



Transcatheter Mitral Valve Repair, Replacement, or Surgery: Data Update

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Define the MR Mechanism, At It Drives The Mode of Therapy!

MITRAL REGURGITATION

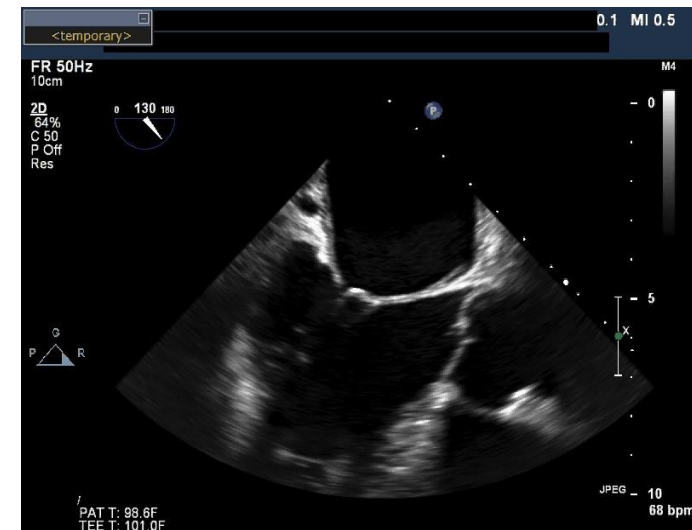
PRIMARY (DEGENERATIVE)



PRIMARY:

- Leaflets
- Subvalvular apparatus
- Chordae and papillary muscles

SECONDARY (FUNCTIONAL)

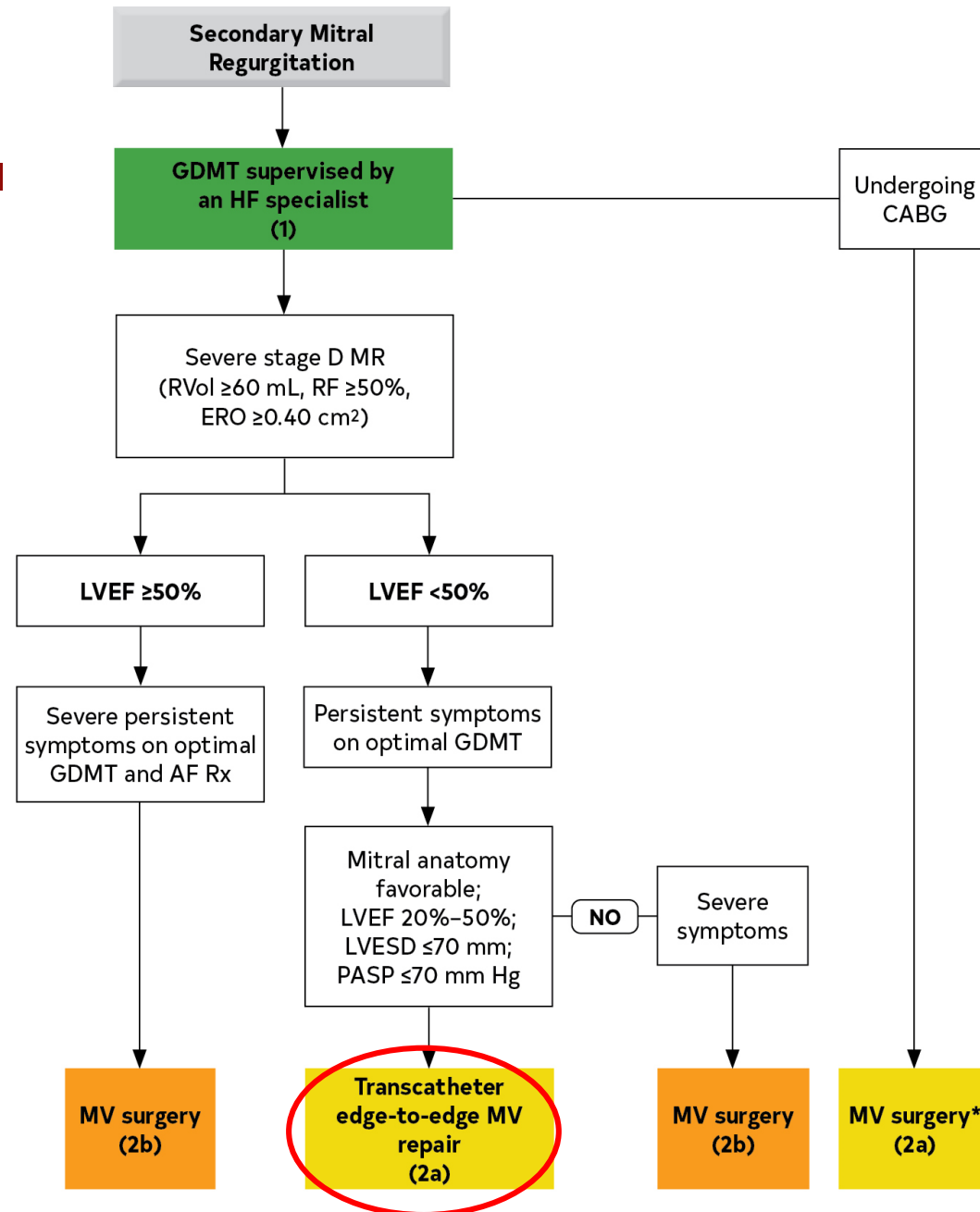


SECONDARY:

- Leaflet tethering
- Mitral annular dilation
- Incomplete coaptation of the mitral valve

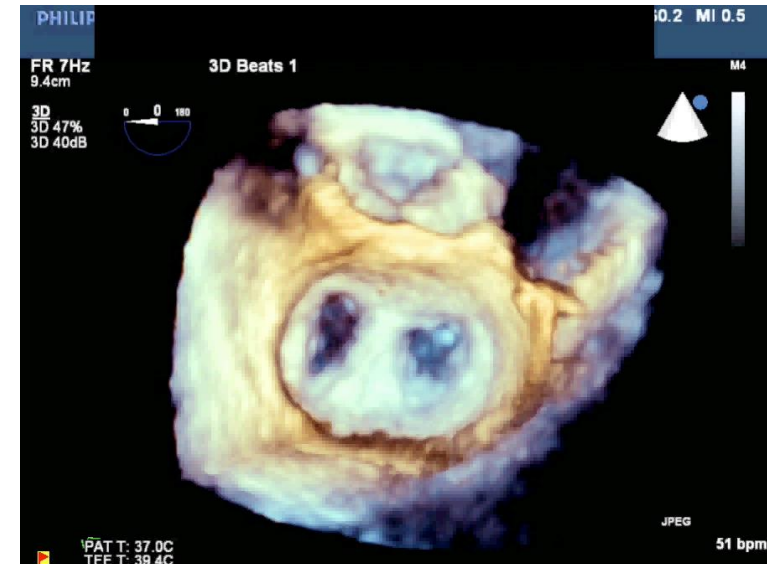
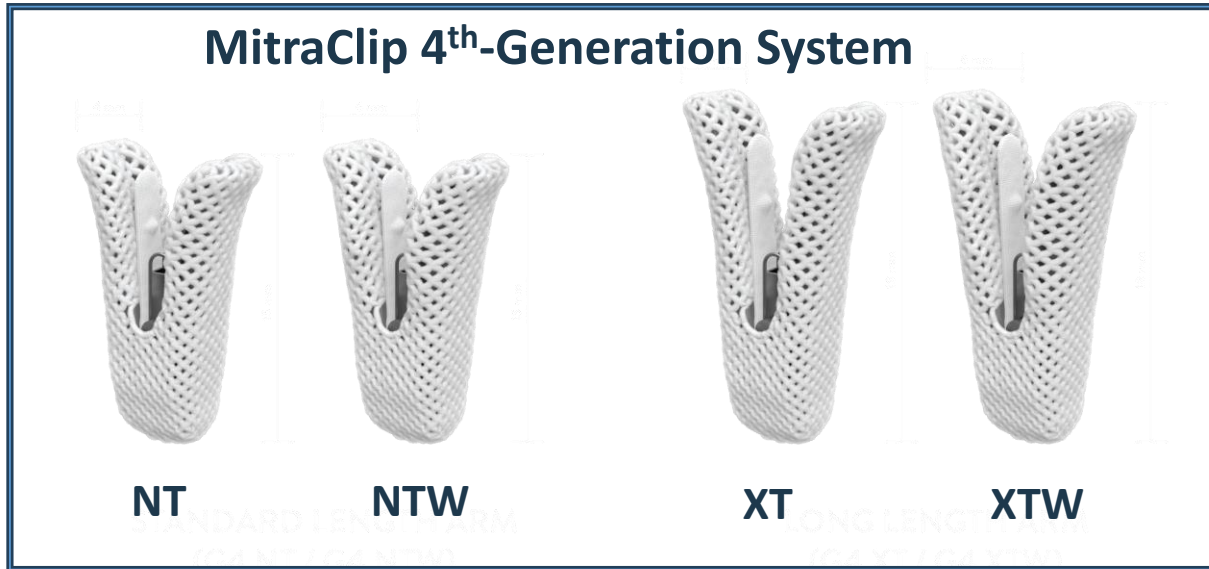
2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: Secondary (Functional) MR

Mitral TEER: Class IIA recommendation, irrespective of surgical risk

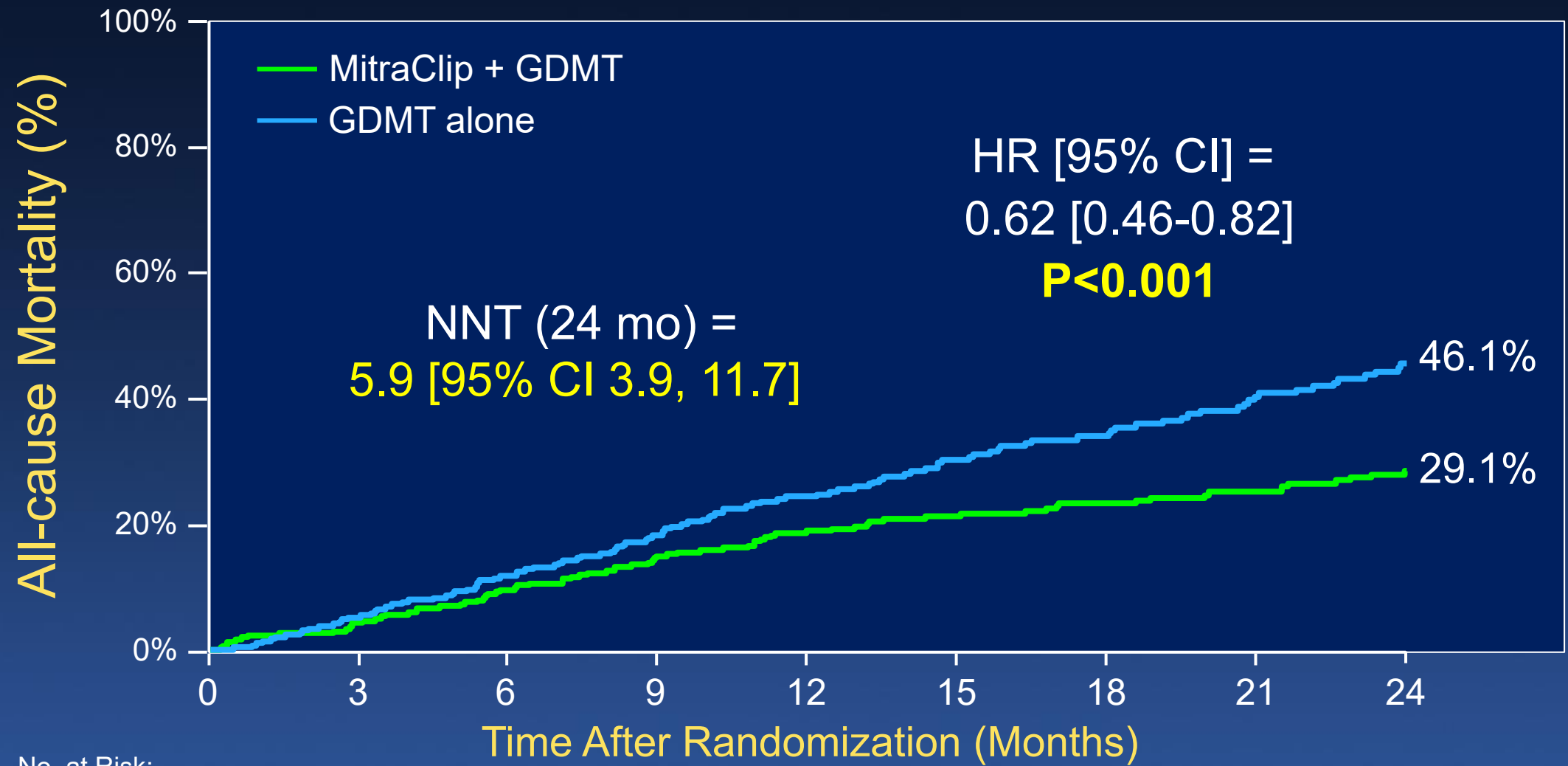




Mitral Transcatheter Edge-to-Edge Repair (TEER): Restoring Leaflet Coaptation



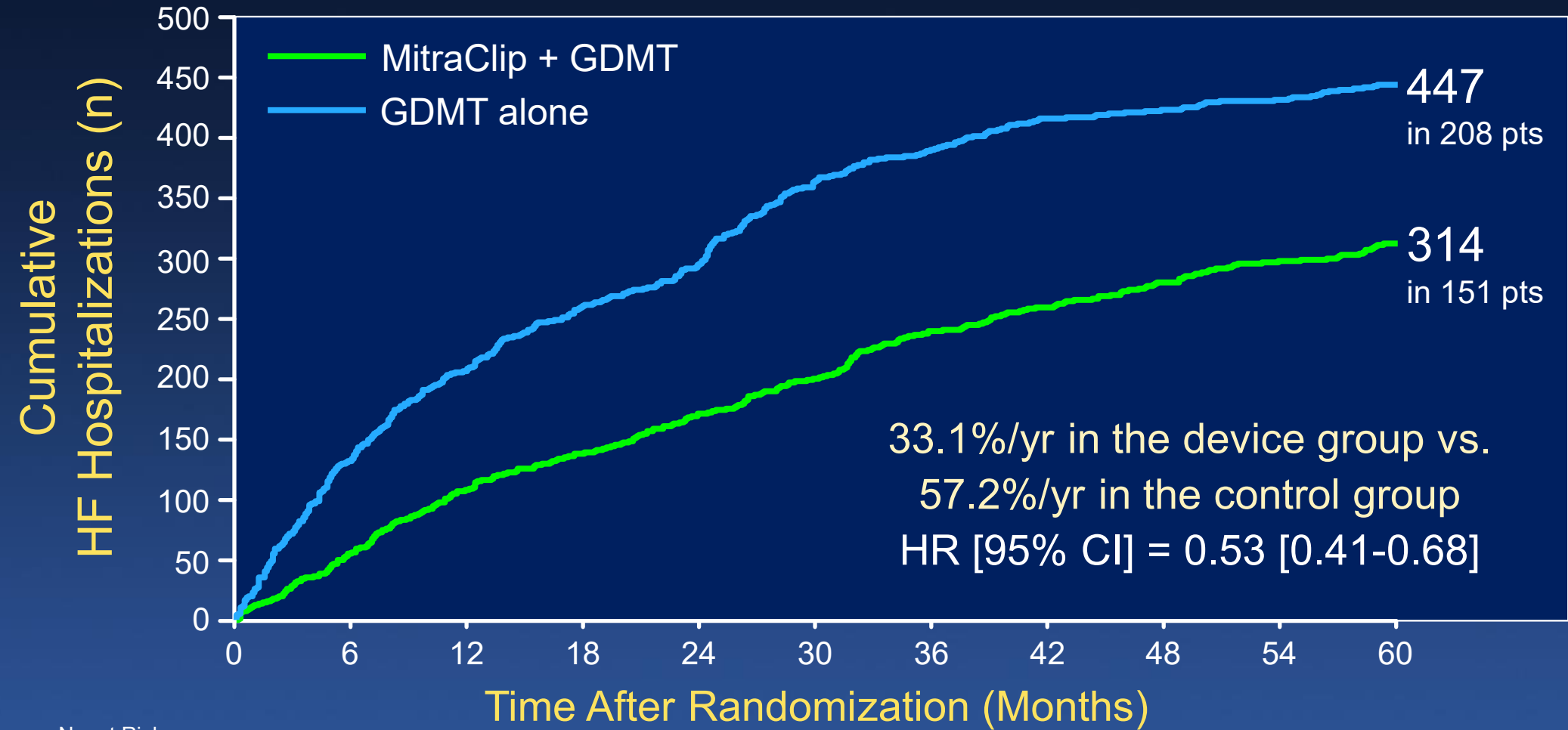
All-cause Mortality



No. at Risk:

MitraClip + GDMT	302	286	269	253	236	191	178	161	124
GDMT alone	312	294	271	245	219	176	145	121	88

Primary Effectiveness: All Heart Failure Hospitalizations Through 5-Year Follow-up



No. at Risk:

MitraClip	302	269	238	219	205	186	167	151	138	124	79
GDMT	312	272	224	188	156	133	120	106	94	84	59

Analyzed using a joint frailty model to account for correlated events and the competing risk of death

Primary Safety: Outcomes Through 5 Years

MitraClip implant attempts (n=293)	30 Days	12 Months	24 Months	36 Months	48 Months	60 Months
All safety events	4 (1.4)	9 (3.3)	13 (5.2)	20 (8.8)	22 (10.1)	23 (10.8)
Device-specific events	4 (1.4)	4 (1.4)	4 (1.4)	4 (1.4)	4 (1.4)	4 (1.4)
- SLDA	2 (0.7)	2 (0.7)	2 (0.7)	2 (0.7)	2 (0.7)	2 (0.7)
- Device embolization	1 (0.3)	1 (0.3)	1 (0.3)	1 (0.3)	1 (0.3)	1 (0.3)
- Endocarditis requiring surgery	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
- Mitral stenosis* requiring surgery	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
- Any device-related complication requiring non-elective CV surgery	1 (0.3)	1 (0.3)	1 (0.3)	1 (0.3)	1 (0.3)	1 (0.3)
Progressive HF unrelated to device complications	0 (0.0)	5 (2.0)	9 (3.8)	16 (7.5)	18 (8.8)	19 (9.5)
- LVAD	0 (0.0)	3 (1.2)	6 (2.6)	11 (5.1)	12 (5.8)	13 (6.5)
- Heart transplantation	0 (0.0)	2 (0.8)	3 (1.3)	7 (3.4)	9 (4.7)	9 (4.7)

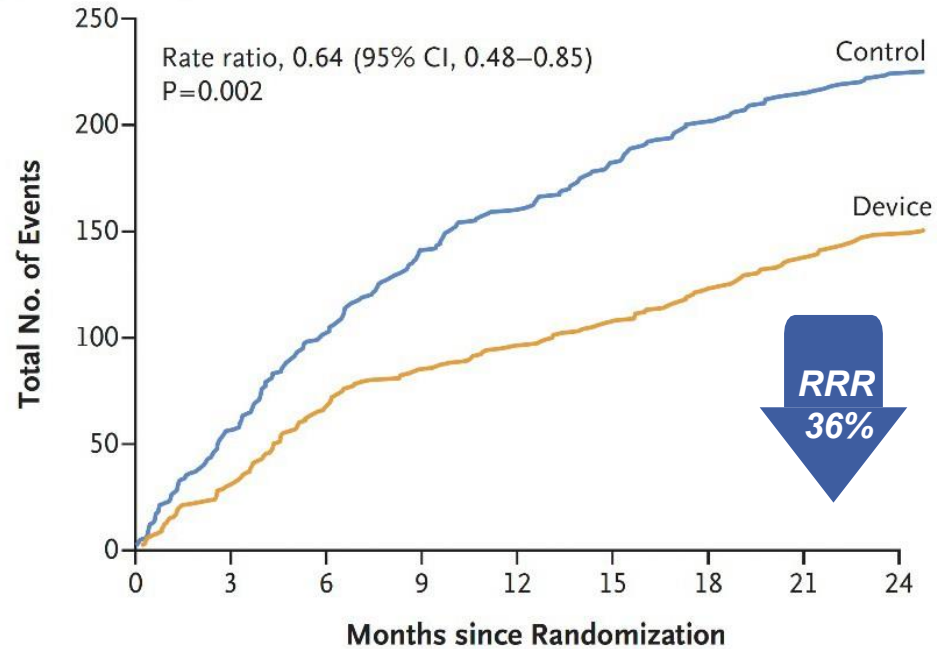
SLDA = single leaflet device attachment. LVAD = left ventricular assist device. *Mitral valve area <1.5 cm² by echo core laboratory measurement.



RESHAPE-HF 2: M-TEER + GDMT vs. GDMT Alone in Patients With Mod-Severe FMR

Mean age 70 yrs, mean LVEF 31±8%, mean EROA 0.23cm²

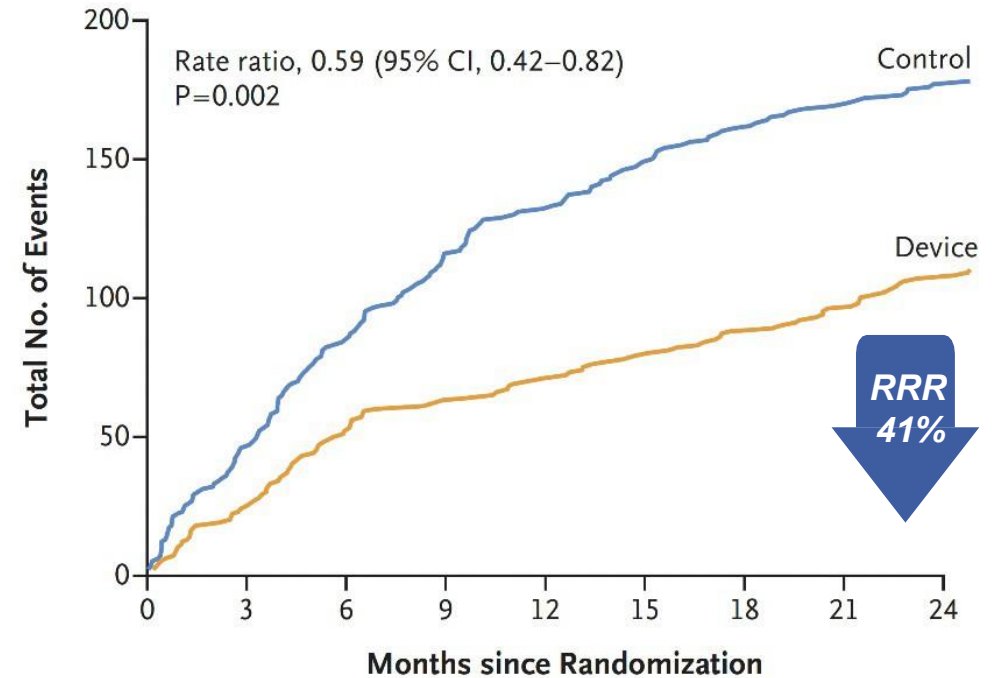
Composite of Hospitalization for Heart Failure or Death from Cardiovascular Causes



No. at Risk

Control	255	240	223	204	189	179	165	155	146
Device	250	241	222	207	197	191	179	170	163

Hospitalization for Heart Failure



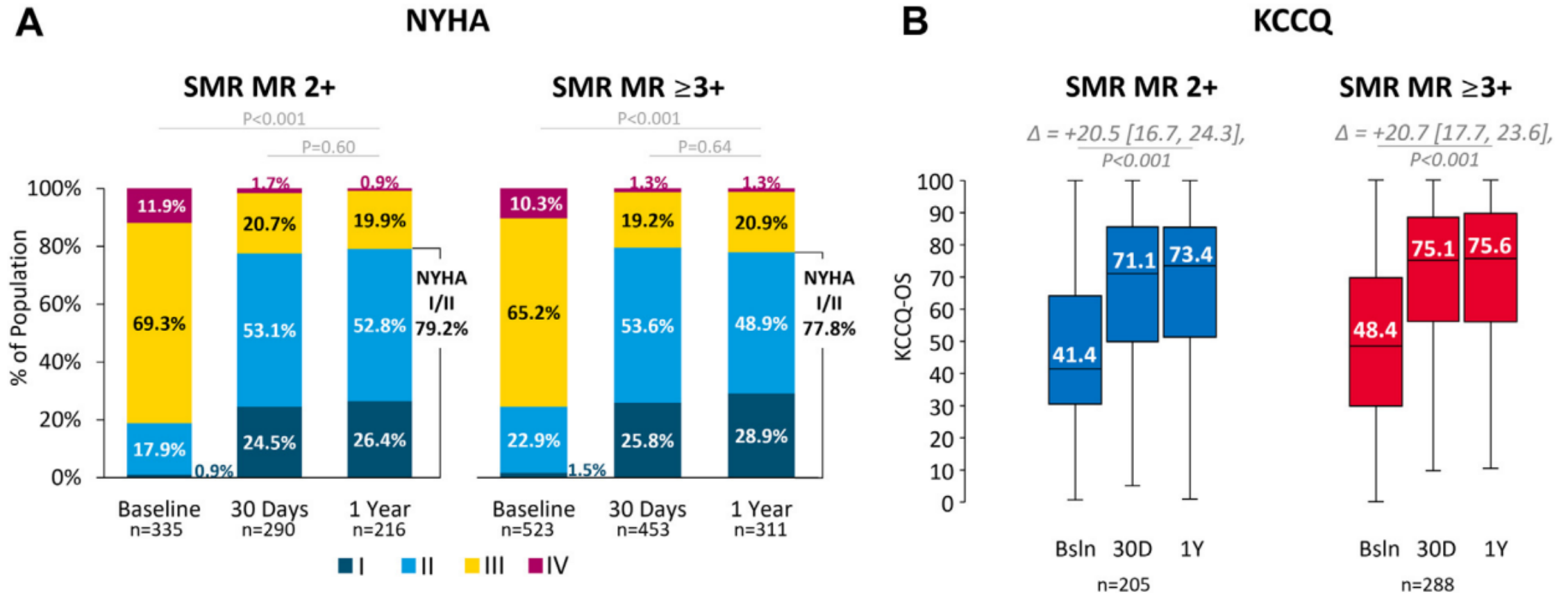
No. at Risk

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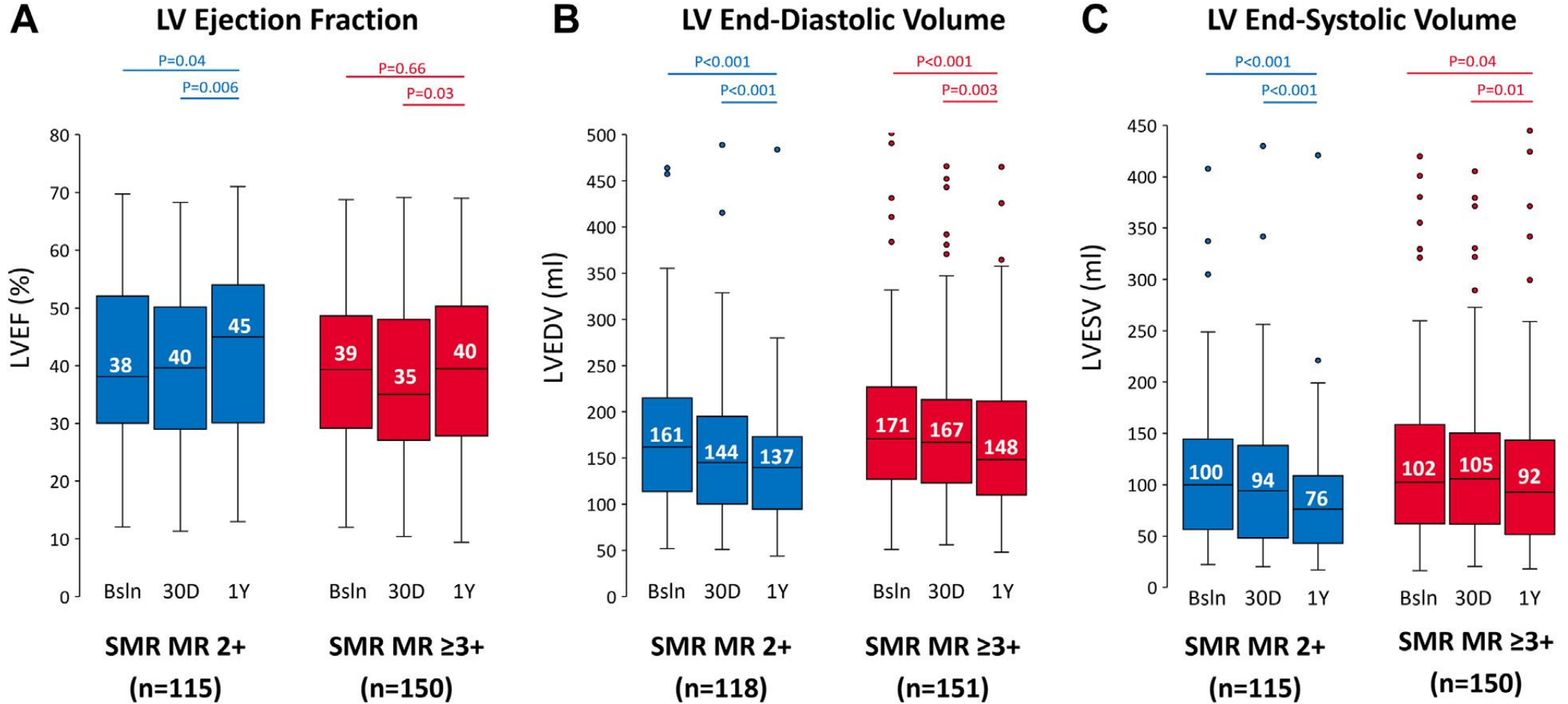
EXPANDED Registry: Cohort of Patients with 2+ FMR (According to Core Echo Lab)

1 year post-MitraClip: MR $\leq 1+$ in 97% of patients





EXPANDED Registry: Cohort of Patients with 2+ FMR (According to Core Echo Lab)

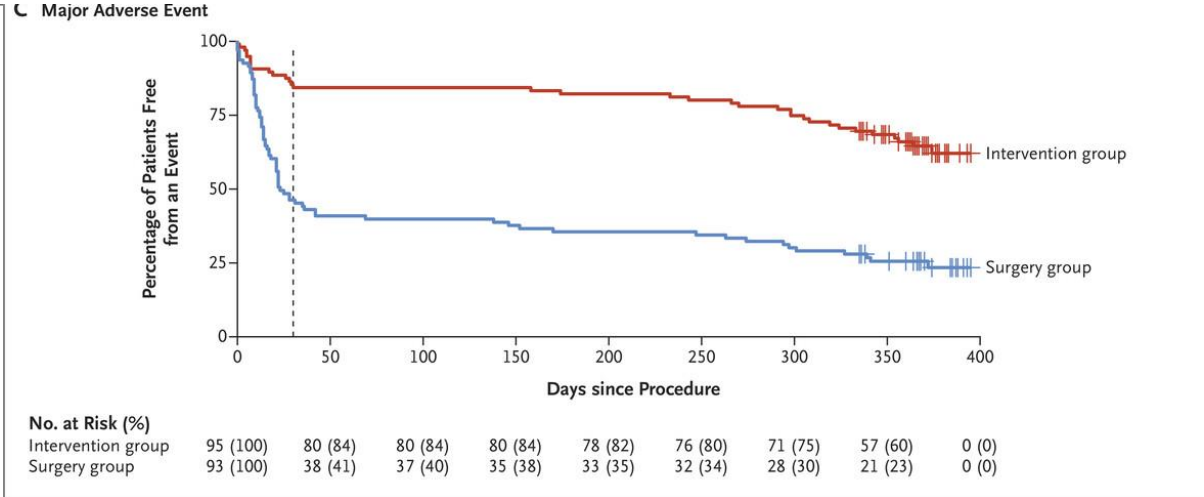
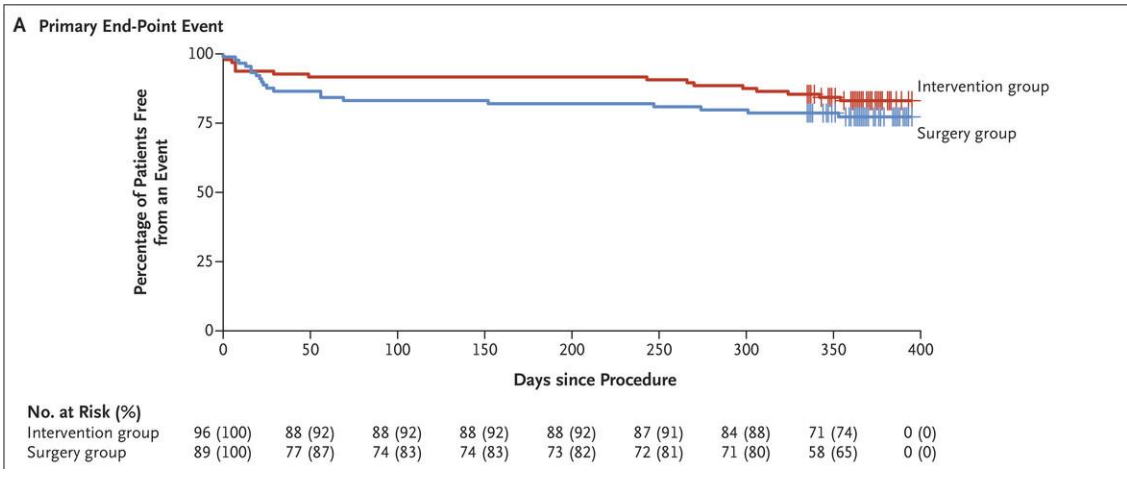




MATTERHORN: Cardiac Surgery vs. M-TEER for Functional MR

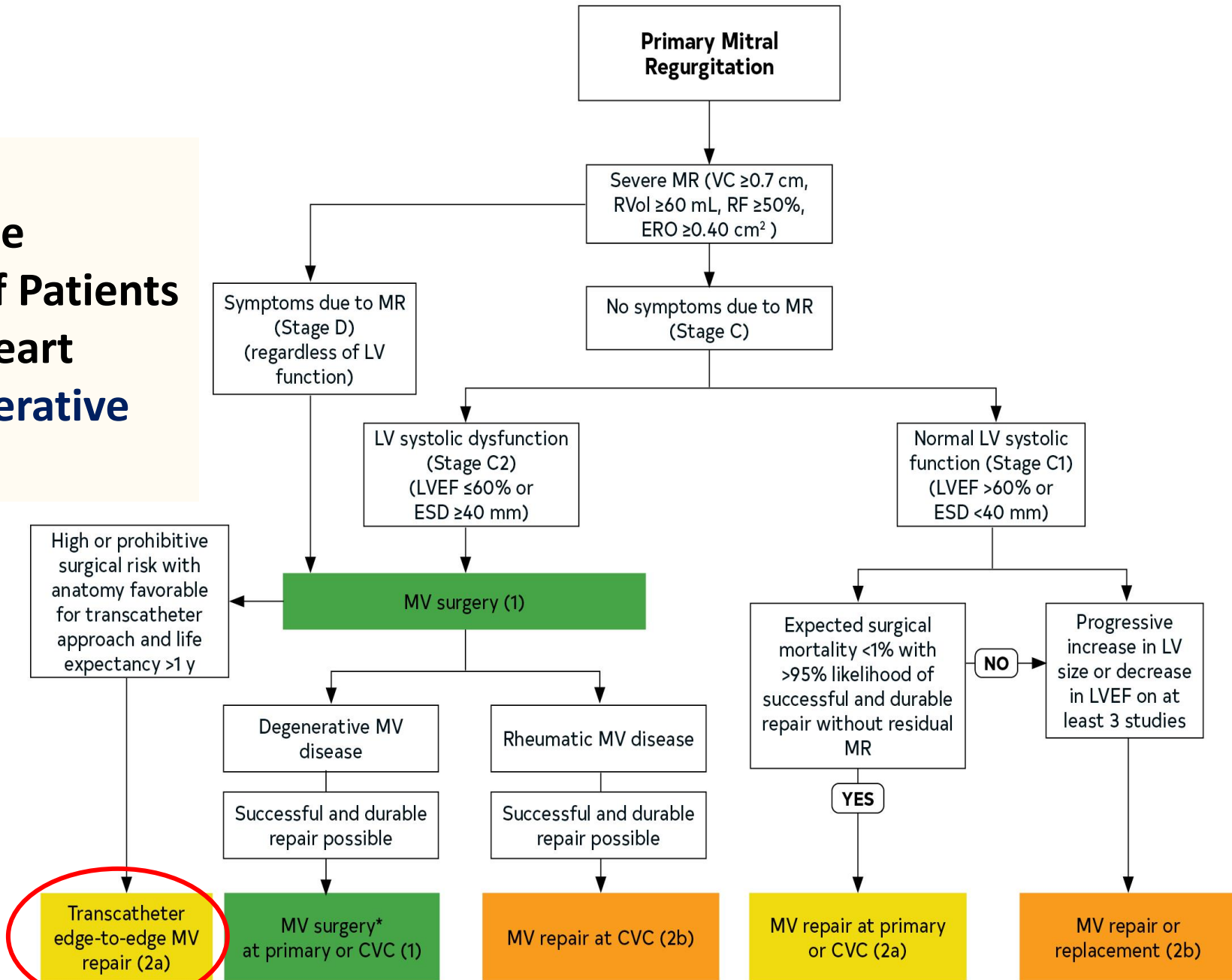
N=208: surgery vs. M-TEER

- **M-TEER non-inferior for efficacy***
- **Safety profile of M-TEER significantly better**

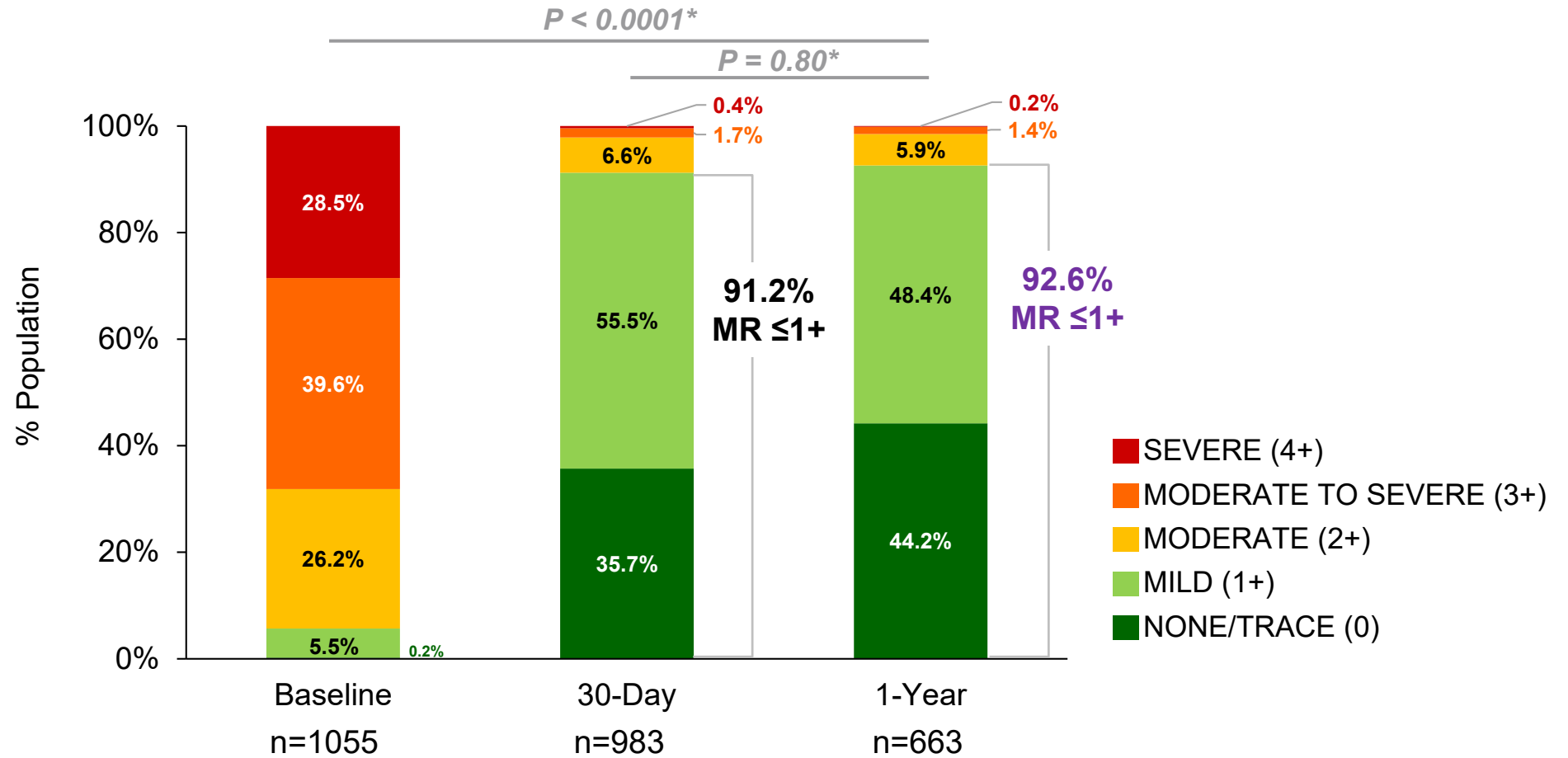


*death from any cause, HF hospitalization, MV reintervention, implantation of an assist device, or stroke)

2020 ACC/AHA Guideline for the Management of Patients with Valvular Heart Disease: Degenerative (Primary) MR



EXPAND G4: Significant and Durable MR Reduction with MitraClip G4



92.6% of subjects achieved MR ≤ 1+ and 98.5% had MR ≤ 2+ at 1 year

MR severity was echo core lab (ECL) assessed

*from paired analysis

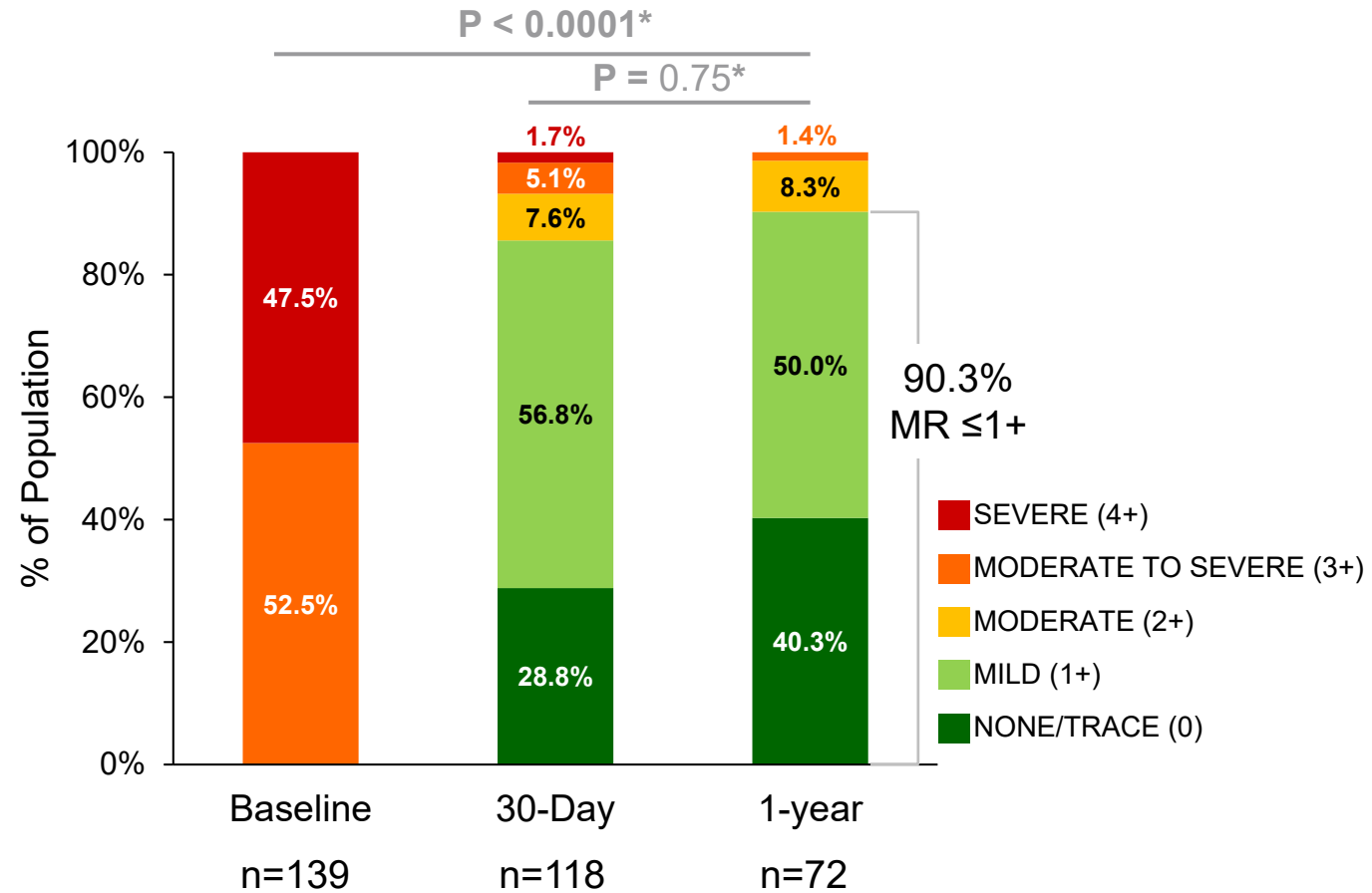
Significant and Durable MR reduction in Complex Anatomies

Complex Anatomy

(N=139, 78.7% PMR)

Defined as MR $\geq 3+$ and at least one of the following

- Primary jet outside A2-P2
- Presence of more than one significant jet
- Presence of wide jet
- Small valve area $< 4\text{cm}^2$
- Mitral annular or leaflet calcification
- Minimal leaflet tissue for attachment (coaptation length $< 2\text{mm}$)
- Presence of severely degenerative leaflets or wide flail gaps ($> 10\text{mm}$) or widths ($> 15\text{mm}$)
- Presence of a Significant Cleft or Scallop
- Bileaflet Flail or Bileaflet Prolapse



90.3% of complex subjects achieved MR $\leq 1+$ at 1 year

REPAIR-MR: Mitral-TEER vs Surgical Repair in Intermediate-Risk Degenerative MR Patients

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

Cardiac Surgeon of the Site Heart Team
Concurs that the Subjects Mitral Valve is
Conducive to Mitral Valve Repair Surgery

NO

Exclude Subject

YES

Subject Meets all Inclusion/Exclusion Criteria
and the 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)

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 ≥ 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

* Zoghbi et al. J Am Soc Echocardiogr. 2017 Apr;30(4):303-371.

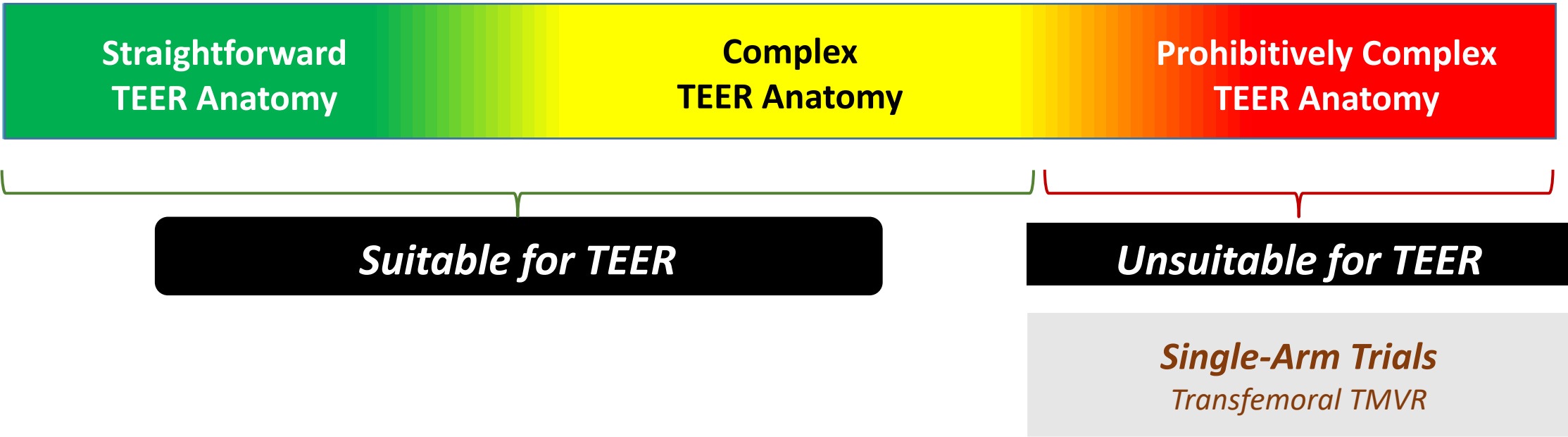
† Subjects in whom planned surgical procedure is replacement will be excluded

‡ As of Jan 11th, 2022



Where Does TMVR Fit Into The Current Treatment Paradigm?

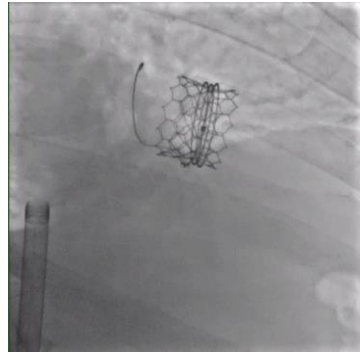
Anatomic Suitability for TEER Intervention in the High Surgical Risk Patient



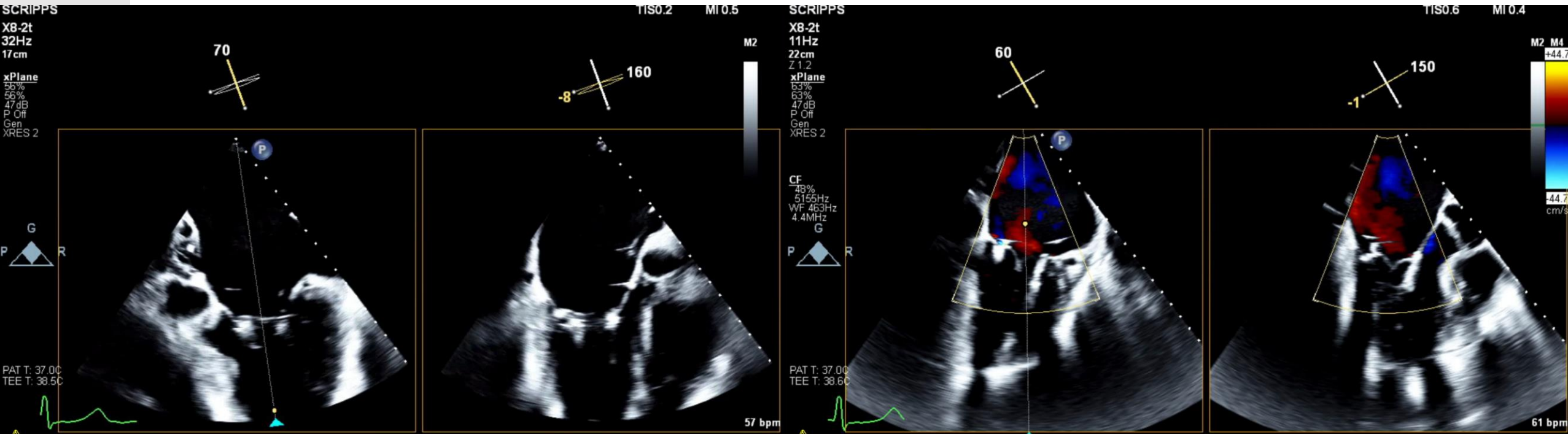


86 yo M with Severe MR, Anatomy Unsuitable for M-TEER (Leaflet Perforation): Treated with Sapien M3 in the ENCIRCLE TRIAL

Implantation of Dock

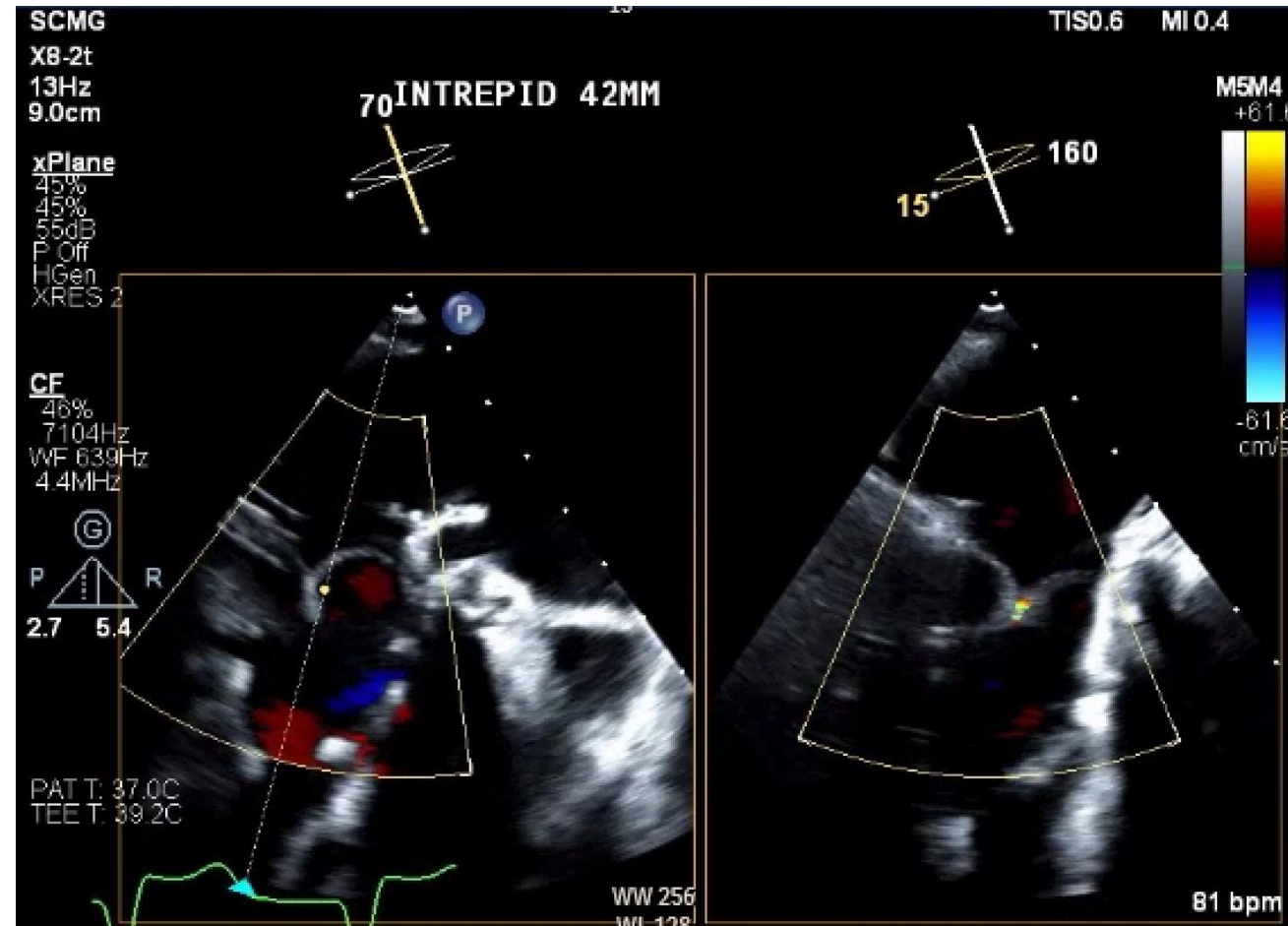
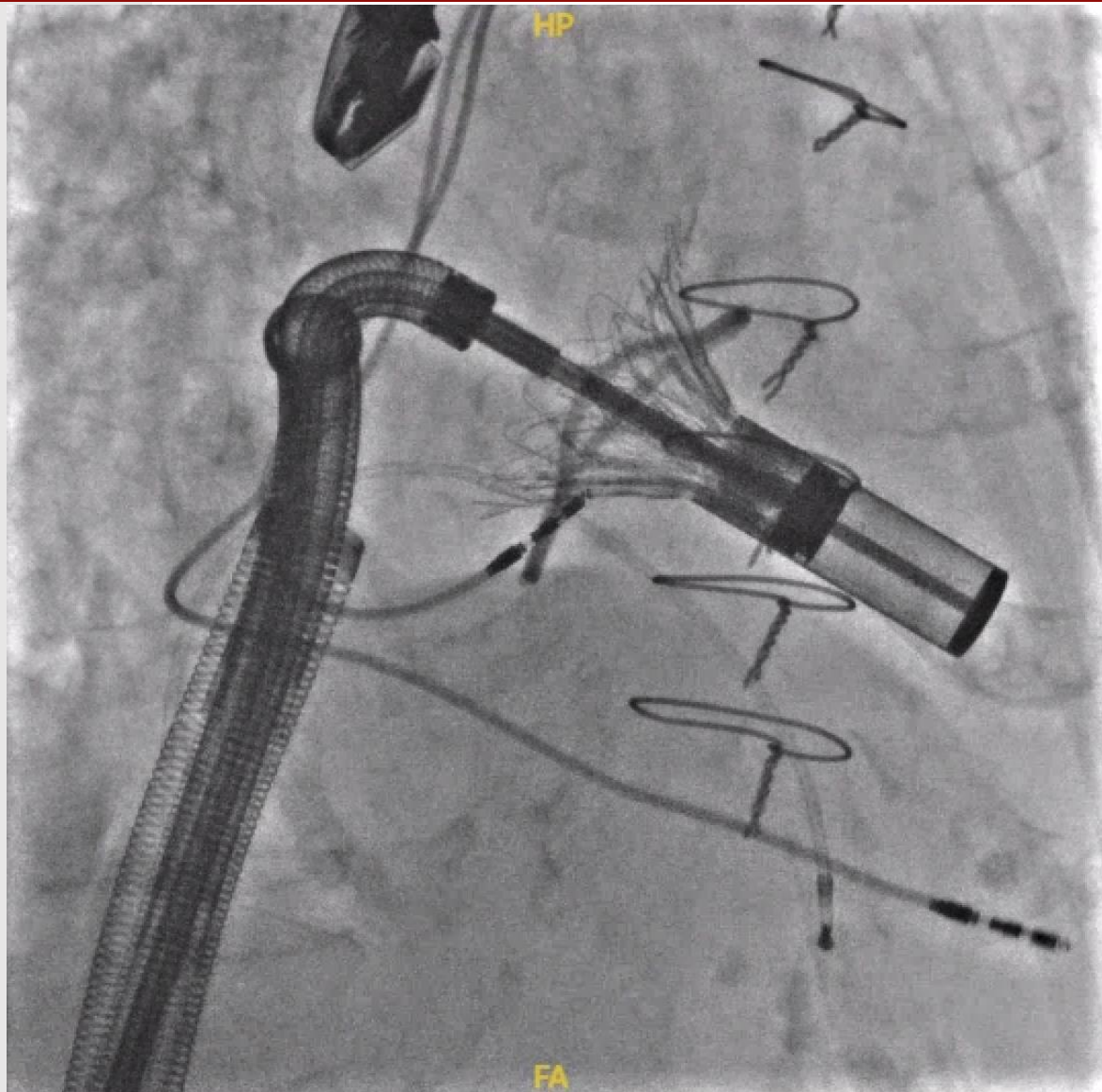
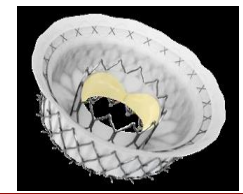


Implantation and deployment of Sapien M3





Medtronic Intrepid Trans-Septal TMVR

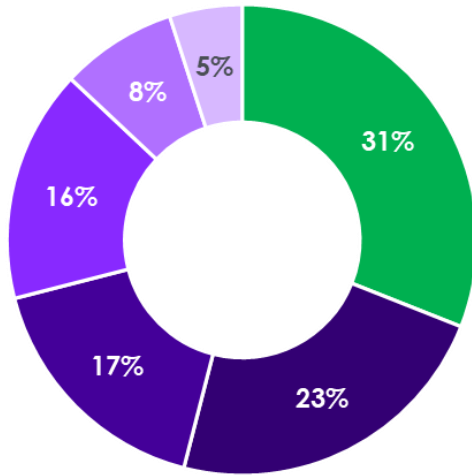


Discharged home POD#1



Anatomical Limitations with First Generation TMVR Devices

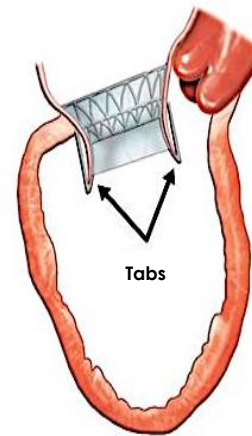
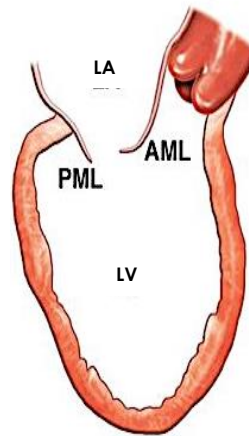
TMVR ANATOMICAL ACCEPTANCE RATES (31%)



- Current Treatable Patients
- Annulus Size
- MAC
- High Risk LVOTO
- LV Size
- Other

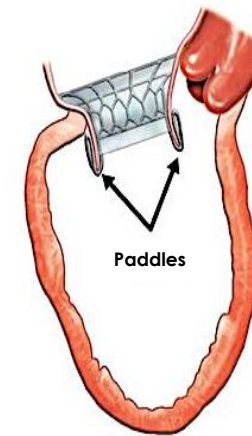
LVOT Obstruction Risks (inc. LV size)

~40%



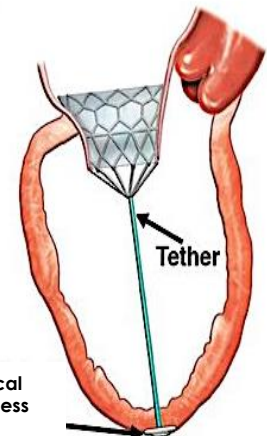
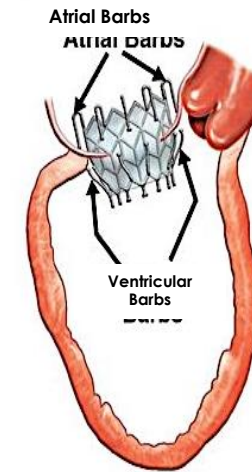
Large Mitral Valve Annulus

~17%



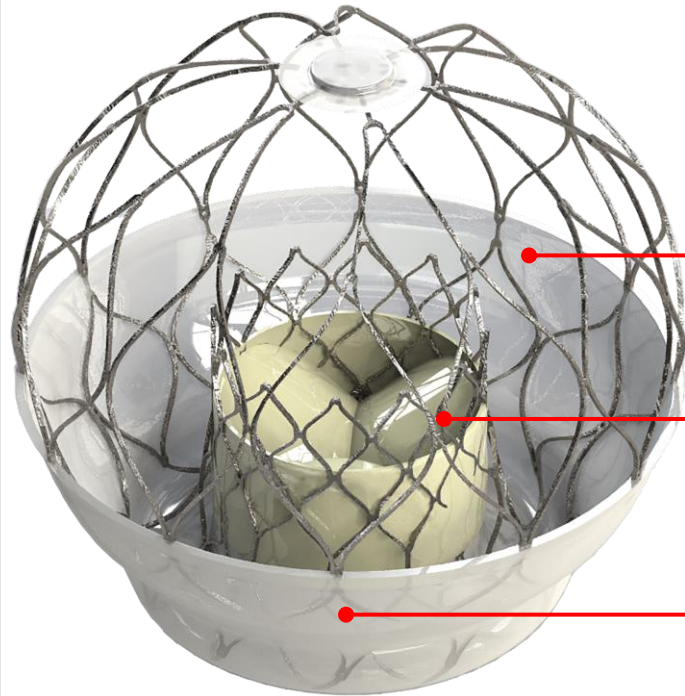
Mitral Annular Calcification

~5%





AltaValve: TMVR with Novel *Atrial* Fixation



STENT FRAME (NITINOL)

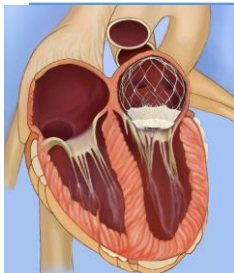
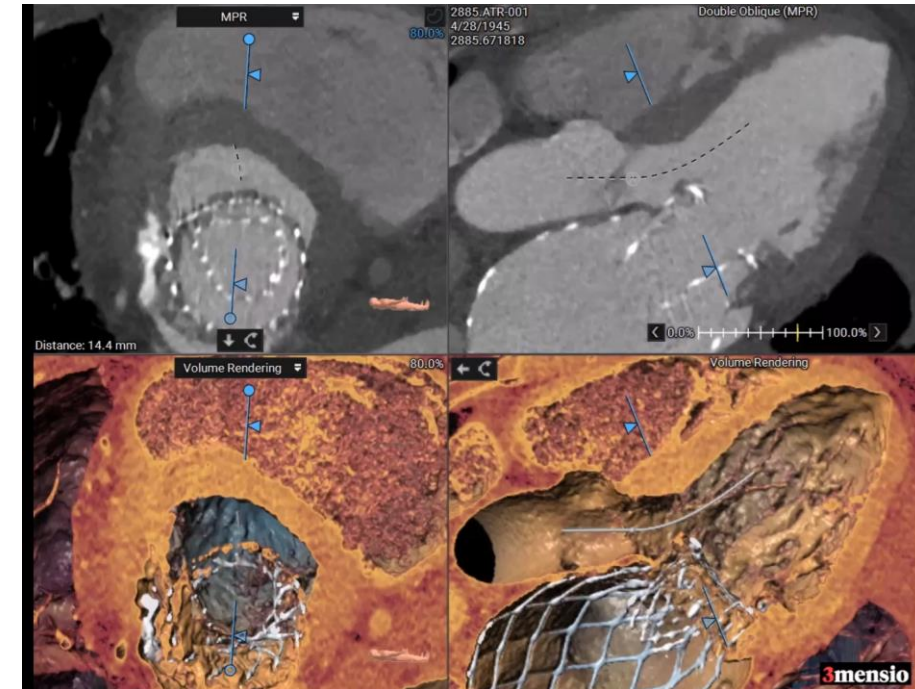
Flexible to conform to LA anatomy

TISSUE VALVE

Bovine pericardium with only **one valve size** for all implants

FABRIC (PET)

Enhances tissue ingrowth, endothelialization and minimizes perivalvular leak

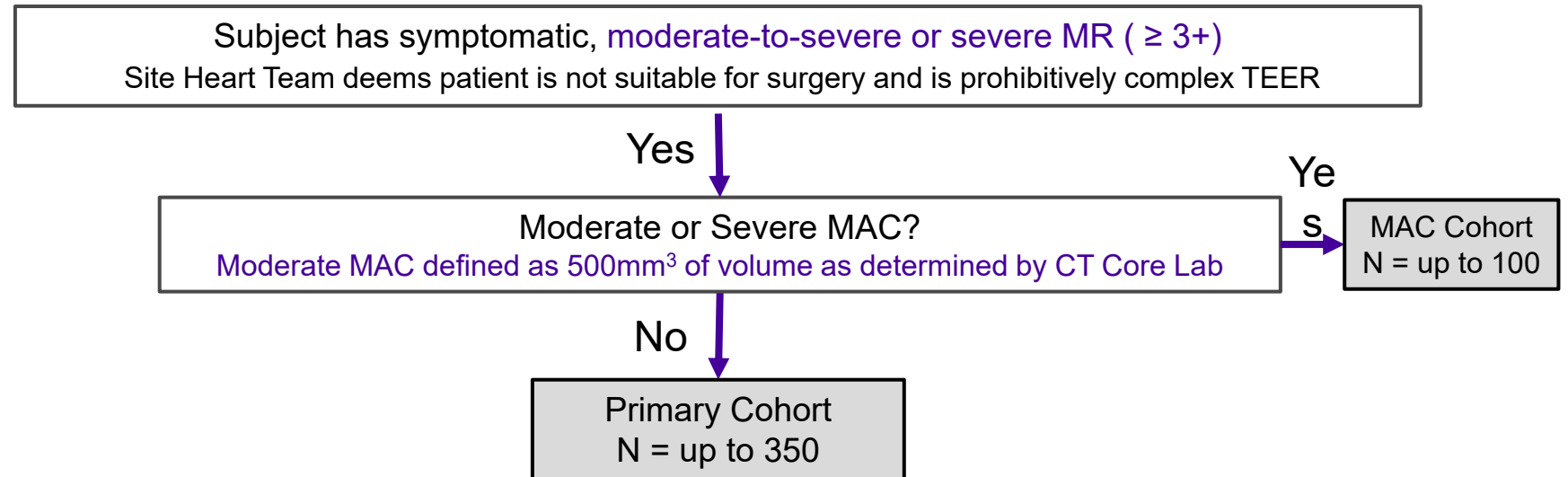
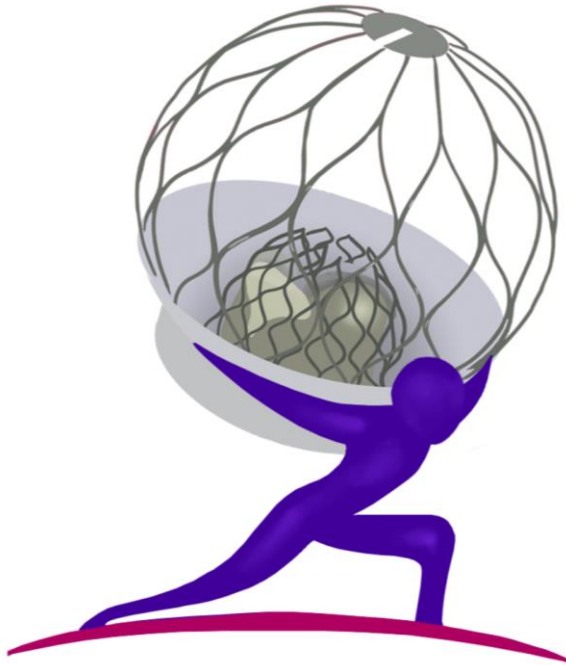


• Atrial Fixation Benefits:

- Minimizes risk of LVOT obstruction
- Preserves native valve: Treat both small & large mitral annulus
- Applicable in both MAC and non-MAC anatomies

A Transseptal Left Atrial System for Treatment of Mitral Regurgitation - ATLAS Trial

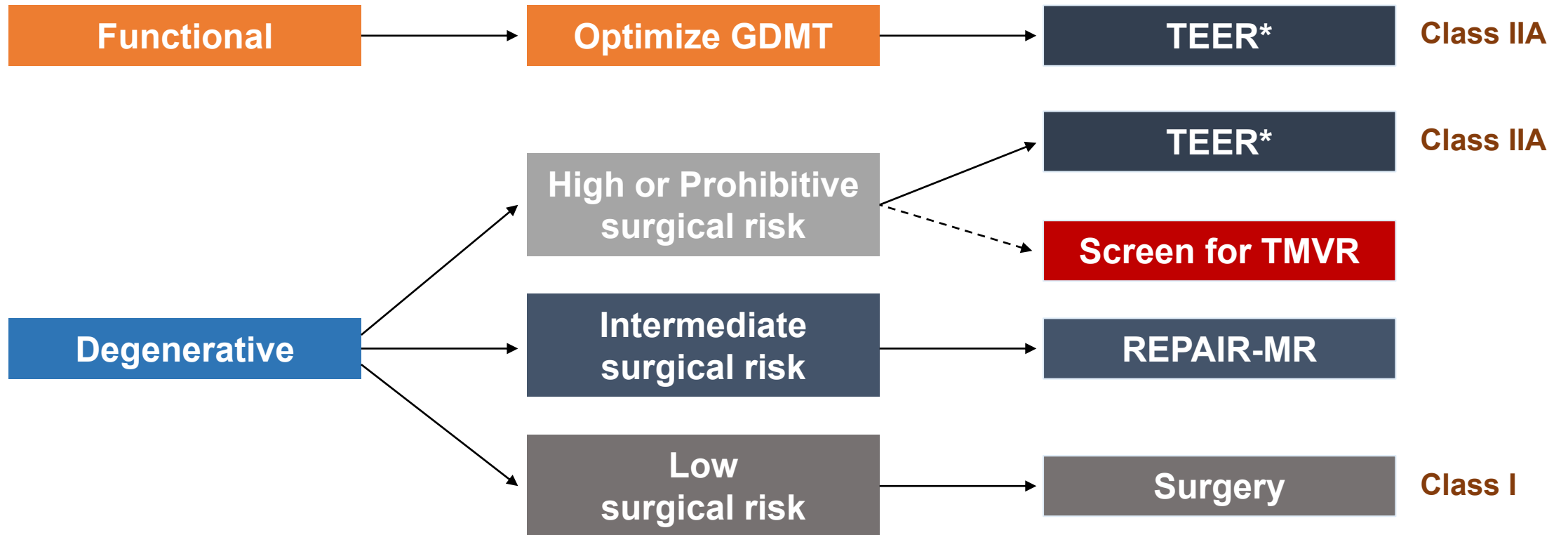
Prospective, multicenter, clinical trial designed to evaluate the safety and performance of the AltaValve System for the treatment of MR in targeted patient population.



Trial commenced enrollment in Europe and United States.



Mitral TEER or Surgery Decision Algorithm Based on MR Mechanism, Anatomy, and Surgical Risk



*If anatomically suitable for TEER. If unsuitable, screen for TMVR clinical trial



Summary

- **Mitral TEER is now the standard-of-care in patients with symptomatic functional MR** despite optimal GDMT
 - 2 RCTs demonstrate improvement in clinical endpoints and QOL in patients with moderate-to-severe and severe FMR
- **MR reduction with M-TEER to $\leq 1+$ in $\geq 90\%$ of patients** with straightforward anatomy
- **REPAIR-MR trial:** mitral TEER vs. surgery in intermediate risk patients with degenerative MR (any patient >75 yrs of age who is not high risk!)
- **TMVR studies** for patients not anatomically suitable for M-TEER
 - Novel designs may reduce anatomical exclusions and increase patient eligibility