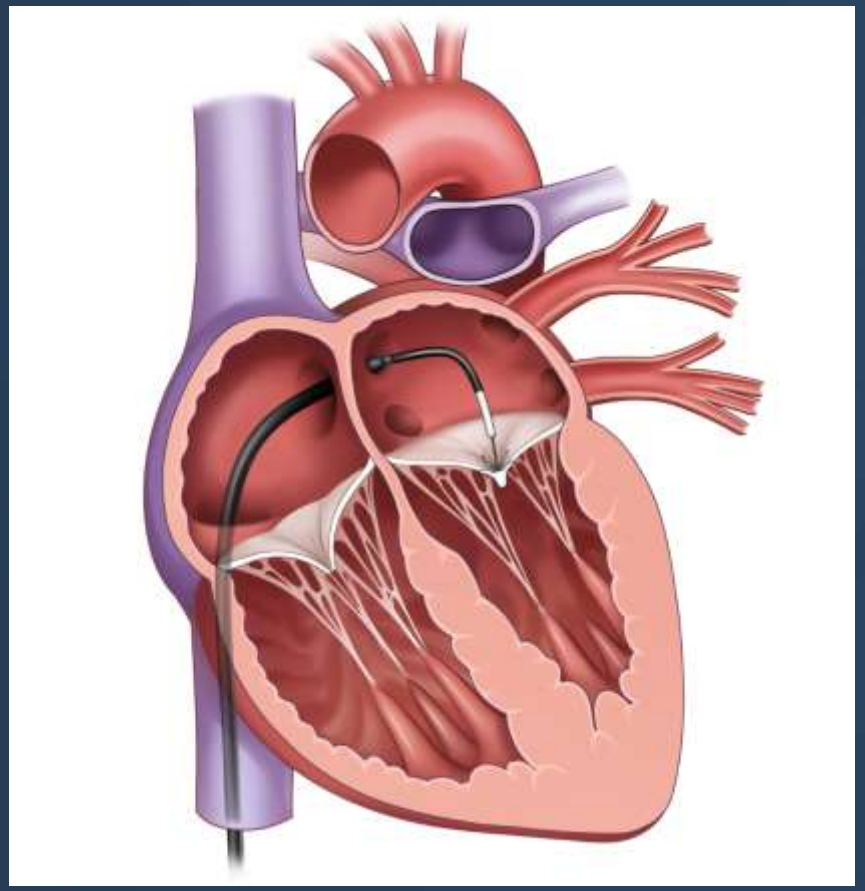
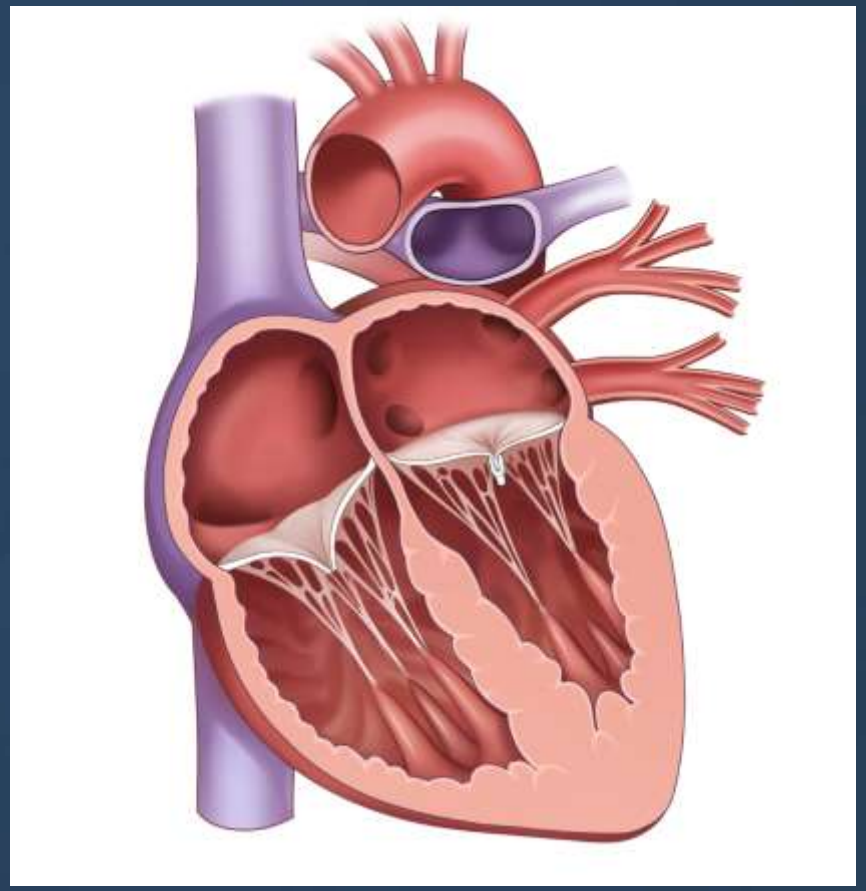
Transcatheter Edge-to-Edge Repair (TEER)

Concept of TEER with MitraClip



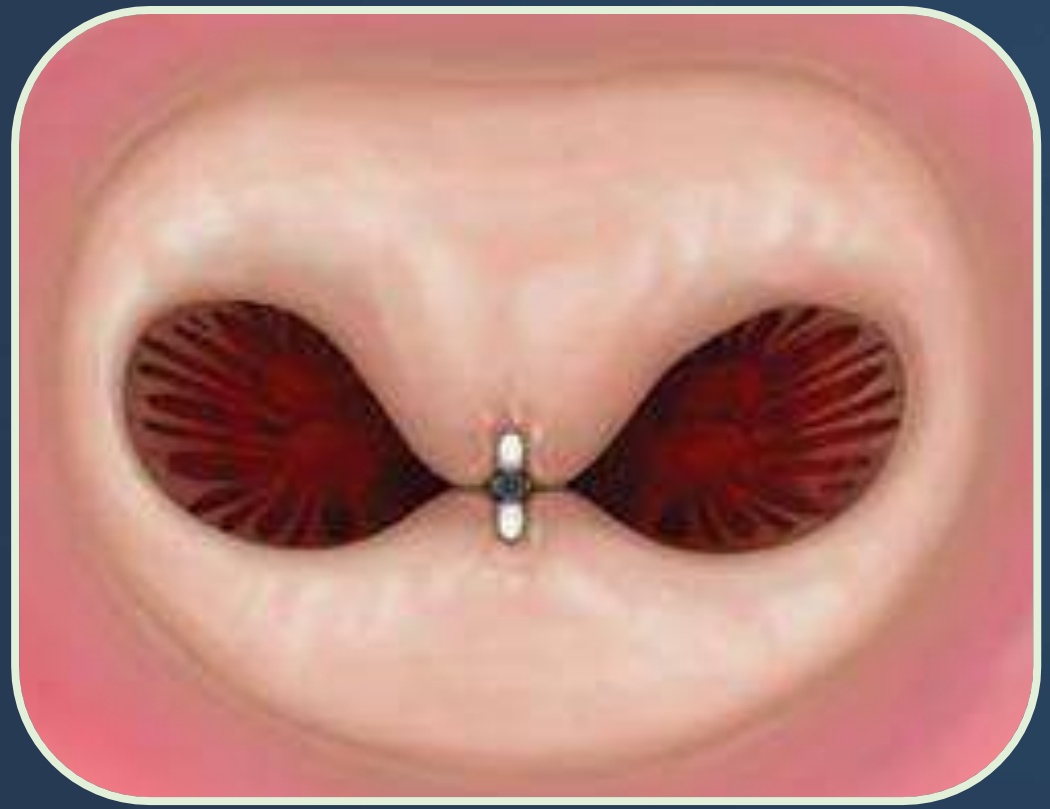


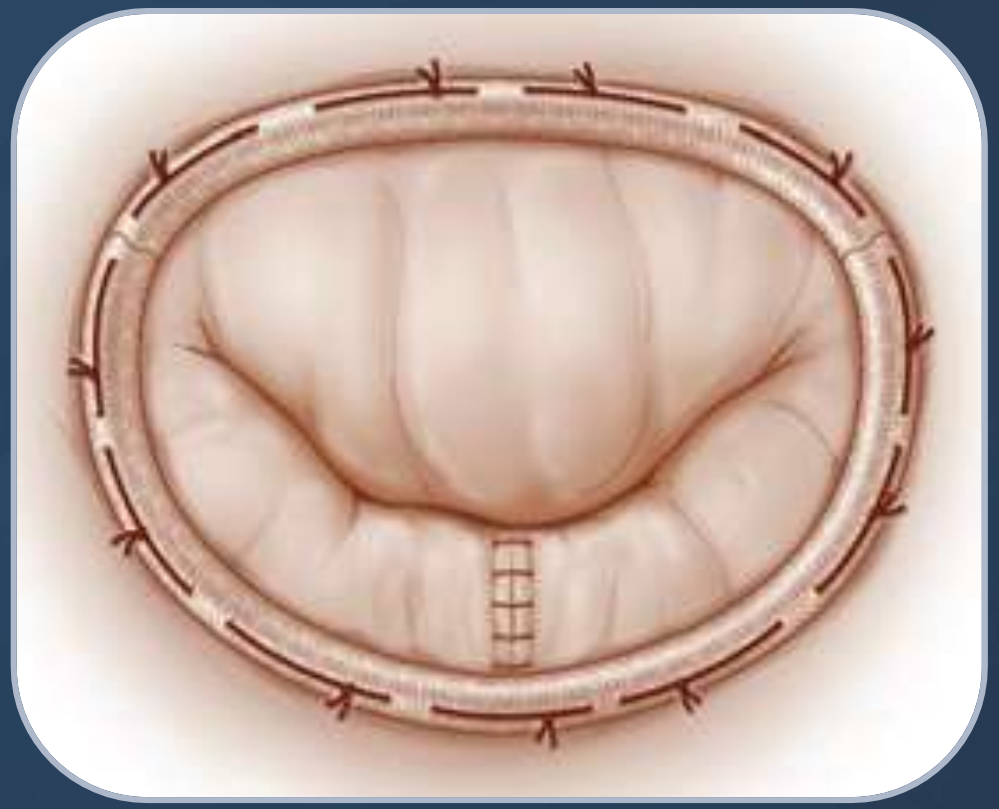
Current Devices of TEER

MitraClip (Abbott)
FDA, CE, KFDA approved

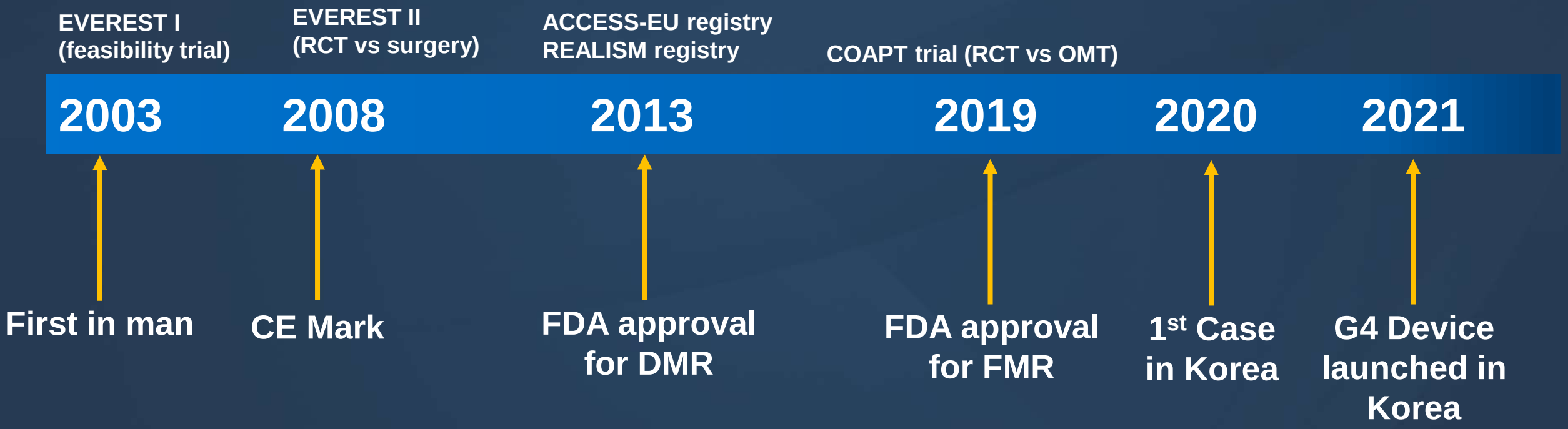
PASCAL (Edwards)
CE approved

MitraClip vs. Surgery





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

Two Types of Mitral Regurgitation

Primary (degenerative) MR: Prolapse/Flail

Secondary (functional) MR: Ventricular Problem

Evidence of TEER for Primary MR

Mitraclip for Primary MR : EVEREST II RCT

279 patients enrolled at 37 sites

Severe MR (3+ or 4+)

73% DMR, 27% FMR

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
Baseline, 30 days, 6 months, 1 year, 18 months, and annually through 5 years

Feldman T et al. NEJM 2011;364:1395-406

EVEREST II Trial

279 patients 2:1 Randomization to Mitraclip vs Surgery

	Percutaneous Repair N=184	Surgery N=95	P value
Age	67.3 ± 12.8	65.7 ± 12.9	0.32
> 75 yr	55 (30%)	26 (27%)	0.68
Male sex	115 (62%)	63 (66%)	0.60
Congestive heart failure	167 / 184 (91%)	74 / 95 (78%)	0.005
Coronary artery disease	86 / 183 (47%)	44 / 95 (46%)	0.99
Atrial fibrillation	59 / 175 (34%)	35 / 89 (39%)	0.42
Diabetes	14 / 184 (8%)	10 / 95 (11%)	0.50
COPD	27 / 183 (15%)	14 / 95 (15%)	0.99
Previous CABG	38 / 184 (21%)	18 / 95 (19%)	0.87
LV ejection fraction, %	60.0 ± 10.1	60.6 ± 11.0	0.65

Feldman T et al. N Engl J Med. 2011 Apr 14;364(15):1395-406.

EVEREST II Trial

279 patients 2:1 Randomization to Mitraclip vs Surgery

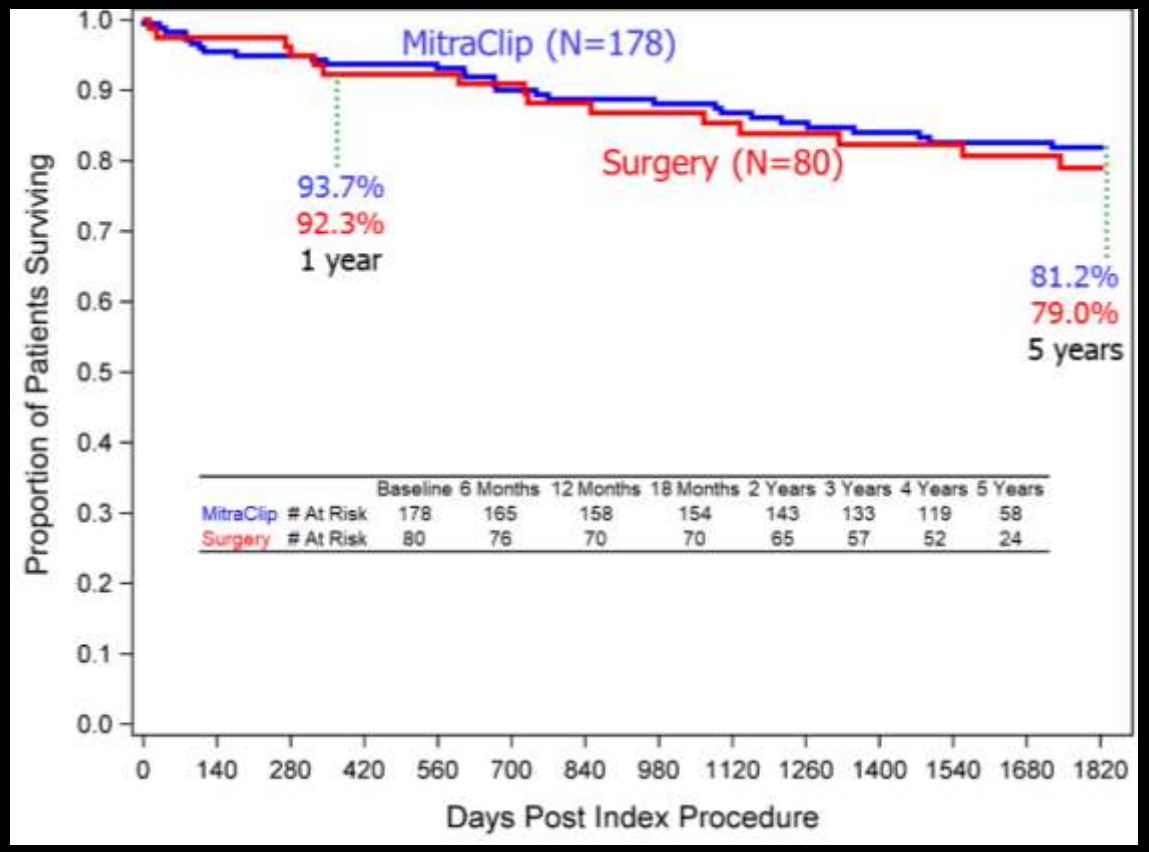
	Percutaneous Repair N=184	Surgery N=95	P value
Primary Efficacy Endpoint at 12 months			
Freedom from death, surgery for MV dysfunction, grade 3+/4+ MR	100 (55%)	65 (73%)	**0.007**
Death	11 (6%)	5 (6%)	1.00
Surgery for MV dysfunction	37 (20%)	2 (2%)	**<0.001**
Grade 3+/4+ MR	38 (21%)	18 (20%)	1.00
Major Adverse Event at 30 days	27 (15%)	45 (48%)	<0.001
Any major adverse event excluding transfusion	9 (5%)	9 (10%)	0.23

Feldman T et al. N Engl J Med. 2011 Apr 14;364(15):1395-406.

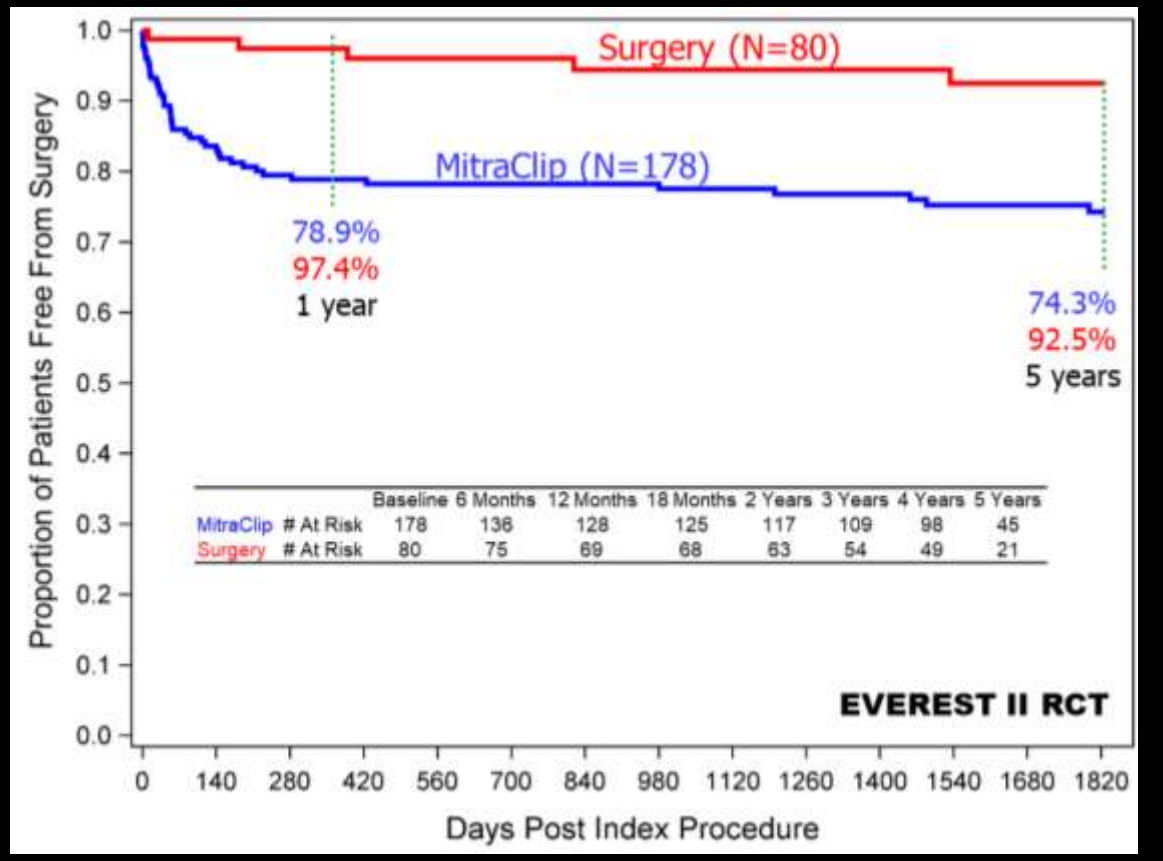
EVEREST II Trial

279 patients 2:1 Randomization to Mitraclip vs Surgery

Freedom from Mortality



Freedom from MV Surgery or Re-operation

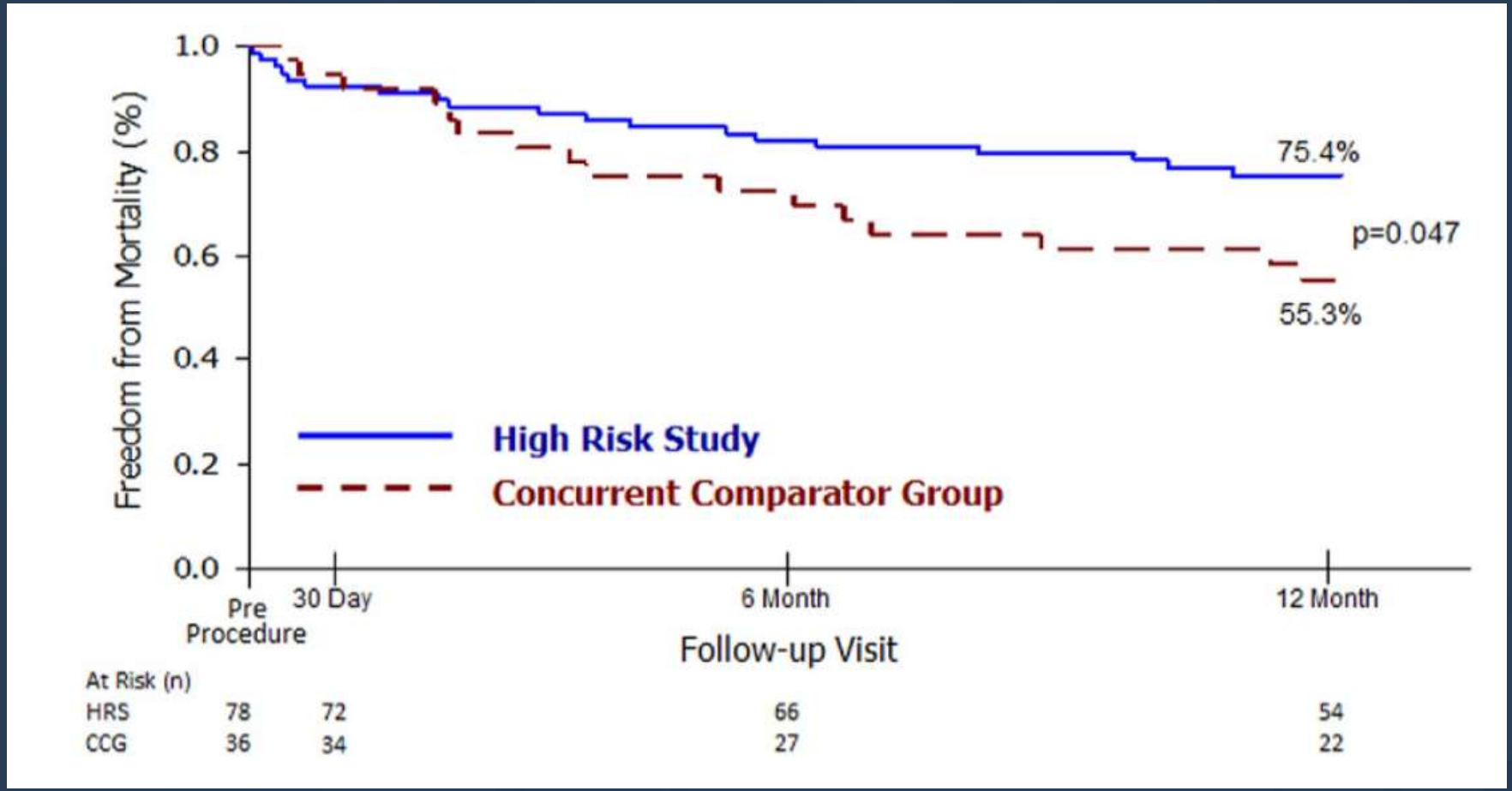


Feldman T et al. N Engl J Med. 2011 Apr 14;364(15):1395-406.

EVEREST II High-Risk Study

76 High Risk Patients compared with 36 Patients with Standard Care

Freedom from Mortality



Whitlow P et al. J Am Coll Cardiol. 2012;59(2):130-9.

2014 & 2017 AHA/ACC Guideline, TMVR for Primary MR

COR	LOE
IIb	B-NR

- 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)

Nishimura R et al. Circulation. 2014.

Real-World outcome of TEER
: 2017 STS/ACC TVT Registry Report

- 2,952 patients in 145 hospitals in US, 2013-2015
- Median age 82, STS-PROM 6.1% (repair), 9.2% (replacement)
- Degenerative MR 86%
- 1 clip in 67%, Post implant none~mild MR in 62%
- Length of stay : 2 days
- In-hospital mortality : 2.7%

Sorajja P et al. JACC. 2017

Real-World outcome of TEER : 2017 STS/ACC TVT Registry Report

	30 days	1 year
Death	5.2%	25.8%
Myocardial Infarction	0.2%	2.5%
Stroke		
Any stroke	1.0%	2.7%
Hemorrhagic stroke	0.4%	0.6%
HF hospitalization	4.7%	20.2%
Mitral Valve Surgery	0.4%	2.1%
Repeat Mitraclip	1.3%	6.2%

Sorajja P et al. JACC. 2017

2020 AHA/ACC Guideline, TEER for Primary MR

COR	LOE
IIa	B-NR

- 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

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

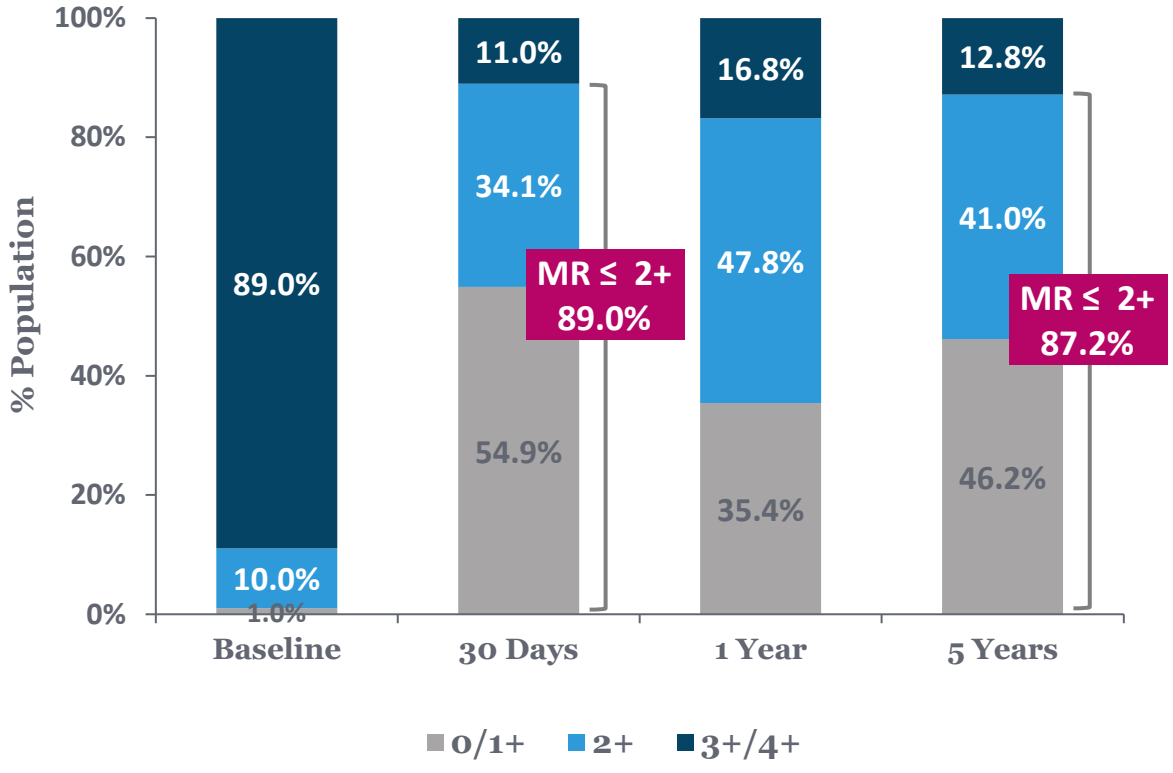
Real-World outcome of TEER
: 2021 STS/ACC TVT Registry Report

	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%	

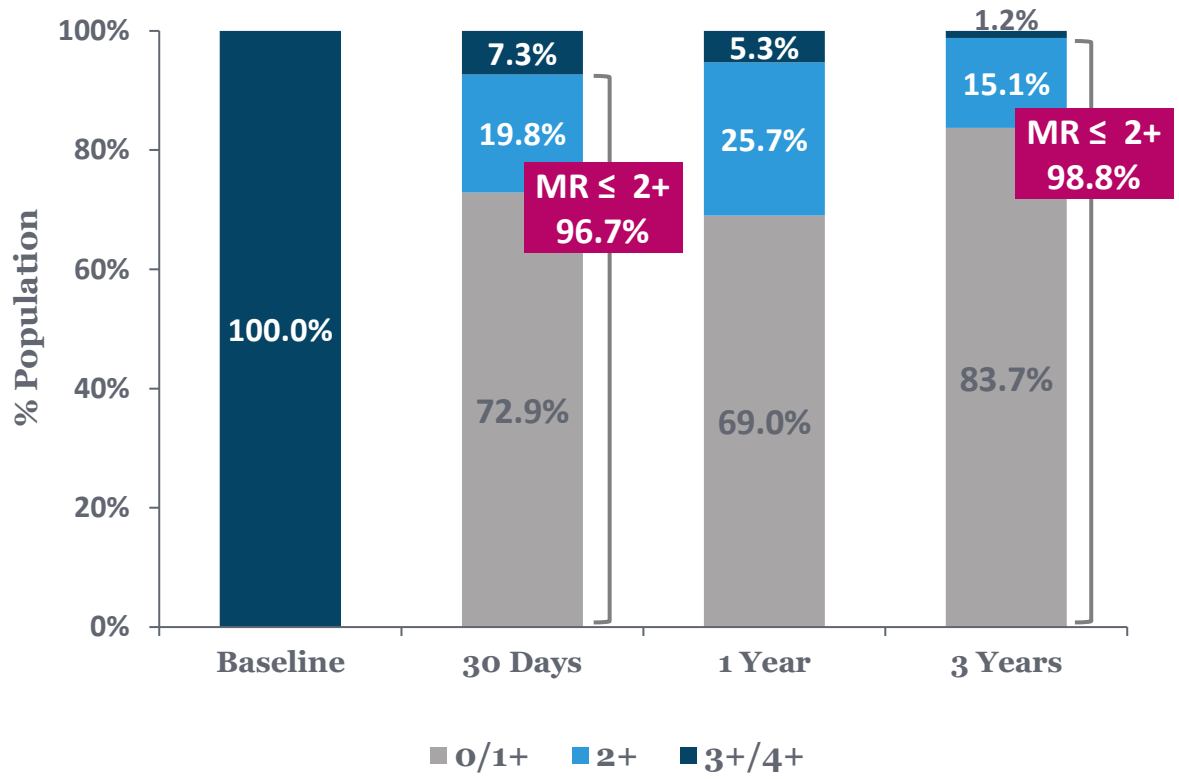
Mack M et al. J Am Coll Cardiol. 2021;78(23):2326-2353.

Durable Results in Longer-term FU

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

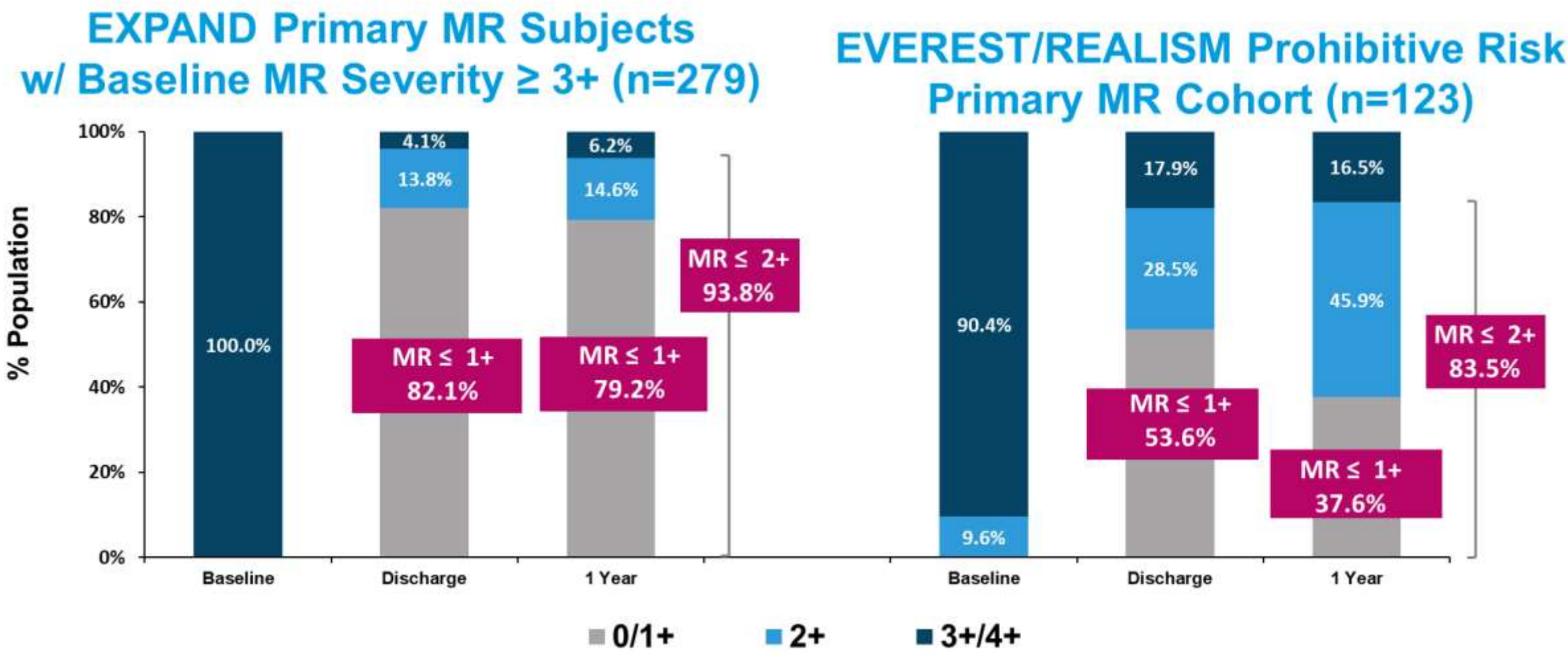


COAPT 3 Year Outcomes[2]
(n=302)



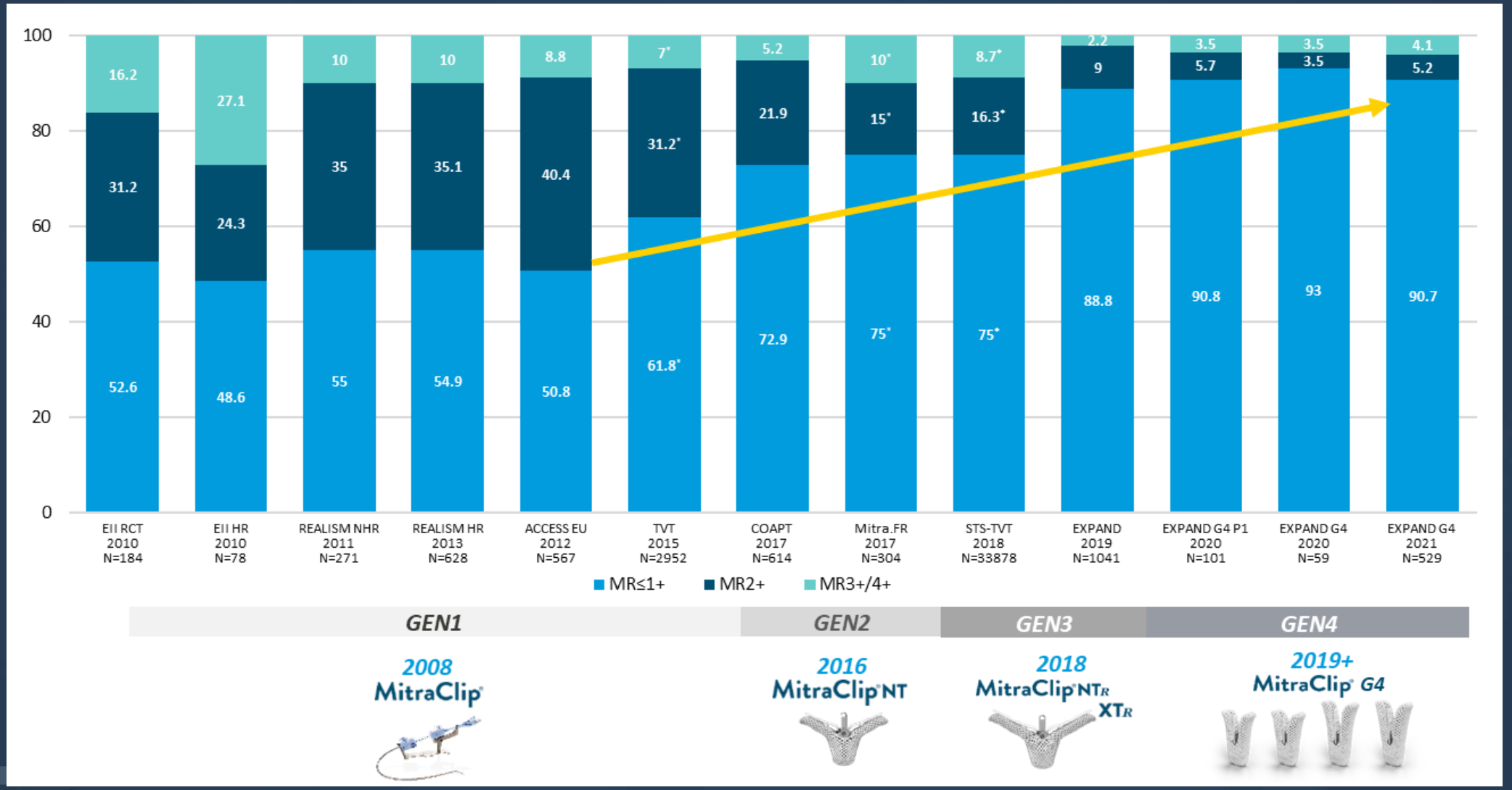
1. EVEREST II REALISM Non High Risk (HR) Cohort, Abbott Internal Data
2. Mack, M.J. et al. J Am Coll Cardiol. 2021;77(8):1029–40.

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



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

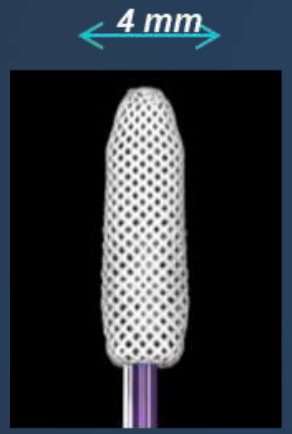
Significant Improvement in MR at 30-days post-TEER Implant Over The Past Years



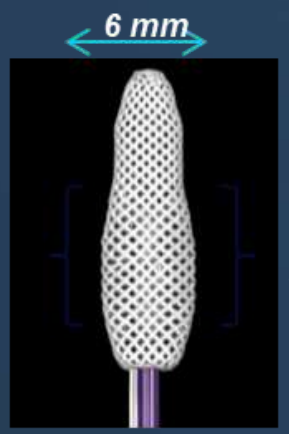
Rinaldi M. TVT 2022 Presentation

Device Update to G4 Mitraclip

Mitraclip™ G4 : Various Length & Width of Clips



50% wider in the grasping area

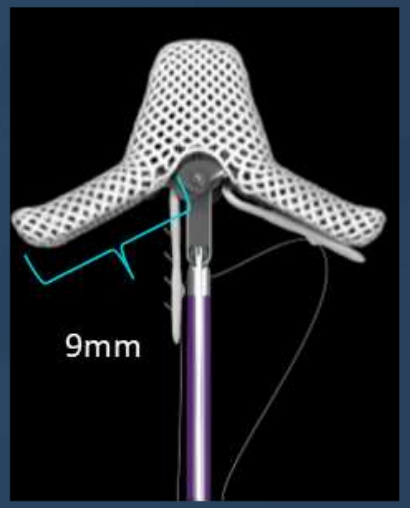


50% wider in the grasping area

NT/XT **NTW/XTW**

MitraClip™ G4

4 Clip sizes

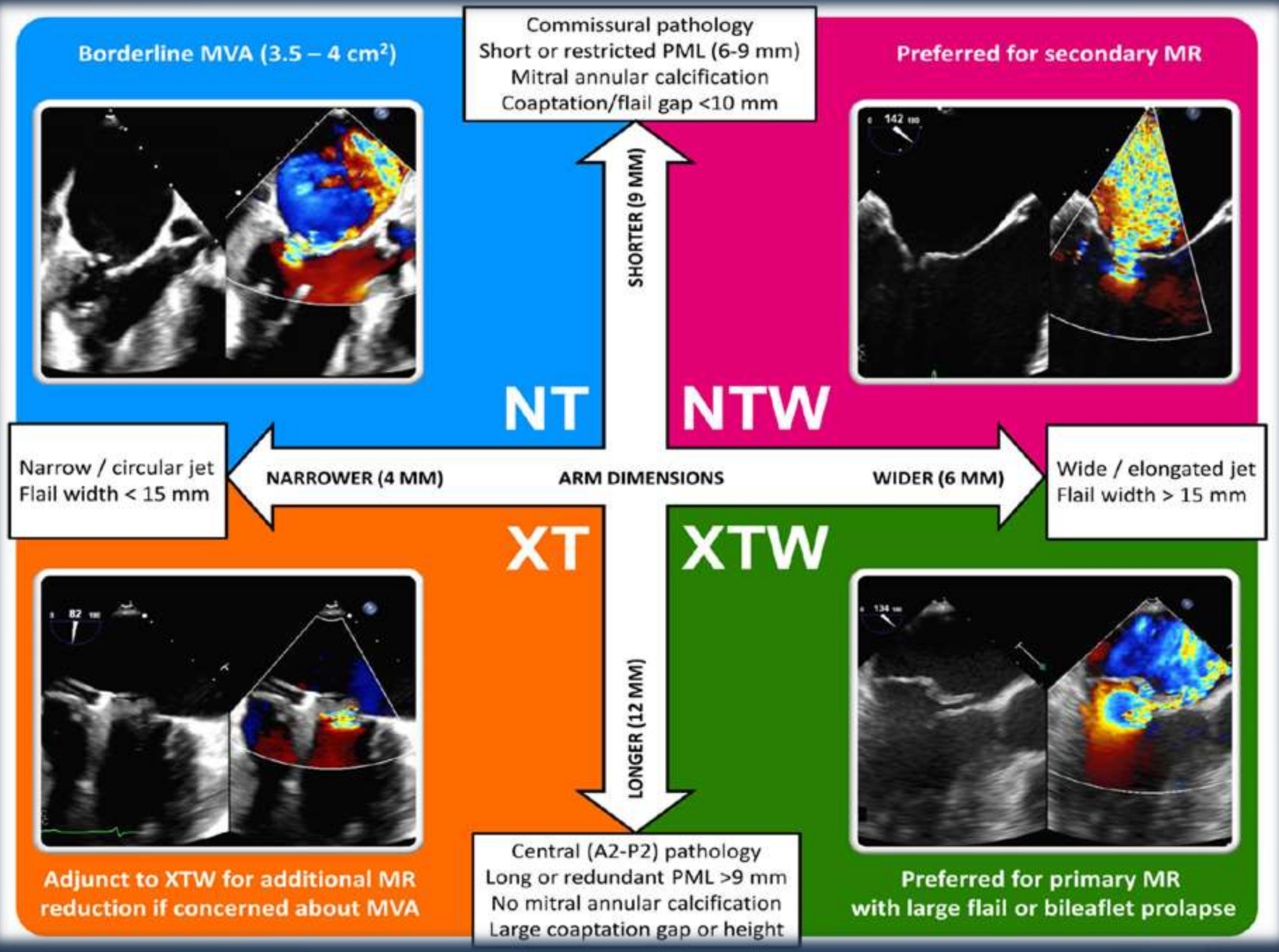


17 mm at 120 degrees
20 mm at 180 degrees

NT/NTW

22 mm at 120 degrees
25 mm at 180 degrees

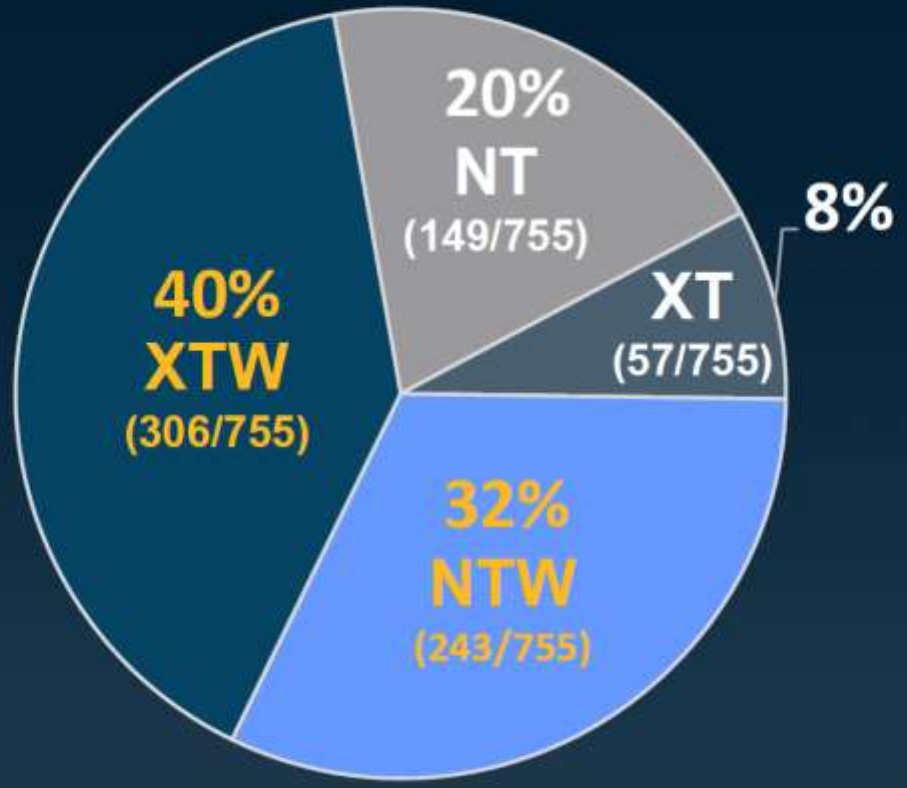
XT/XTW



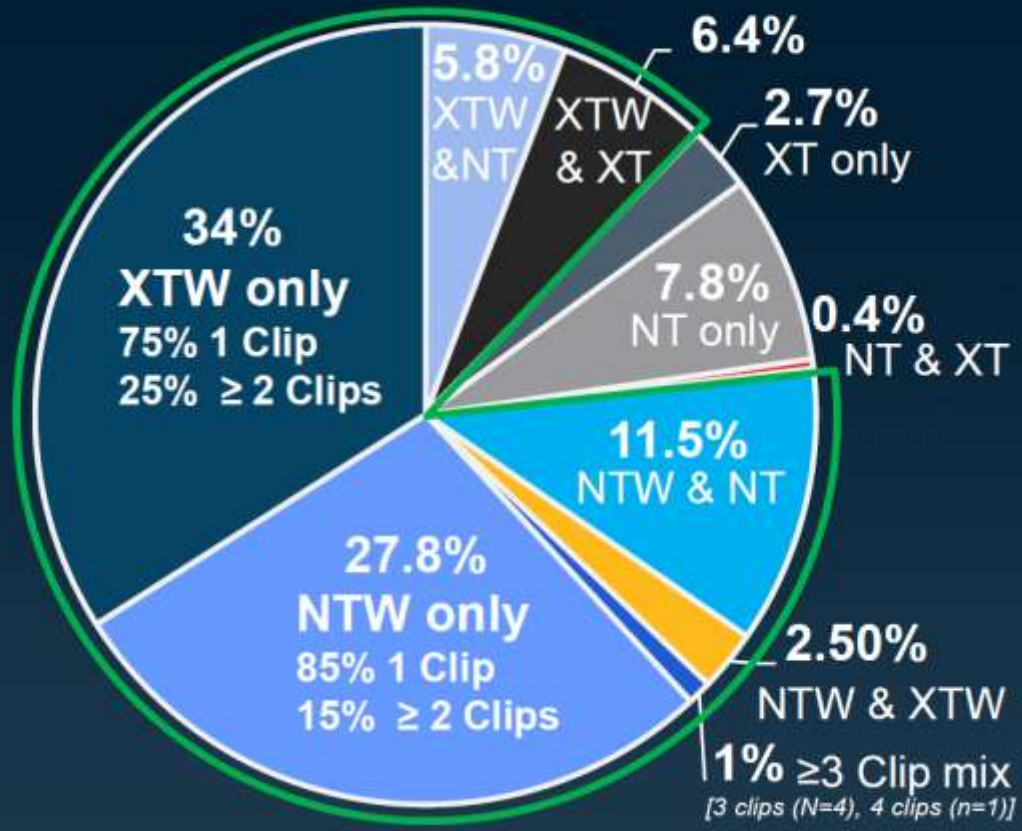
Garcia-Sayan E et al. Catheter Cardiovasc Interv. 2021;98(4):E626-E636.

Clips Used in EXPAND G4 Registry (N=529)

Clip Size Usage (total clips implanted = 755)

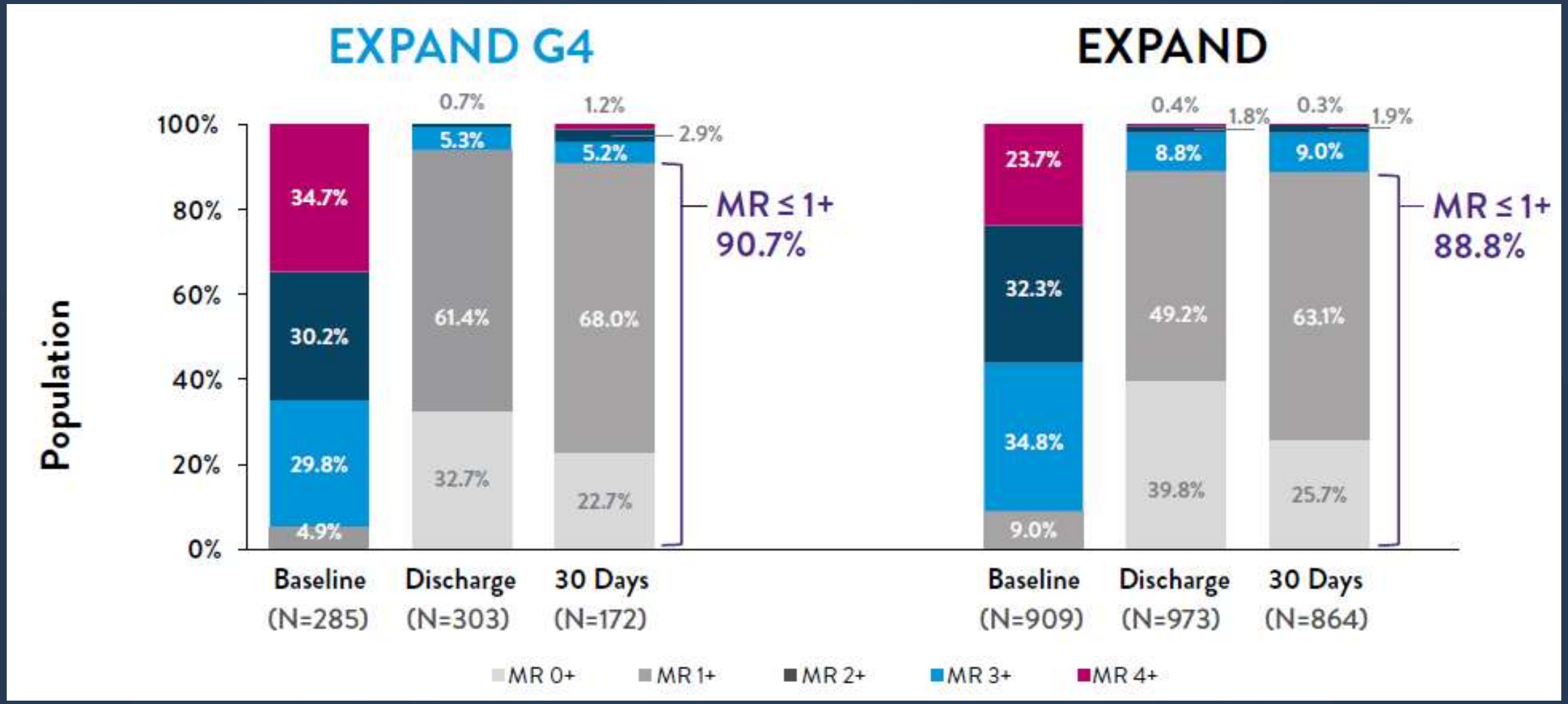


Clip Mix (N=514, 13 Clip combinations)



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

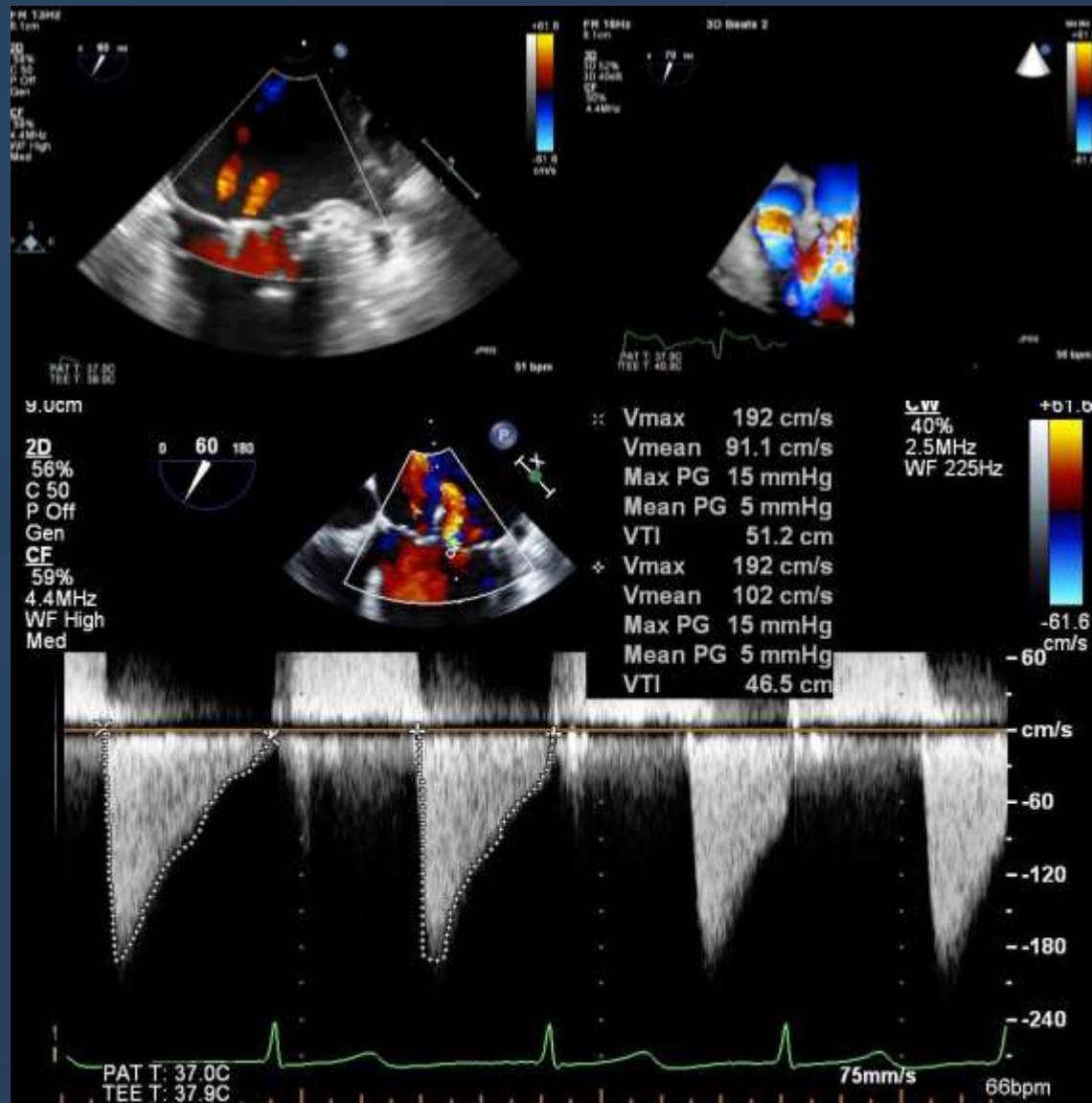
	TVT Registry 30-Day (N=2,952)	EXPAND 30-Day (N=1,041)	EXPAND 1-Year (N=1,041)	EXPAND G4 30-Day (N=529)
All-cause Death	5.2% (96)	2.3% (24)	14.9% (147)	**1.5% (7)**
MI	0.2% (3)	0.0% (0)	1.2% (12)	**0.0% (0)**
Stroke	1.0% (17)	1.2% (8)	1.7% (18)	**0.0% (0)**
Ischemic stroke	0.6% (11)	1.0% (6)	N/A	**0.0% (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?

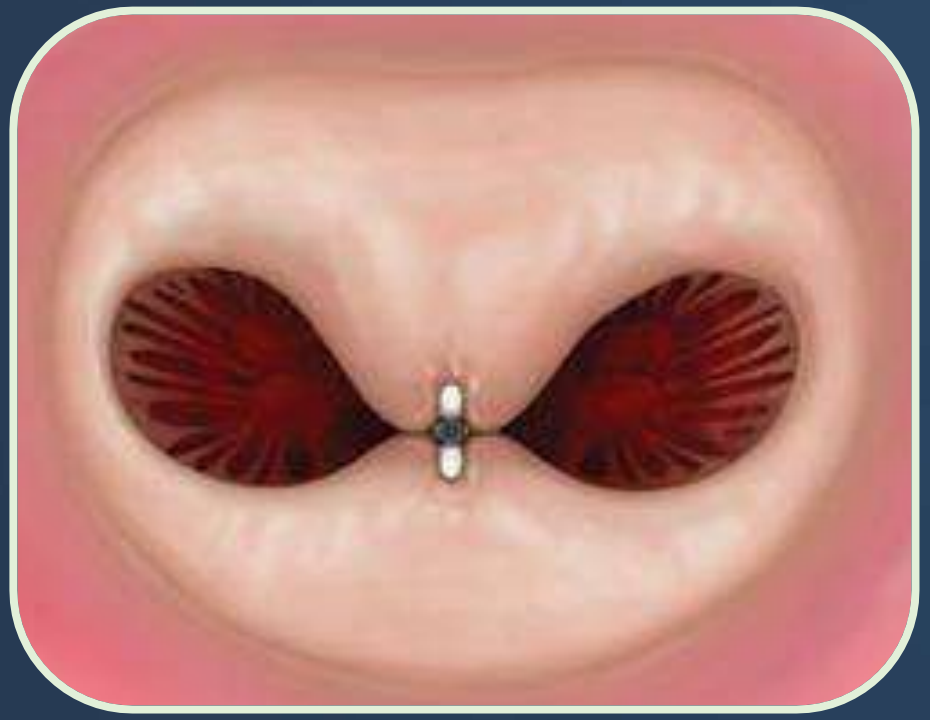
- MR reduction (≤ 2+)
  - "achievable" MR result will depend on starting MVA, baseline MR, etc
  - **Acceptable MR reduction ("success") may vary among patients**
- Absence of significant MS
  - Mean gradient ≤ 5 mmHg
  - Increased gradients did OK in COAPT (MG +/- 7 mmHg), in secondary MR…



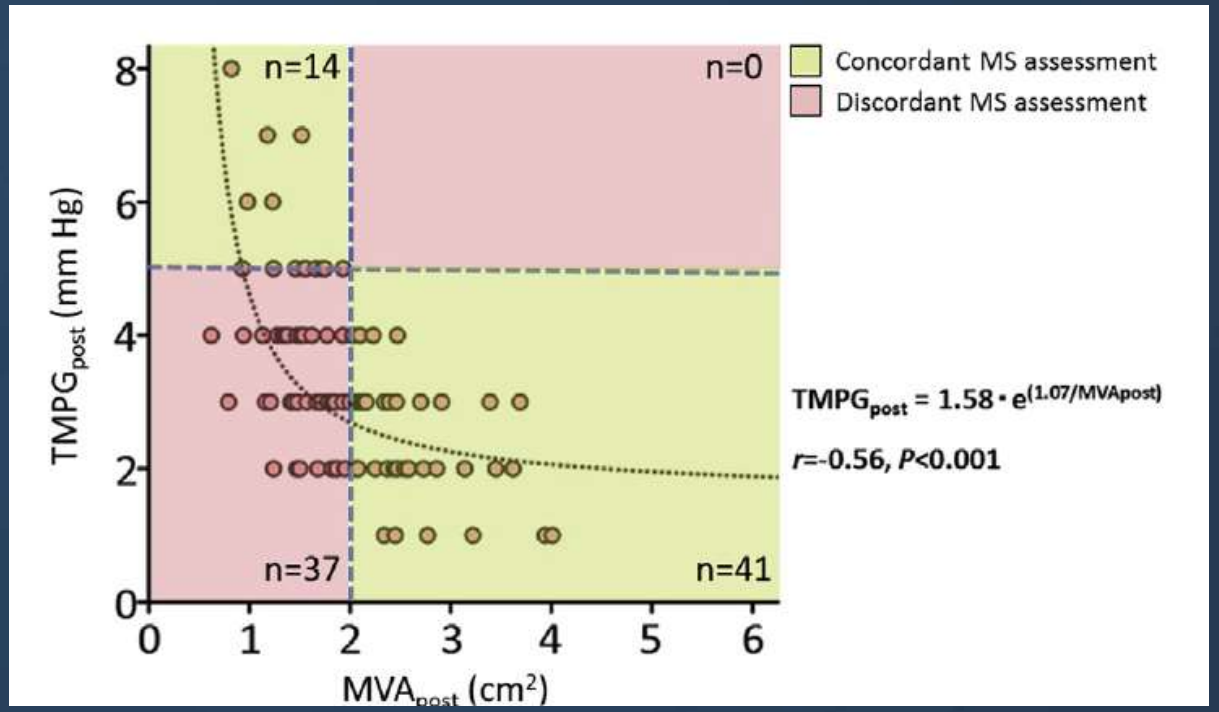
Halaby R et al. JACC CV Interv. 2021

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.

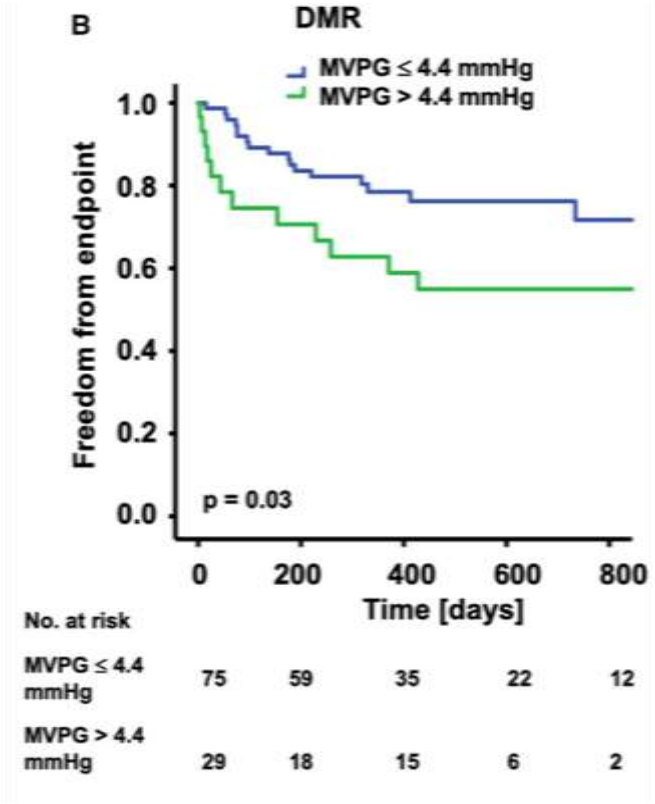
Predictor of Increased MV Gradient after TEER

- 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.

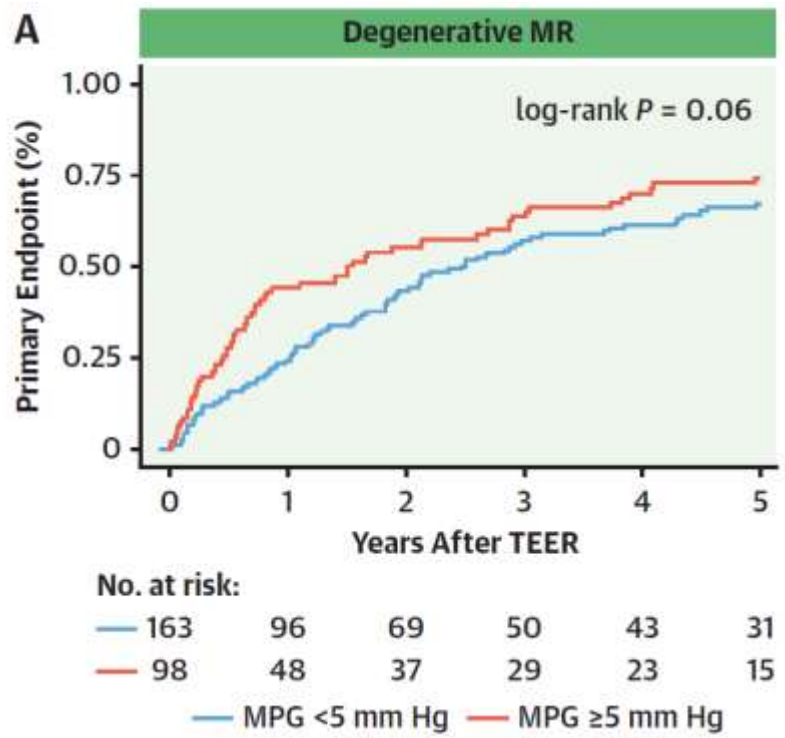
Contrasting Results of Impact of High Transmitral Gradient after TEER for Primary MR

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



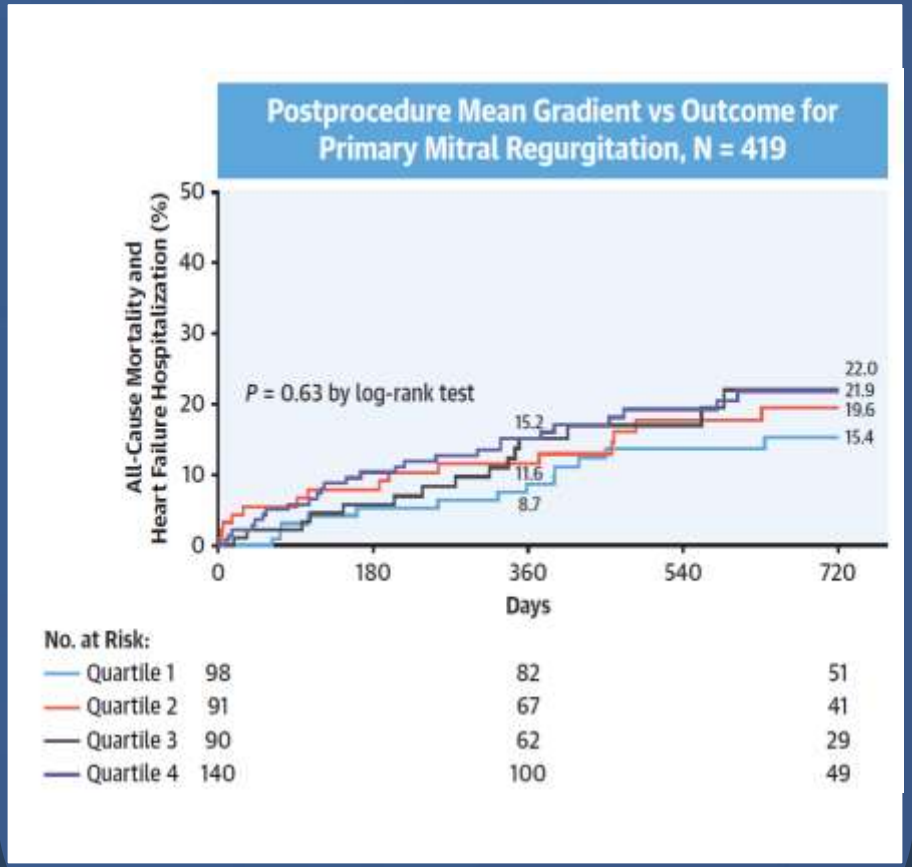
Patzelt J et al. JAHA. 2019;8:e011366.

265 from German Single Center
Mortality, HF Hospitalization



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

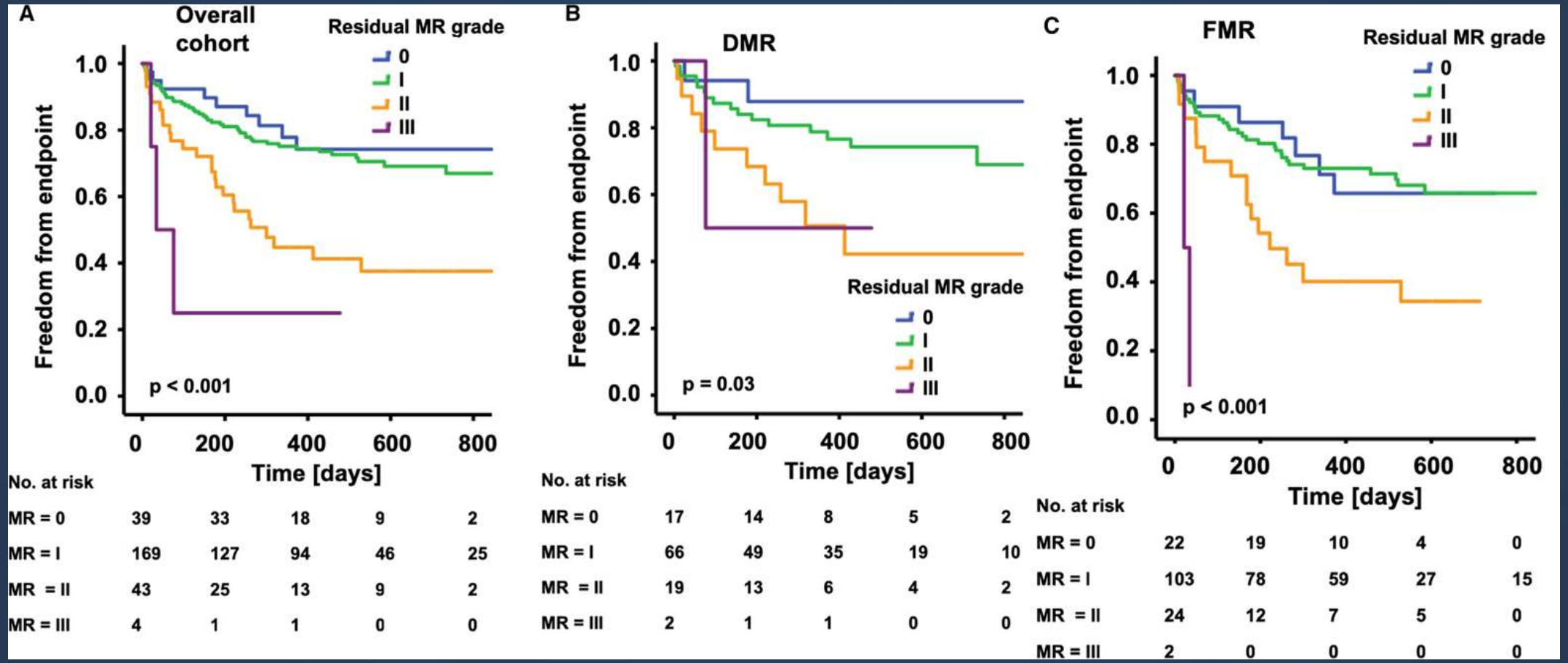
419 from US Single Center
Mortality



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

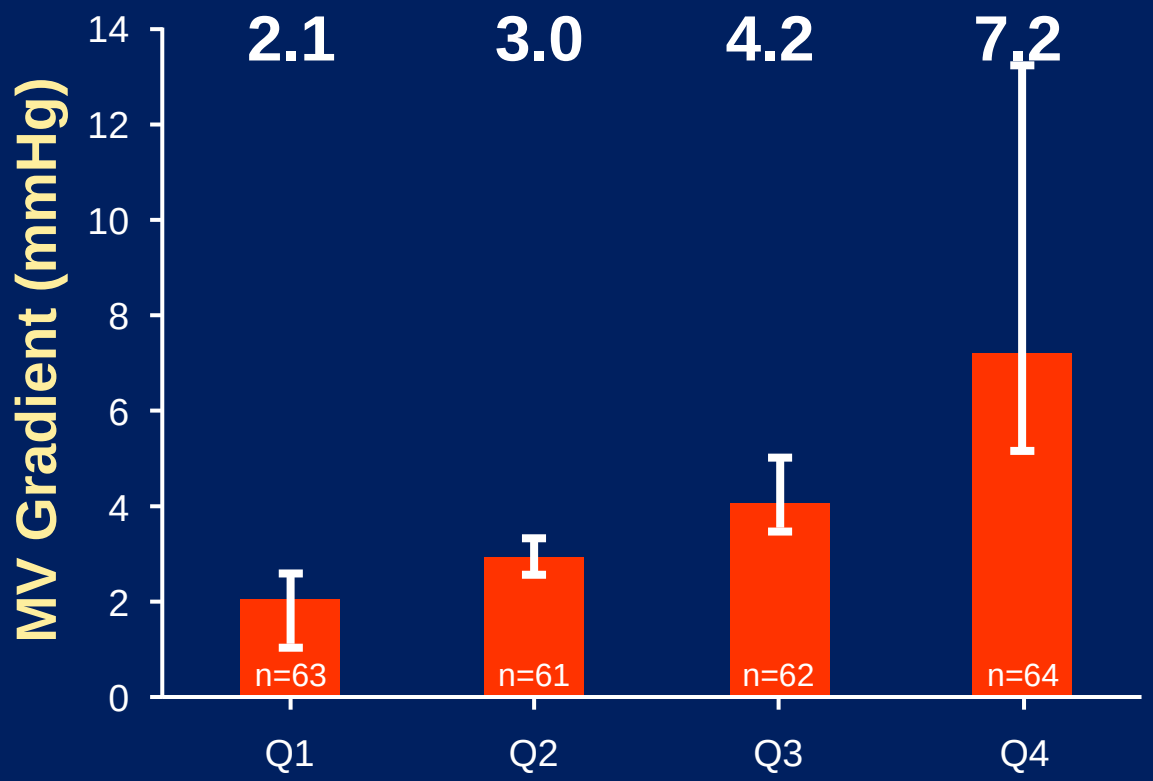


Patzelt J et al. J Am Heart Assoc. 2019;8:e011366.

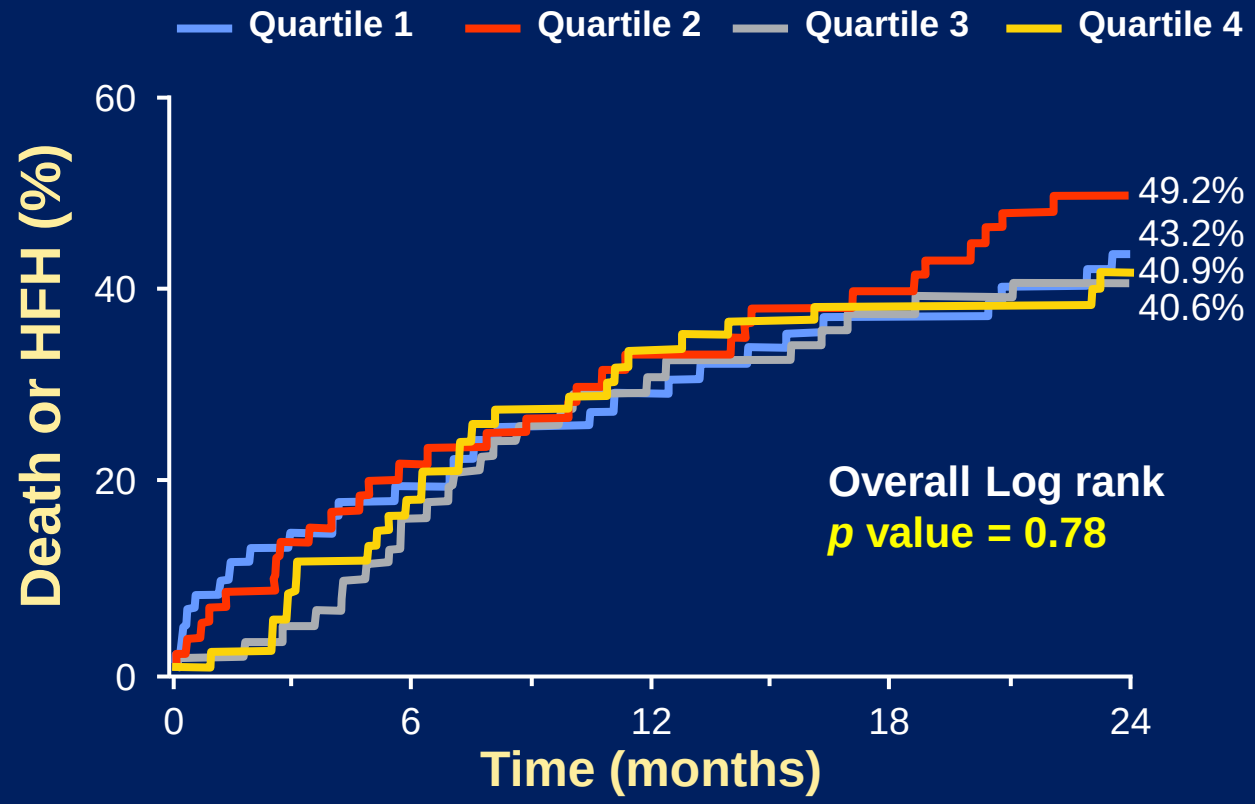
High Transmitral Gradient after TEER was NOT associated with Worse Outcome in COAPT Trial (Secondary MR)

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

Mitral Valve Gradient by Quartile



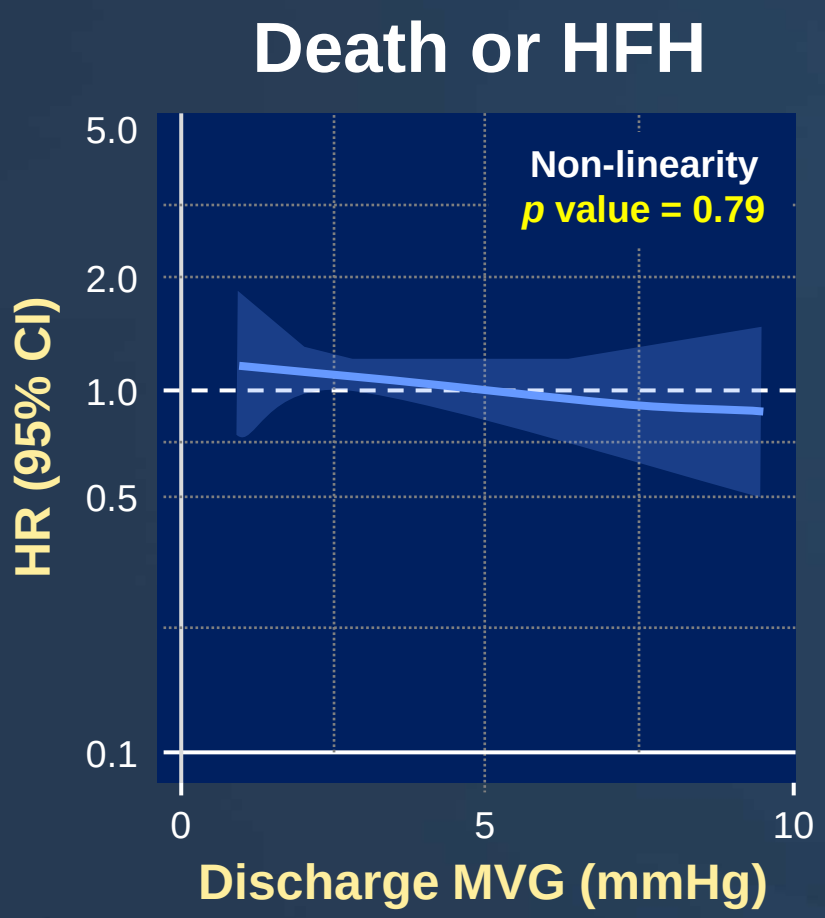
Death or HF Hospitalization

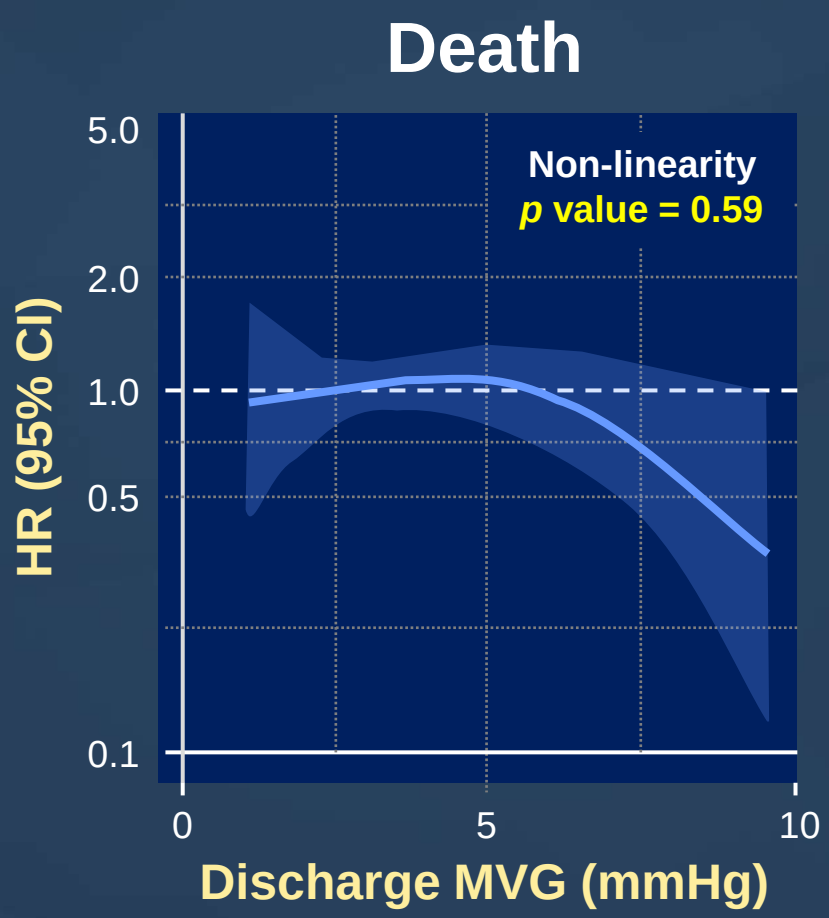


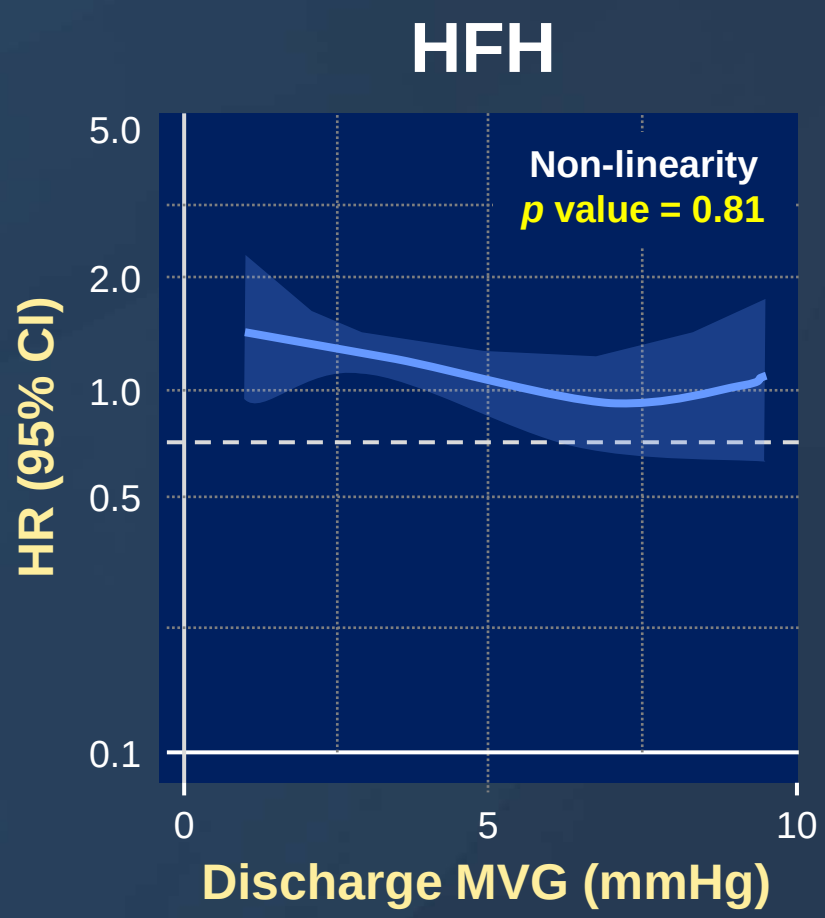
Halaby R et al. JACC Cardiovasc Interv. 2021;14(8):879-889.

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

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







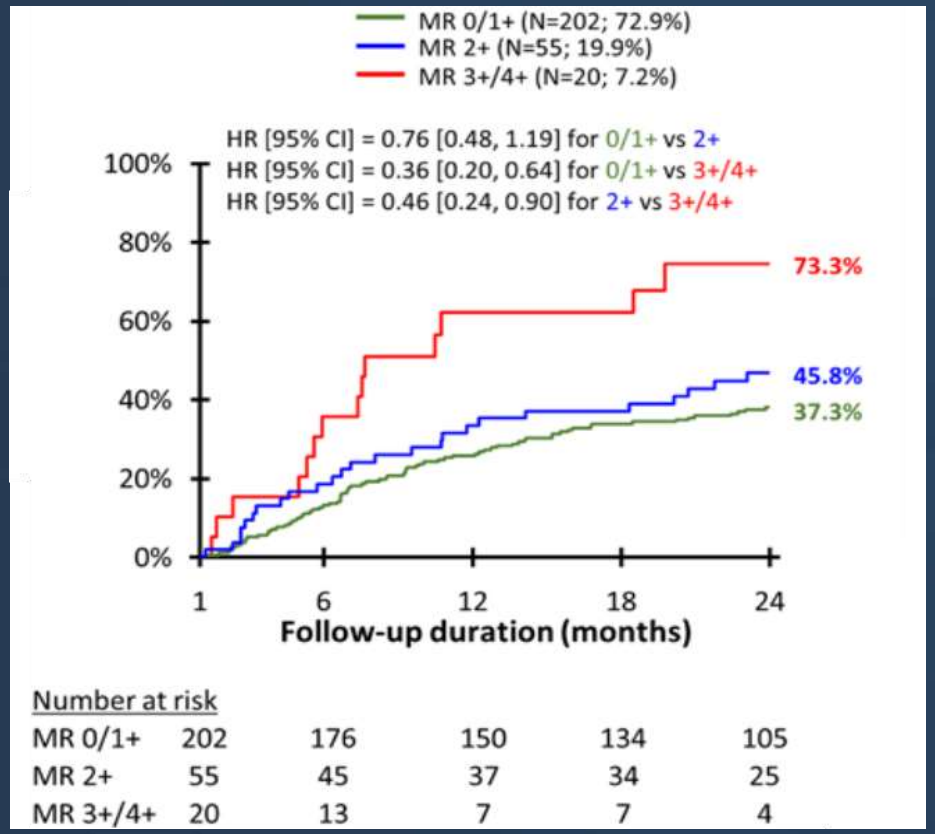
Halaby R et al. JACC Cardiovasc Interv. 2021;14(8):879-889.

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

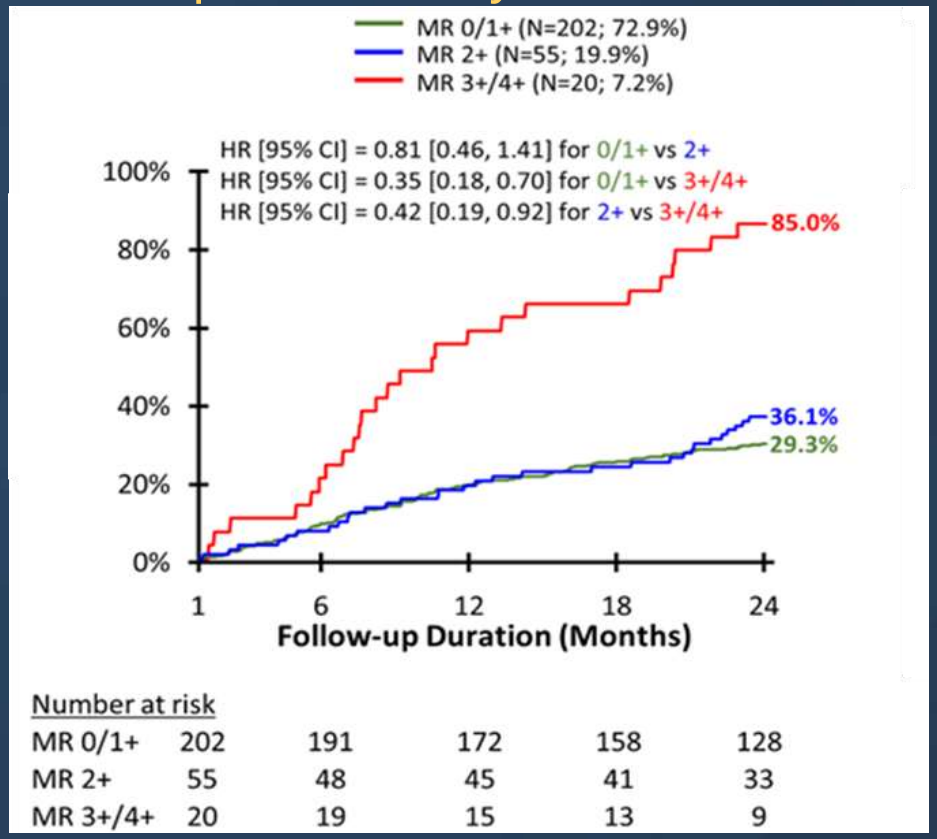
MR Reduction was Strong Predictor of Clinical Outcome

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



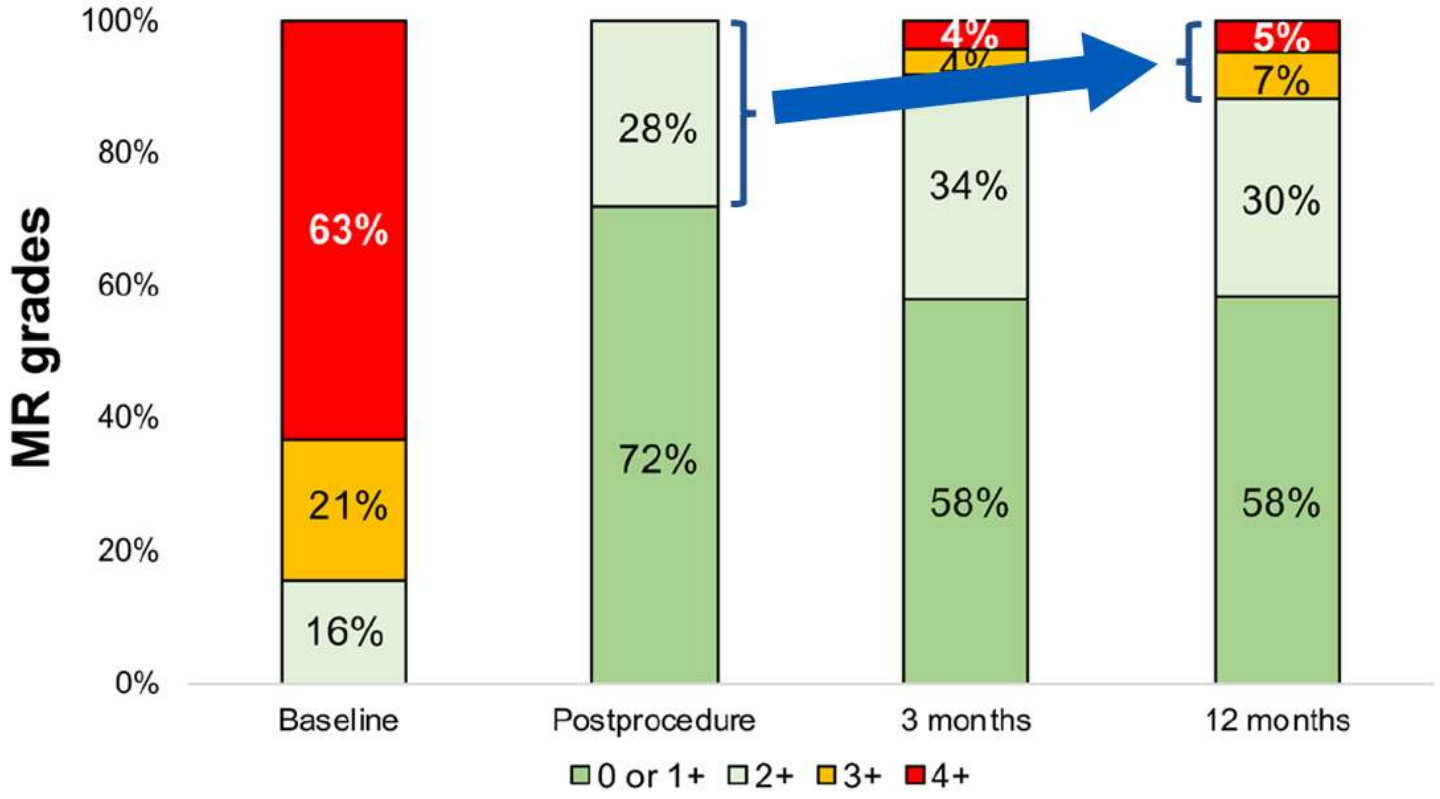
HF Hospitalization by Residual MR

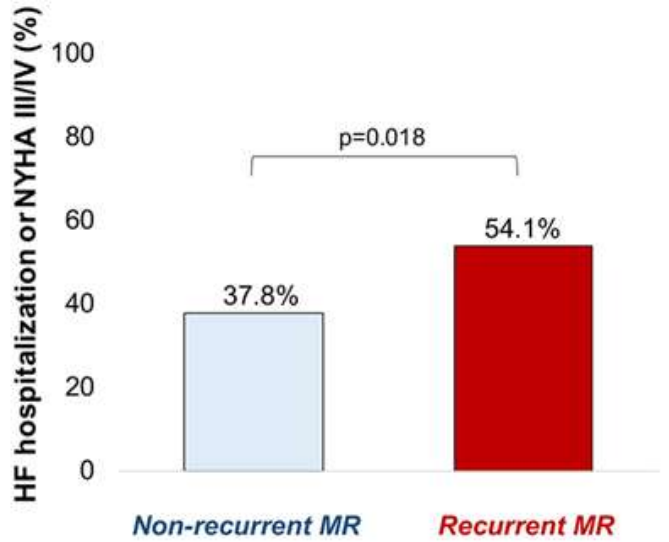


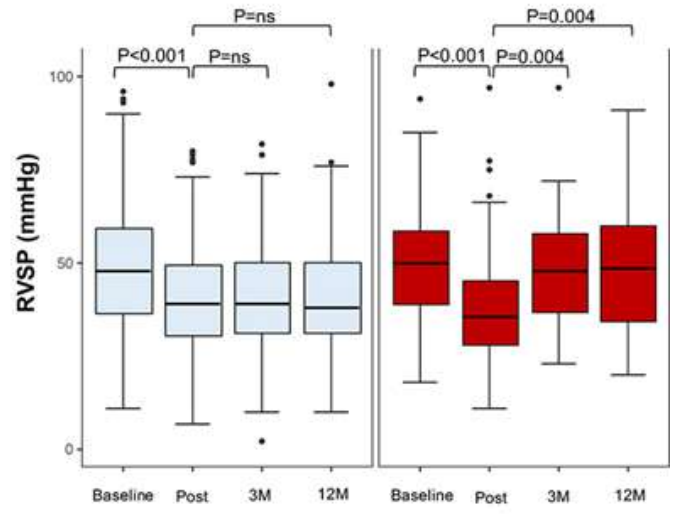
Kar S et al. Circulation. 2021;144:426-37.

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



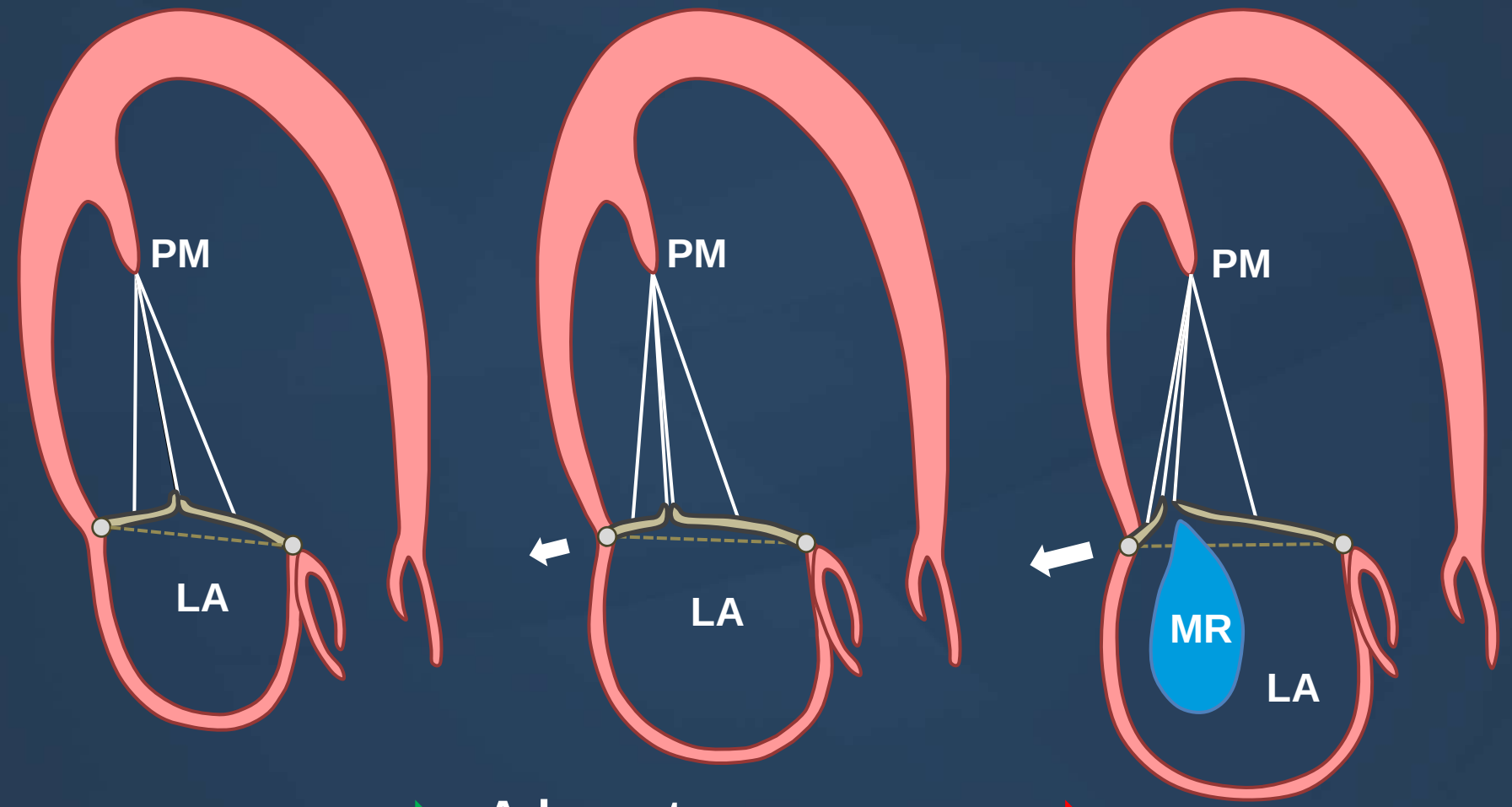




Sugiura A et al. Circ Cardiovasc Interv. 2022;15(3):e010895.

TEER in Atrial Functional MR

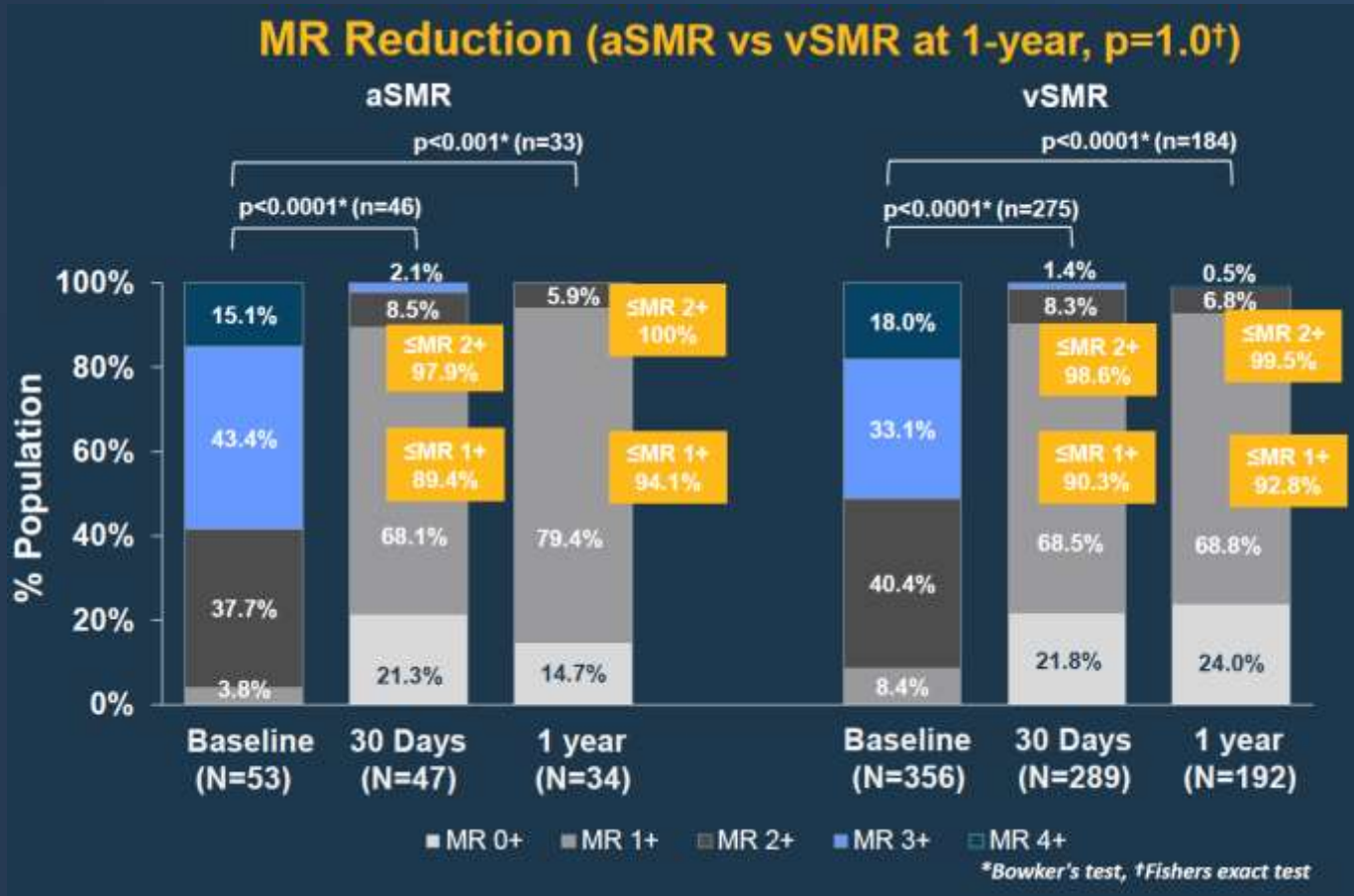
Isolated Annular Dilation Develops Atrial FMR in AF

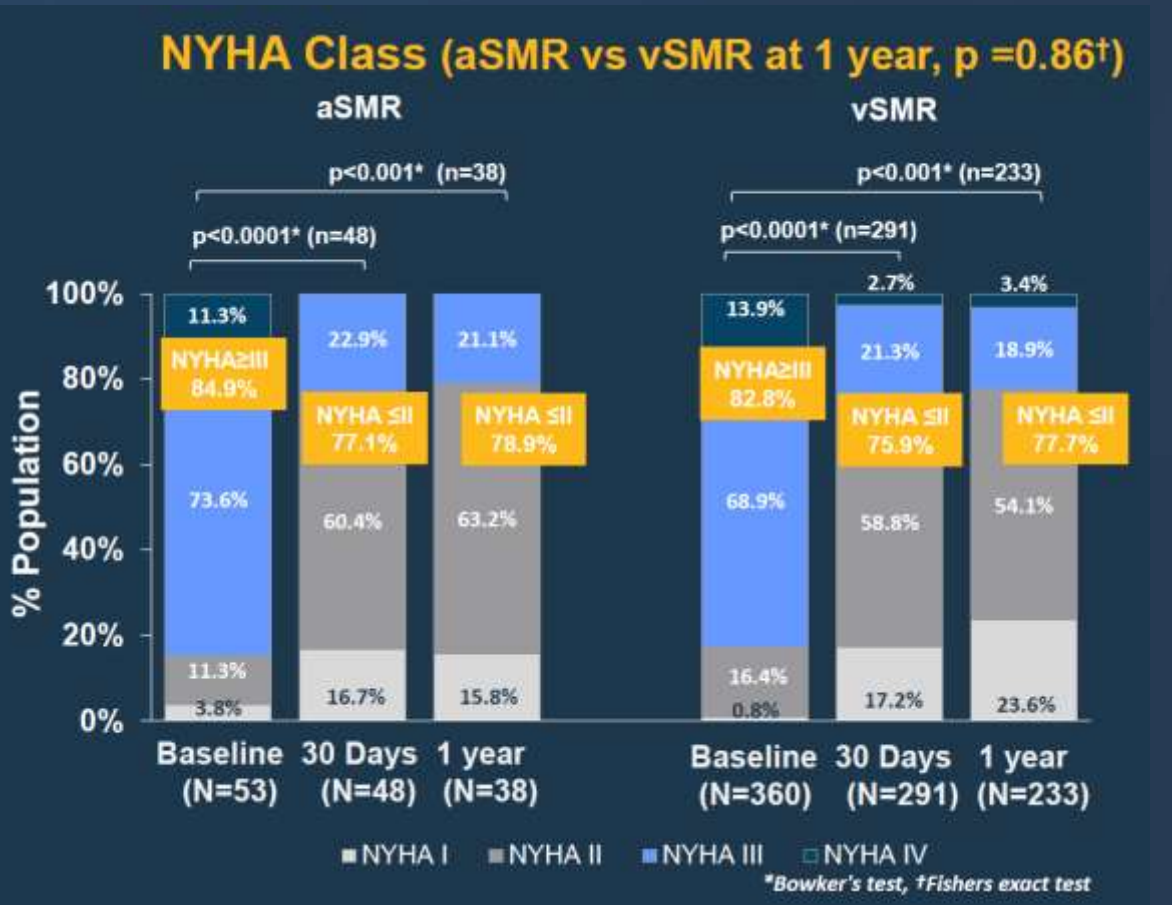


Kim DH et al.
JACC Imaging.
2019;12:665–

TEER in Atrial FMR : Global EXPAND study

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



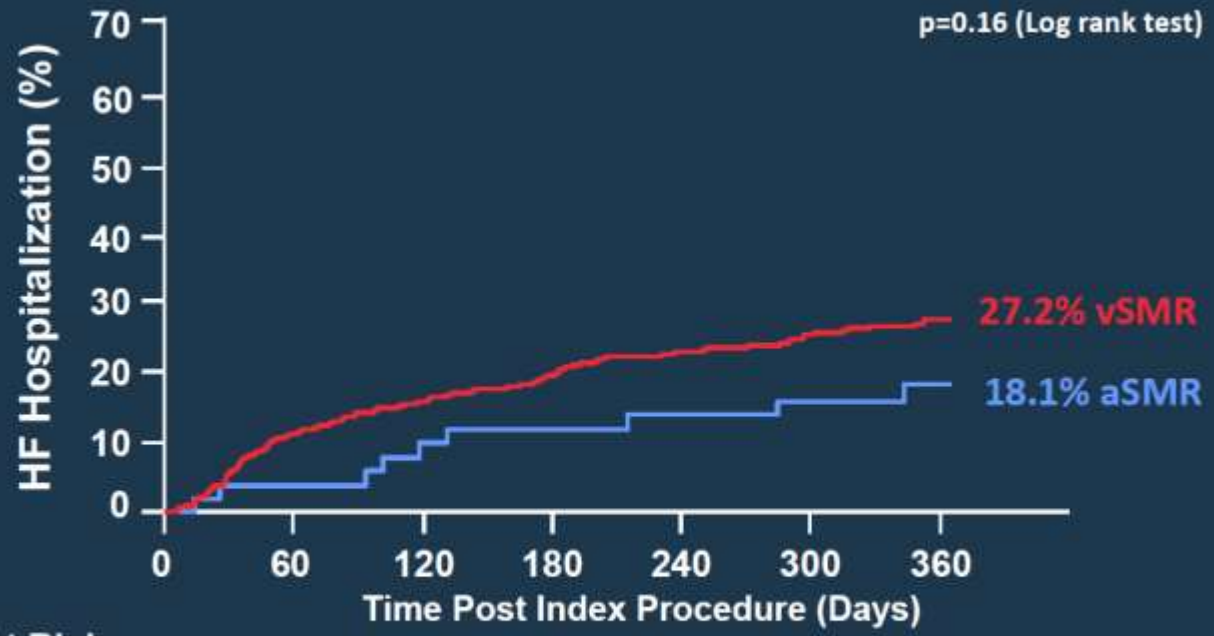


Sodhi et al. Presented at TCT 2021

TEER in Atrial FMR : Global EXPAND study

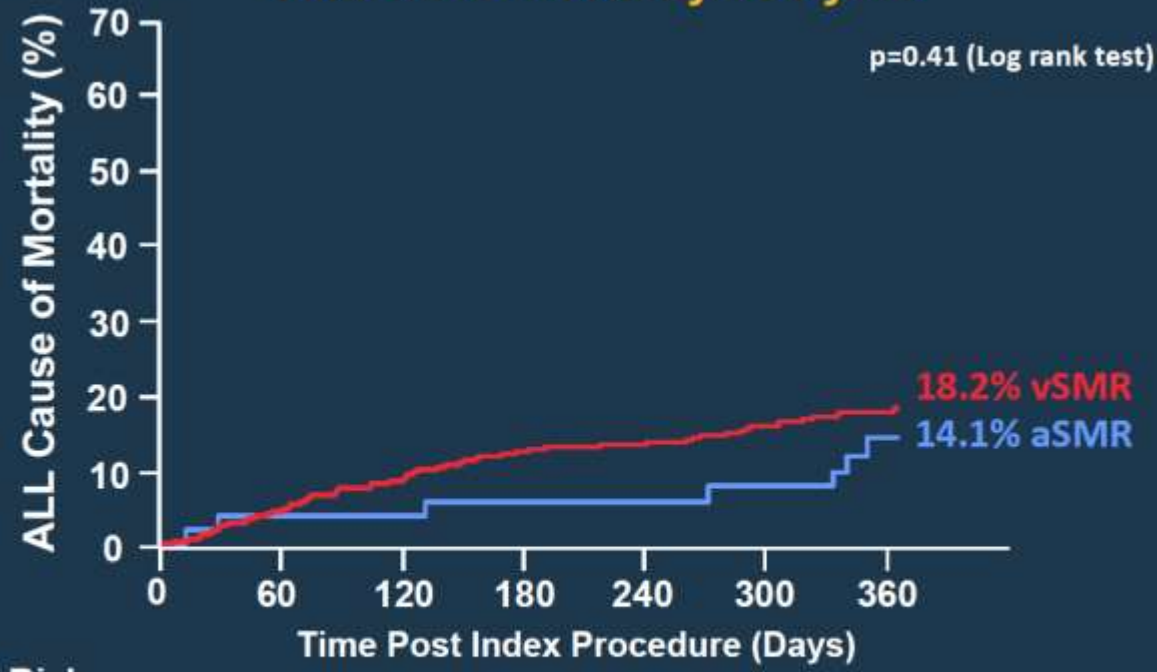
N=53, LV EF ≥45% without RWMA, AF with Dilated LA

HF Hospitalization at 1 year



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

All-Cause mortality at 1 year



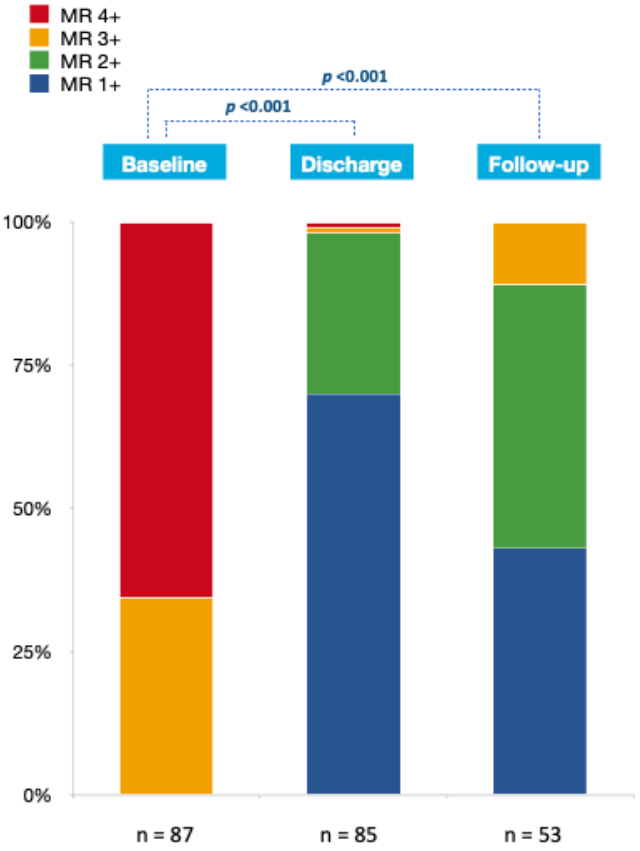
At Risk				
aSMR	53	50	49	29
vSMR	360	349	292	183

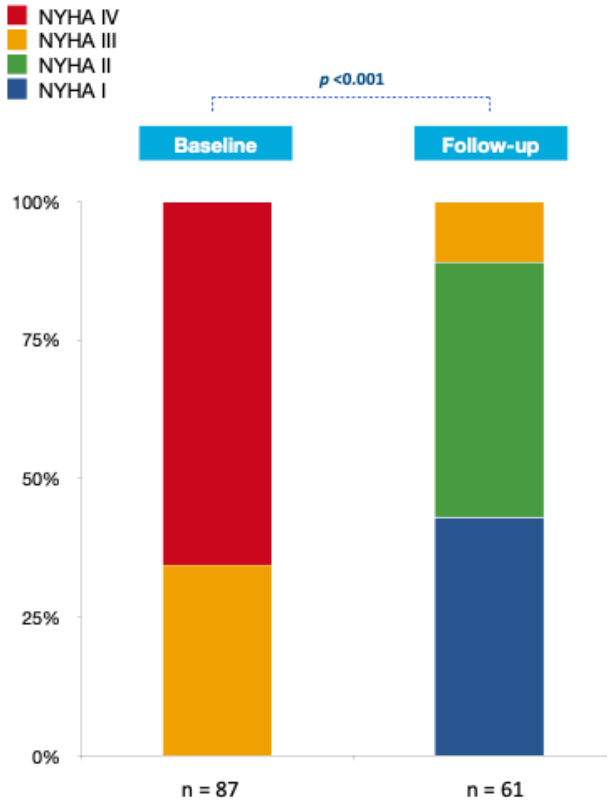
HFH, based on each patient's first occurrence of HF Hospitalization.

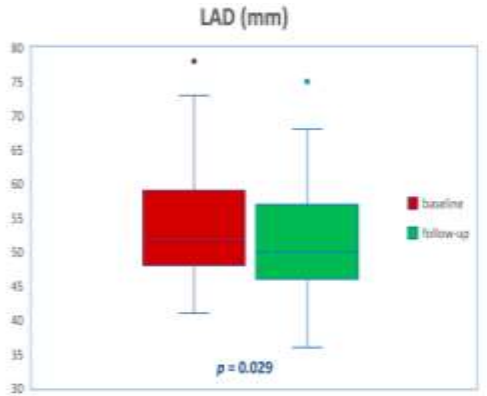
Sodhi et al. Presented at TCT 2021

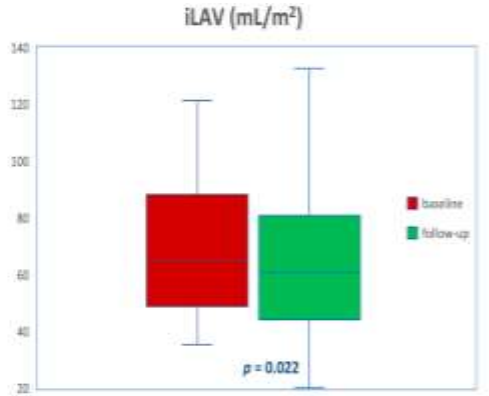
TEER in Atrial FMR : MITRA-TUNE

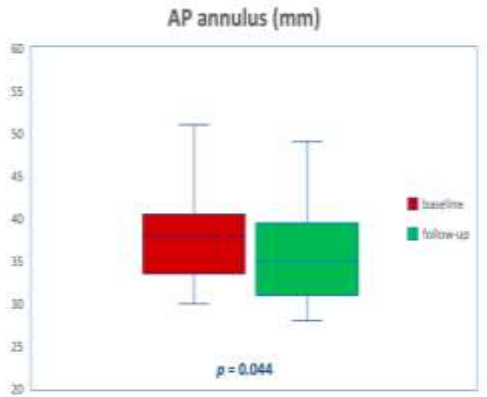
N=87 (7.6% of FMR), LV EF ≥50%, LVEDD <55mm, AF
81 YO, 61% female, STS 4%

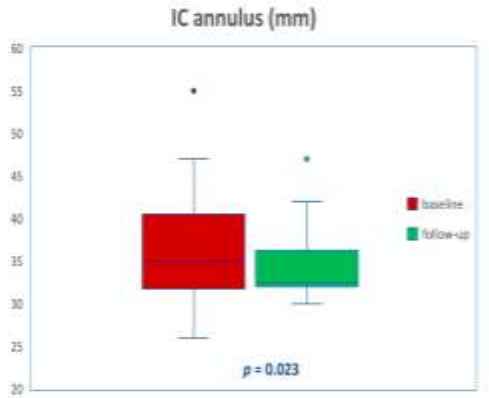








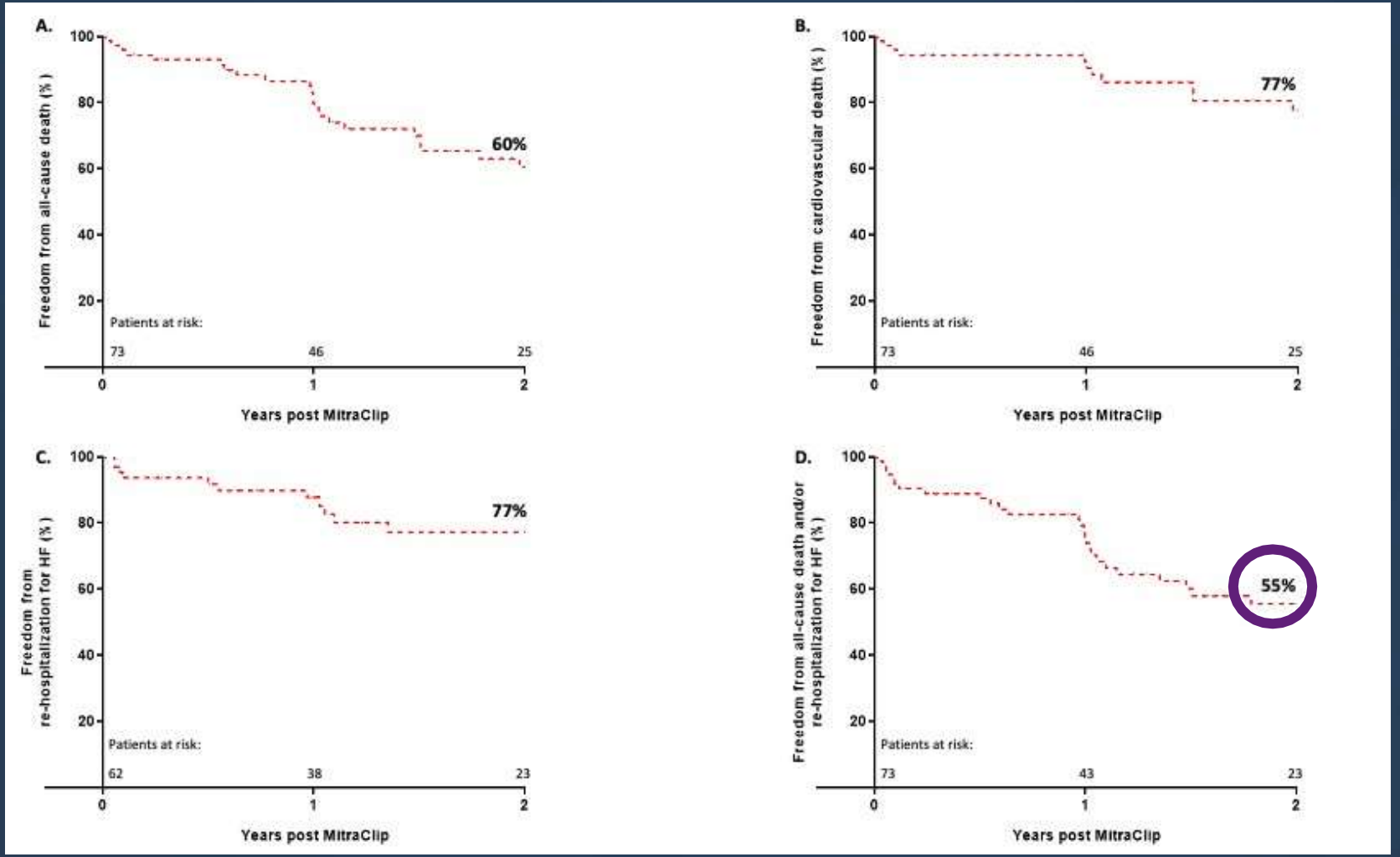




Rubbio AP et al. IJC 2022;349:39-45

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

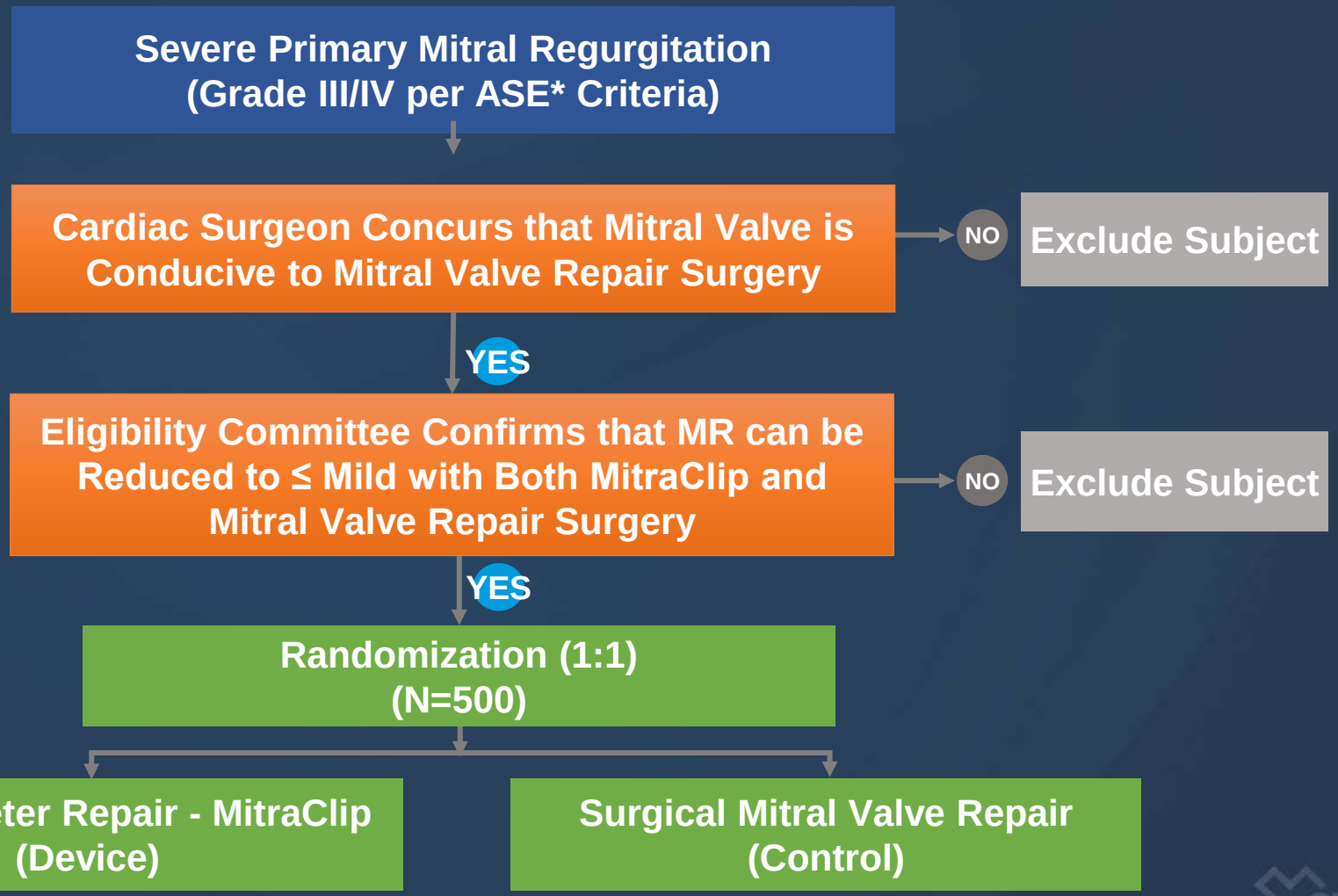
REPAIR MR

MitraClip vs. Surgery for Moderate Surgical Risk

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

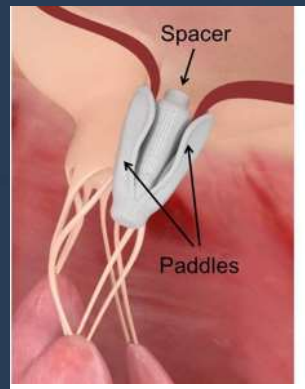
Patient Population

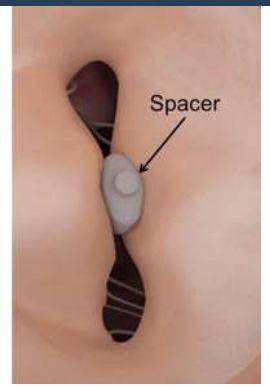
- Subject is symptomatic (NYHA Class II/III/IV) or asymptomatic (LVEF ≤ 60%, Pulmonary Artery Systolic Pressure > 50 mmHg, or LVESD > 40 mm)
- Subject is at least 75 years of age, OR if younger than 75 years, then has:
  - STS-PROM Score ≥ 2%, OR
  - Presence of other comorbidities which may introduce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



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

CLASP IID RCT (PASCAL)





Patients with Clinically Significant Mitral Regurgitation N=1275

Heart Team Assessment

- MR 3+ to 4+ as assessed by echo core lab
- Eligible for transcatheter mitral valve repair
- Patient suitable for both devices

DMR

CLASP IID (prohibitive risk)

- PASCAL Repair System
- MitraClip System

FMR

CLASP IIF

- PASCAL Repair System + GDMT
- MitraClip System + GDMT

Follow-up: 30 days, 6 months, 1 year and annually through 5 years

Primary Endpoints, Non-Inferiority
- MR severity reduction at 6 months
- Major adverse events (MAEs) at 30 days

Primary Endpoints, Non-Inferiority
- All-cause mortality and HF rehospitalization at 2 years
- Major adverse events (MAEs) at 30 days

Currently Enrolling | **Approved and Enrolling Soon**

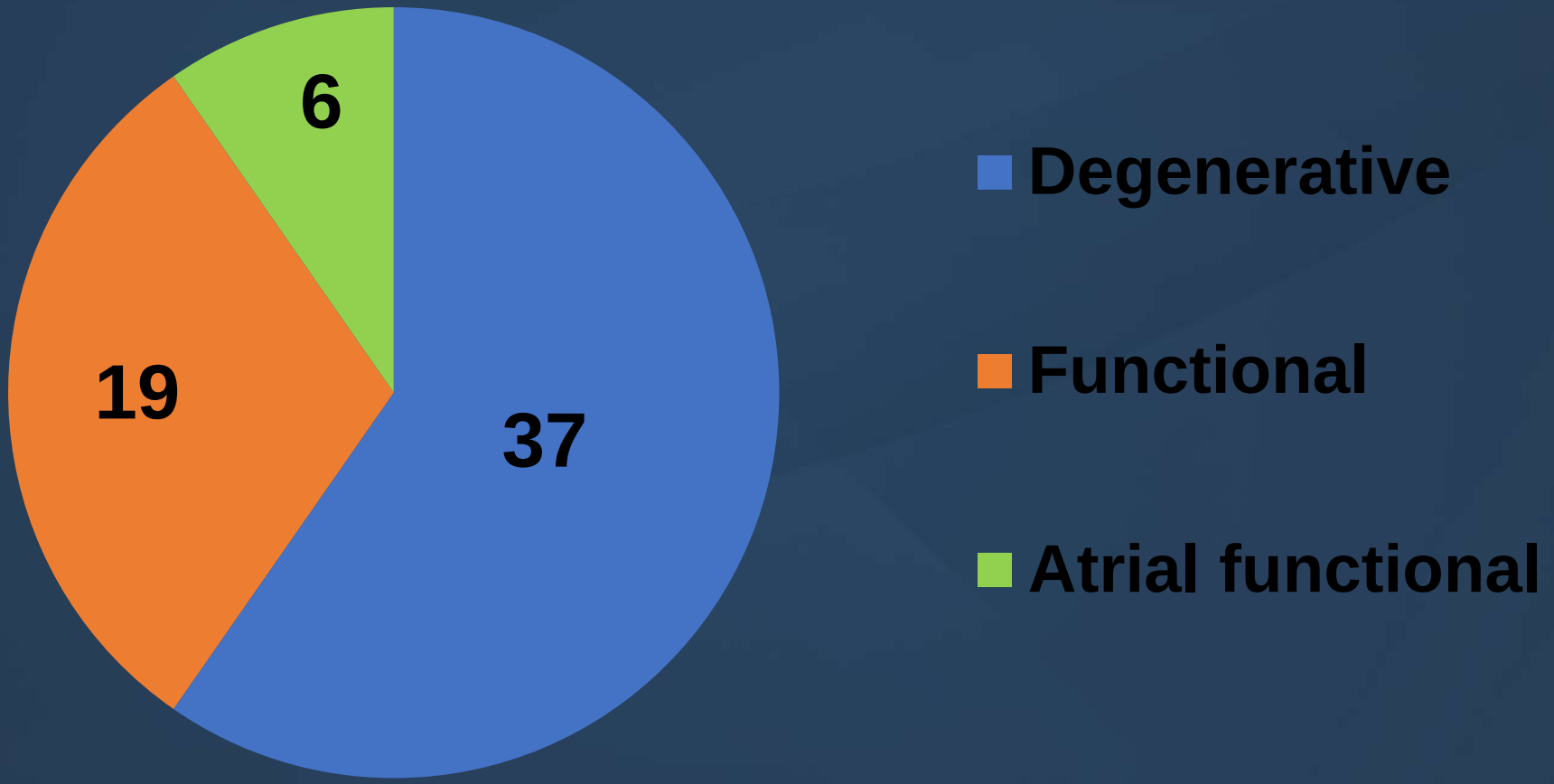
NCT03706833 PI : Scott Lim, MD, Robert Smith MD., Linda Gillam, MD

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.
- Another strong competitor (PASCAL) is coming.

Asan Medical Center Experience

MitraClip Indication in AMC (N=62)



10 among 15 patients with ischemic CMP had posterolateral wall akinesia

Mitraclips Used in AMC

	Primary MR N=37	Secondary MR N=25
Median number of clips	1.6	1.8
1 clip implanted	14 (38%)	6 (24%)
2 clips implanted	22 (59%)	16 (64%)
3 clips implanted	1 (3%)	1 (4%)
First clip used in G4 era		
Wide clips (NTW/XTW)	15	20
Narrow clips (NT/XT)	5	0

"G4" Clips Used in AMC

	Primary MR N=20	Secondary MR N=20
First Clip		
NTW	7 (35%)	3 (15%)
XTW	8 (40%)	17 (85%)
NT	1 (5%)	
XT	4 (20%)	
Second Clip	11	14
NTW	4 (36%)	7 (50%)
XTW	2 (18%)	2 (14%, Atrial)
NT	2 (18%)	4 (29%)
XT	3 (27%)	1 (7%)