Mitral Clip-Ready for Primetime?

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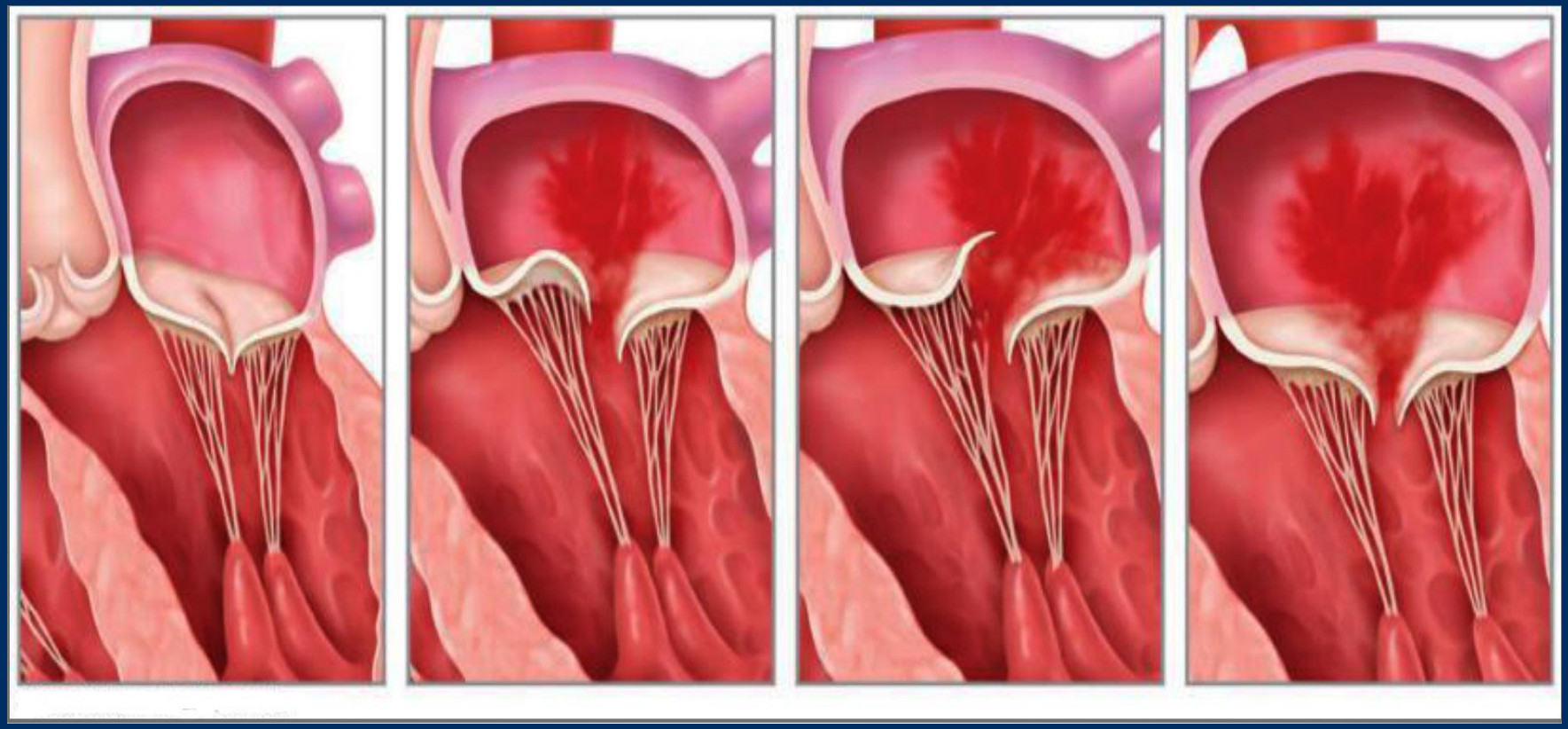
Disclosures

- Chiesi Pharma-Cosultant

Objectives:

- Overview mitral valve regurgitation as a problem.
- Review data for Mitral clip approval and indications.
- Identify patients that may be candidates for Mitral Clip.

Etiology of Mitral Regurgitation (MR)



Normal

Degenerative MR
- Prolapse

Degenerative MR
- Flail

Functional MR
Ischemic vs. Non-ischemic

- Due to dilated LV, mitral annulus or regional disruption of LV, MV apparatus

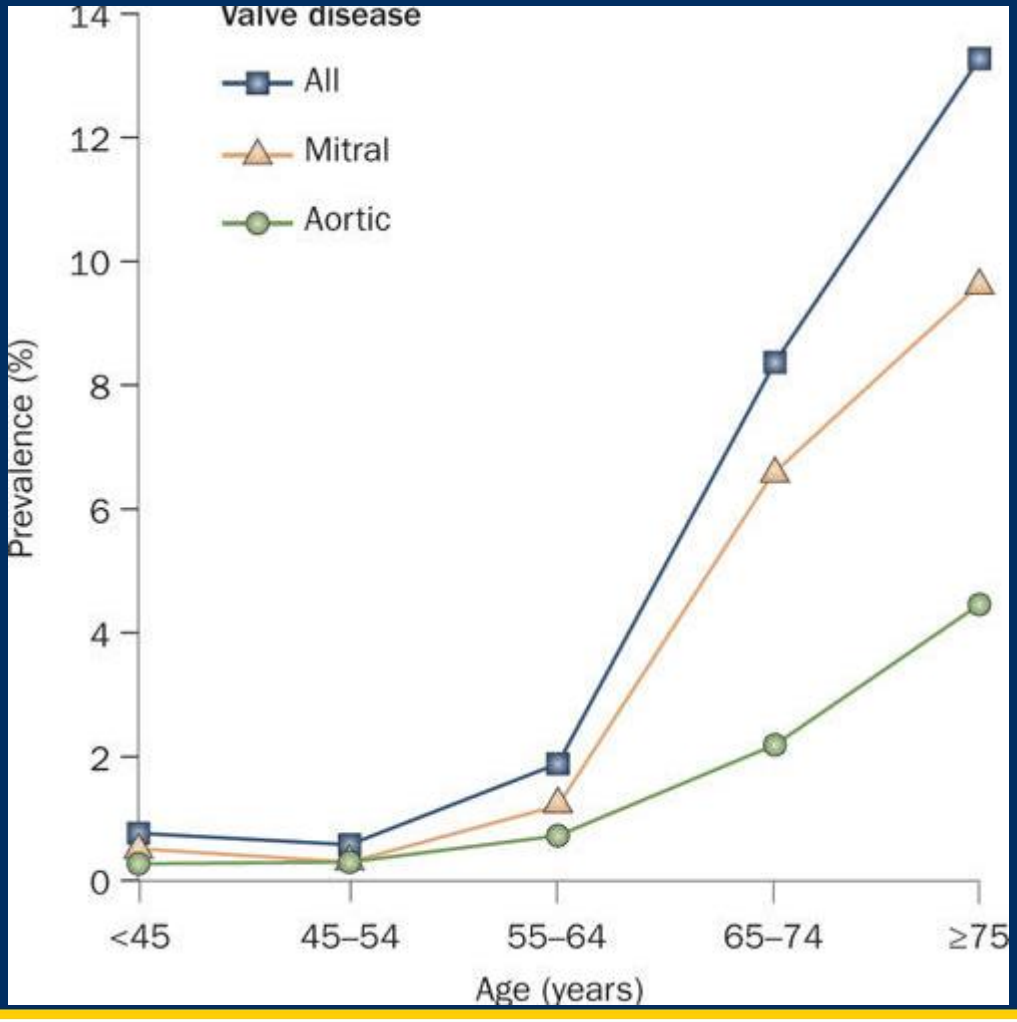
MR Mechanism

- **Degenerative MR**
  - Also known as primary or organic MR
  - Usually caused by an anatomic defect of one or more structures comprising the mitral valve apparatus—the annulus, the leaflets, the chordae tendineae, and the papillary muscles
  - "Disease of the mitral valve/apparatus"
- **Functional MR**
  - Also known as secondary MR
  - Results from left ventricular (LV) dysfunction and dilation, which causes otherwise normal valve components to fail and results in MR
  - "Disease of the ventricle"

Source: Enriquez-Sarano, M et al. *Lancet*. 2009;373:1382-94.

Mayo Clinic (www.mayoclinic.com)

Prevalence of Mitral valve disease



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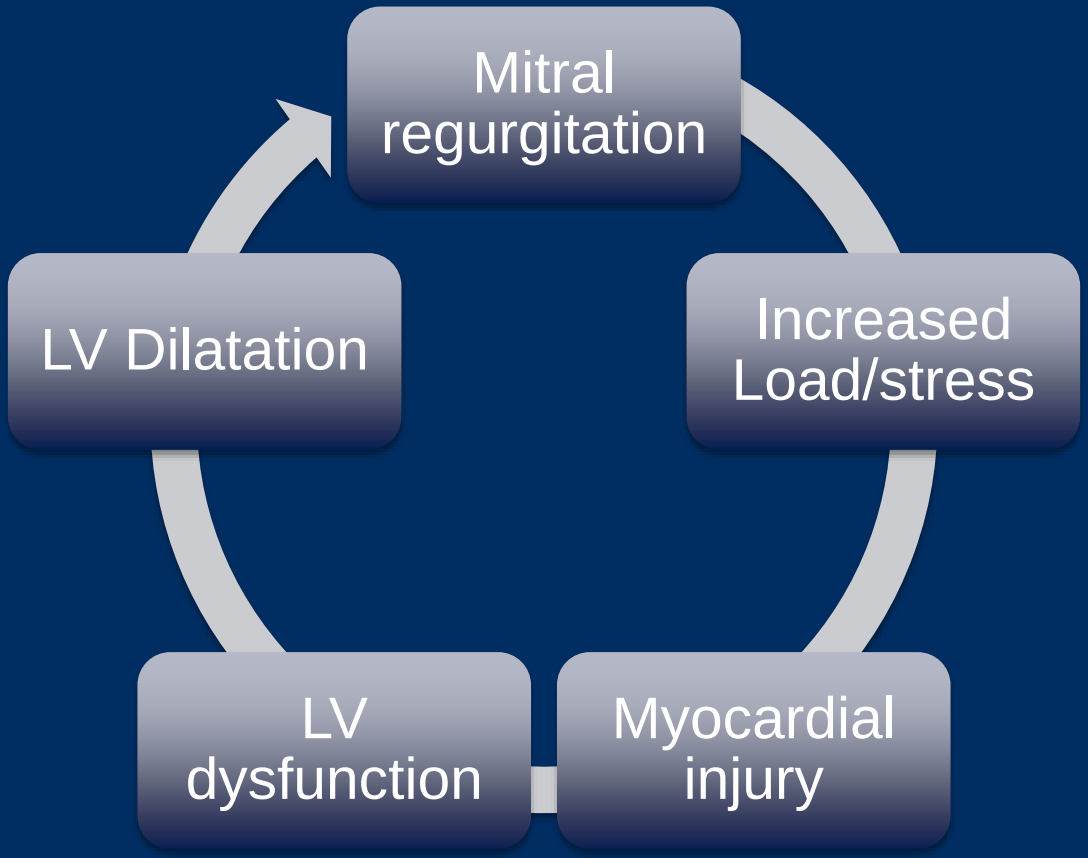
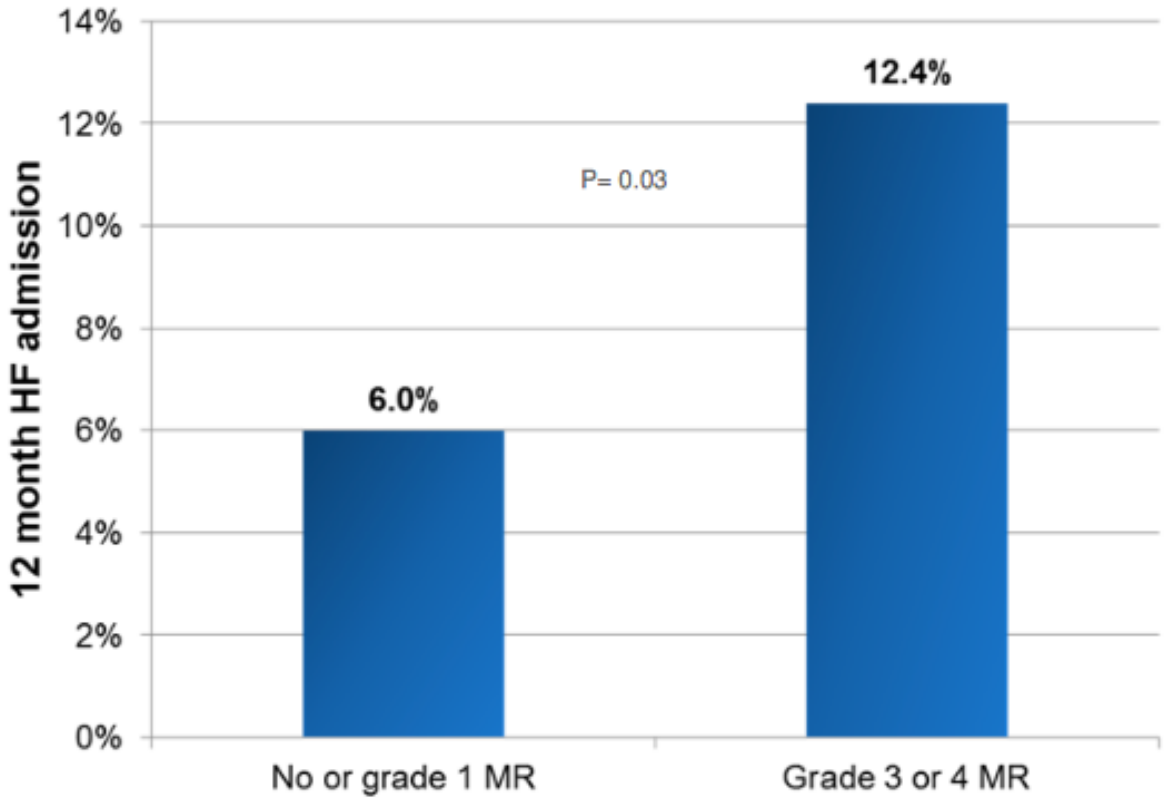
Nkomo et al. Lancet 2006;368:1005-11

Congestive Heart Failure

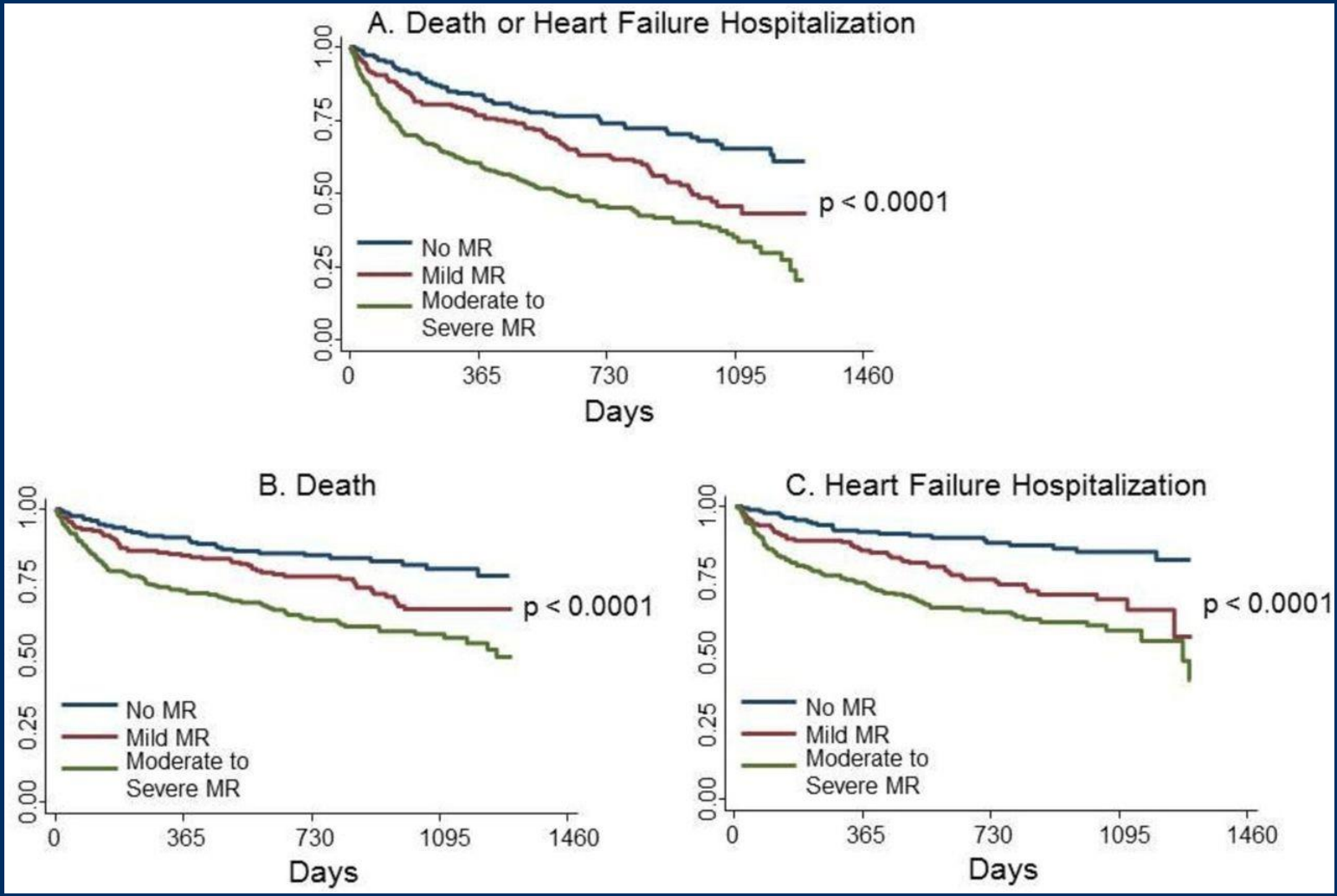


Hospital Admissions for CHF (doubled)



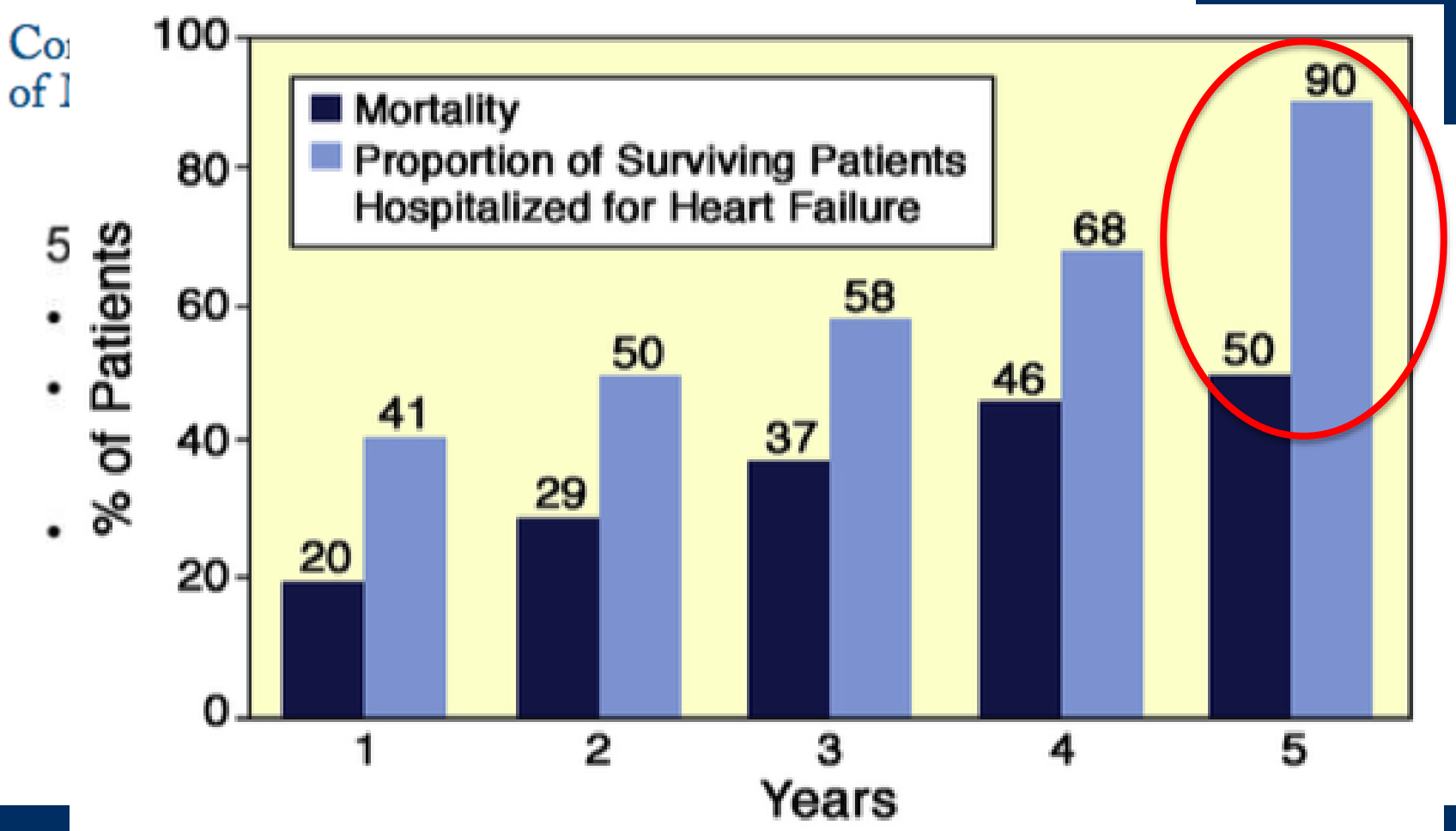
Markwick et al, TCT 2012

Impact of MR on Survival



Samer Mowakeaa et al. Open Heart 2018;5:e000745

Prevalence and Outcomes of Unoperated Patients With Severe Symptomatic Mitral Regurgitation and Heart Failure



Goel et al. JACC 2014 63(2):185-186.

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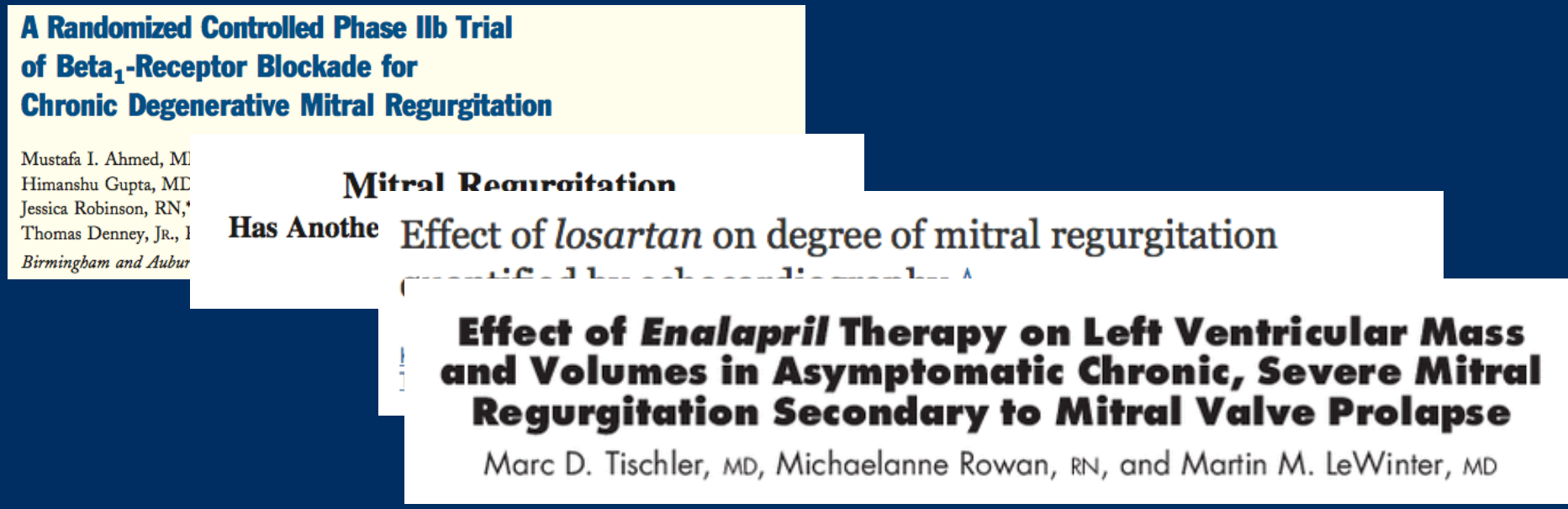
When to consider any intervention?

- Mod-severe mitral valve regurgitation
  - Symptoms (dyspnea) or
  - LV dilatation or reduced EF (<60%) or
  - Pulmonary HTN (PASP >50 mmHg)
  - Asymptomatic (good operator/institution outcomes)

Medical Therapy



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Circulation: Heart Failure. 2013;6:624-626
AJC. 1998;82(2):242-245
Ahmen et al. JACC. 2012;60(9):833-8.

PRACTICE GUIDELINE

2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the American Association for Thoracic Surgery, American Society of Echocardiography, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons

CLASS IIa

1. Medical therapy for systolic dysfunction is reasonable in symptomatic patients with chronic primary MR (stage D) and LVEF less than 60% in whom surgery is not contemplated (382–386). *(Level of Evidence: B)*

CLASS III: No Benefit

1. Vasodilator therapy is not indicated for normotensive asymptomatic patients with chronic primary MR (stages B and C1) and normal systolic LV function (386–391). *(Level of Evidence: B)*

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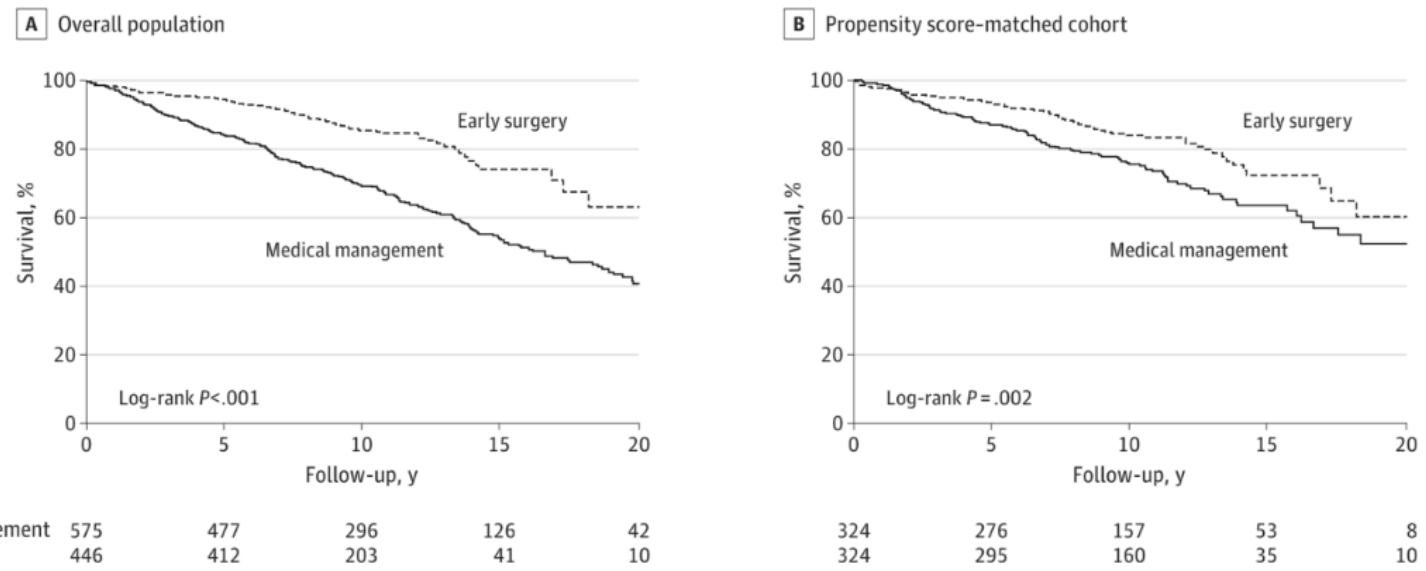
Original Investigation

Association Between Early Surgical Intervention vs Watchful Waiting and Outcomes for Mitral Regurgitation Due to Flail Mitral Valve Leaflets

Rakesh M. Suri, MD, DPhil; Jean-Louis Vanoverschelde, MD; Francesco Grigioni, MD, PhD; Hartzell V. Schaff, MD; Christophe Tribouilloy, MD; Jean-Francois Avierinos, MD; Andrea Barbieri, MD; Agnes Pasquet, MD; Marianne Huebner, PhD; Dan Rusinaru, MD; Antonio Russo, MD; Hector I. Michelena, MD; Maurice Enriquez-Sarano, MD

Figure 1. Survival After Diagnosis of Mitral Regurgitation Due to Flail Mitral Leaflet According to Initial Treatment Strategy



Long-term survival following early surgery vs initial medical management overall population (A) and in the propensity score–matched cohort (B).

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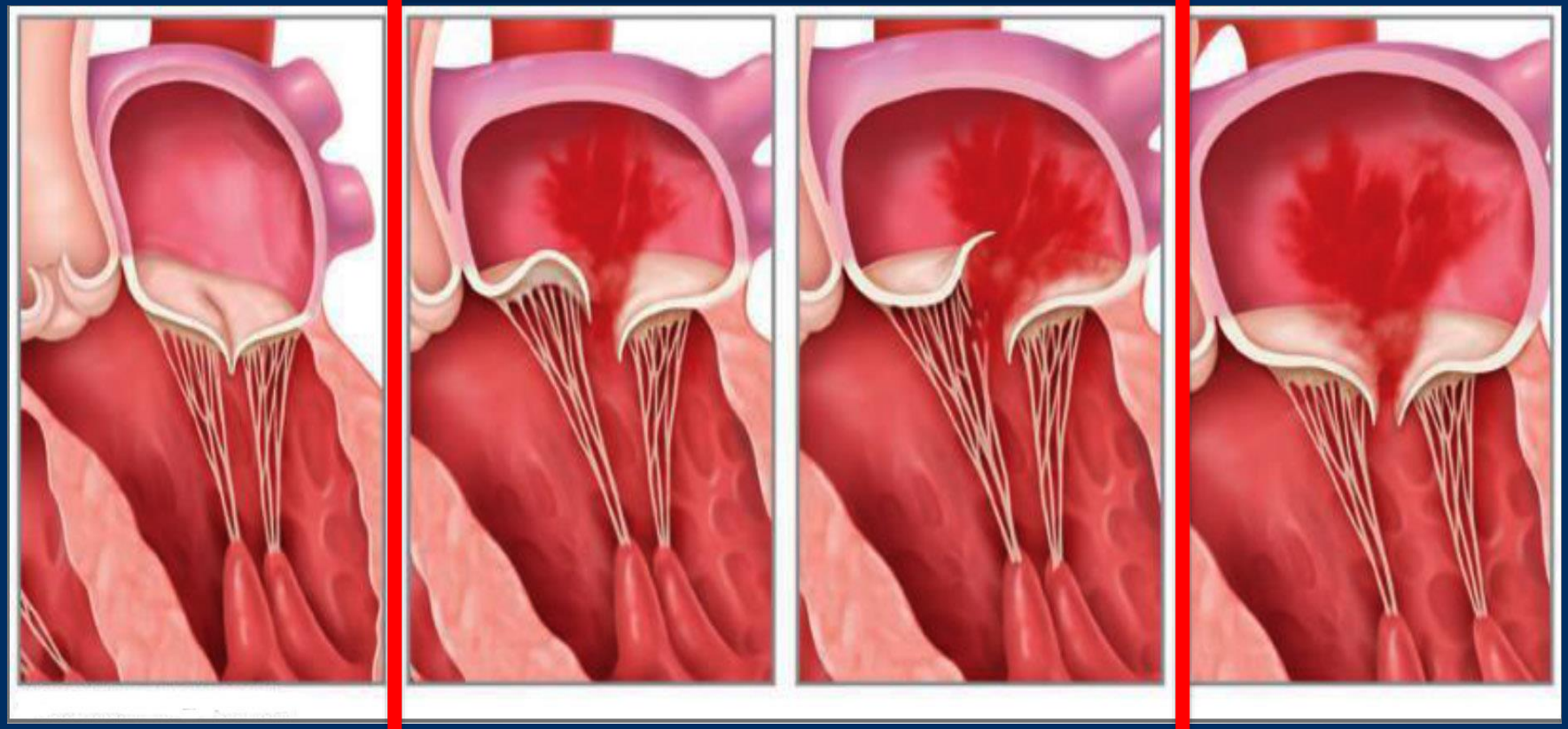
JAMA. 2013;310(6):609-616. doi:10.1001/jama.2013.8643

Etiology of Mitral Regurgitation (MR)



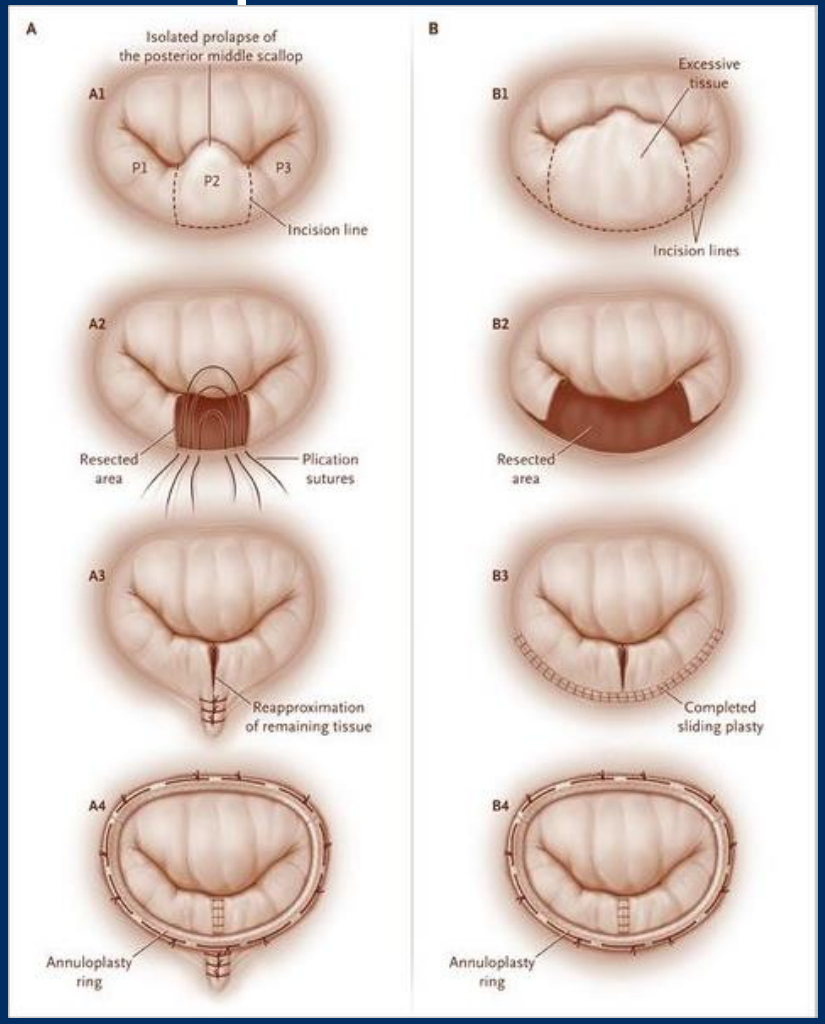
Normal

Degenerative MR
- Prolapse

Degenerative MR
- Flail

Functional MR
Ischemic vs. Non-ischemic

Mitral Valve Repair



http://heartsurgeryinfo.com/minimally-invasive-mitral-valve-repair/

General Principles of Therapy for MR Etiology

Primary MR

No Medical Therapy
(Diuretics palliative)

Surgery for symptoms or LV dysfunction
(Repair > Replacement)

Consider prophylactic repair for low risk with long term survival

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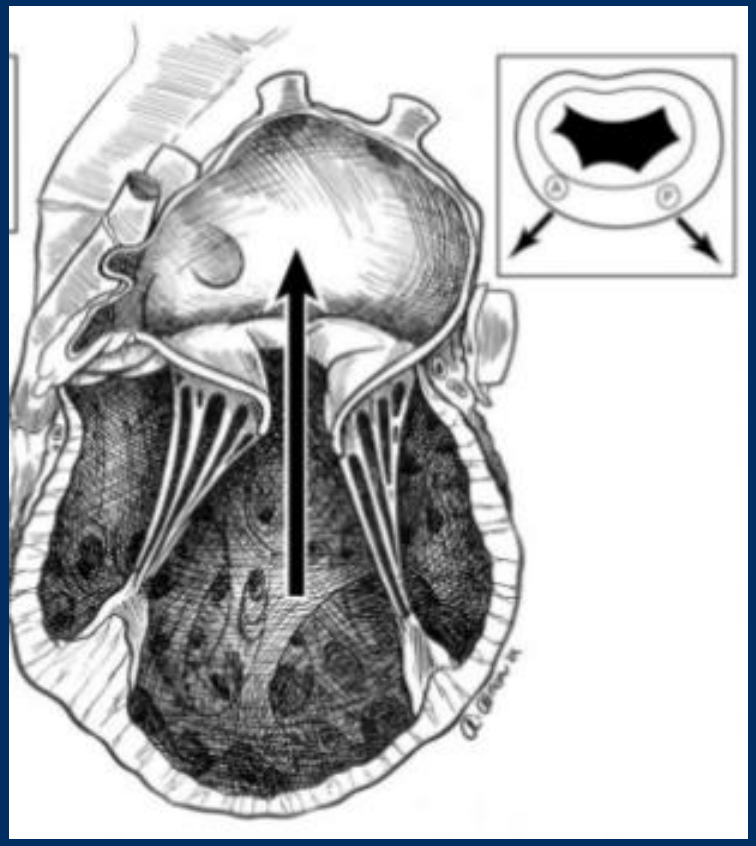
Surgery

	Class	Level
Mitral valve repair should be the preferred technique when it is expected to be durable.	I	C
Surgery is indicated in symptomatic patients with LVEF > 30% and LVESD < 55 mm.	I	B
Surgery should be considered in patients with severe LV dysfunction (LVEF < 30% and/or LVESD > 55 mm) refractory to medical therapy with high likelihood of durable repair and low comorbidity.	IIa	C
Surgery may be considered in patients with severe LV dysfunction (LVEF < 30% and/or LVESD > 55 mm) refractory to medical therapy with low likelihood of durable repair and low comorbidity.	IIb	C

Mitral valve repair is reasonable in asymptomatic patients with chronic severe primary MR (stage C1) with preserved LV function (LVEF >60% and LVESD <40 mm) in whom the likelihood of a successful and durable repair without residual MR is greater than 95% with an expected mortality rate of less than 1% when performed at a Heart Valve Center of Excellence (101,106–112).

General Principles of Therapy for MR Etiology



Secondary MR

Medical

Therapy first

(BB,ACE/ARB, Aldactone, Diuretics)

CRT

Surgery only in highly selected pts with CHF

(Restrictive annuloplasty ring +/- LV restoration)

(Class 3/4 symptomatic and acceptable surgical risk)

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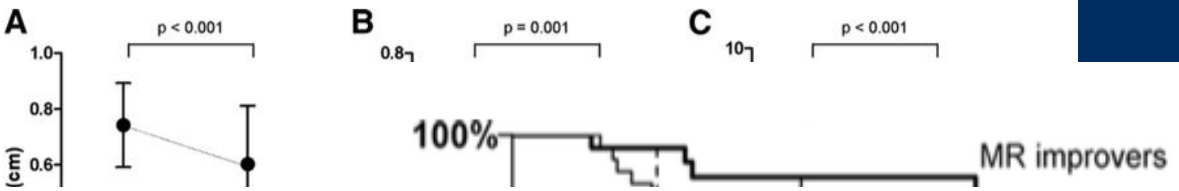
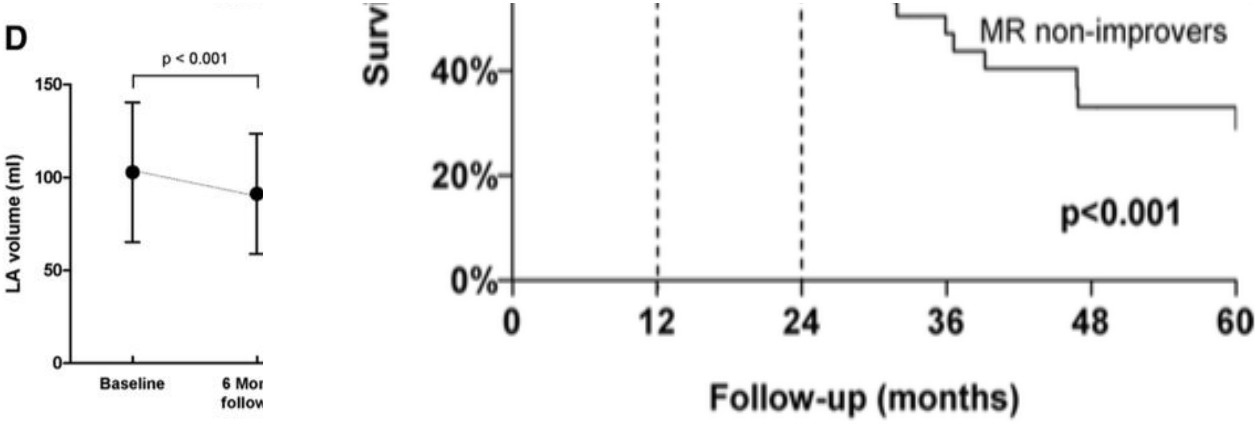
Cardiac Resynchronization Therapy as a Therapeutic Option in Patients With Moderate-Severe Functional Mitral Regurgitation and High Operative Risk

Rutger J. van Bommel, MD; Nina Ajmone Marsan, MD; Victoria Delgado, MD, PhD; C. Jan Willem Borleffs, MD, PhD; Eva P.M. van Rijnsoever, MSc; Martin J. Schalij, MD, PhD; Jeroen J. Bax, MD, PhD



Conclusions—Cardiac resynchronization therapy is a potential therapeutic option in heart failure patients with moderate-severe functional MR and high risk for surgery. Improvement in MR results in superior survival after CRT. (***Circulation*. 2011;124:912-919.**)



Bommel et al. Circulation. 2011;124:912-19

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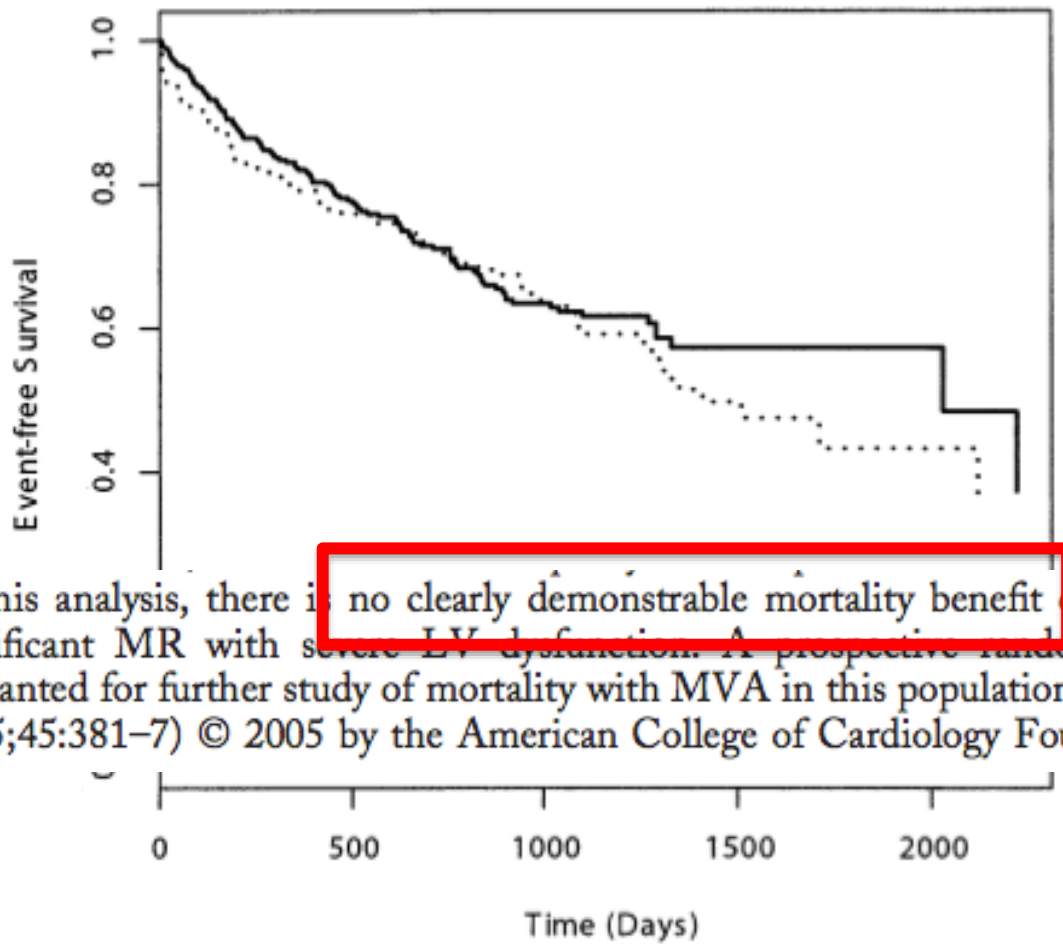
Impact of Mitral Valve Annuloplasty on Mortality Risk in Patients With Mitral Regurgitation and Left Ventricular Systolic Dysfunction



CONCLUSIONS In this analysis, there i no clearly demonstrable mortality benefit onferred by MVA for significant MR with s LV dysfunction. A prospective randomized control trial is warranted for further study of mortality with MVA in this population. (J Am Coll Cardiol 2005;45:381–7) © 2005 by the American College of Cardiology Foundation

Wu et al. JACC;45(3):381-7

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Functional MR

- Main problem is the LV dysnfunction
  - ICMP vs NICMP
- Ofter high risk for surgery
- High recurrence rate after repair
- No improvement in survival

Therefore, there is a need for a less invasive and safer option of FMR patients

Secondary/function MR

	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

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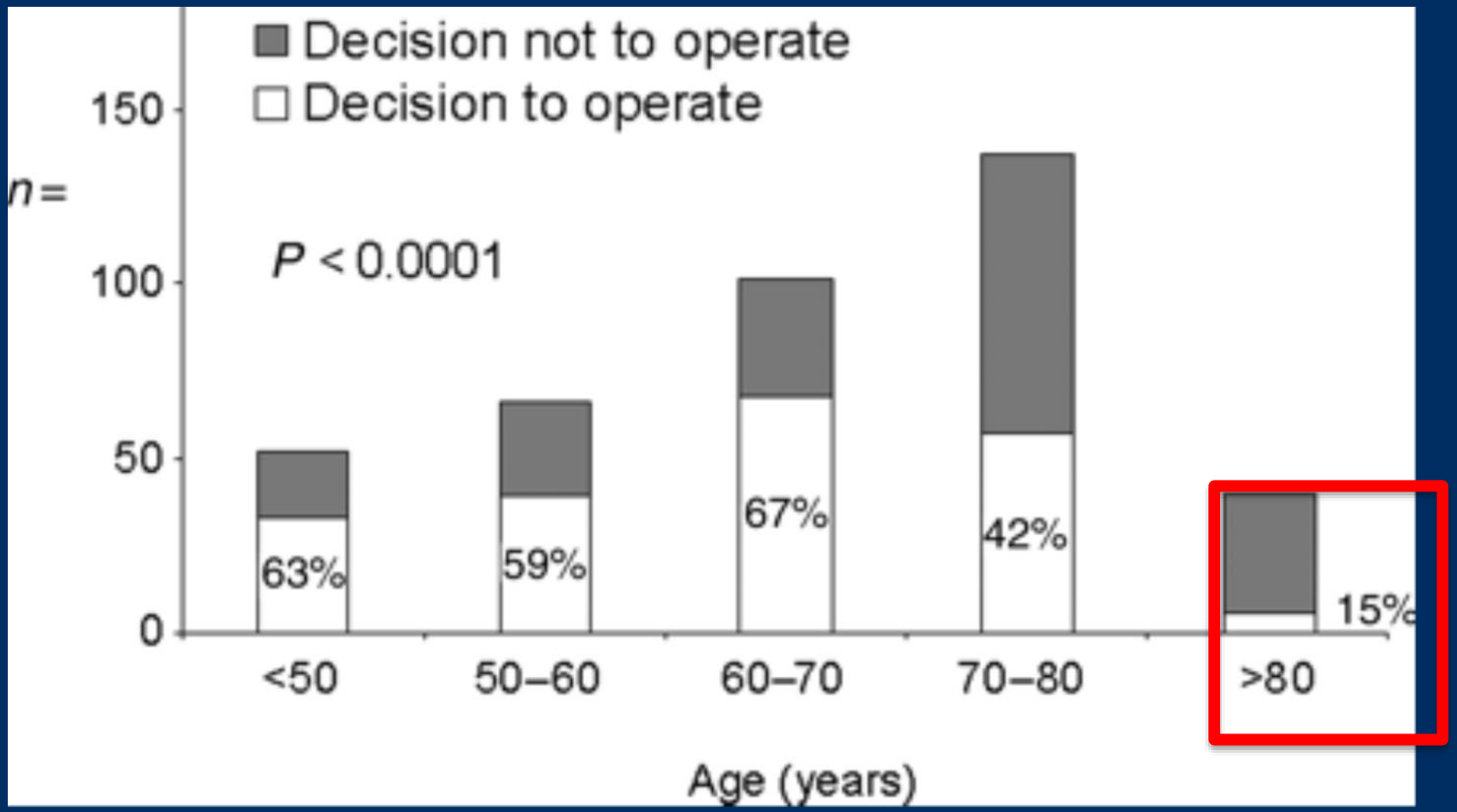
CLINICAL PRACTICE GUIDELINE: FOCUSED UPDATE

2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease

IIb	B

Transcatheter mitral valve repair may be considered for severely symptomatic patients (NYHA class III to IV) with chronic severe primary MR (stage D) who have favorable anatomy for the repair procedure and a reasonable life expectancy but who have a prohibitive surgical risk because of severe comorbidities and remain severely symptomatic despite optimal GDMT for heart failure (HF) (124).

Who are denied surgery? (Age)



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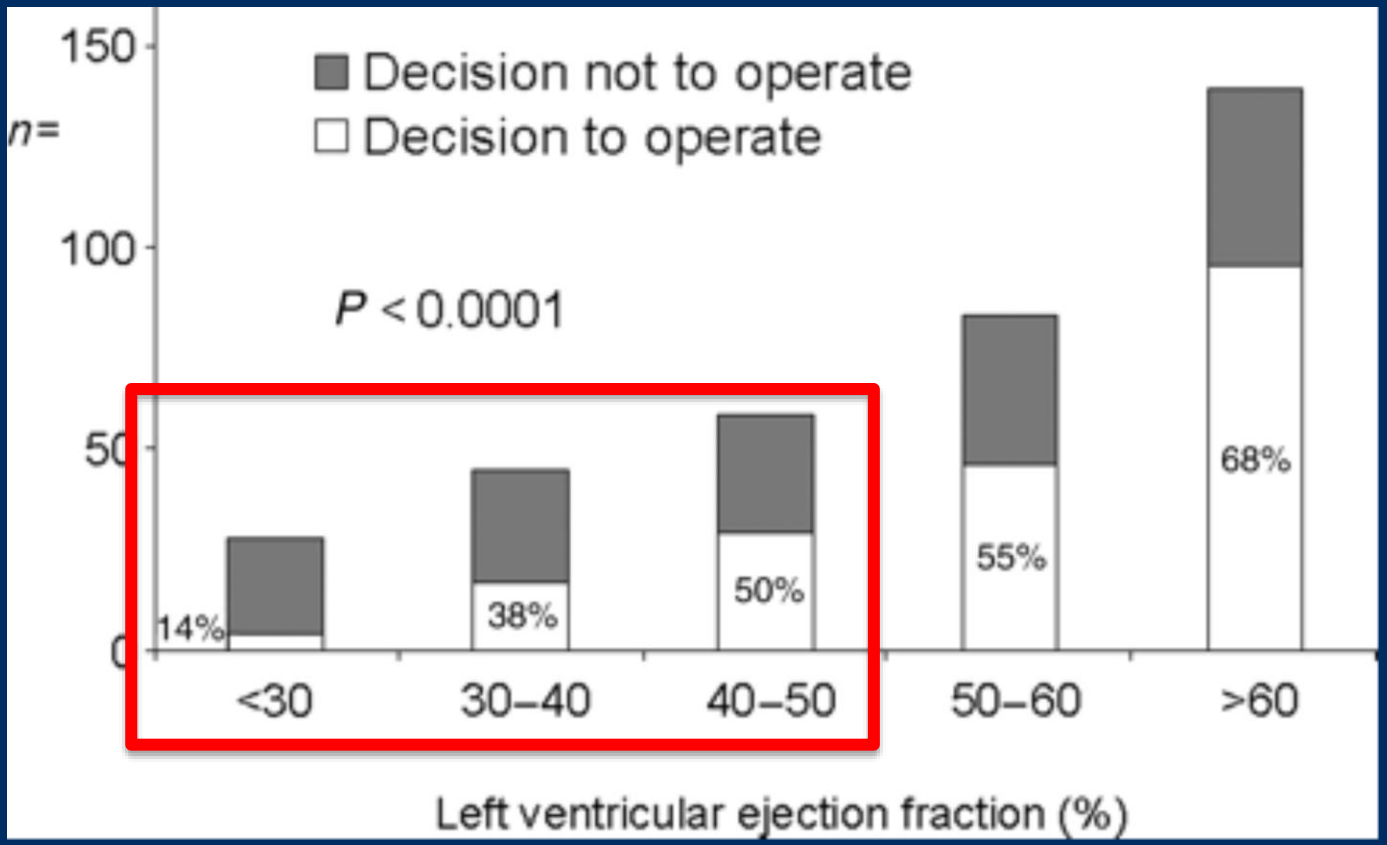
Eur Heart J. 2007;28(11):1358-1365.

Ejection Fraction



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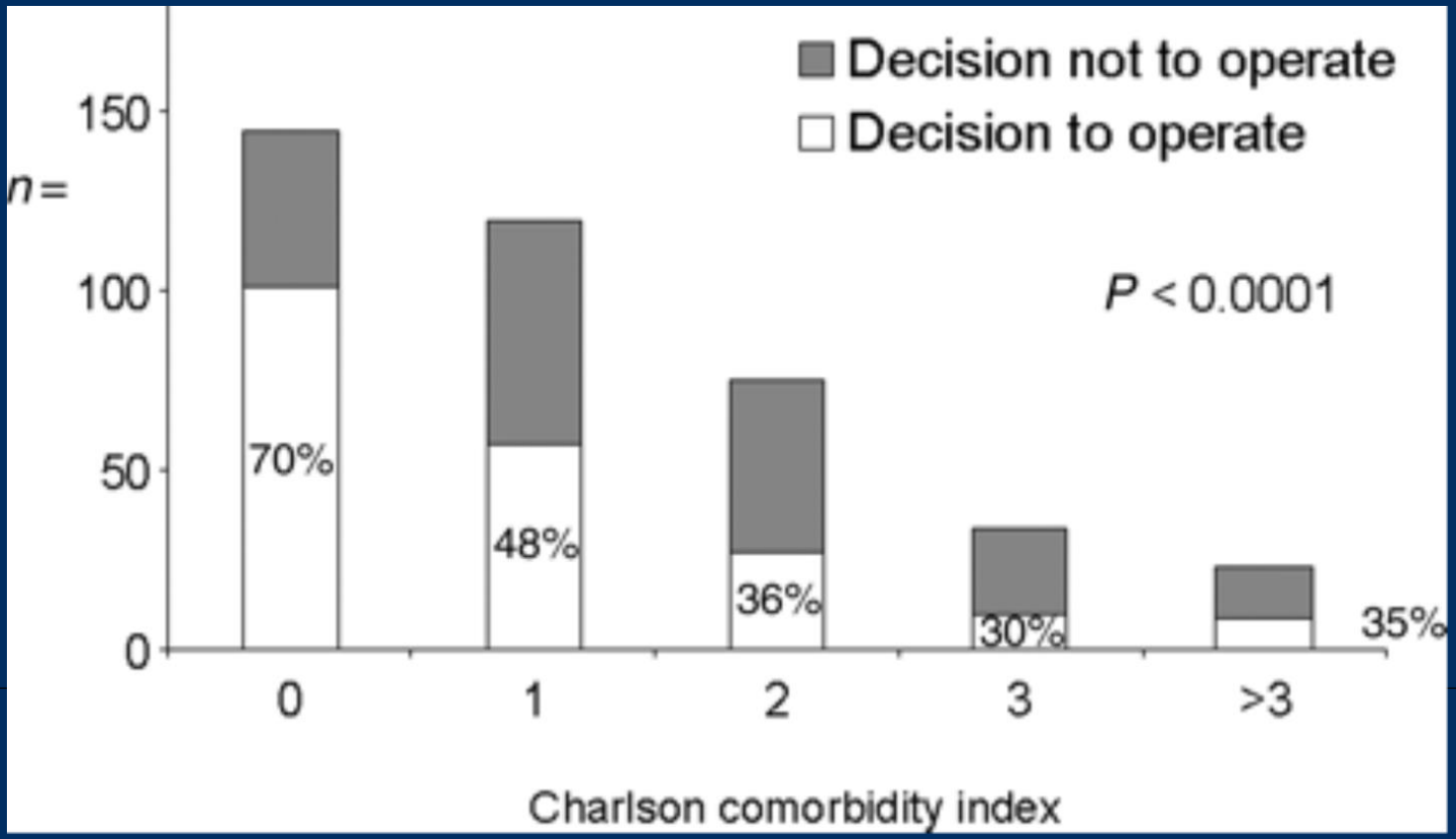
Eur Heart J. 2007;28(11):1358-1365.

Comorbidities



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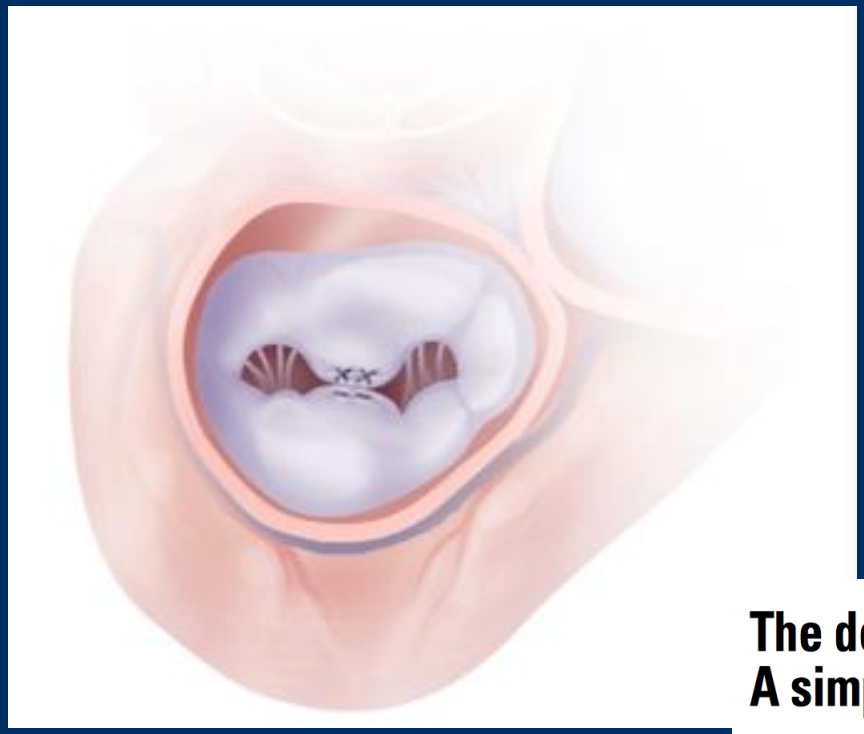
Eur Heart J. 2007;28(11):1358-1365.

Alfieri Stitch (double orifice)



Alfieri stitch

- 1991
- Surgically-treated patients (most in addition with annuloplasty)
- Durable effect for 12 years

The double-orifice technique in mitral valve repair: A simple solution for complex problems

Ottavio Alfieri, MD

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Alfieri et al. J Thorac Cardiovasc Surg 2001;122:647-81
Alfieri et al. J Thorac Cardiovasc Surg 2003;126:1987-97

The double-orifice technique in mitral valve repair: A simple solution for complex problems

1992-2000

Ottavio Alfieri, MD

TABLE 1. Cause of mitral insufficiency

Cause	n	%
Degenerative	210	80.8
Rheumatic	25	9.6
Endocarditis	16	6.1
Ischemic	6	2.3
Other*	3	1.2
Total	260	100

*Functional MR in dilated cardiomyopathy (2 patients) and amyloidosis (1 patient).

TABLE 2. Mechanism of mitral insufficiency

Mechanism of MR	n	%
Bileaflet prolapse	148	56.9
Anterior leaflet prolapse	68	26.2
Posterior leaflet prolapse	31	11.9
Lack of coaptation without prolapse	13	5.0
Restricted motion	9	
Free-edge erosion	4	

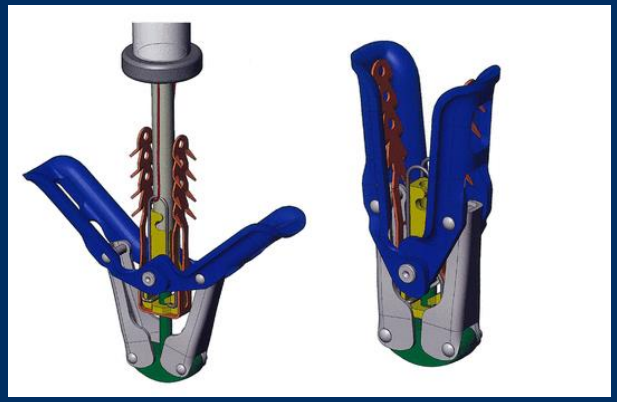
Conclusions: The effectiveness and durability of the central double-orifice technique were assessed in this study. This type of repair can be a useful addition to the surgical armamentarium in mitral valve reconstruction.

Percutaneous Mitral Repair With the MitraClip System

Safety and Midterm Durability in the Initial EVEREST (Endovascular Valve Edge-to-Edge REpair Study) Cohort

Figure 2 The MitraClip Device

The device is covered with polyester fabric to facilitate tissue in-growth. The distal gripping element helps with leaflet fixation. The clip delivery system exits through a guide catheter.



Feldman et al. JACC 2009;54:686-94

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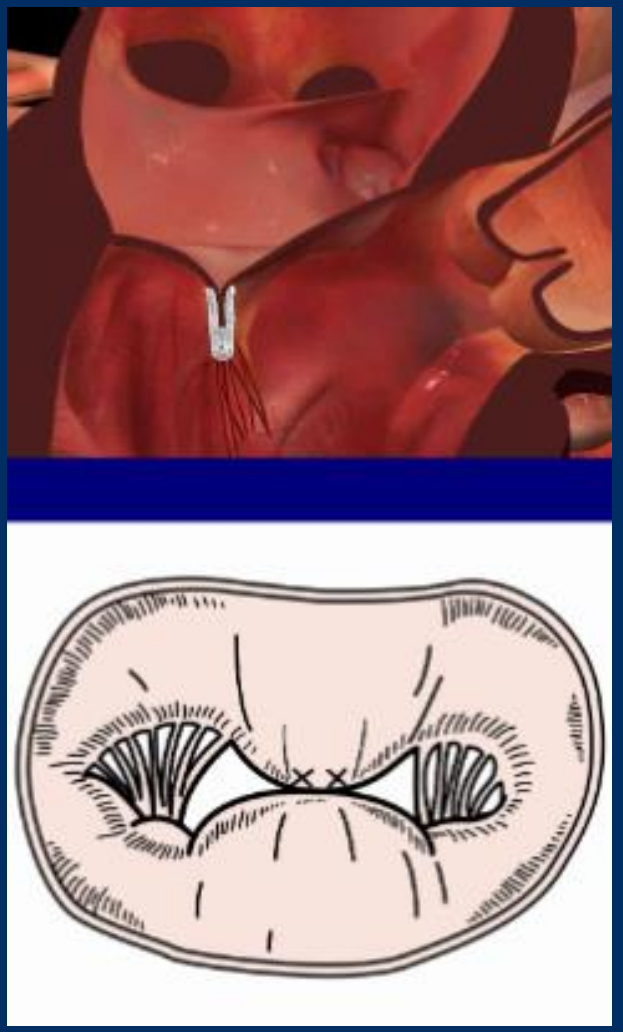
MitraClip Concepts

- Helps coaptation
  - Reduction of MR
- Creation of tissue bridge
  - Limits annular dilatation
  - Helps in durability
- Restrains LV (regional effect)
  - Helps LV remodeling



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http://resources.mitraclip.com/image-video-gallery.aspx

Procedural Goals

- Reduce MR <2+
- Abolish pulmonary vein flow reversal
- Achieve above results while maintaining a mean mitral inflow gradient <5-7 mmHg.

Study	Population	N
EVEREST I (Feasibility)	Feasibility patients	55
EVEREST II (Pivotal)	Pre-randomized patients	60
EVEREST II (Pivotal)	Non-randomized patients (High risk Study)	78
EVEREST II (Pivotal)	Randomized patients (2:1 Clip to Surgery)	184 Clip 95 Surgery
REALISM (Contd Access)	Non-randomized patients	899
Compassionate/ Use	Non-randomized patients	66
ACCESS Europe Phase I	Non-randomized patients	567
ACCESS Europe Phase II	Non-randomized patients	286
Commercial Use	Commercial patients	>40,000

>45,000

Percutaneous Mitral Repair With the MitraClip System

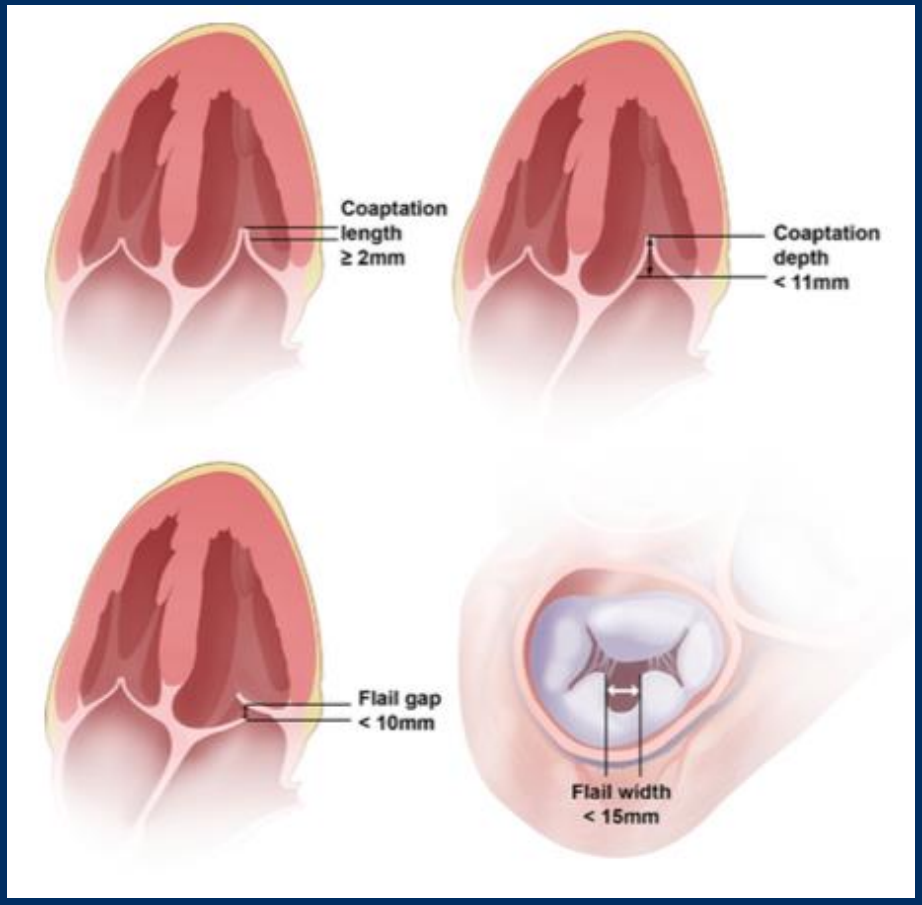
Safety and Midterm Durability in the Initial EVEREST (Endovascular Valve Edge-to-Edge REpair Study) Cohort

Ted Feldman, MD,* Saibal Kar, MD,† Michael Rinaldi, MD,‡ Peter Fail, MD,§
James Hermiller, MD,‖ Richard Smalling, MD, PHD,¶ Patrick L. Whitlow, MD,#
William Gray, MD,** Reginald Low, MD,†† Howard C. Herrmann, MD,‡‡ Scott Lim, MD,§§
Elyse Foster, MD,‖‖ Donald Glower, MD,¶¶ for the EVEREST Investigators

Conclusions Percutaneous repair with the MitraClip system can be accomplished with low rates of morbidity and mortality and with acute MR reduction to < 2+ in the majority of patients, and with sustained freedom from death, surgery, or recurrent MR in a substantial proportion (EVEREST I; NCT00209339. EVEREST II; NCT00209274). (J Am Coll Cardiol 2009;54:686–94) © 2009 by the American College of Cardiology Foundation

Key Anatomical Inclusions

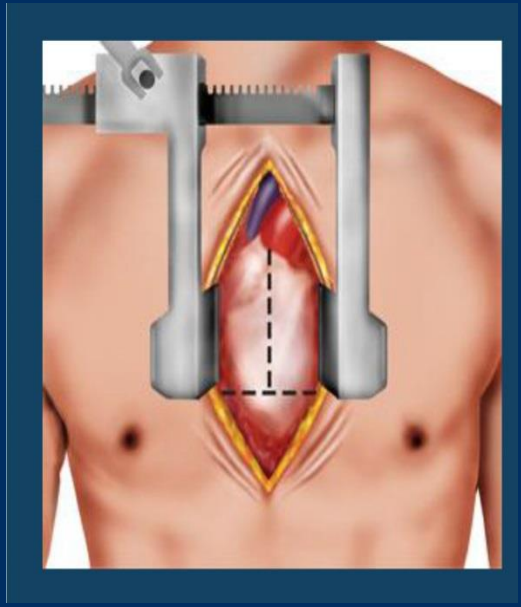
- +3-+4 MR
- LVEF >25%
- LVESD<55%
- Primary regurgitant jet originating from mal-coaptation of A2-P2
- DMR pts: Flail width (<15 mm) and flail gap (<10 mm)
- FMR pts: Coaptation length (>2mm)



EVEREST II Randomized Clinical Trial

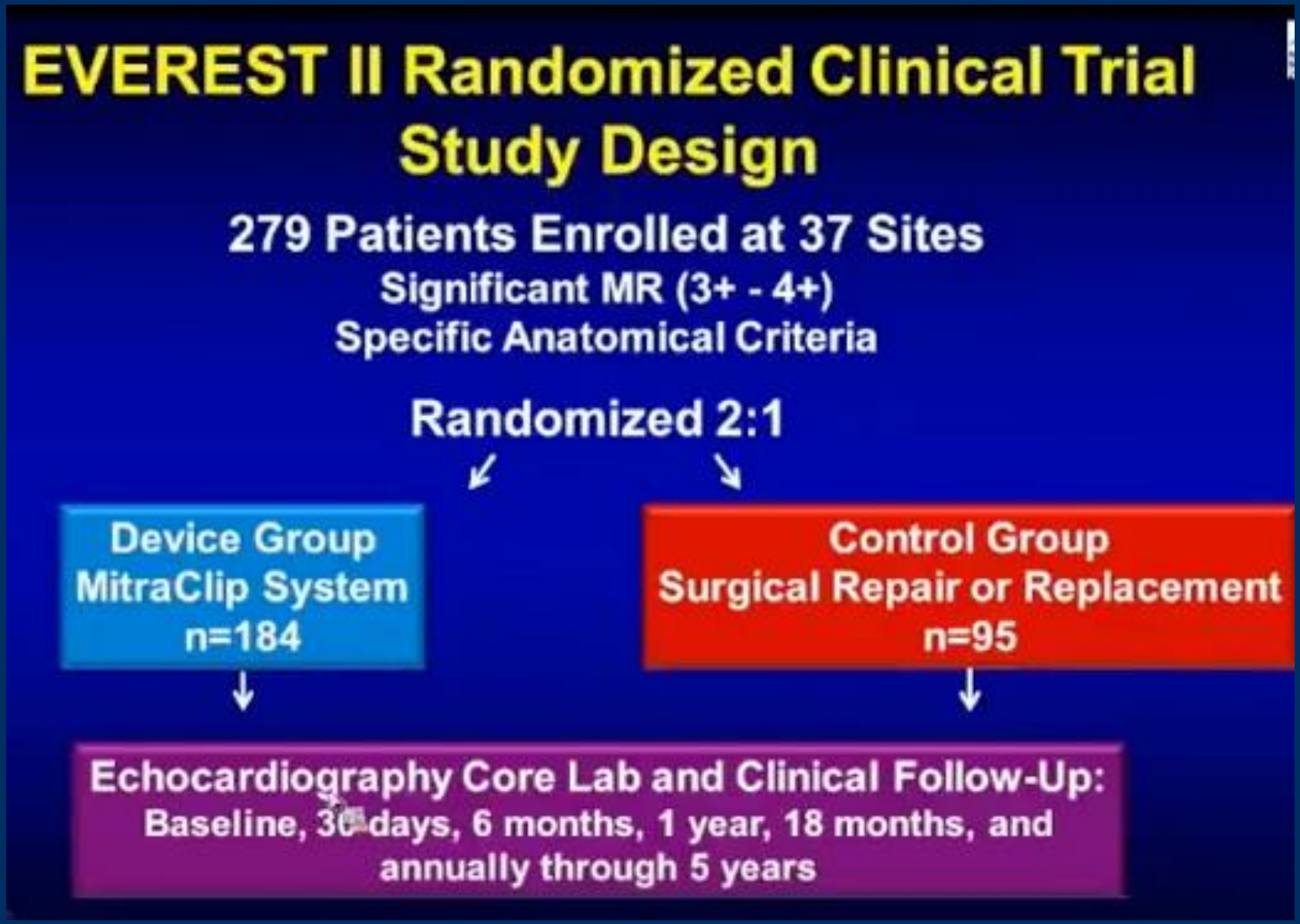
Surgical and Percutaneous Therapy for Mitral Regurgitation

Mitral Valve Surgery
Repair/Replacement



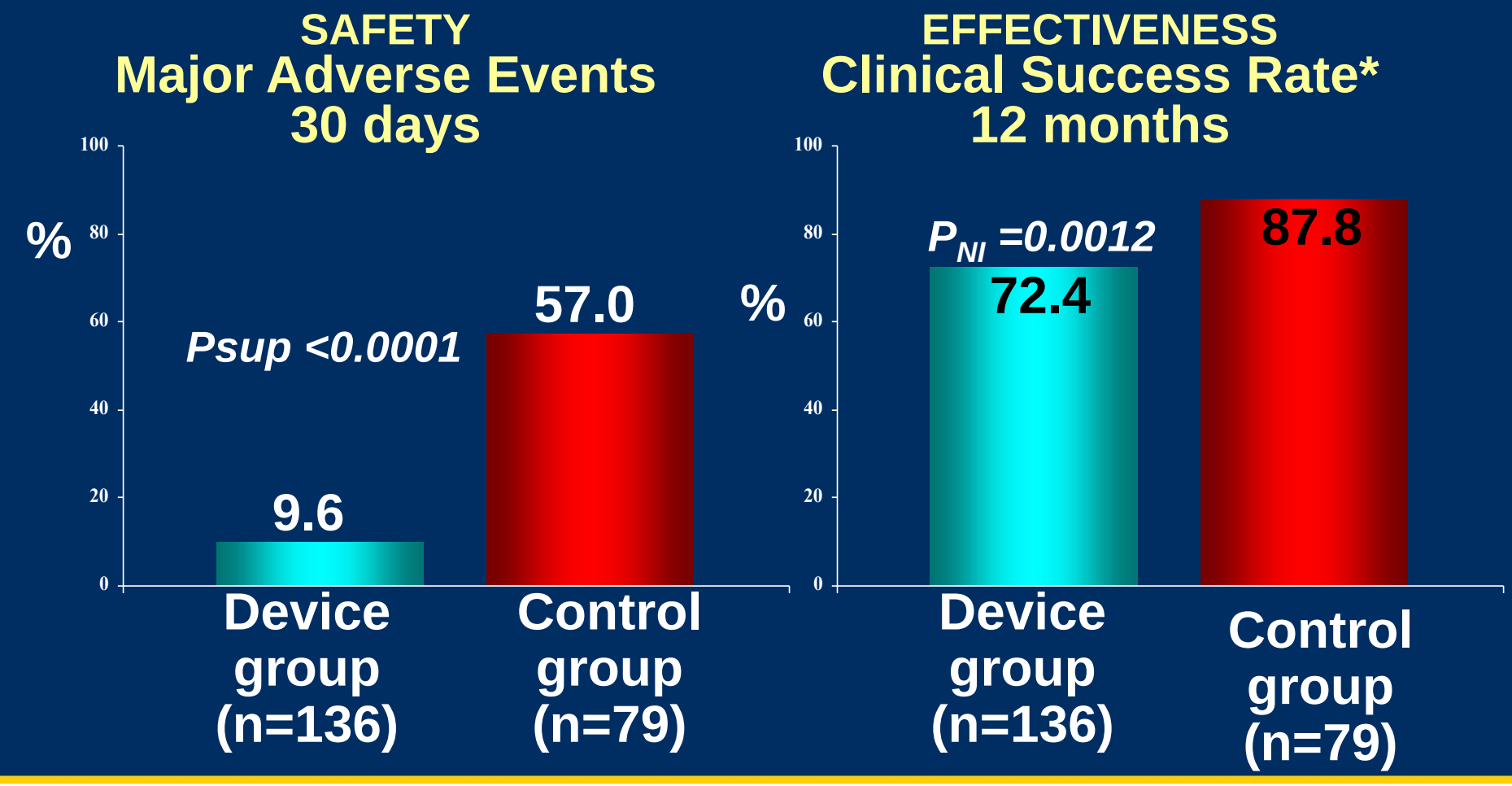
or

Catheter Based Mitral Valve Repair
MitraClip System


EVEREST II Randomized Clinical Trial
Study Design
279 Patients Enrolled at 37 Sites
Significant MR (3+ - 4+)
Specific Anatomical Criteria
Randomized 2:1
Device Group
MitraClip System
n=184
Control 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

EVEREST II (Endovascular Valve Edge-to-Edge Repair) Study

Primary Endpoints Per Protocol Cohort



*Freedom from the combined outcome of death, MV surgery or re-operation for MV dysfunction, MR >2+ at 12 Month

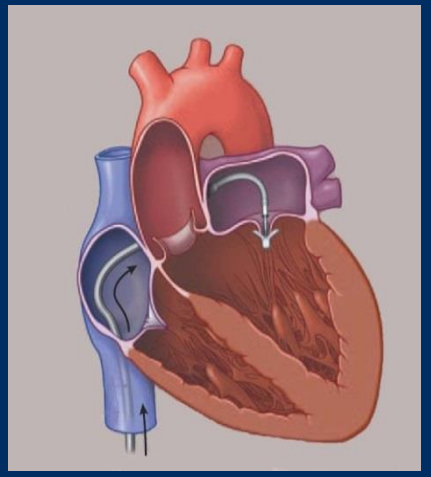
Feldman T et al, ACC 2010

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 14, 2011 VOL. 364 NO. 15

Percutaneous Repair or Surgery for Mitral Regurgitation

Ted Feldman, M.D., Elyse Foster, M.D., Donald D. Glower, M.D., Saibal Kar, M.D., Michael J. Rinaldi, M.D., Peter S. Fail, M.D., Richard W. Smalling, M.D., Ph.D., Robert Siegel, M.D., Geoffrey A. Rose, M.D., Eric Engeron, M.D., Catalin Loghin, M.D., Alfredo Trento, M.D., Eric R. Skipper, M.D., Tommy Fudge, M.D., George V. Letsou, M.D., Joseph M. Massaro, Ph.D., and Laura Mauri, M.D., for the EVEREST II Investigators*



BACKGROUND

Mitral-valve repair can be accomplished with an investigational procedure that involves the percutaneous implantation of a clip that grasps and approximates the edges of the mitral leaflets at the origin of the regurgitant jet.

CONCLUSIONS

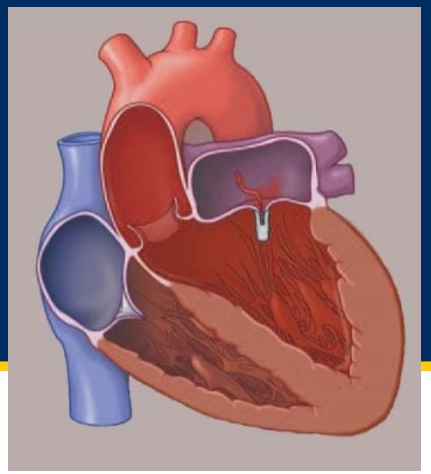
Although percutaneous repair was less effective at reducing mitral regurgitation than conventional surgery, the procedure was associated with superior safety and similar improvements in clinical outcomes.

RESULTS

At 12 months, the rates of the primary end point for efficacy were 55% in the percutaneous-repair group and 73% in the surgery group (P=0.007). The respective rates of the components of the primary end point were as follows: death, 6% in each group; surgery for mitral-valve dysfunction, 20% versus 2%; and grade 3+ or 4+ mitral regurgitation, 21% versus 20%. Major adverse events occurred in 15% of patients in the percutaneous-repair group and 48% of patients in the surgery group at 30 days (P<0.001). At 12 months, both groups had improved left ventricular size, New York Heart Association functional class, and quality-of-life measures, as compared with baseline.

CONCLUSIONS

Although percutaneous repair was less effective at reducing mitral regurgitation than conventional surgery, the procedure was associated with superior safety and similar improvements in clinical outcomes. (Funded by Abbott Vascular; EVEREST II ClinicalTrials.gov number, NCT00209274.)



Feldman et al. NEJM 2011:364;678

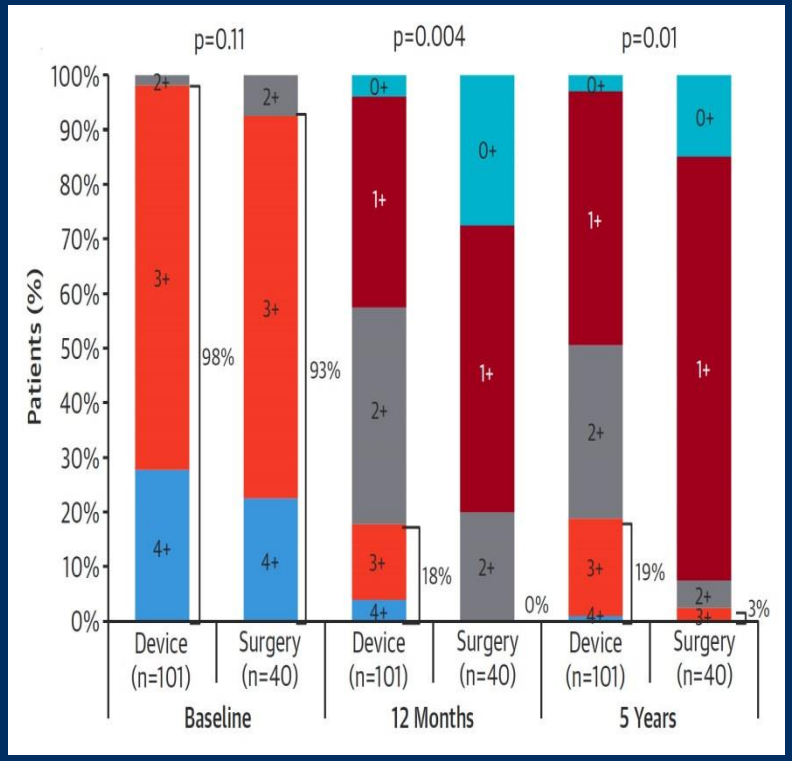
Randomized Comparison of Percutaneous Repair and Surgery for Mitral Regurgitation

5-Year Results of EVEREST II

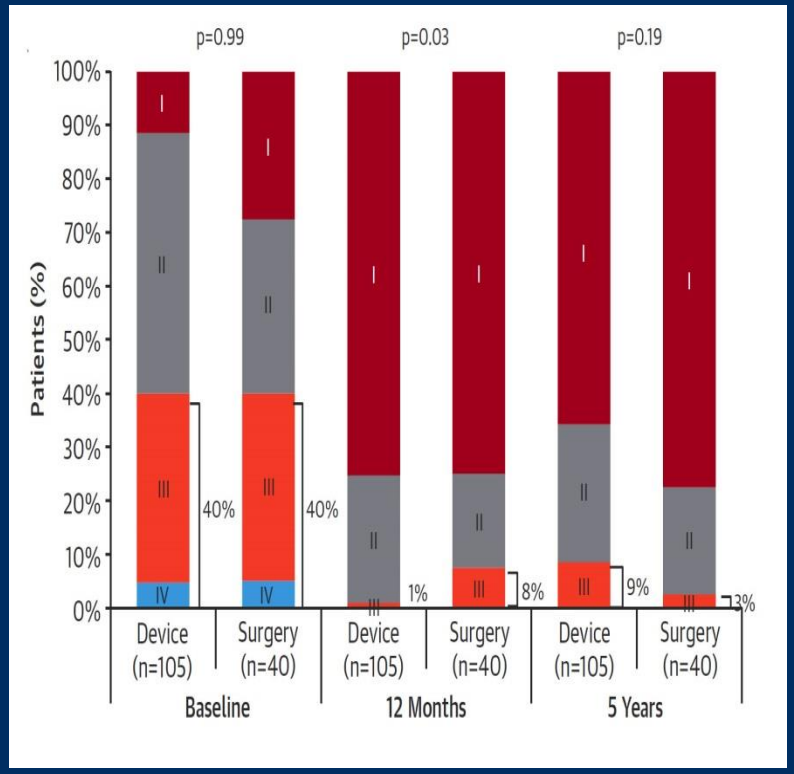
Ted Feldman, MD,* Saibal Kar, MD,† Sammy Elmariah, MD, MPH,‡§ Steven C. Smart, MD,* Alfredo Trento, MD,‖ Robert J. Siegel, MD,† Patricia Apruzzese, MS,§ Peter Fail, MD,¶ Michael J. Rinaldi, MD,# Richard W. Smalling, MD, PhD,** James B. Hermiller, MD,†† David Heimansohn, MD,‡‡ William A. Gray, MD,§§ Paul A. Grayburn, MD,‖‖ Michael J. Mack, MD,¶¶ D. Scott Lim, MD,## Gorav Ailawadi, MD,*** Howard C. Herrmann, MD,††† Michael A. Acker, MD,‡‡‡ Frank E. Silvestry, MD,††† Elyse Foster, MD,§§§ Andrew Wang, MD,‖‖‖ Donald D. Glower, MD,¶¶¶ Laura Mauri, MD,§### for the EVEREST II Investigators

EVEREST II Trial: Severity of MR and Heart Failure Symptoms Post-Treatment

Echocardiographic Severity of MR

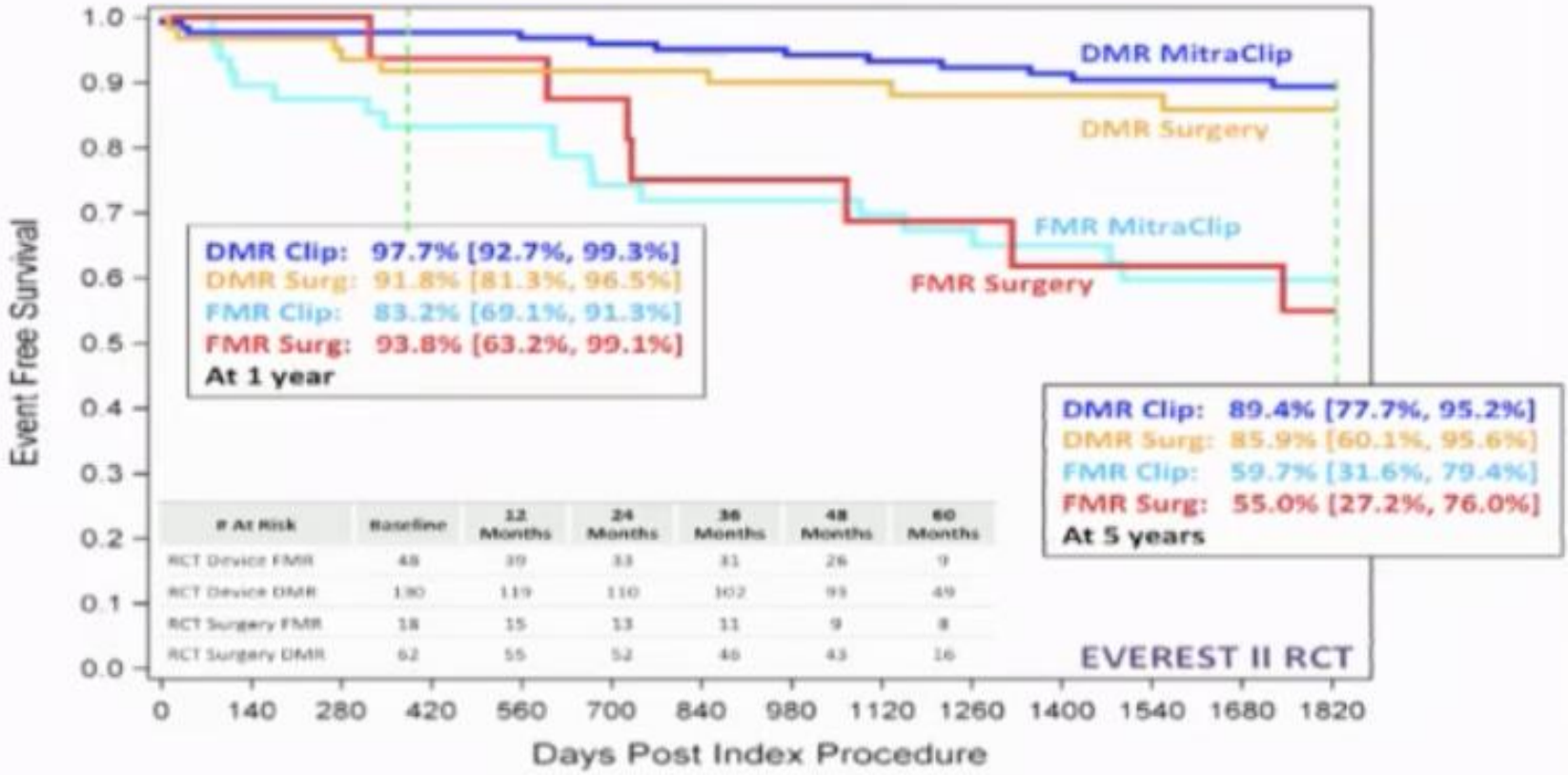


NYHA Functional Class



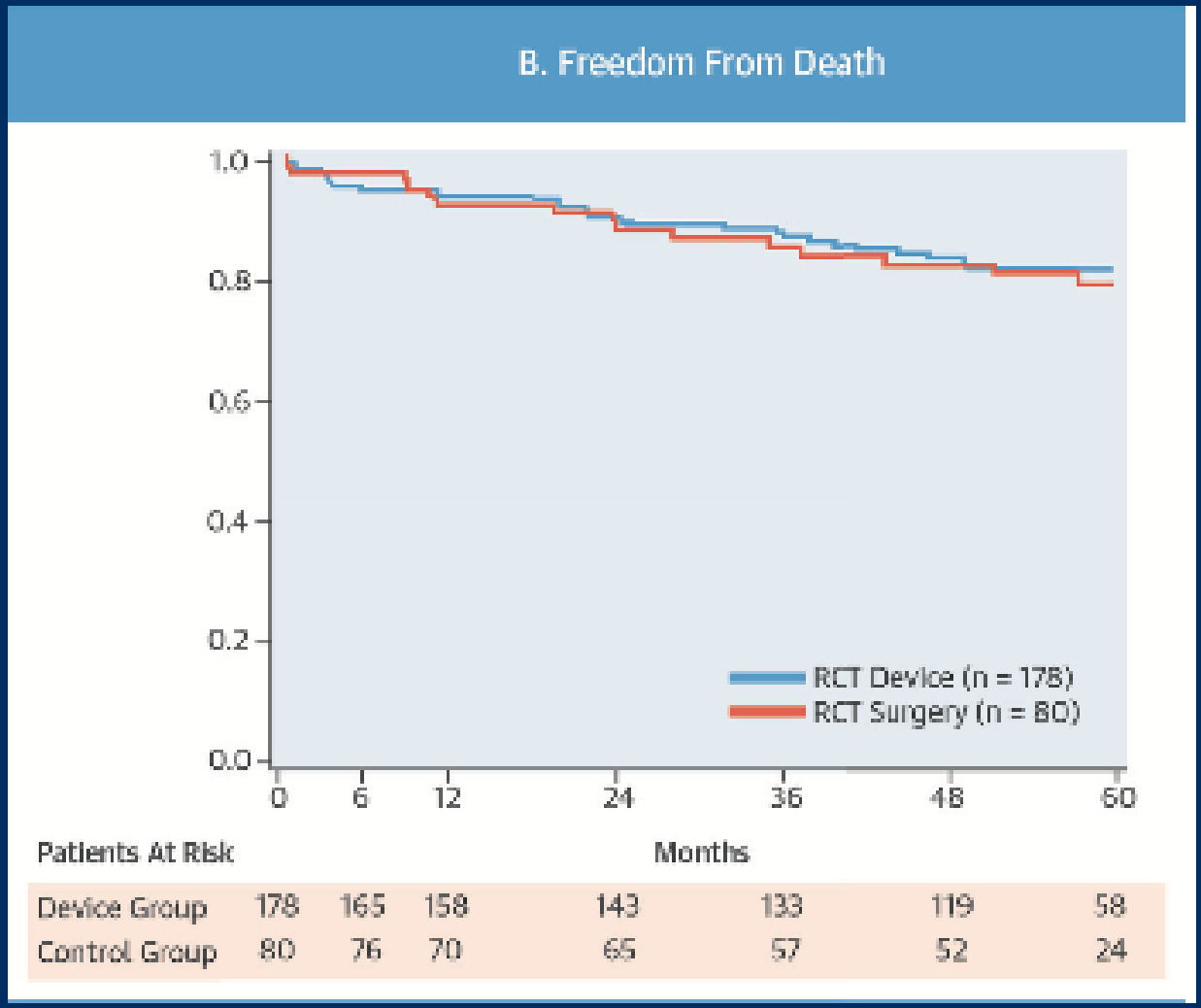
Feldman et al. JACC 2015;66:2844-54.

Freedom From Mortality & Reintervention



Feldman et al. JACC 2015;66:2844-54.

EVEREST II Trial: 5-Year Clinical Outcomes – Percutaneous Repair and Surgery for Mitral Regurgitation

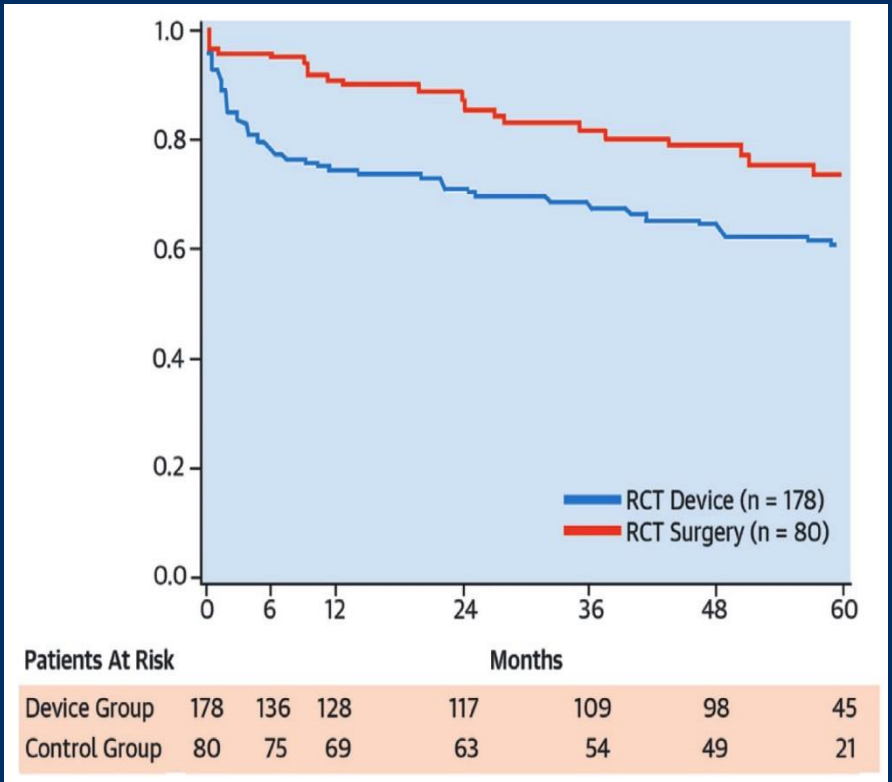


Patients At Risk							
Device Group	178	165	158	143	133	119	58
Control Group	80	76	70	65	57	52	24

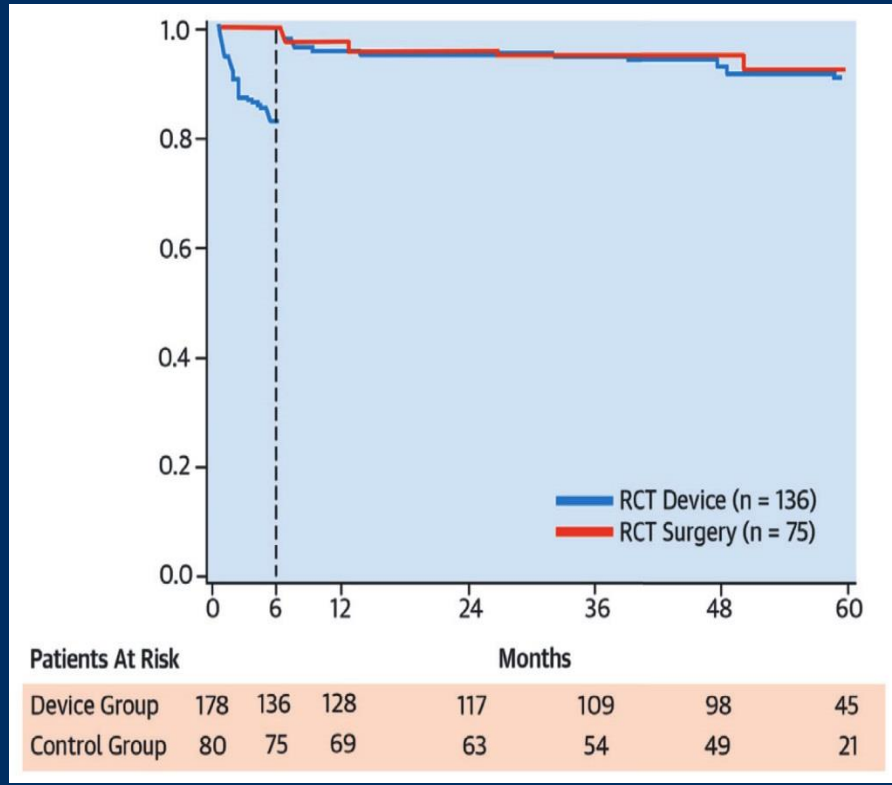
Feldman et al. JACC 2015;66:2844-54.

EVEREST II Trial: 5-Year Clinical Outcomes – Percutaneous Repair and Surgery for Mitral Regurgitation

Freedom from Death, MV Surgery or Reoperation



Landmark Analysis of Freedom from Death, MV Surgery or Reoperation Beyond 6 Months



Feldman et al. JACC 2015;66:2844-54.

Randomized Comparison of Percutaneous Repair and Surgery for Mitral Regurgitation

5-Year Results of EVEREST II

Ted Feldman, MD,* Saibal Kar, MD,† Sammy Elmariah, MD, MPH,‡§ Steven C. Smart, MD,* Alfredo Trento, MD,‖ Robert J. Siegel, MD,† Patricia Apruzzese, MS,§ Peter Fail, MD,¶ Michael J. Rinaldi, MD,# Richard W. Smalling, MD, PhD,** James B. Hermiller, MD,†† David Heimansohn, MD,‡‡ William A. Gray, MD,§§ Paul A. Grayburn, MD,‖‖ Michael J. Mack, MD,¶¶ D. Scott Lim, MD,## Gorav Ailawadi, MD,*** Howard C. Herrmann, MD,††† Michael A. Acker, MD,‡‡‡ Frank E. Silvestry, MD,††† Elyse Foster, MD,§§§ Andrew Wang, MD,‖‖‖ Donald D. Glower, MD,¶¶¶ Laura Mauri, MD,§### for the EVEREST II Investigators

ABSTRACT

BACKGROUND In EVEREST II (Endovascular Valve Edge-to-Edge Repair Study), treatment of mitral regurgitation (MR)

CONCLUSIONS Patients treated with percutaneous repair more commonly required surgery for residual MR during the first year after treatment, but between 1- and 5-year follow-up, comparably low rates of surgery for MV dysfunction with either percutaneous or surgical therapy endorse the durability of MR reduction with both repair techniques. (EVEREST II Pivotal Study High Risk Registry; NCT00209274) (J Am Coll Cardiol 2015;66:2844–54) © 2015 by the American College of Cardiology Foundation.

p = 0.003) with percutaneous repair. After percutaneous repair, 78% of surgeries occurred within the first 6 months. Beyond 6 months, rates of surgery and moderate-to-severe MR were comparable between groups. Five-year mortality rates were 20.8% and 26.8% (p = 0.4) for percutaneous repair and surgery, respectively. In multivariable analysis, treatment strategy was not associated with survival.

CONCLUSIONS Patients treated with percutaneous repair more commonly required surgery for residual MR during the first year after treatment, but between 1- and 5-year follow-up, comparably low rates of surgery for MV dysfunction with either percutaneous or surgical therapy endorse the durability of MR reduction with both repair techniques. (EVEREST II Pivotal Study High Risk Registry; NCT00209274) (J Am Coll Cardiol 2015;66:2844–54) © 2015 by the American College of Cardiology Foundation.

Feldman et al. JACC 2015;66:2844-54.

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Improved Functional Status and Quality of Life in Prohibitive Surgical Risk Patients With Degenerative Mitral Regurgitation After Transcatheter Mitral Valve Repair

D. Scott Lim, MD,* Matthew R. Reynolds, MD, MSc,†‡ Ted Feldman, MD,§ Saibal Kar, MD,‖ Howard C. Herrmann, MD,¶ Andrew Wang, MD,# Patrick L. Whitlow, MD,** William A. Gray, MD,†† Paul Grayburn, MD,‡‡ Michael J. Mack, MD,‡‡ Donald D. Glower, MD#

METHODS A prohibitive-risk DMR cohort was identified by a multidisciplinary heart team that retrospectively evaluated high-risk DMR patients enrolled in the EVEREST (Endovascular Valve Edge-to-Edge Repair Study) II studies.

RESULTS A total of 141 high-risk DMR patients were consecutively enrolled; 127 of these patients were retrospectively identified as meeting the definition of *prohibitive risk* and had 1 year follow-up (median: 1.47 years) available. Patients were elderly (mean age: 82.4 years), severely symptomatic (87% New York Heart Association class III/IV), and at prohibitive surgical risk (STS score: 13.2 ± 7.3%). TMVR (MitraClip) was successfully performed in 95.3%; hospital stay was 2.9 ± 3.1 days. Major adverse events at 30 days included death in 6.3%, myocardial infarction in 0.8%, and stroke in 2.4%. Through 1 year, there were a total of 30 deaths (23.6%), with no survival difference between patients discharged with MR ≤1+ or MR 2+. At 1 year, the majority of surviving patients (82.9%)

TMVR in prohibitive surgical risk patients is associated with safety and good clinical outcomes, including decreases in re-hospitalization, functional improvements, and favorable ventricular remodeling, at 1 year.

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

Results of the EVEREST II Study

Donald D. Glower, MD,* Saibal Kar, MD,† Alfredo Trento, MD,† D. Scott Lim, MD,‡ Tanvir Bajwa, MD,§‖ Ramon Quesada, MD,¶ Patrick L. Whitlow, MD,# Michael J. Rinaldi, MD,** Paul Grayburn, MD,†† Michael J. Mack, MD,†† Laura Mauri, MD,‡‡§§ Patrick M. McCarthy, MD,‖‖ Ted Feldman, MD¶¶

ABSTRACT

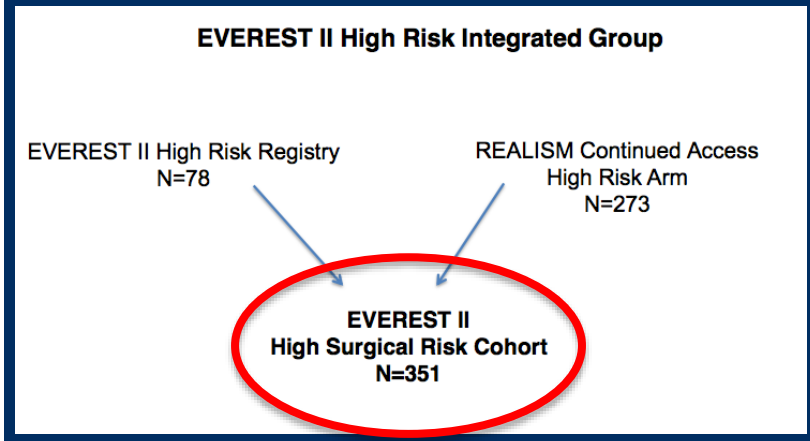
BACKGROUND The EVEREST II (Endovascular Valve Edge-to-Edge REpair STudy) High-Risk registry and REALISM Continued Access Study High-Risk Arm are prospective registries of patients who received the MitraClip device (Abbott Vascular, Santa Clara, California) for mitral regurgitation (MR) in the United States.

OBJECTIVES The purpose of this study was to report 12-month outcomes in high-risk patients treated with the percutaneous mitral valve edge-to-edge repair.

METHODS Patients with grades 3 to 4+ MR and a surgical mortality risk of ≥12%, based on the Society of Thoracic Surgeons risk calculator or the estimate of a surgeon coinvestigator following pre-specified protocol criteria, were enrolled.

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 80% 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%.

CONCLUSIONS The percutaneous mitral valve device significantly reduced MR, improved clinical symptoms, and decreased LV dimensions at 12 months in this high-surgical-risk cohort. (Endovascular Valve Edge-to-Edge REpair STudy [EVERESTIIRCT]; NCT00209274) (J Am Coll Cardiol 2014;64:172-81) © 2014 by the American College of Cardiology Foundation.

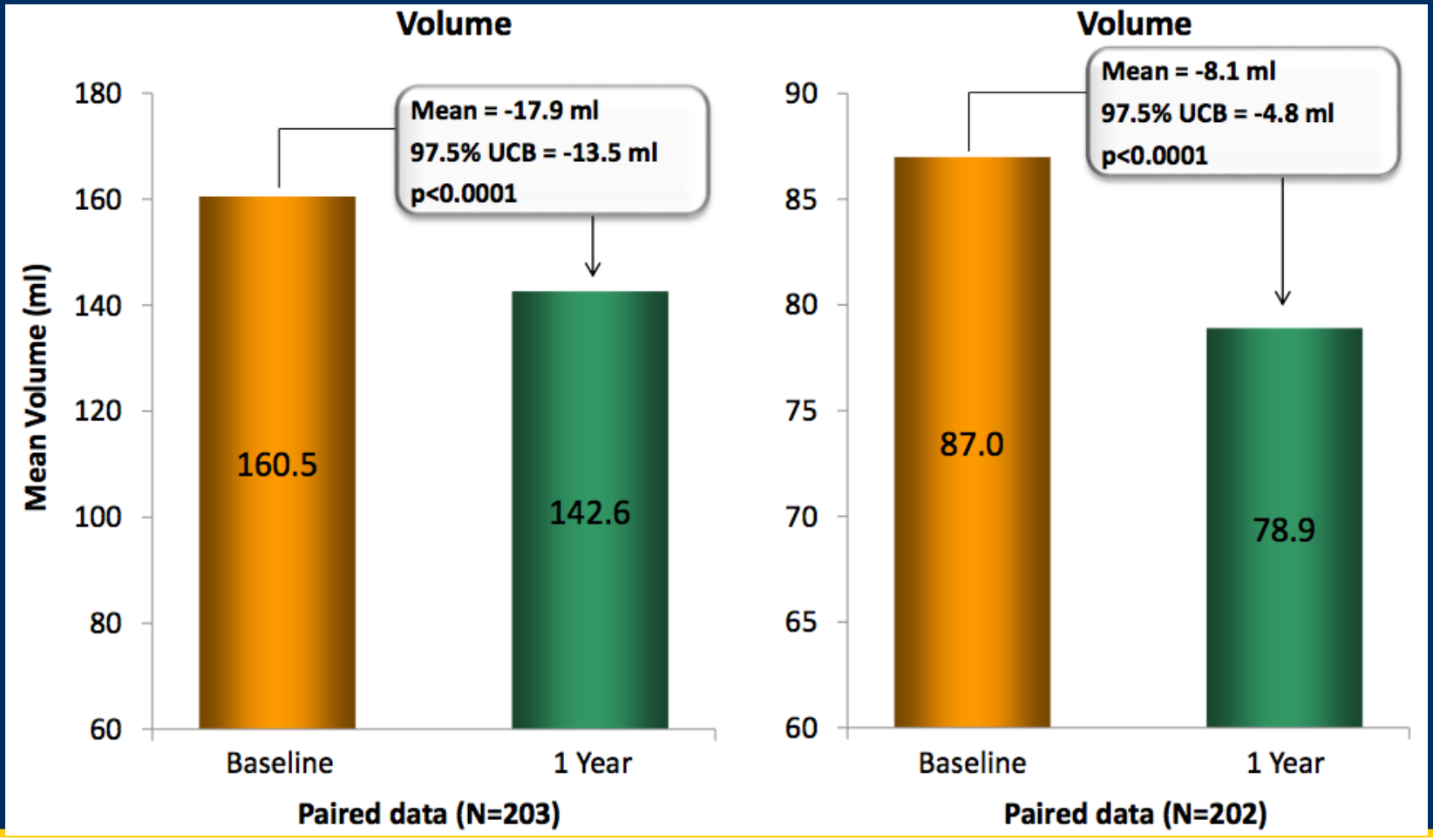


Glower et al. JACC 2014;64:172-81

EVEREST II High Risk Surgical Cohort

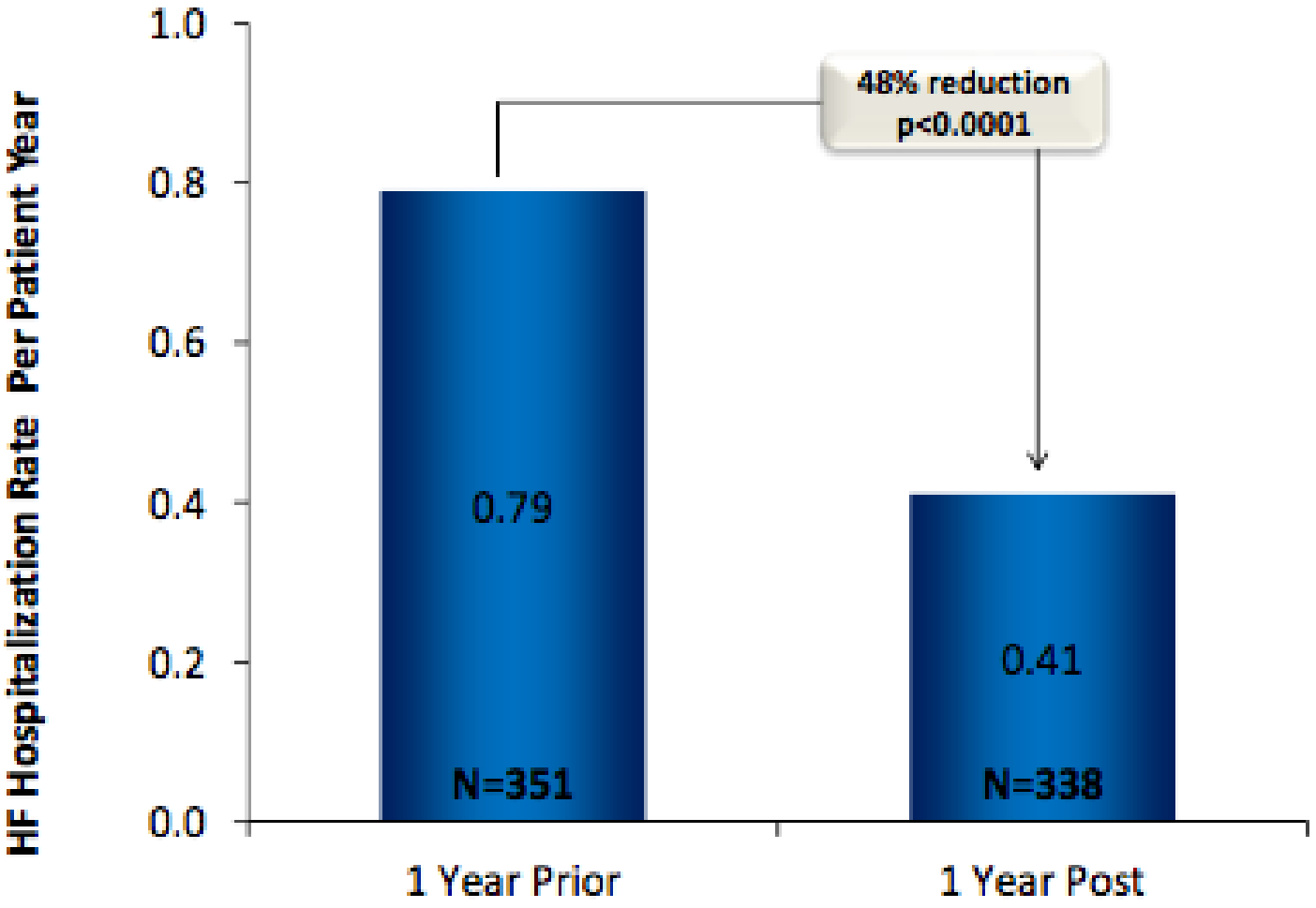
	n=351
Age	76 ± 11
Predicted Surgical Mortality Risk, (%)	18.2±8.4
NYHA Functional Class III or IV	85%
Atrial Fibrillation	69%
Mitral Regurgitation Grade ≥ 3+	86%
Left Ventricular Ejection Fraction (%)	47.5 ± 14.2
Functional MR	70%
30 day Mortality	6.8%
Home ± home health care	91.7 %
MR Grade I-II at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

LV Volumes



Glower et al JACC 2014;64:172-181

Hospitalizations for Heart Failure



Glower et al JACC 2014;64:172-181

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Glower et al JACC 2014;64:172-181

Prospective Registries

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

MitraClip for Severe Symptomatic Mitral Regurgitation in Patients at High Surgical Risk: A Comprehensive Systematic Review

TABLE I. Demographic Characteristics of Patients Undergoing MitraClip Implantation or Mitral Valve Surgery

Study	*N*	Age, year ± SD	Male (%)	COPD (%)	DM (%)	CAD (%)	IRF (%)	EuroSCORE, Mean ± SD	STS Score, Mean ± SD	EF (%)	FMR (%)	DMR (%)
MitraClip implantation												
Schillinger et al. [11]	1,064	75*	62	19	29	57	50	23*	12*	–	61	39
Sürder et al. [12]	100	77 ± 19	67	20	13	45	50	19*	–	48 ± 19	62	38
Chan et al. [13]	27	74 ± 12	63	–	–	–	–	27 ± 12	14 ± 9	40 ± 17	56	44
Grasso et al. [14]	117	72 ± 10	67	21	34	49	38	12 ± 14	–	–	76	24
Tamburino et al. [15]	31	71*	100	0	32	45	19	14 ± 12	10 ± 9	42 ± 17	56	42
Auricchio et al. [16]	51	70 ± 9	86	29	22	47	72	30 ± 19	14 ± 15	27± 9	73	27
Van den Branden et al. [17]	52	73 ± 10	69	27	21	67	69	27 ± 17	10 ± 8	37± 14	90	10
Pleger et al. [18]	59	77*	69	0	32	49	–	25 ± 3	11 ± 2	39 ± 8	36	20
Franzen et al. [19]	51	73 ± 10	68	–	–	49	–	28 ± 22	16 ± 11	36 ± 17	69	31
Paranskaya et al. [20]	85	78 ± 6	56	28	40	–	56	24± 12	12 ± 7	43 ± 17	57	44
Divchev et al. [21]	33	78 ± 7	58	27	39	81	–	24 ± 14	30 ± 15	38 ± 16	70	30
Lim [29]	351	75 ± 11	61	29	38	82	9	–	11 ± 8	45± 14	70	30
Maisano et al. [22]	567	74 ± 10	64	–	30	62	42	23 ± 18	–	35*	77	23
Conradi et al. [23]	95	72 ± 8	64	28	40	53	9	34 ± 19	–	36 ± 13	31	56
Tramasso et al. [30]	52	68 ± 9	83	21	27	71	58	22 ± 5	–	28 ± 10	100	0
Neuss et al. [24]	157	74 ± 10	68	–	37	–	–	22 ± 17	–	41± 17	73	27
Treede et al. [25]	202	75 ± 9	63	34	35	72	51	36 ± 21	–	44 ± 16	65	35
Rudolph et al. [26]	104	74 ± 9	41	41	33	65	55	36*	–	–	23	66
Mitral valve surgery												
STS (MVR) [27]	463	75 ± 9	53	53	48	33	36	–	17*	49± 16	–	–
STS (MVRp)[27]	2,760	69±9	40	39	46	49	30	–	18*	53 ± 14	–	–
Parker et al. [28]	42	67± 9	27	16	12	–	12	33 ± 23	–	24 ± 6	100	0
Total												
MitraClip	3,195	74 ± 10	65	24	31	34	42	26 ± 15	14 ±10	38 ± 15	60	40
MVS	3,265	73 ± 13	42	41	46	29	31	–	17*	52 ± 16	–	–

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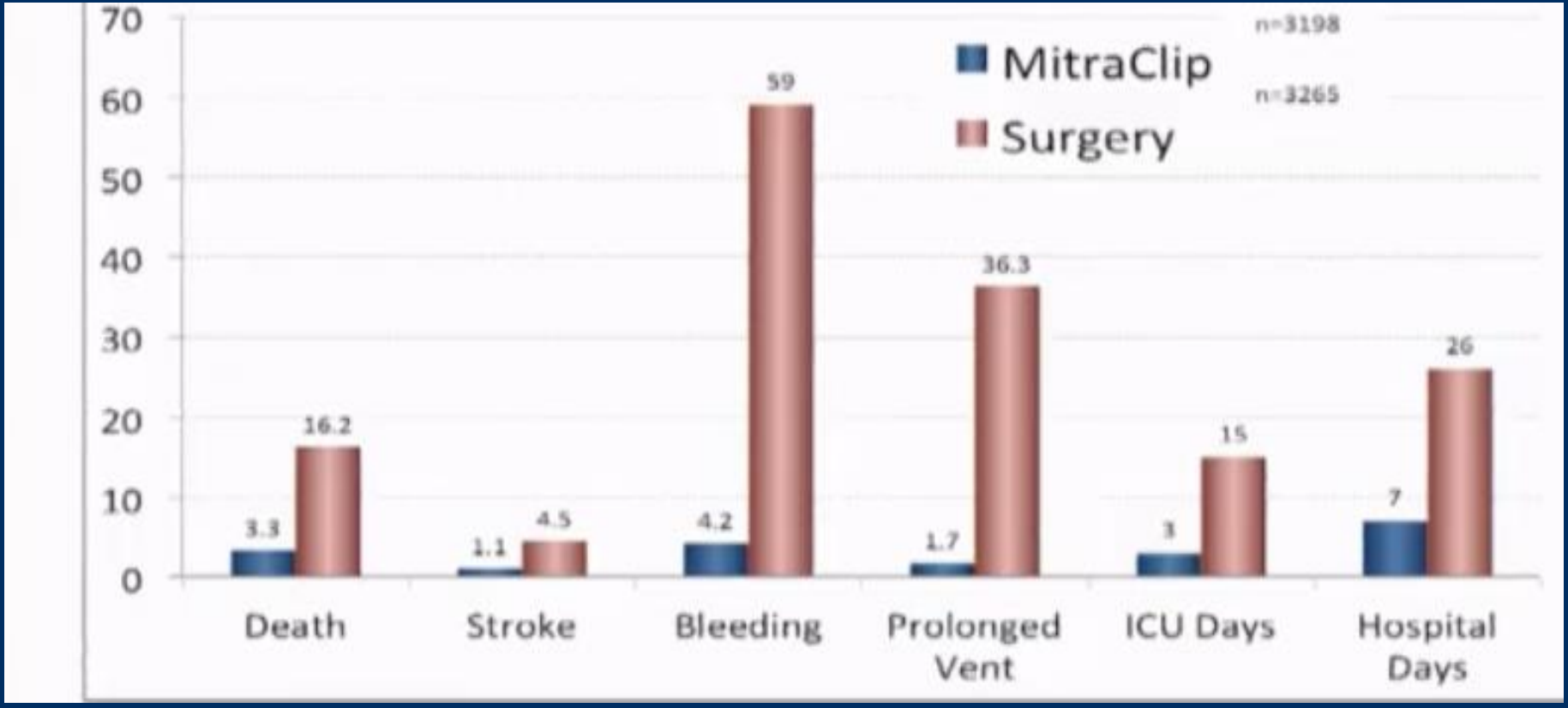
Philip et al. Cath Cardiovasc Intervent 2014;84:581

MitraClip for Severe Symptomatic Mitral Regurgitation in Patients at High Surgical Risk: A Comprehensive Systematic Review



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Philip et al. Cath Cardiovasc Intervent 2014;84:581

Procedural Success

A systematic review of the MitraClip system for high surgical risk candidates

Table 2 Summary of postoperative outcomes in high risk patients undergoing mitral valve repair using MitraClip

Author	30 day mortality (%)	Acute procedural success (%)	Successful clip implantation (%)	Number of clips implanted (%)			Early need for surgery (%)	Clip related chordal rupture (%)	Transseptal complication (%)	Partial clip detachment (%)	Transfusion of ≥2 units (%)	Median length of hospital stay (days)
				1	2	3 or more						
Altiok[12]	–	97	100	77	23	0	–	–	–	–	–	–
Treede[15]	3.5	92	97	62	32	4	5.4	–	–	–	–	12±10*
Pleger[16]	0	–	92	73	27	0	–	–	–	–	2.8	–
Schillinger[19]	2.7	84	99	–	–	–	0	–	–	5.3	0	–
Paranskaya[20]	4.7	97	–	17	55	28	1.2	–	–	2.4	–	–
Grasso[25]	0.9	100	–	59	40	1	0	–	–	0	0.9	
Ihlemann[29]	6.2	100	–	75	25	0	6.2	6.2	–	12.5	–	6±3*
Chan[30]	0	93	–	41	52	–	–	–	–	–	–	–
Van den Branden[31]	3.6	–	96	84	11	2	1.8	–	1.8	3.6	3.6	5
Sürder[34]	1.0	85	–	54	40	4	3.0	2.0	3.0	5.0	–	7
Auricchio[35]	7.8	95	–	51	49	0	2.0	2.0	–	–	9.8	–
Whitlow[48]	7.7	72†	96	–	–	–	0	–	1.2	–	17.9	–
Weighted mean	3.3	91	97.5	57	37	5	2.3	2.4	2.17	6.2	5.7	NA

Procedure success

Munkholm-Larsen S, et al. Heart 2014;100:473–478

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

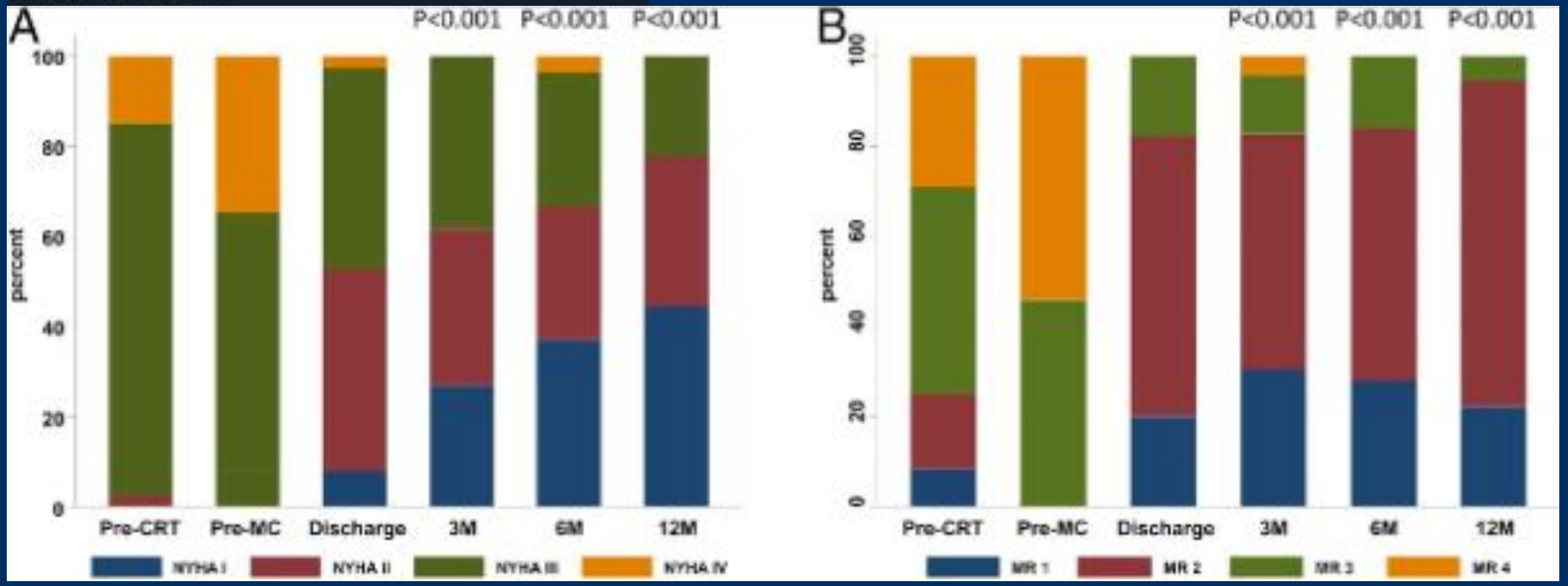
Angelo Auricchio, MD, PHD,* Wolfgang Schillinger, MD,† Sven Meyer, MD,‡ Francesco Maisano, MD,§ Rainer Hoffmann, MD,‖ Gian Paolo Ussia, MD,¶ Giovanni B. Pedrazzini, MD,* Jan van der Heyden, MD,# Simona Fratini, MD, PHD,** Catherine Klersy, MD, MSC,†† Jan Komtebedde, DVM,* Olaf Franzen, MD,‡ on behalf of the PERMIT-CARE Investigators

Lugano, Switzerland; Göttingen, Hamburg, and Aachen, Germany; Milan, Catania, L'Aquila, and Pavia, Italy; and Nieuwegein, the Netherlands

J Am Coll Cardiol. 2011 Nov 15;58(21):2183-9

51 severely symptomatic CRT non responders with grade 3 or 4 MR underwent MitraClip treatment,

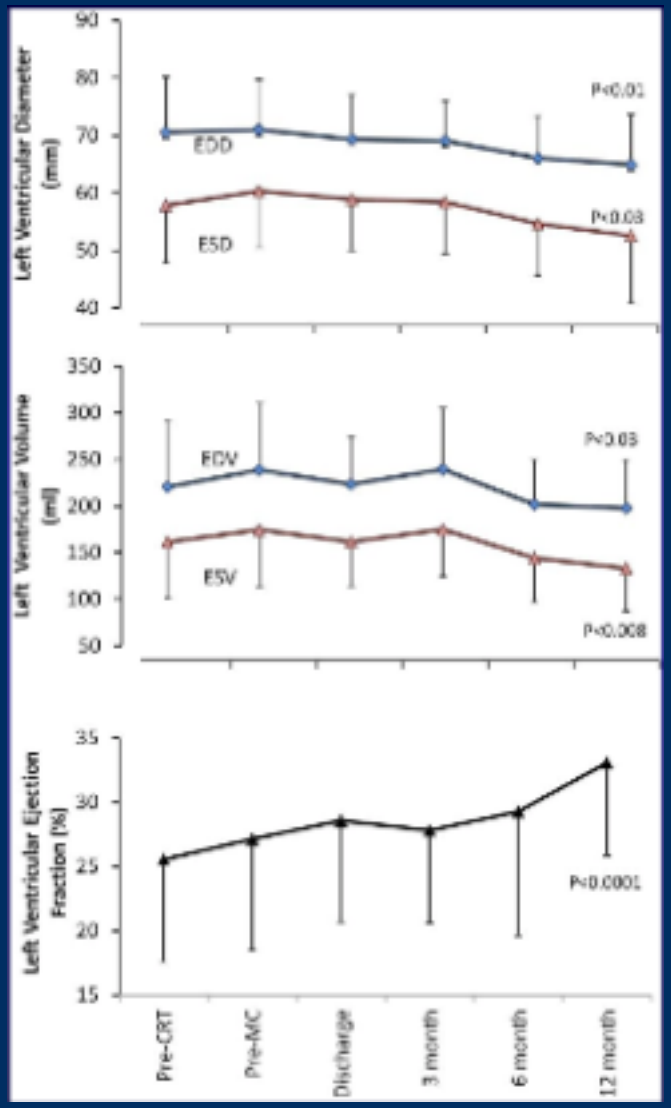
PERMIT-CARE study
Improvement Over Time



NYHA p<0.001

MR Grade p<0.001

Auricchio et al. JACC 2001;58:2183-9



LVEDD p<0.01
LVESD p<0.03

LVEDV p<0.03
LVESV p<0.008

EF p<0.0001

Auricchio et al. JACC 2001;58:2183-9

PERMIT CARE Study
Correction of MR in CRT Non- responders

"MitraClip Improves Symptoms and Promotes Reverse Remodeling"

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Auricchio et al. JACC 2001;58:2183-9

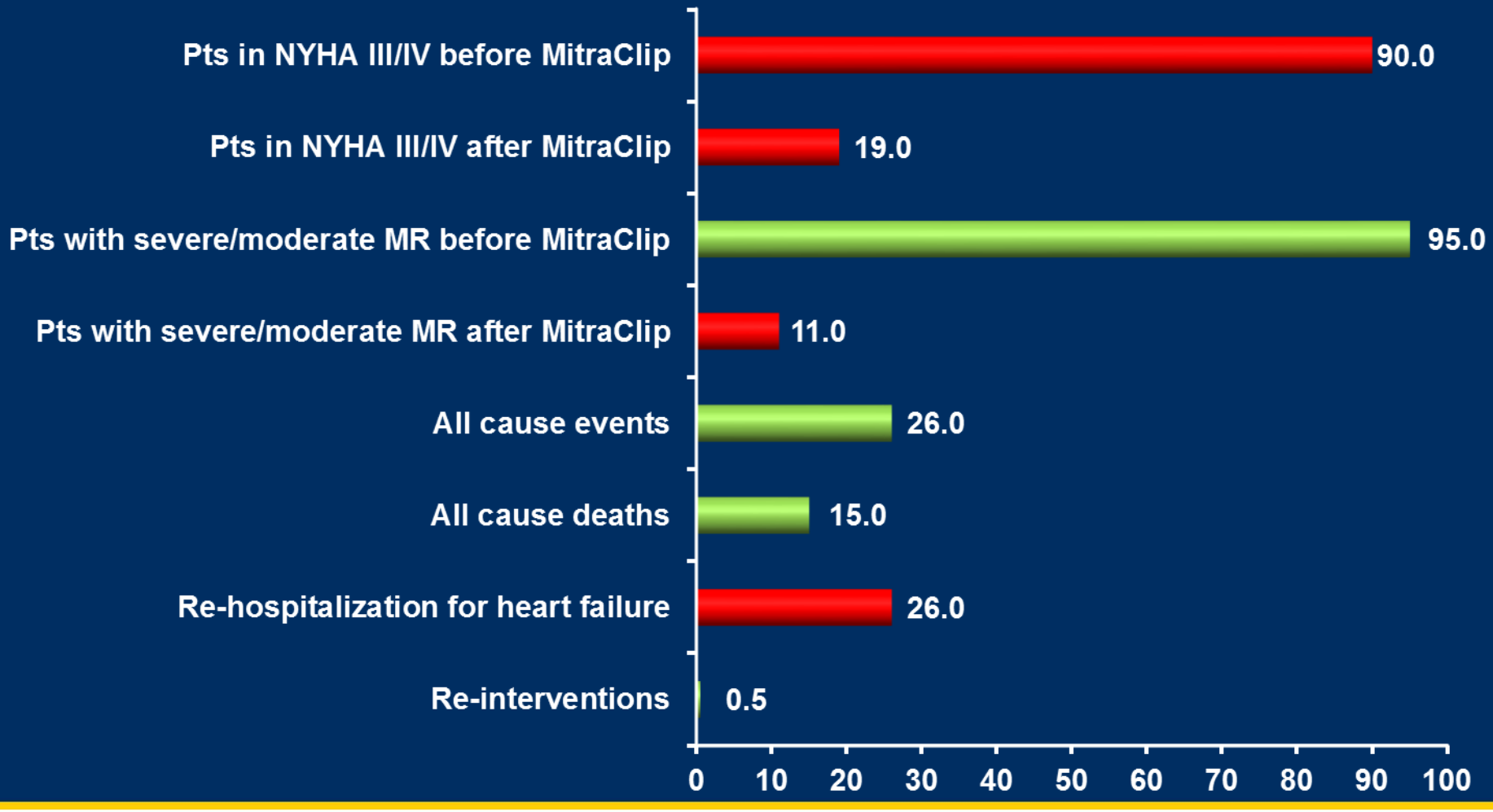
The American Journal of Cardiology

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]

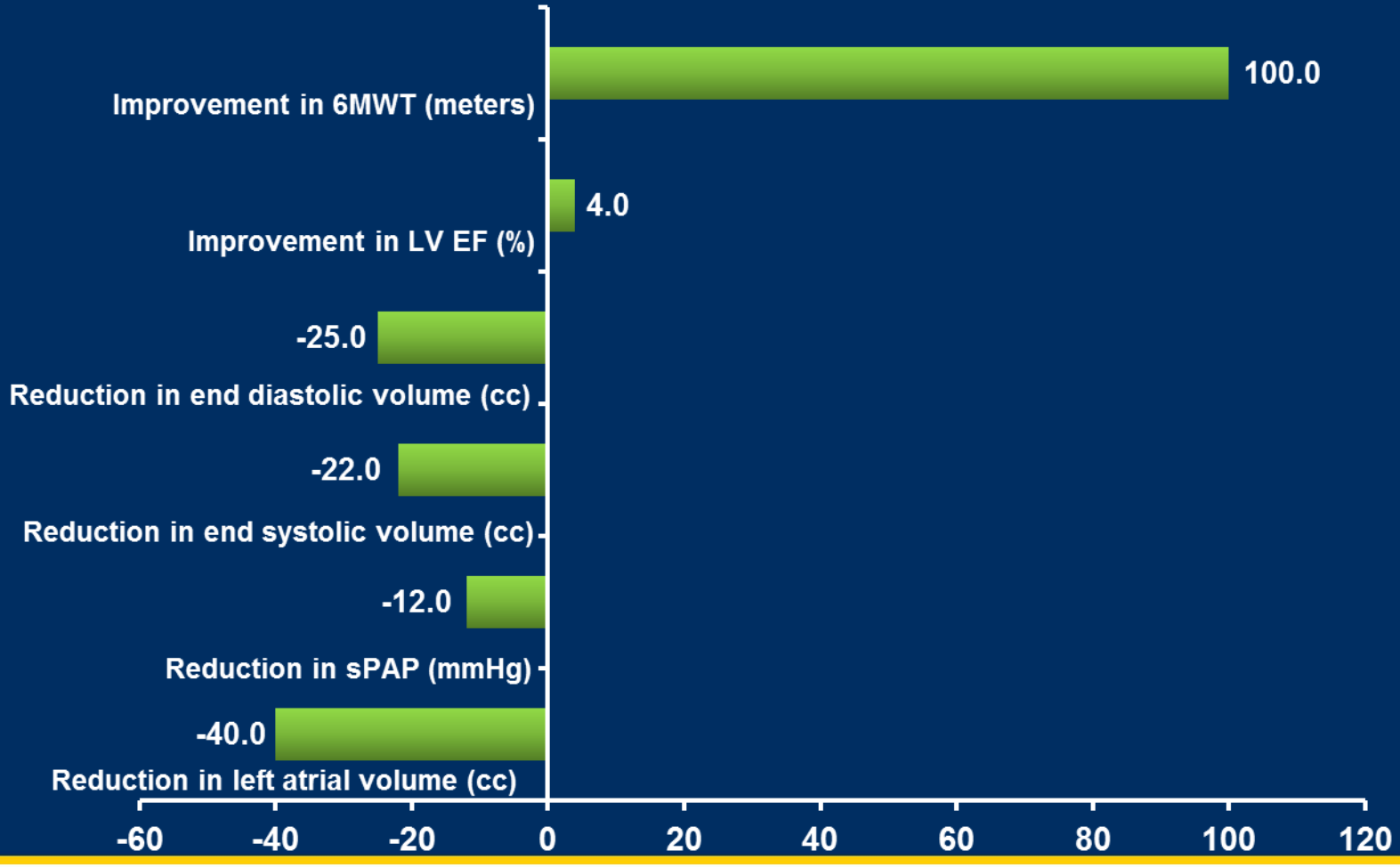
(Am J Cardiol 2015;116:325–331)

Adverse Clinical Events at Follow-Up of 9 Months



D'ascenzo et al., Am J Cardiol 2015;116:325

Change of Functional and Echocardiographic Data at Follow-Up



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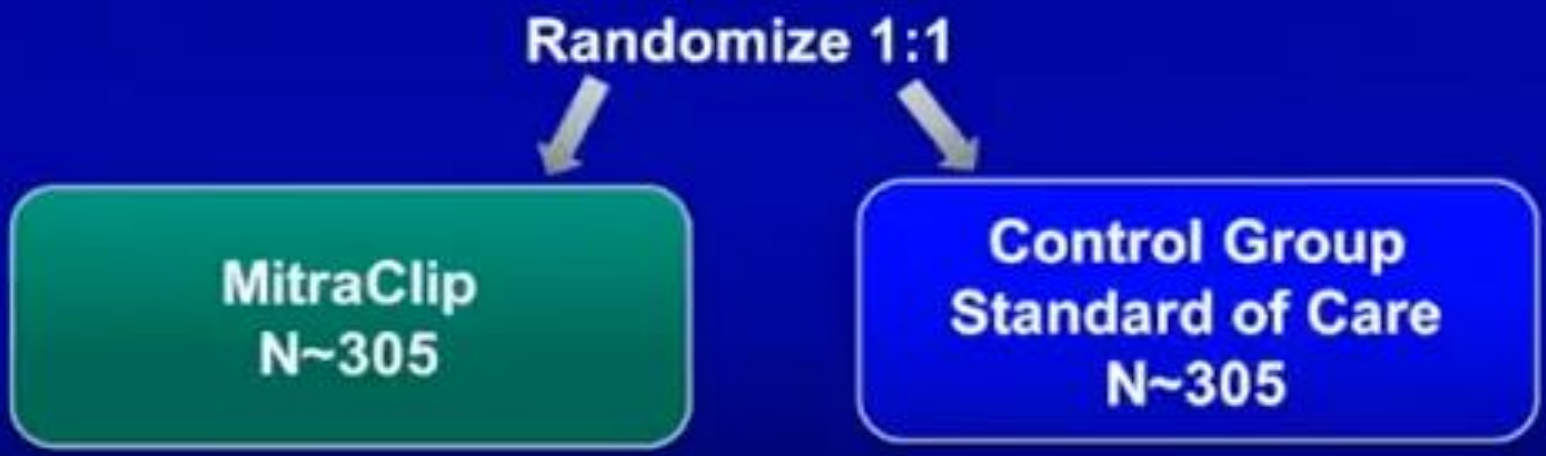
D'ascenzo et al., Am J Cardiol 2015;116:325

COAPT Trial Design

~610 Patients Enrolled at Up to 100 Sites

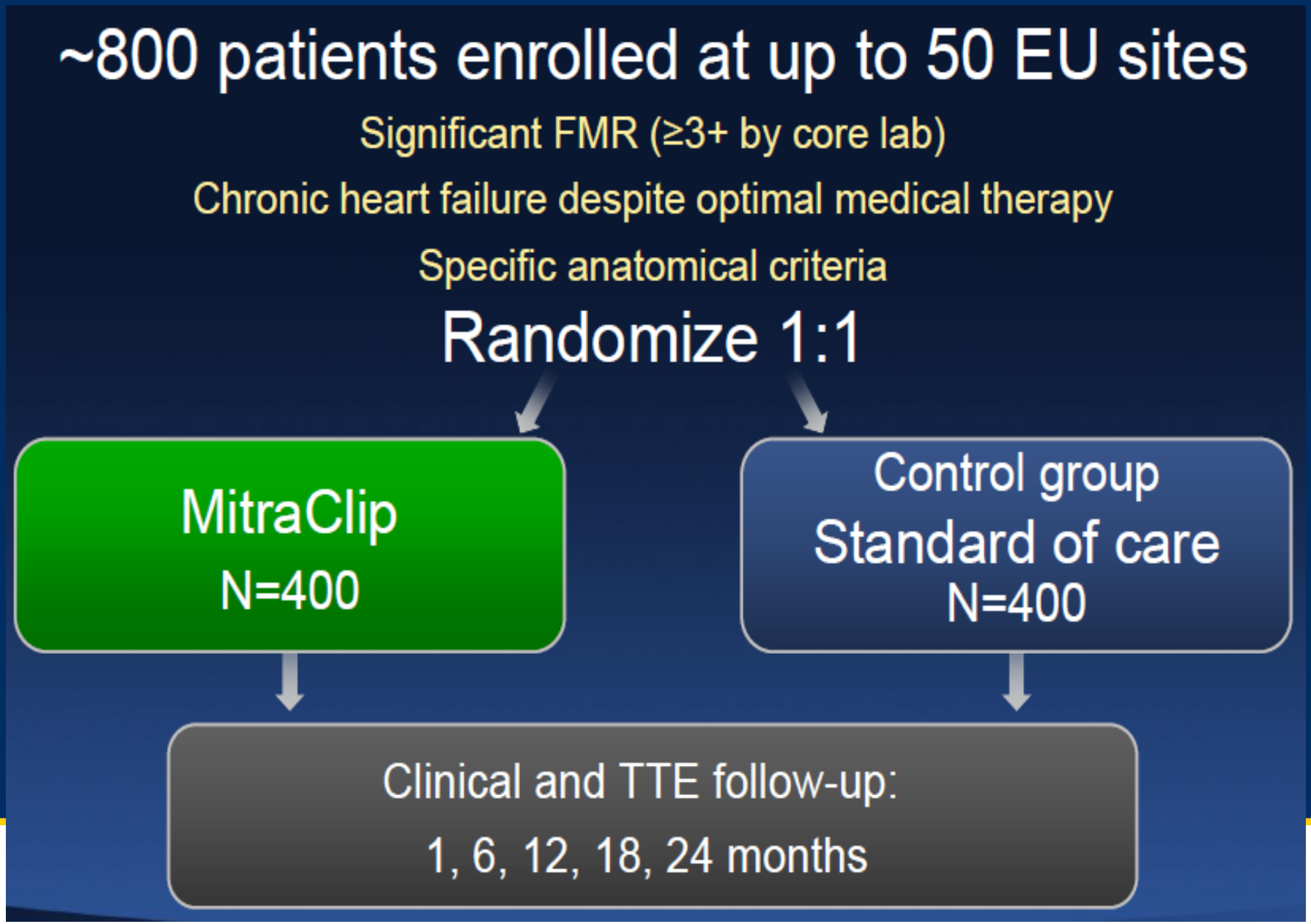
Symptomatic HF treated with maximally tolerated guideline directed medical therapy
Significant FMR (≥3+ by Echo Core Lab)
Not appropriate for MV surgery as determined by site's Local Heart Team
Valve anatomy eligible for MitraClip treatment



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

Primary Endpoint: Hospitalization for heart failure within 2 years

RESHAPE-HF: Trial design



Who to treat with MitraClip?

- Severe MR (+3-4)
- Primary MR (Flail, prolapse) or mixed etiology
- Symptomatic
- High operative risk for surgery

Who not to treat?

- Non high risk patient
- Small mitral orifice area (<3.0 cm2)
- Severe leaflet calcification
- Other anatomical exclusion

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CLINICAL PRACTICE GUIDELINE: FOCUSED UPDATE

2017 AHA/ACC Focused Update of the 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease

IIb	B

Transcatheter mitral valve repair may be considered for severely symptomatic patients (NYHA class III to IV) with chronic severe primary MR (stage D) who have favorable anatomy for the repair procedure and a reasonable life expectancy but who have a prohibitive surgical risk because of severe comorbidities and remain severely symptomatic despite optimal GDMT for heart failure (HF) (124).

Take Home Messages for MitraClip Percutaneous Approaches for Ischemic/Functional MR

- MitraClip therapy is FDA approved for symptomatic patients with severe MR of degenerative etiology (DMR) who are poor surgical candidates

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Take Home Messages for MitraClip Percutaneous Approaches for Ischemic/Functional MR

- MitraClip therapy is FDA approved for symptomatic patients with severe MR of degenerative etiology (DMR) who are poor surgical candidates
- COAPT and RESHAPE Trials will add additional information for patients with symptomatic FMR in high surgical risk
- MitraClip registries in FMR have shown acceptable results in high surgical risk pts
  - Improve NYHA Class, durable improvement in MR, functional improvement in 6 min walking test, reverse LV remodeling

Review Questions

Review Questions

- 1. Which of the **following are statements regarding outcomes of MitraClip in the EVEREST Trial are TRUE:**
  - Surgery is safer then MitraClip at 30 days
  - Surgery is inferior to MitraClip in effectiveness
  - Majority of MitraClip pts had severe residual MR
  - MitraClip was well tolerated with equal symptomatic relief compared to surgery

Review Questions

True or False

Aortic valve disease is more prevalent than mitral valve disease?

Review Question

A target endpoint for the mitral valve clip success:

a. Mean mitral inflow gradient <10 mmHg
b. Resolution of pulmonary flow reversal.
c. Resolution of mitral valve regurgitation.
d. Percutaneous closure of the septal puncture at conclusion of case.

Evidence based references:

1. Nkomo et al. Burden of valvular heart diseases: a population-based study. Lancet 2006;368:1005-11

2. Nishimura et. al. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease. JACC. 2014;63(22):e57-185.

3. Glower et al. Percutaneous Mitral Valve Repair for Mitral Regurgitation in High-Risk Patients. Results of the EVEREST II study. JACC 2014;64:172-81.