

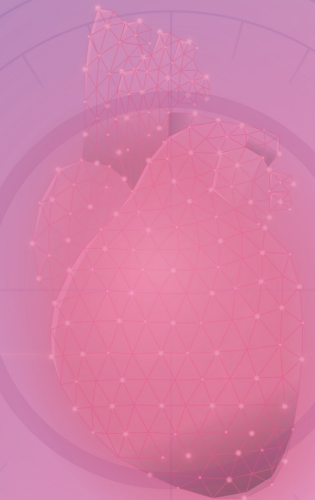


MitraClip for Low, Intermediate, and High-Risk Patients

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Disclosures

- None



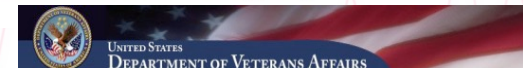
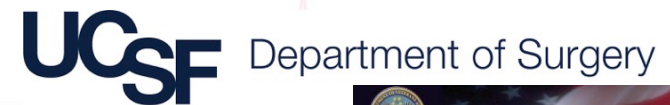
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Outline

Primary MR

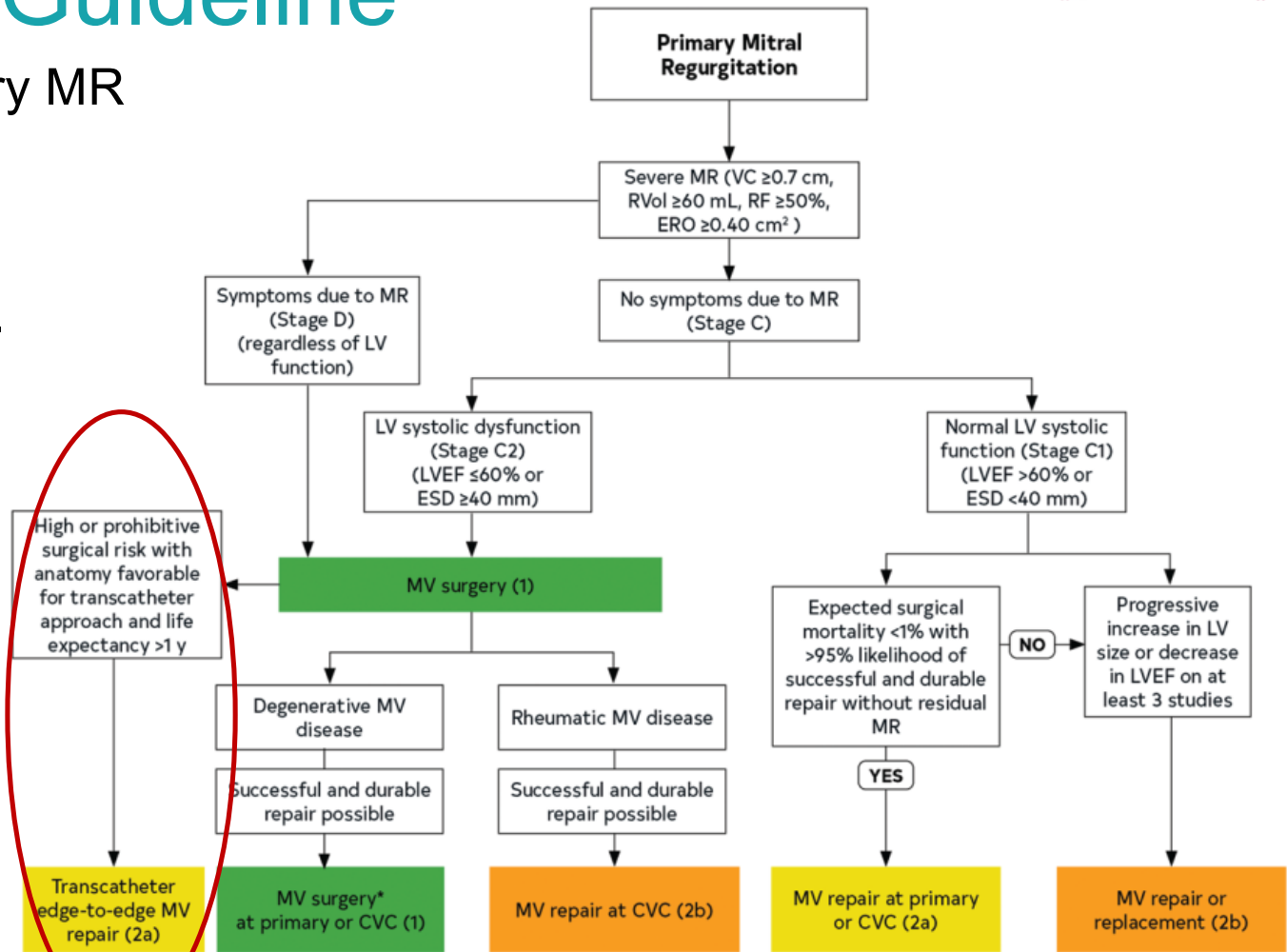
- Guidelines
- High or Prohibitive Risk: EVEREST II 5 yr
- EXPAND G4 1 yr
- STS/ACC TVT Registry: High, Intermediate, Low STS-PROM Risk
- Intermediate and Low Risk Trials



2020 ACC/AHA Guideline

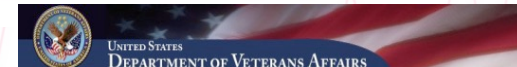
Valvular Heart Disease: Primary MR

- 2a B-NR: Severe sx MR with primary MR, high or prohibitive surgical risk: M-TEER is reasonable if anatomy is favorable for TEER and life expectancy is at least 1 yr.



Otto et al. *Circulation* 2021;143:e00-e00

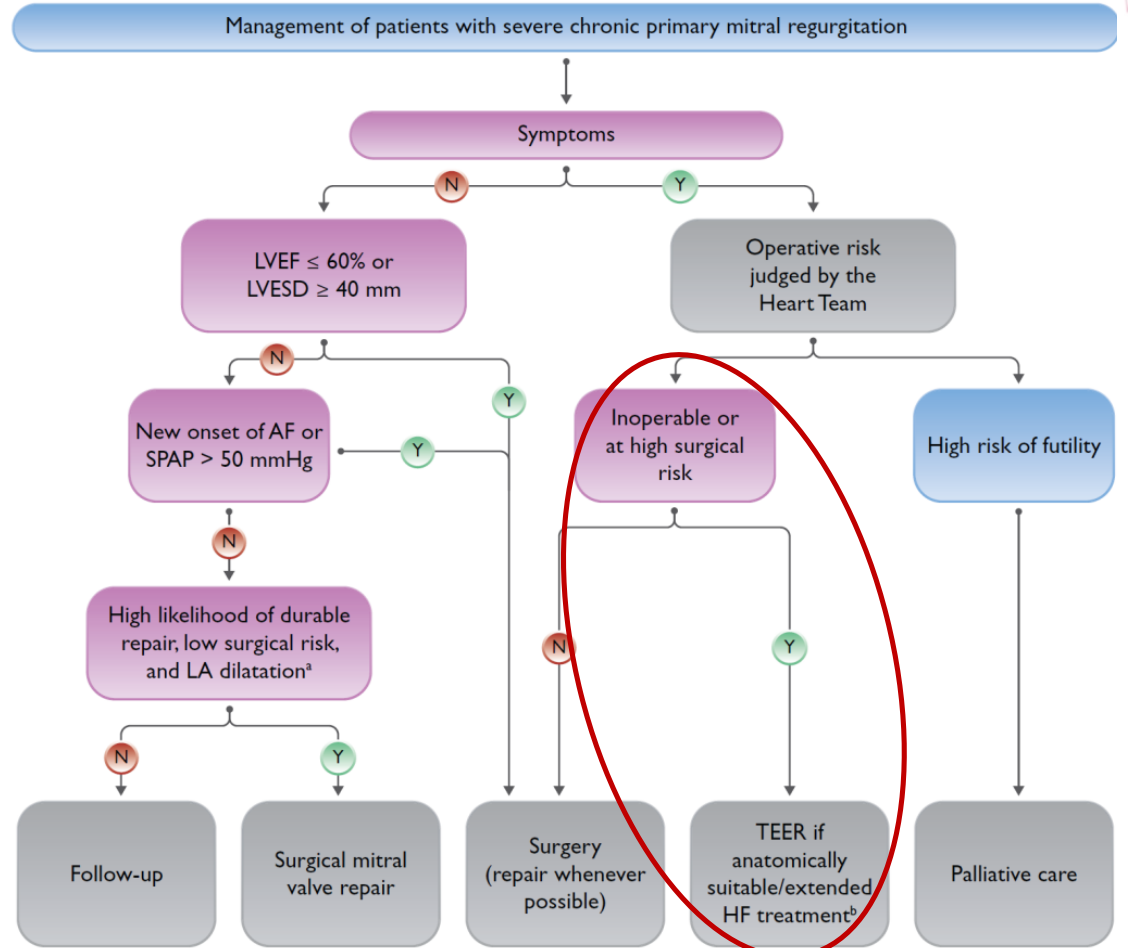
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2021 ESC/EACTS Guidelines

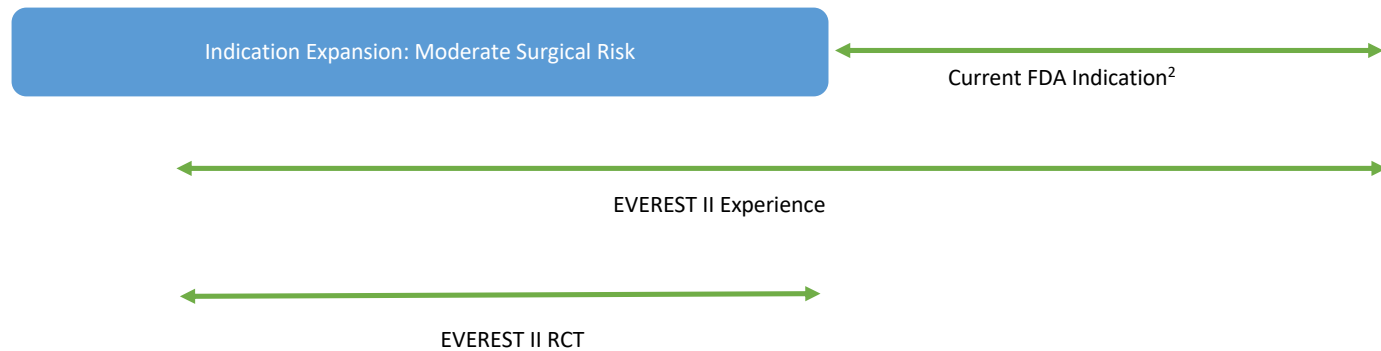
Valvular Heart Disease: Primary MR

- 2b B: M-TEER may be considered in High or prohibitive surgical risk: severe sx MR, anatomically suitable, and when procedure not considered futile

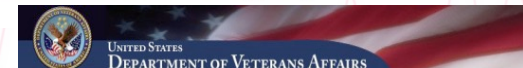
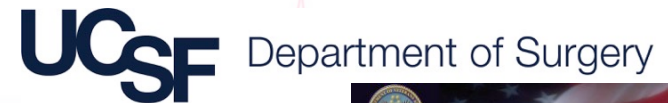


Background: Current risk scale

Low Risk	Intermediate Risk	High Risk	Prohibitive Risk
<ul style="list-style-type: none"> • STS PROM < 4%, AND • No Frailty, AND • No Major Organ system compromise, AND • No Procedure-specific impediment 	<ul style="list-style-type: none"> • STS PROM 4-8%, OR • 1 Index Frailty, OR • 1 Organ system compromise, OR • Possible procedure-specific impediment 	<ul style="list-style-type: none"> • STS PROM > 8%, OR • ≥ 2 Indices Frailty, OR • No more than 2 Organ systems compromise, OR • Possible procedure-specific impediment 	<ul style="list-style-type: none"> • Risk of death with surgery at 1 year > 50%, OR • ≥ 3 Organ systems compromise, OR • Severe procedure-specific impediment



Slide Courtesy of Gorav Ailawadi MD and Gilbert Tang MD



Nishimura, Otto, Bonow et al. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease. Circulation. 2014;129:2440-2492

5-Year Results of EVEREST II Trial

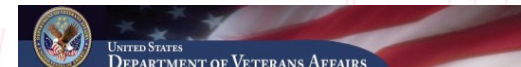
Randomized Comparison of Percutaneous Repair and Surgery for Mitral Regurgitation Endovascular Edge-to-Edge Repair Study

- Multicenter, randomized, nonblinded trial of MitraClip vs surgery for MR to 5-yr f/u in 2013.
- 279 pts enrolled at 37 North American centers, 2005-2008
- 2:1 ratio perc n=178 or surgery n=80
- Eligibility: mod-sev 3+ or sev 4+ chronic MR, sx with LVEF >25% and LVESD ≤55mm OR asx with 1 or more: LVEF 25-60%, LVESD ≥40mm, new onset AF, or PASP >50mmHg at rest or >60mmHg with exercise
- Anatomic inclusion: primary regurgitant jet A2 and P2 MV, both functional and degenerative
- Endpoints: freedom from death, surgery for MV dysfunction, and 3+/4+ MR; freedom from death; freedom from surgery for MV dysfunction; freedom from death and surgery for MV dysfunction



Feldman et al. J Am Coll Card 2015;66:2844-54

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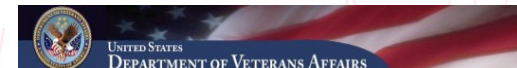
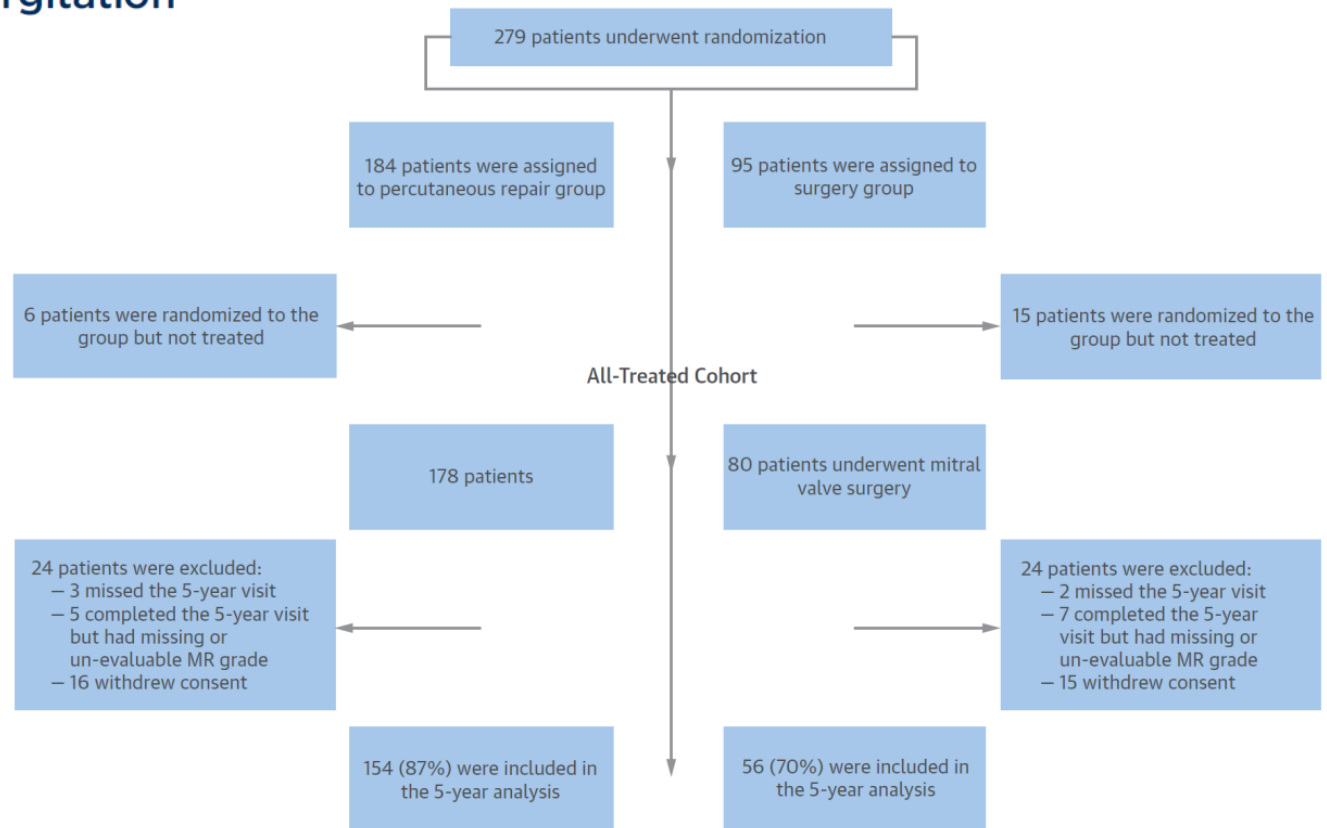


5-Year Results of EVEREST II Trial

Randomized Comparison of Percutaneous Repair and Surgery for Mitral Regurgitation

Endovascular Edge-to-Edge Repair Study

- Mitraclip: single 50.6%, double clip 38.2%, not deployed 11.2%
- Single leaflet device detachment (SLDA) n=9 within 1 yr, n=1 at 14 mo
 - All underwent surgery: 5 MVR and 5 MVr
- No device embolization
- MS n=1, underwent MVR

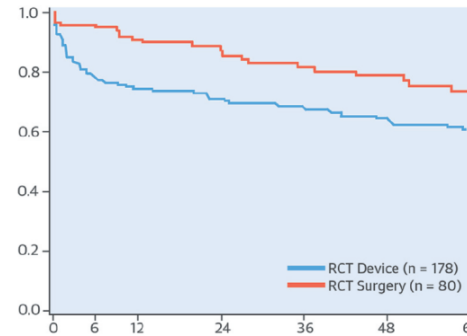


5-Year Results of EVEREST II Trial

Randomized Comparison of Percutaneous Repair and Surgery for Mitral Regurgitation

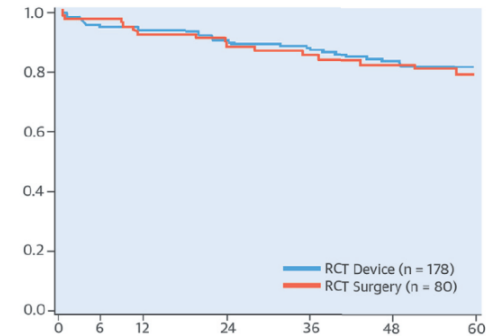
- Freedom from death, surgery & 3+/4+ MR at 5 yrs superior for surgery 64% vs Mitraclip 44%, $p=0.01$
- No difference in death: surgery 20.8% vs TEER 26.8%, $p=0.36$
- Need for reoperation/surgery > for TEER 28% vs surgery 9%, $p=0.003$
- 3+/4+ MR > for TEER 12% vs surgery 2%, $p=0.02$

A. Freedom From Death, MV Surgery or Reoperation



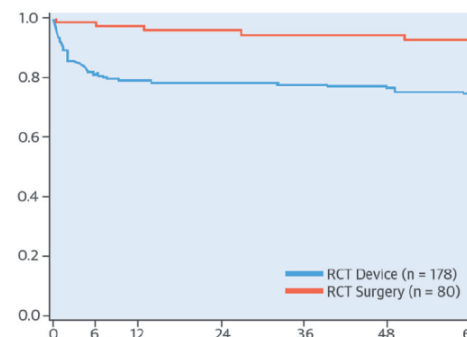
Patients At Risk	Months						
	0	6	12	24	36	48	60
Device Group	178	136	128	117	109	98	45
Control Group	80	75	69	63	54	49	21

B. Freedom From Death



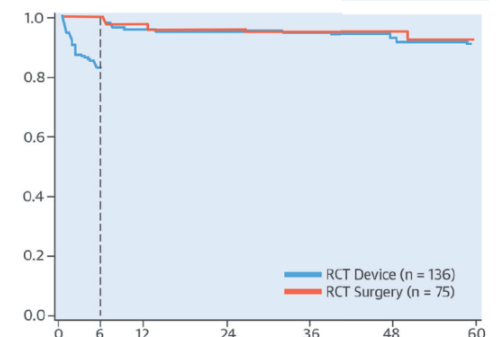
Patients At Risk	Months						
	0	6	12	24	36	48	60
Device Group	178	165	158	143	133	119	58
Control Group	80	76	70	65	57	52	24

C. Freedom From MV Surgery or Reoperation



Patients At Risk	Months						
	0	6	12	24	36	48	60
Device Group	178	136	128	117	109	98	45
Control Group	80	75	69	63	54	49	21

D. Landmark Analysis of Freedom From MV Surgery or Reoperation Beyond 6 Months



Patients At Risk	Months						
	0	6	12	24	36	48	60
Device Group	178	136	128	117	109	98	45
Control Group	80	75	69	63	54	49	21



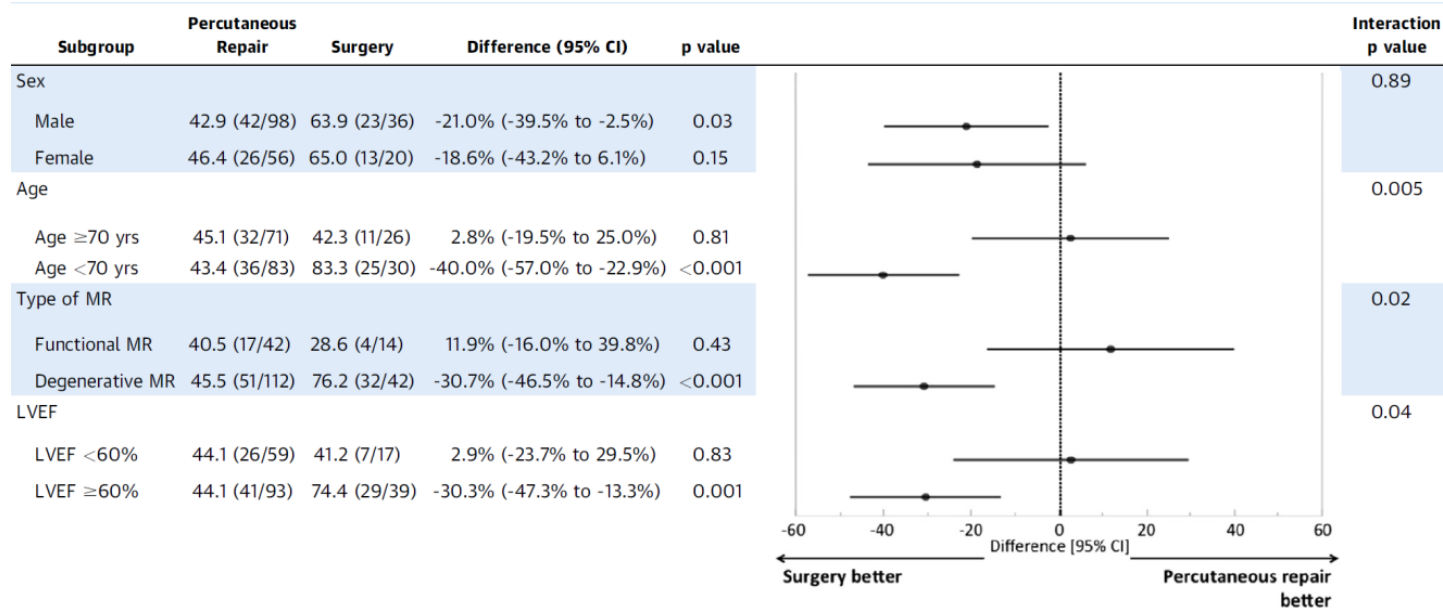
Feldman et al. J Am Coll Card 2015;66:2844-54

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5-Year Results of EVEREST II Trial

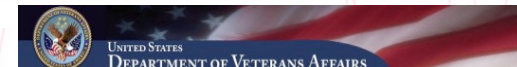
Randomized Comparison of Percutaneous Repair and Surgery for Mitral Regurgitation



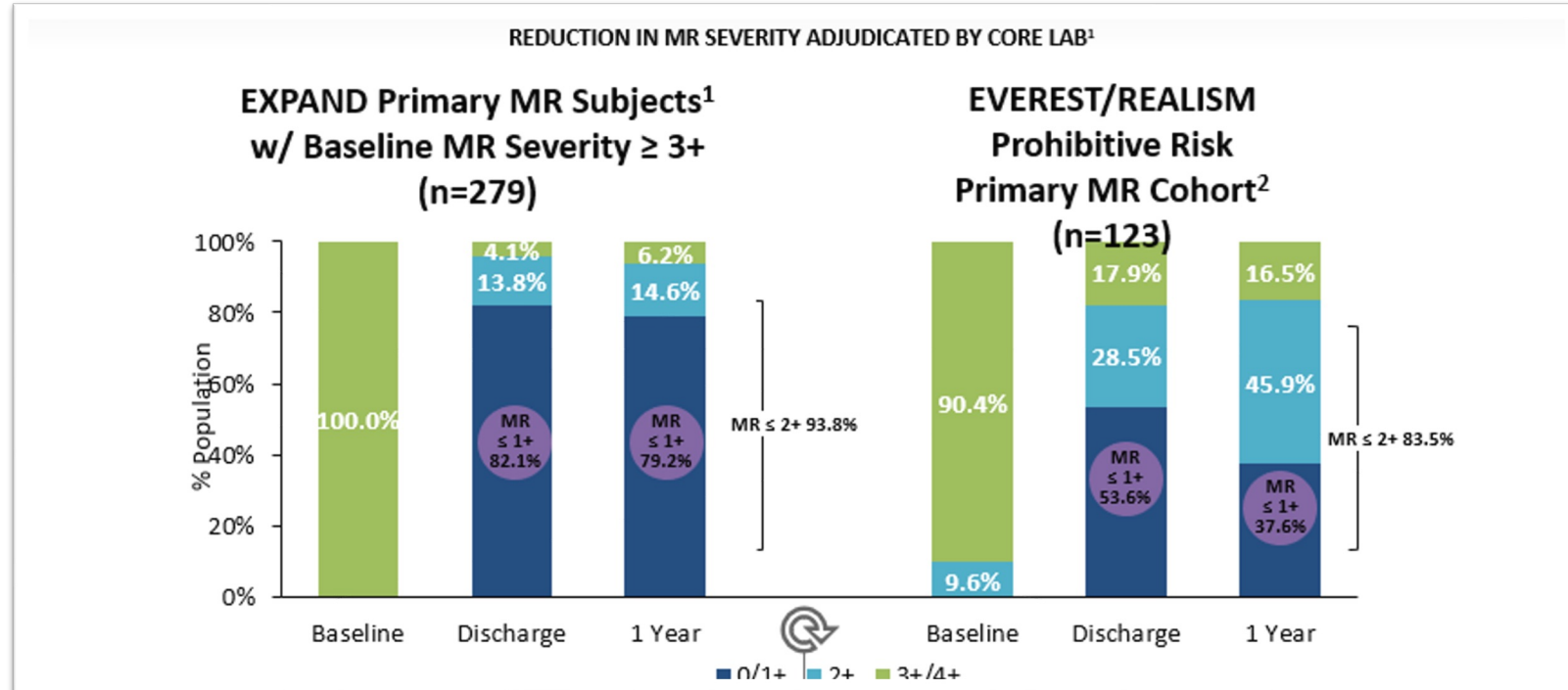
- Surgery performed better than TEER in younger pts (<70).
- Surgery better for degenerative MR than TEER.
- Surgery better for LVEF ≥60%



Feldman et al. J Am Coll Card 2015;66:2844-54



Outcomes Improved with Experience and New Generation Devices



- Significant durable MR reduction with MitraClip therapy in contemporary use (EXPAND) compared to historical trials (EVEREST/REALISM)

Courtesy of Gilbert Tang MD and Gorav Ailawadi MD



Feldman et al. J Am Coll Card 2015;66:2844-54



1-Yr Results EXPAND G4

1-Year Outcomes With Fourth-Generation Mitral Valve Transcatheter Edge-to-Edge Repair From the EXPAND G4 Study

- 4th generation MitraClip G4: 2 wider clip sizes (NTW, XTW), independent grasping feature, improved clip deployment sequence
- Objective:** 1-yr outcomes G4 system in contemporary real-world



EXPAND G4 Study Design

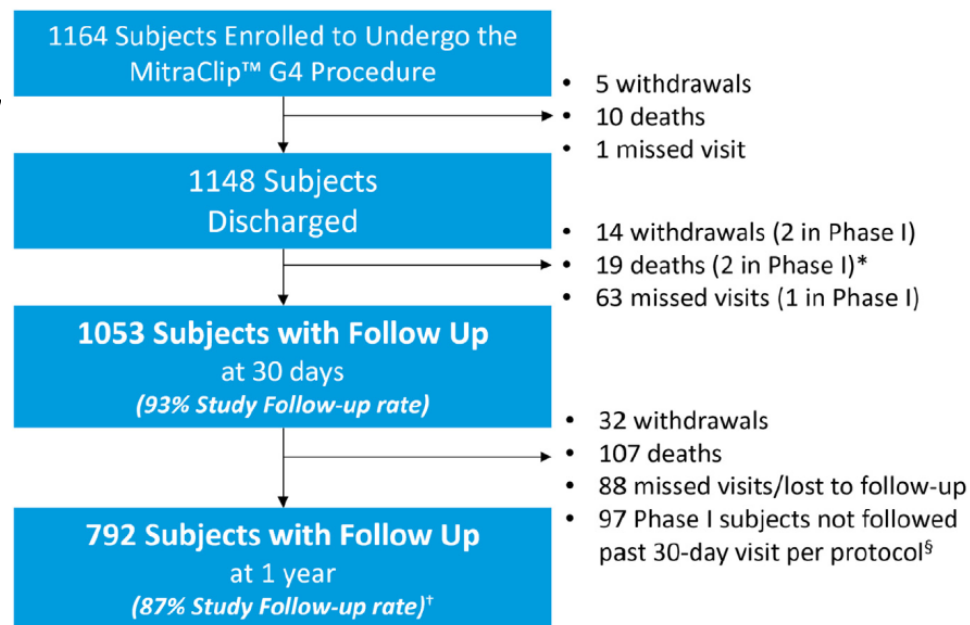
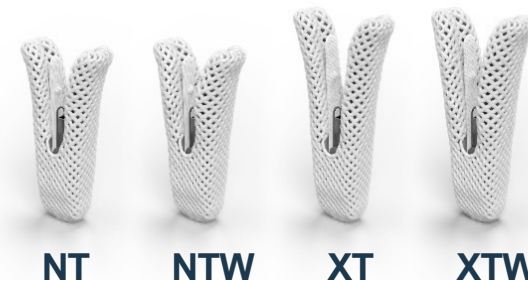
- Prospective, multi-center, international, single arm study
- Primary and secondary MR
- N=1164 pts M-TEER 2020-2022, 60 centers US, Canada, Europe and Japan



Follow Up: Discharge, 30d, and yearly through 5yrs



Key Outcome Measures: All-cause mortality, HFH, MR severity, functional capacity NYHA class, QOL (KCCQ)



Von Bardeleben et al. J Am Coll Card Intv 2023;

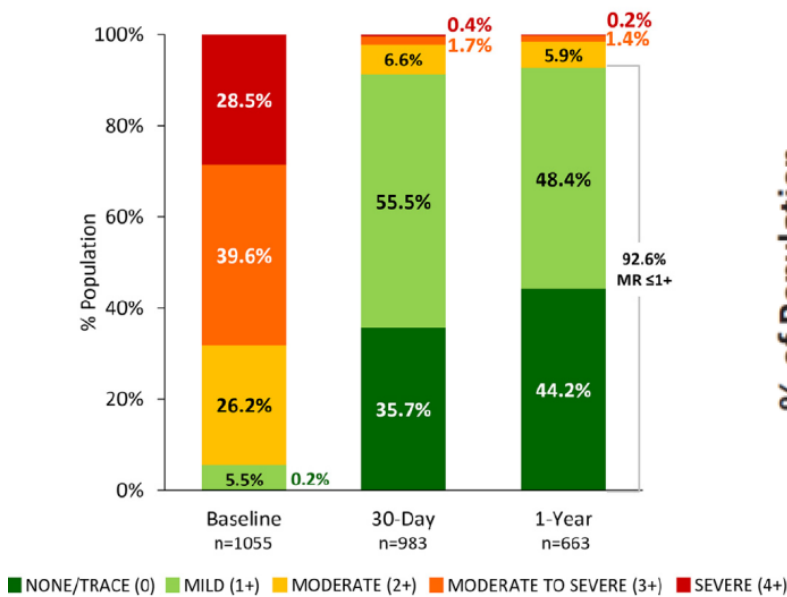
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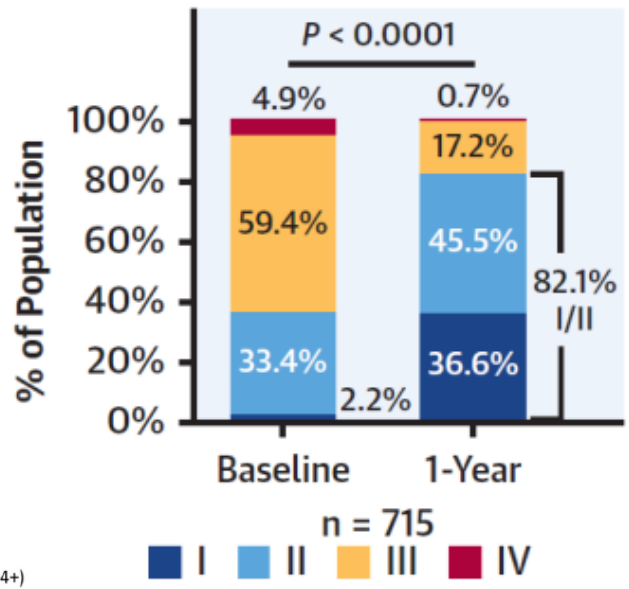
1-Yr Results EXPAND G4

1-Year Outcomes With Fourth-Generation Mitral Valve Transcatheter Edge-to-Edge Repair From the EXPAND G4 Study

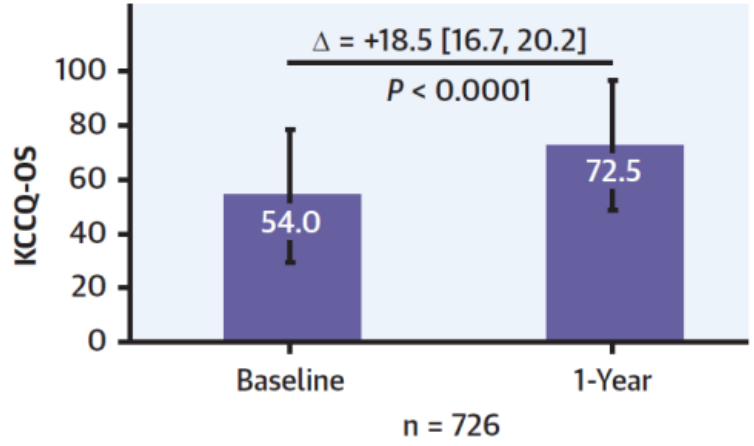
MR Grade in All Subjects



NYHA Functional Class Improvement through 1 Year



Improvement in Quality of Life through 1 Year



- 93% had MR ≤1+, 82% NYHA I/II, KCCQ score improved by 18.5 point



Von Bardeleben et al. J Am Coll Card Intv 2023;

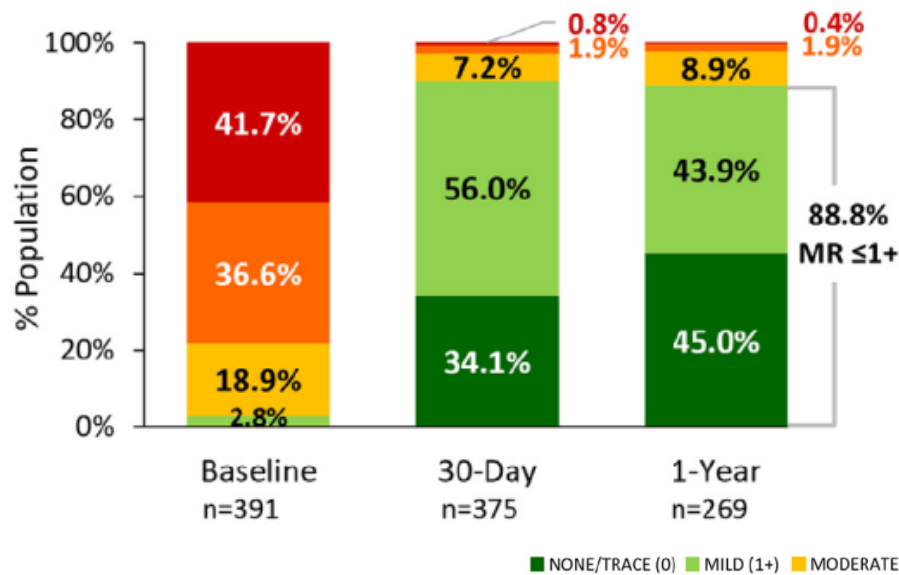


1-Yr Results EXPAND G4

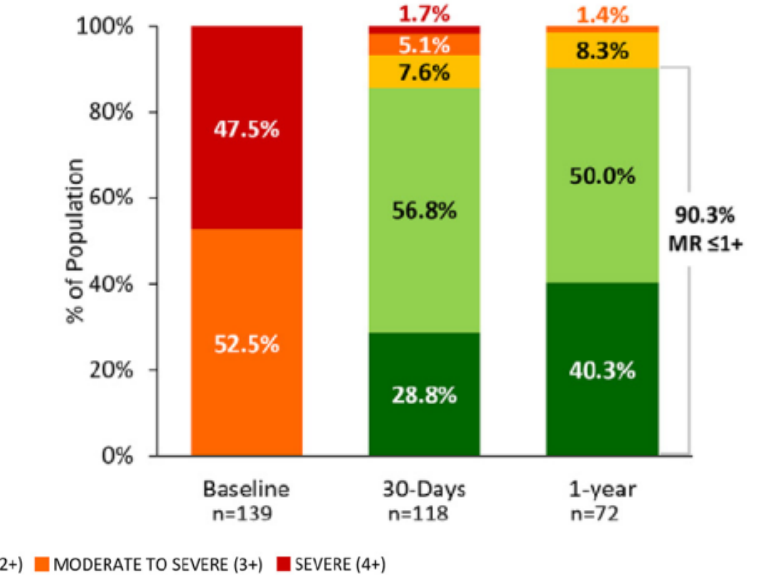
Primary MR

1-Year Outcomes With Fourth-Generation Mitral Valve Transcatheter Edge-to-Edge Repair From the EXPAND G4 Study

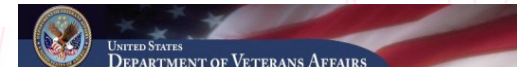
A MR Grade in All PMR Subjects



A MR Grade in Subjects with Complex Anatomy



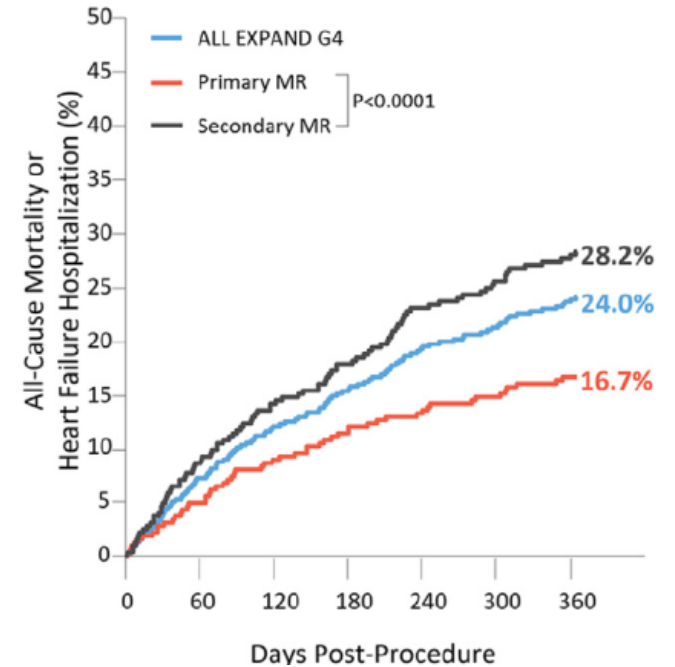
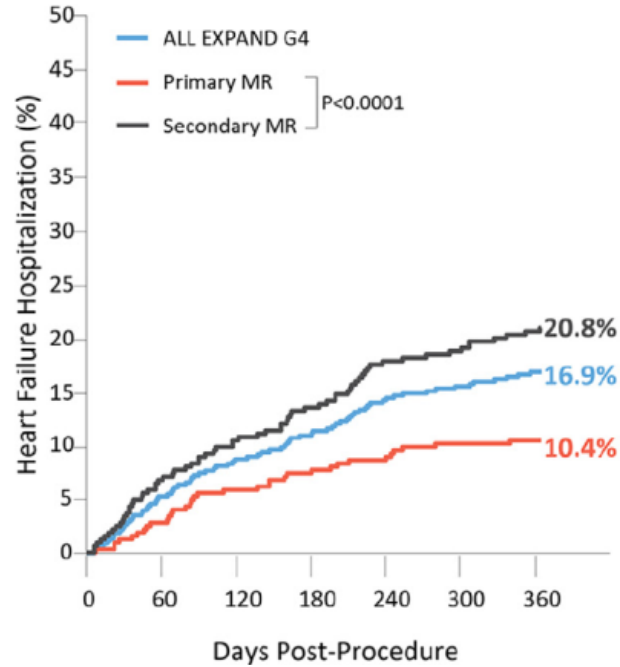
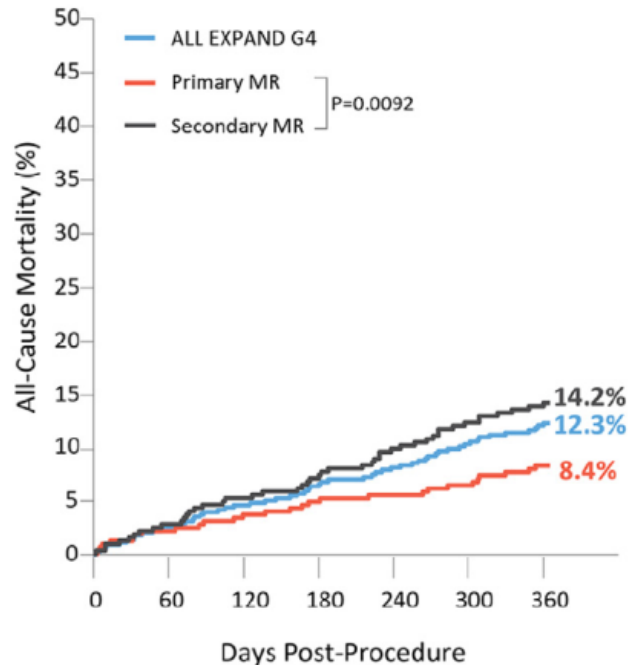
- Primary MR (43%): 89% had ≤1+ MR
- With complex anatomy 90% had ≤1+ MR



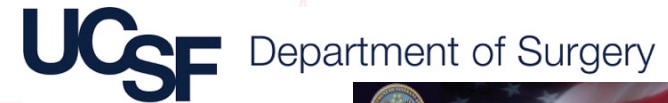
Von Bardeleben et al. J Am Coll Card Intv 2023;

1-Yr Results EXPAND G4

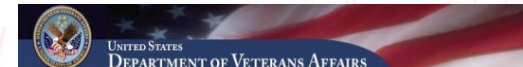
1-Year Outcomes With Fourth-Generation Mitral Valve Transcatheter Edge-to-Edge Repair From the EXPAND G4 Study



Primary MR had less all-cause mortality, less heart failure hospitalizations, and less combined endpoint



Von Bardeleben et al. J Am Coll Card Intv 2023;



Real World Data M-TEER by Surgical Risk

JAMA | Original Investigation

Transcatheter Mitral Valve Repair for Degenerative Mitral Regurgitation

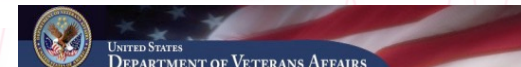
STS/ACC TVT Registry

- All pts mod-sev or sev degenerative MR TMVr in US 2014-2022
- STS-PROM risk: high $\geq 8\%$, intermediate 2-8%, low $< 2\%$
- TMVr N=60883 Mitraclip total: N=19088 degenerative MR mod-sev or sev
 - N=1929 (10.1%) low risk STS $< 2\%$, 12973 (68%) intermediate, 4186 (21.9%) high risk
- Median age 82 (IQR 76-86); 48% women; 78% NYHA class III/IV
- Median STS MVr risk 4.6% (2.8-7.4%)



Makkar et al. JAMA 2023;329(20):1778-88

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Real World Data M-TEER by Surgical Risk

JAMA | Original Investigation

Transcatheter Mitral Valve Repair for Degenerative Mitral Regurgitation

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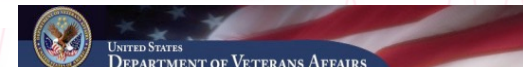
- MR success = mod or less residual MR, no sev MS (<10mmHg)
- MR success 95% at procedure, 93% at discharge, 89% at 30d
- MR success increased 82% 2014 to 92% 2022

Mean mitral valve gradient, mm Hg	≥10	Unsuccessful procedure		2067/18 766 (11.0%)
	>5 to <10	Mild MR or less and mitral gradient 5-10 mm Hg 2221/18 766 (11.8%)	Moderate MR and mitral gradient 5-10 mm Hg 1207/18 766 (6.4%)	Unsuccessful procedure
	≤5	Mild MR or less and mitral gradient ≤5 mm Hg 9824/18 766 (52.4%)	Moderate MR and mitral gradient ≤5 mm Hg 3447/18 766 (18.4%)	
		Mild MR or less	Moderate MR	Higher than moderate MR
Residual MR				



Makkar et al. JAMA 2023;329(20):1778-88

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Real World Data M-TEER by Surgical Risk

JAMA | Original Investigation

Transcatheter Mitral Valve Repair for Degenerative Mitral Regurgitation

STS/ACC TVT Registry

■ In hospital and 30-d Outcomes

- In-Hospital mortality 1.1%; at 30d 2.7% (STS-PROM 4.6%)
- CVA 0.6%; at 30d 1.2%
- Need for unplanned cardiac surgery or intervention 1.1%; at 30d 0.97%
- SLDA 0.9%; Device Embolization 0.08%
- Median LOS 1 day (IQR 1-3d)

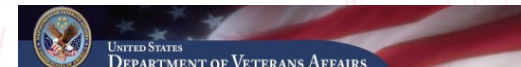
■ 1 yr Outcomes

- Death 15.4%
- Mitral valve reintervention 3.4%
- HF admission 9.3%



Makkar et al. JAMA 2023;329(20):1778-88

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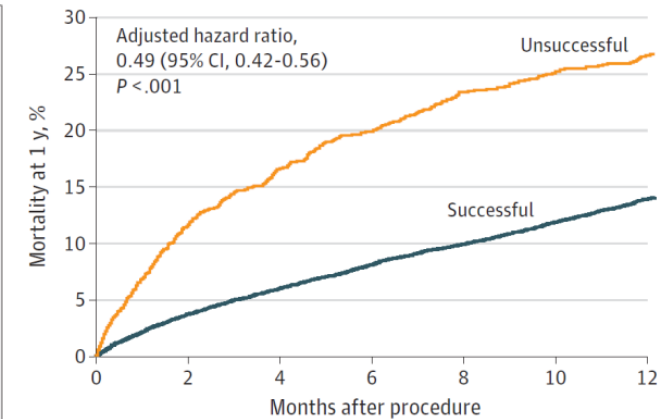
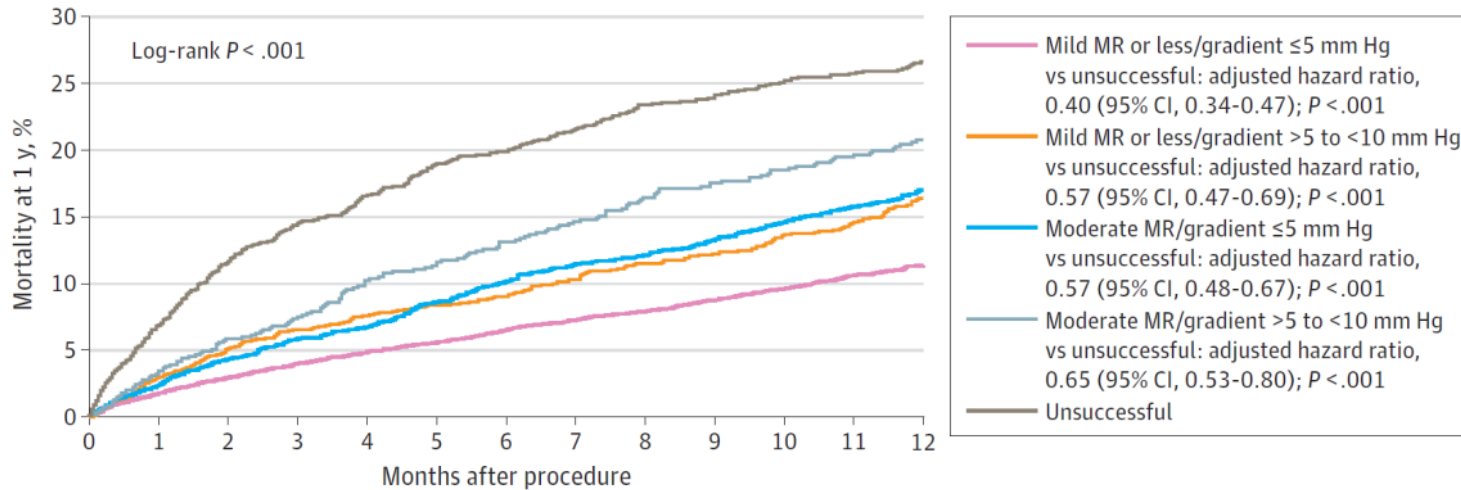


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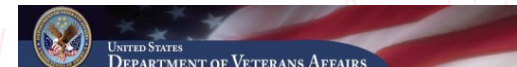


- MR success 95% at procedure, 93% at discharge, 89% at 30d
 - MR success increased 82% 2014 to 92% 2022
 - Pts mild MR or less & gradient < 10 mmHg increased from 45% 2014 to 72% 2022.
- Pts with better MR success had lower 1-yr mortality



Makkar et al. JAMA 2023;329(20):1778-88

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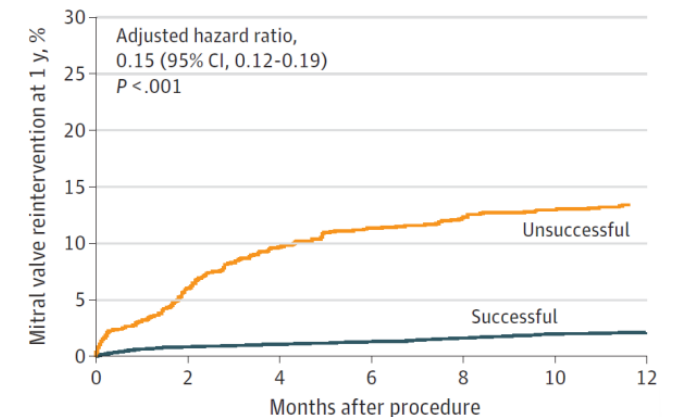
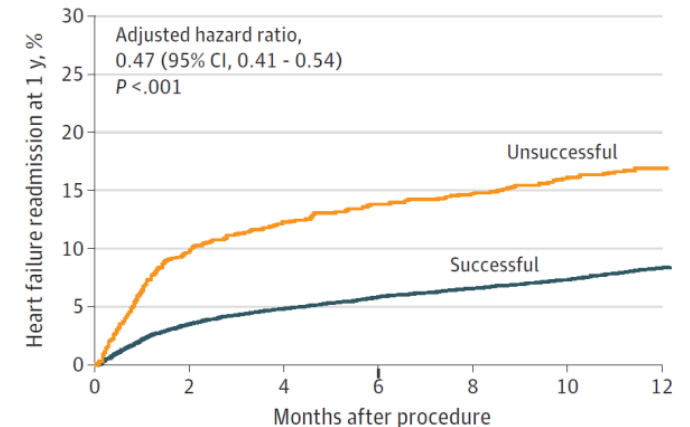
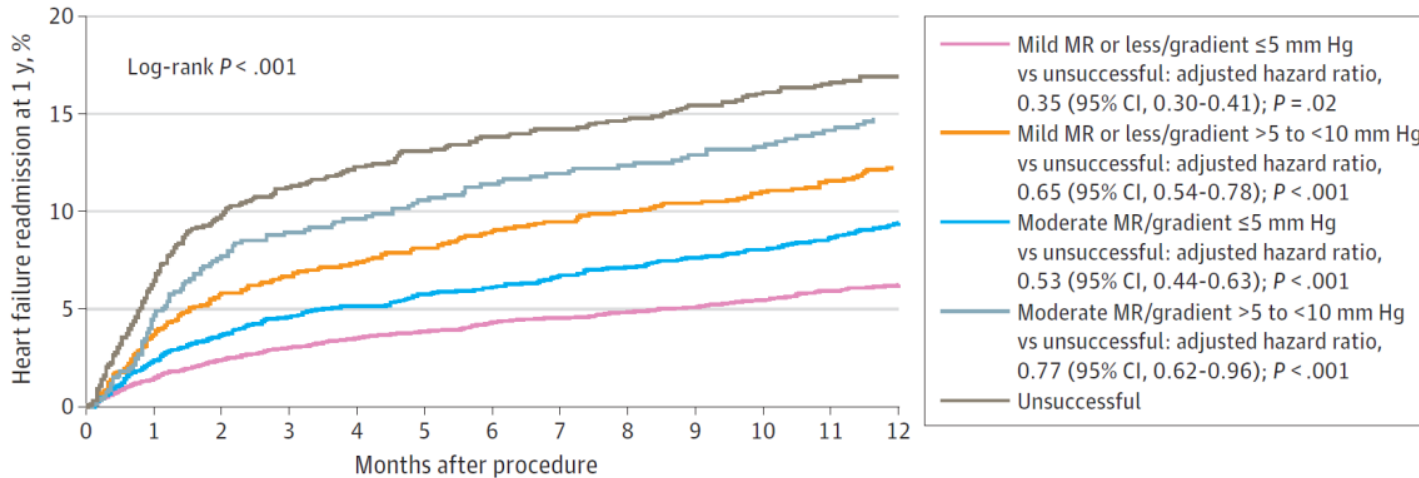


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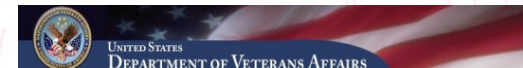


- Level of MR success impacted HF readmission
- Pts with procedure success had significantly reduced HF readmission, and MV reintervention rates at 1yr than those with unsuccessful TEER



Makkar et al. JAMA 2023;329(20):1778-88

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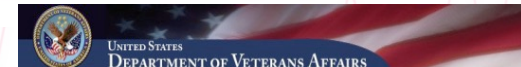
Ongoing Randomized Trials of TEER

Intermediate and Low Risk

- REPAIR MR: MitraClip vs Surgical Mitral Valve Repair for Severe Primary MR in pts of Intermediate Surgical Risk
- PRIMARY: TEER versus Surgical Mitral Repair in pts ≥ 65 years old with Primary Degenerative MR of any Surgical Risk (Low, Intermediate, or High)



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REPAIR MR Clinical Trial

Percutaneous MitraClip™ Device or Surgical Mitral Valve **RE**pair in **PA**tients with **Pr**ima**Ry** **M**itral **R**egurgitation who are Candidates for Surgery (REPAIR-MR)

Prospective, randomized, controlled, multi-center clinical trial of the MitraClip™ device in patients with severe primary mitral regurgitation, whose mitral valve has been determined to be suitable for correction by MR repair surgery.



Courtesy of Gilbert Tang MD and Gorav Ailawadi MD

McCarthy et al. J Am Heart Assoc 2023;12:e027504

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REPAIR MR Clinical Trial

Patient Population

- Symptomatic, or asymptomatic (LVEF \leq 60%, PA Systolic Pressure $>$ 50 mmHg, or LVESD $>$ 40 mm)
- \geq 75 years of age, OR if younger:
 - STS-PROM Score \geq 2%, OR
 - Presence of other comorbidities which may introduce a potential surgical specific impediment

Severe Primary Mitral Regurgitation
(Grade III/IV per ASE* Criteria)

Cardiac Surgeon of the Site Heart Team
Concurs that the Mitral Valve can be
repaired with a high degree of success

NO → Exclude Subject

YES

Subject Meets all Inclusion/Exclusion Criteria
and the Eligibility Committee Confirms that
MR can be Reduced to \leq Mild with Both
MitraClip and Mitral Valve Repair Surgery

NO → Exclude Subject

YES

Randomization (1:1)
(N=500)

Transcatheter Repair - MitraClip
(Device)

Surgical Mitral Valve Repair
(Control)



REPAIR MR Trial: Noninferiority Design

Primary and Secondary Endpoints

PRIMARY ENDPOINTS

- **Co-Primary Endpoint #1:** All-cause mortality, stroke, cardiac hospitalization, or acute AKI requiring renal replacement therapy at **2 yrs** (any cardiac hospitalizations in the first 30d post treatment will be excluded)
- **Co-Primary Endpoint #2:** Proportion of subjects with \leq **Moderate MR** ($\leq 2+$), w/o MVR, and w/o recurrent MV intervention (surgical or percutaneous) to **2 yrs**.

SECONDARY ENDPOINTS

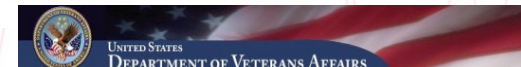
- **MR \leq Mild** ($\leq 1+$) at 30d post-index procedure among survivors
- Hospital LOS from procedure to home discharge (days)
- Discharge to home post index hospitalization
- QOL improvement of at least 10 points at **2 yrs** assessed using KCCQ (Kansas City Cardiomyopathy Questionnaire) compared to baseline among survivors
- **Severe Symptomatic Mitral Stenosis** at **1 yr**



McCarthy et al. J Am Heart Assoc 2023;12:e027504



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Percutaneous or Surgical Repair In Mitral Prolapse And Regurgitation for ≥ 65 Years



PRIMARY Trial

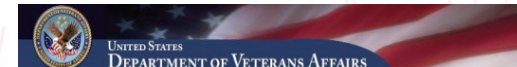
- **Primary aim:** Evaluate long-term effectiveness and safety of MV TEER vs surgical repair in primary DMR.
- **Secondary aim:** Analyze relationship btw adequacy of MR correction at **1 yr** post randomization and long-term clinical outcomes (death, HF hospitalizations/urgent care visits, valve re-interventions, and QOL).
- **Tertiary aim:** Evaluate patient-centered outcomes (QOL, functional status, discharge location).



Courtesy of Gilbert Tang MD and Gorav Ailawadi MD

ClinicalTrials.gov ID NCT05051033

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PRIMARY Trial Design

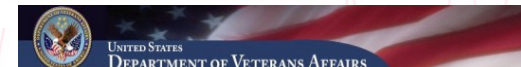


- Prospective, multi-national, open-label, randomized trial comparing TEER to surgical repair (1:1 ratio) degenerative MR
- Trial conducted in U.S., Canada, Germany, Spain, Belgium and UK and is designed as a **strategy trial**: all devices approved for use in a country may be eligible to be used
- The trial uses a **superiority design**

Courtesy of Gilbert Tang MD and Gorav Ailawadi MD



ClinicalTrials.gov ID NCT05051033



PRIMARY Inclusion Criteria

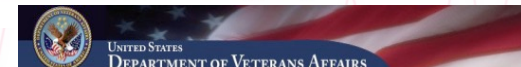


- ≥ 65 years of age with mod-sev 3+ or severe 4+ primary, degenerative MR by TTE
- Local heart team verified clinical indications for MV intervention and both surgical and transcatheter edge-to-edge repair strategies are anatomically suitable
- Low, intermediate or high surgical risk



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PRIMARY Endpoints

Primary Outcome Measure



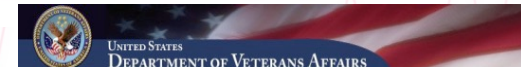
- Composite at **≥3yrs**:
 - All-cause mortality
 - Any mitral re-intervention including intra-operative conversion to replacement
 - Heart failure hospitalizations (adjudication committee)
 - ≥ 2+ (moderate) MR (core-lab adjudicated)
- **Primary safety endpoint: stroke + major bleed**

Courtesy of Gilbert Tang MD and Gorav Ailawadi MD



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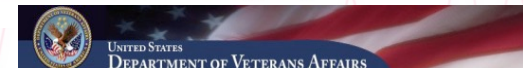
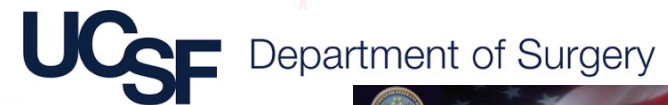


Randomized Trials of TEER vs. Surgery

EVEREST II (2011)	PRIMARY	REPAIR-MR	MITRA-HR
Abbott	NIH	Abbott	France
All-comers (30% FMR)	DMR All-comers >60 years	DMR Moderate risk	DMR High risk
Non-inferiority	Superiority	Non-inferiority	Non-inferiority
MitraClip vs Surgery	TEER vs. Surgery	MitraClip vs. Surgery	MitraClip vs Surgery
A) 1-year death, MV surgery, >3+ MR B) Death, MI, surgery, stroke, renal failure, infection, >48 h ventilation, AF, >2 units blood	A) 3-6 year death, any mitral reintervention, heart failure hospitalization, $\geq 2+$ MR B) Stroke + major bleed	A) 2-year death, stroke, heart failure hospitalization, dialysis B) 2-year $\leq 2+$ MR without replacement or reintervention	1-year death, unplanned cardiovascular rehospitalization, mitral re-intervention
272	450 - 650	500	330



Courtesy of Gilbert Tang MD and Gorav Ailawadi MD





Thank you

