

Transcatheter Therapy for Mitral Regurgitation from MAC- Where are we in 2026

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Disclosure of Relevant Financial Relationships

Within the prior 24 months, I have had a financial relationship with a company producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients:

<u>Nature of Financial Relationship</u>	<u>Ineligible Company</u>
Grant/Research Support	None
Consultant Fees/Honoraria	Medtronic, Edwards, Shockwave
Individual Stock(s)/Stock Options	None
Royalties/Patent Beneficiary	None
Executive Role/Ownership Interest	None
Other Financial Benefit	None

All Relevant Financial Relationships have been mitigated.

MAC with mitral dysfunction: common, lethal, hard to fix

~10%

of adults over 60 have mitral annular calcification

6–14%

periprocedural mortality reported for mitral surgery in MAC — well above non-MAC cohorts

None

medical therapies that slow or reverse MAC

Why every option is hard

- 1 Surgery**
Debridement risks AV-groove disruption and LV rupture; hybrid strategies are increasingly used
- 2 TEER**
Calcified leaflets limit grasping and leave gradients; 1-yr mortality trended higher than non-MAC (19.7% vs 11.3%)
- 3 Patient**
Elderly, frail, AF, CKD; nearly half of a recent MAC cohort had prior TAVR/SAVR

Case 1

- 82 yo F presented with worsening HF
 - Remote SAVR and CABG
 - V-i-V TAVR with a 23 mm Evolut 2022
 - COPD – remote diagnostic lung partial resection
 - Pulmonary hypertension

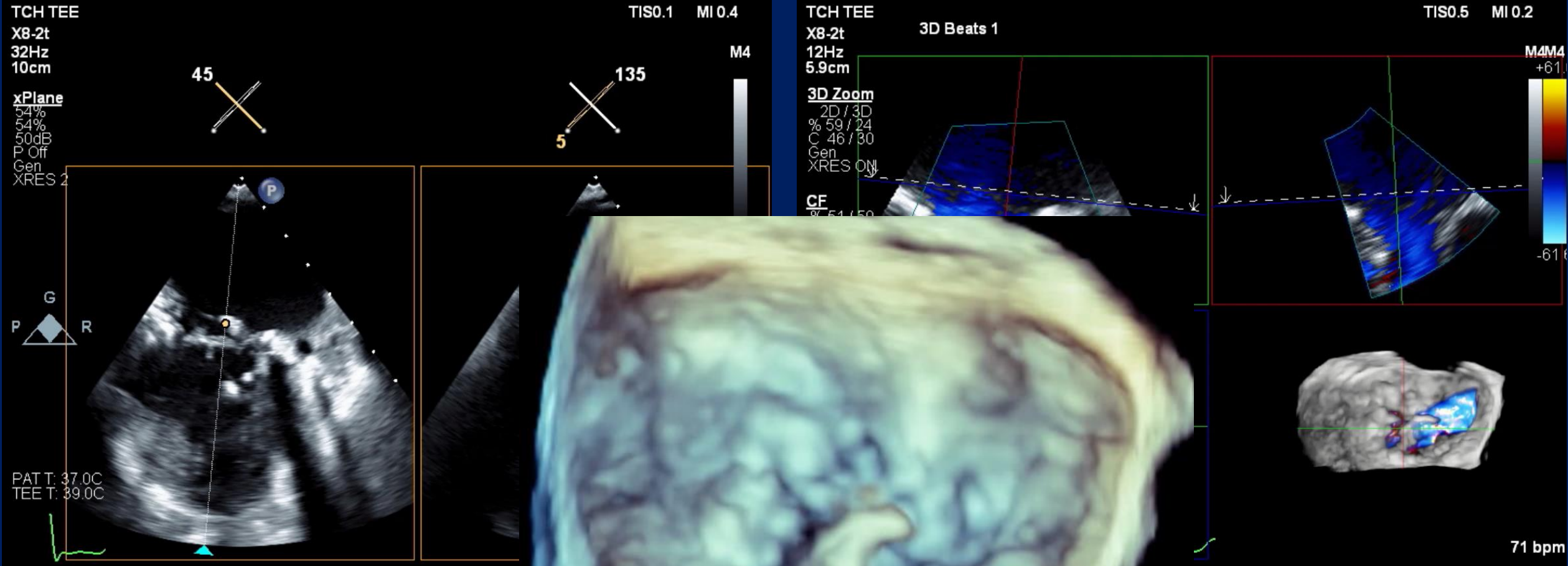
Echo:

- EF of 61 %
- RV dilated, preserved systolic function
- Severe MR. Mean gradient of 4 mmHg
- Severe TR

RHC:

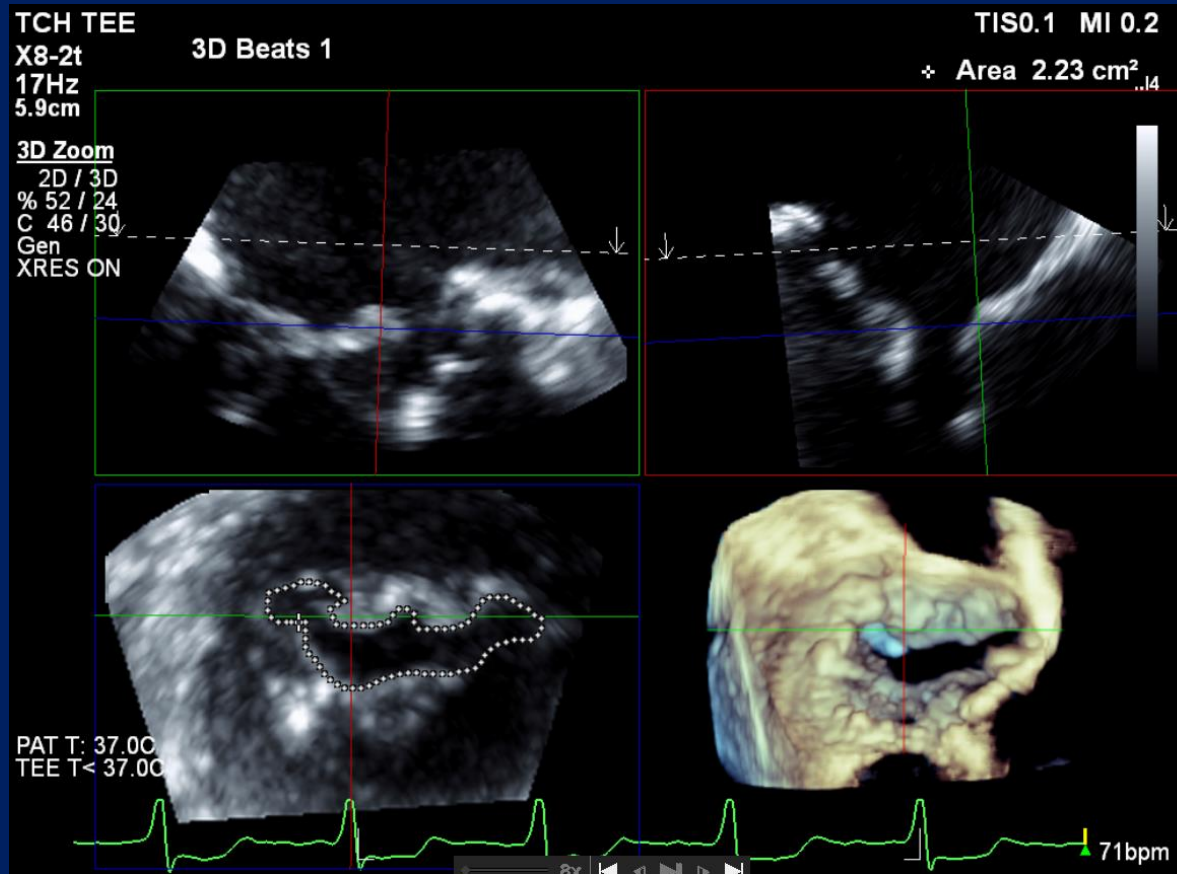
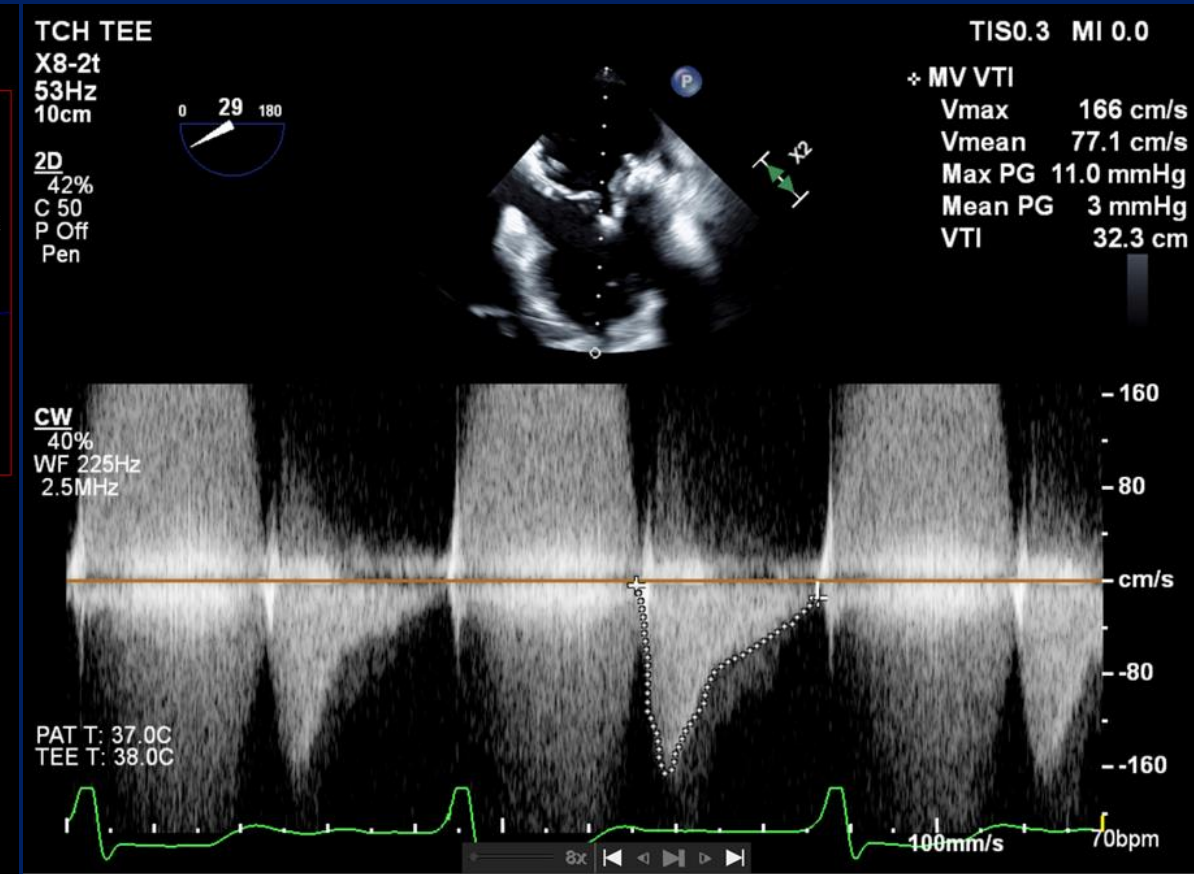
- Wedge 23 mmHg
- RA 16mmHg
- RV 82/7 mmHg
- PA: 78/27/48 mmHg
- A0: 112/70 mmHg
- Derived
 - PVR 10 woods
 - SVR 2225 Dynes. Sed/cm5
 - CO 2.4 L/min CI 1.6 l/min/m2

Severe MAC with Flail P2



Planimetry of 2.2 cm²

Mean gradient of 3 mmHg
at 70 bpm



Options for MR in MAC

- M-TEER
- TMVR- S3 in Mac – Off label
 - Dedicated Valve platforms
 - Transeptal
 - » Edwards M3 – FDA Approved – 29 Fr
 - » Medtronic Intrepid – Awaiting FDA Approval – 29 Fr
 - Transapical
 - » Abbott Tendyne- FDA Approved – Transapical – 36 Fr

CTA for comprehensive assessment of transcatheter treatment options



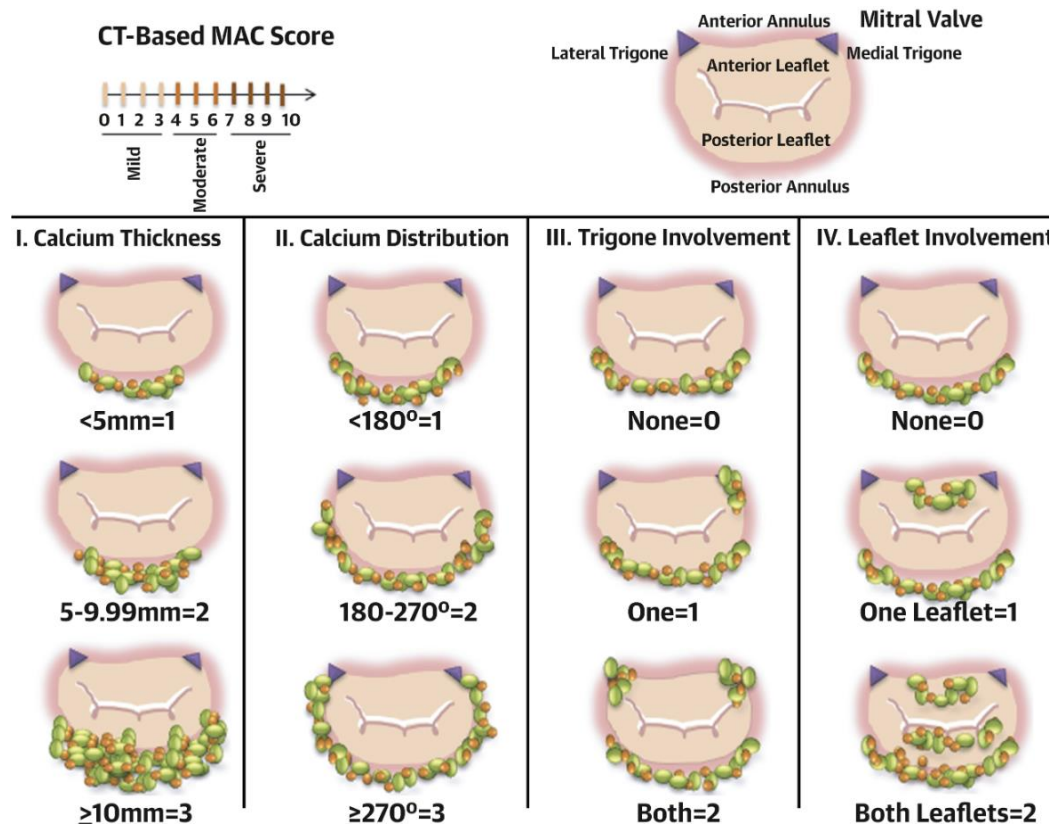
- M-TEER

- Possible if no leaflet ca, MV gradient not too high, small MV area.

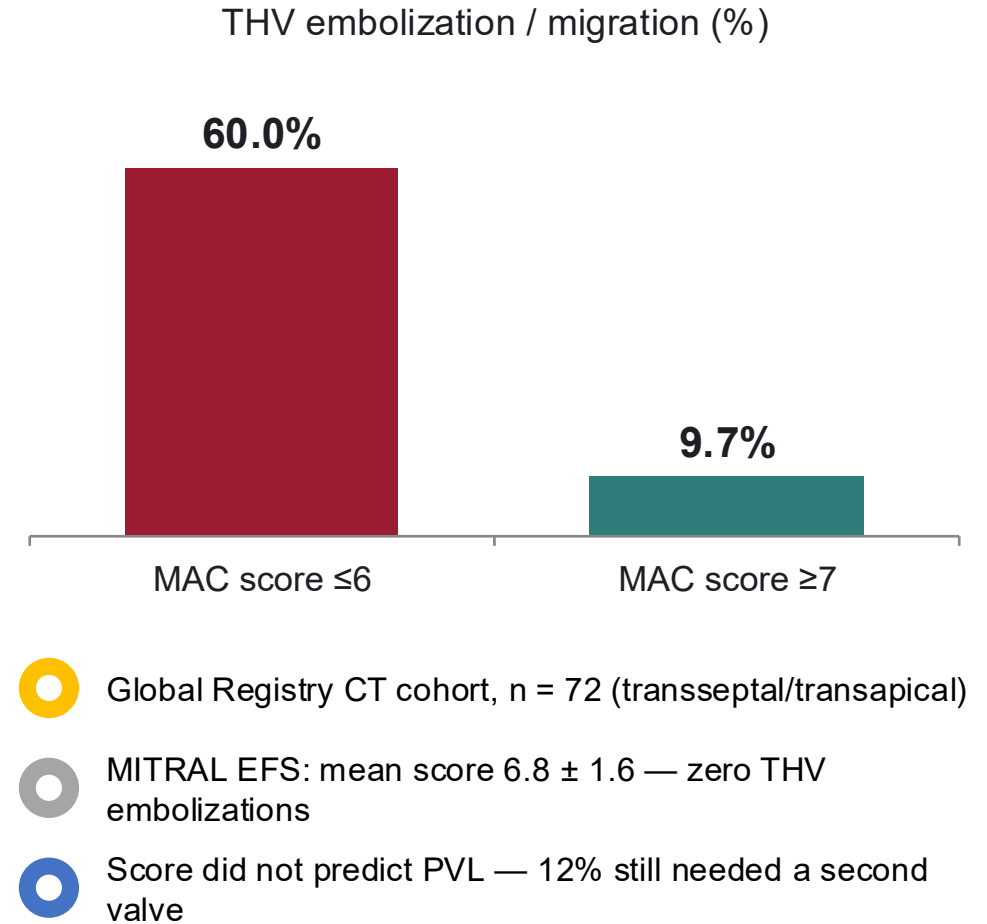
- TMVR :

- Intrepid , Encircle, Tendyne
- S3 in MAC

TMVR –S3 in MAC- Calcium is the anchor: the CT MAC score



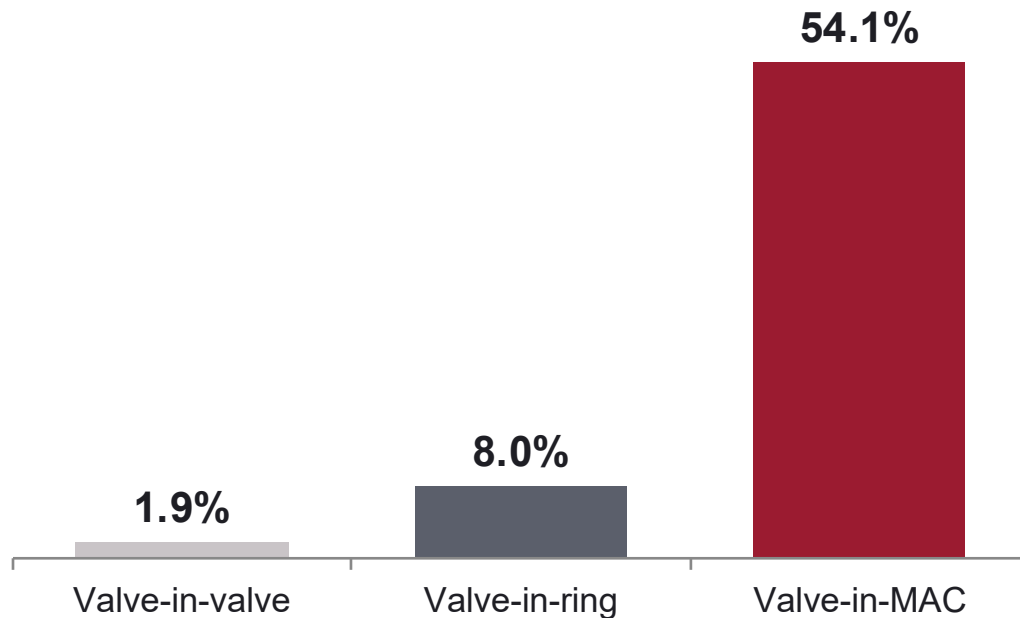
Thicker, more circumferential calcium with trigone and anterior-leaflet involvement = better anchoring and less embolization.



Guerrero M et al, JACC CVI 2020;13:1945-57; editorial 'Big MAC, Hold the Valve', JACC CVI 2020; Guerrero M, SOLACI-SOCIME 2025 (MITRAL EFS CT data).

Neo-LVOT obstruction: Dominant procedural threat

LVOT obstruction after TMVR (Δ mean gradient ≥ 10 mmHg)



TMVR Registry, $n = 194$ (37 ViMAC)

34.6% vs 2.4%

procedural mortality with vs without LVOT obstruction

$\leq 1.7 \text{ cm}^2$

neo-LVOT predicts LVOTO

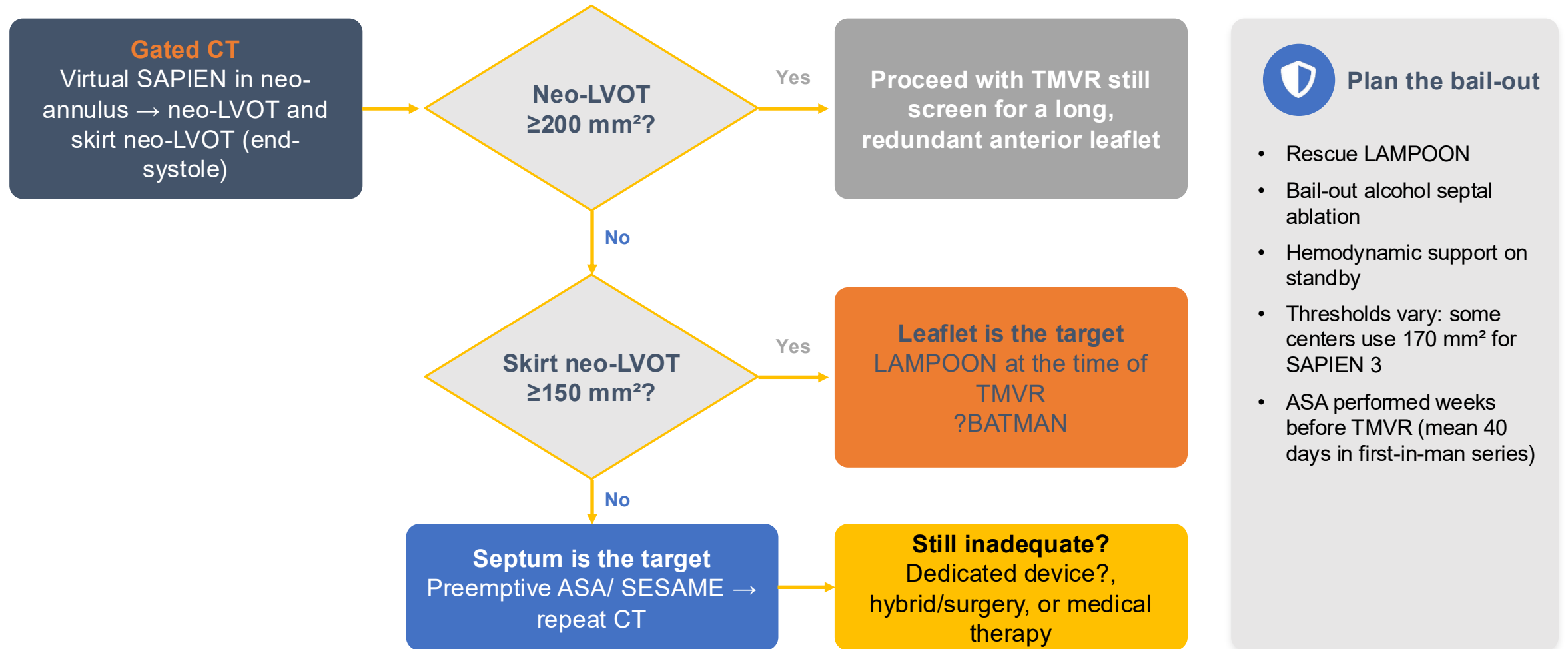
10–11%

clinically reported LVOTO after ViMAC in TVT and Global registries

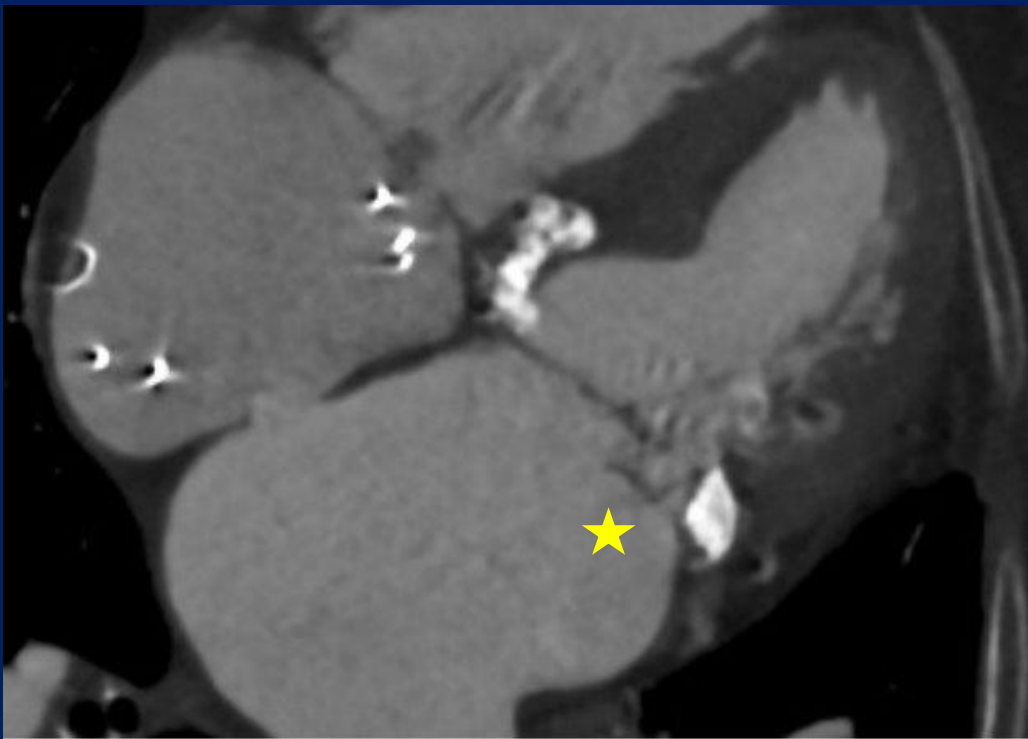
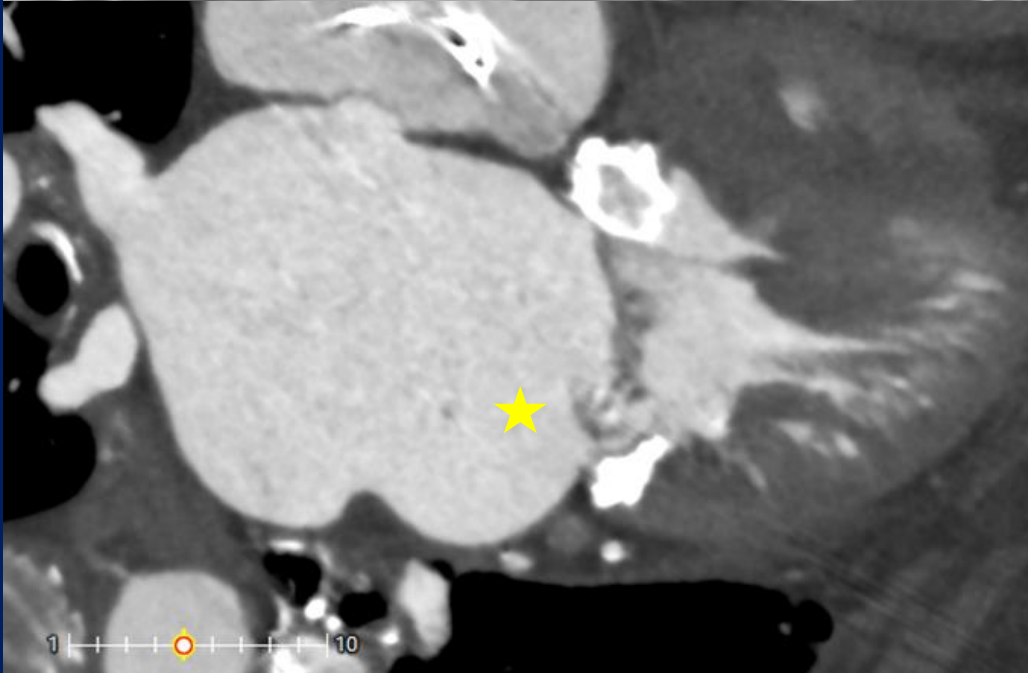
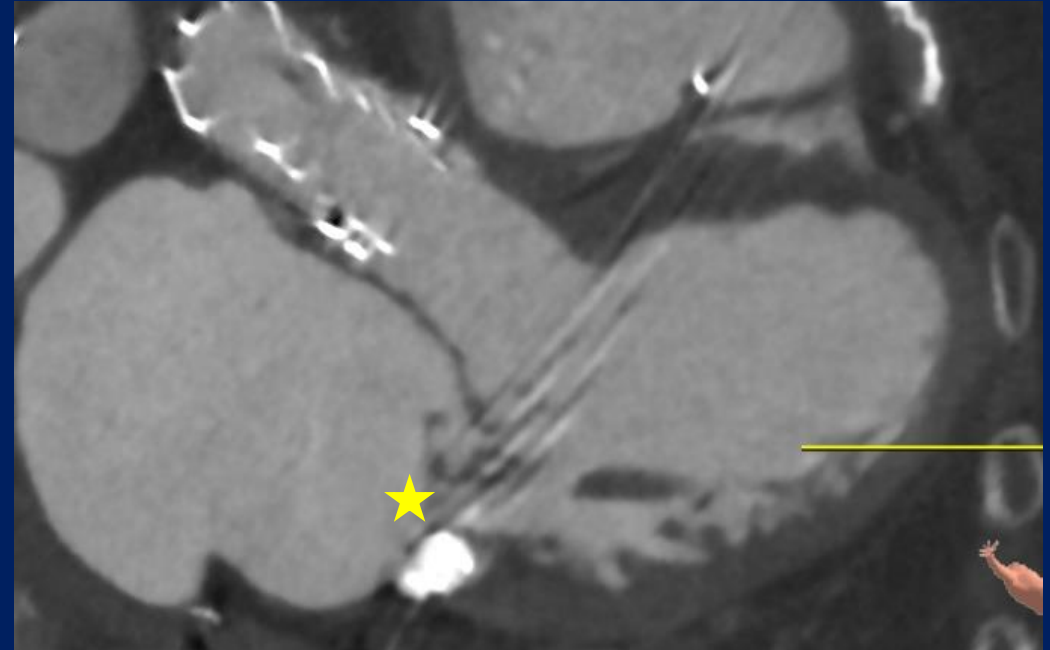
Simulation caveat: 3D neo-LVOT models are least accurate in ViMAC (mean predicted-vs-actual difference $-73 \pm 61 \text{ mm}^2$ vs ~ -21 to -23 mm^2 for ViV/ViR) — build in margin.

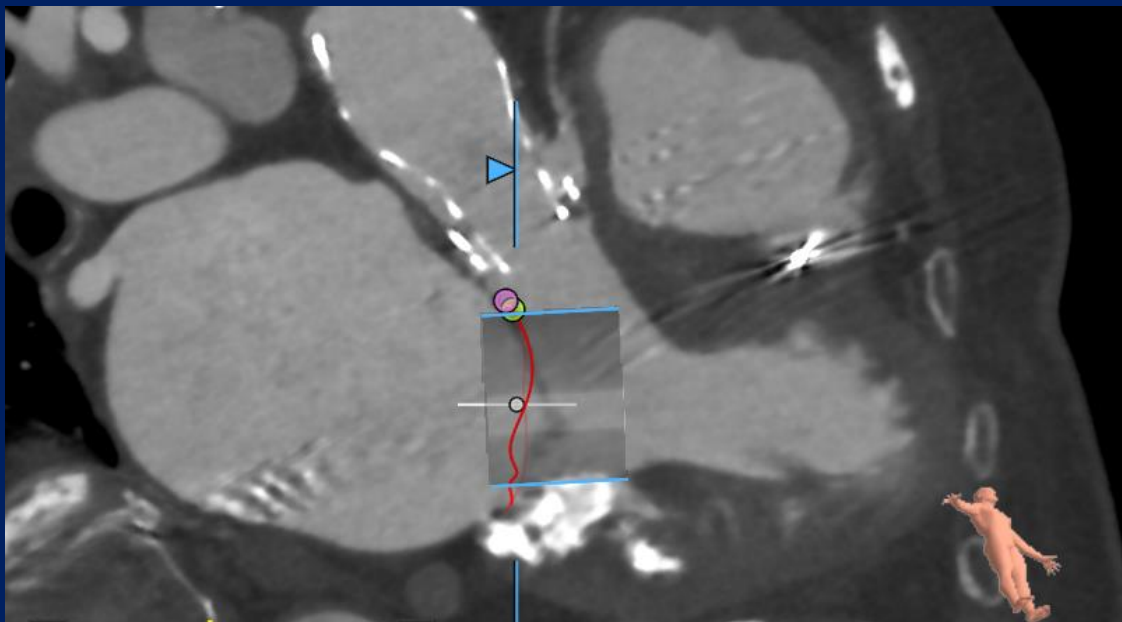
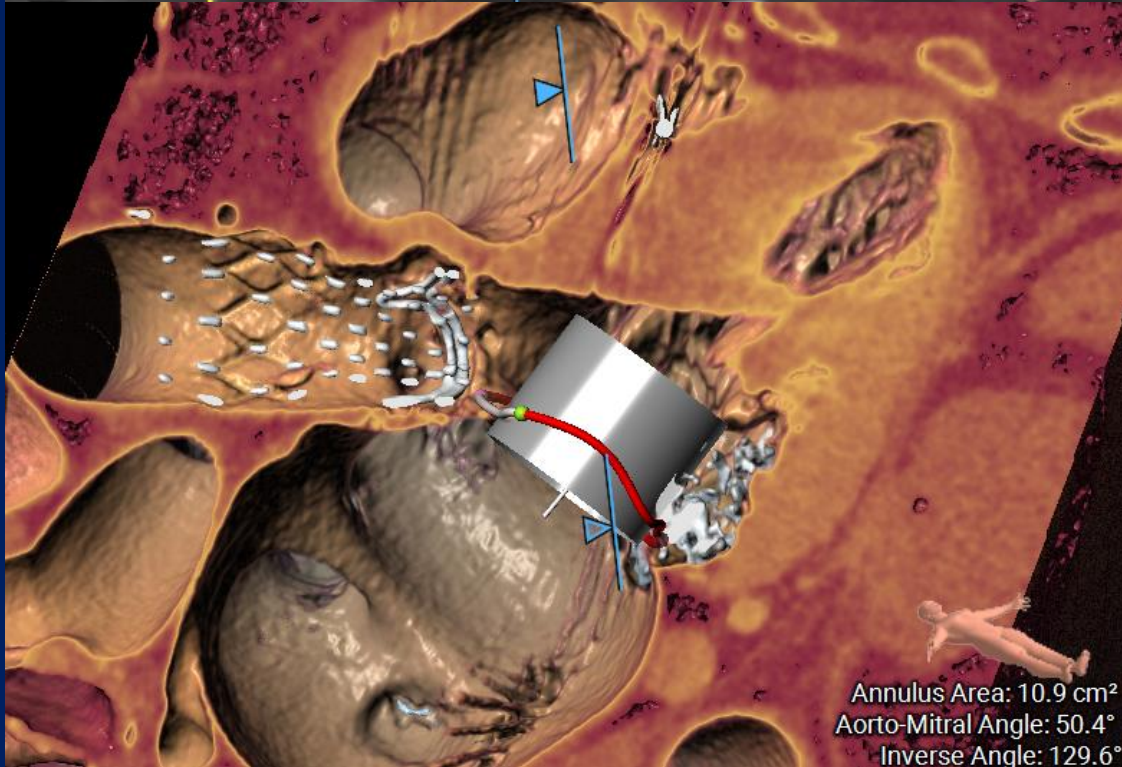
Yoon SH et al, JACC CI 2019;12:182-93; Wang DD et al, CCI 2018;92:379-87; Guerrero M et al, Circ CI 2020;13:e008425; Guerrero M et al, JACC 2018;71:1841; Accuracy of 3D neo-LVOT simulations, 2024 (PMID 39506471).

LVOT before TMVR: a planning algorithm



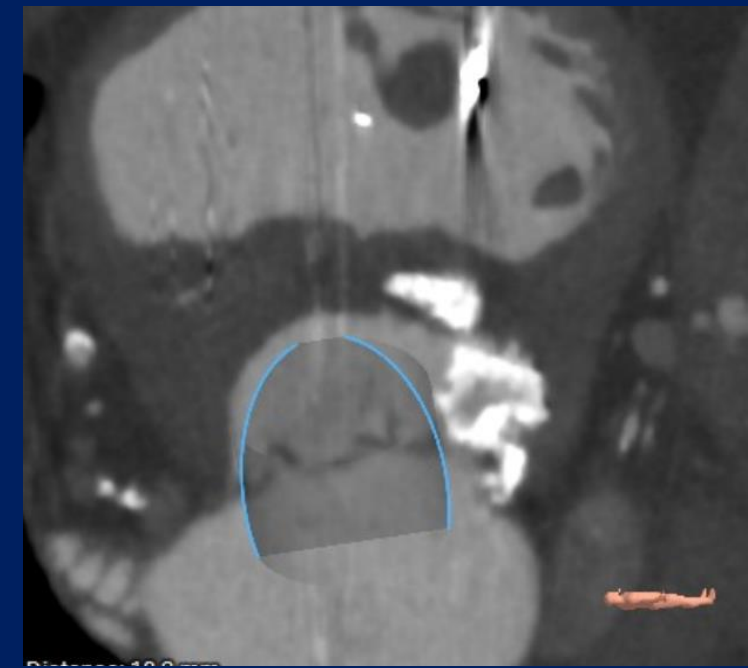
Framework adapted from MITRAL II protocol (NCT04408430) and NHLBI LAMPOON IDE (Khan JM et al, JACC 2019;73:2521; JACC CI 2024); Wang DD et al, JACC CI 2019;12:1268; Wong et al, CCI 2023; Khan JM et al, JACC CI 2019;12:1283 (rescue LAMPOON).





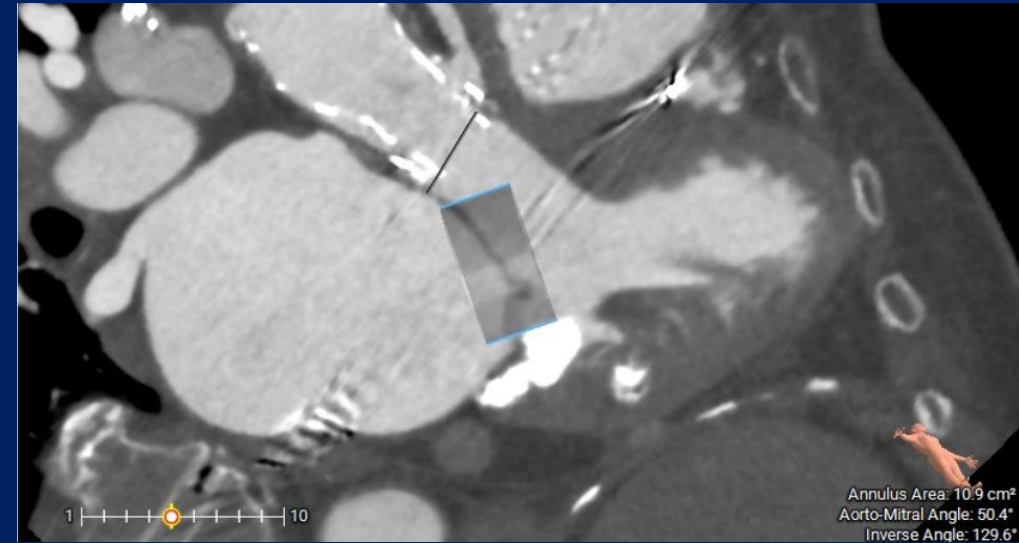
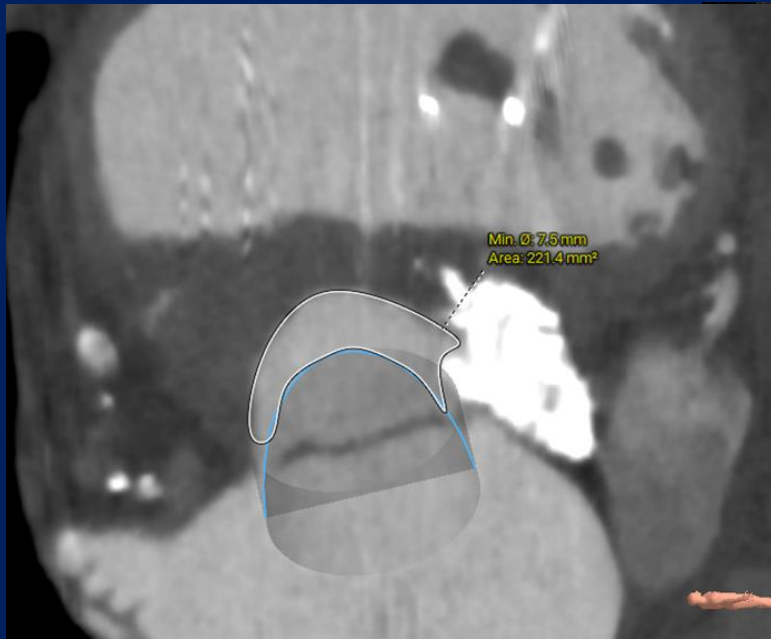
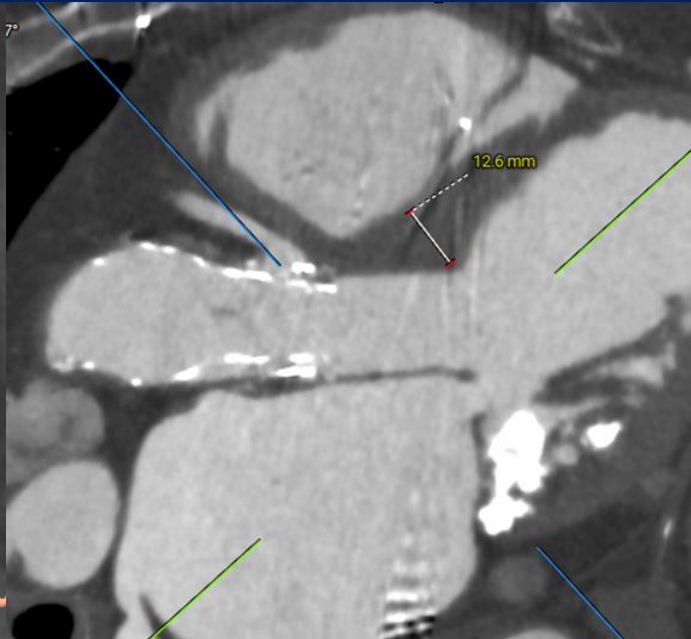
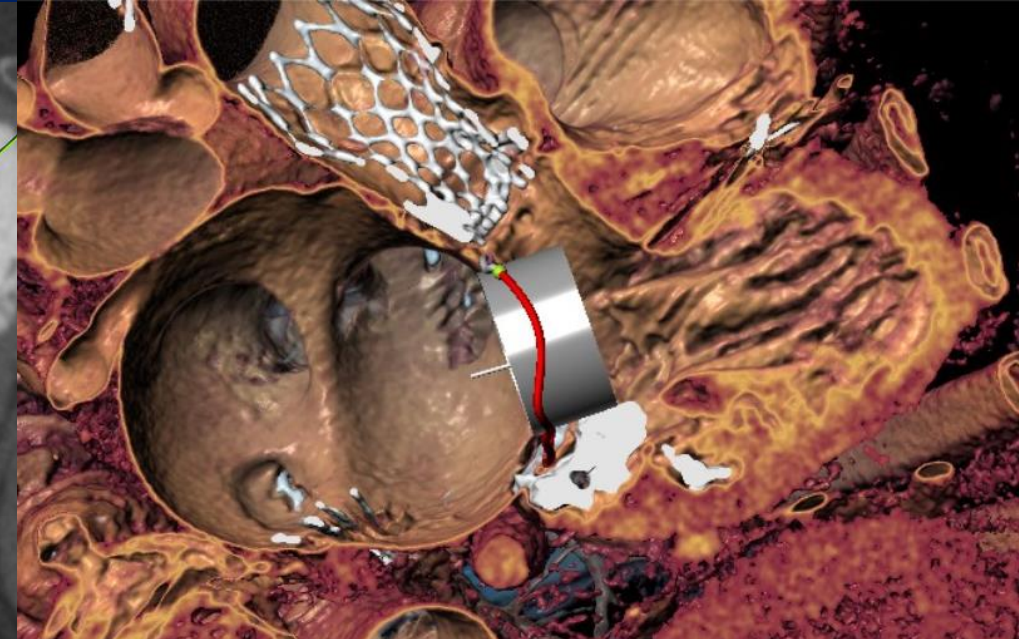
TMVR

- Not a research TMVR candidate due to comorbidities
- Encircle M3 not a candidate- (not enough room 1 cm below the annulus)
- Neo LVOT at 151 mm²





- Off label Valve in MAC using the TAVR and anterior anchor.
- Neo skirt LVOT 221mm²
- Leaflet modification, BATMAN, LAMPOON

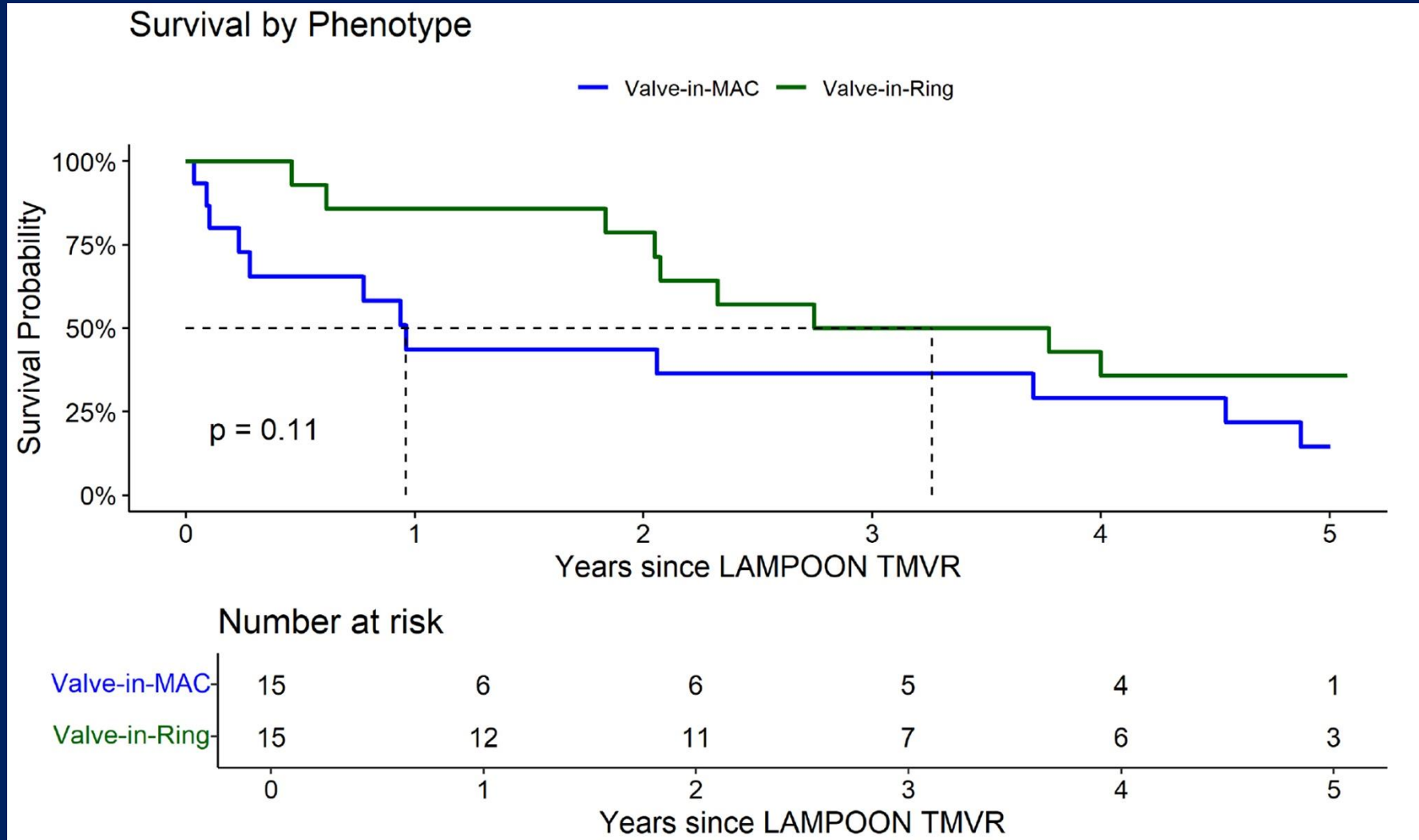


LVOT modification: what the evidence shows

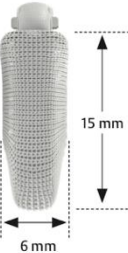
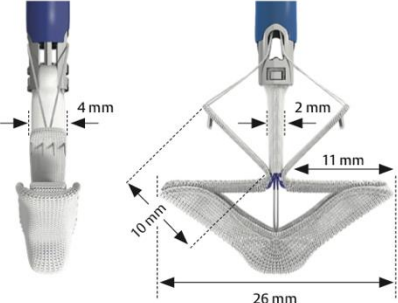
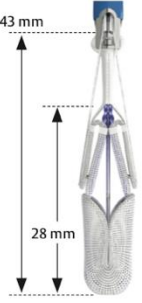
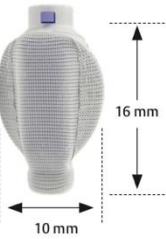
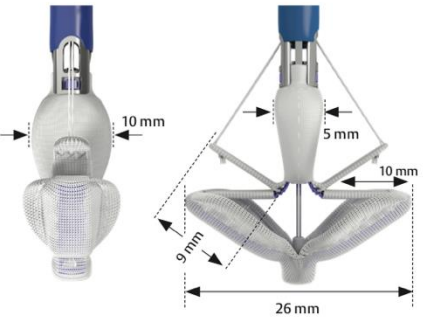
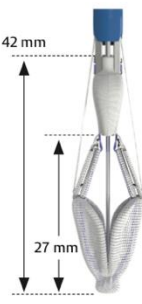
Strategy	Evidence	Key results	Watch-outs
Preemptive ASA	Wang, JACC CI 2019 — 30 pts, 6 US centers	Median neo-LVOT +111 mm ² ; TMVR in 19 (100% success) a mean 40 days later; post-TMVR 30-day mortality 5.3%	2 deaths after ASA before TMVR; pacemaker 16.7%; needs a suitable septal perforator
LAMPOON (prospective)	NHLBI IDE, JACC 2019 — 30 pts (15 ViMAC)	Laceration successful in 100%; 30-day survival 93%	ViMAC survival 44% at 1 y, 15% at 5 y; skirt neo-LVOT <150 mm ² later excluded
LAMPOON (real world)	STS/ACC TVT Registry 2019–25 — 9,250 TMVR, 569 sites	LAMPOON in 8.9%; freedom from LVOTO 95.5%; 30-day mortality ViMAC 23.7% (n = 221) vs ViV 8.3%, ViR 6.1%	Only 17 sites with ≥10 cases; native-valve 1-year mortality >40%
Septal RF ablation / SESAME	Permitted in MITRAL II; NHLBI SESAME EFS (NCT06269640)	Transcatheter septal reduction when perforator anatomy precludes ASA	Investigational; outcome data pending

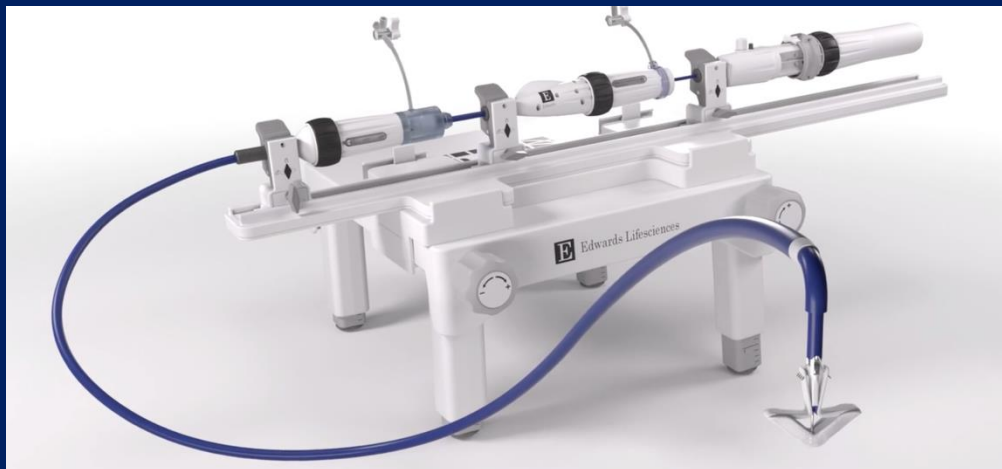
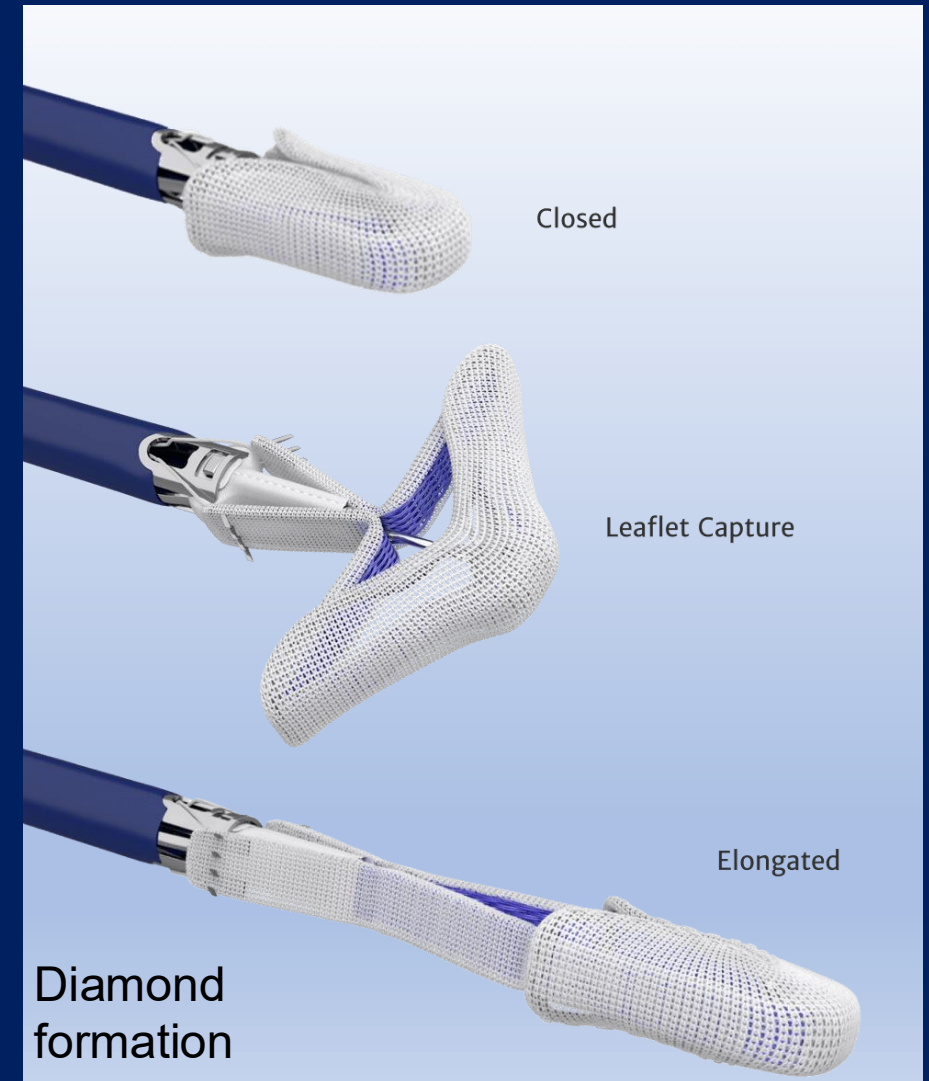
Wang DD et al, JACC CI 2019;12:1268-79; Wong et al, CCI 2023 (PMID 37855165); Khan JM et al, JACC 2019;73:2521 and JACC CI 2024 (5-year LAMPOON); Khan JM, LAMPOON Trends and Outcomes (TVT Registry), New York Valves 2026; NCT04408430; NCT06269640.

LAMPOON- TMVR in MAC



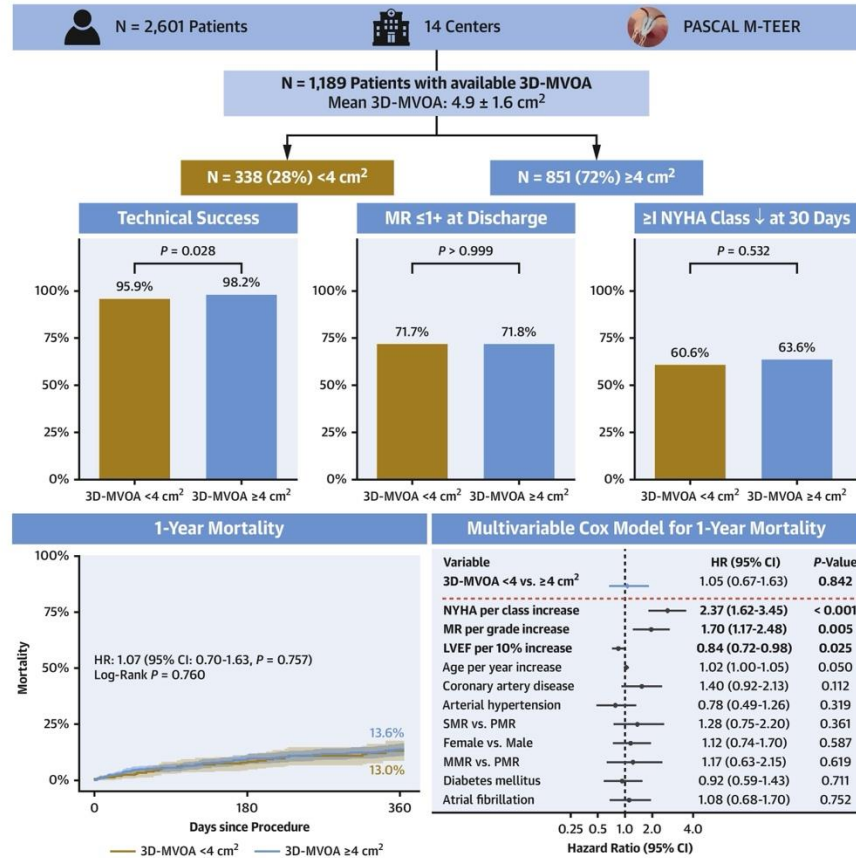
Edwards Pascal Precision

	Closed	Leaflet - Capture - Ready	Elongated
PASCAL Ace	 <p>15 mm 6 mm</p>	 <p>4 mm 2 mm 11 mm 10 mm 26 mm</p>	 <p>43 mm 28 mm</p>
PASCAL	 <p>16 mm 10 mm</p>	 <p>10 mm 5 mm 10 mm 9 mm 26 mm</p>	 <p>42 mm 27 mm</p>



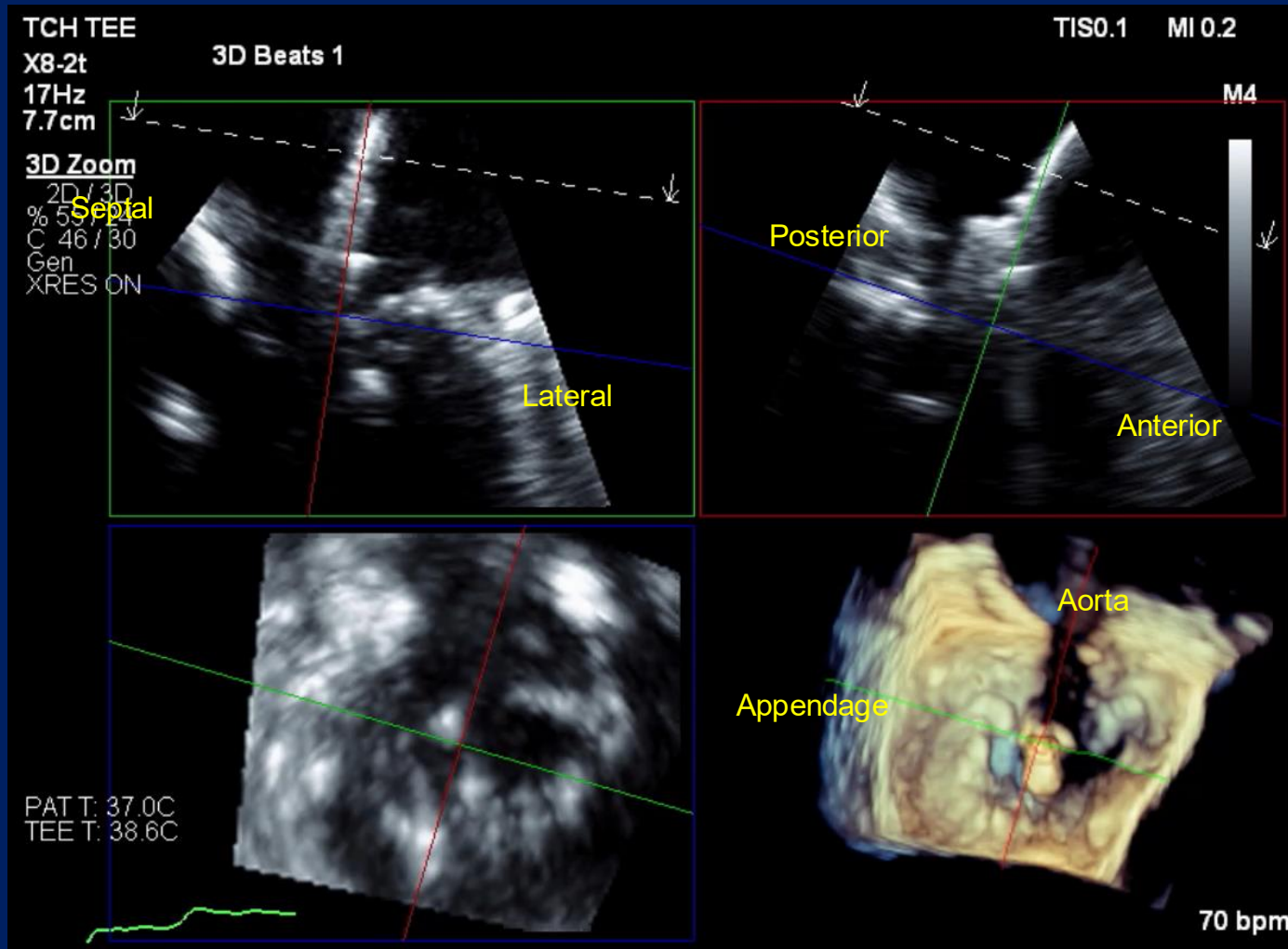
Small Mitral Valve Orifice Area in Mitral Valve TEER: The REPAIR Study

CENTRAL ILLUSTRATION: PASCAL M-TEER for Small 3D-MVOA: The REPAIR Study



- In a real-world PASCAL M-TEER population ~1/3 of patients are being treated with 3D-MVOA $< 4 \text{ cm}^2$
- Technical success was achieved more frequently in patients with 3D-MVOA $\geq 4 \text{ cm}^2$ than in patients with $< 4 \text{ cm}^2$
- MR reduction to $\leq 1+$ at discharge and ≥ 1 NYHA class improvement to 30 days occurred with equal frequency
- 1-year survival was similar among patients with 3D-MVOA < 4 and $\geq 4 \text{ cm}^2$
- PASCAL M-TEER in 3D-MVOA $< 4 \text{ cm}^2$ is technically feasible but requires careful procedural planning

Mitral TEER with Pascal

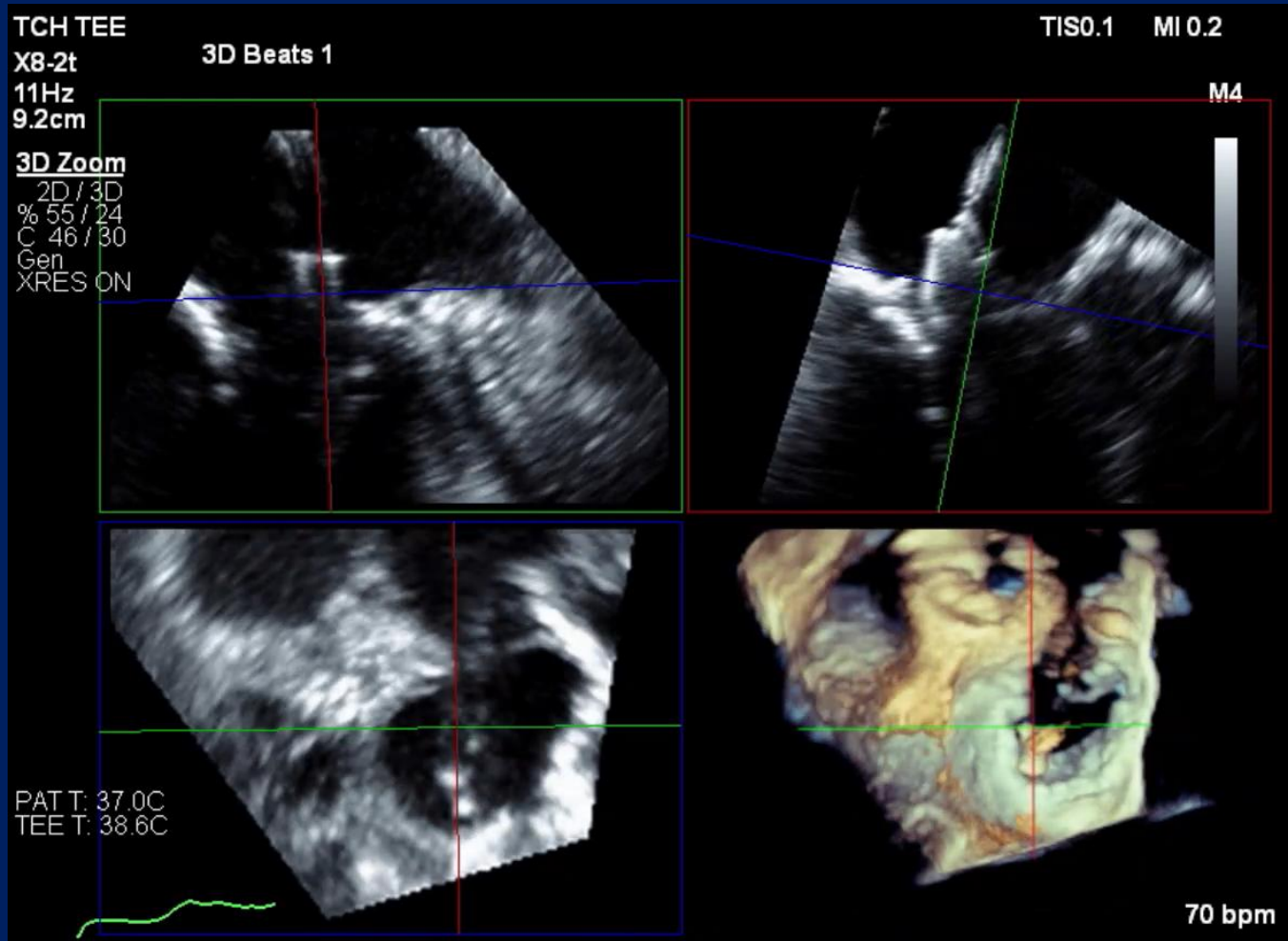
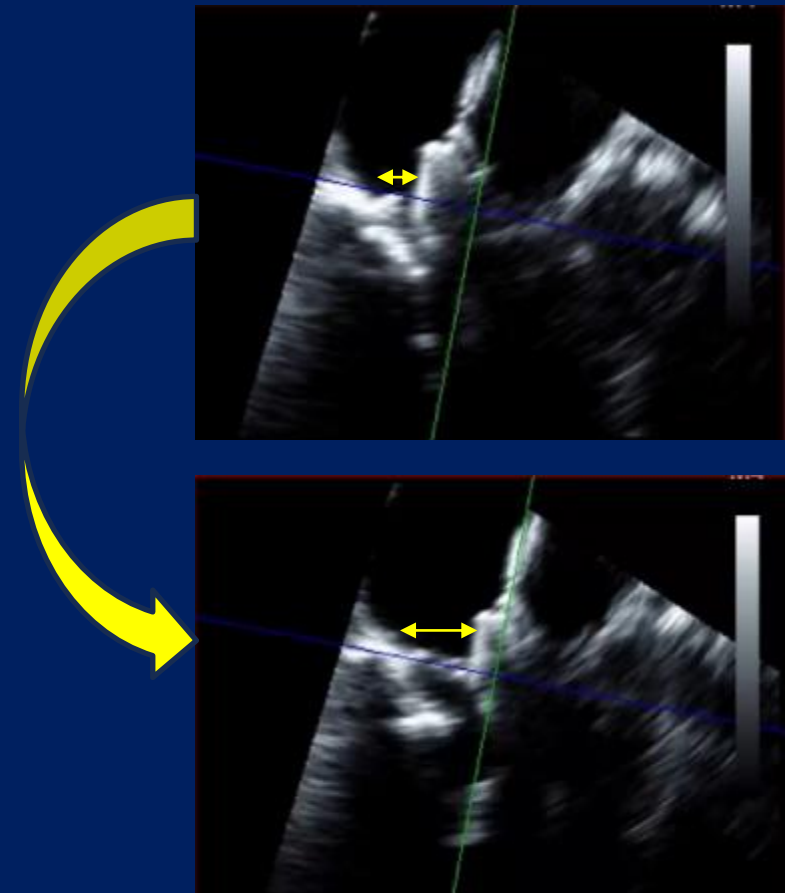


Alignment

- Minimize manipulation below the valve
- Co-axiality
 - Septal – lateral
 - Anterior - posterior

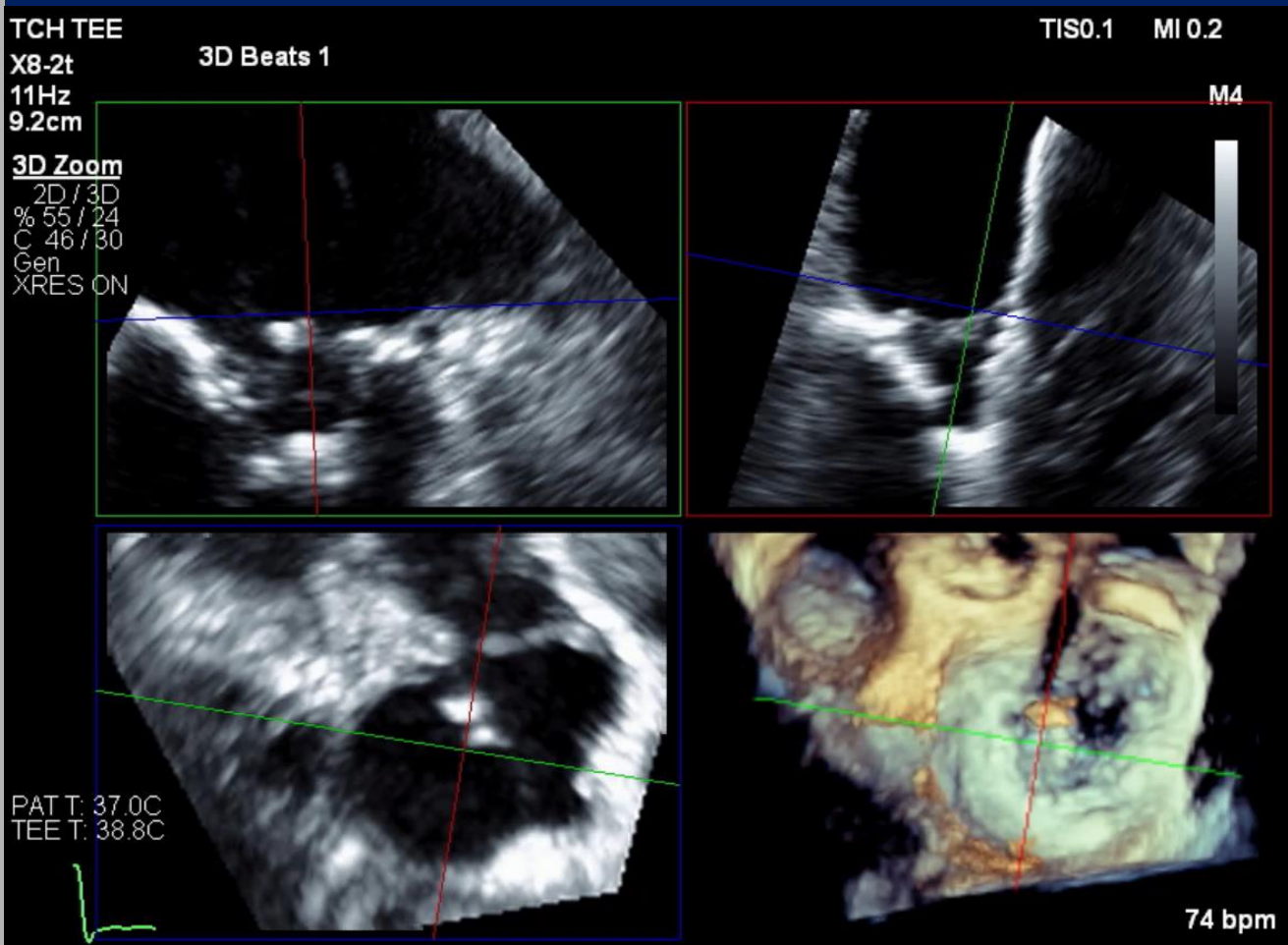
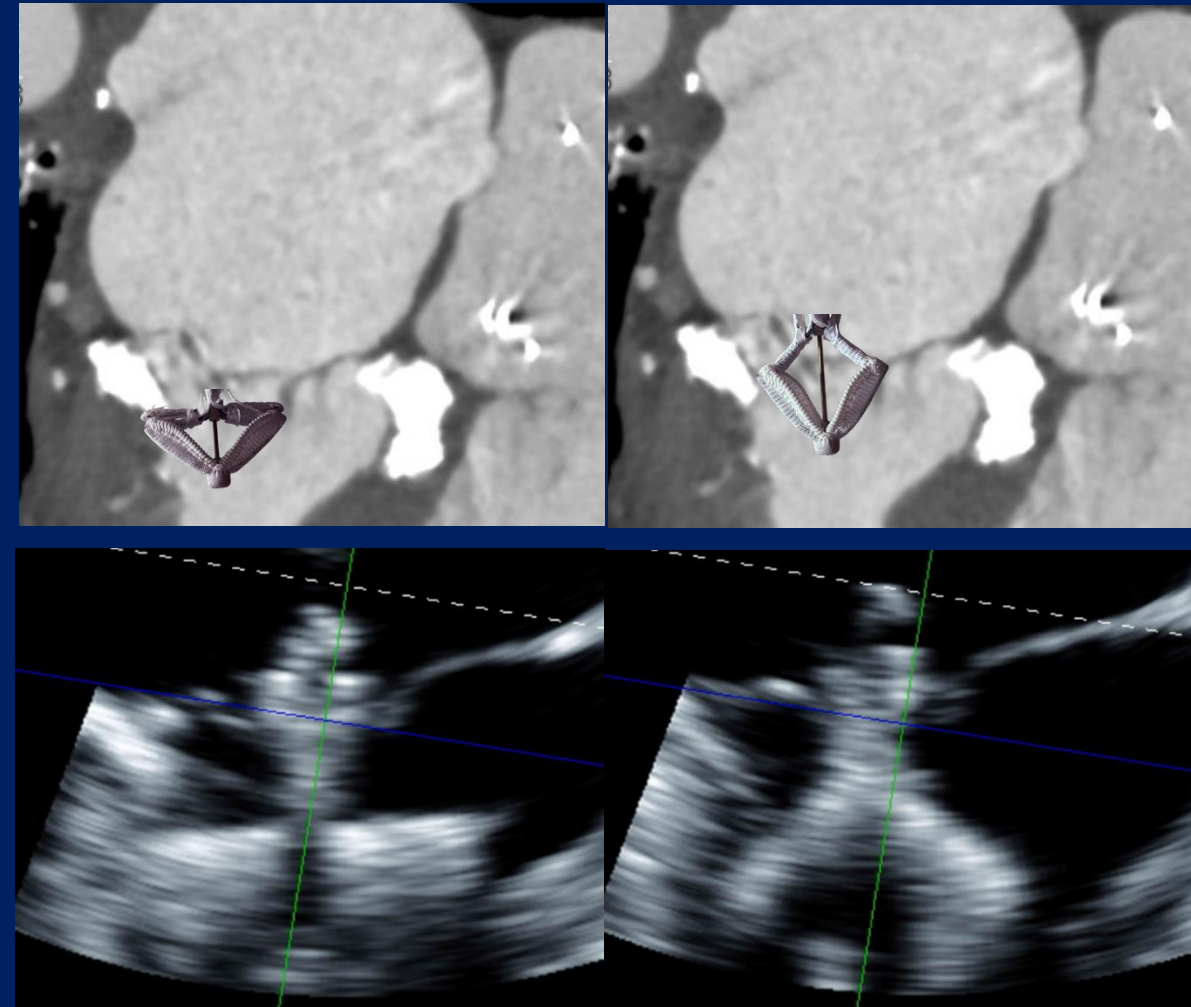
Crossing Valve

- Anterior position to avoid the posterior MAC



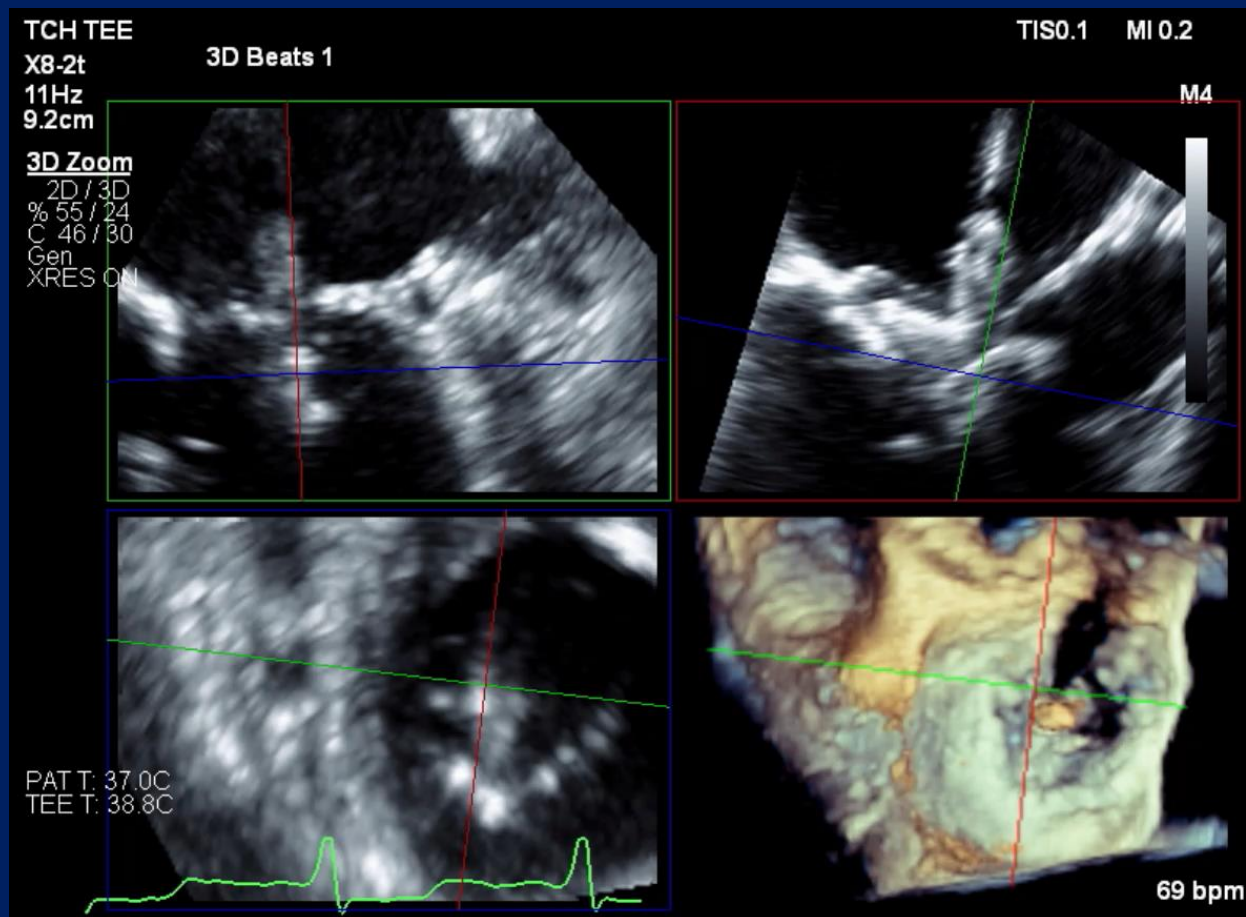
Arms opened below the leaflets

- Interaction with the MAC preventing up for pulling up
- **Diamond shape configuration**

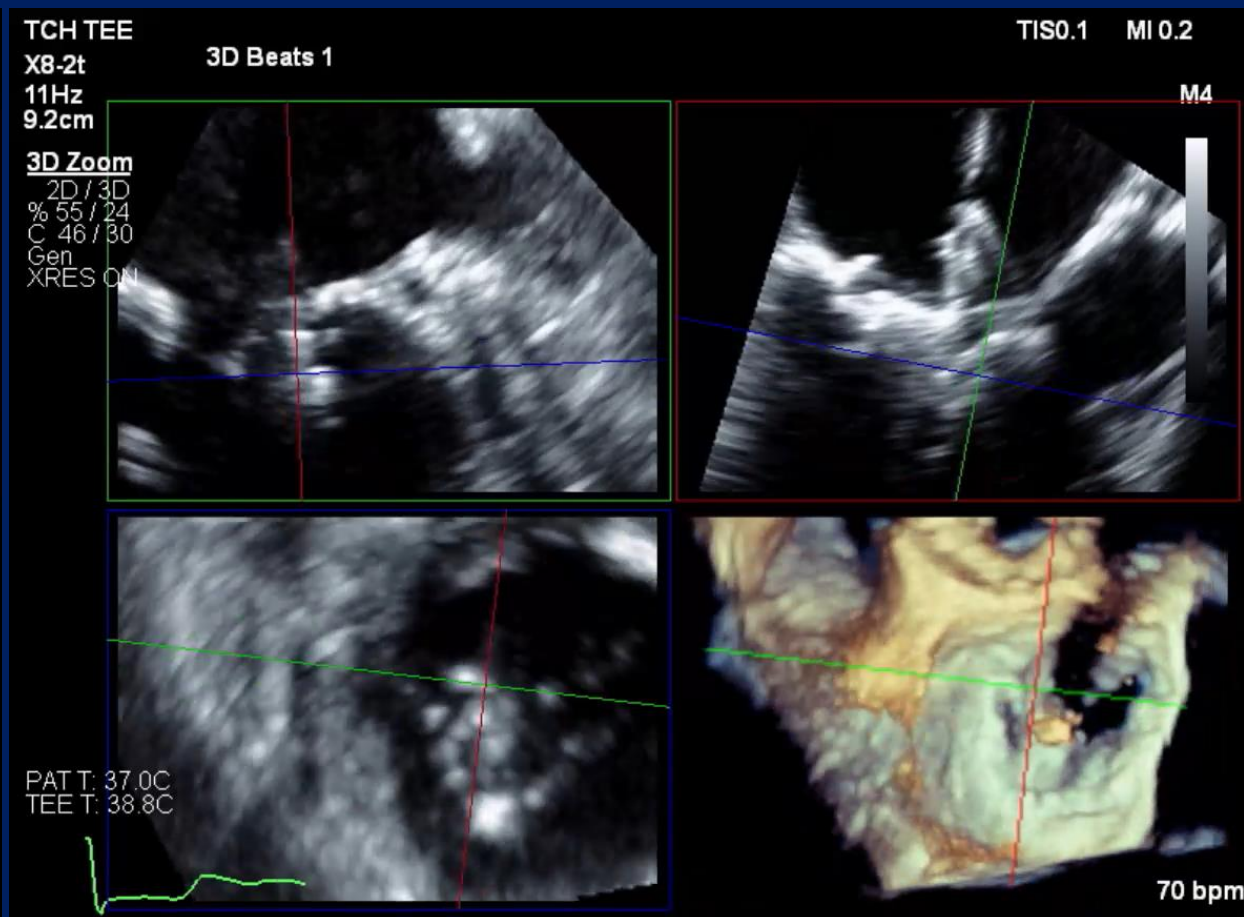


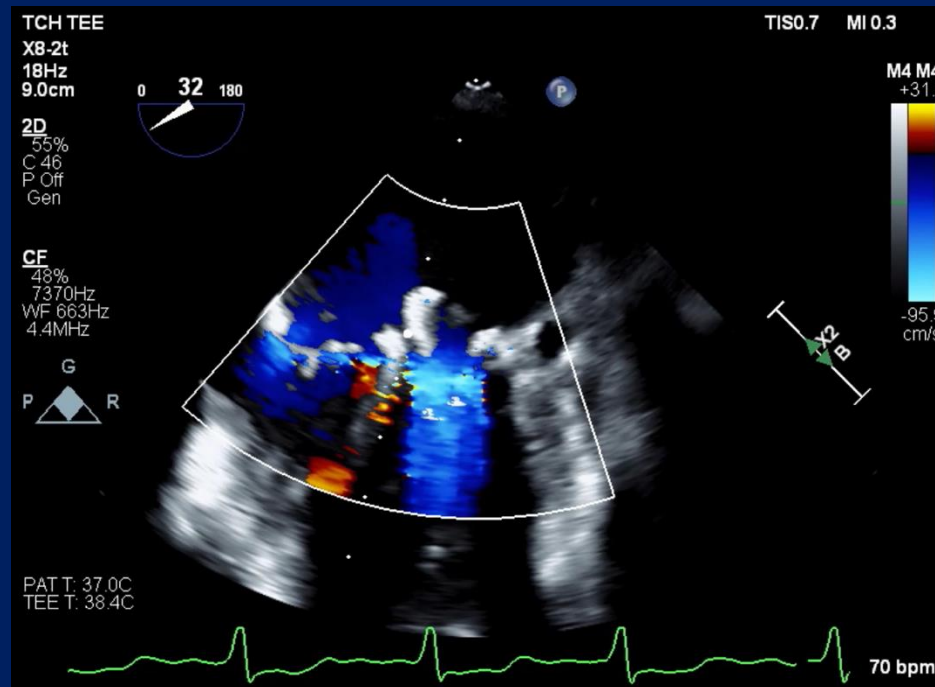
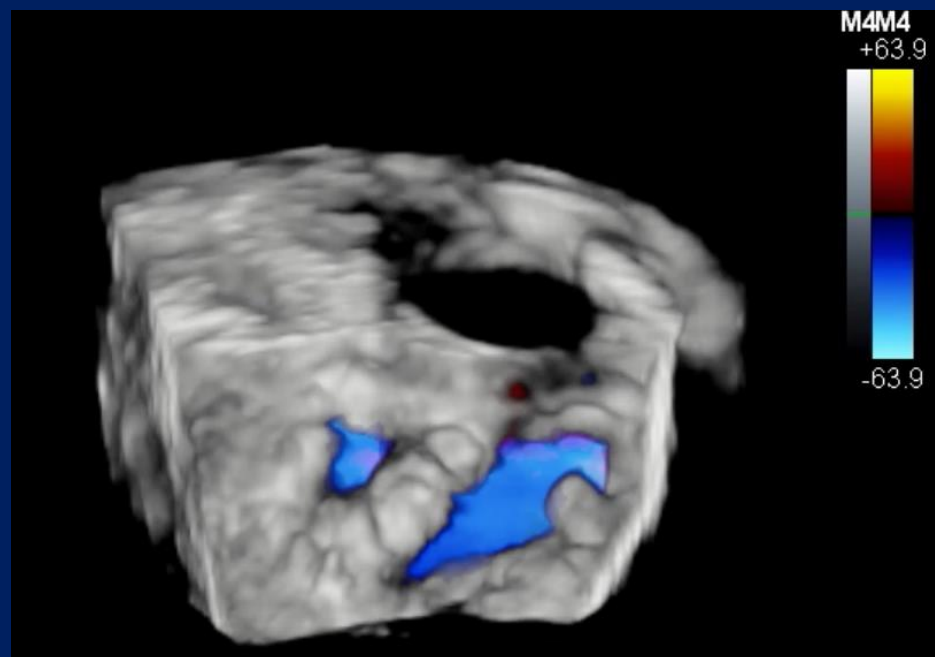
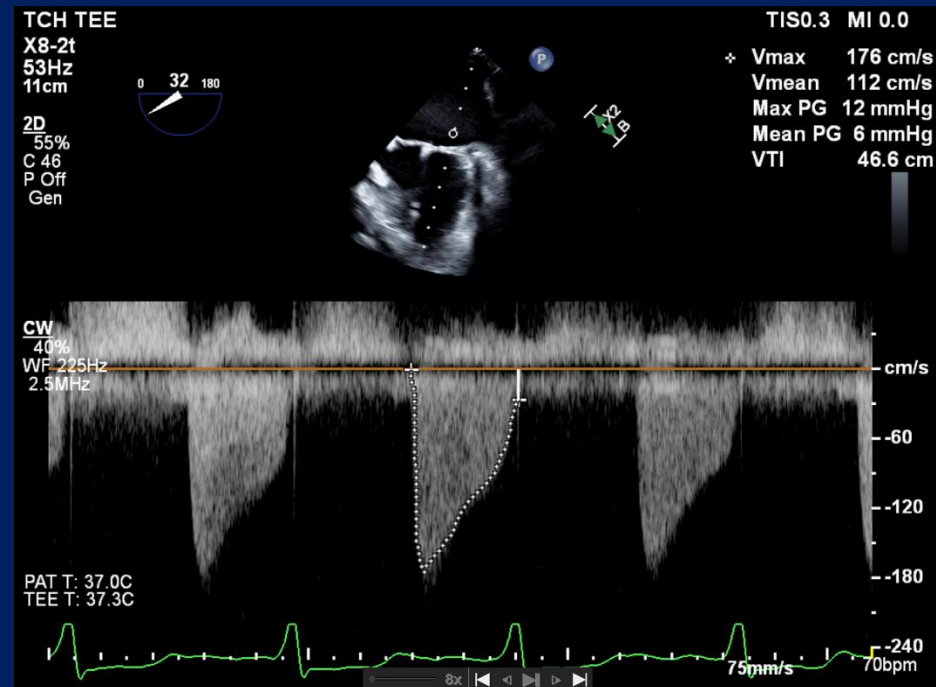
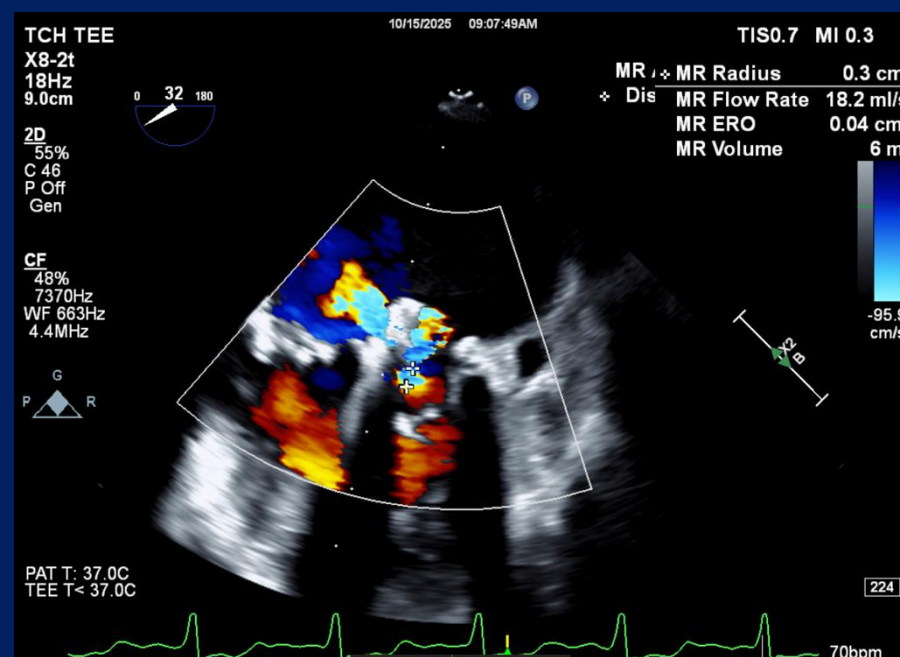
Sequential leaflet capture

Anterior leaflet



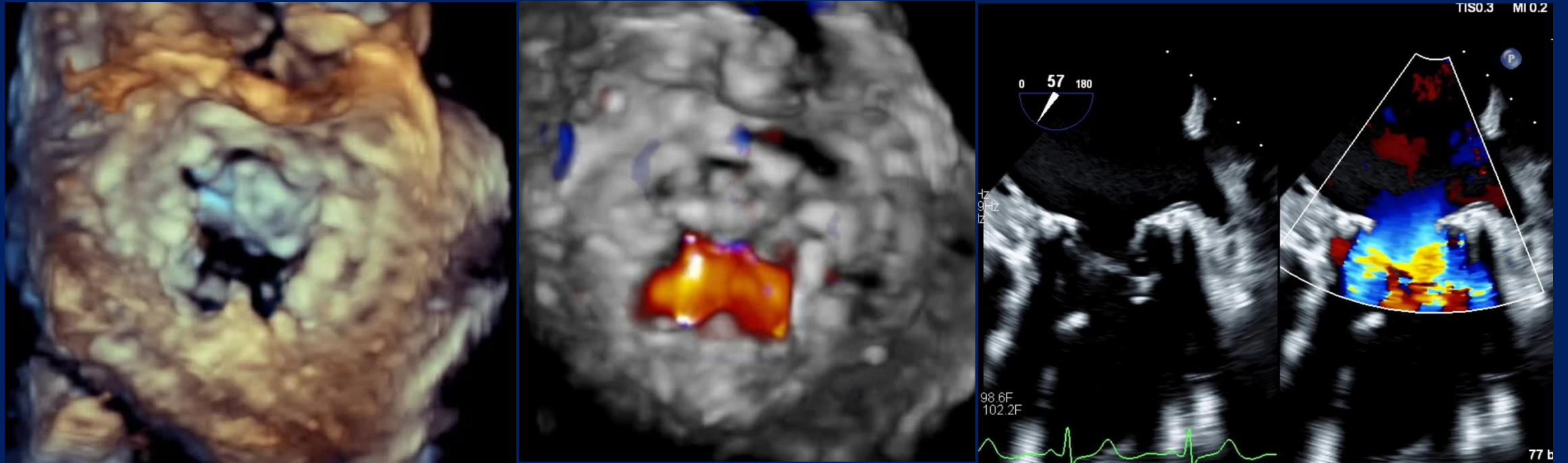
Posterior leaflet





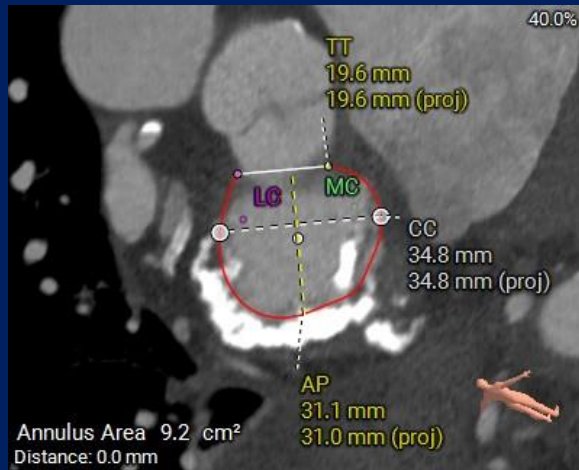
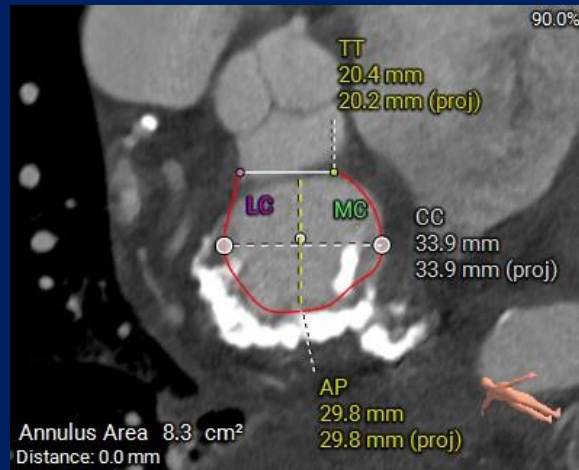
Case 2

- 65 yr lady ESRD, severe MAC, MR
- Recurrent HF admissions



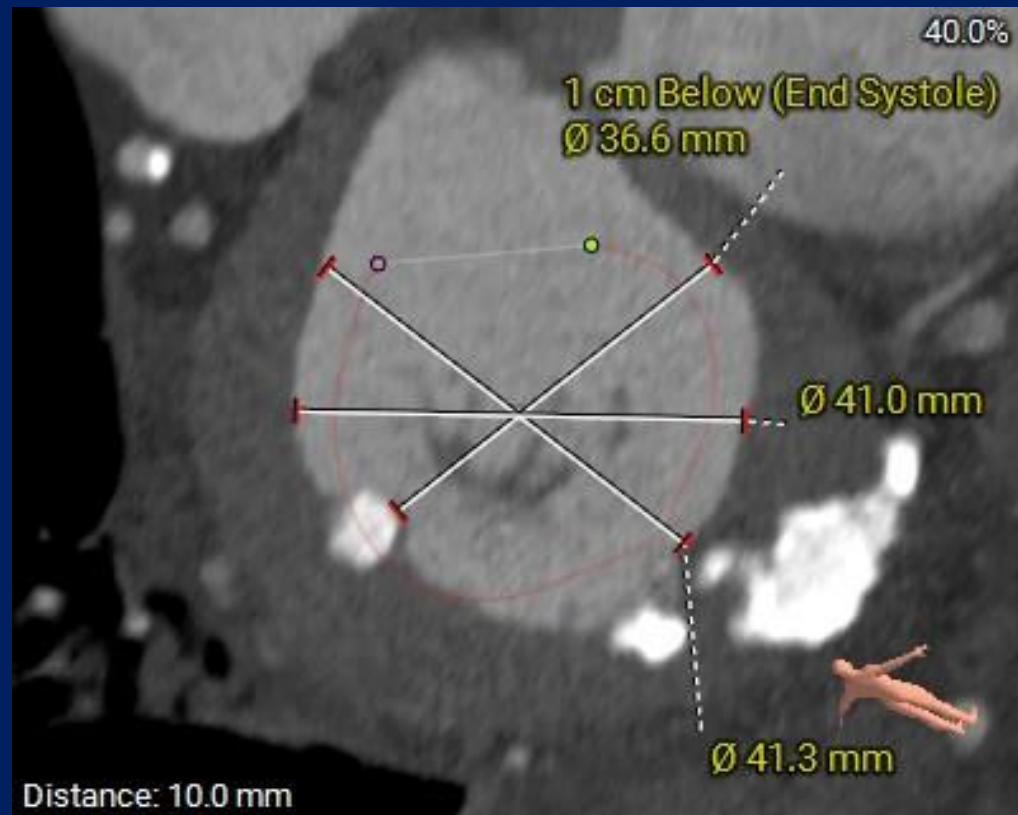
CTA for TMVR Evaluation

1. Off label S3 in MAC
2. Edwards M3

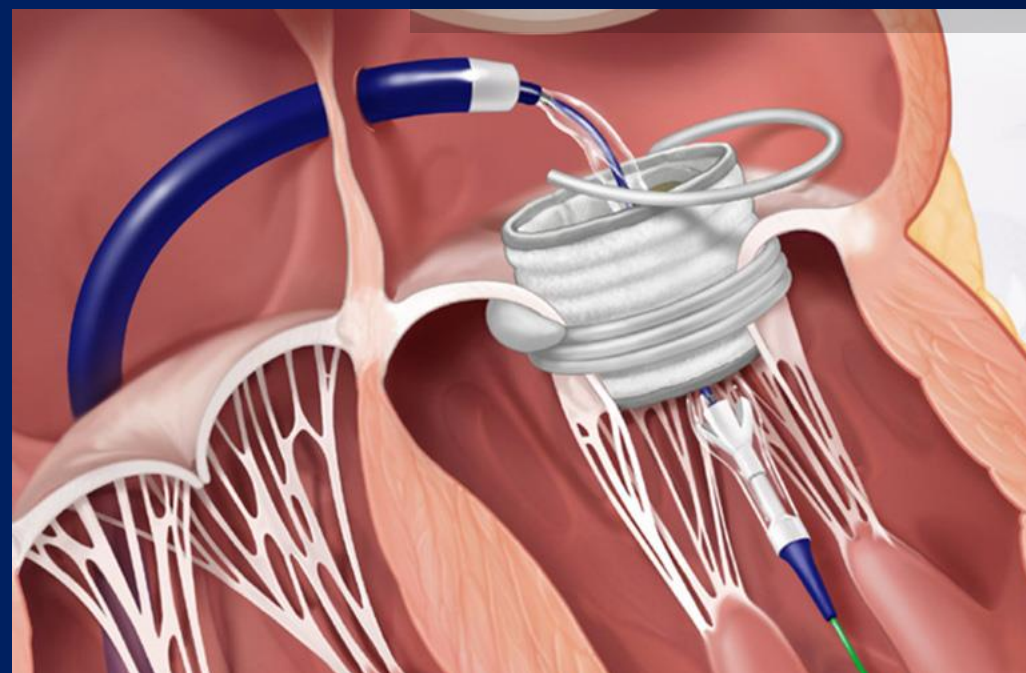


TMVR Evaluation

1. Off label S3 in MAC
2. Edwards M3



Edwards M3



Study Design

SAPIEN M3 System TransCatheter MIttral Valve ReplaCement via Transseptal AccEss

Prospective, single-arm, multicenter study

Purpose: Establish safety and effectiveness of the SAPIEN M3 system in patients with symptomatic MR $\geq 3+$, unsuitable for surgery or commercially available transcatheter treatment options as assessed by heart team

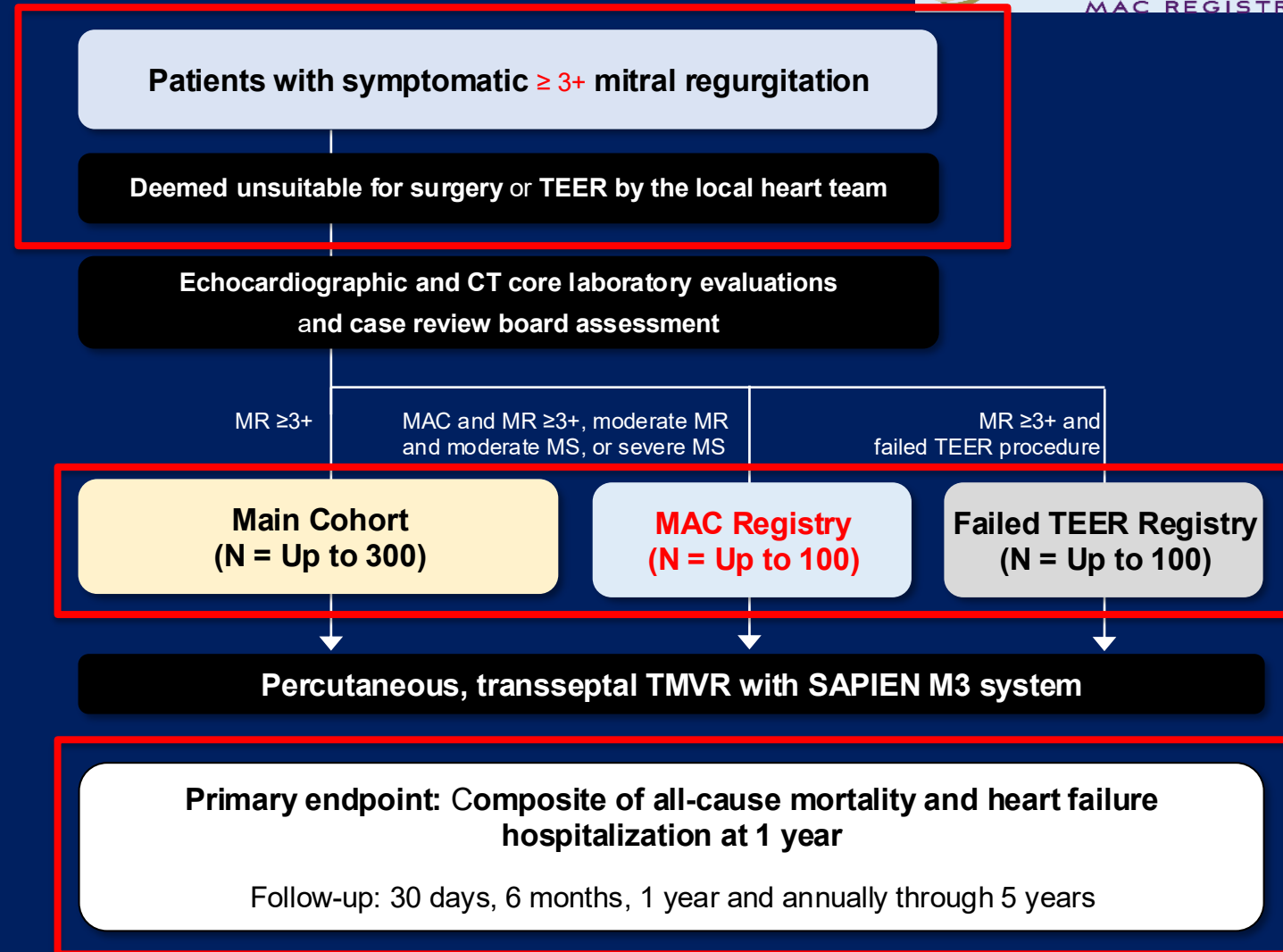
Principal Investigators:

John Webb, MD; David Daniels, MD; Mayra Guerrero, MD

ClinicalTrials.gov: NCT04153292

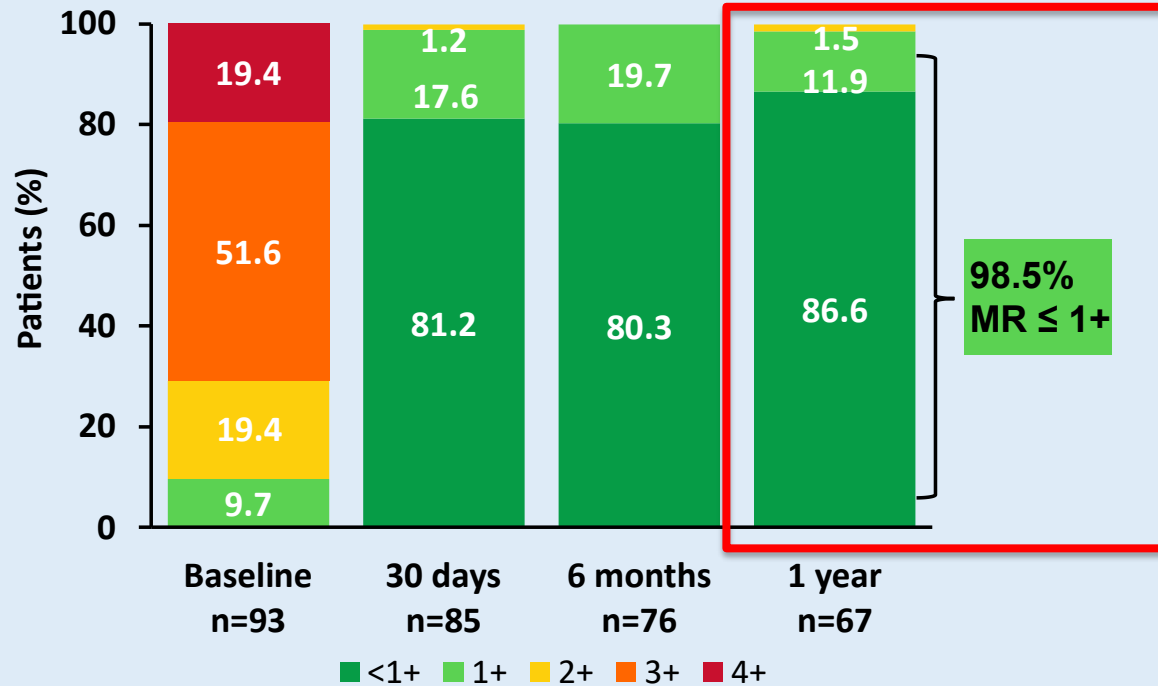
Trial Oversight:

- Echocardiographic Core Laboratory
- Computed Tomography Core Laboratory
- Case Review Board
- Clinical Events Committee
- Data Safety Monitoring Board

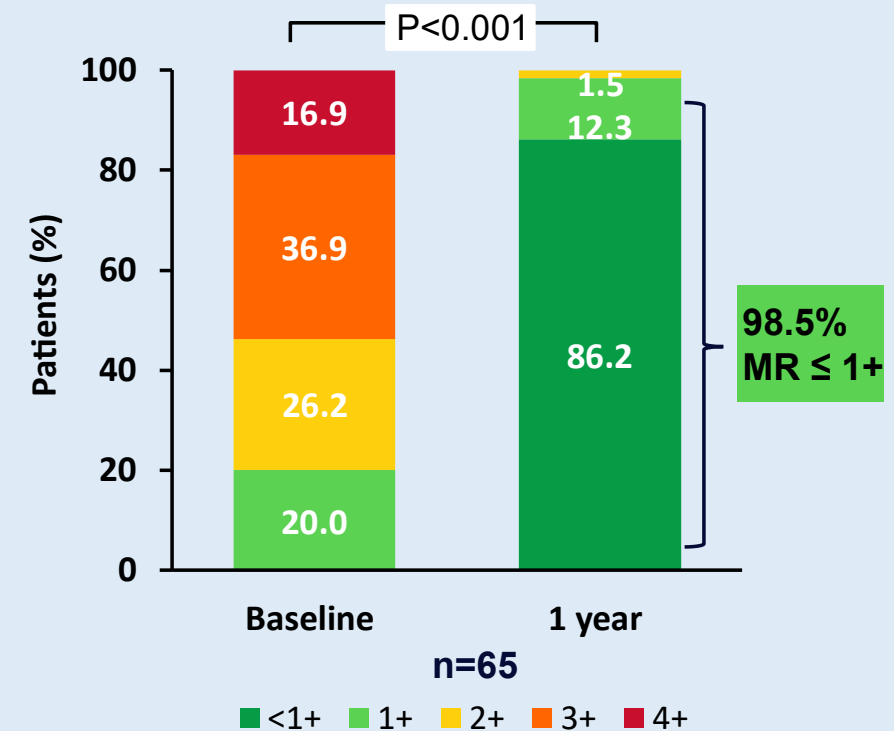


MR Severity

Unpaired



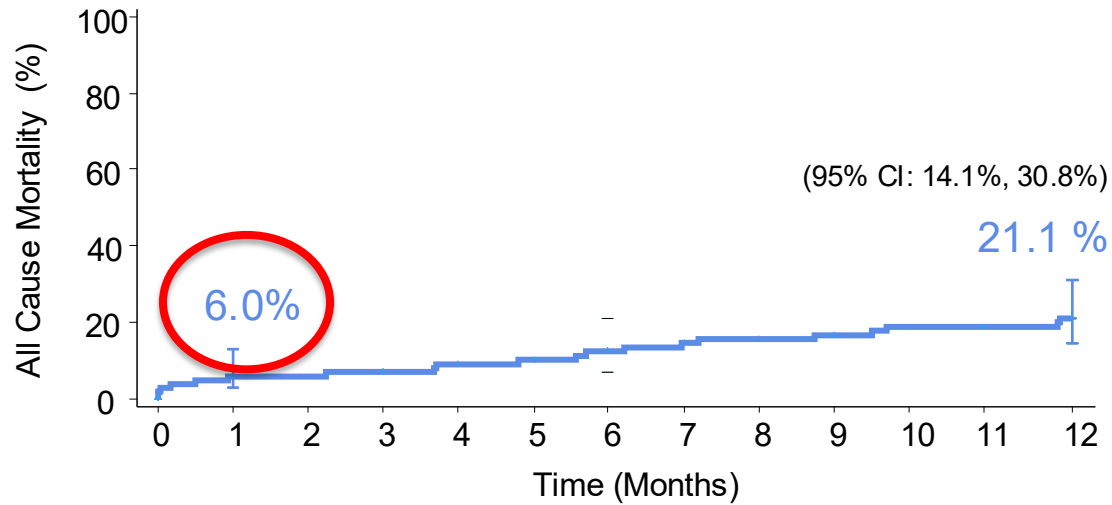
Paired



>98% patients had MR ≤1+ at 1 Year

Primary Endpoint Components

All-cause Mortality

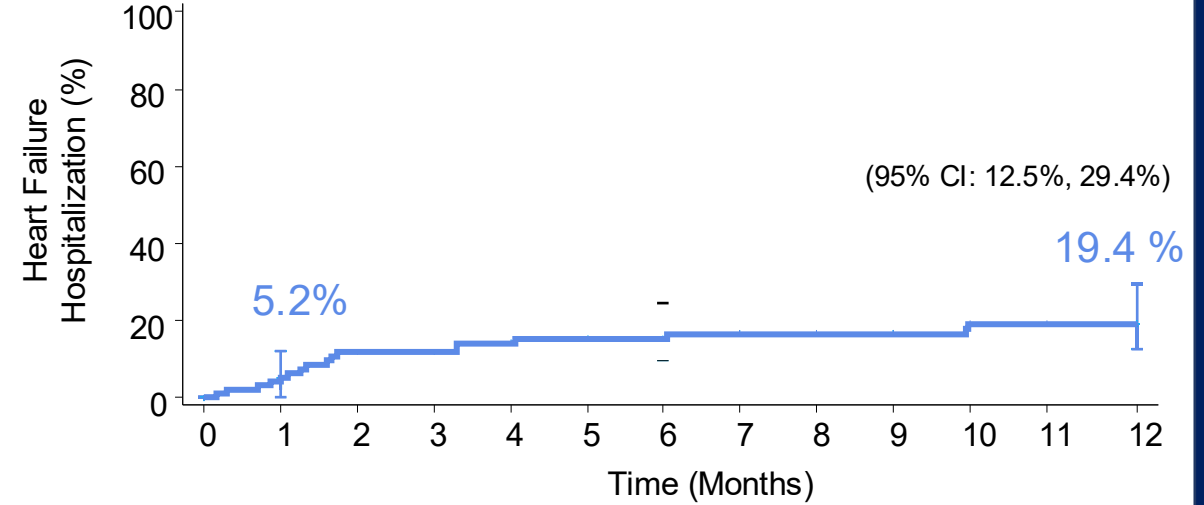


No. at Risk: 100 94

81

73

Heart Failure Hospitalization



No. at Risk: 100 90

69

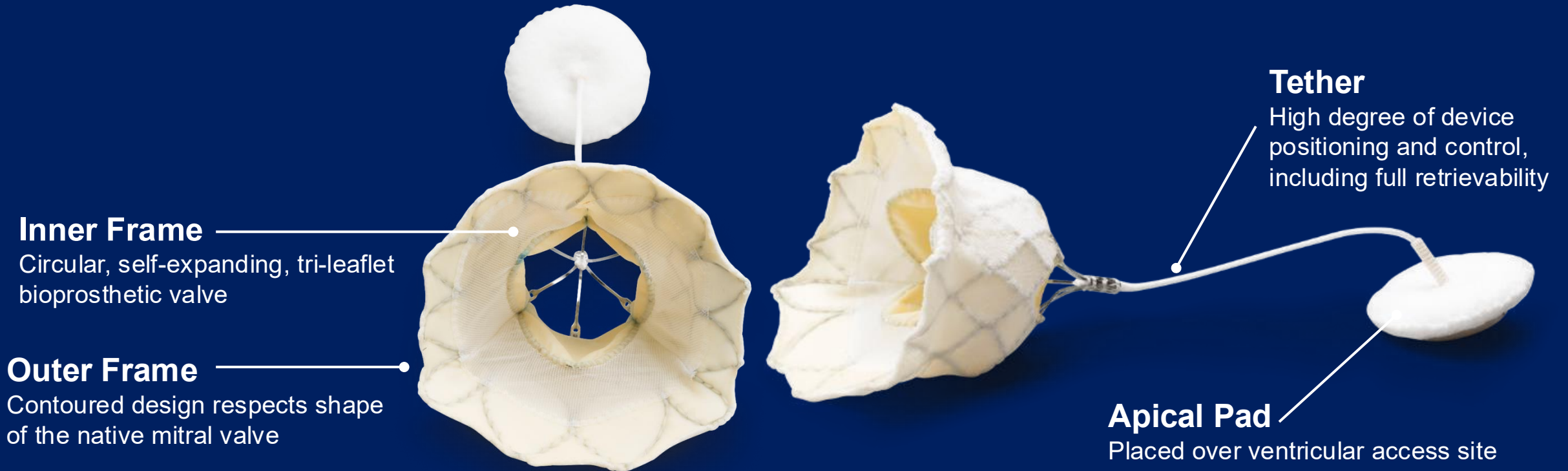
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Graphs show Kaplan-Meier estimated rates with 95% CIs.

Tendyne TMVR System

Designed for the Mitral Anatomy to Eliminate MR

Dual-frame design provides customized anatomic fit and maintains stable hemodynamic performance

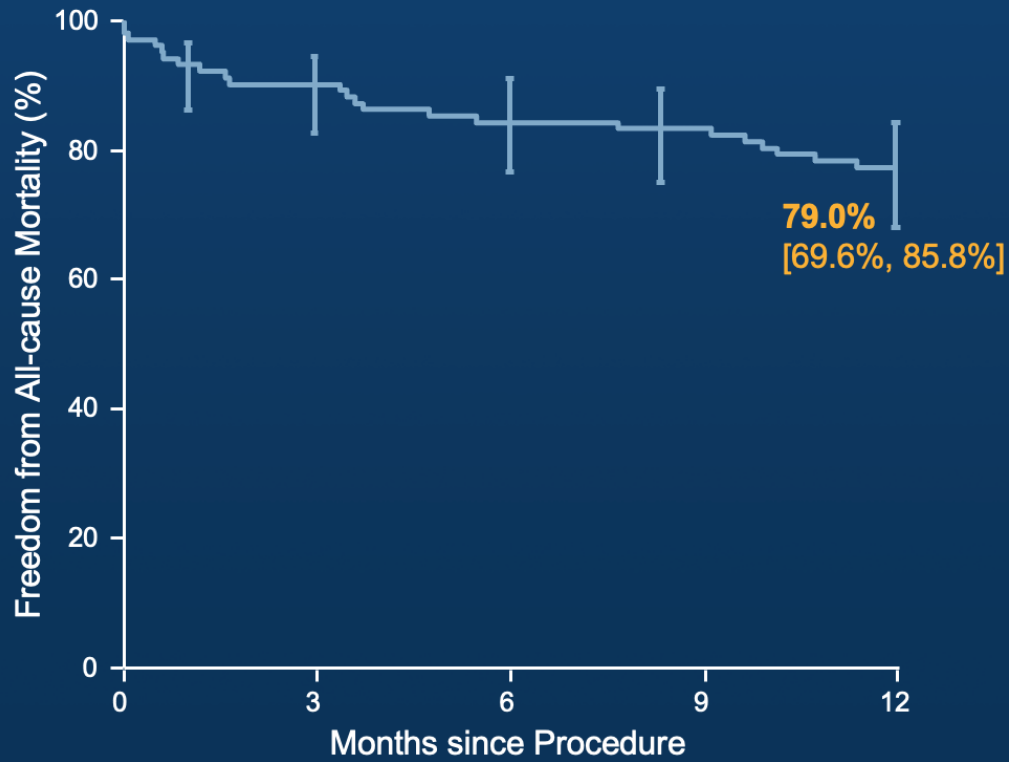


Five size options to meet the needs of diverse anatomies

34- 36 Fr Transapical

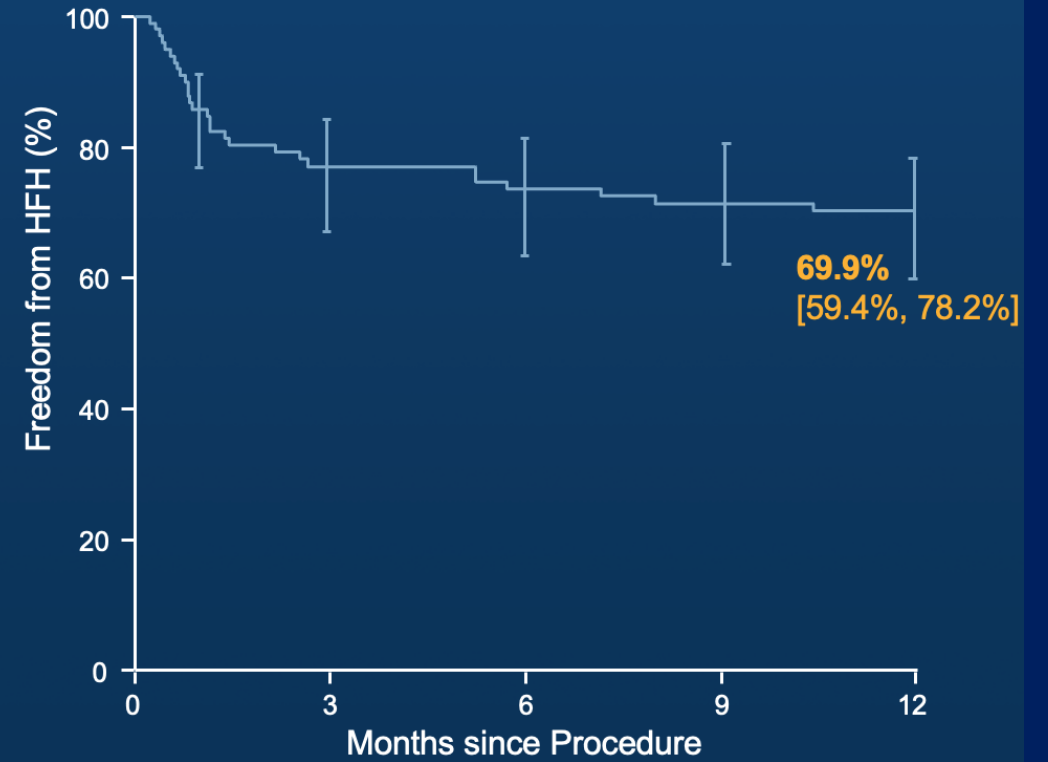
Tendyne Summit-MAC Trial

All-Cause Mortality



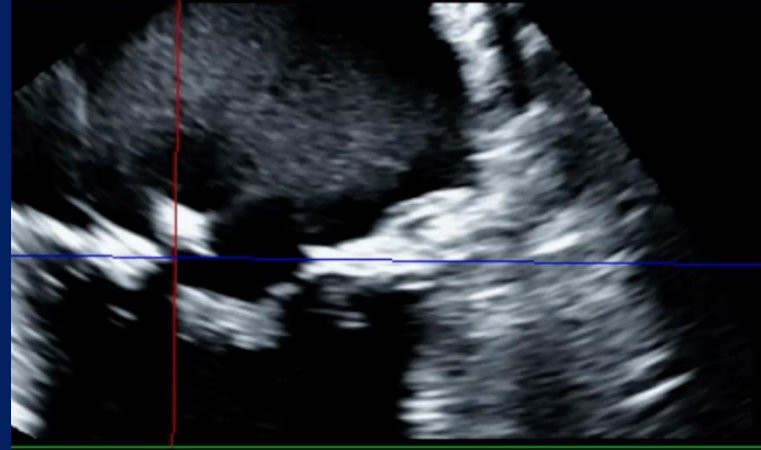
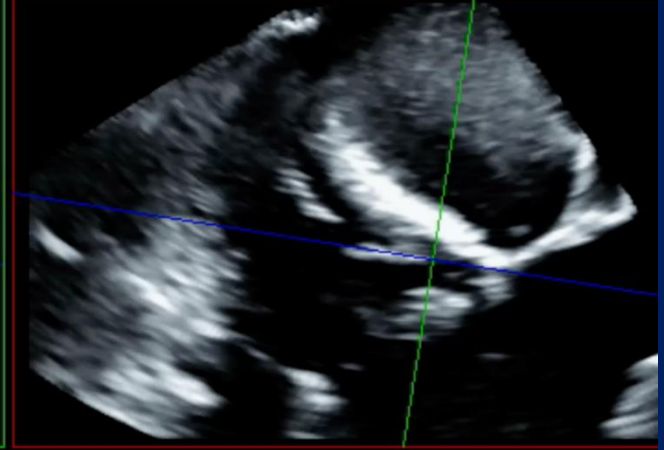
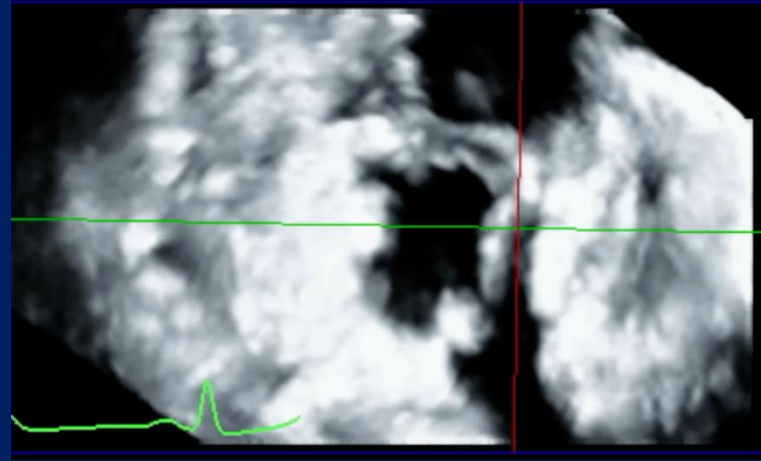
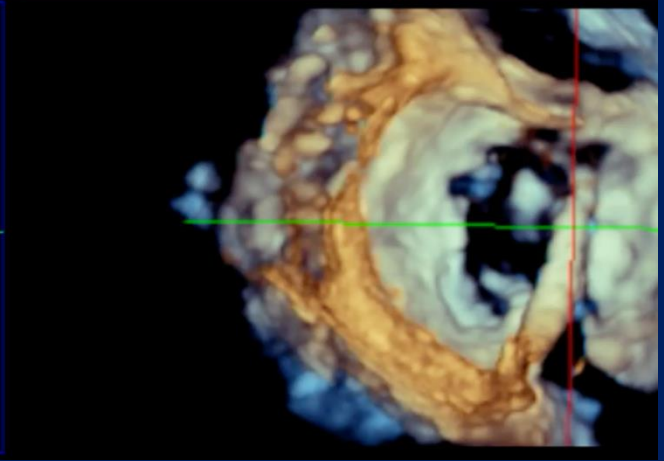
No. at Risk 103 90 85 83 72

Heart Failure Hospitalization

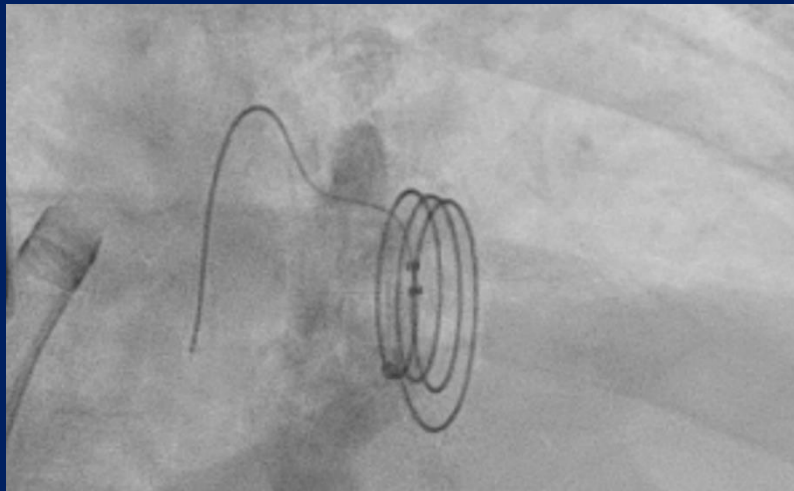
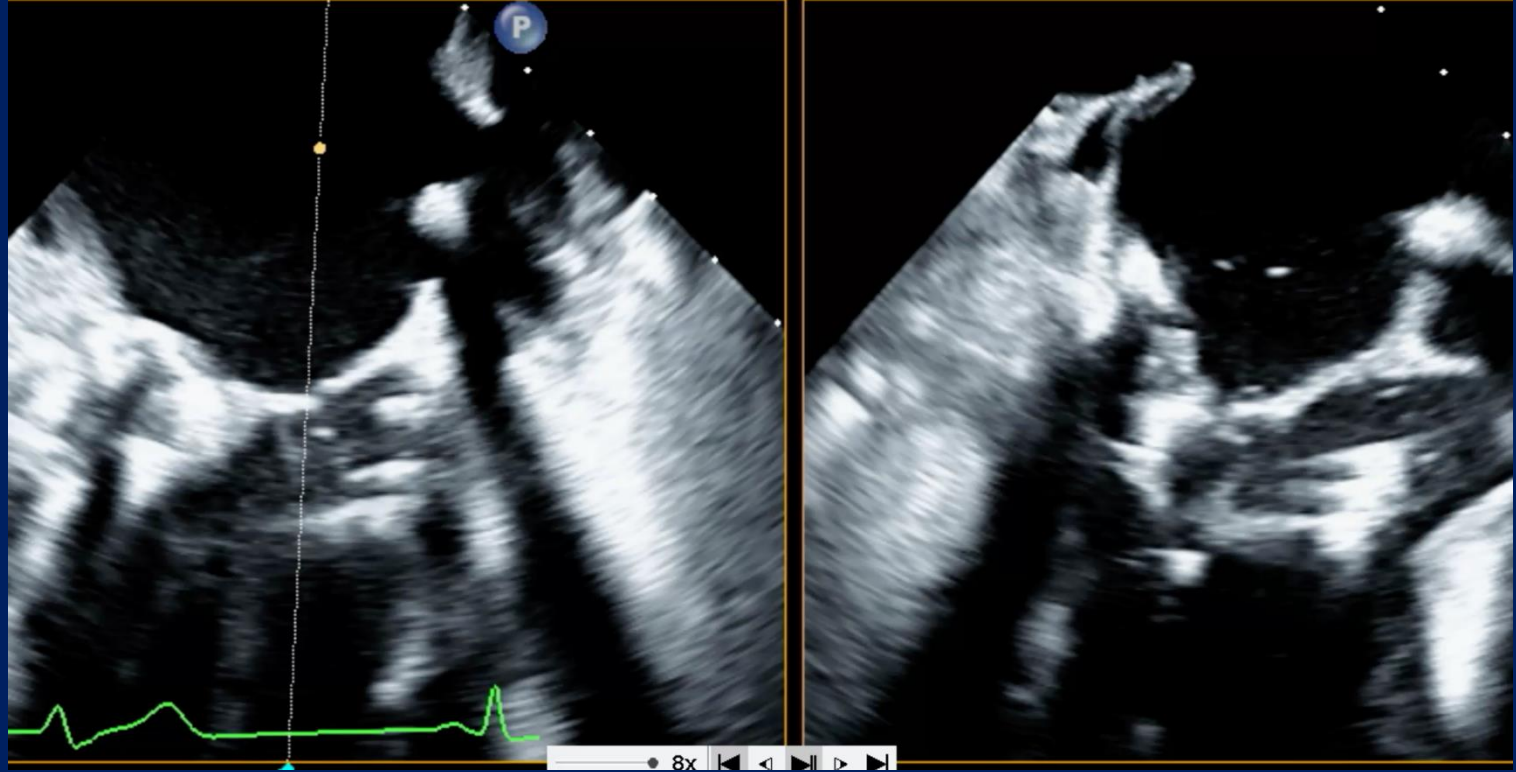


No. at Risk 103 68 64 61 55

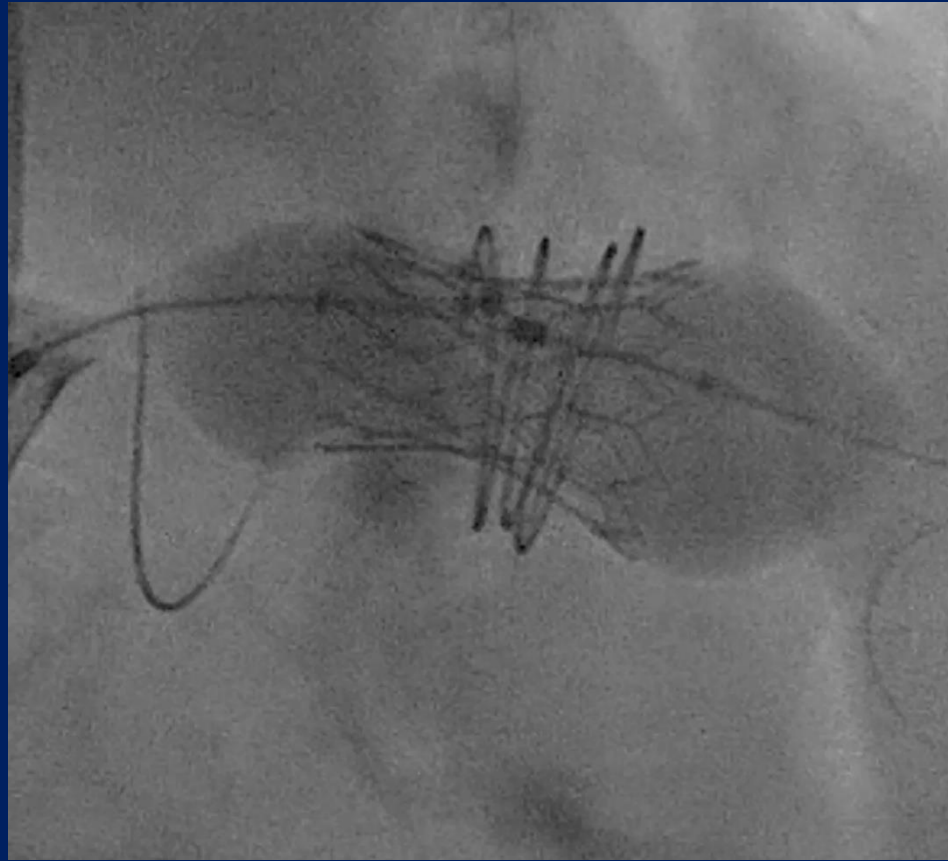
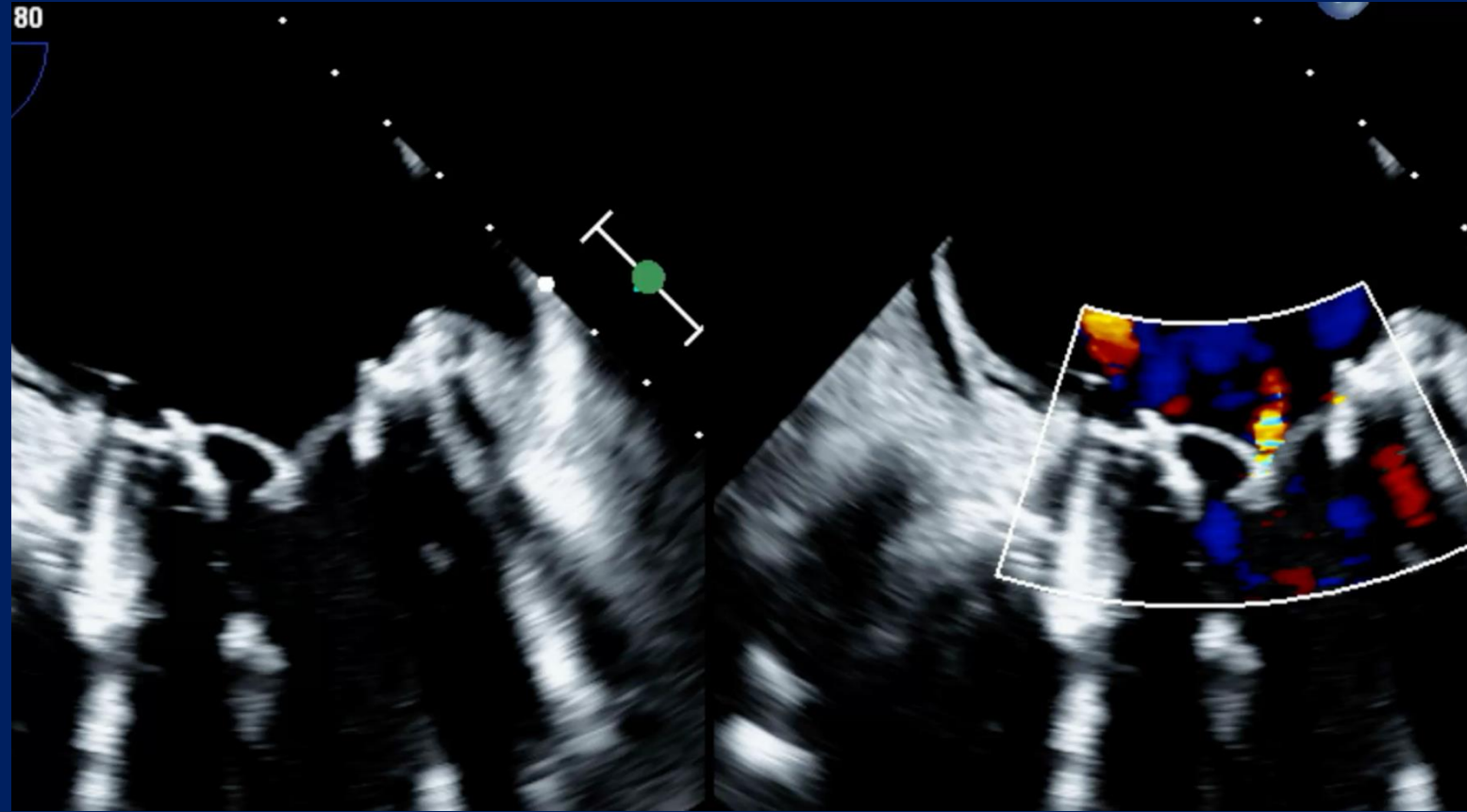
M3- Dock Deployment



M3- Dock Deployment



M3 Valve Deployment



Conclusion

- MAC associated MR is a difficult disease to treat
- Edwards Pascal TEER with its safe retrieval from chordal entrapment can be useful even in small valve area.
- Patients with adequate NeoLVOT can be treated successfully with Edwards M3 or Tendyne
- Sapien in MAC with leaflet or septal modification reserved for patients with no other options. (1 yr Mortality high)
- Newer Valves – Medtronic Intrepid can accommodate even smaller NeoLVOT- 100sqmm.

