How We Treat Patients with Secondary MR in Heart Failure

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TCTAP 2018, Seoul

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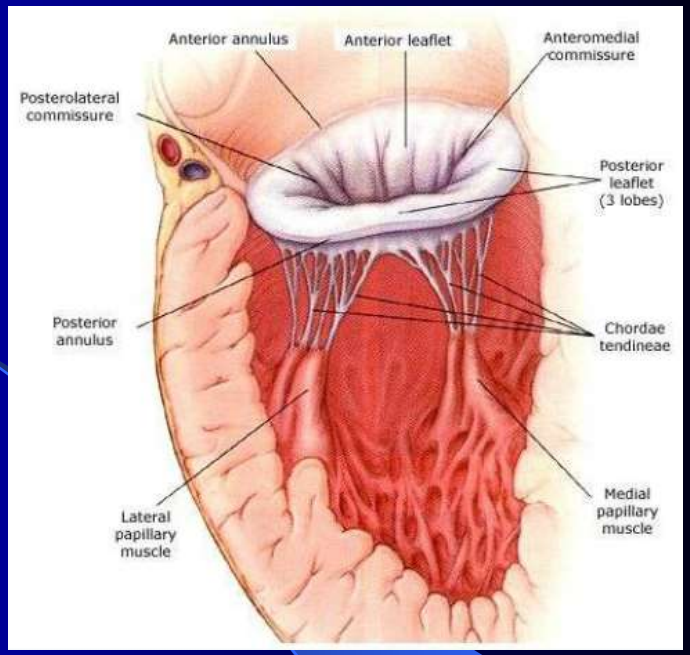
Disclosure

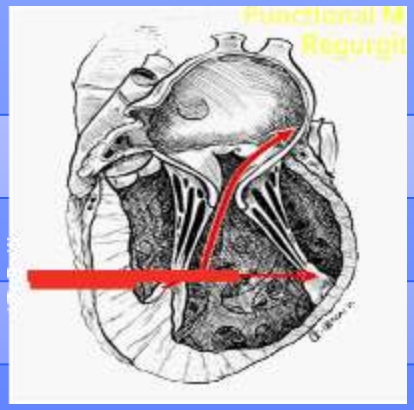
Consultant: **Edwards Lifesciences**

JC Medical Inc.

Etiology of MR

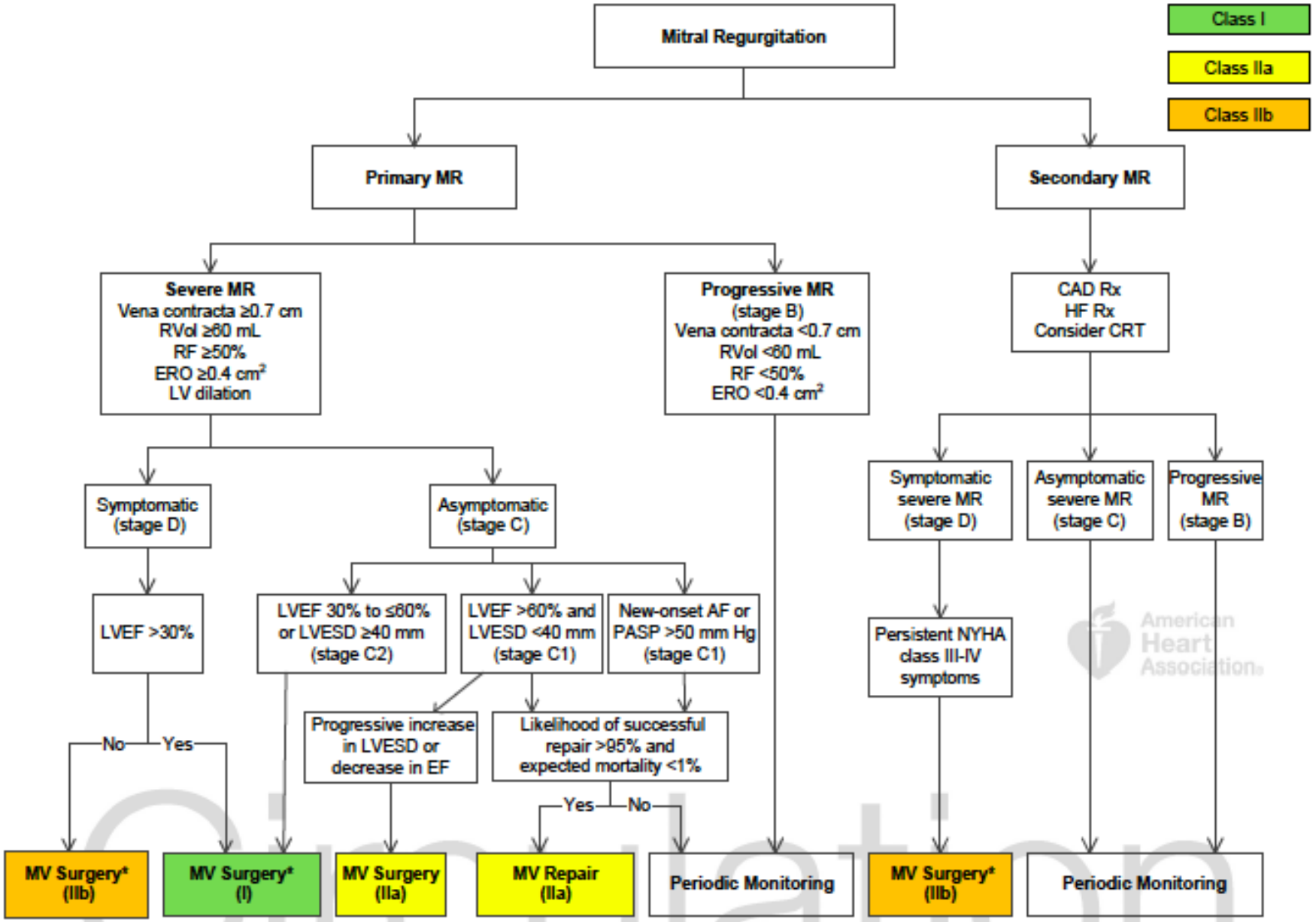


Acute	Chronic Primary	Chronic Secondary
Chordal rupture	Myxomatous	Ischemic
Endocarditis	Endocarditis	Dilated cardiomyopathy
Papillary muscle rupture	Mitral annular/leaflet calcification	
Trauma	Congenital (claft)	
Acute MI	Rheumatic	
	Radiation	
	Collagen vascular disease	



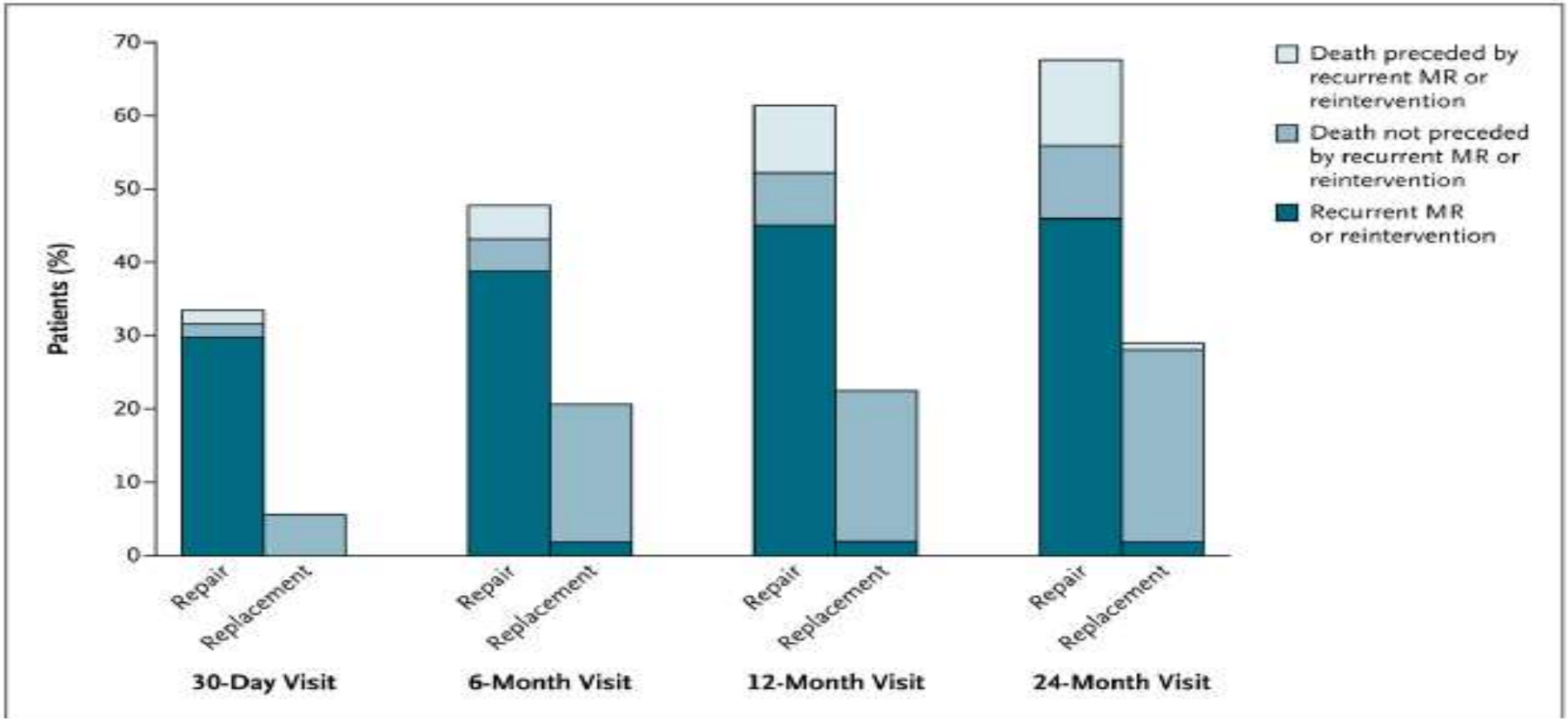
Nishimura, et al.
2017 AHA/ACC Focused Update on VHD

Figure 2. Indications for Surgery for MR (Updated Figure 4 From the 2014 VHD guideline)



High Cumulative Failure of MV Repair for ischemic MR

METHODS—We randomly assigned 251 patients to mitral-valve repair or replacement. Patients were followed for 2 years, and clinical and echocardiographic outcomes were assessed.



Failure of the intervention was defined as death, moderate or severe mitral regurgitation (MR) as seen on transthoracic echocardiography, or mitral-valve reintervention.

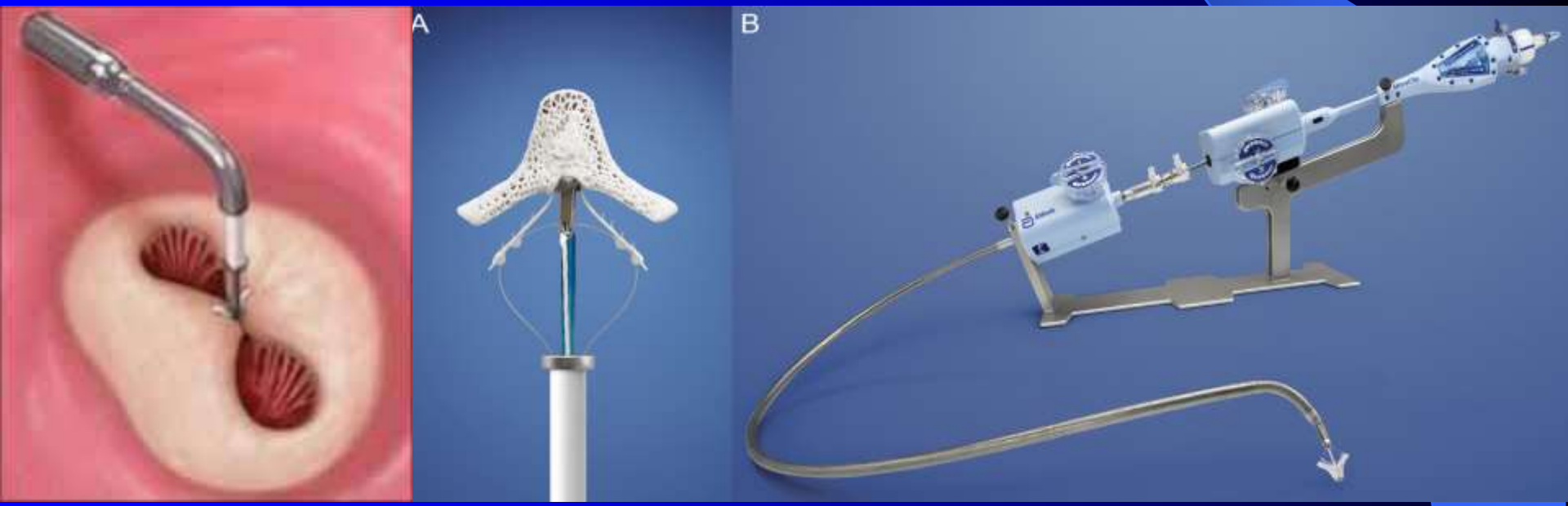
N Engl J Med. 2016 January 28; 374(4): 344–353

Transcatheter MV Repair

Percutaneous Edge-to-Edge Repair

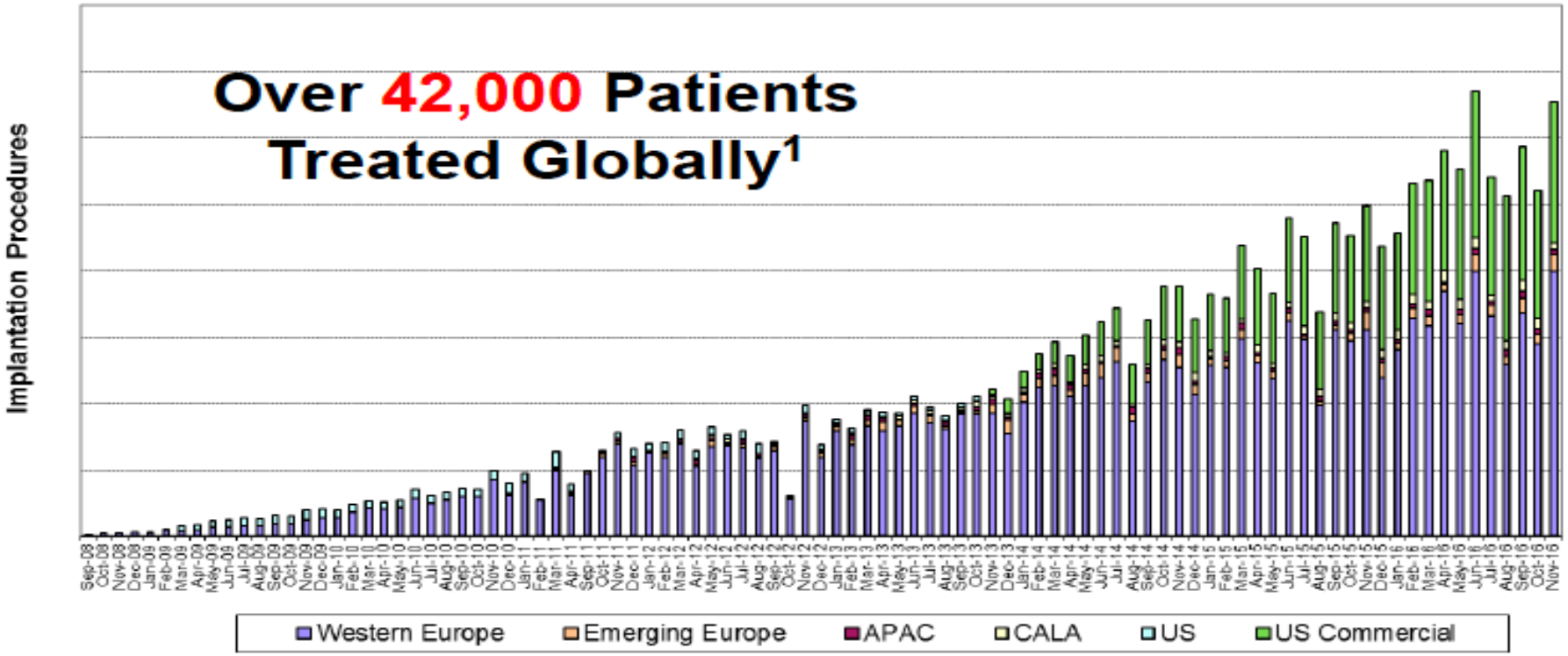
MitraClip

- FDA approval for degenerative MR in high risk patients
- Ongoing clinical trial on the treatment of functional MR



MitraClip is an FDA approved therapy for degenerative MR in high-risk patients

Global MitraClip Experience



1. Includes clinical and commercial procedures as of 30/11/2016. Source: Data on file at Abbott Vascular

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

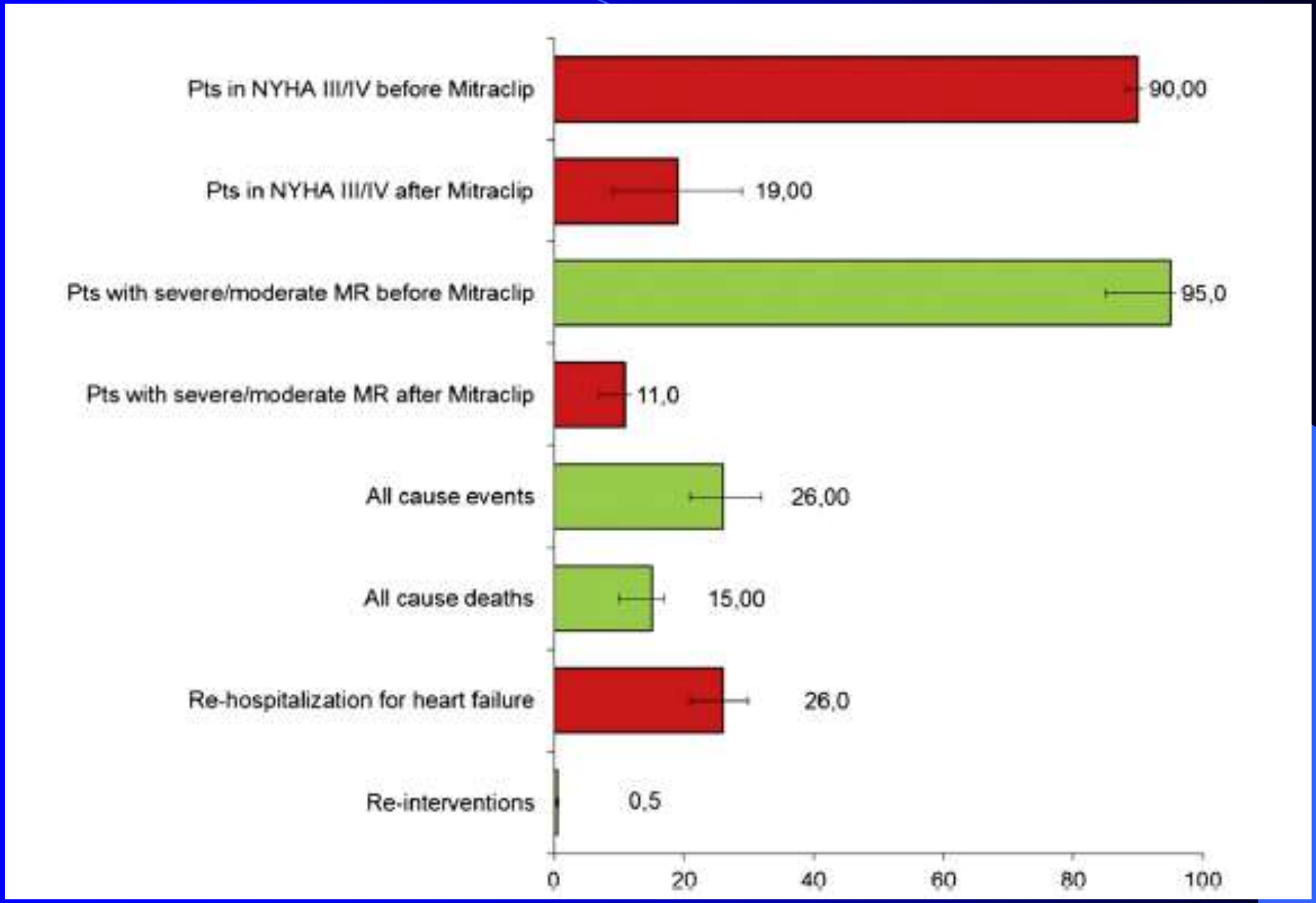
Fabrizio D'ascenzo, MD[a], Claudio Moretti, MD[a], Walter Grosso Marra, MD[a], Antonio Montefusco, MD[a], Pierluigi Omede, MD[a], Salma Taha, MD[a,b,*], Davide Castagno, MD[a], Oliver Gaemperli, MD[c], Maurizio Taramasso, MD[d], Simone Frea, MD[a], Stefano Pidello, MD[e], Volker Rudolph, MD[f], Olaf 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)

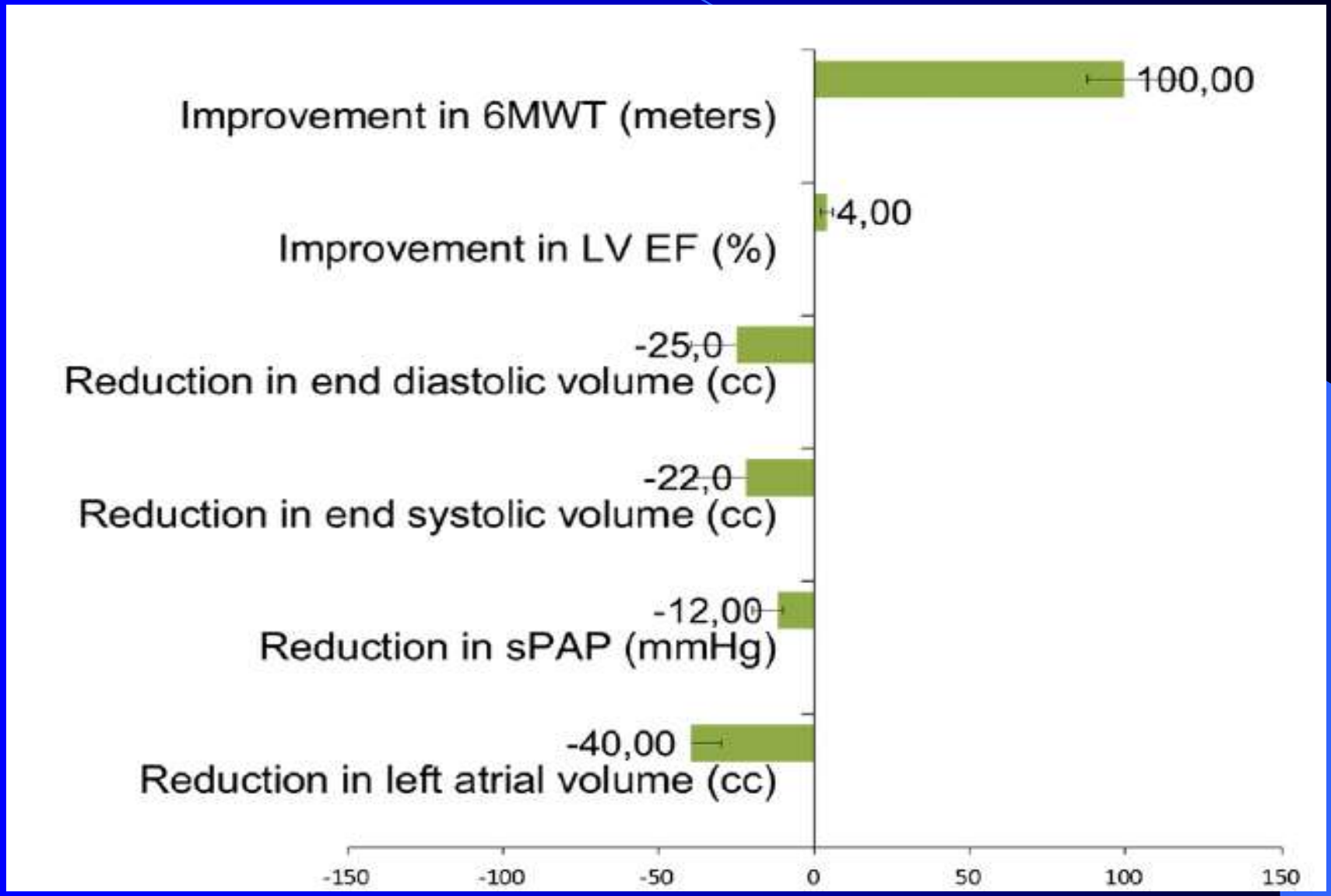
Echocardiographic features of included patients (all variables are reported as continuous or percentages with median, first and third quartiles)

	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)

Adverse Events at follow-up of 9 months



Change in functional and Echo data at follow-up



Systemic Review

Transcatheter Mitral Valve Repair With MitraClip for Symptomatic Functional Mitral Valve Regurgitation

Rodrigo Mendirichaga, MD[a], Vikas Singh, MD[b,*], Vanessa Blumer, MD[a], Manuel Rivera, MD[a], Alex P. Rodriguez, MD[a], Mauricio G. Cohen, MD[a], William W. O'Neill, MD[c], and Sammy Elmariah, MD, MPH[b]

- 12 studies including 1695 patients
- LVEF 32.5%
- Acute procedural success (residual MR ≤2 or reduction ≥1) 89%
- Survival to hospital discharge 98%, at 30-day 97%, at 12 months 82%

Safety outcomes

	CVA/TIA	AF	MI	Acute renal failure	Bleeding requiring transfusion	Vascular complication requiring intervention	Cardiac tamponade	Urgent cardiovascular surgery
Auricchio, 2011	0 (0)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	1 (2)	1 (2)
Braun, 2014	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Giannini, 2016	0 (0)	2 (3)	0 (0)	1 (2)	4 (7)	0 (0)	0 (0)	0 (0)
ACCESS-EU, 2013	2 (1)	-	3 (1)	20 (5)	15 (4)	-	4 (1)	-
Matsumoto, 2014	2 (2)	-	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Nickenig, 2014	0 (0)	57 (13)	-	-	44 (10)	4 (1)	3 (1)	-
Ondrus, 2016	1 (4)	-	-	-	-	-	1 (4)	2 (8)
Taramasso, 2014	0 (0)	5 (4)	0 (0)	23 (21)	-	-	-	1 (1)
Vandendriessche, 2014	1 (2)	-	-	-	3 (7)	-	1 (2)	2 (5)

Percutaneous Edge-to-Edge Repair

There are only sparse data to indicate that correcting MR prolongs life or even improves symptoms over an extended time.

Percutaneous edge-to-edge repair for secondary mitral regurgitation is a low-risk option, but its efficacy to reduce mitral regurgitation remains inferior to surgery.

Percutaneous edge-to-edge repair can improve symptoms, functional capacity and quality of life and may induce reverse LV remodeling.

A survival benefit of both surgery and percutaneous edge-to-edge repair, compared with 'optimal' medical therapy, has not yet been proven.

COAPT Trial

Objective

- To evaluate the safety and effectiveness of the MitraClip System for treatment of functional mitral regurgitation (FMR ≥3+) in symptomatic heart failure subjects who are treated per standard of care and who have been determined by the site's local heart team as not appropriate for mitral valve surgery

COAPT Trial

Primary Endpoints

Primary Effectiveness (minimum 1-year follow-up on all patients)

- Recurrent heart failure hospitalizations

Primary Safety (1 year)

- Composite of Single Leaflet Device Attachment (SLDA), device embolizations, endocarditis requiring surgery, Echocardiography Core Laboratory confirmed mitral stenosis requiring surgery, and any device related complications requiring non-elective cardiovascular surgery at 12 months

COAPT Trial: Design

~610 patients enrolled at up to 100 sites

Symptomatic HF treated with maximally tolerated guideline directed medical therapy
Significant FMR (≥3+ by echo core lab)
Not appropriate for MV surgery as determined by site's local heart team
Valve anatomy eligible for MitraClip treatment

Randomize 1:1

MitraClip N~305	Control group Standard of care N~305

Clinical and TTE follow-up: Baseline, treatment, 1-week (phone),
1, 6, 12, 18, 24, 36, 48, 60 months

Primary efficacy endpoint: Hospitalization for heart failure within 2 years
Primary safety endpoint: Device-related complications at 1 year

Principal Investigators: Gregg Stone, Michael Mack
Heart Failure Co-Principal Investigators: William Abraham, JoAnn Lindenfeld

Sponsor: Abbott Vascular

TCT-138

Cardiovascular Outcomes Assessment of MitraClip® Therapy in Heart Failure Patients with Functional Mitral Regurgitation (The COAPT Trial): Baseline Characteristics and Preliminary 2-Year Outcomes of the Roll-In Cohort

Michael Mack,[1] William Abraham,[2] JoAnn Lindenfeld,[3] Neil Weissman,[4] Steven Marx,[5] Jeff Ellis,[6] Lori Anne Crosson,[7] Yu Shu,[8] Hong Nie,[6] Gregg Stone[9]

METHODS Subjects enrolled in COAPT have ≥3+ FMR, are symptomatic despite maximally tolerated guideline-directed medical therapy, and have LVESD ≤70 mm and LVEF ≥20% - ≤50%. A Central Eligibility Committee confirms that each subject has been optimally medically treated and will not undergo MV surgery. Endpoints include NYHA Class, Six Minute Walk Distance (6MWD) and echo measures analyzed by an independent core lab.

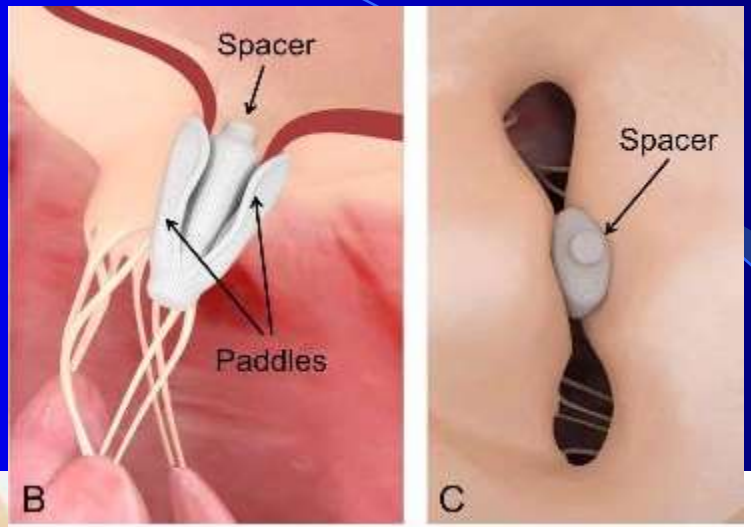
RESULTS 51 roll-in subjects (mean age 75 yrs, 63% male) were enrolled at 34 centers. Baseline co-morbidities included CAD (82%), renal disease (63%), prior CABG (53%) and COPD (43%). Mean STS score was 11±7% and 71% were NYHA class III/IV. Baseline 3+/4+ FMR was present by core lab analysis in 55%/45% of patients (65% due to ischemic cardiomyopathy (CM), 35% idiopathic CM). LVEF was 37±11% and mean 6MWD was 235±121m. The Clip implant rate was 94% (mean 1.3 Clips), 30-day complications were infrequent, and 30-day mortality was zero. Adverse events and functional measures were assessed through 2 years (Table).

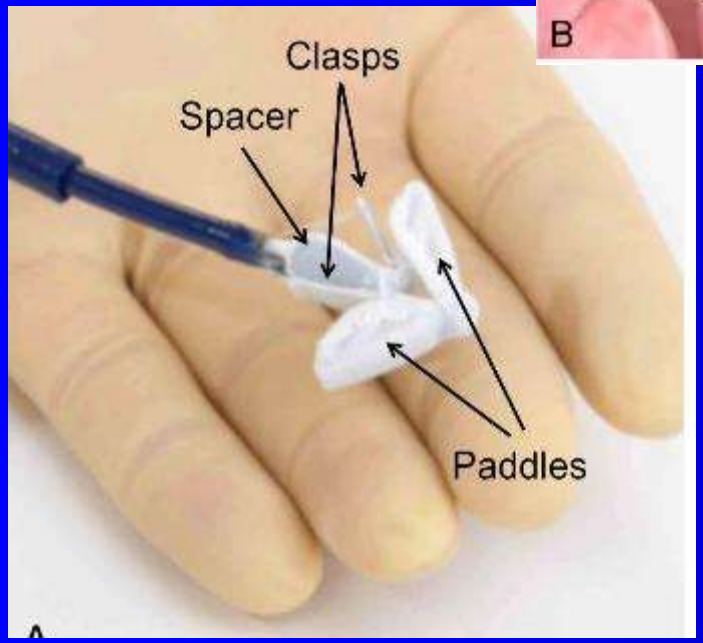
Outcome

	30 Days	1 Year	2 Years
Death	0% (0/51)	16.0% (8/50)	23.9% (11/46)
Stroke	0% (0/51)	2.0% (1/50)	4.3% (2/46)
Heart failure hospitalization	11.8% (6/51)	28.0% (14/50)	37.0% (17/46)
NYHA class III/IV	44.0% (22/50)	31.6% (12/38)	44.8% (13/29)
NYHA improvement by ≥1 class	56.0% (28/50)	60.5% (23/38)	41.4% (12/29)
MR ≤2+ (core lab)	80.9% (38/47)	82.9% (29/35)	80.8% (21/26)
Change in LV end-diastolic volume (ml)	-2 ± 26 (36/39 paired)	-7 ± 33 (22/23 paired)	-2 ± 42 (18/18 paired)
Change in 6MWD (m)	13 ± 112 (45/46 paired)	15 ± 94 (32/32 paired)	28 ± 95 (24/24 paired)
Change in KCCQ overall summary score	14 ± 26 (49/49 paired)	13 ± 17 (37/37 paired)	12 ± 21 (27/27 paired)

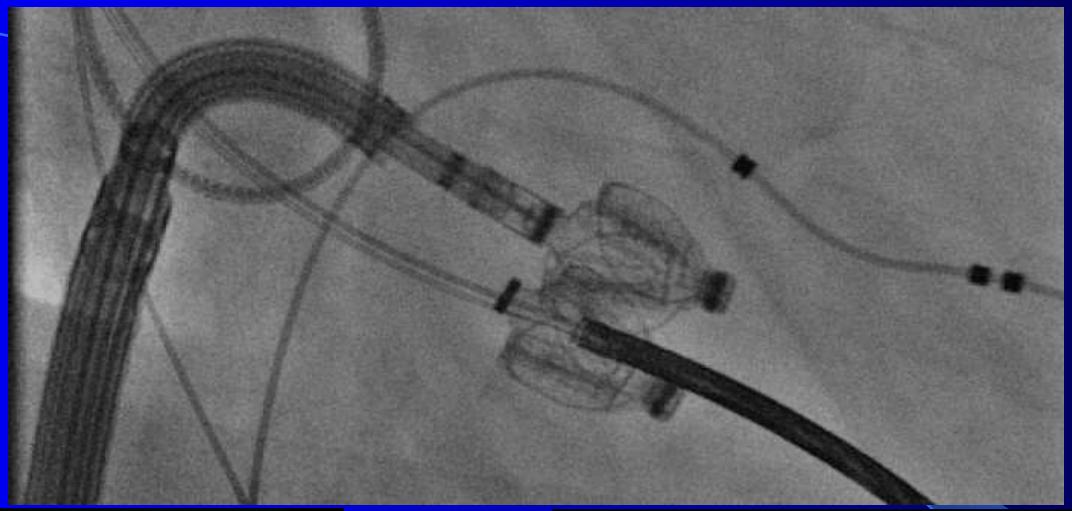
COAPT results are expected to be available in the last quarter of 2018

Other “clips”

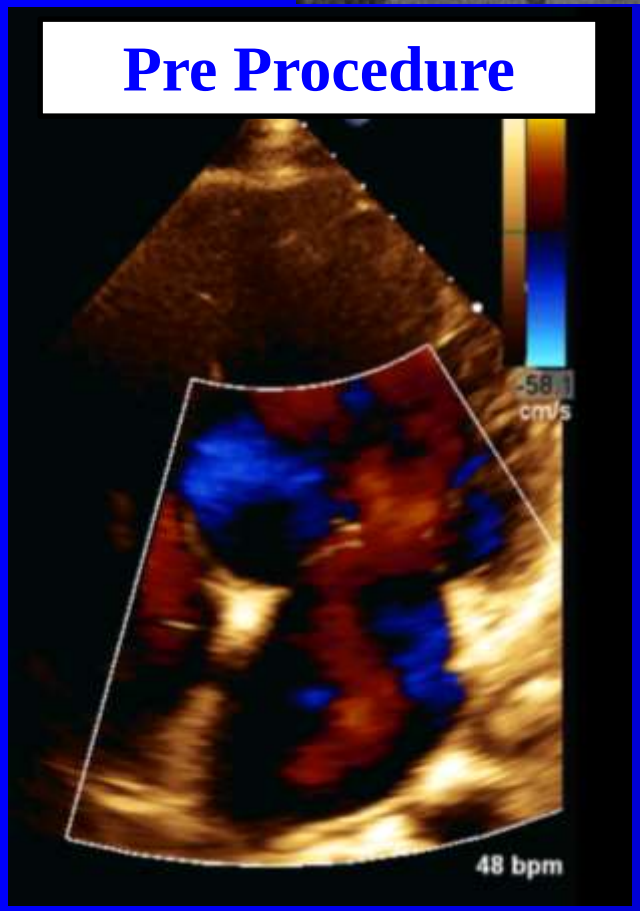




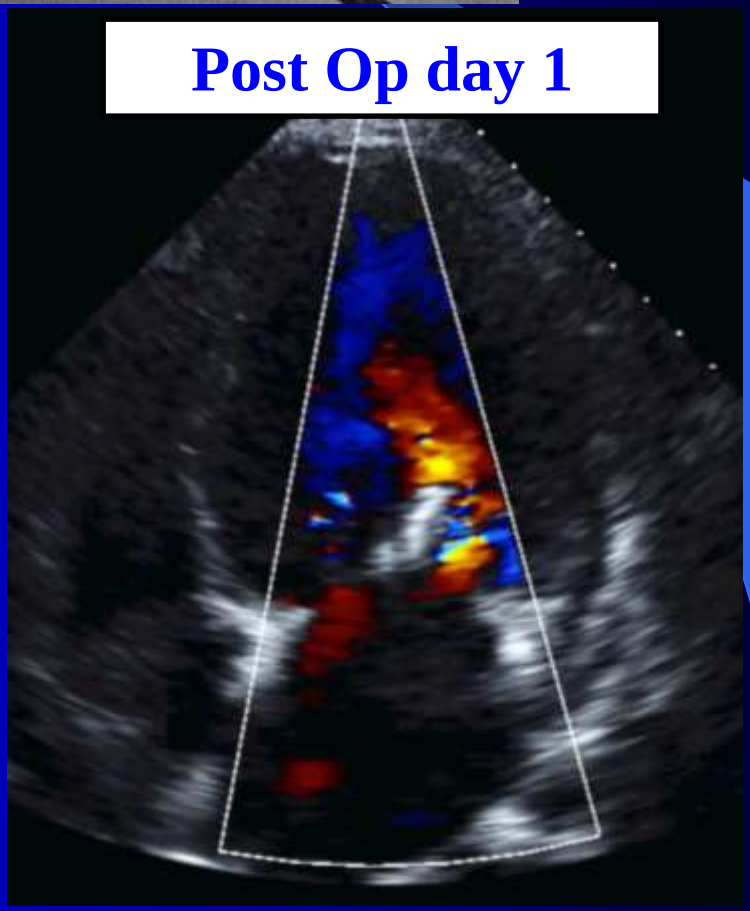
Edwards PASCAL Repair System



Pre Procedure



Post Op day 1



The CLASP Study
Edwards PASCAL TrAnScatheter Mitral Valve RePair System Study
Study 2016-05

Study Overview

CLASP

Study Design: Multi-center (up to 15 sites), multinational, prospective, single arm, safety and clinical outcome study

N= 130 subjects
Adult subjects with clinically significant, symptomatic, mitral regurgitation who are at hight risk for standard mitral repair or replacement, or for whom surgery whill not be offered as a treatment option as assessed by the Heart Team.

FUP: 30 days, 6 months, 1 year, 2 years, 3 years

Primary Endpoint: hierarchical composite of all-cause mortality or recurrent heart failure hospitalization at 6 months

Clinical Experience with PASCAL:

- As of today **N= 27** Compassionate Use Cases or Special Access Cases performed worldwide
- Late Breaking Trial presentation at EuroPCR 2017 and accepted publication in Lancet

	Sites
Australia	**The Prince Charles Hospital, Brisbane, Australia**
	Royal Prince Alfred Hospital, Campertown, Australia
Canada	St. Michael's Hospital, Toronto, Canada
	St. Paul's Hospital, Vancouver, Canada
	Sunnybrook Health Sciences Centre, Toronto, Canada
Germany	Universitäts Krankenhaus Eppendorf, Hamburg, Germany
	Universitätsklinik Bonn, Bonn, Germany
Greece	Hygeia Hospital, Athens, Greece
Italy	San Raffaele, Milano, Italy
Switzerland	Inselspital, Universitätsspital Bern, Bern, Switzerland
	Universität Zürich, Zurich, Switzerland

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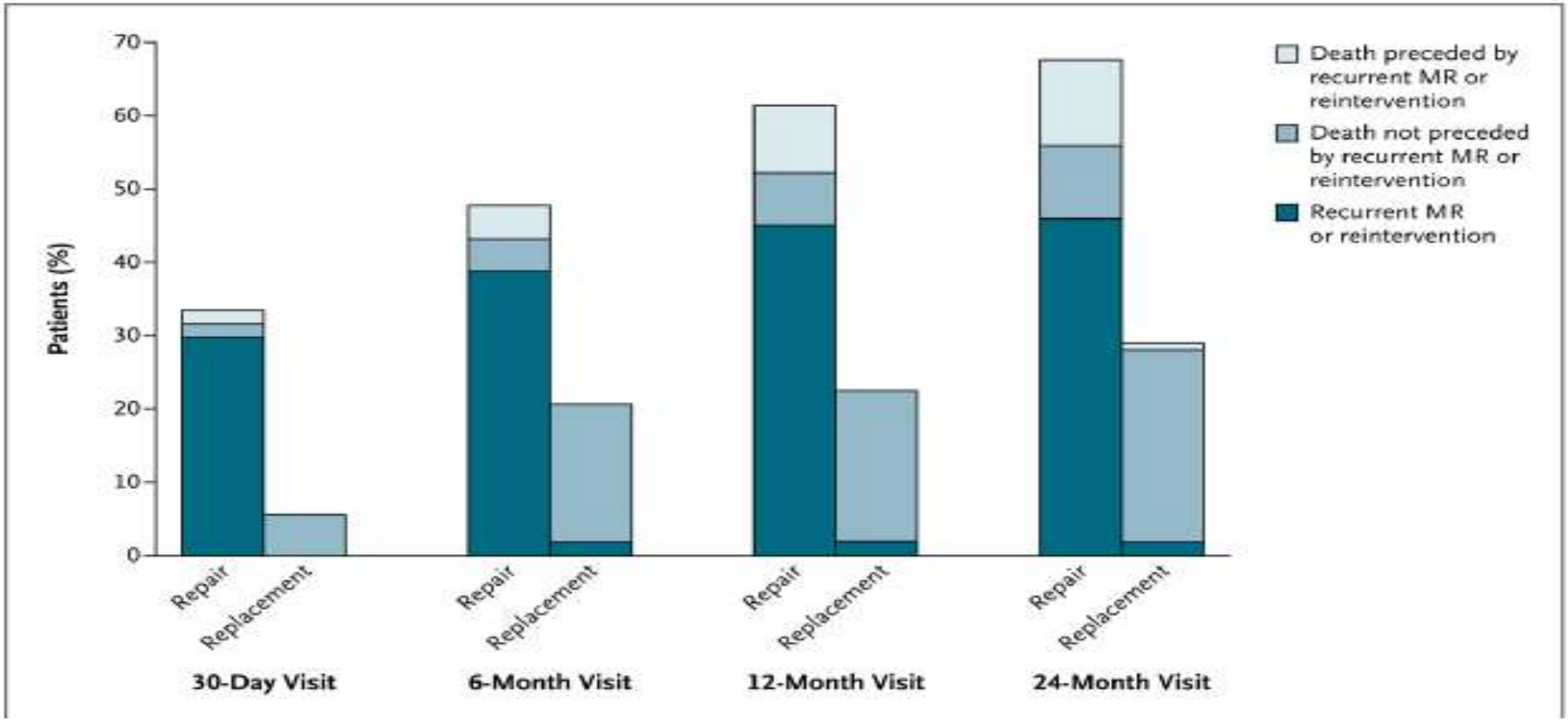

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TMVR First in Human Experience

12 cases
Feasibility Trial
pending

Edwards CardiAQ
June 2012

24 cases
Feasibility Trial
CE Mark Trial

Neovasc Tiara
Jan 2014

38 cases
Pivotal Trial

Medtronic Intrepid
Nov 2014

5 cases
Feasibility Trial

Highlife
Feb 2016

>10 cases

Edwards M3
Aug 2017

Abbott Tendyne
Feb 2013

>50 cases
Feasibility Trial
completed
EU CE Mark Trial

Edwards Fortis
Feb 2014

23 cases
Program
Discontinued

NaviGate
Oct 2015

Caisson
June 2016

< 10 cases
Feasibility Trial

Patient selection and indications

	FMR	
	Low risk	High risk
Best medical care	Yes	Yes
Surgical repair or replacement	Yes	?
Transcatheter repair	?	Current practice COAPT trial
TMVR	no	?
Heart transplant	Meet criteria	

Interdisciplinary Rounds
Decision-making

- Interventional cardiologists
- Cardiac surgeons (Valve repair surgeon)
- Echocardiologist
- Radiologist
- Anesthetist
- THV nurses
- Other specialists

Centre for
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