

Role of Transcatheter Repair in Moderate Risk Primary MR Patients



LOS ROBLES
HEALTH SYSTEM



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Disclosure Statement of Financial Interest



Within the past 12 months, I or my spouse/partner have had a financial interest/arrangement or affiliation with the organization(s) listed below.

AFFILIATION/FINANCIAL RELATIONSHIP

COMPANY

Grant/Research Support

Co-Principal investigator of the Repair MR trial and EXPAND trial

Co-Principal investigator of the PINNACLE FLX and CHAMPION Trials, Steering committee member of the Triluminate trial. Executive committee member of the RELIEVE HF trial.

Consulting Fees/Honoraria

Abbott, Boston Scientific, Medtronic, Peija Medical, Intershunt

Major Stock Shareholder/Equity

None

Royalty Income

None

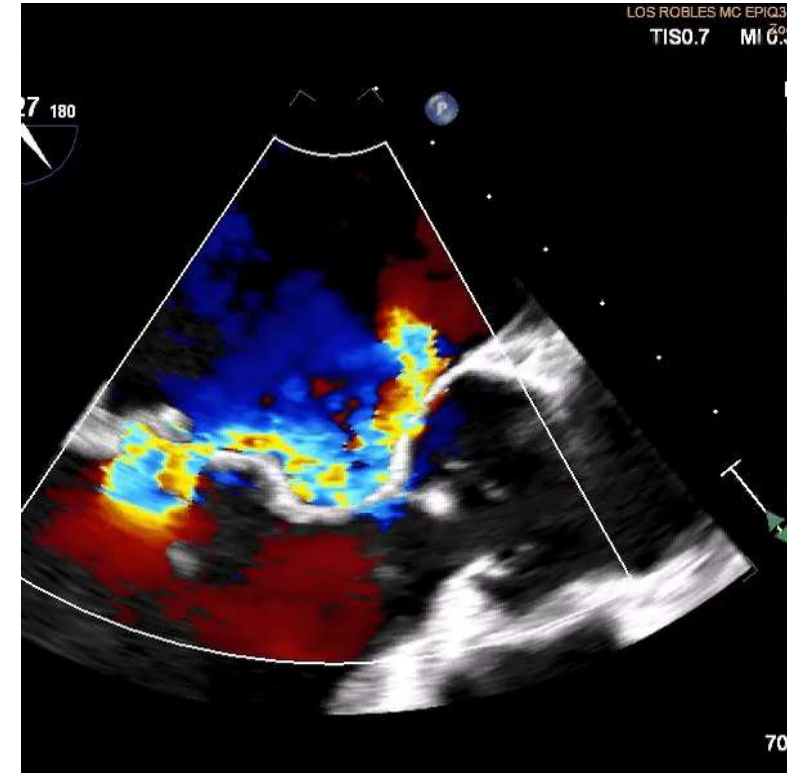
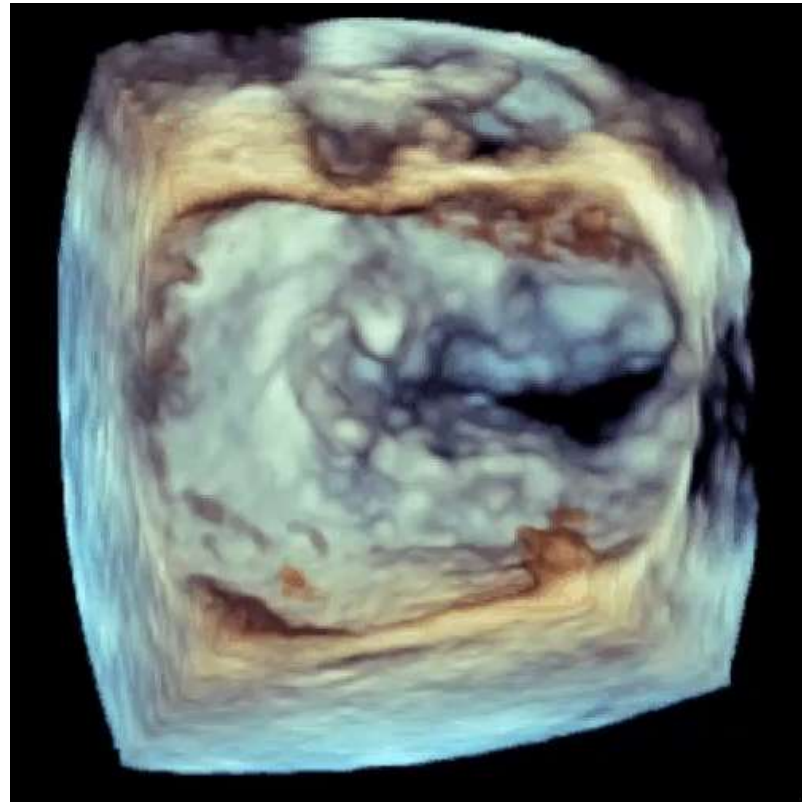
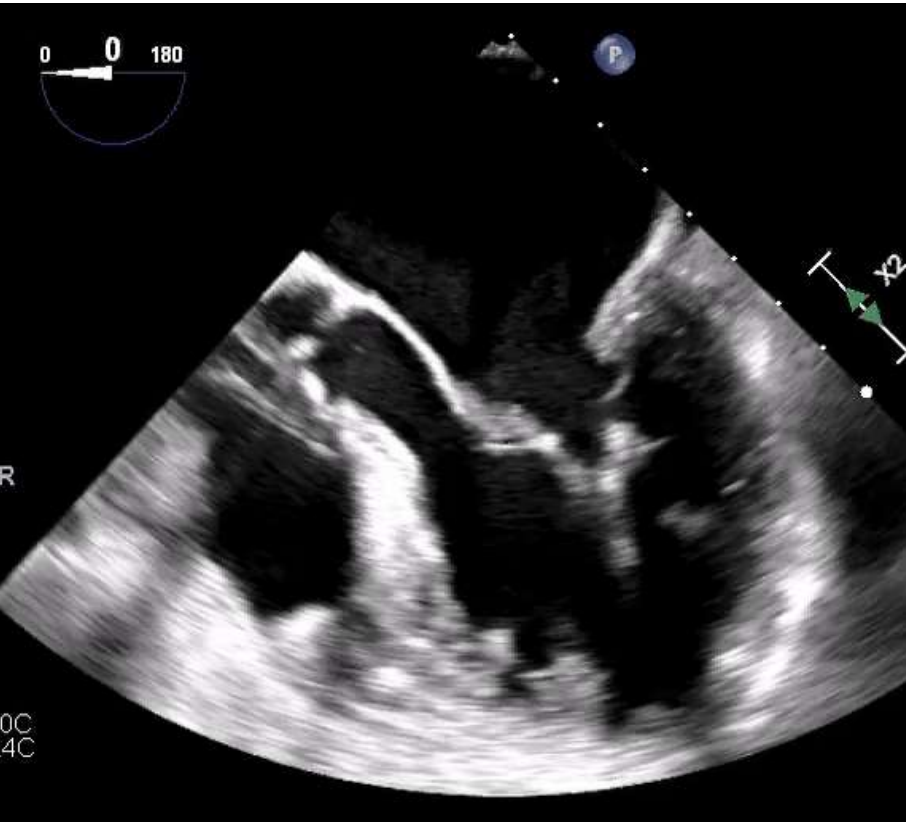
Ownership/Founder

None

Intellectual Property Rights

None

75 year old lady, Jehovah's Witness, mild mitral annular calcification (STS score for mortality < 2)



ACC/AHA valvular heart disease guidelines; Intervention for Patients with Chronic Primary MR



COR	LOE	Recommendations
1	B-NR	1. In symptomatic patients with severe primary MR (Stage D), mitral valve intervention is recommended irrespective of LV systolic function.
1	B-NR	2. In asymptomatic patients with severe primary MR and LV systolic dysfunction (LVEF \leq 60%, LVESD \geq 40 mm) (Stage C2), mitral valve surgery is recommended.
1	B-NR	3. In patients with severe primary MR for whom surgery is indicated, mitral valve repair is recommended in preference to mitral valve replacement when the anatomic cause of MR is degenerative disease, if a successful and durable repair is possible.
2a	B-NR	4. In asymptomatic patients with severe primary MR and normal LV systolic function (LVEF \geq 60% and LVESD \leq 40 mm) (Stage C1), mitral valve repair is reasonable when the likelihood of a successful and durable repair without residual MR is $>$ 95% with an expected mortality rate of $<$ 1%, when it can be performed at a Primary or Comprehensive Valve Center.

Surgical repair
Whenever
Technically
possible

ACC 2021 guidelines: Intervention for Patients with Chronic Primary MR (TEER has only a narrow indication)



COR	LOE	Recommendations
2a	B-NR	6. In severely symptomatic patients (NYHA class III or IV) with primary severe MR and high or prohibitive surgical risk, transcatheter edge-to-edge repair (TEER) is reasonable if mitral valve anatomy is favorable for the repair procedure and patient life expectancy is at least 1 year.
2b	B-NR	7. In symptomatic patients with severe primary MR attributable to rheumatic valve disease, mitral valve repair may be considered at a Comprehensive Valve Center by an experienced team when surgical treatment is indicated, if a durable and successful repair is likely
3: Harm	B-NR	8. In patients with severe primary MR where leaflet pathology is limited to less than one half the posterior leaflet, mitral valve replacement should not be performed unless mitral valve repair has been attempted at a Primary or Comprehensive Valve Center and was unsuccessful.

¹ Otto et al. J Am Coll Cardiol. 2021 Feb 2;77(4):450-500.

What is Moderate Surgical Risk for Primary MR?



TABLE 8 Risk Assessment for Surgical Valve Procedures

Criteria	Low-Risk SAVR (Must Meet ALL Criteria in This Column)	Low-Risk Surgical Mitral Valve Repair for Primary MR (Must Meet ALL Criteria in This Column)	High Surgical Risk (Any 1 Criterion in This Column)	Prohibitive Surgical Risk (Any 1 Criterion in This Column)
STS=predicted risk of death*	<3% AND	<1% AND	>8% OR	Predicted risk of death or major morbidity (all-cause) >50% at 1 y OR
Frailty†	None AND	None AND	≥2 Indices (moderate to severe) OR	≥2 Indices (moderate to severe) OR
Cardiac or other major organ system compromise not to be improved postoperatively‡	None AND	None AND	1 to 2 Organ systems OR	≥3 Organ systems OR
		None		

Moderate Risk?

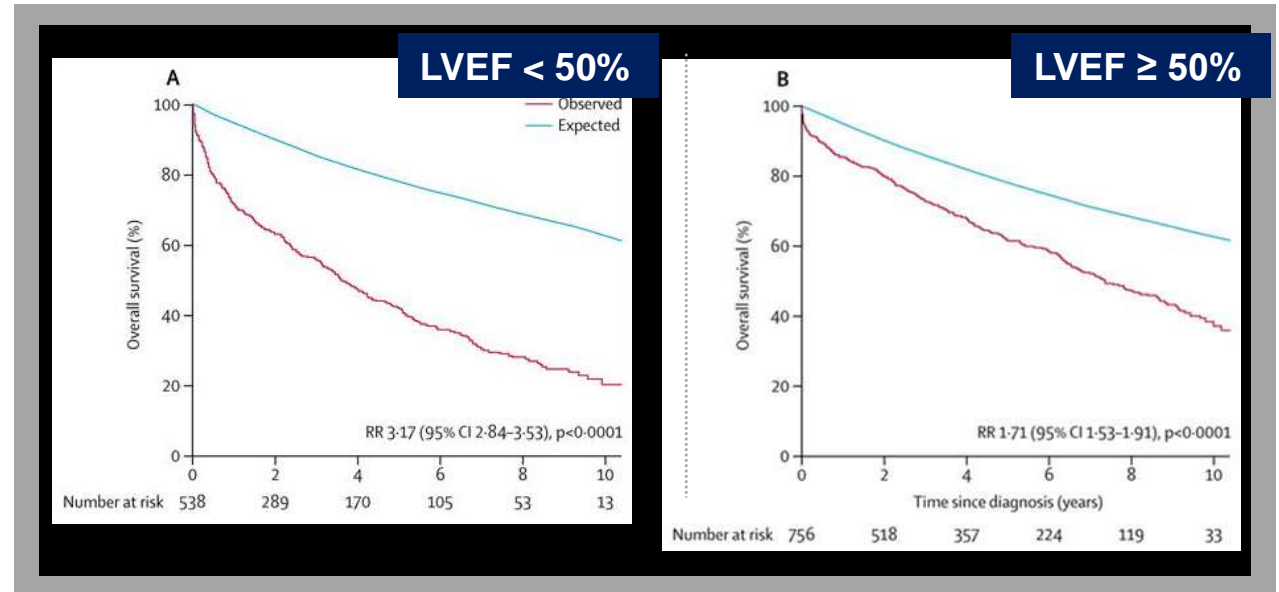
Low risk defined as STS score < 1% without any comorbidities in the most recent guidelines; No mention of moderate surgical risk for primary MR in the Guidelines.

¹ Otto et al. J Am Coll Cardiol. 2021 Feb 2;77(4):450-500.

Undertreatment of Degenerative MR in the community



“ Mitral surgery was ultimately done in only 198 (15%) of 1294 patients...in 164 (29%) of 571 with primary regurgitation. Excess mortality and HF and substantial surgical undertreatment underscore the limits of the current mitral regurgitation standards and suggests that new strategies to improve treatment and outcomes of mitral regurgitation should be tested.¹



Survival after diagnosis of isolated moderate or severe mitral regurgitation, stratified by left-ventricular ejection fraction (LVEF) at diagnosis in Olmsted County residents (median age: 77)

¹Dziadzko et al. Lancet. 2018; 391: 960–969.

Impact of Age in Isolated Mitral Valve Repair



J. MAXWELL CHAMBERLAIN MEMORIAL PAPER FOR ADULT CARDIAC SURGERY

Longitudinal Outcome of Isolated Mitral Repair in Older Patients: Results From 14,604 Procedures Performed From 1991 to 2007

Vinay Badhwar, MD, Eric D. Peterson, MD, Jeffrey P. Jacobs, MD, Xia He, MS, J. Matthew Brennan, MD, Sean M. O'Brien, PhD, Rachel S. Dokholyan, MPH, Kristopher M. George, MD, Steven F. Bolling, MD, David M. Shahian, MD, Fredrick L. Grover, MD, Fred H. Edwards, MD, and James S. Gammie, MD

AGE RANGE	OPERATIVE MORTALITY
65-69 years	1.7%
70-74 years	1.9%
75-79 years	3.4%
80+ years	4.3%

Age is a strong predictor of morbidity and mortality in mitral valve repair with an age of 75 years being a key inflection point

Mitral Valve Repair Surgery:

Operative Outcomes



STS Report – 2019

Operative / In-hospital mortality for Mitral Valve Repair

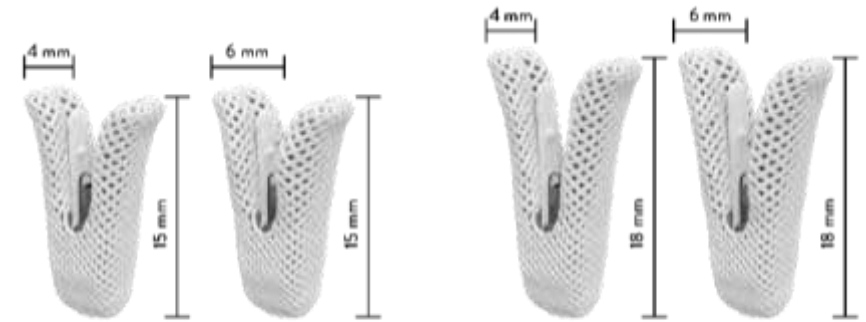
	25th PERCENTILE	50th PERCENTILE	75th PERCENTILE
MV Repair	0.3%	0.6%	1.2%

25% of patients who undergo surgical mitral valve repair have an STS score > 1.2%

Transcatheter Edge-to-Edge Repair for Primary MR



- Despite its safety, effectiveness in select patients, TEER with MitraClip has only a narrow indication for the treatment of primary MR in the US
 - **Primary MR:** Prohibitive risk defined as an STS PROM Repair Score $\geq 6\%$ or frailty or other clinical factors that may introduce a procedure-specific impediment
- Over 100,000 patients treated worldwide
- The MitraClip™ is currently in its 4th generation with new features to simplify the procedure, particularly for patients with complex anatomies
- TEER with PASCAL device is currently in clinical trial for prohibitive risk primary MR



STANDARD LENGTH ARM
(G4 NT / G4 NTW)

LONG LENGTH ARM
(G4 XT / G4 XTW)



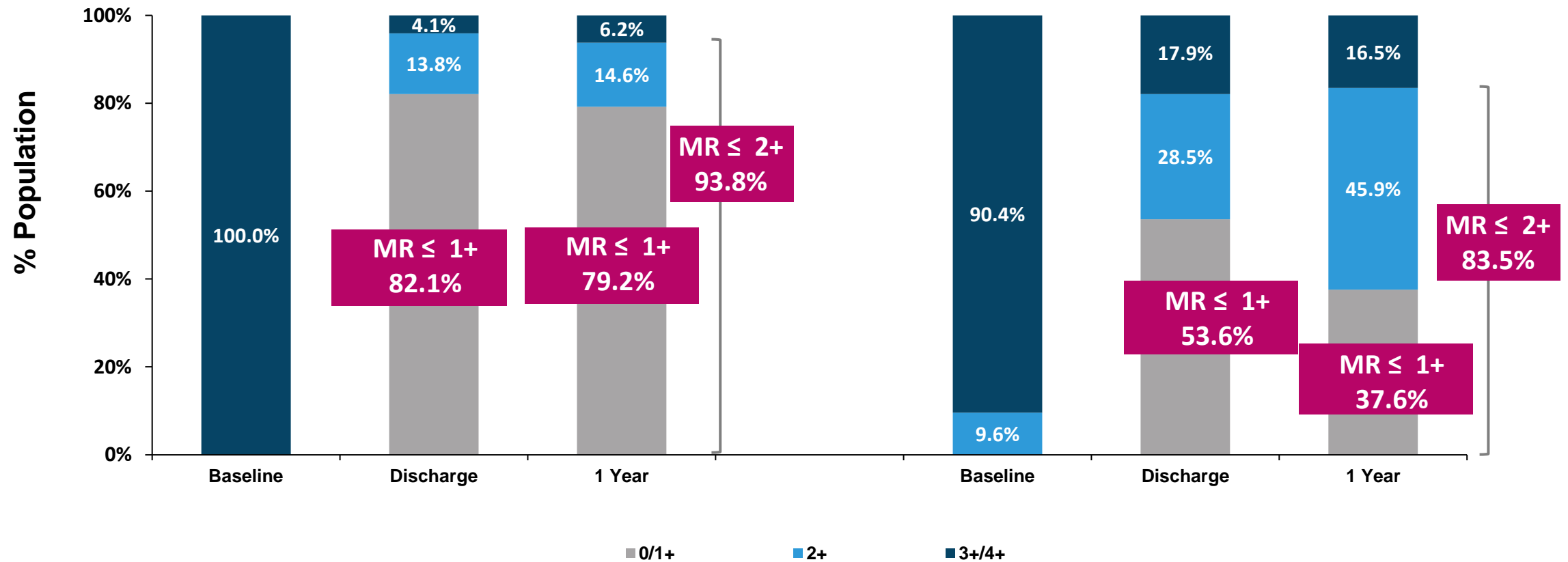
Contemporary MitraClip™ Outcomes:

Improvements in MR Reduction with New Generation MitraClip™ Systems



EXPAND Primary MR Subjects¹
w/ Baseline MR Severity ≥ 3+ (n=279) (2017-2019)

EVEREST/REALISM Prohibitive Risk
Primary MR Cohort² (n=123) (2010-2013)



¹Kar et al. TCT 2020, Late Breaking Clinical Trial Presentation

²Lim et al. ACC 2018 Presentation

Concomitant Tricuspid Repair in Patients with Degenerative Mitral Regurgitation

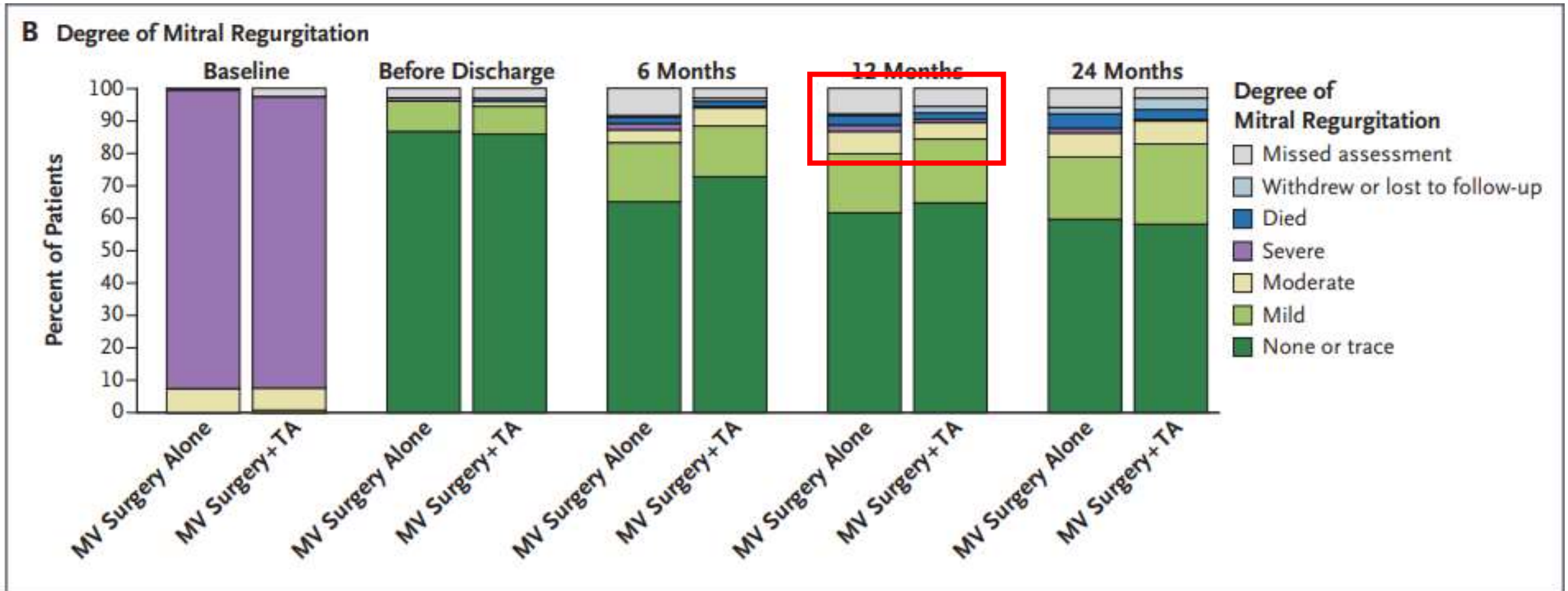


Figure B: The degree of mitral regurgitation among the patients who were undergoing mitral-valve (MV) surgery alone or MV surgery plus tricuspid annuloplasty (TA) during the 2 years after randomization.

TEER in Moderate Surgical Risk:

REPAIR MR: Objectives and Design



SCIENTIFIC OBJECTIVE

Compare the clinical outcome of MitraClip™ device versus surgical repair in patients with severe primary MR who are:

- Moderate Surgical Risk
- Have a mitral valve conducive to repair

TRIAL DESIGN

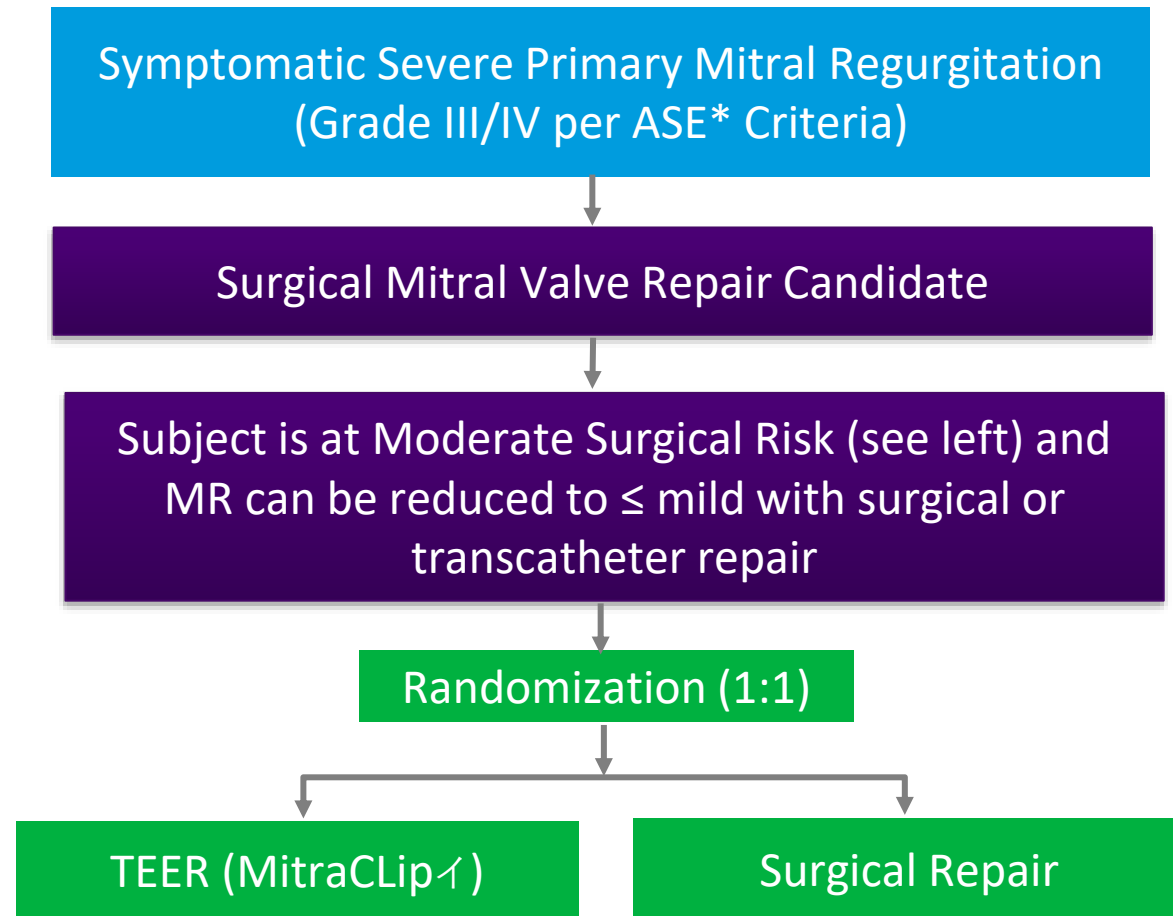
- Prospective, randomized, multi-center study, to be conducted in United States, Canada, and Europe
- 500 subjects enrolled at up to 60 sites in United States, Canada, & Europe
- Principal Investigators: Dr. Patrick McCarthy (Northwestern) and Dr. Saibal Kar (Los Robles)
- Echo Core-Laboratory: Medstar Washington University Hospital (Dr. Federico Asch and Dr. Neil Weissman)



MitraClip in Moderate Surgical Risk: REPAIR MR: Design



- Subject is at least 75 years of age, OR if younger than 75 years, then has:
 - STS-PROM Score $\geq 2\%$, OR
 - Presence of other comorbidities which may introduce a potential surgical specific impediment



MitraClip in Moderate Surgical Risk:



REPAIR MR: Trial Endpoints

PRIMARY ENDPOINTS

- Co-Primary Endpoint #1: All-cause mortality, stroke, cardiac hospitalization, or acute kidney injury requiring renal replacement therapy at 2 years (any cardiac hospitalizations in the first 30 days post treatment will be excluded).
- Co-Primary Endpoint #2: Proportion of subjects with moderate or less MR ($\leq 2+$), without mitral valve replacement, and without recurrent mitral valve intervention (surgical or percutaneous) from the time of index procedure through 2 years.

SECONDARY ENDPOINTS

- Proportion of subjects with MR \leq Mild at 30 days post-index procedure among survivors
- Hospital length of stay from procedure to home discharge (days)
- Proportion of subjects discharged to home post index hospitalization
- Quality of life improvement assessed using the Kansas City Cardiomyopathy Questionnaire (KCCQ) of at least 10 points at 2 years compared to baseline among survivors
- Severe Symptomatic mitral stenosis at 1 year

SUBJECT FOLLOW-UP

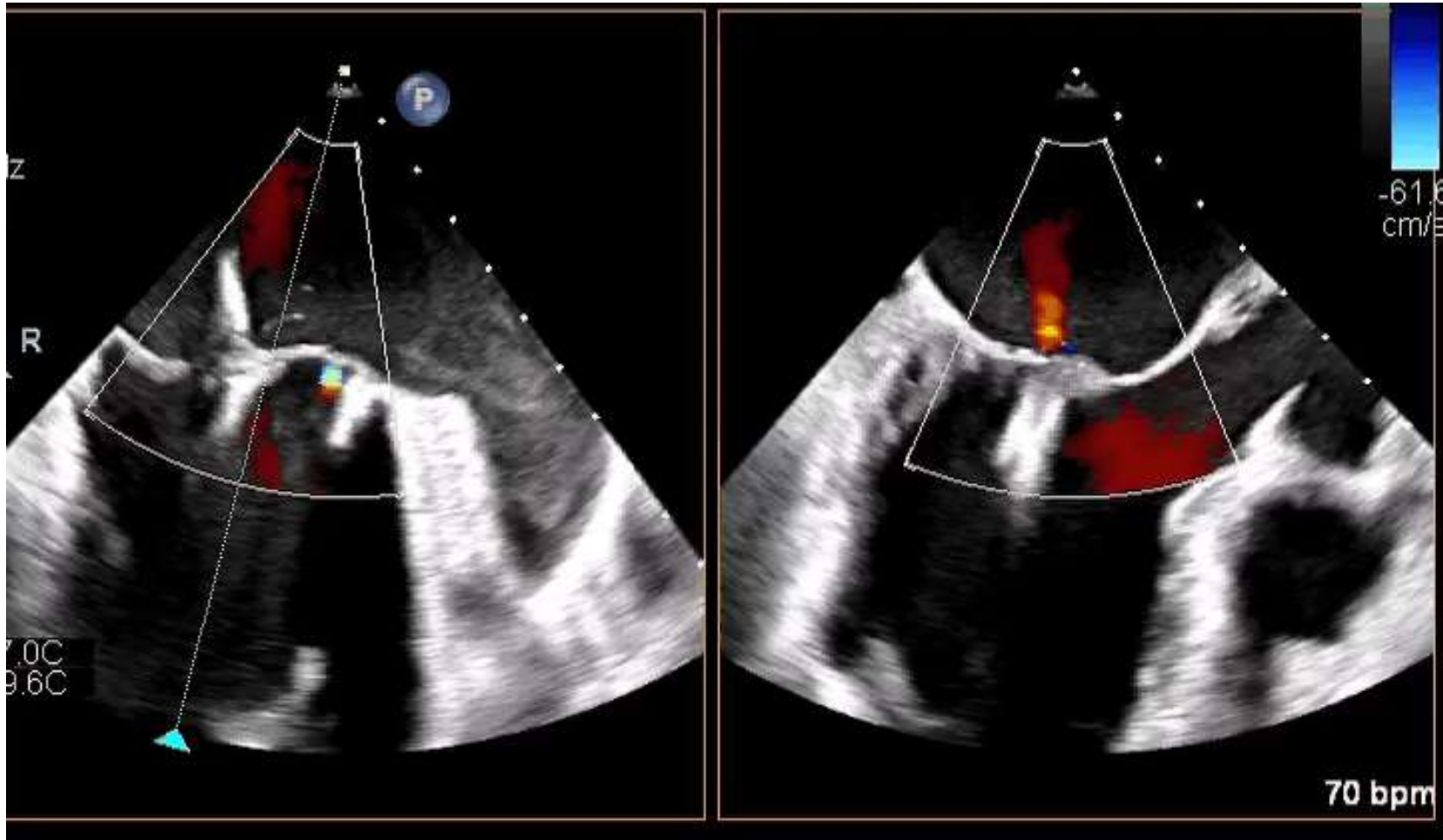
- Screening, Baseline, Index Procedure, Discharge, 30 days, 6 months, 1 year, 18 months, and annually from 2 **to 10 years**

Patient was reluctant to have surgery



- The cardiologist (MR), and heart team without a batting an eye, thought it was reasonable to perform MitraClip procedure
 - 75 years old
 - Some mitral annular calcification
 - Jehovah's Witness
 - Claimed that there was a high likelihood of significant reduction of MR
- Surgical risk is in the eye of the beholder

Disappearance of MR following one XTW Clip



MitraClip for intermediate risk primary MR



- The goal of the study, is to evaluate alternative treatment options, for the right patient population:
 - where there is (i) an unmet clinical need and (ii) equipoise between surgical and transcatheter repair
- We did not combine Echo parameters with hard clinical end points.
 - therefore, the need for two co-primary endpoints
- For the first time, we will have objective, long-term, core lab and CEC adjudicated data for contemporary surgical and transcatheter techniques.

Conclusions



- TEER in Intermediate Risk Primary MR, Will Follow the TAVR's Footsteps
- REPAIR MR, as currently designed, is the right trial for primary MR:
 - *The patient population and the associated benefit-risk will help advance patient care for moderate risk patients*
 - *The randomized nature of the study is intended to increase and improve guideline support for MitraClip™*

TEER in for a Intermediate risk primary MR



- Procedural outcomes associated with MitraClip™ has improved significantly since the early EVEREST II experience.¹
- Mitral valve disease continues to be under treated in the community, where only a minority of affected patients undergo mitral surgery, even when surgical treatment options are available.²
- With improvements in procedural experience, advanced imaging, and availability of new generation devices, the time is NOW to bring a safe and effective transcatheter treatment option for elderly patients who may be candidates for surgery but may also benefit from a MitraClip!

The Time is NOW to evaluate TEER in Intermediate Risk!

¹ Kar et al. Core Lab Adjudicated Contemporary Clinical Outcomes at 1 Year with MitraClip NTR/XTR System from Global EXPAND Study

² Dziadzko et al. Lancet. 2018; 391: 960–969/ Survival after diagnosis of isolated moderate or severe mitral regurgitation, stratified by left-ventricular ejection fraction (LVEF) at diagnosis in Olmsted County residents