Controversies and Hot Topics

MitraClip Will Be the Dominant Therapy in Severe FMR - Predicting COAPT

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COEX

Seoul, Korea

NorthShore University HealthSystem
Evanston Hospital

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Disclosure Information

The following relationships exist:

Grant support: Abbott, BSC, Cardiokinetics, Edwards, WL Gore
Consultant: Abbott, BSC, Mitralign, WL Gore

Off label use of products and investigational devices will be discussed in this presentation

Therapy for MR

	Degenerative	**Functional**
Low Surgical Risk	Surgical Mitral Repair	?
High Surgical Risk	Commercial MitraClip	Global Practice COAPT

Clinical Outcomes Assessment of the MitraClip Percutaneous Therapy for High Surgical Risk

COAPT TRIAL

~430 patients enrolled at up to 75 US sites

Significant FMR ≥3+ core lab; EF<50%; CHF hospitalization or BNP>300

High risk for mitral valve surgery- Local Heart Team

Specific valve anatomic criteria

Randomize 1:1

MitraClip

Control group Standard of care

Safety: Composite death, stroke, worsening renal function, LVAD implant, heart transplant at 12 months

Effectiveness: Recurrent heart failure hospitalizations

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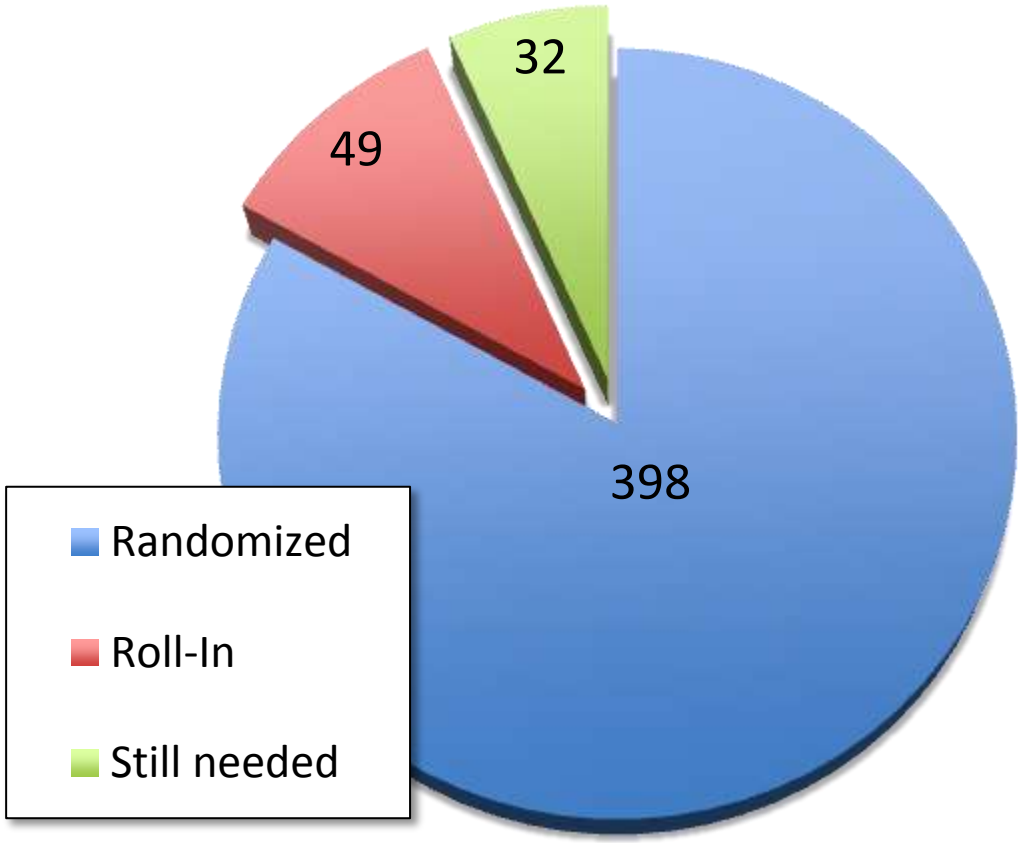
COAPT Enrollment Apr 25, 2016

83 active sites



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Key **Inclusion** Criteria (ii)

- The subject has had at least 1 HF hospitalization in the 12 months prior to enrollment and/or a corrected BNP ≥300 pg/ml or nT-proBNP ≥1500 pg/ml measured within 90 days prior to registration
- Subject has been adequately treated per applicable standards for CAD, LV dysfunction, MR or HF (CRT, revascularization, and/or GDMT)
- The primary regurgitant jet is non-commissural. If secondary jets exist, they must be considered clinically significant.
- Creatinine obtained within prior 14 days less than local laboratory upper limit of normal (ULN)

Clinical Investigational Plan 11-512: Version 6.0, September 8, 2014, approved by FDA October 15, 2014.

Primary Endpoints

Primary Effectiveness

- Recurrent heart failure hospitalizations through 24 months (analyzed when last subject completes 12 months follow-up)

Primary Safety

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

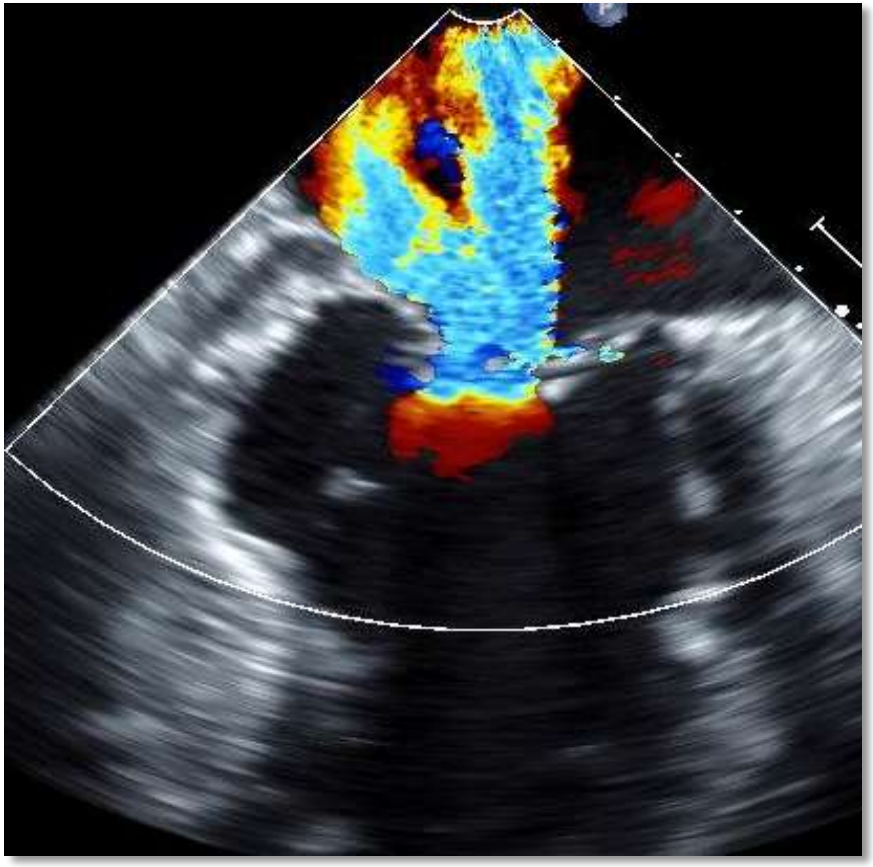
Clinical Investigational Plan 11-512: Version 6.0, September 8, 2014, approved by FDA October 15, 2014.

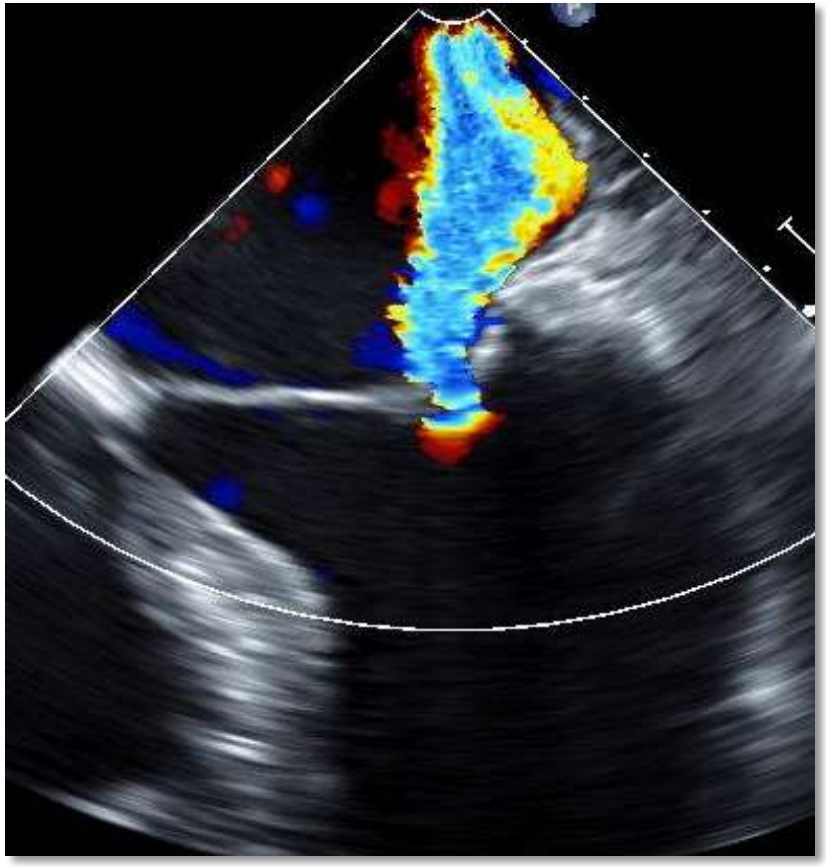
COAPT will be positive!

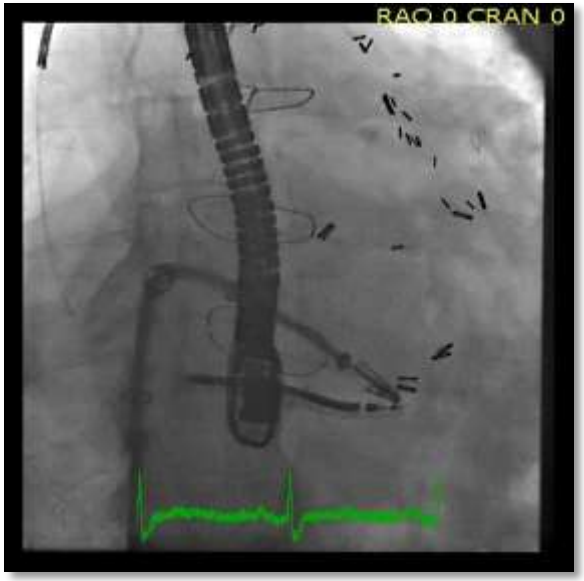
COAPT Case Example

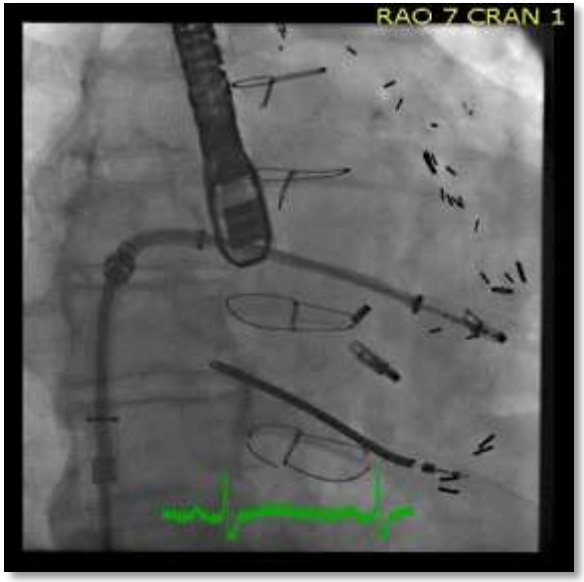
- a 72YO male with history of prior posterior, inferior and lateral MI, CABG with patent grafts
- severe mitral regurgitation and acute and chronic systolic and diastolic heart failure, LVEF 45%
- recent HF hospitalization was 1/5-1/9/2015 with weight gain, LE edema, SOB with exertion and BNP > 2500
- STS risk score for replacement: 10.9% and for repair: 7.35%

TEE Pre









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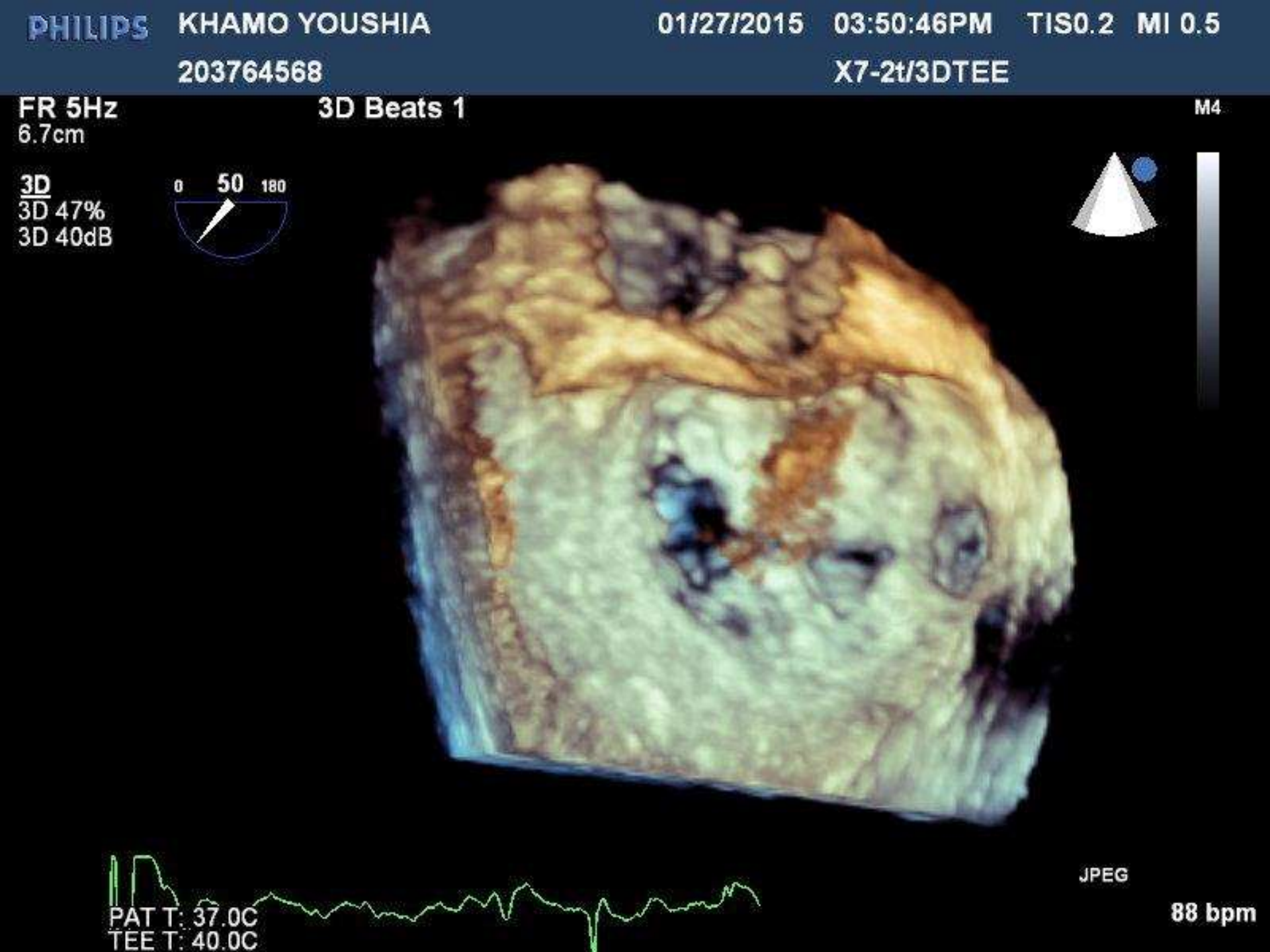
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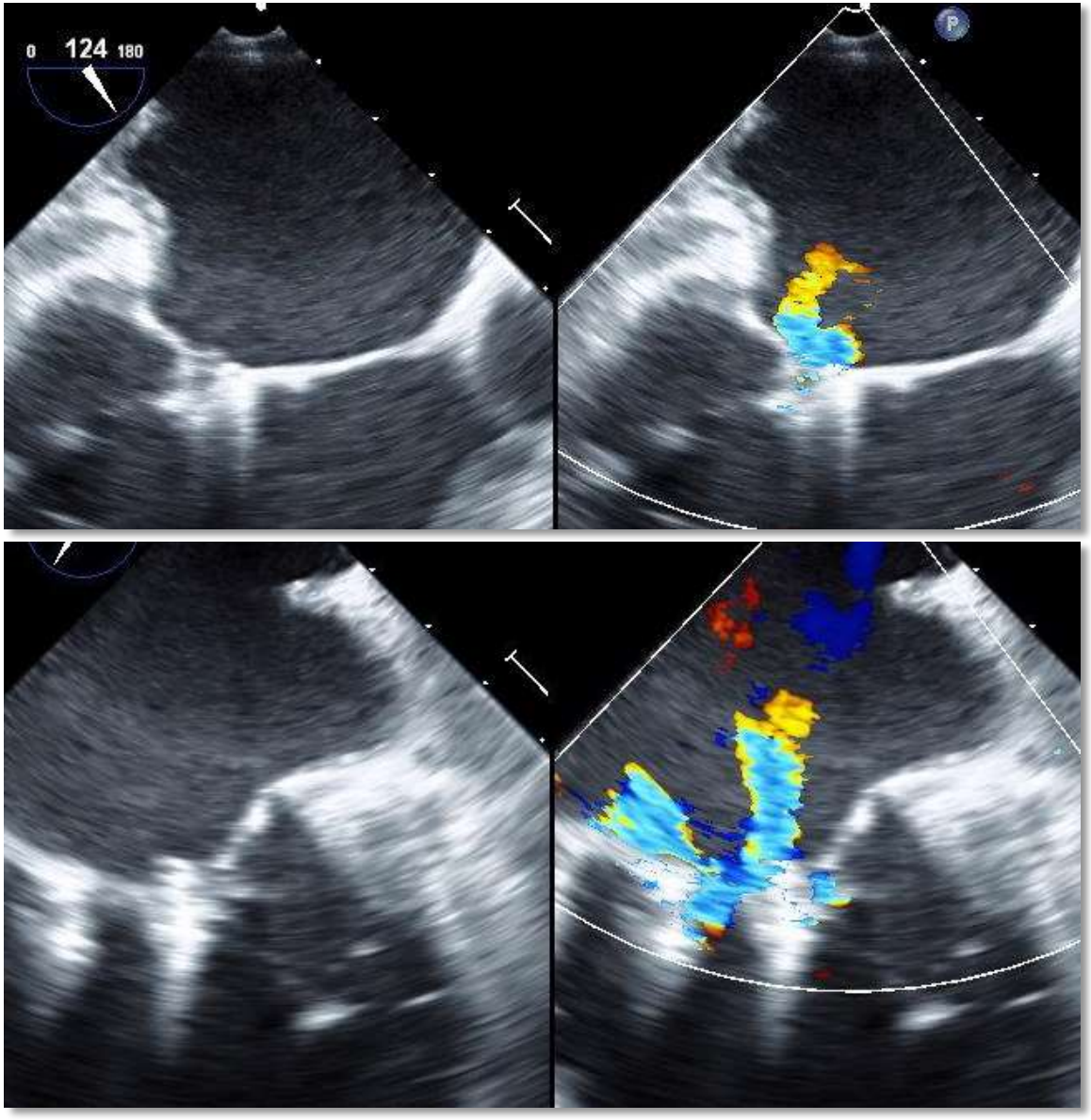

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Percutaneous Mitral Valve Repair for Mitral Regurgitation in High-Risk Patients

Results of the EVEREST II Study

Donald
Ramon
Michae

RESULTS In the studies, 327 of 351 patients completed 12 months of follow-up. Patients were elderly (76 ± 11 years of age), with 70% having functional MR and 60% having prior cardiac surgery. The mitral valve device reduced MR to ≤2+ in 86% of patients at discharge ($n = 325$; $p < 0.0001$). Major adverse events at 30 days included death in 4.8%, myocardial infarction in 1.1%, and stroke in 2.6%. At 12 months, MR was ≤2+ in 84% of patients ($n = 225$; $p < 0.0001$). From baseline to 12 months, left ventricular (LV) end-diastolic volume improved from 161 ± 56 ml to 143 ± 53 ml ($n = 203$; $p < 0.0001$) and LV end-systolic volume improved from 87 ± 47 ml to 79 ± 44 ml ($n = 202$; $p < 0.0001$). New York Heart Association functional class improved from 82% in class III/IV at baseline to 83% in class I/II at 12 months ($n = 234$; $p < 0.0001$). The 36-item Short Form Health Survey physical and mental quality-of-life scores improved from baseline to 12 months ($n = 191$; $p < 0.0001$). Annual hospitalization rate for heart failure fell from 0.79% pre-procedure to 0.41% post-procedure ($n = 338$; $p < 0.0001$). Kaplan-Meier survival estimate at 12 months was 77.2%.

The percutaneous mitral valve device significantly reduced MR, improved clinical symptoms, and decreased LV dimensions at 12 months in this high-surgical-risk cohort.

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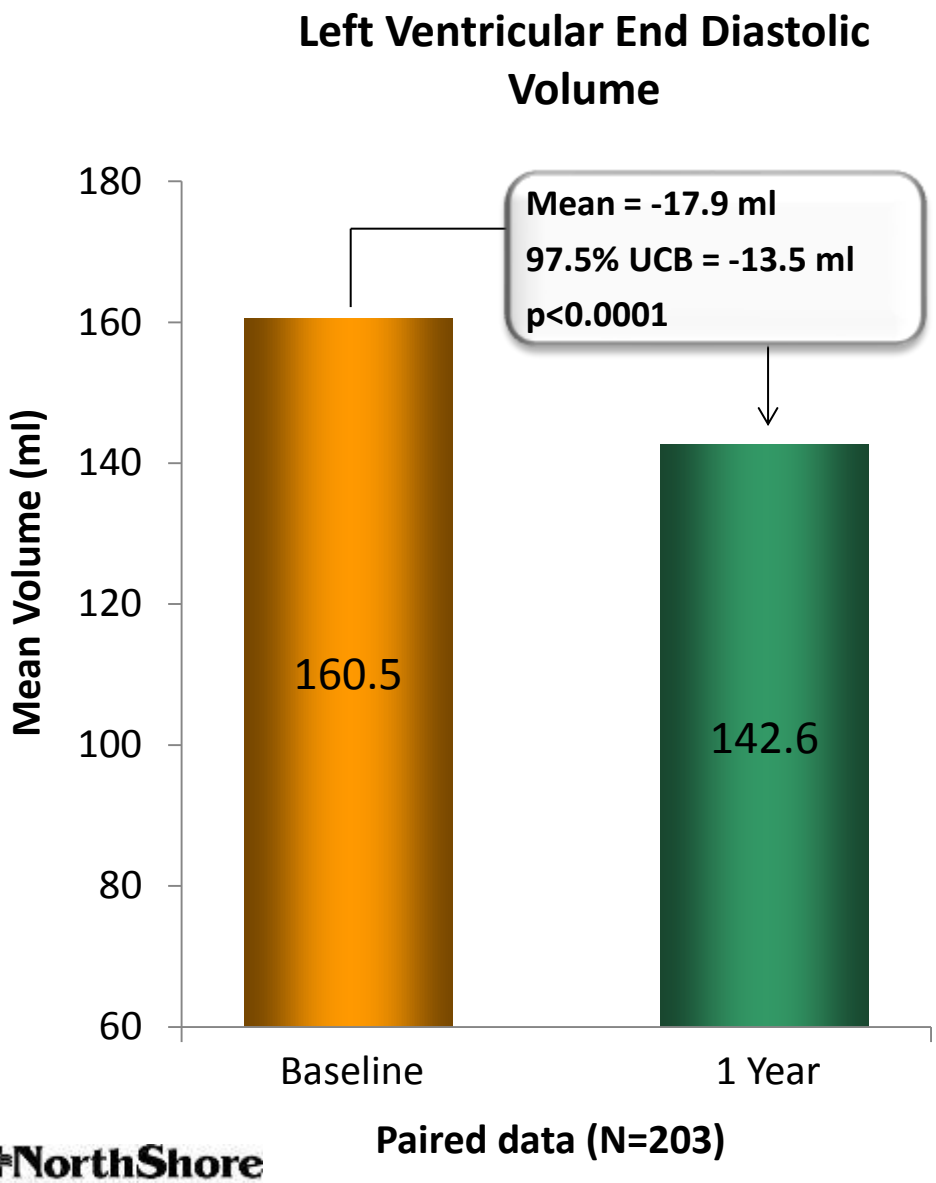
J Am Coll Cardiol 2014;64:172–81

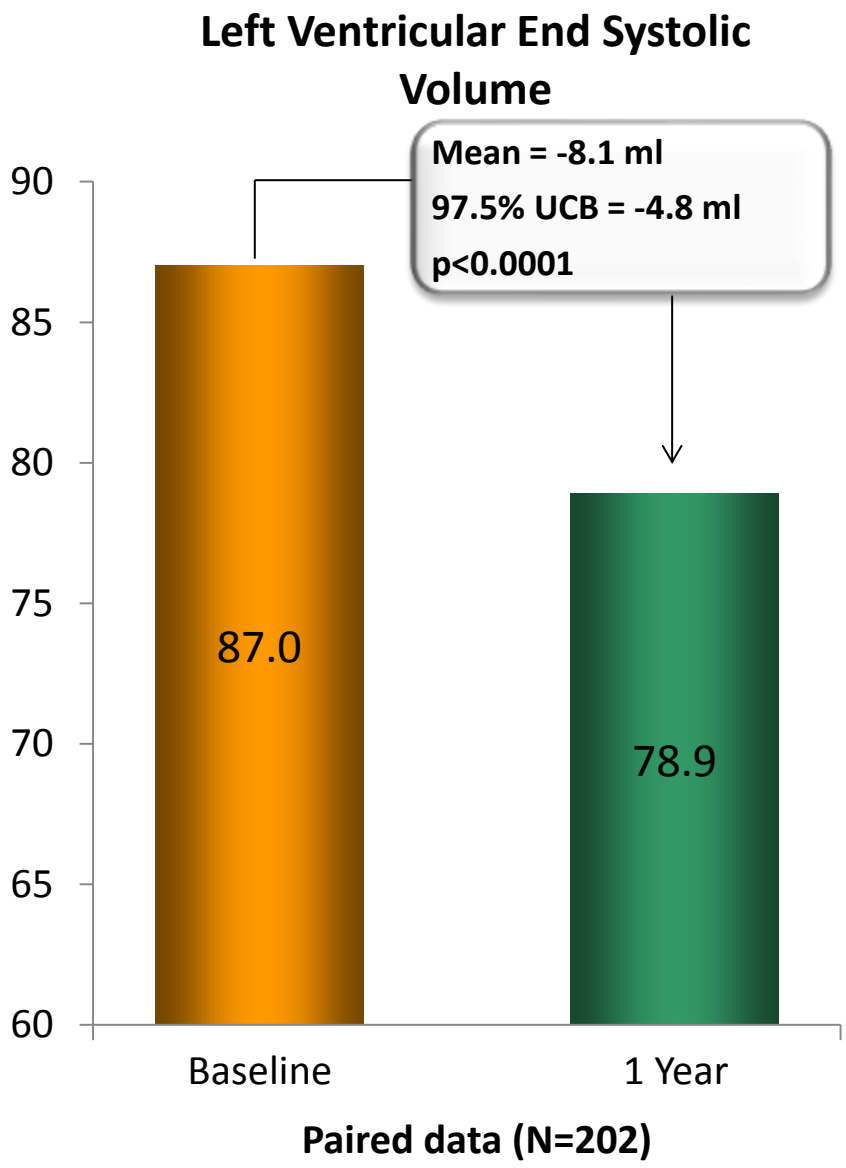
The EVEREST II High Surgical Risk Cohort

	n=351
Age	76 ± 11
Predicted Surgical Mortality Risk, (%)	18.2±8.4
NYHA Functional Class III or IV	85%
Atrial Fibrillation	69%
Mitral Regurgitation Grade ≥ 3+	86%
Left Ventricular Ejection Fraction (%)	47.5 ± 14.2
Functional MR	70%
30 day Mortality	6.8%
Home ± home health care	91.7 %
MR Grade I-II at 2 years	87%
Decrease LV EDV/ESV at 1 year	17.9 / 8.1 ml
Event Free Survival 1 year	77.1%

ACC 2013

Left Ventricular Volumes





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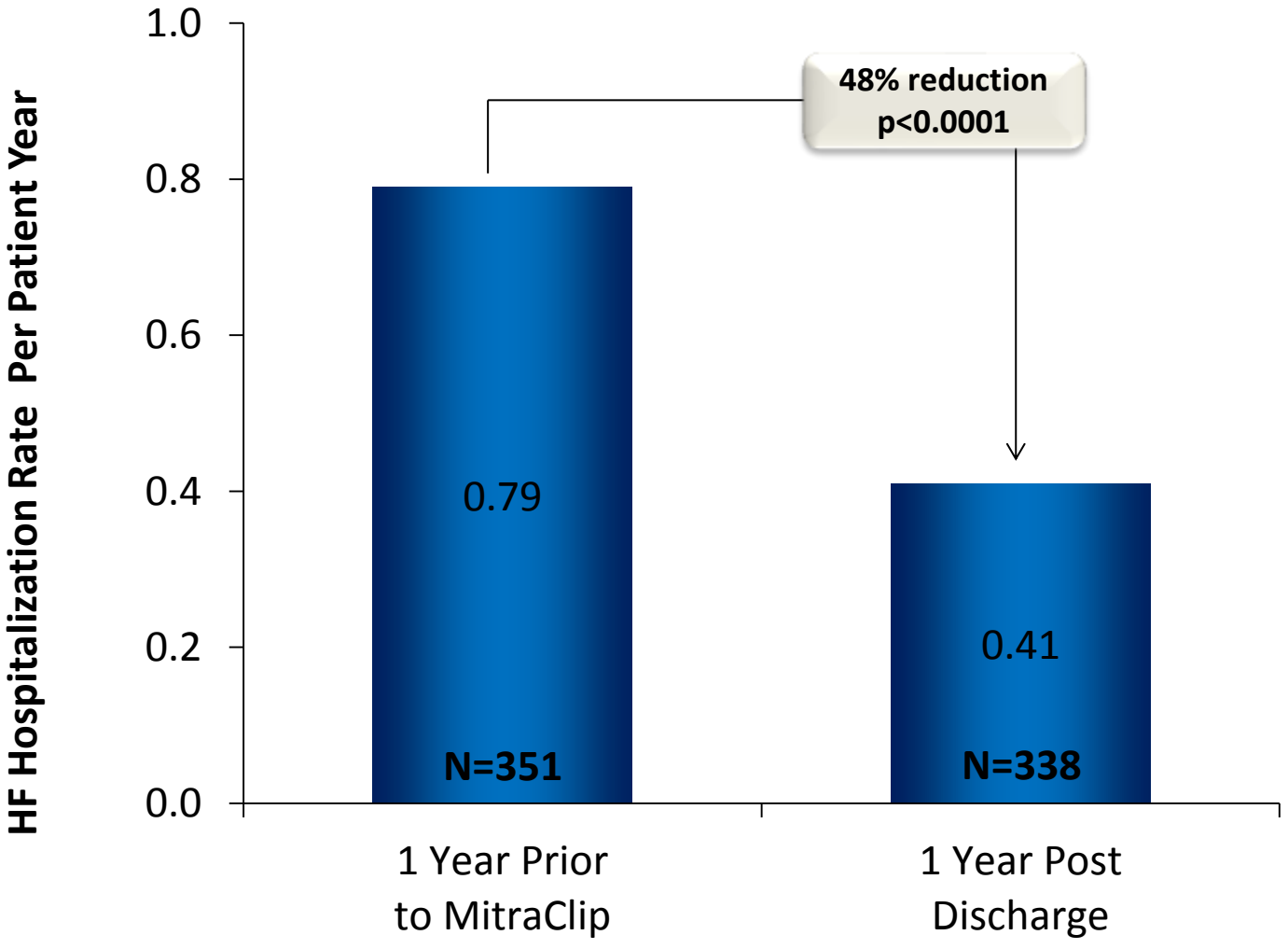
Hospitalizations for Heart Failure



Registries

Prospective-Multicenter

Study	n
REALISM US Continued Access	899
REALISM Compassionate/Emergency Use	66
ACCESS Europe Phase I	567
ACCESS Europe Phase II	286
German Transcatheter Mitral Valve Interventions (TRAMI)	1002
GRASP-It	304
MitraSwiss registry nationwide	265
Sentinel Registry EURObservational Research Programme ESC	628
MitraClip Asia-Pacific Registry (MARS)	145
ANZ MitraClip Registry	45

COAPT will be positive **??**

The EVEREST II High Surgical Risk Cohort

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Event Free Survival 1 year	77.1%

ACC 2013

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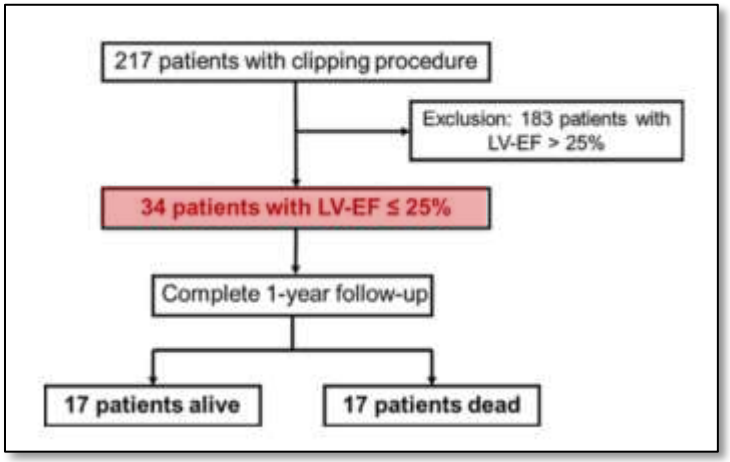
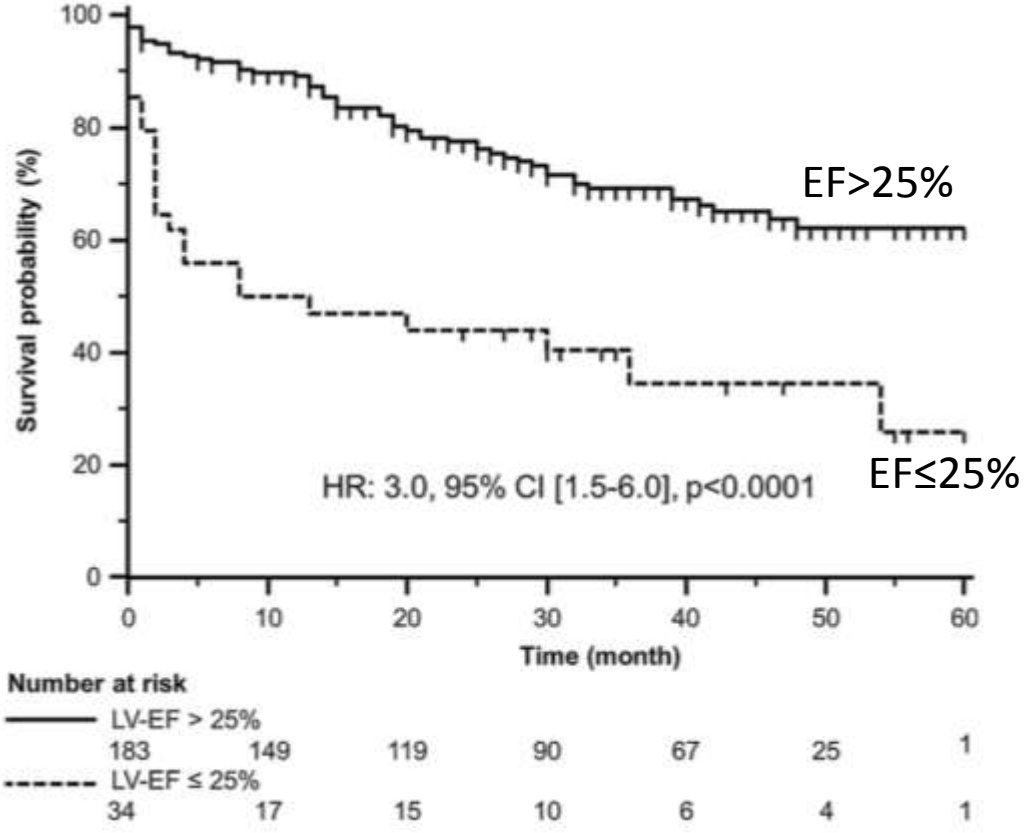
Long-Term Outcome of Patients with Severe Biventricular Heart Failure after MitraClip

Predictive valve of LVEF



None of the patients met the inclusion criteria of EVEREST II



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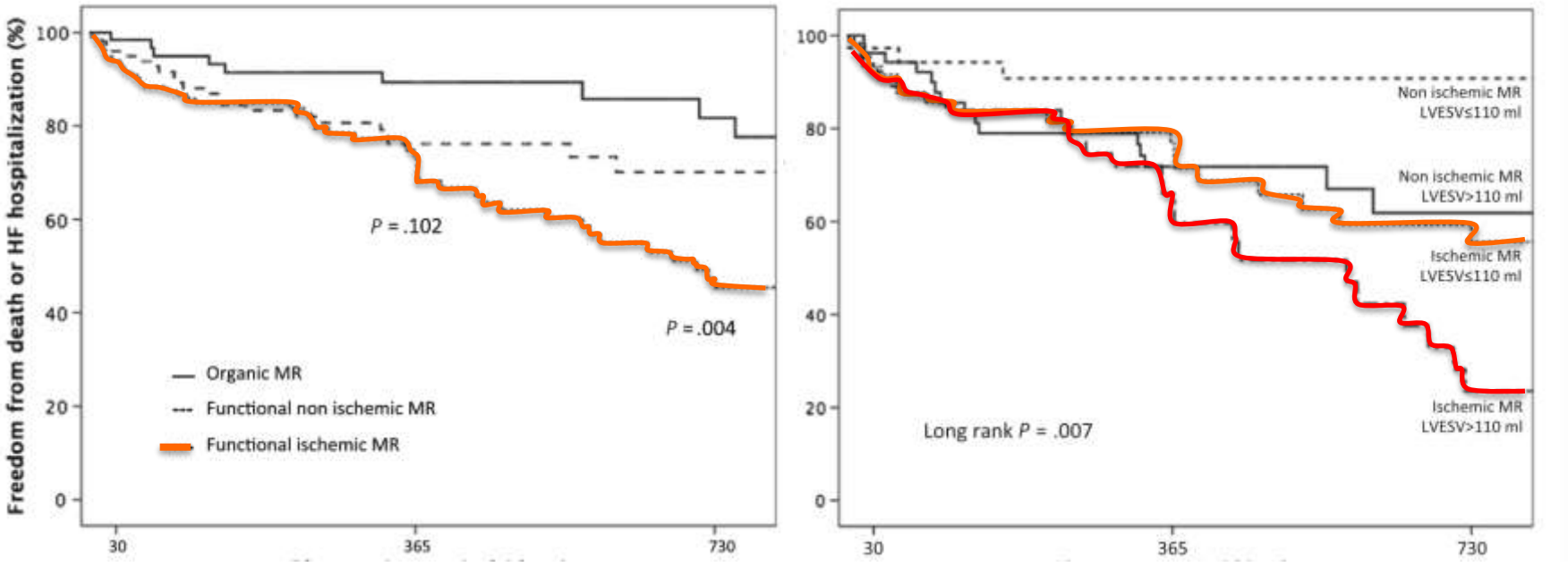
J Interven Cardiol 2015;28:164–171

Predictors of outcome after edge-to-edge percutaneous mitral valve repair



Baseline ischemic functional etiology, severely dilated ventricles, or advanced heart failure and those undergoing unsuccessful procedures carried the worst prognosis

n=304

Capodanno D: Am Heart J 2015;170:187-95

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Key **Inclusion** Criteria (ii)

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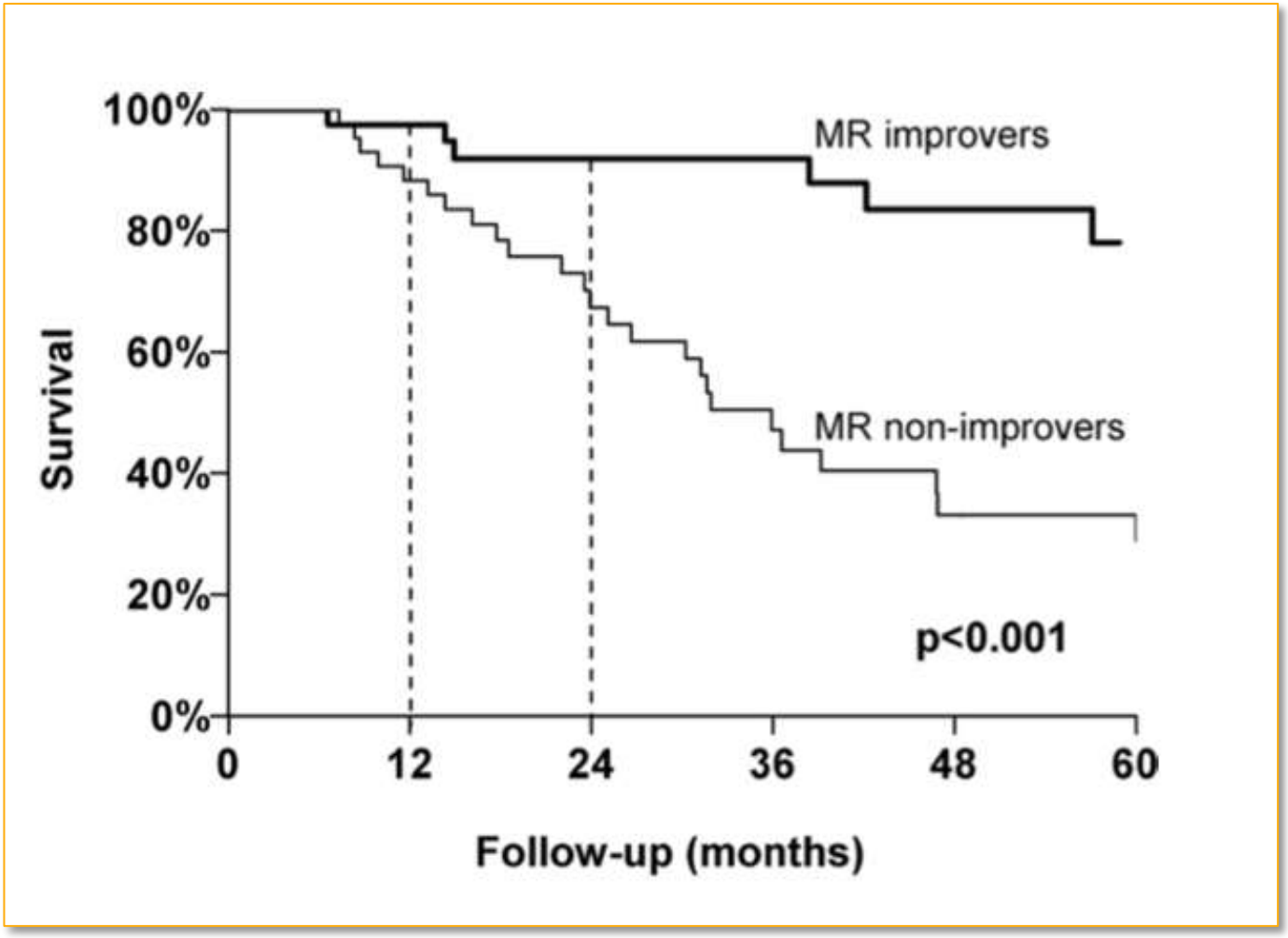
- Subject has been adequately treated per applicable standards for CAD, LV dysfunction, MR or HF (CRT, revascularization, and/or GDMT)
- The primary regurgitant jet is non-commissural. If secondary jets exist, they must be considered clinically significant.
- CrCl as obtained within prior 14 days less than local laboratory upper limit of normal (ULN)

Clinical Investigational Plan 11-512: Version 6.0, September 8, 2014, approved by FDA October 15, 2014.

CRT in Patients With Moderate-Severe Functional MR and High Operative Risk (2)



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Circulation. 2011;124:912-919

Correction of Mitral Regurgitation in Nonresponders to Cardiac Resynchronization Therapy by MitraClip Improves Symptoms and Promotes Reverse Remodeli

Angelo Auricchio, MD, PHD,* Wolfgang Schillinger, MD,† Sven Meyer, MD,‡
Francesco Maisano, MD,§ R
Giovanni B. Pedrazzini, MD
Catherine Klersy, MD, MSc
on behalf of the PERMIT-C

Lugano, Switzerland; Götting
Milan, Catania, L'Aquila, an

n	51
Age years	70±9
Ischemic etiology	73%
STS %	13.9±15
LVEF (echo) %	27±9

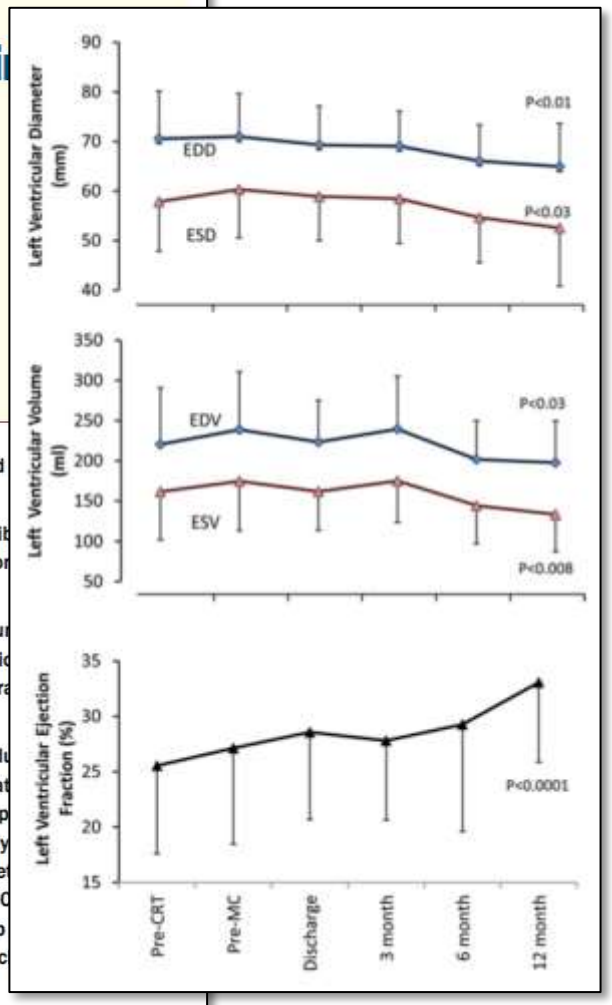
Objectives This study e … and remodeling …

Background Moderate to … ntrit… no response… lition… tion in select patients with significant FMR.

Methods Fifty-one severely symptomatic CRT nonresponders with significant FMR (grade ≥2, 100%) u… treatment. Changes in New York Heart Association functional class, degree of FMR, LV ejectio… LV end-diastolic/end-systolic volumes (EDV/ESV) before and after (3, 6, and 12 months) Mitra… were recorded. Mortality data, including cause of death, were collected.

Results MC treatment was feasible in all patients (49% 1 clip, 46% 2 clips). There were 2 periprocedu… follow-up was 14 months (25th to 75th percentile: 8 to 17 months). New York Heart Associat… improved acutely at discharge (73%) and continued to improve progressively during follow-up… $p < 0.001$). The proportion of patients with significant residual FMR (grade ≥2) progressively… follow-up (regression model, $p < 0.001$). Reverse LV remodeling and improved LVEF were de… with further improvement at 12 months (regression model, $p = 0.001$, $p = 0.008$, and $p = 0$… and LVEF, respectively). Overall 30-day mortality was 4.2%. Overall mortality during follow-up… person-years (95% confidence interval: 10.3 to 38.3). Nonsurvivors had more compromised c… ditions, longer QRS duration, and a more dilated heart.

Conclusions FMR treatment with the MitraClip in CRT nonresponders was feasible, safe, and demonstrated improved functional class, increased LVEF, and reduced ventricular volumes in about 70% of these study patients. (J Am Coll Cardiol 2011;58:2183–9) © 2011 by the American College of Cardiology Foundation



J Am Coll Cardiol 2011;58:2183–9

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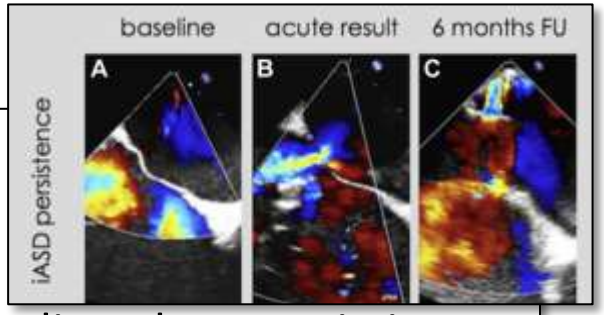
Persistence of Iatrogenic ASD After MitraClip

A Note of Caution



- 66 patients
- persistent iASD in 50% of cases
- patients with iASD not different vs without ASD baseline characteristics
- procedures took longer for iASD (82±39.7min vs. 68.9±45.5 min; p<0.05)
- less decrease of PASP for iASD (1.6±14.1 mmHg vs. 9.3±17.4 mmHg; p 0.02)
- Patients with iASD
  - more often NYHA Class >II after FU (57% vs. 30%; p 0.04)
  - higher levels of N-terminal pro-BNP(6,667.3±7,363.9 ng/dl vs. 4,835.9±6,681.7 ng/dl; p<0.05)
  - less improvement in 6-min walking distances (20.8±107.4 m vs. 114.6±116.4 m; p<0.001).
- **Patients with iASD showed higher death rates during 6 months** (16.6% vs. 3.3%; p<0.05).
  - Cox regression found that only persistence of iASD (p<0.04) associated with 6-month survival.

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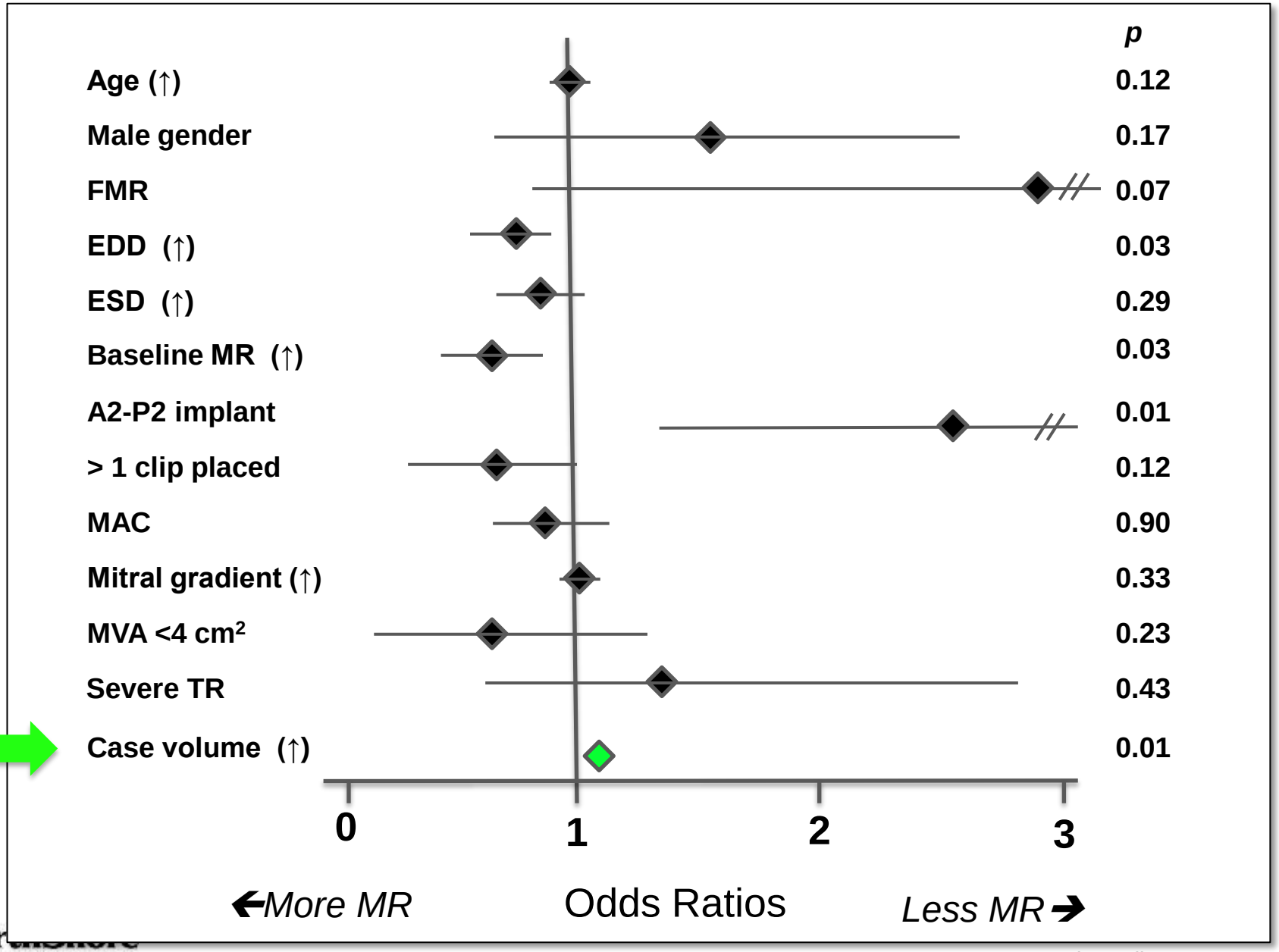
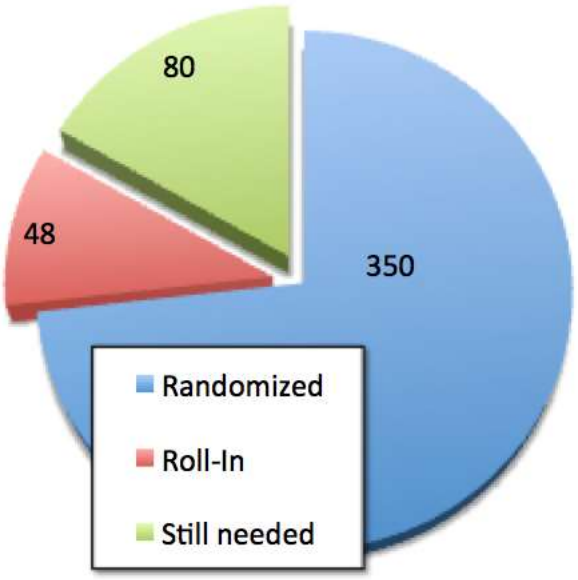
Schueler R, Öztürk C, Wedekind JA, Werner N, Stöckigt F, Mellert F, Nickenig G, Hammerstingl C. JACC Cardiovasc Interv. 2015 Mar;8(3):450-9

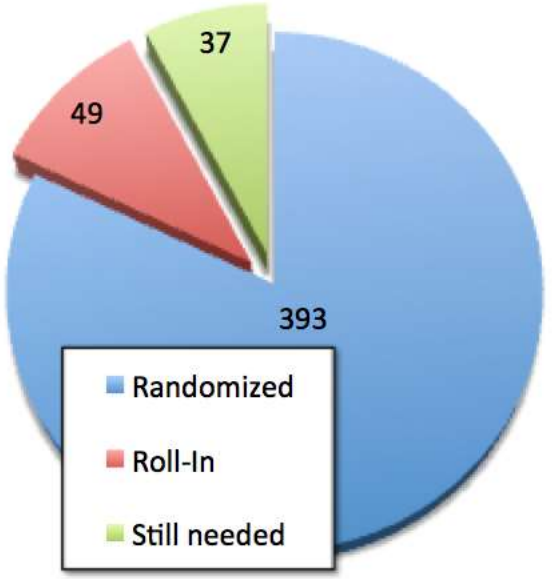
TVT Registry: Residual MR



COAPT Enrollment



Feb 16th
81 active sites



Apr 11th
83 active sites

MitraClip RCTs in Functional MR

1348 patients

Heart failure and FMR

MitraClip vs. GDMT or MV Surgery

- **COAPT – 430**
- **MITRA-FR – 288**
- **RESHAPE-HF-2 – 420**
- **MATTERHORN (vs MVS) –210**