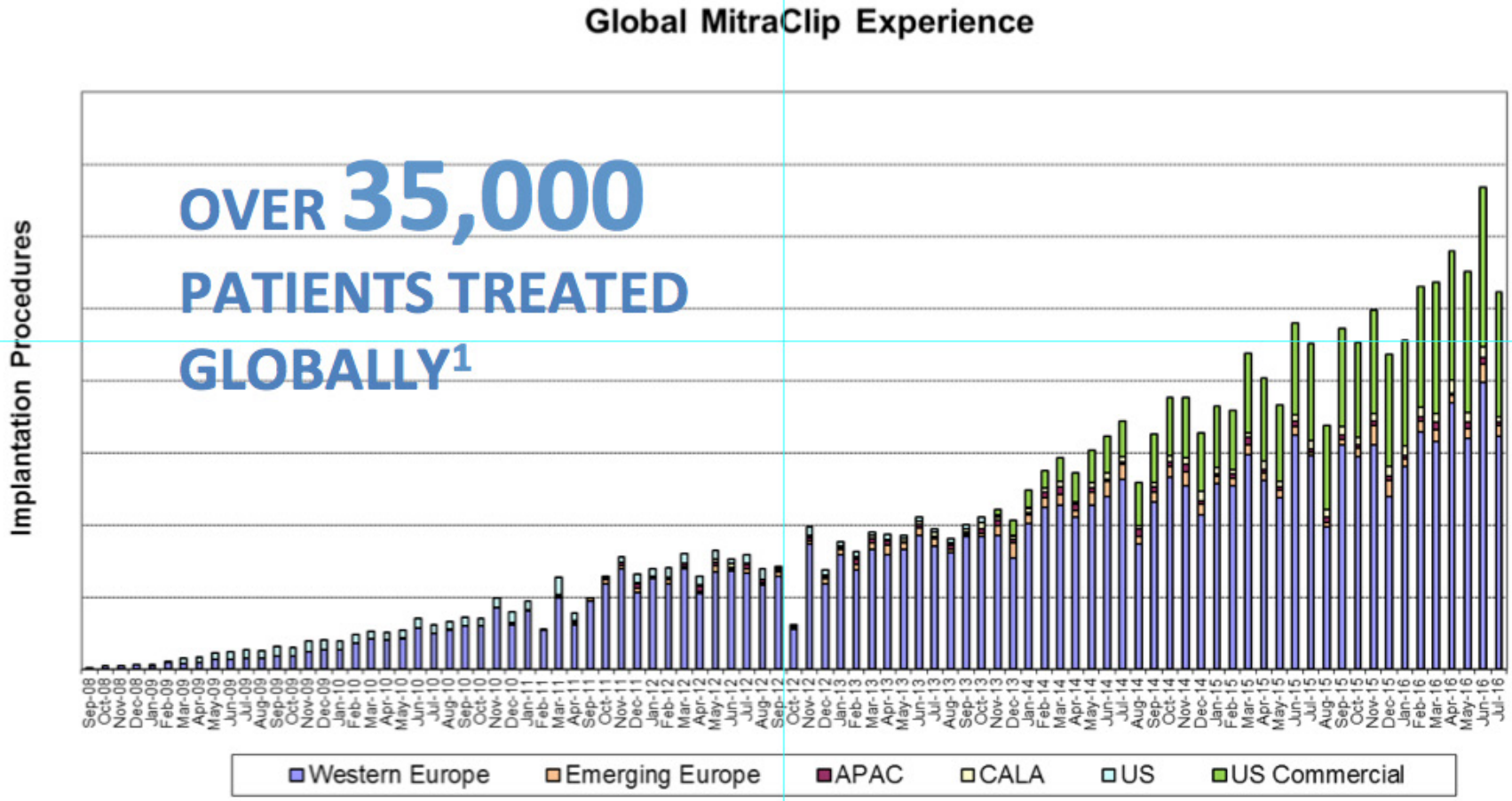
Catheter-Based Mitral Valve Repair

MitraClip System



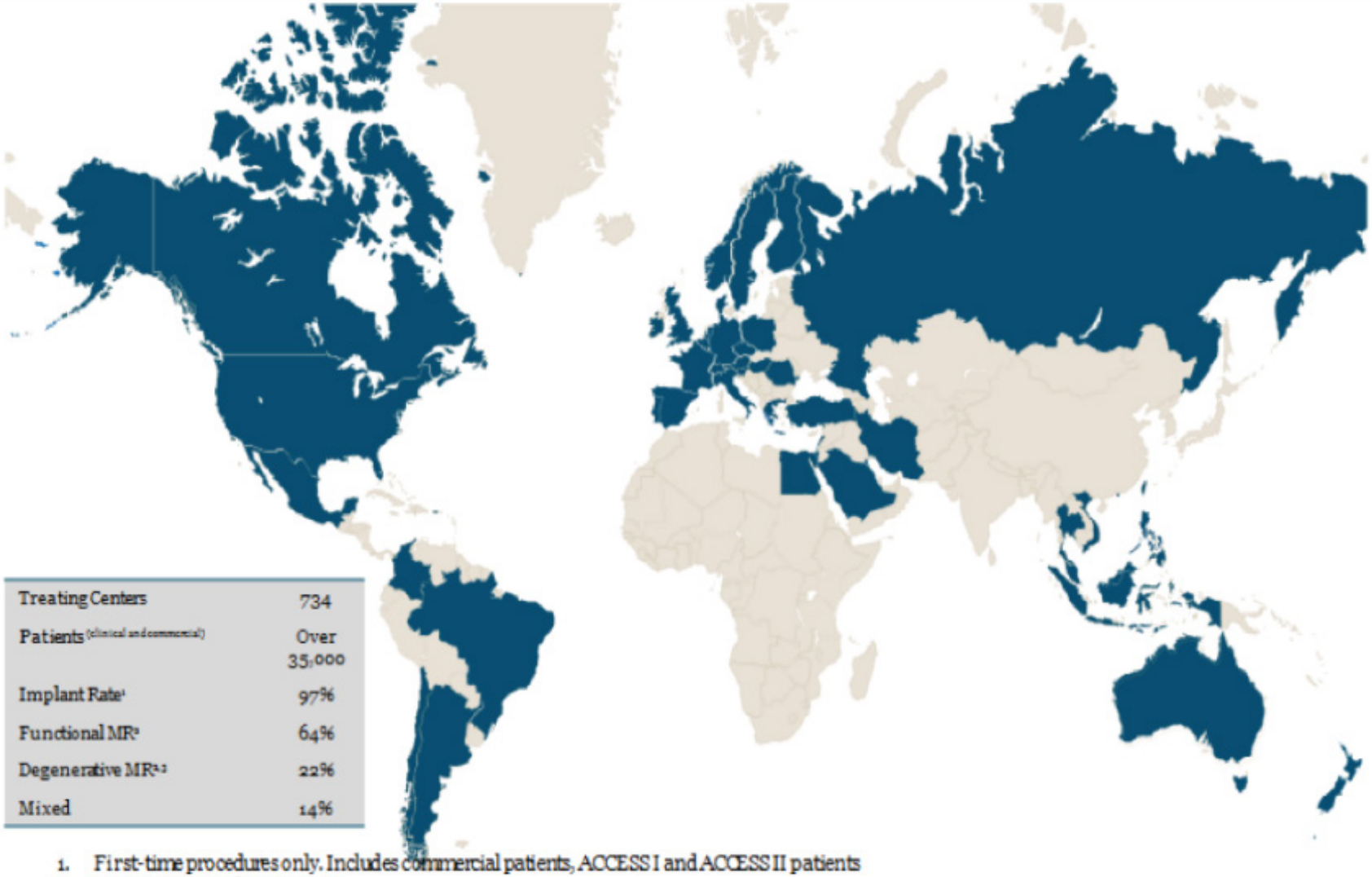


GLOBAL MITRACLIP EXPERIENCE



1. Includes clinical and commercial procedures as of 31/07/2016. Source: Data on file at Abbott Vascular

MITRACLIP THERAPY CURRENT GLOBAL ADOPTION



Treating Centers	734
Patients (clinical and commercial)	Over 35,000
Implant Rate[1]	97%
Functional MR[2]	64%
Degenerative MR[2,3]	22%
Mixed	14%

1. First-time procedures only. Includes commercial patients, ACCESS I and ACCESS II patients
2. OUS Commercial Experience
3. Etiology not inclusive of U.S. cases as of 14/04/2014

Data As of July 31, 2016. Source: Data on file at Abbott Vascular

2014

Survival of Transcatheter Mitral Valve Repair Compared With Surgical and Conservative Treatment in High-Surgical-Risk Patients

Martin J. Swaans, MD,* Annelies L. M. Bakker, MD,* Arash Alipour, MD, PhD,* Martijn C. Post, MD, PhD,*

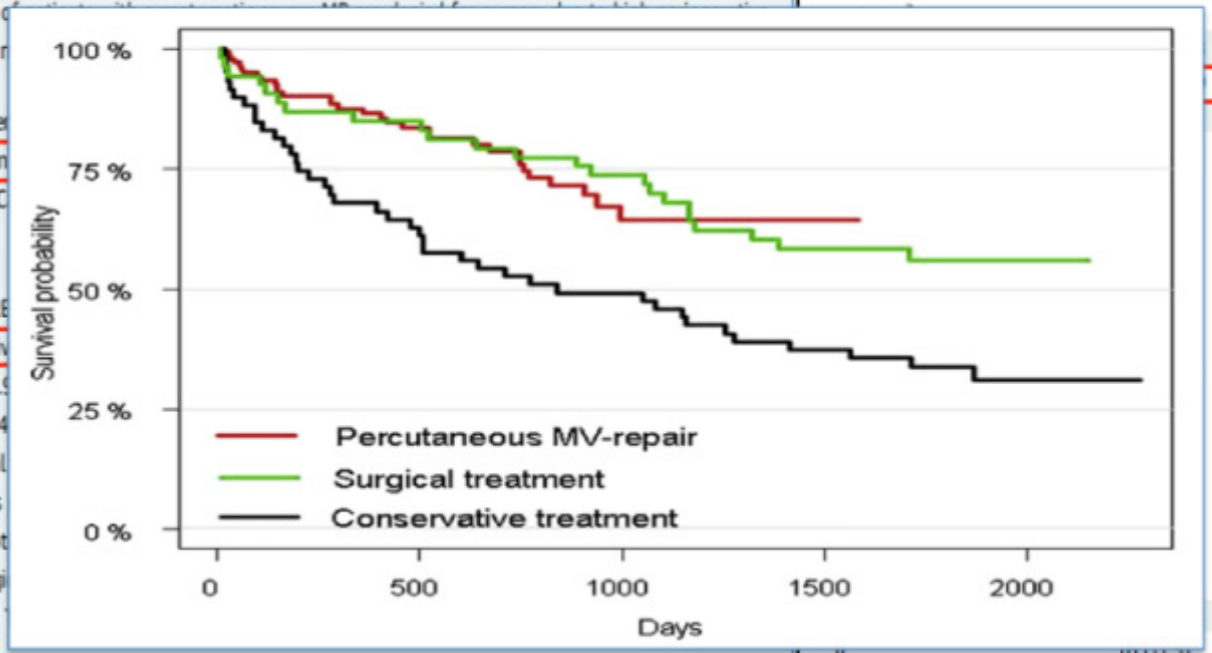
OBJECTIVES The goal of this study was to compare survival between transcatheter mitral valve (MV) repair using MitraClip system (Abbott Vascular, Santa Clara, California), MV-surgery, and conservative treatment in high-surgical-risk patients symptomatic with severe mitral valve regurgitation (MR).

BACKGROUND Up to 50% o… risk. Transcatheter MV repair r…

METHODS Consecutive patie… (n = 53) and conservatively (n… logistic European System for C… as judged by the heart team.

RESULTS The log EuroSCORE… (14.2 ± 8.9%) and conservativ… higher in surgical patients (43.9… and conservatively treated (34… groups showed similar survival… survived. The same trend was… controlling for risk factors, bot… to 0.78, p = 0.006) and surgi… conservatively treated group. … 2.16, p = 0.430).

CONCLUSIONS Despite a higher log EuroSCORE, high-surgical-risk patients with symptomatic severe MR treated with transcatheter MV repair show similar survival rates compared with surgically treated patients, with both displaying survival benefit compared with conservative treatment. (J Am Coll Cardiol Intv 2014;7:875-81) © 2014 by the American College of Cardiology Foundation.



Characteristic	MitraClip	High-Risk Surgery	Conservative Treatment
No.	139	53	59
Age, yrs	74.6 ± 9.4	70.2 ± 9.5	71.7 ± 9.6
Male, %	94 (67.6)	27 (50.9)	32 (54.2)
		26.7 ± 5.3	26.5 ± 4.5
		43.9 ± 14.4	34.5 ± 16.5
		14.2 ± 8.9	18.7 ± 13.2
		28 (52.8)	25 (42.4)
		10 (18.9)	17 (28.8)
		27 (50.9)	24 (40.7)
		15 (28.3)	19 (32.2)
		28 (52.8)	45 (76.3)
		13 (24.5)	25 (42.4)
		5 (9.4)	9 (15.3)
		9 (17.0)	11 (18.6)
		1 (1.9)	2 (3.4)
		9 (17.0)	18 (30.5)
		11 (20.8)	14 (23.7)
		28 (52.8)	26 (44.1)
		14 (26.4)	19 (32.2)
II	[illegible]	6 (11.3)	8 (13.6)
III	91 (65.5)	38 (71.7)	35 (59.3)
IV	32 (23.0)	9 (17.0)	16 (27.1)
Etiology			
FMR	107 (77.0)	31 (58.5)	48 (81.3)
DMR	25 (18.0)	17 (32.1)	4 (6.8)
Mixed	7 (5.0)	5 (9.4)	7 (11.9)

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

Fabrizio D'ascenzo, MD[a], Claudio Moretti, MD[a], Walter Grosso Marra, MD[a], Antonio Montefusco, MD[a], Pierluigi Omede, MD[a], Salma Taha, MD[a,b,*], Davide Castagno, MD[a], Oliver Gaemperli, MD[c], Maurizio Taramasso, MD[d], Simone Frea, MD[a], Stefano Pidello, MD[e], Volker Rudolph, MD[f], Olaf Franzen, MD[g], Daniel Braun, MD[h], Cristina Giannini, MD[i], Huseyin Ince, MD[j], Leor Perl, MD[k], Giuseppe Zoccai, MD[l], Sebastiano Marra, MD[a], Maurizio D'Amico, MD[a], Francesco Maisano, MD[m], Mauro Rinaldi, MD[a], and Fiorenzo Gaita, MD[a]

(Am J Cardiol 2015;116:325–331)

Baseline features of included patients (all variables are reported as continuous or percentages with median, first and third quartiles)

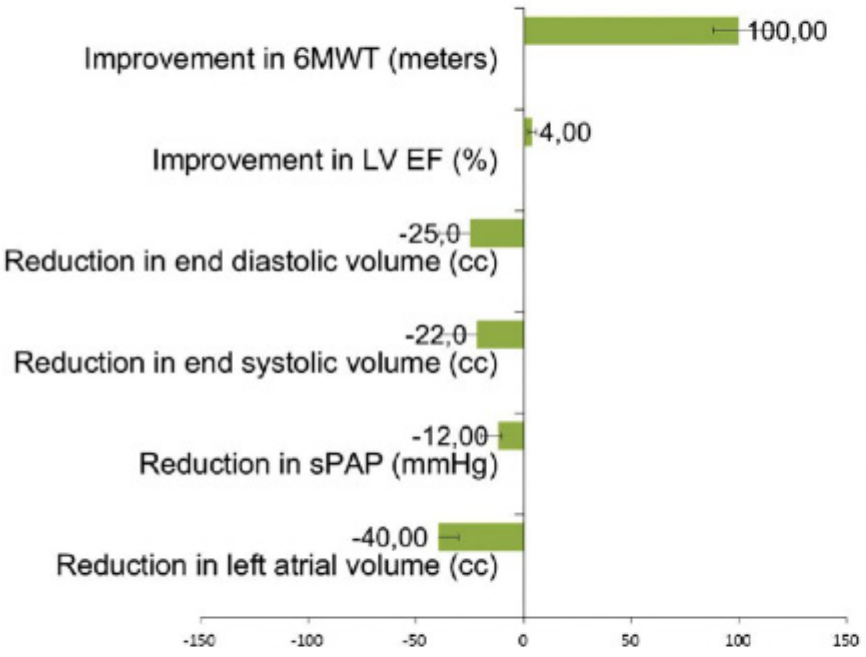
	9 studies, 875 patients
Age (years)	71 (69-73)
women	23-38 (34%)
Hypertension	54-74 (70%)
Diabetes mellitus	22-40 (33%)
Coronary heart disease	63-75 (70%)
Previous myocardial infarction	34-53 (43%)
Non ischemic heart disease	25-37(30%)
Atrial fibrillation	41-56 (51%)
Intracardiac defibrillator/Cardiac resynchronization therapy	65-81 (72%)
Logistic Euroscore	18-28 (24)
STS score	8-14 (12)
NYHA class III/IV	88-98 (90%)
Baseline 6 minute walk test (meters)	220-262 (230)

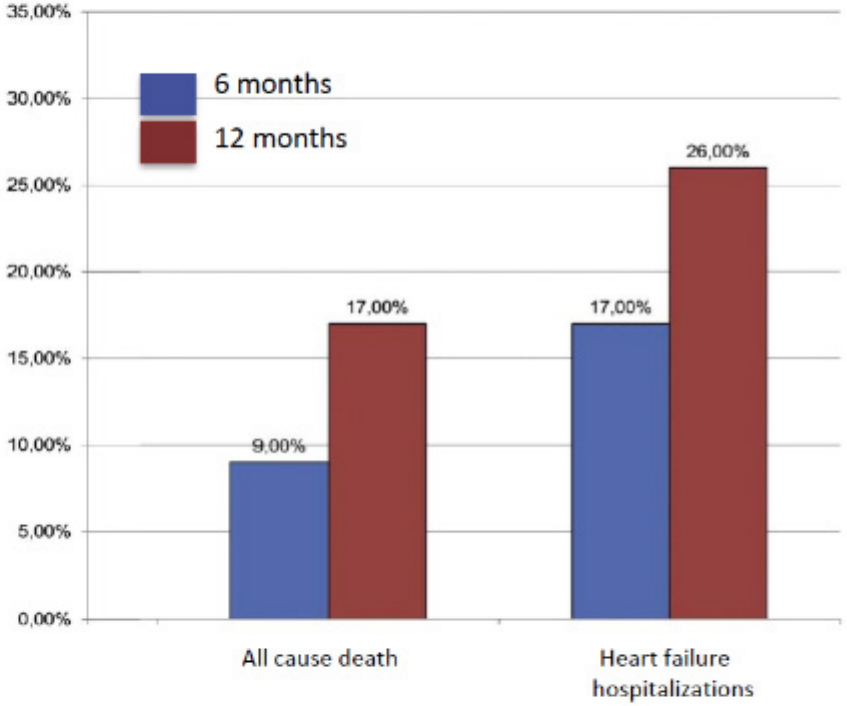
Echocardiographic features of included patients (all variables are reported as continuous or percentages with median, first and third quartiles)

	9 studies, 875 patients
Left ventricle ejection fraction (%)	29- 36(34%)
Left ventricle end diastolic volume (ml)	192-229 (212)
Left ventricle end systolic volume (ml)	124-182 (152)
Systolic pulmonary artery pressure (mmHg)	32-54 (33)
Left atrial volume (ml)	118-129 (125)

Meta-Analysis of Mitraclip in Functional MR

9 studies, 875 patients, STS median 12%,





significant improvement in functional class and remodeling, even with severely dilated hearts, although efficacy limited in atrial fibrillation

D'ascenzo F: Am JCardiol 116:325-331,2015

Comparison of MitraClip RCTs in FMR

	COAPT	RESHAPE-HF
N patients, sites	420 @ 75 US sites	800 @ 75 EU sites
Control arm	Medical Rx	Medical Rx
FMR grade (core lab)	3+ - 4+	3+ - 4+
NYHA class	II, III, or ambulatory IV	III or ambulatory IV
Other inclusion criteria	HF hosp <12 mos or BNP ≥400 pg/ml or nT-proBNP ≥1600 pg/ml	-
LVEF	≥20% - ≤50%	≥15% - ≤40%
LV volumes	LVESD ≤70 mm	LVEDD ≥55 mm
Primary efficacy endpoint (superiority)	Recurrent HF hospitalization (ITT)	Death or recurrent HF hospitalization (ITT)
Primary safety endpoint (noninf)	SLDA, device embolizations, endocarditis/MS/device-related complications requiring non-elective CV surgery	-
Health Economics	Assessed	Assessed

TMVR LANDSCAPE

TMVI technologies with active clinical programs under protocol	4	Abbott Tendyne; Edwards CardiAQ; Medtronic Twelve; Neovasc
TMVI technologies FIH studies <24 months	5	Cephea; M-Valve; Caisson; Highlife; Valtech
TMVI technologies with valves in development	11+	Braile; Navigate; Venus; HT Consultant; MitralHeal; Direct Flow; Verso; Micro Interventional; SinoMed; TransMural Systems; MitrAssist

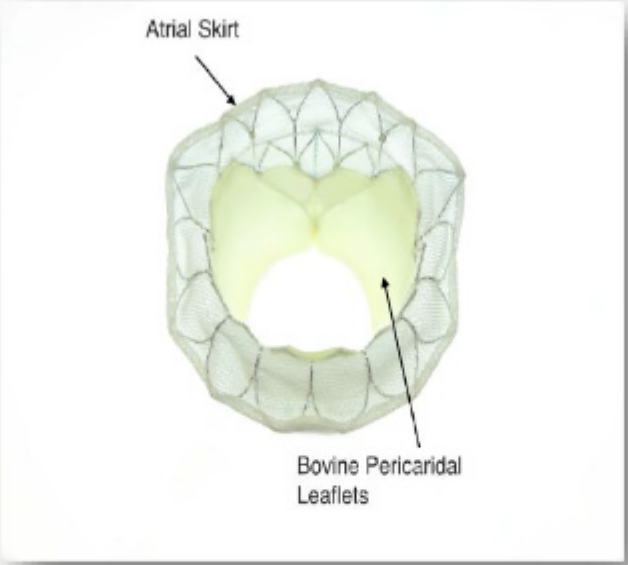
Tendyne

- Valve
  - Porcine Pericardial
- Stent
  - Inner circular and outer D-Shaped Self-Expanding Nitinol Frame
- Anchoring
  - Tether to Left Ventricular Apex
- Delivery
  - Transapical- 32 Fr

CardiAQ

- Valve
  - Porcine pericardium
- Stent
  - Nitinol self expanding
- Anchoring
  - 12 X2 opposing atrial and ventricular anchors
- Delivery
  - Transapical
  - Transfemoral

Neovasc Tiara



- Valve
  - Bovine pericardium
- Stent
  - D-shaped
  - Nitinol self-expanding
- Anchoring
  - Ventricular anchors fix the valve onto fibrous trigone and posterior annulus
- Delivery
  - Transapical- 32F

TMVR PROs

- WILL ELIMINATE MR
- CAN TREAT ALL PATHOLOGIES
- REPRODUCIBLE
- WILL ALLOW VIV IMPLANT AT LATER STAGE
- PRESERVES THE MITRAL APPARATUS

TMVR CONs

- LARGE VALVE SIZE
- CLOSING PRESSURES ARE HIGHER
- ANCHORING HAS TO BE LEAFLEST/ANNULUS BASED
- LV OBSTRUCTION IS A POSSIBILITY

SUMMARY

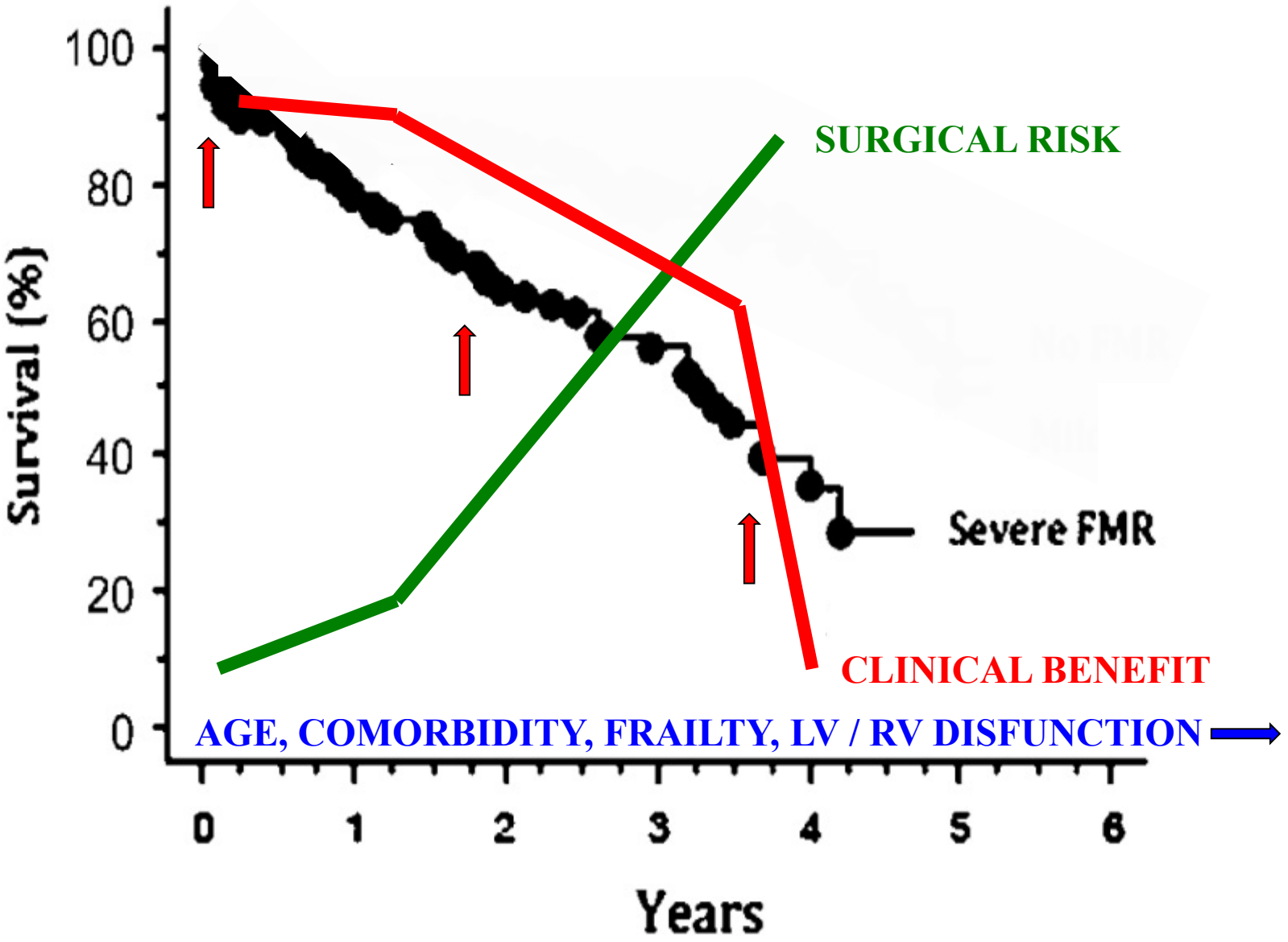
- SURGERY CAN BE VERY EFFECTIVE
  - Morbidity, mortality and durability concerns
  - Repair vs replacement remain controversial
- THERE IS AN UNMET CLINICAL NEED
- PERCUTANEOUS REPAIR PARTLY MEETS THIS NEED
  - Efficacy variable, durability unknown
  - Combined procedures complex and expensive
  - May prevent subsequent TMVI ?
- TMVI EFFICACY, SAFETY AND DURABILITY PROMISING
  - Remains to be proven

What is a “Window of opportunity

A window of opportunity is a short period during wich an otherwise unaittainable opportunity exists.

After the window of opportunity closes, the opportunity ceases to exist.

SEVERE MR: windows of opportunities




If a window of
opportunity
appears, don't pull
down the shade.
~Tom Peters