Recent Clinical Data Update of MitraClip

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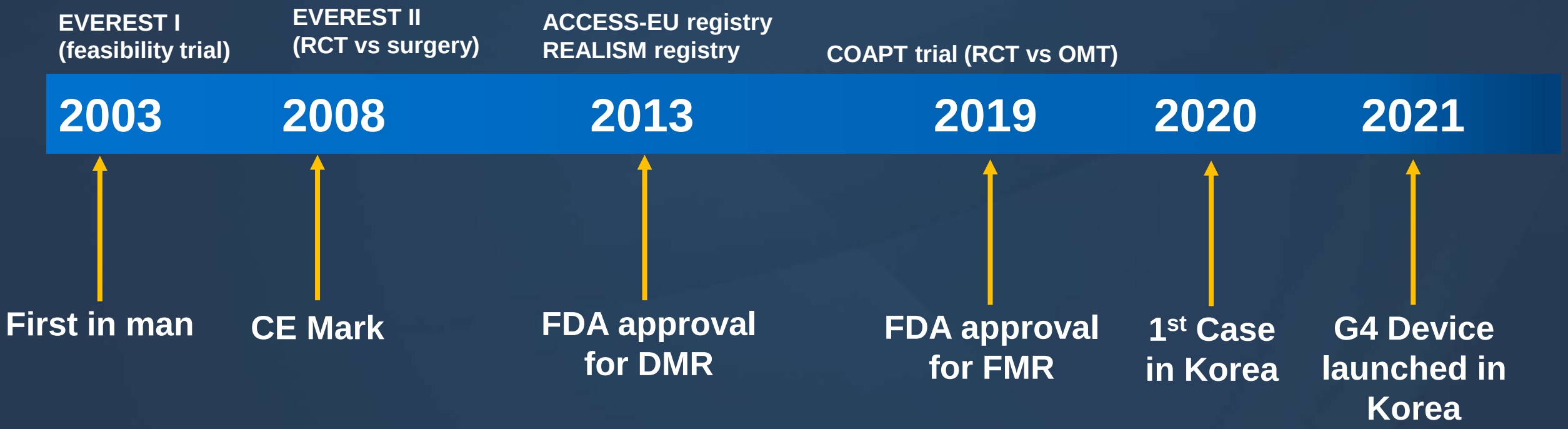
Status of MitraClip



2020 AHA/ACC Guideline Indication of TEER

- **Primary MR (IIA, B)**
  - Severely symptomatic MR (NYHA III-IV)
  - High or prohibitive surgical risk
  - Favorable anatomy

- **Secondary MR (IIA, B)**
  - Chronic severe symptomatic MR after optimal GDMT (NYHA II-IV)
  - LVEF 20-50% & LVESD ≤70 mm & PASP ≤70 mmHg
  - Appropriate anatomy

Otto CM et al. J Am Coll Cardiol 2020 Dec 17

Updated Outcome Data

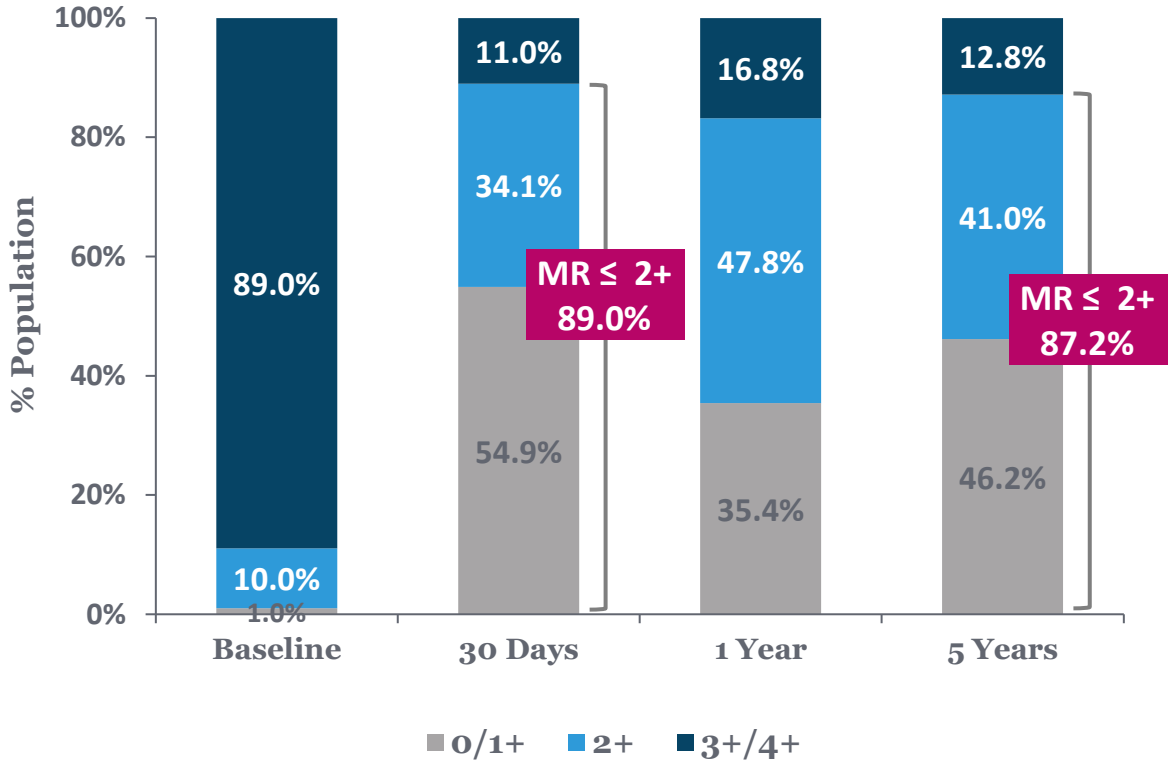
Real-World outcome of TEER
: 2021 STS/ACC TVT Registry Report

	In-hospital	30-day
Death	2.2%	4.5%
Stroke	0.7%	1.3%
MV reintervention	0.6%	1.1%
Single leaflet device attachment	1.0%	1.3%
Atrial fibrillation	2.1%	2.9%
Major bleeding	2.2%	4.7%
Major vascular access site complications	0.4%	0.5%
Moderate-severe / Severe mitral insufficiency	8.7%	
MV mean gradient > 5 mmHg	26.3%	

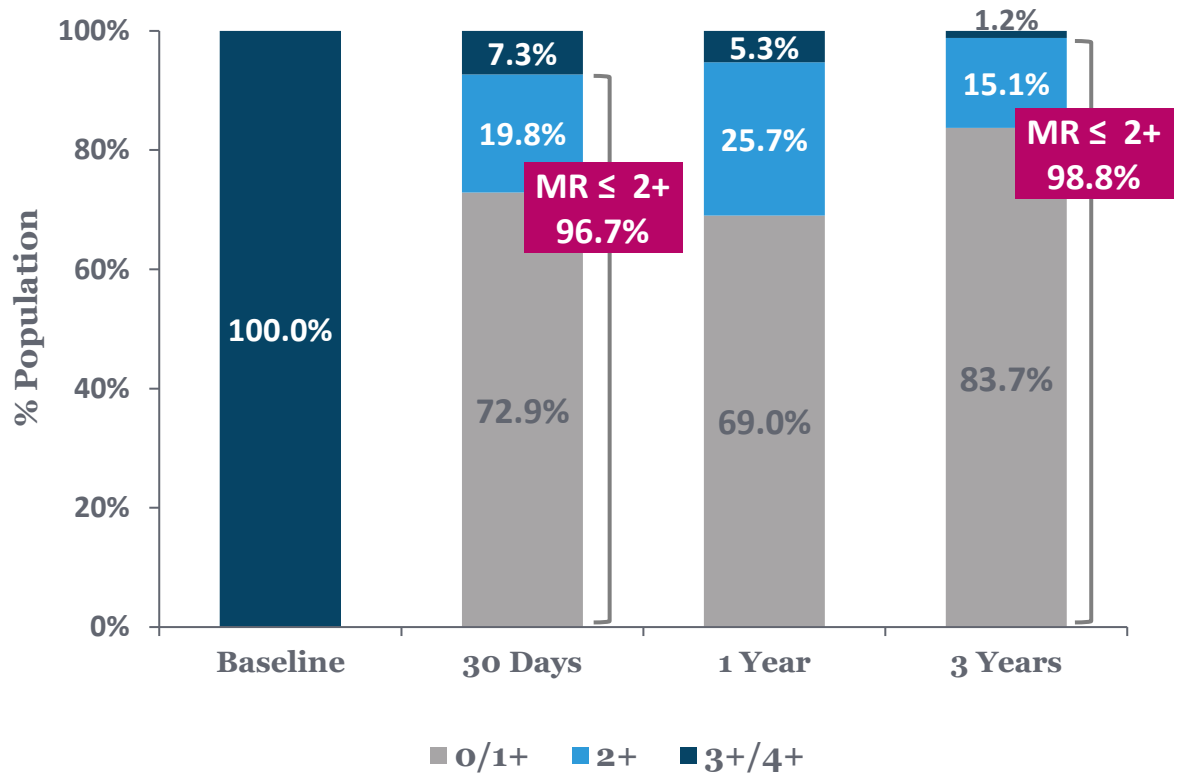
Mack M et al. J Am Coll Cardiol. 2021;78(23):2326-2353.

Durable Results in Longer-term FU

EVEREST II REALISM 5 Year Outcomes[1]
(n=264)

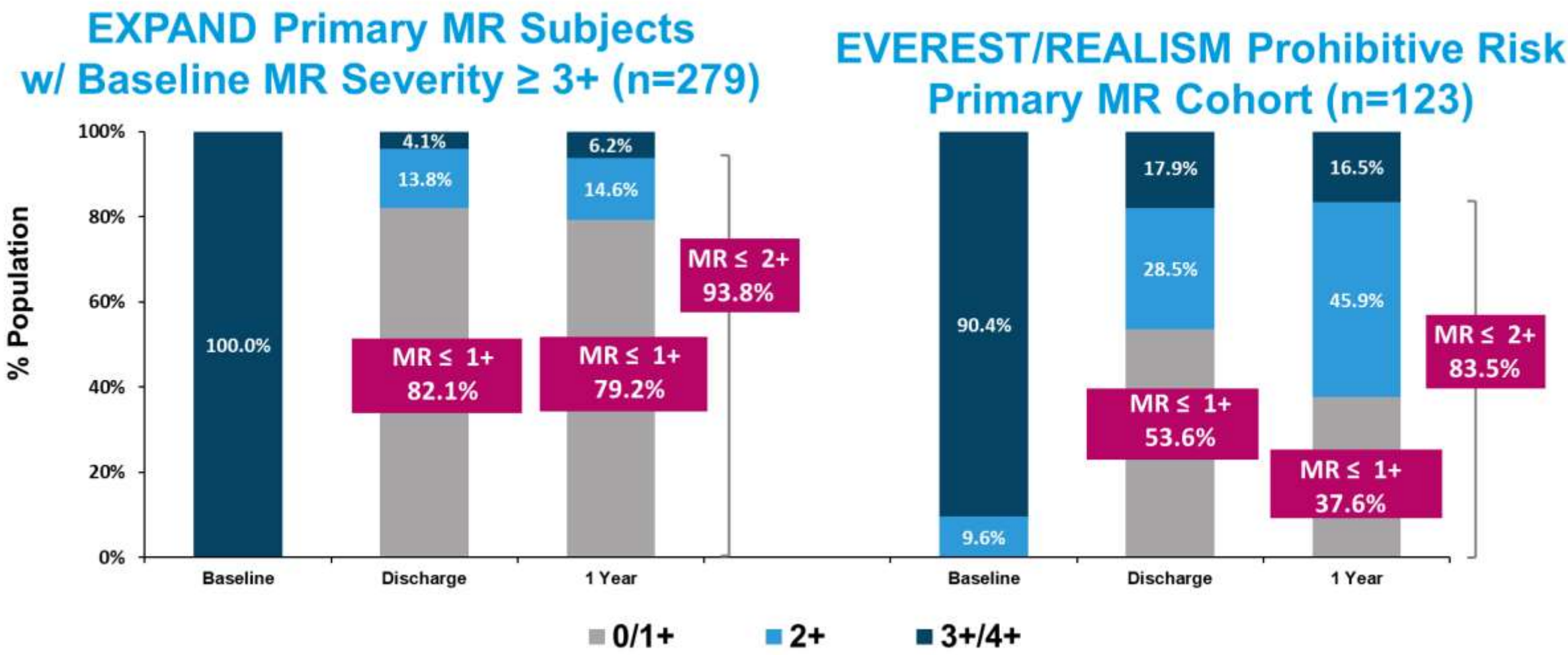


COAPT 3 Year Outcomes[2]
(n=302)



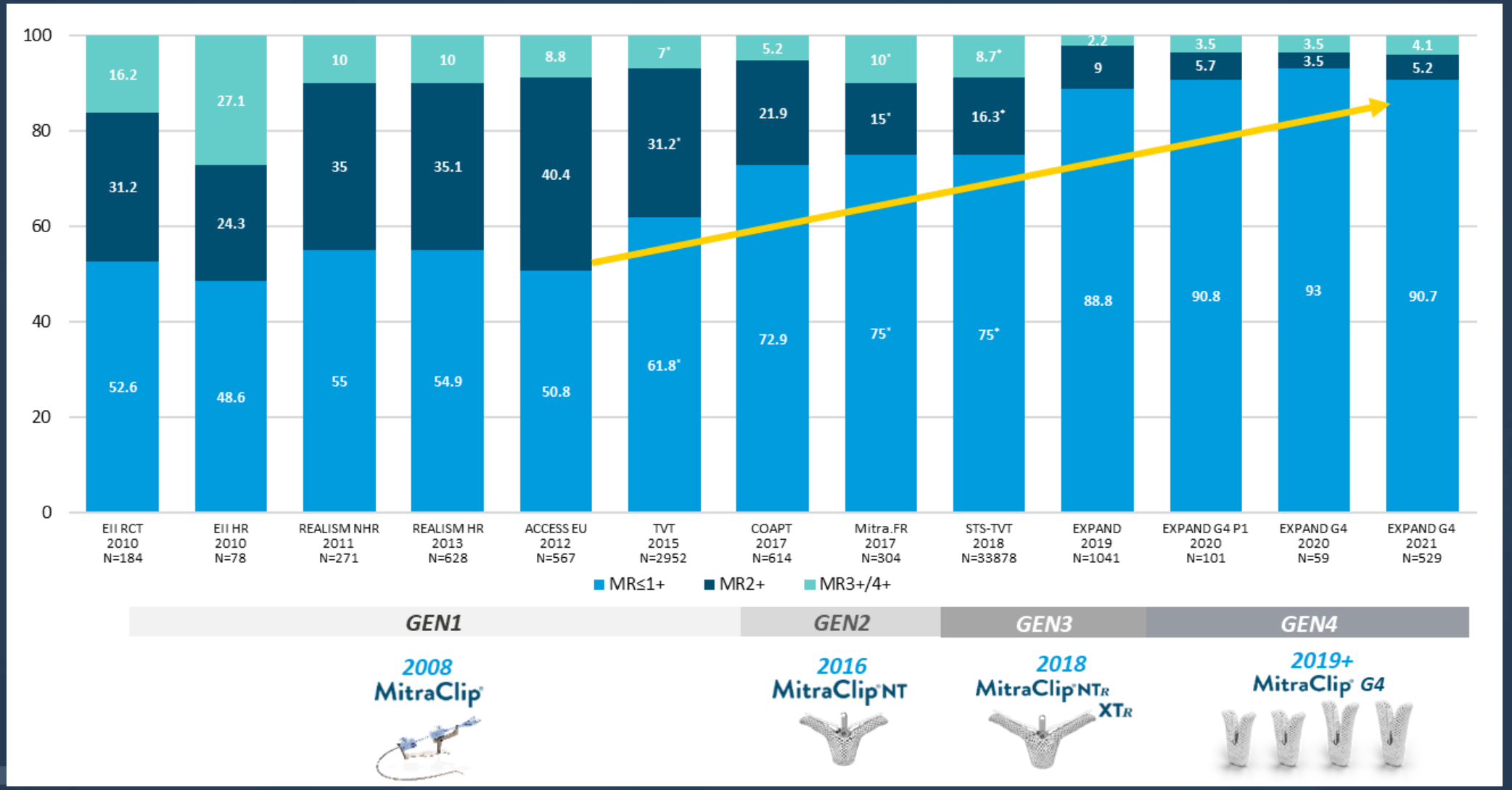
1. EVEREST II REALISM Non High Risk (HR) Cohort, Abbott Internal Data
2. Mack, M.J. et al. J Am Coll Cardiol. 2021;77(8):1029–40.

Higher MR Reduction (about 80% MR ≤1+ at 1-year)



Kar et al. TCT 2020, Presentation, Lim et al. ACC 2018 Presentation

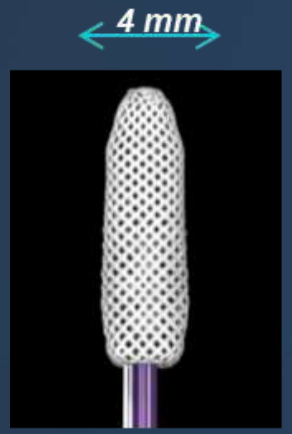
Significant Improvement in MR at 30-days post-TEER Implant Over The Past Years



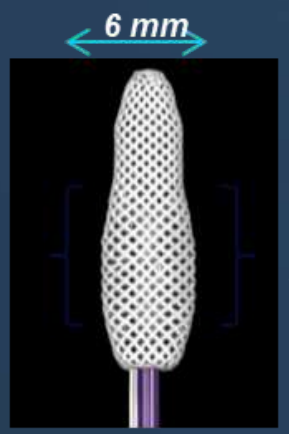
Rinaldi M. TVT 2022 Presentation

Updated Data with Newer G4 MitraClip

Mitraclip™ G4 : Various Length & Width of Clips



50% wider in the grasping area

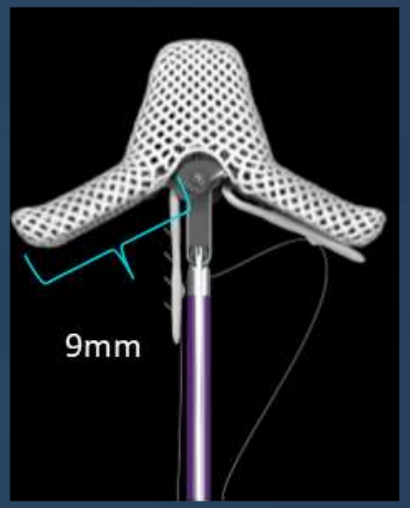


50% wider in the grasping area

NT/XT **NTW/XTW**

MitraClip™ G4

4 Clip sizes

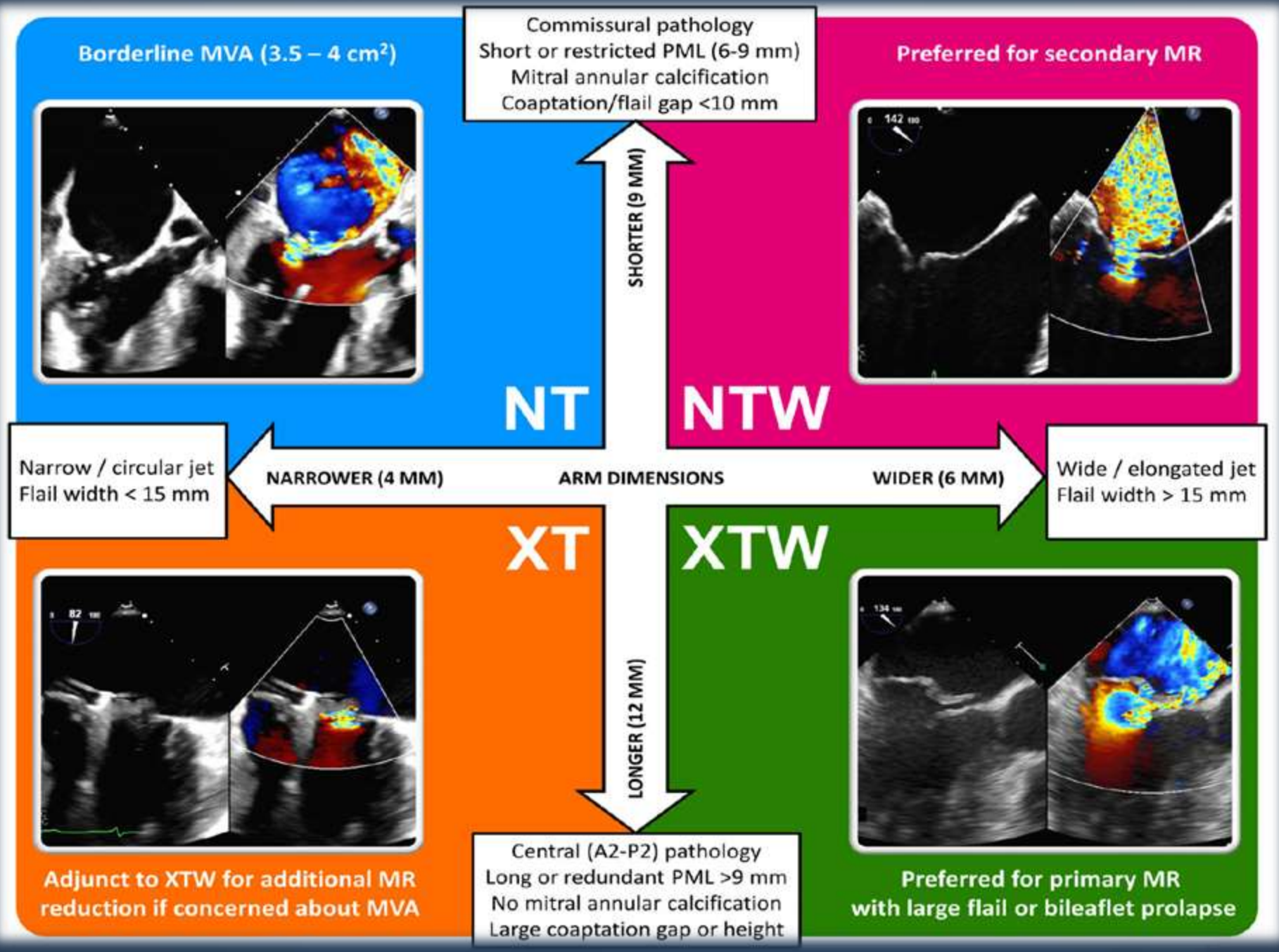


17 mm at 120 degrees
20 mm at 180 degrees

NT/NTW

22 mm at 120 degrees
25 mm at 180 degrees

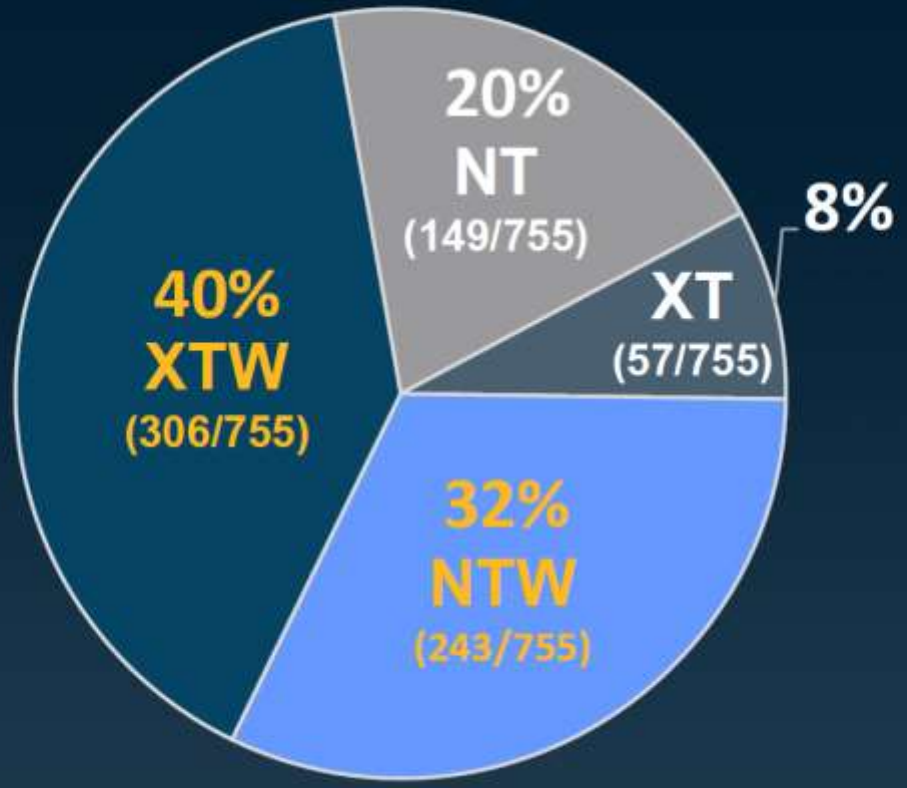
XT/XTW



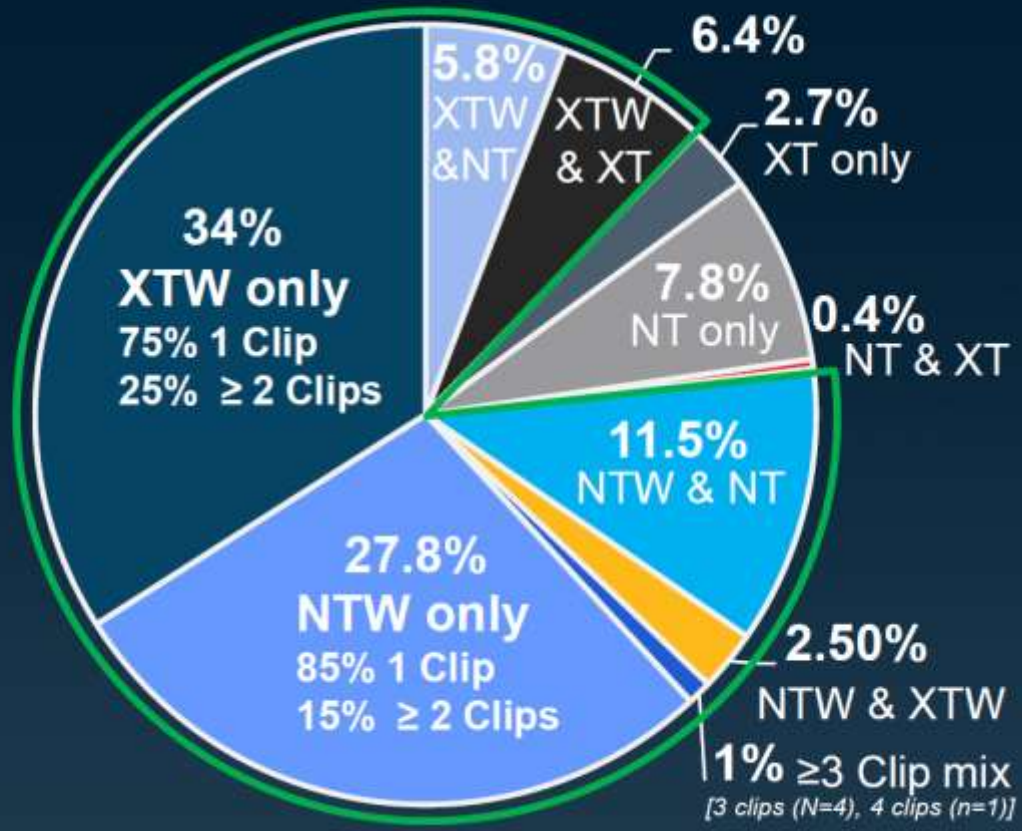
Garcia-Sayan E et al. Catheter Cardiovasc Interv. 2021;98(4):E626-E636.

Clips Used in EXPAND G4 Registry (N=529)

Clip Size Usage (total clips implanted = 755)

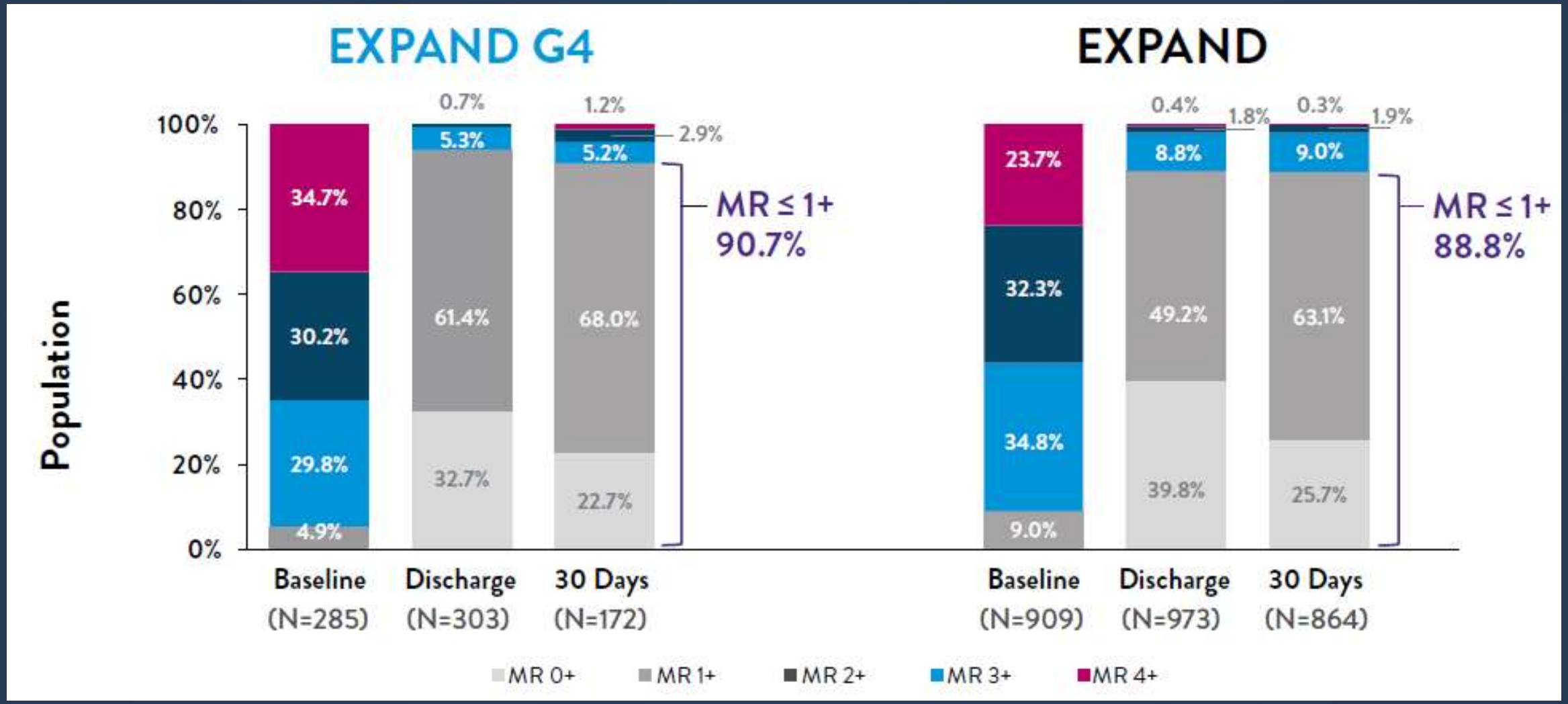


Clip Mix (N=514, 13 Clip combinations)



Rodriguez E. Presented at TCT 2021

MR Severity in EXPAND G4 Registry



Rodriguez E. Presented at TCT 2021.

Real-World Safety & Durability of G4 Mitraclip

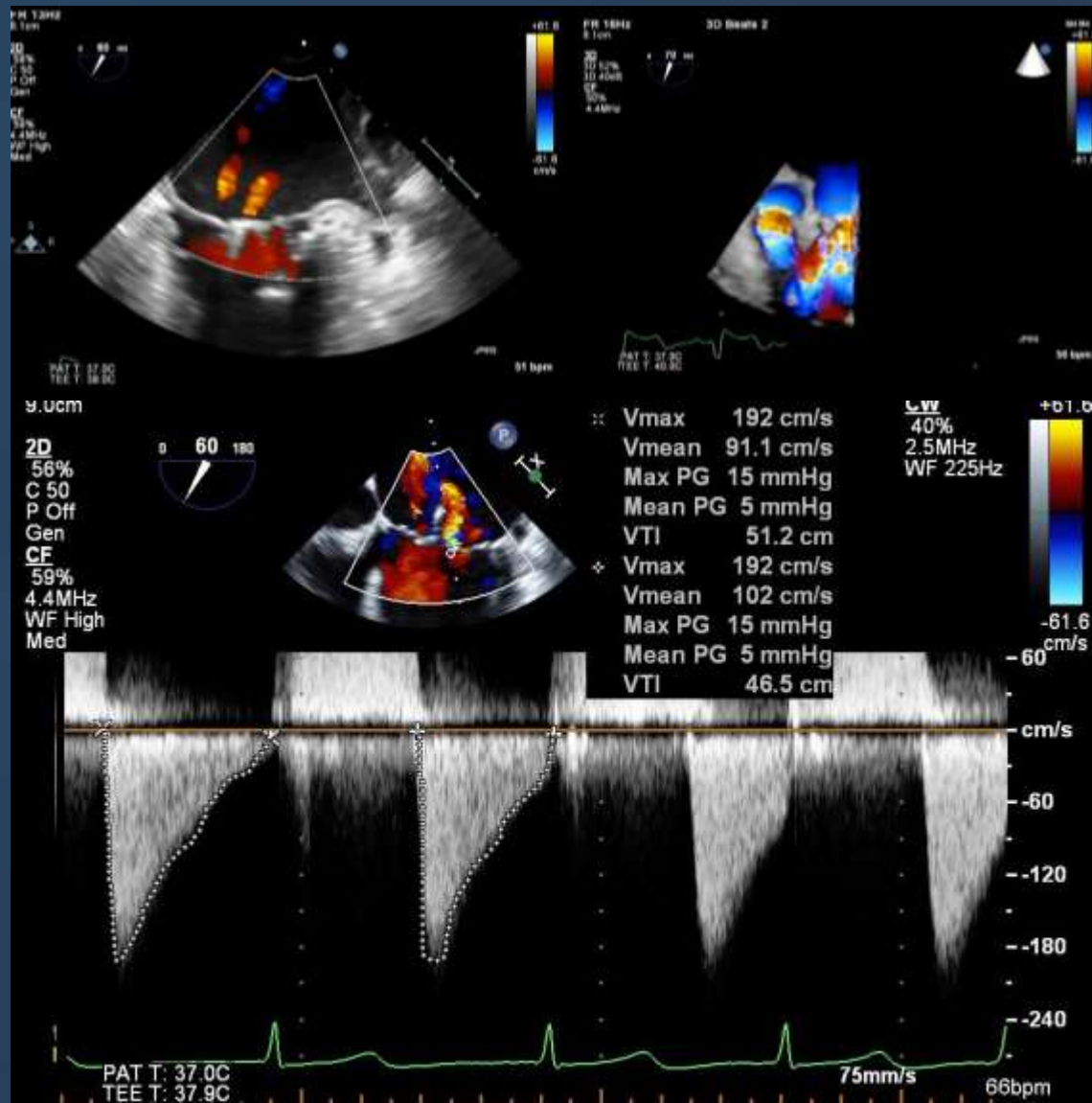
	TVT Registry 30-Day (N=2,952)	EXPAND 30-Day (N=1,041)	EXPAND 1-Year (N=1,041)	EXPAND G4 30-Day (N=529)
All-cause Death	5.2% (96)	2.3% (24)	14.9% (147)	**1.5% (7)**
MI	0.2% (3)	0.0% (0)	1.2% (12)	**0.0% (0)**
Stroke	1.0% (17)	1.2% (8)	1.7% (18)	**0.0% (0)**
Ischemic stroke	0.6% (11)	1.0% (6)	N/A	**0.0% (0)**
Non-elective CV surgery for device related complications	N/A	1.1% (11)	N/A	**0.8% (4)**
Leaflet Adverse Events	1.5% (17)	2.0% (20)	2% (20)	**1.1% (6)**
SLDA	1.5% (4)	1.7% (18)	1.7% (18)	**1.1% (6)**

Rinaldi M. TVT 2022 Presentation

Optimal Procedural Outcomes

How to define TEER success?

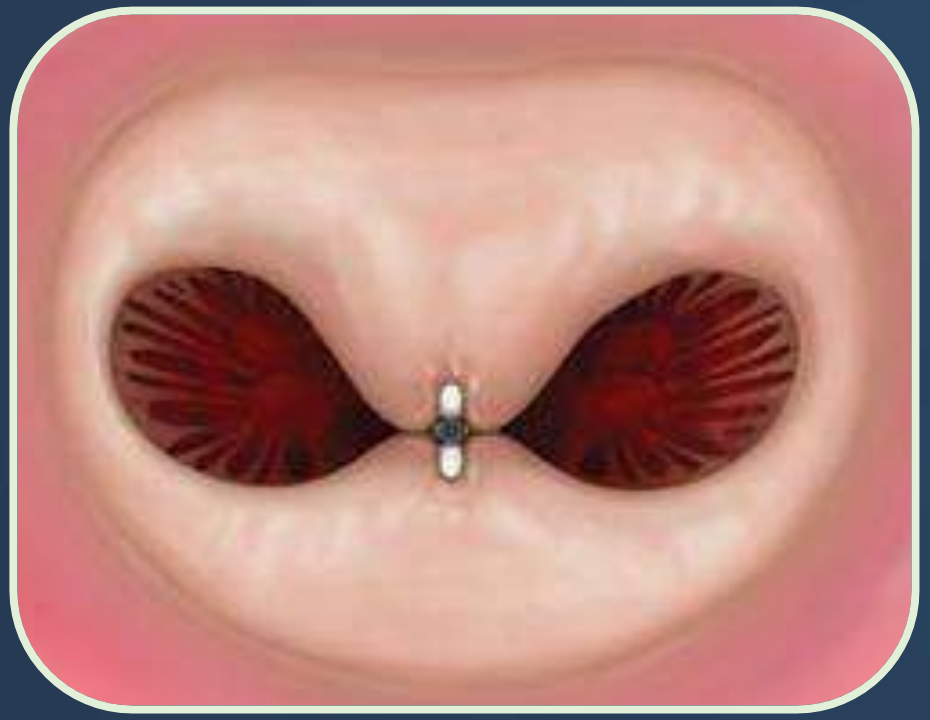
- MR reduction (≤ 2+)
  - "achievable" MR result will depend on starting MVA, baseline MR, etc
  - **Acceptable MR reduction ("success") may vary among patients**
- Absence of significant MS
  - Mean gradient ≤ 5 mmHg
  - Increased gradients did OK in COAPT (MG +/- 7 mmHg), in secondary MR…



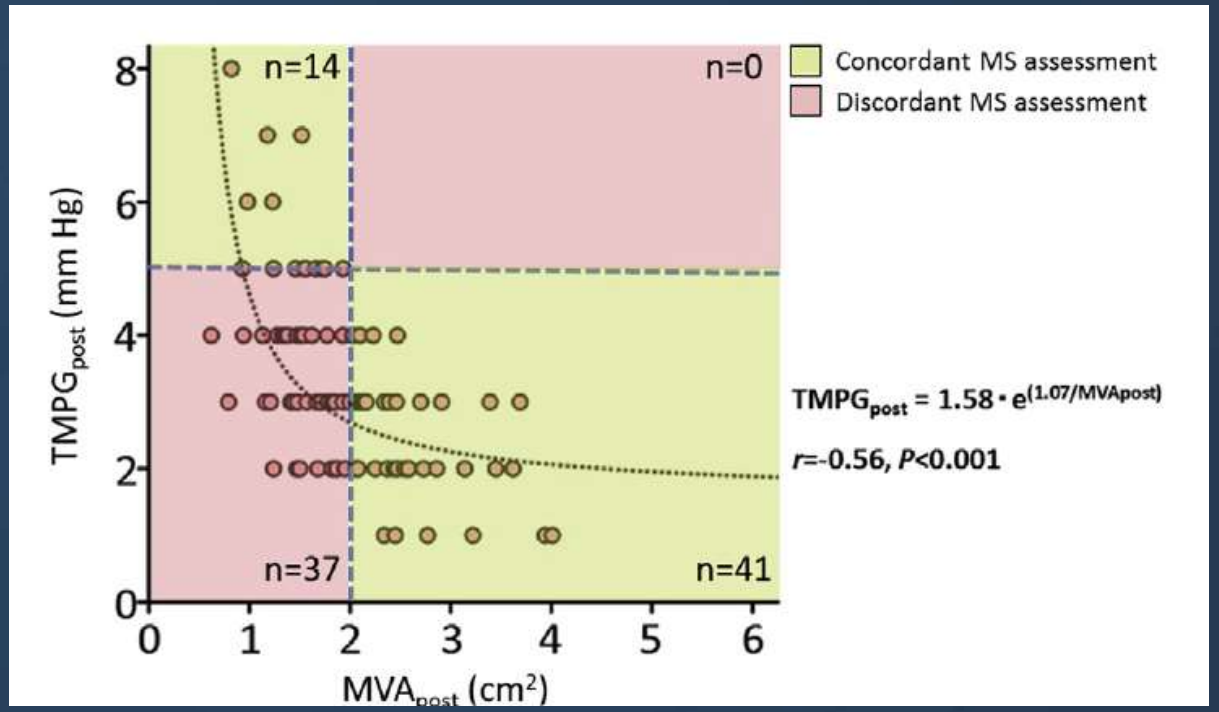
Halaby R et al. JACC CV Interv. 2021

TEER Reduces MV Area, therefore Increase MV Gradient

Double-edged Sword of TEER



MVA & mean MV gradient after Mitraclip



Utsunomiya H et al. Am J Cardiol. 2017;120:662-669.

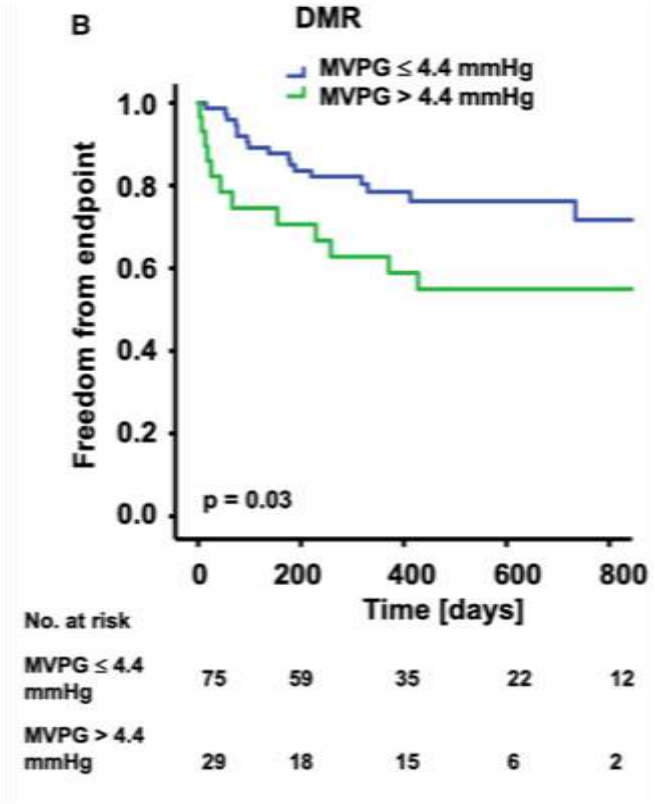
Predictor of Increased MV Gradient after TEER

- MV Orifice Area ≤ 4.0 cm^2
- Baseline Mitral Gradient ≥ 4mmHg
- Mitral Annular Calcification
- Hemodialysis
- More Clips used
- Higher Residual MR (Increased Blood Flow over MV)

Neuss M et al. JACC CV Interv. 2017;10:931-9. Thaden JJ et al. J Am Heart Assoc. 2018;7:e007315.
Oguz D et al. Catheter Cardiovasc Interv. 2021;98:E932-E937.

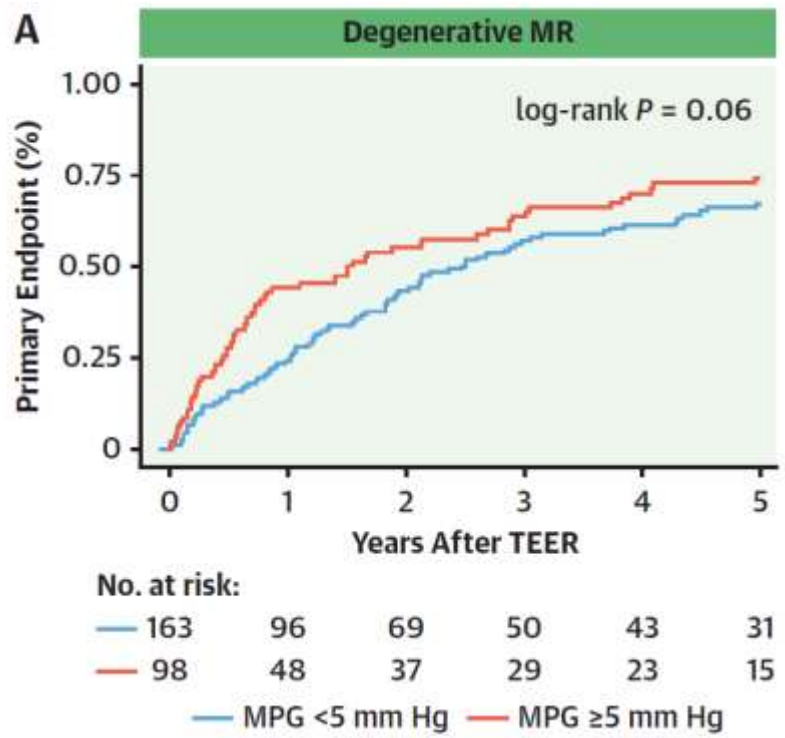
Contrasting Results of Impact of High Transmitral Gradient after TEER for Primary MR

255 from German Single Center
Mortality, MV Surgery, Redo, LVAD



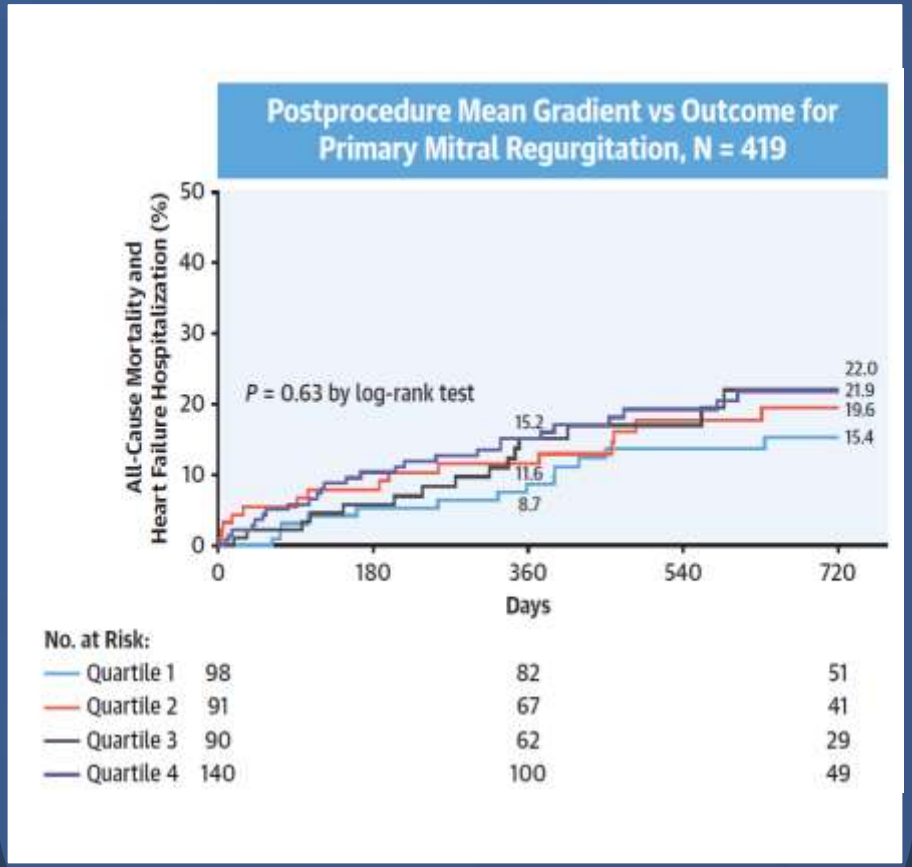
Patzelt J et al. JAHA. 2019;8:e011366.

265 from German Single Center
Mortality, HF Hospitalization



Koell B et al. JACC Interv. 2022;15:922-34.

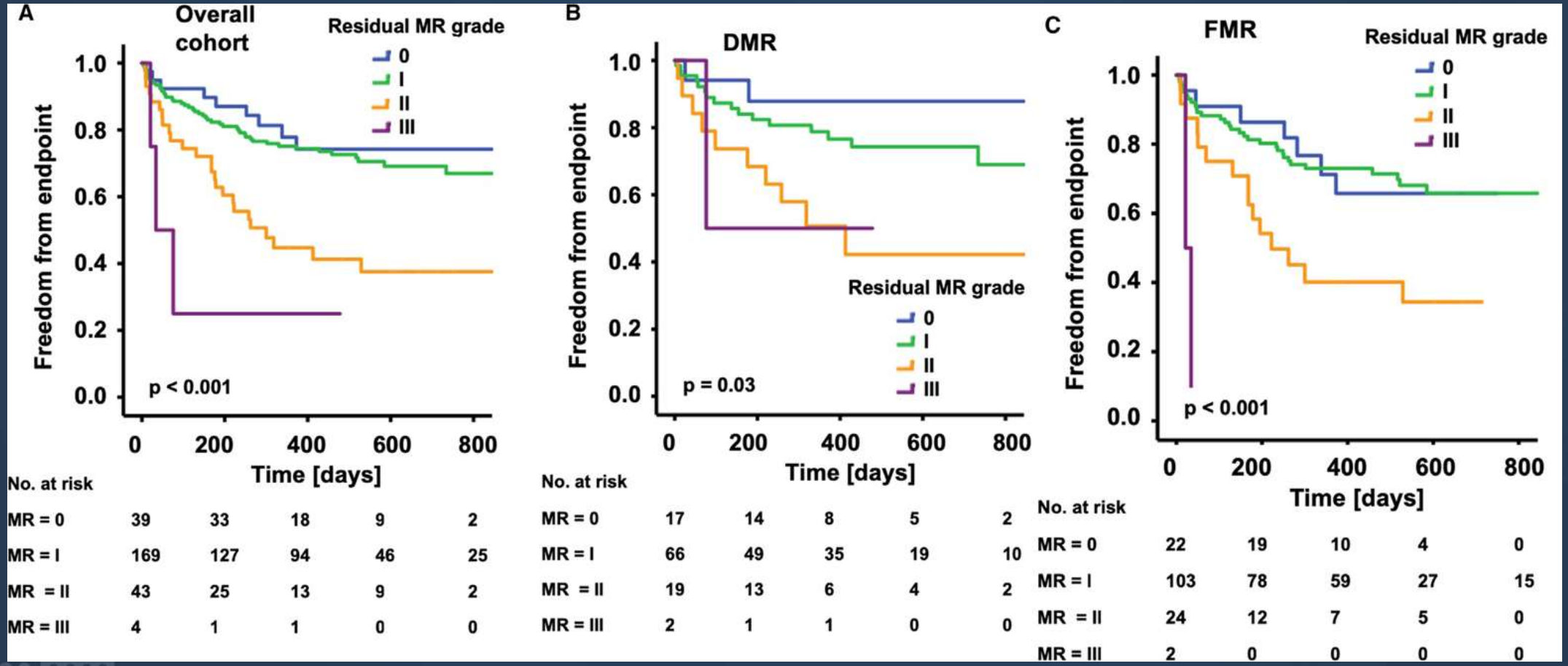
419 from US Single Center
Mortality



Yoon S et al. JACC Interv. 2022;15:935-45.

Residual MR was Stronger Predictor than MV Gradient

255 Patients from German Single Center from 2014 to 2017, Primary 41%, Secondary 59%
Clinical Outcome: All-cause mortality, MV Surgery, LVAD, or Redo TEER

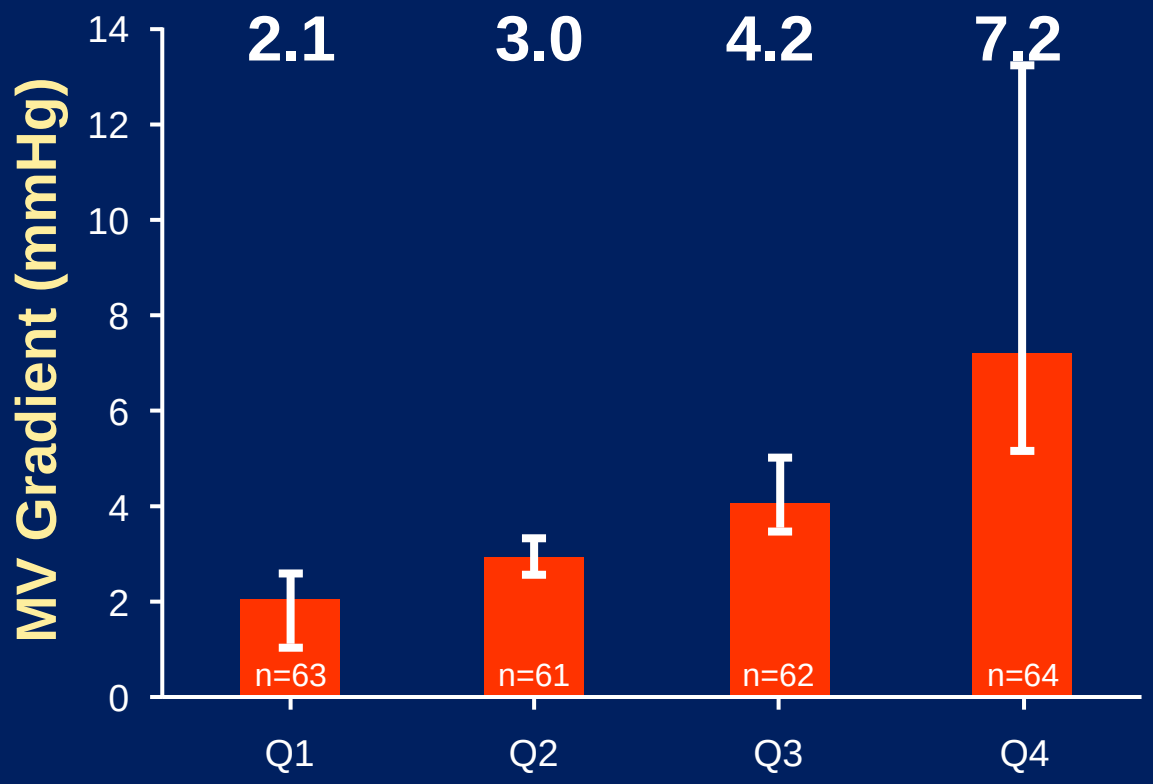


Patzelt J et al. J Am Heart Assoc. 2019;8:e011366.

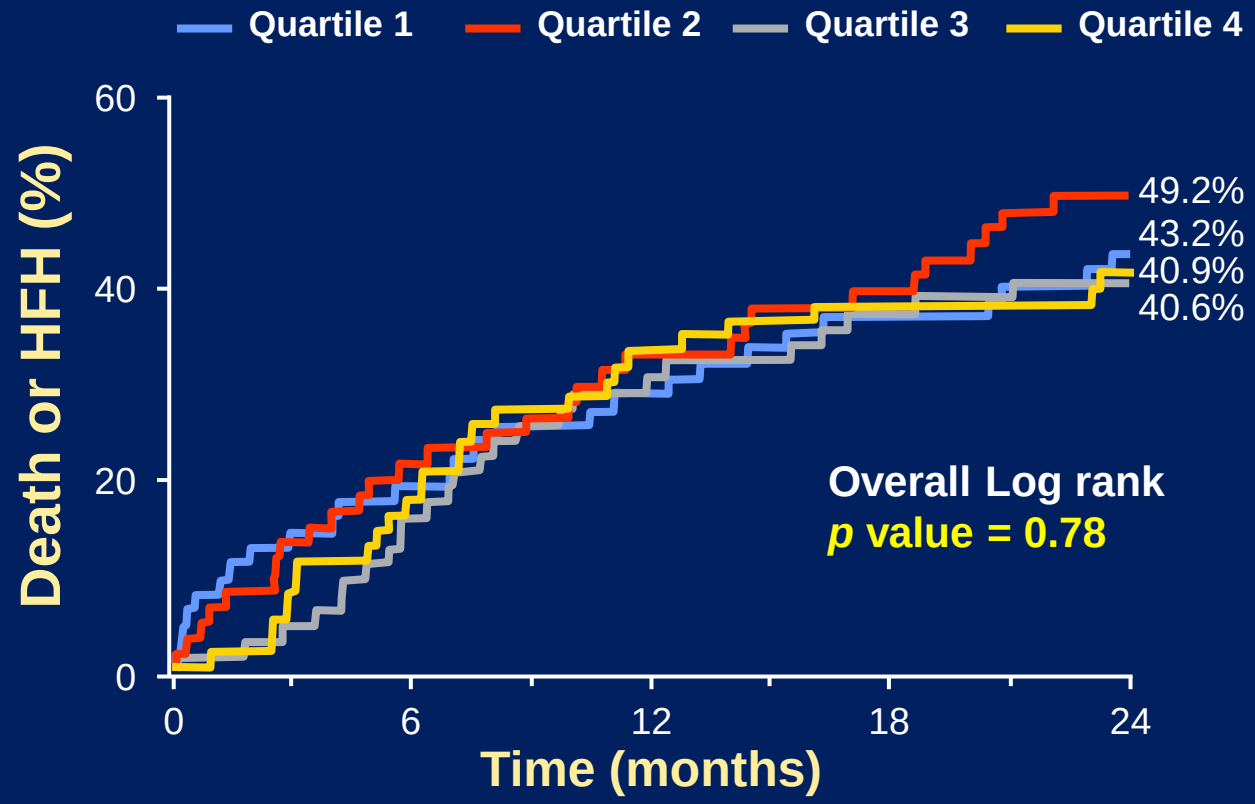
High Transmitral Gradient after TEER was NOT associated with Worse Outcome in COAPT Trial (Secondary MR)

Mean discharge TTE MVG after MitraClip was 4.2 ± 2.2 mmHg (range 1 to 13.2 mmHg)*

Mitral Valve Gradient by Quartile



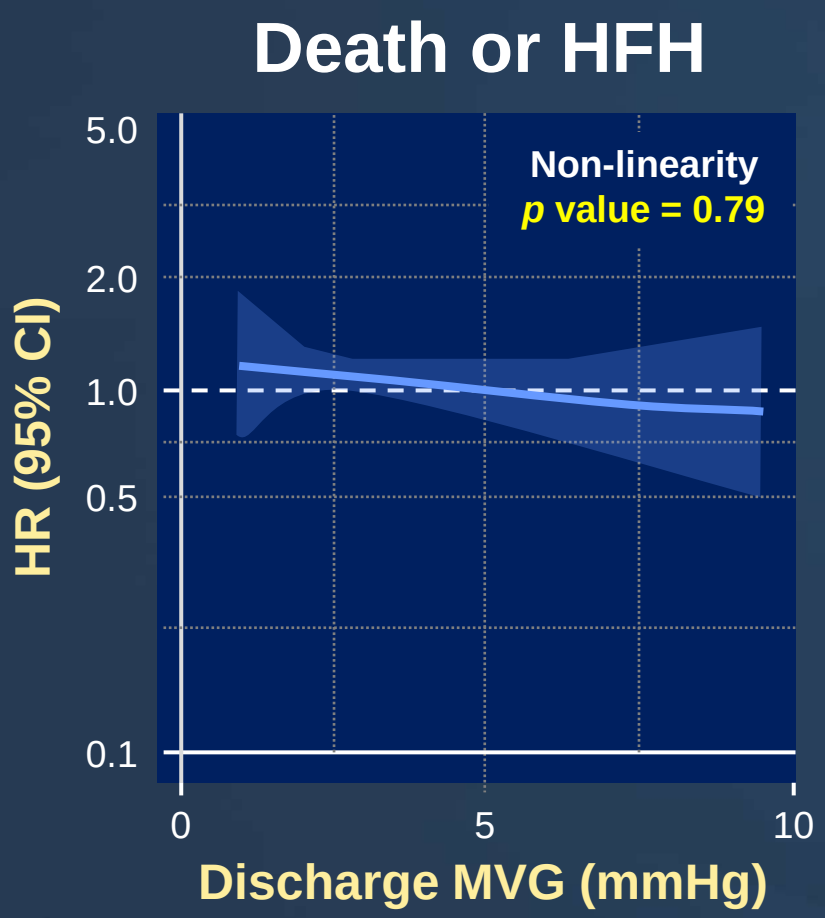
Death or HF Hospitalization

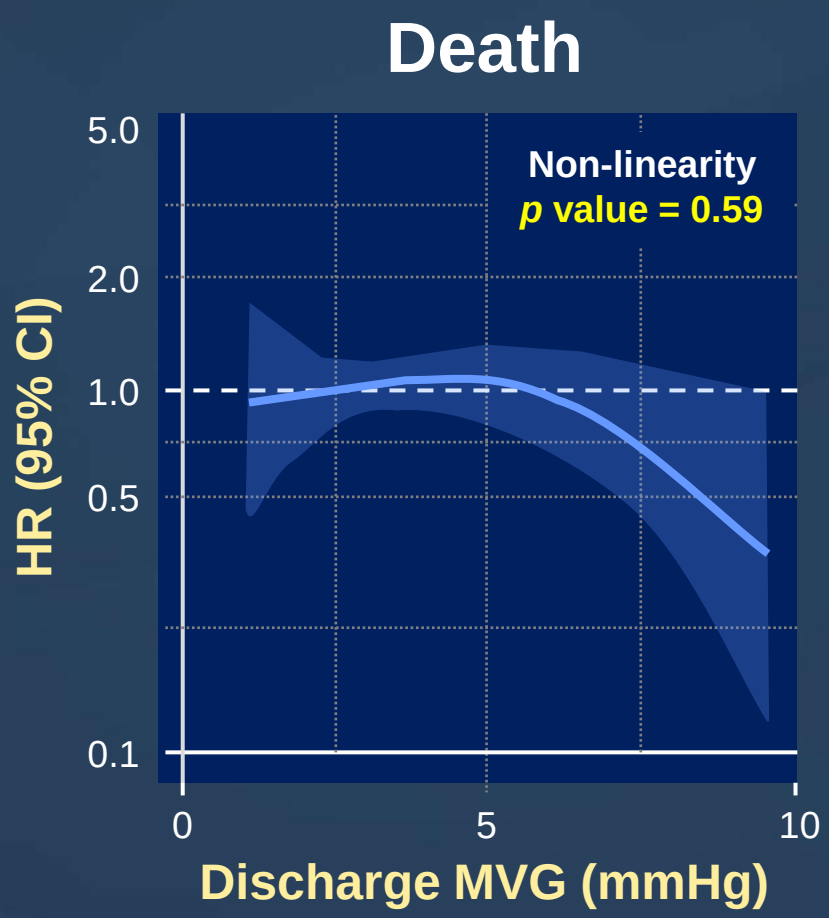


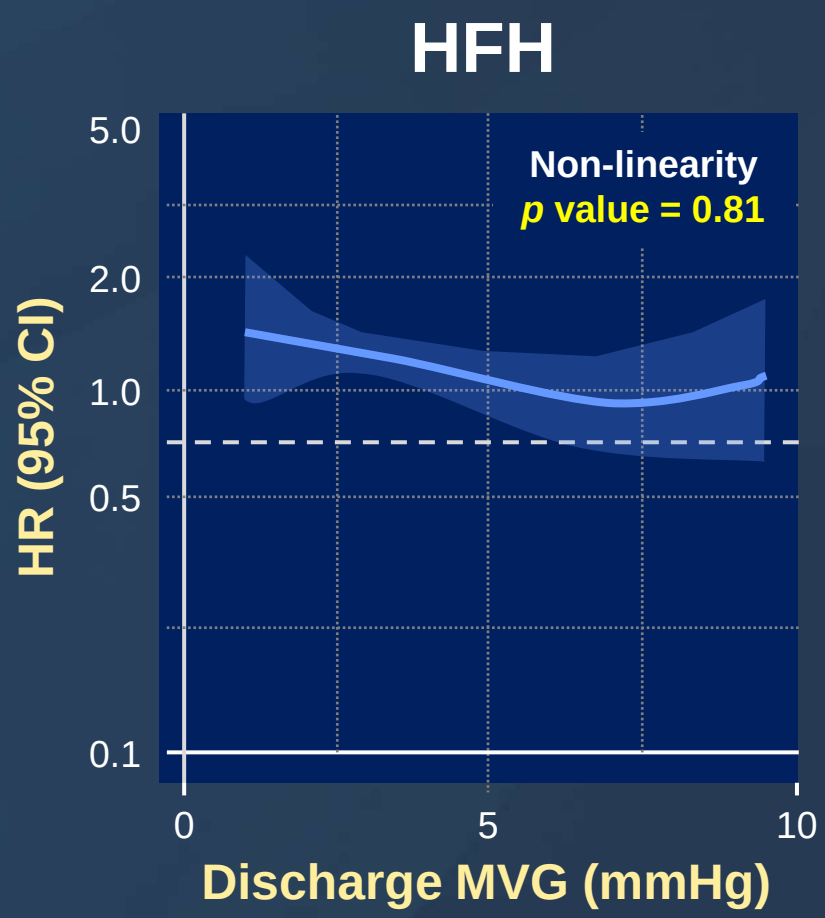
Halaby R et al. JACC Cardiovasc Interv. 2021;14(8):879-889.

*Median [IQR] = 3.5 [2.6, 5.1]

Impact of MV Gradient after TEER in COAPT Trial (Secondary MR)







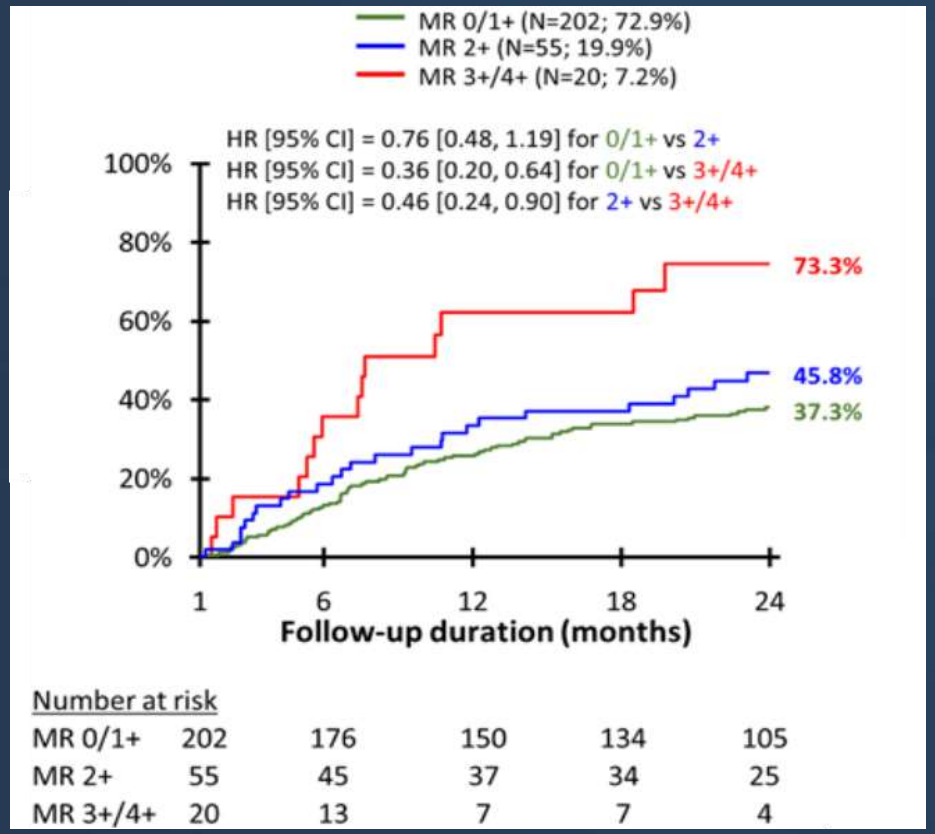
Halaby R et al. JACC Cardiovasc Interv. 2021;14(8):879-889.

*Median [IQR] = 3.5 [2.6, 5.1]

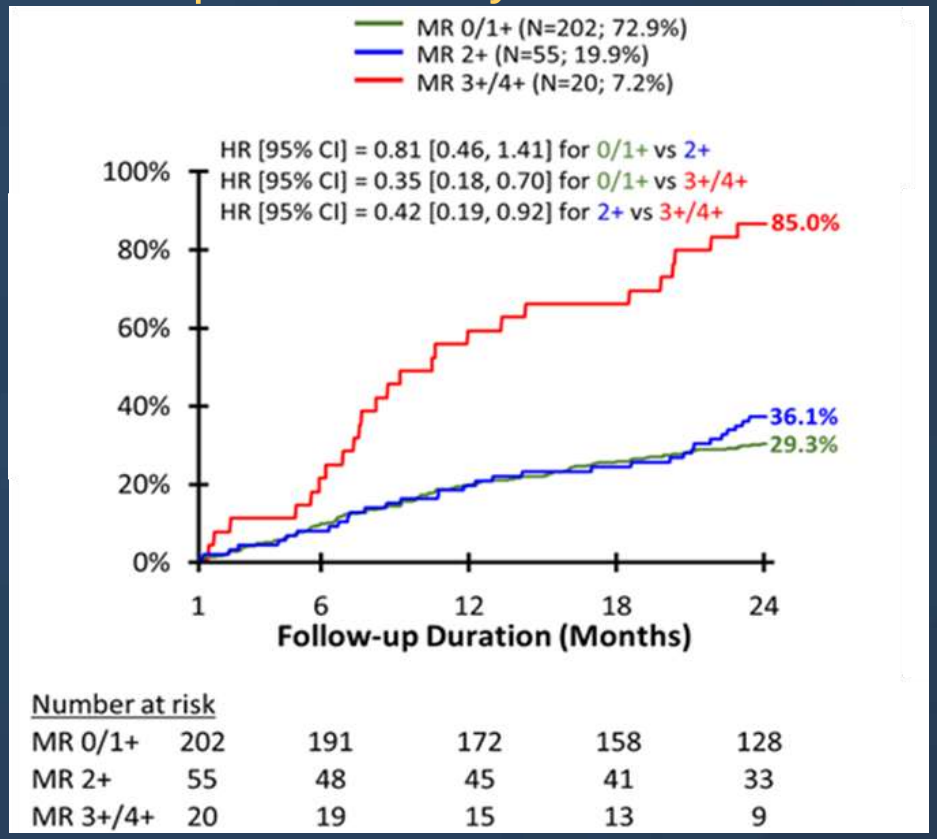
MR Reduction was Strong Predictor of Clinical Outcome

277 Secondary MR Patients after TEER from COAPT Trial
Benefits of MR Reduction Might Outweigh the Adverse Effects of Increased MV Gradient

Death or HFH by Residual MR



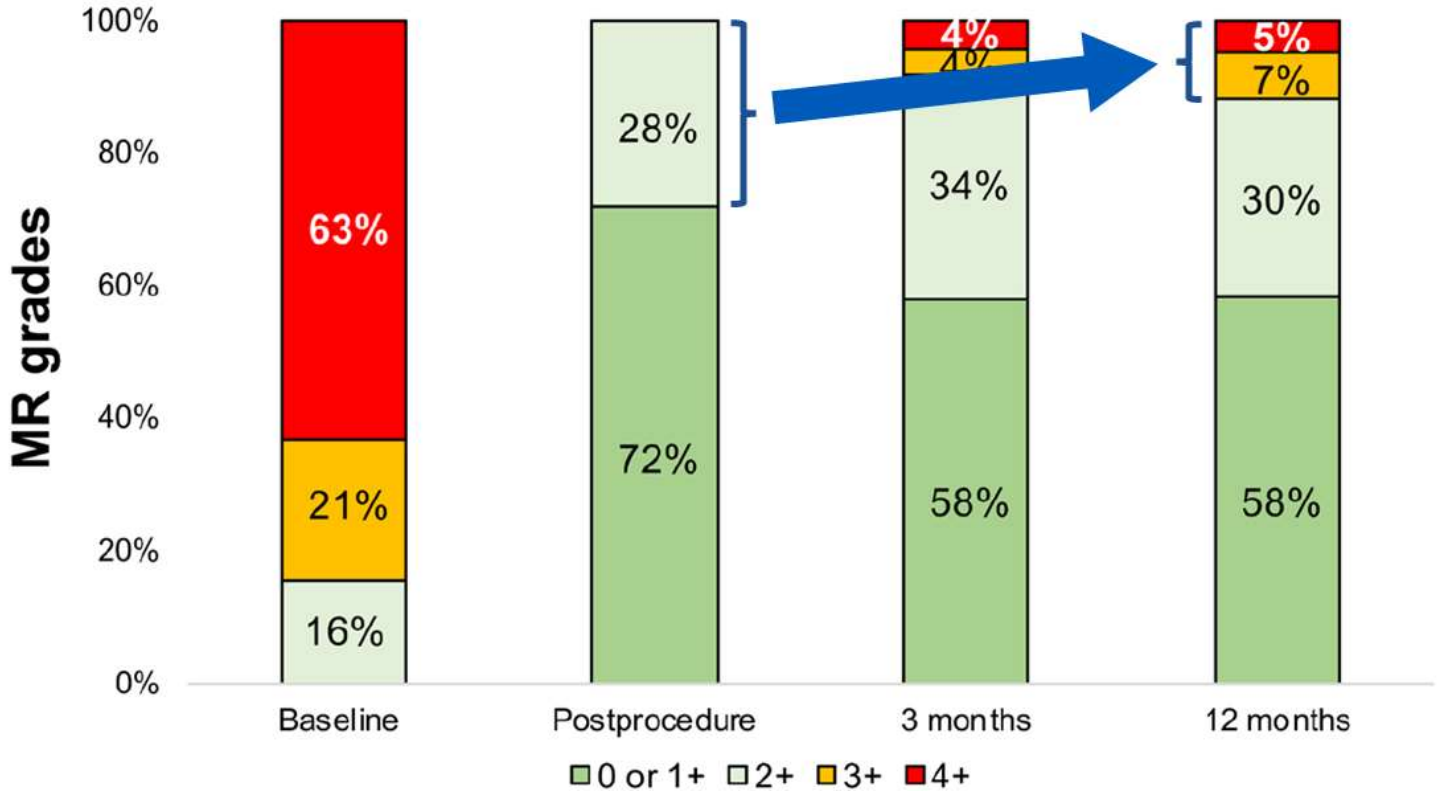
HF Hospitalization by Residual MR

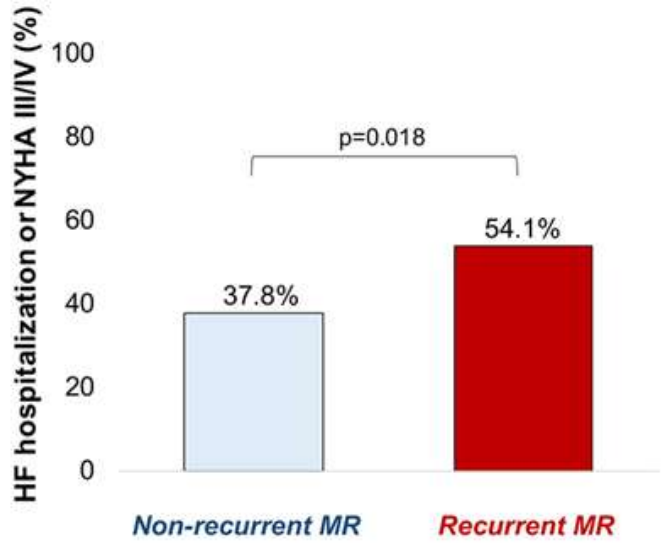


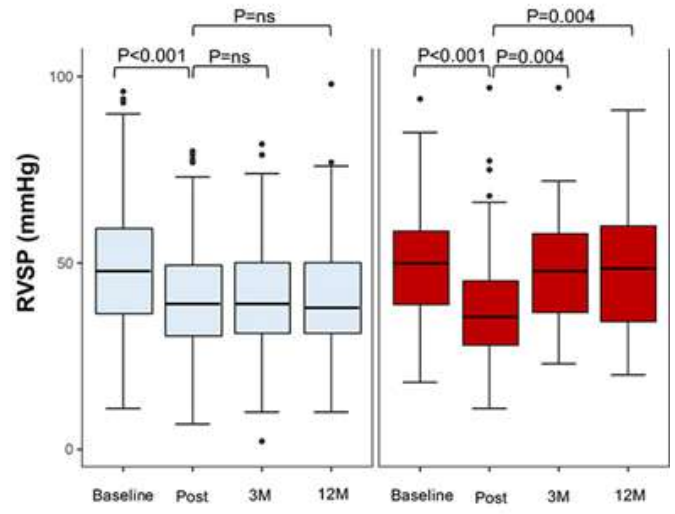
Kar S et al. Circulation. 2021;144:426-37.

Deleterious Hemodynamic Effect of Recurrent MR

- German Single center, MR to ≤2+ after Mitraclip (N=685)
- 61 (8.9%) patients developed recurrent MR within 12 months
- Predictor of Recurrent MR : MR 2+, Flail leaflet



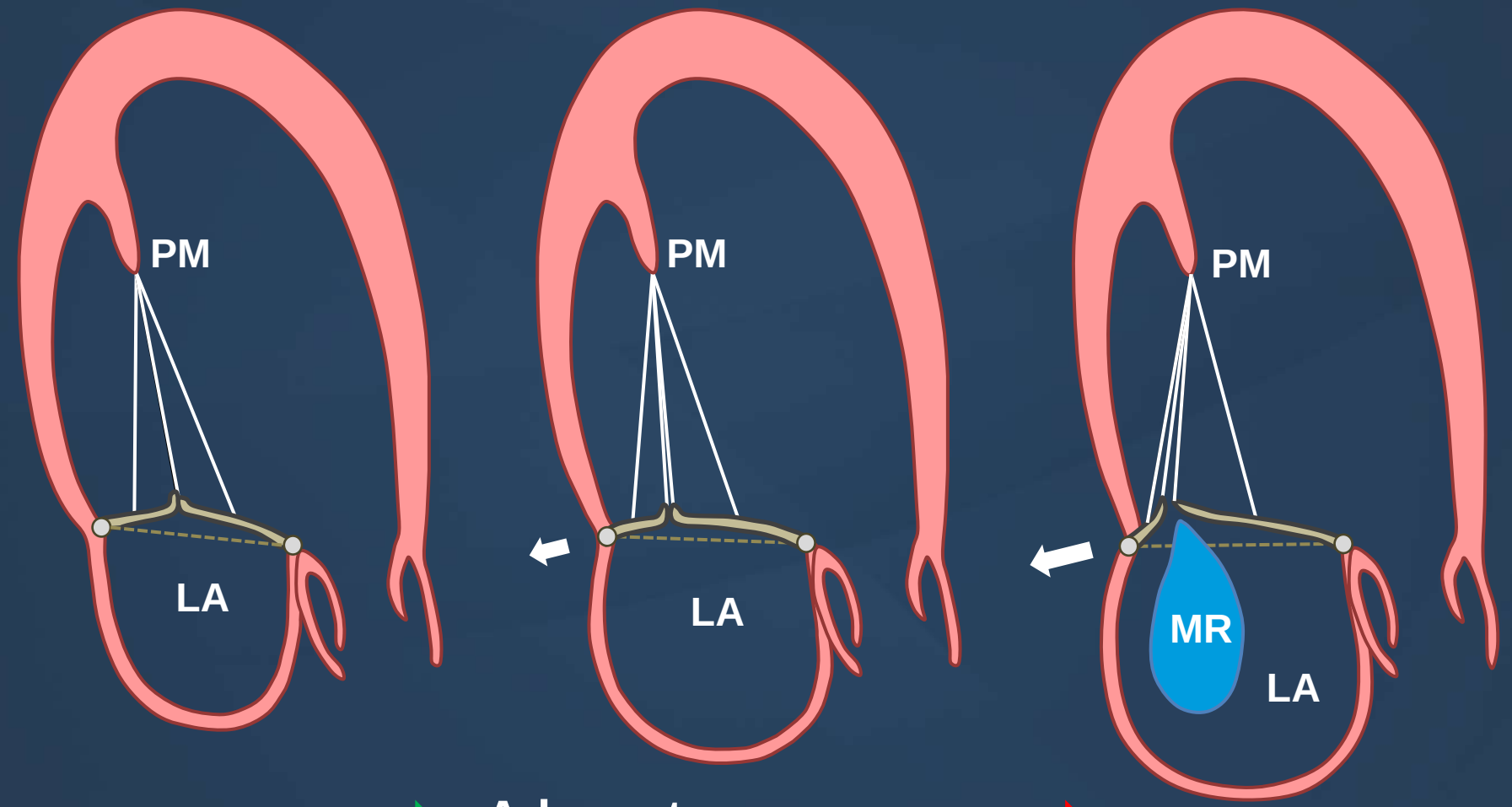




Sugiura A et al. Circ Cardiovasc Interv. 2022;15(3):e010895.

TEER in Atrial Functional MR

Isolated Annular Dilation Develops Atrial FMR in AF



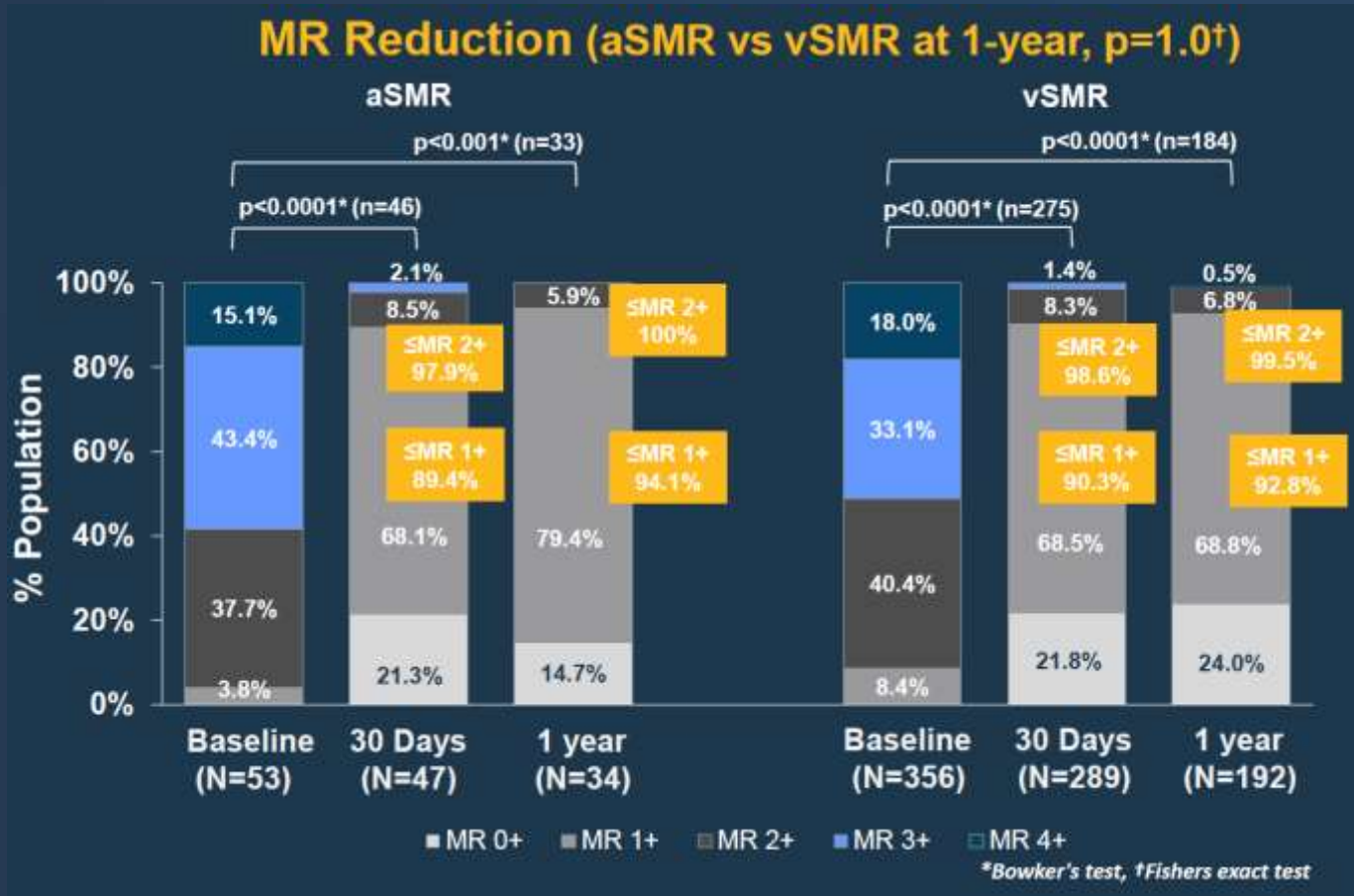
Normal → Adequate Leaflet Adaptation → Inadequate Leaflet Adaptation

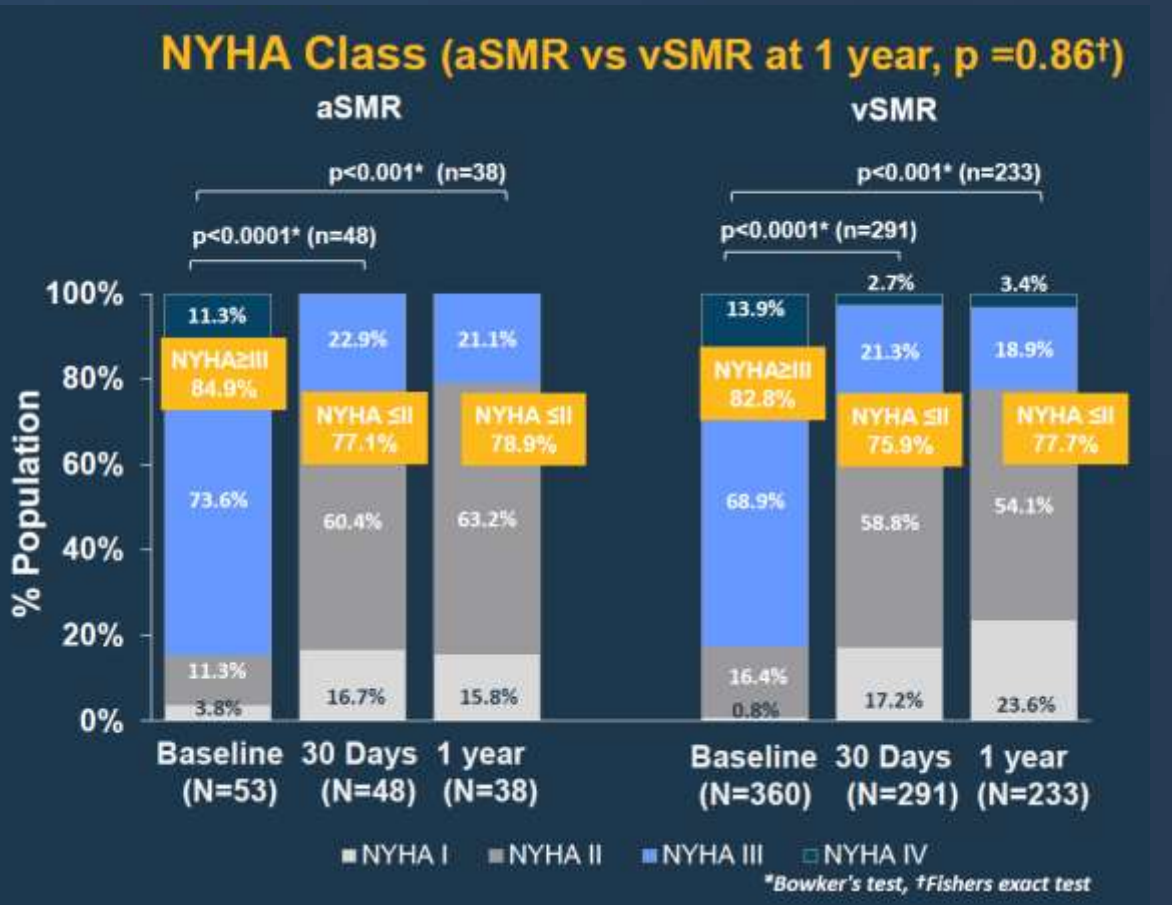
NSR | AF

Kim DH et al. JACC Imaging. 2019;12:665–

TEER in Atrial FMR : Global EXPAND study

N=53, LV EF ≥45% without RWMA, AF with Dilated LA



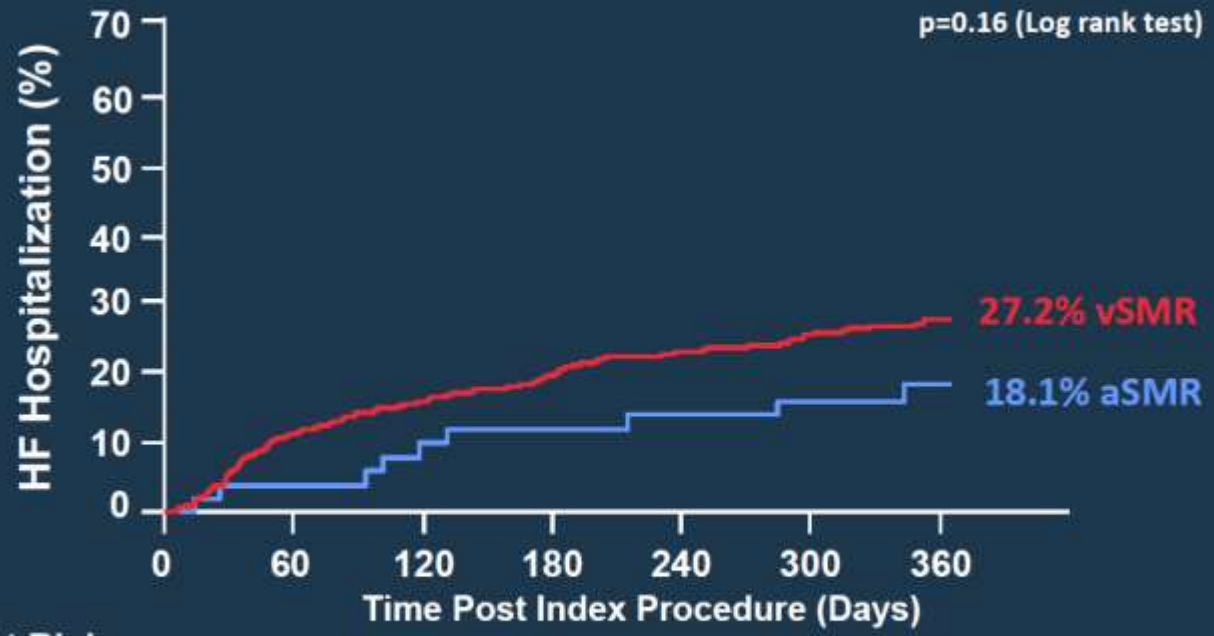


Sodhi et al. Presented at TCT 2021

TEER in Atrial FMR : Global EXPAND study

N=53, LV EF ≥45% without RWMA, AF with Dilated LA

HF Hospitalization at 1 year



At Risk				
aSMR	53	49	44	24
vSMR	360	333	251	144

All-Cause mortality at 1 year

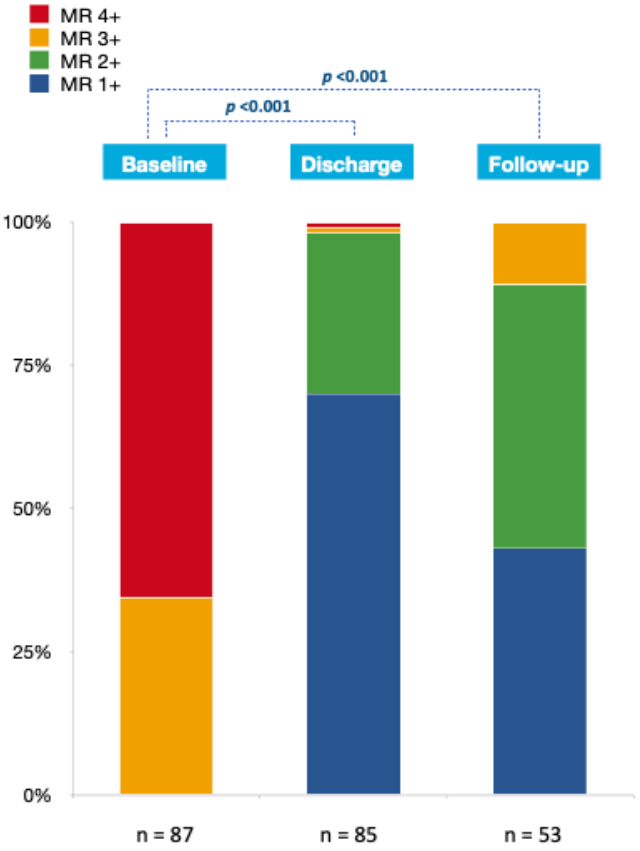
At Risk				
aSMR	53	50	49	29
vSMR	360	349	292	183

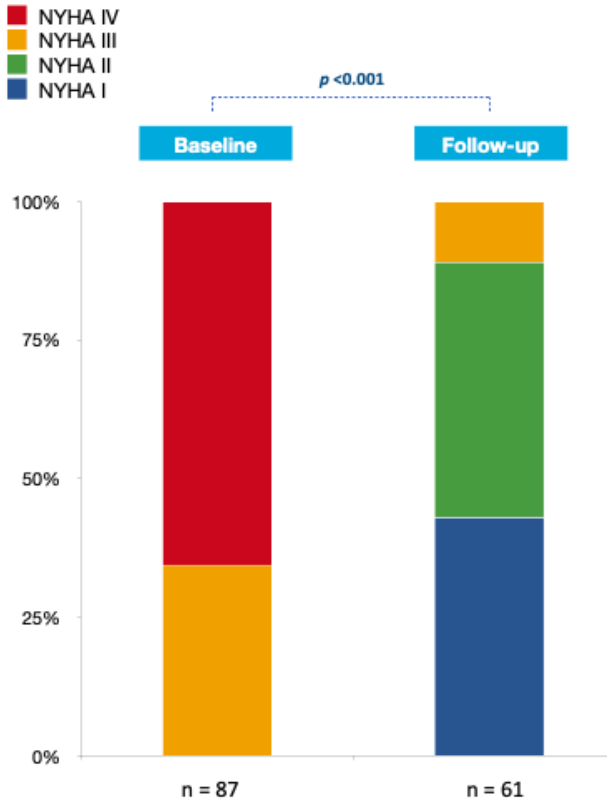
HFH, based on each patient's first occurrence of HF Hospitalization.

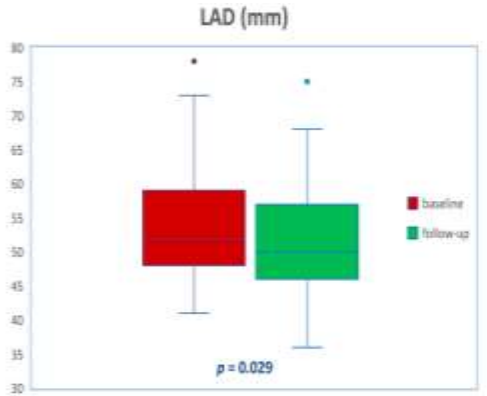
Sodhi et al. Presented at TCT 2021

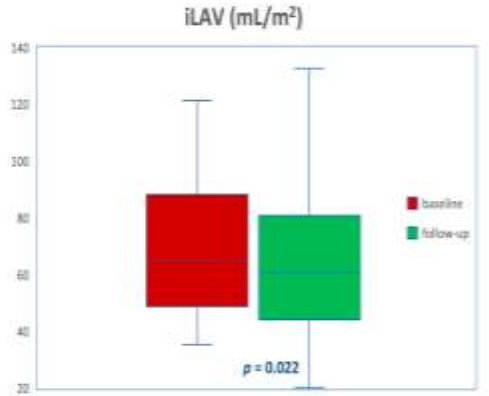
TEER in Atrial FMR : MITRA-TUNE

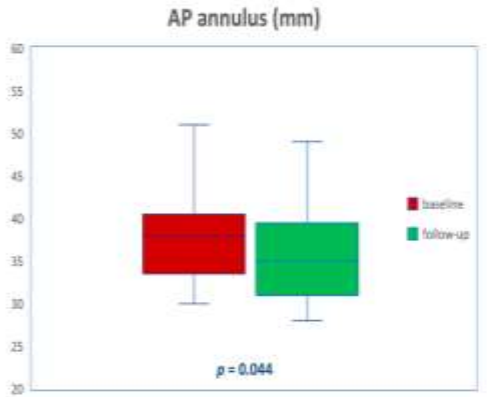
N=87 (7.6% of FMR), LV EF ≥50%, LVEDD <55mm, AF
81 YO, 61% female, STS 4%

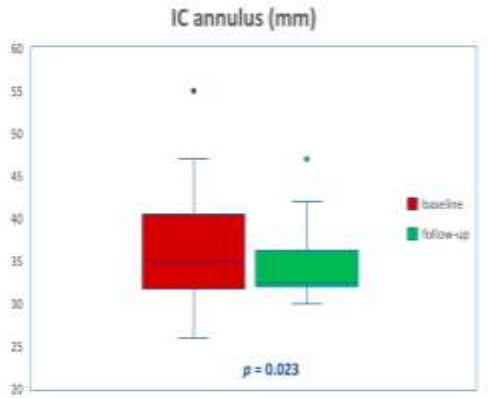








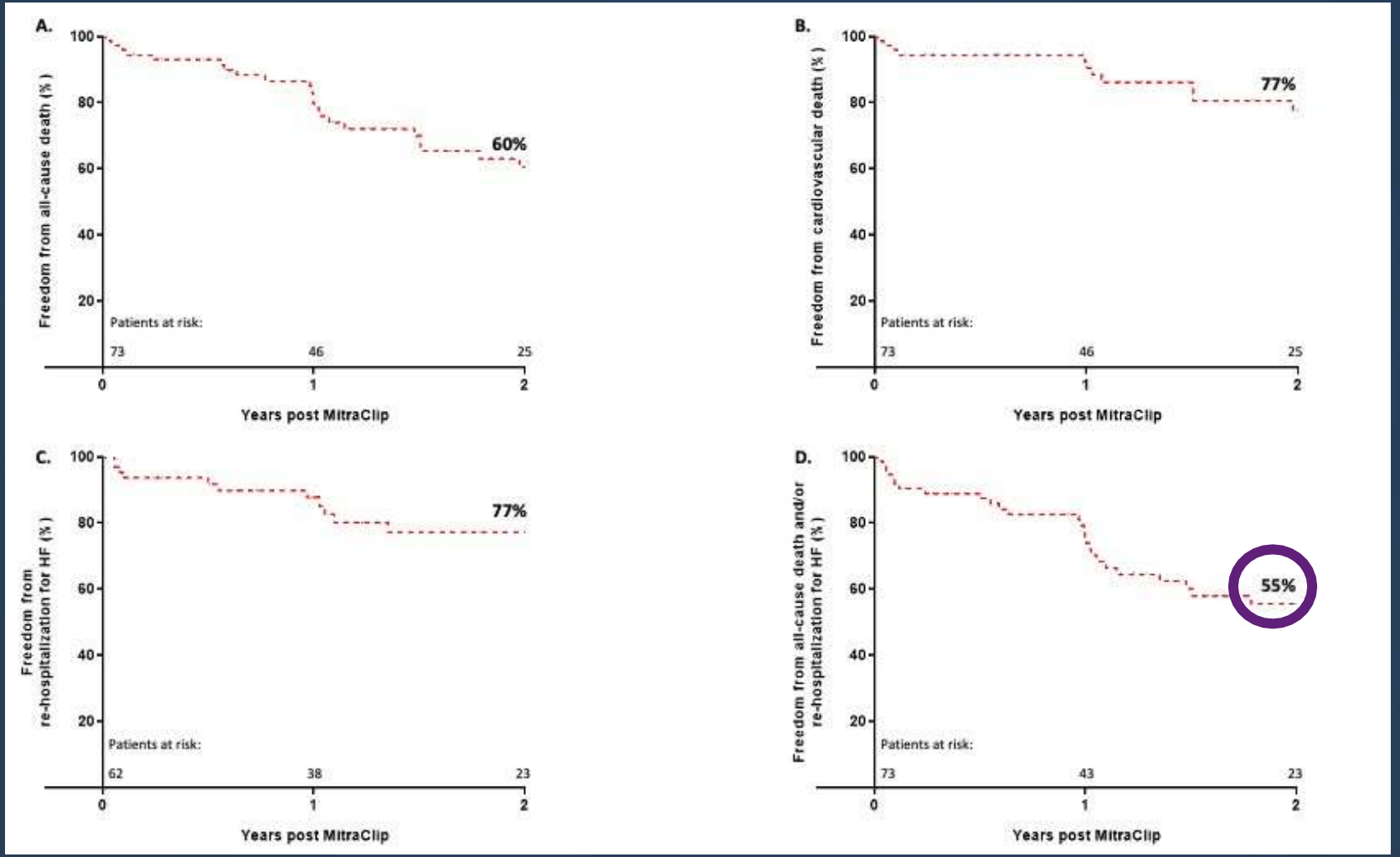




Rubbio AP et al. IJC 2022;349:39-45

TEER in Atrial FMR : MITRA-TUNE

83% device success, 2% in-hospital death, 5% 30-day mortality



Rubbio AP et al. IJC 2022;349:39-45

Ongoing Clinical Trials

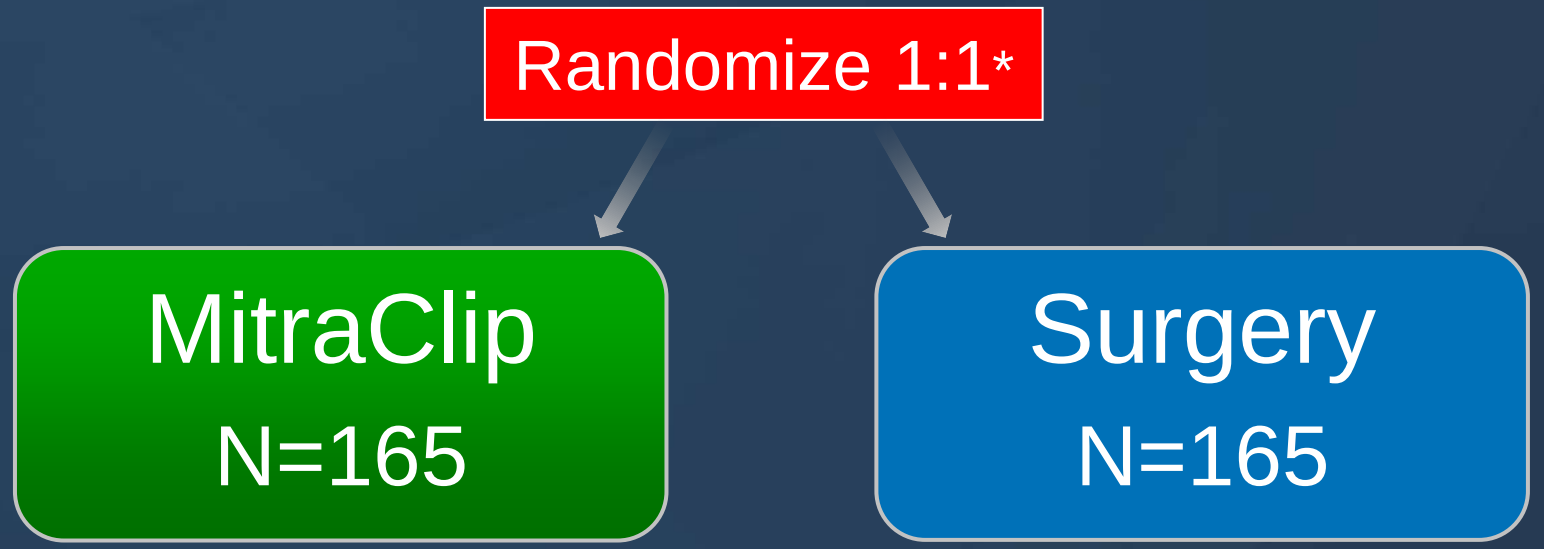
MITRA-HR

MitraClip vs. Surgery for High Surgical Risk Primary MR

Primary Endpoint: All-cause mortality, unplanned hospitalizations for HF and MV reintervention at 12 month (non-inferiority)

Table 1. Inclusion criteria of the MITRA-HR trial.

Primary mitral regurgitation grade 3+ or 4+
New York Heart Association Class II to IV
Mitral valve anatomy appropriate to MitraClip therapy and mitral valve surgery (repair or replacement)
High surgical risk defined by the local Heart Team as: – age ≥75 years and an intermediate MVARC risk (STS score [repair] ≥6%, or one frailty index [mild][1], or one compromised major organ system[2], or one possible procedure-specific impediment[3]) or – age <75 years and a high MVARC risk (STS score [repair] >8%, or two frailty indices [moderate to severe][1], or no more than two compromised organ systems[2], or one possible procedure-specific impediment[3])
Isolated mitral valve pathology
If revascularisation procedures are required, they must be performed more than 30 days from the intervention (day 0)
Affiliation to French social security
[1,2,3] details in Supplementary Appendix 1



PI : Patrice Guerin MD. NCT03271762.
Piriou N et al. EuroIntervention 2019;15:e329-e335.

REPAIR MR

MitraClip vs. Surgery for Moderate Surgical Risk

Primary Endpoint: Death, Stroke, Cardiac Hospitalization, AKI requiring RRT at 2 yrs

Patient Population

- Subject is symptomatic (NYHA Class II/III/IV) or asymptomatic (LVEF ≤ 60%, Pulmonary Artery Systolic Pressure > 50 mmHg, or LVESD > 40 mm)
- Subject is at least 75 years of age, OR if younger than 75 years, then has:
  - STS-PROM Score ≥ 2%, OR
  - Presence of other comorbidities which may introduce a potential surgical specific impediment

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

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Cardiac Surgeon Concurs that Mitral Valve is Conducive to Mitral Valve Repair Surgery → NO → Exclude Subject

↓ YES

Eligibility Committee Confirms that MR can be Reduced to ≤ 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)

PI : Patrick McCarthy MD, Saibal Kar MD. NCT04198870.

Summary : Clinical Update of MitraClip

- Real-world registries showed higher efficacy, safety, and durability with contemporary MitraClip G4 devices.
- Obtaining optimal MR reduction was the key for better long-term clinical outcome.
- Reduction of MR seems more important than reducing transmitral gradient, especially in secondary MR patients.
- MitraClip is trying to widen its indication to moderate-risk primary MR or atrial functional MR.