Advances in Structural Heart Disease

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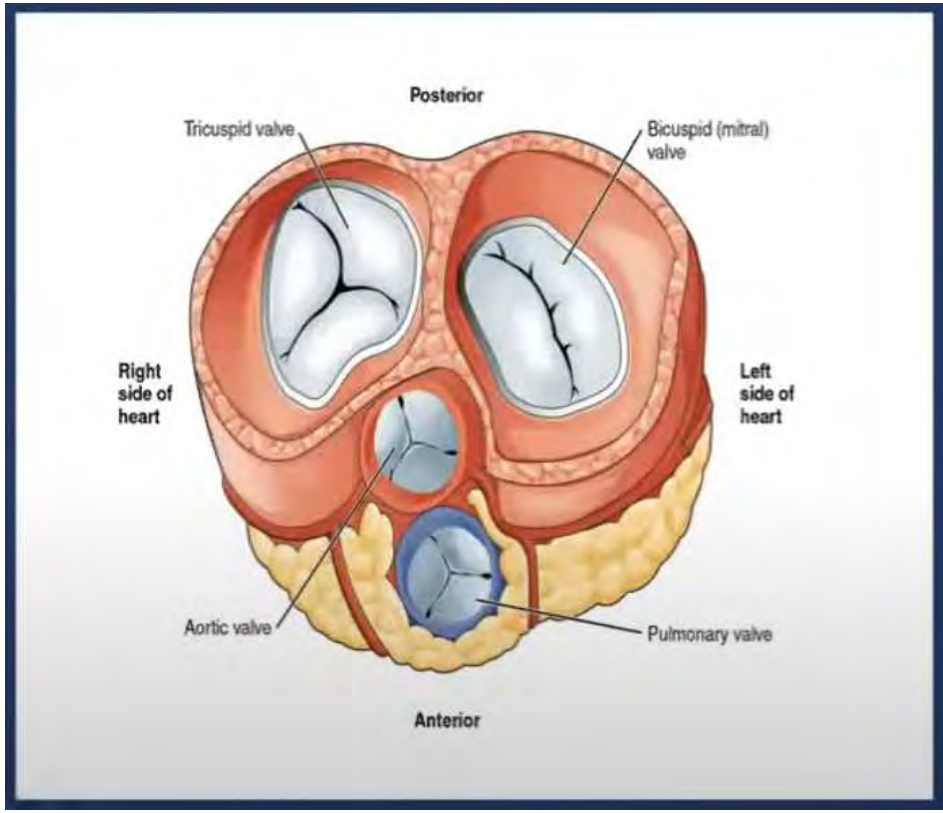
Disclosure

I have no financial conflicts of interest to disclose

Objectives

- Review state of the art of structural heart disease therapies in 2024
- The Heart Team in 2024
- Currently available transcatheter, minimally invasive surgical options for valvular heart disease

Transcatheter Therapies for Valvular Heart Diseases



Aortic

Mitral

Pulmonic

Tricuspid

"A valve is a device or natural object that regulates, directs or controls the flow of a fluid by opening, closing, or partially obstructing various passageways"

How do valves fail?

- Stenosis
- Regurgitation

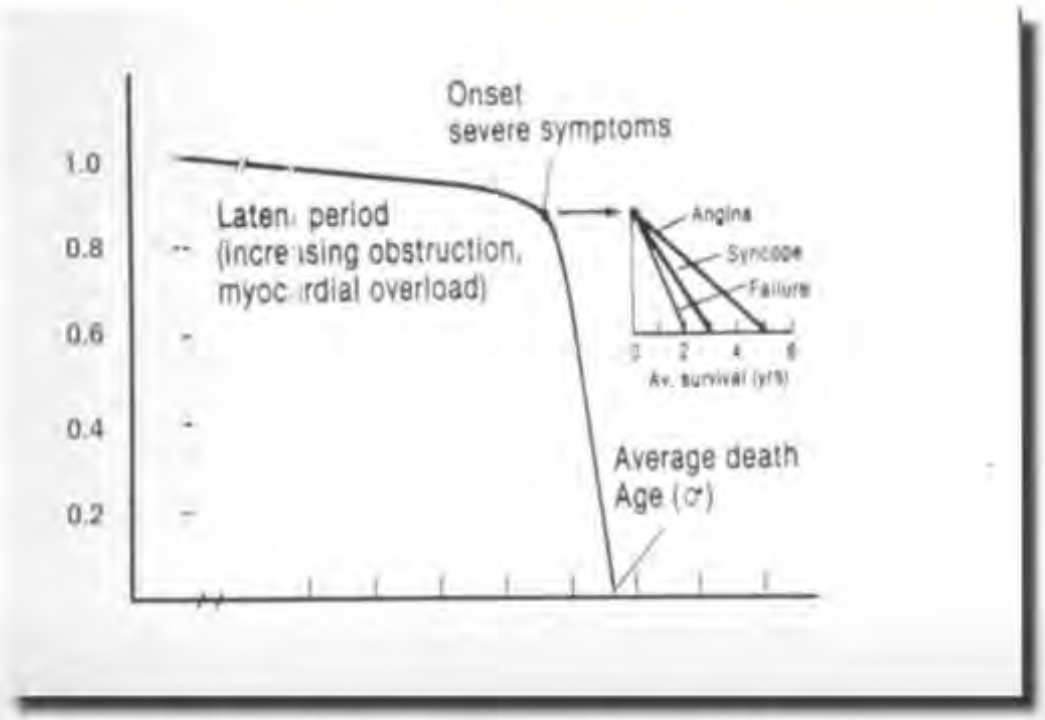
How to fix a broken valve?

- Repair
- Replacement

Aortic Valve

AS

Natural History of Aortic Stenosis



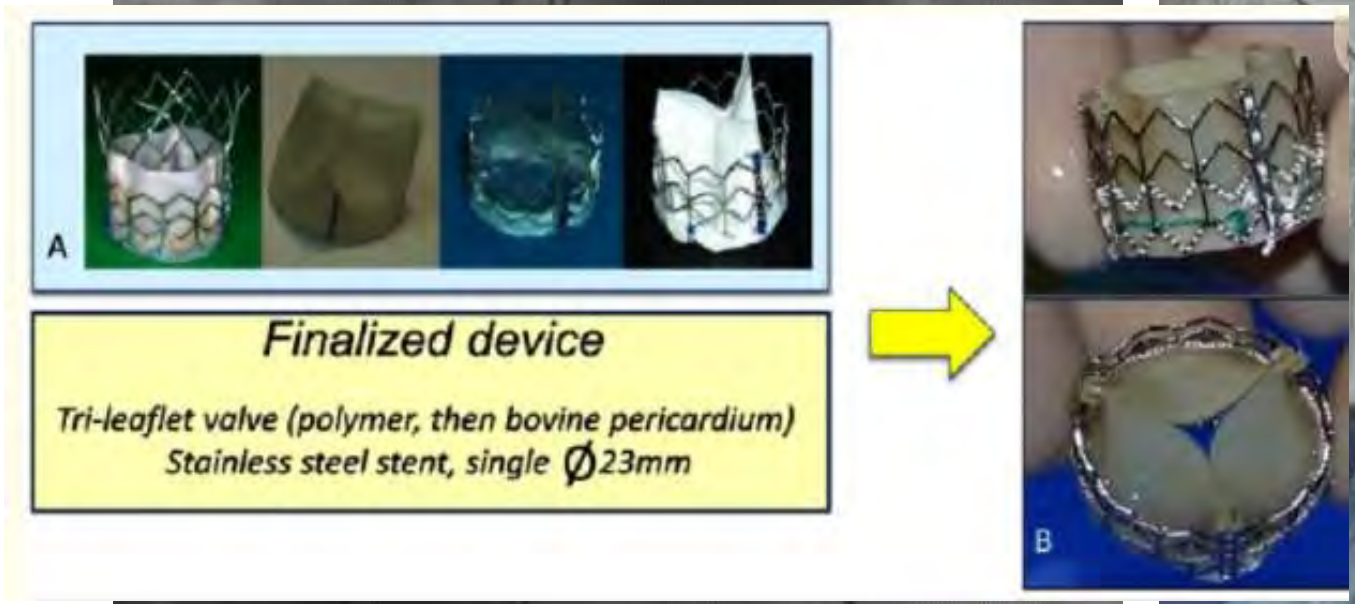
"Surgical intervention should be performed Promptly once … minor symptoms occur"

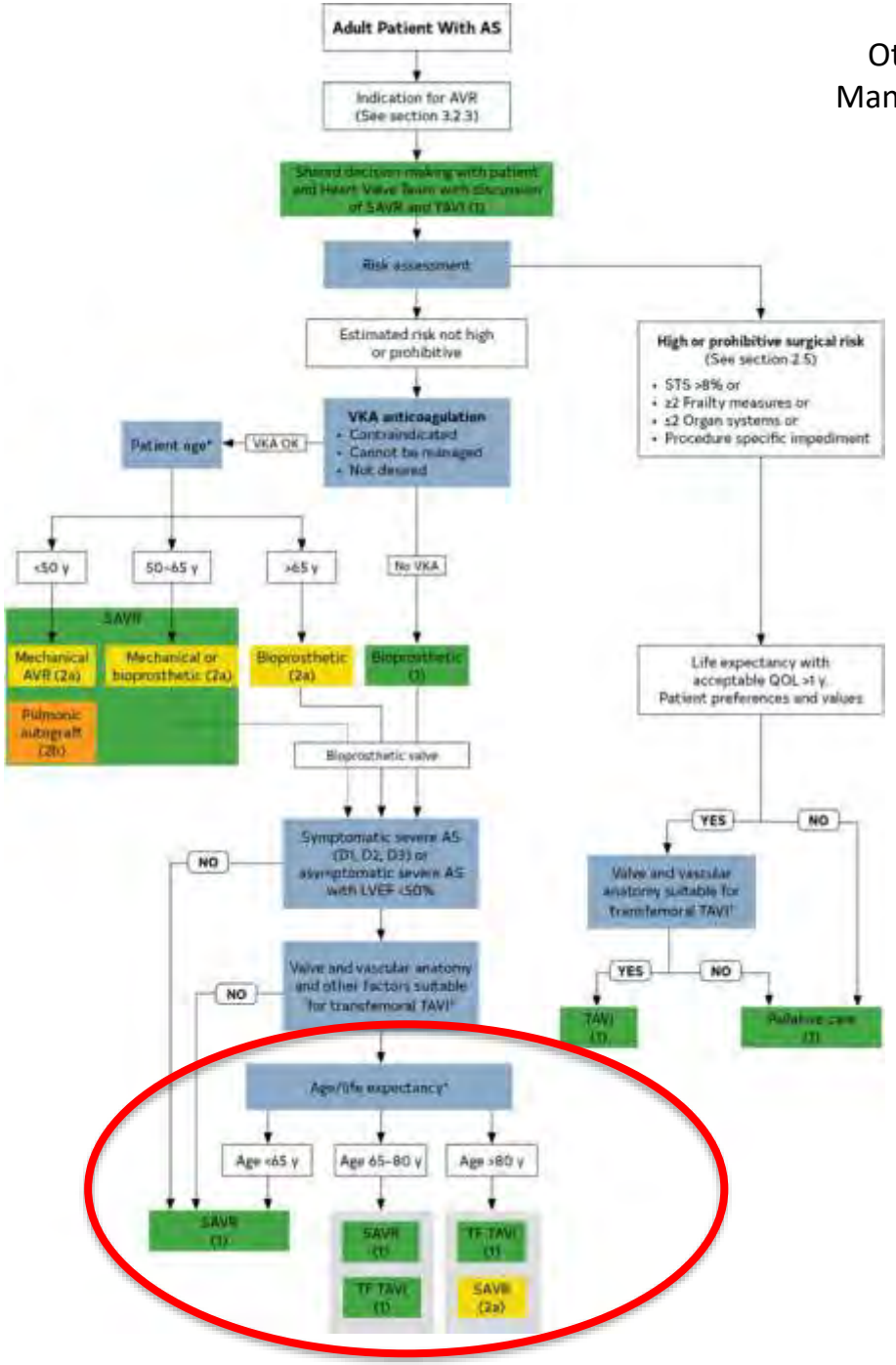
Surgical AVR improves survival, symptoms, and LV function

Sources: Ross J Jr, Braunwald E. Aortic stenosis. *Circulation 1968;38*
C.M. Otto. Valve Disease: Timing of Aortic Valve Surgery. Heart 2000.

April 16, 2002 – First in Man TAVR via Transseptal Approach

On April 16, 2002, at the Charles Nicolle University Hospital in Rouen, France, the Interventional Cardiologist, Professor Alain Cribier performed the first transcatheter aortic valve replacement procedure in the world.
He used a Percutaneous Valve Technology (PVT) percutaneous heart valve.





Otto C, Nishimura R, et al. 2020 ACC/AHA Guideline for the Management of Patients With Valvular Heart Disease. J Am Coll Cardiol. 2021 Feb, 77 (4) e25–e197

The Heart Team – Then and Now

Now – The Role of The Heart Team has Gotten More Complicated!

- Treatment focus has now shifted from the first to the second aortic intervention (i.e., to the treatment of bioprosthetic failure), regardless of whether the first intervention is SAVR or TAVR.

- **Anatomy:**
  - Will redo TAVR be straightforward or complex (i.e., require leaflet modification)?
  - Will coronary access be an issue, both now and with future THV in THV?

- **Durability:**
  - Bioprosthetic vs mechanical valve
  - How long will a bioprosthetic valve last?

- **Hemodynamics:**
  - What size (ID) and type of SAVR will be used?
  - Will the SAVR be compatible with future VIV TAVR?

- **Other Considerations:**
  - Significant mitral or tricuspid valve disease
  - Multivessel or significant CAD
  - Patient preference

Mature Space (20th anniversary of TAVR)

New Transcatheter Heart Valves (THV) for AS

Indication Expansion

New Transcatheter Heart Valves (THV) for AR

April 16, 2002; FIM-TAVI; Rouen, FR

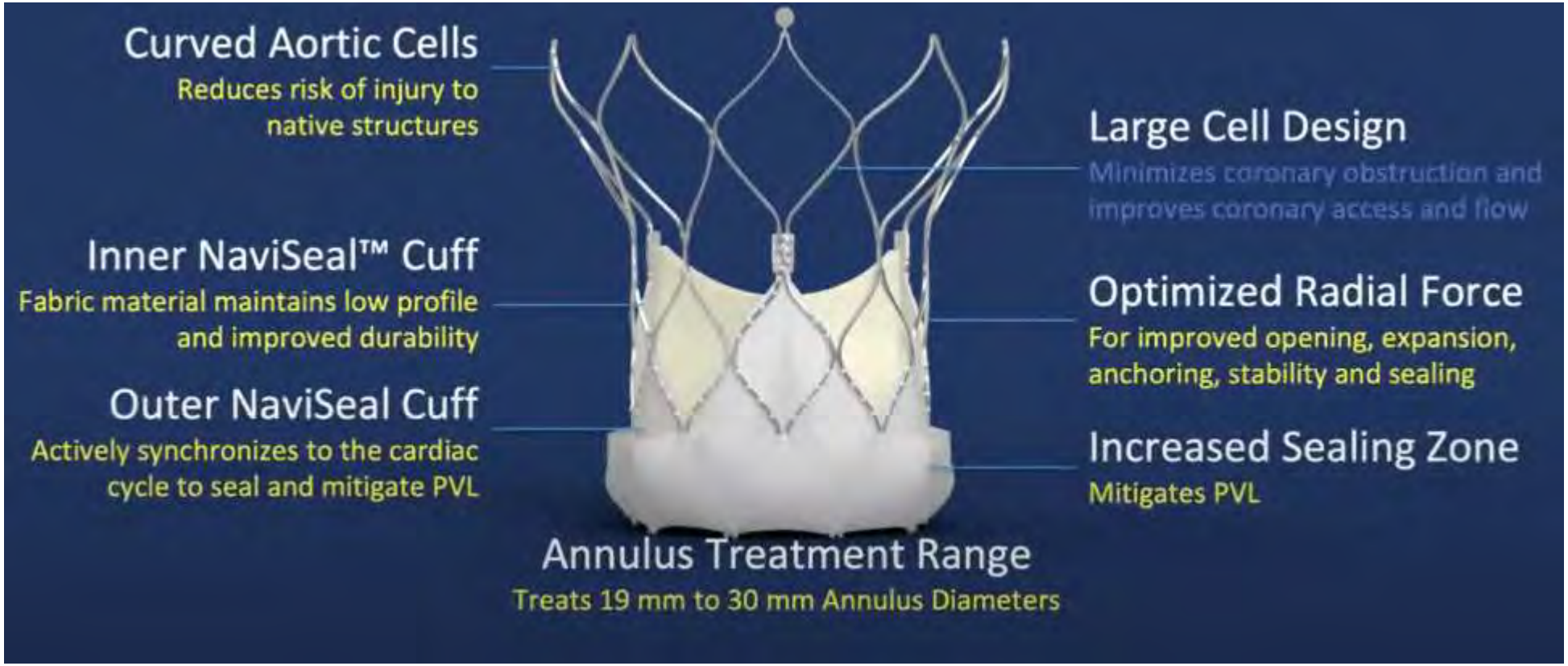
15 min post-TAVI

EDWARDS SAPIEN

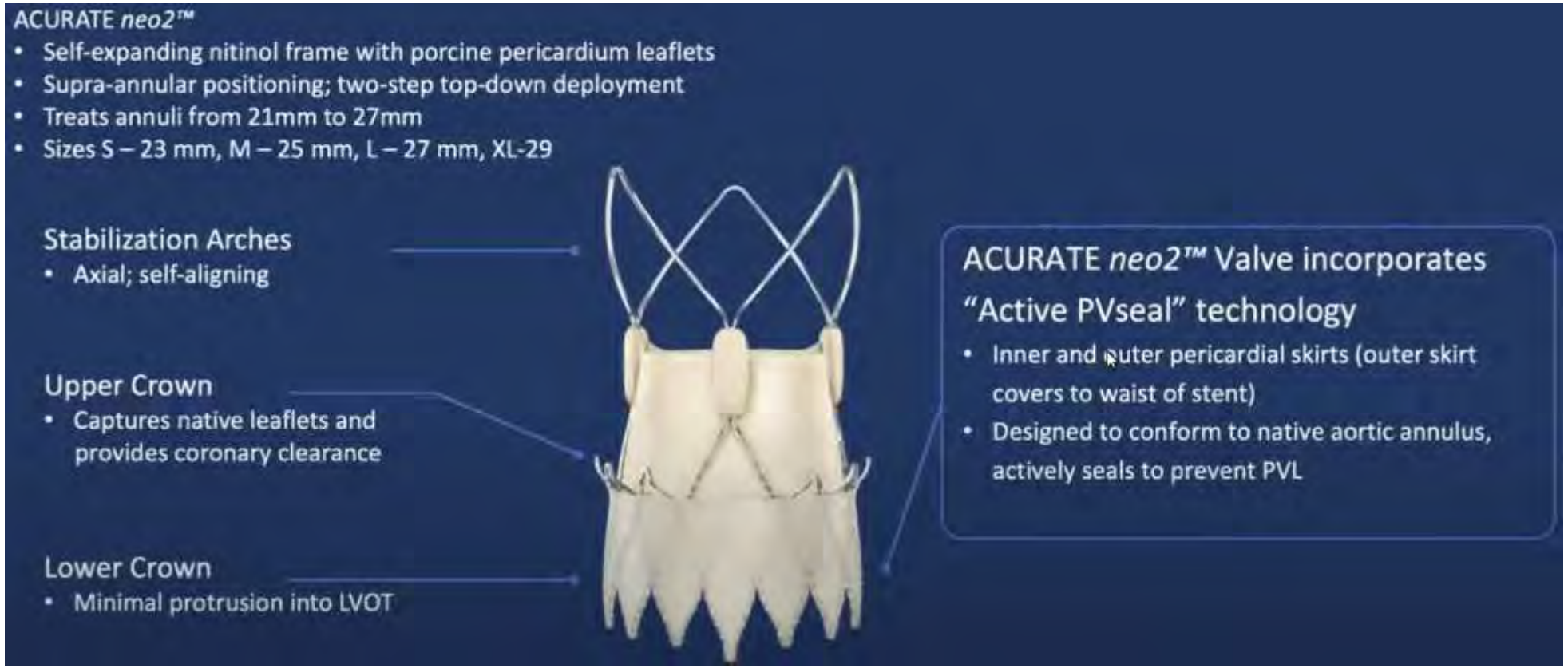
Medtronic Evolut

4 FDA-approved TAVR valves expected to be in the US market in 2024-2025!!

Navitor THV


Curved Aortic Cells
Reduces risk of injury to native structures
Inner NaviSeal™ Cuff
Fabric material maintains low profile and improved durability
Outer NaviSeal Cuff
Actively synchronizes to the cardiac cycle to seal and mitigate PVL
Large Cell Design
Minimizes coronary obstruction and improves coronary access and flow
Optimized Radial Force
For improved opening, expansion, anchoring, stability and sealing
Increased Sealing Zone
Mitigates PVL
Annulus Treatment Range
Treats 19 mm to 30 mm Annulus Diameters

ACURATE neo 2 THV



Sapien X4

Enhancing versatility and control to provide personalized TAVR treatment

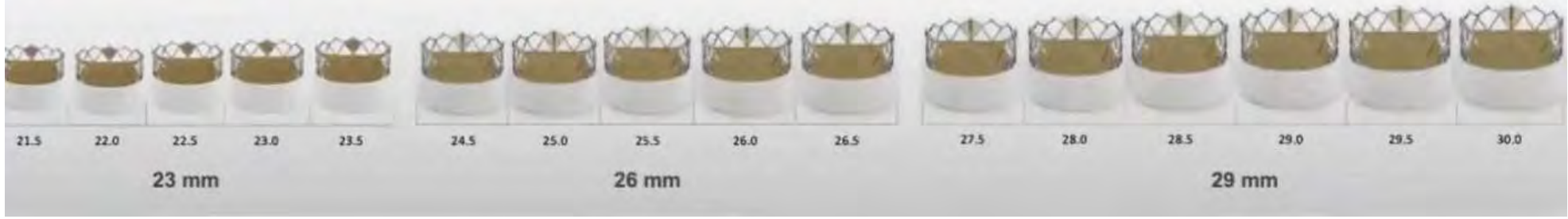
Adjustable valve sizes to optimize the index procedure while enabling lifetime therapy management (PCI, TAV in TAV)

SAPIEN 3 Ultra

4 valve sizes (3 mm increments)

SAPIEN X4

3 valve sizes, 16 deployment diameters (0.5 mm increments)



Expanding TAVR Indications – Asymptomatic and Moderate AS

Interpreting Symptoms is Difficult

Interpreting symptoms is difficult, especially in elderly and sedentary populations.

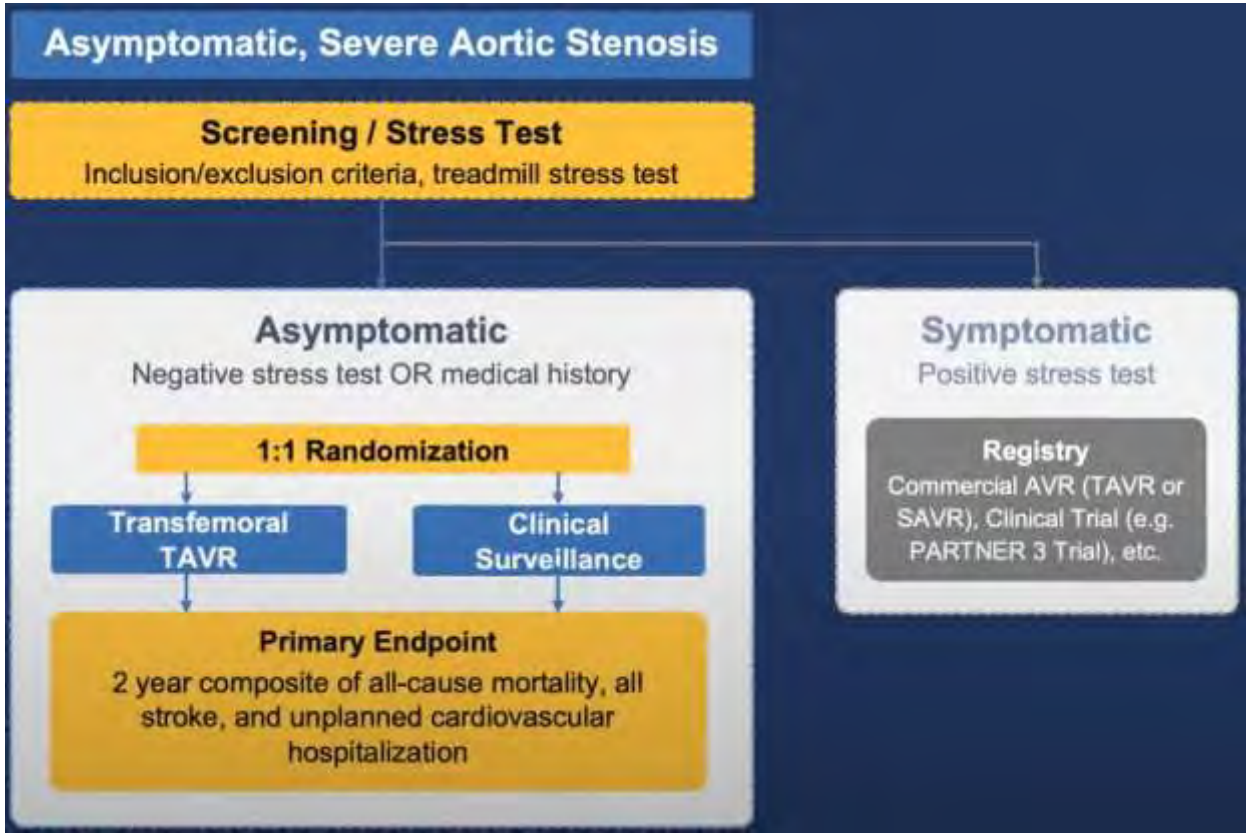
up to **49%**

Up to 49% of patients that report no symptoms at time of diagnosis have an abnormal stress test.[4]

These patients have a 6-fold increased risk of cardiac death. AVR is recommended.

Stages/Criteria	Stage 0	Stage 1	Stage 2	Stage 3	Stage 4
	No Cardiac Damage	LV Damage	LA or Mitral Damage	Pulmonary Vasculature or Tricuspid Damage	RV Damage
Echocardiogram		Increased LV Mass Index >115 g/m² (Male) >95 g/m² (Female)	Indexed LA Volume >35 mL/m²	Systolic Pulmonary Hypertension >60 mm Hg	Moderate-Severe Right Ventricular Dysfunction
		E/e' >14	Moderate-Severe Mitral Regurgitation	Moderate-Severe Tricuspid Regurgitation	
		LV Ejection Fraction <50%	Atrial Fibrillation		

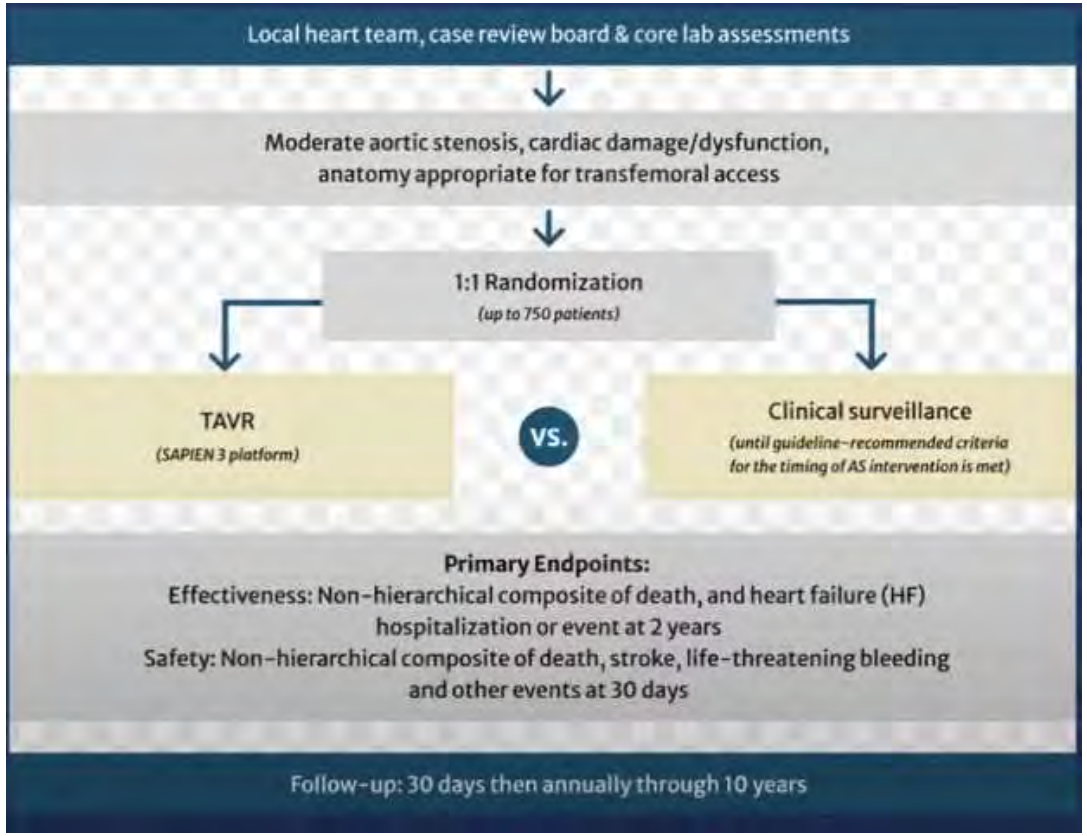
Early TAVR Trial



Généreux P, Schwartz A, Oldemeyer B, Cohen DJ, Redfors B, Prince H, Zhao Y, Lindman BR, Pibarot P, Leon MB. Design and rationale of the evaluation of transcatheter aortic valve replacement compared to surveillance for patients with asymptomatic severe aortic stenosis: The EARLY TAVR trial. Am Heart J. 2024 Feb;268:94-103. doi: 10.1016/j.ahj.2023.11.019. Epub 2023 Dec 4. PMID: 38056546.

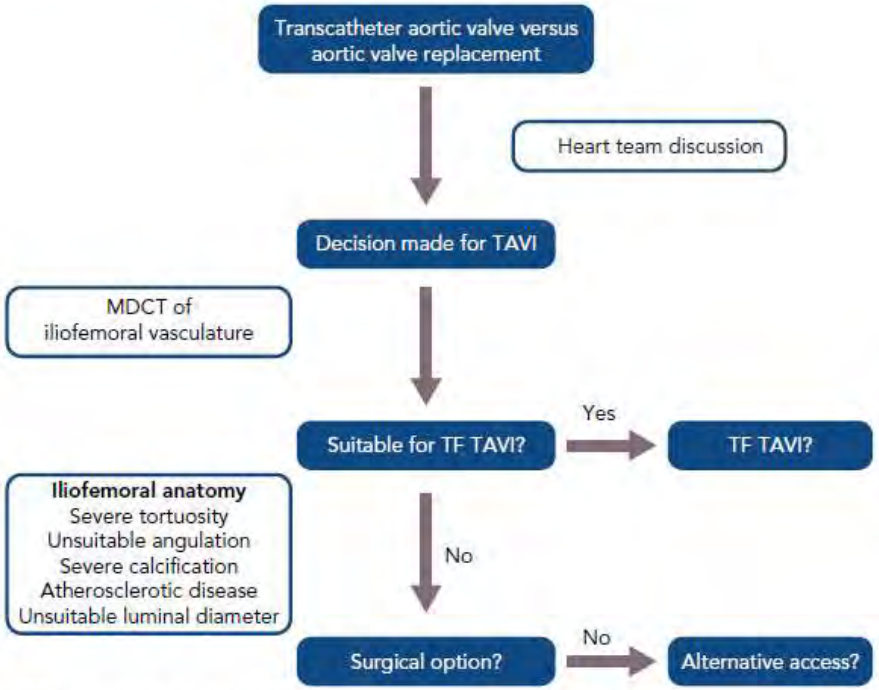
Moderate AS

THE PROGRESS TRIAL



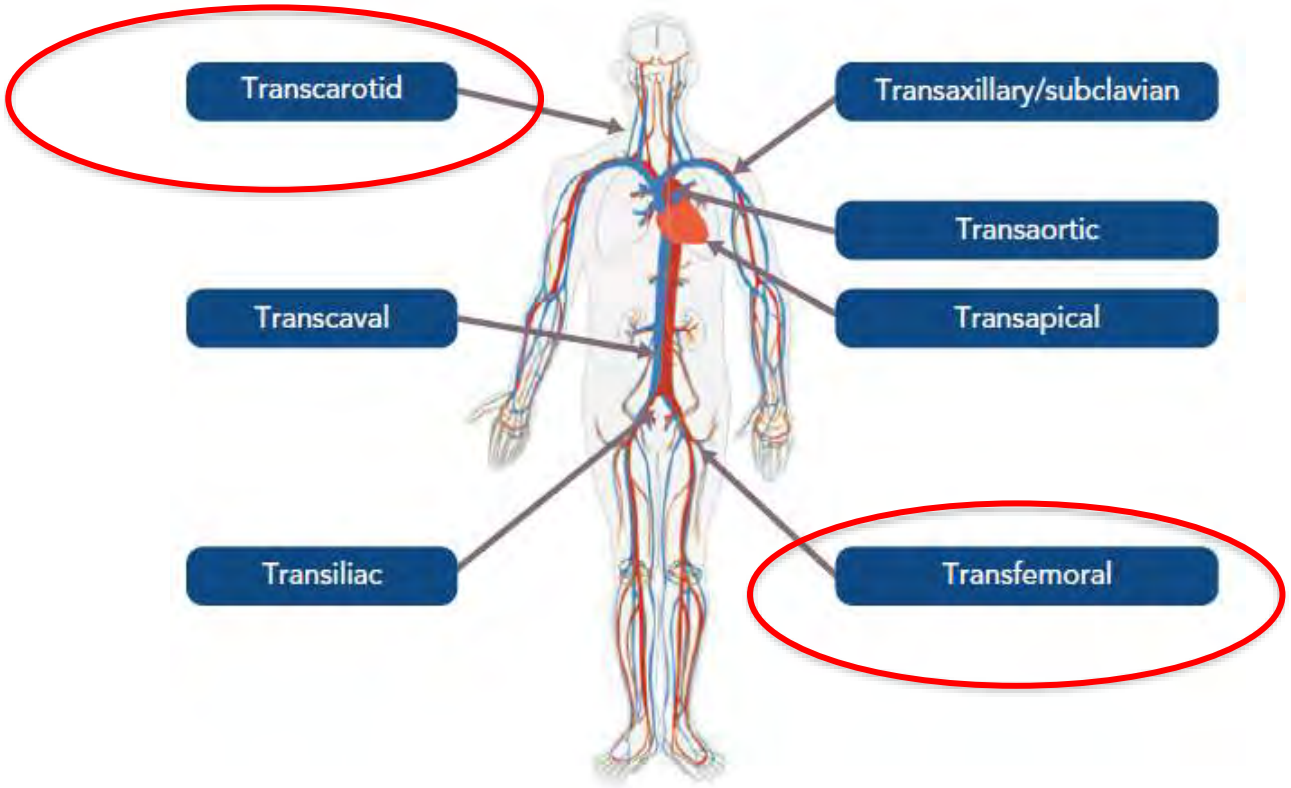
Access Sites for TAVR & Alternative Access TAVR

Figure 1: Algorithm for Deciding if Patient is a Candidate for Alternative Access Transcatheter Aortic Valve Implantation



MDCT = multiple detector CT; SAVR = surgical aortic valve replacement; TAVI = transcatheter aortic valve implantation; TF = transfemoral.

Figure 2: Access Options in Modern Transcatheter Aortic Valve Implantation

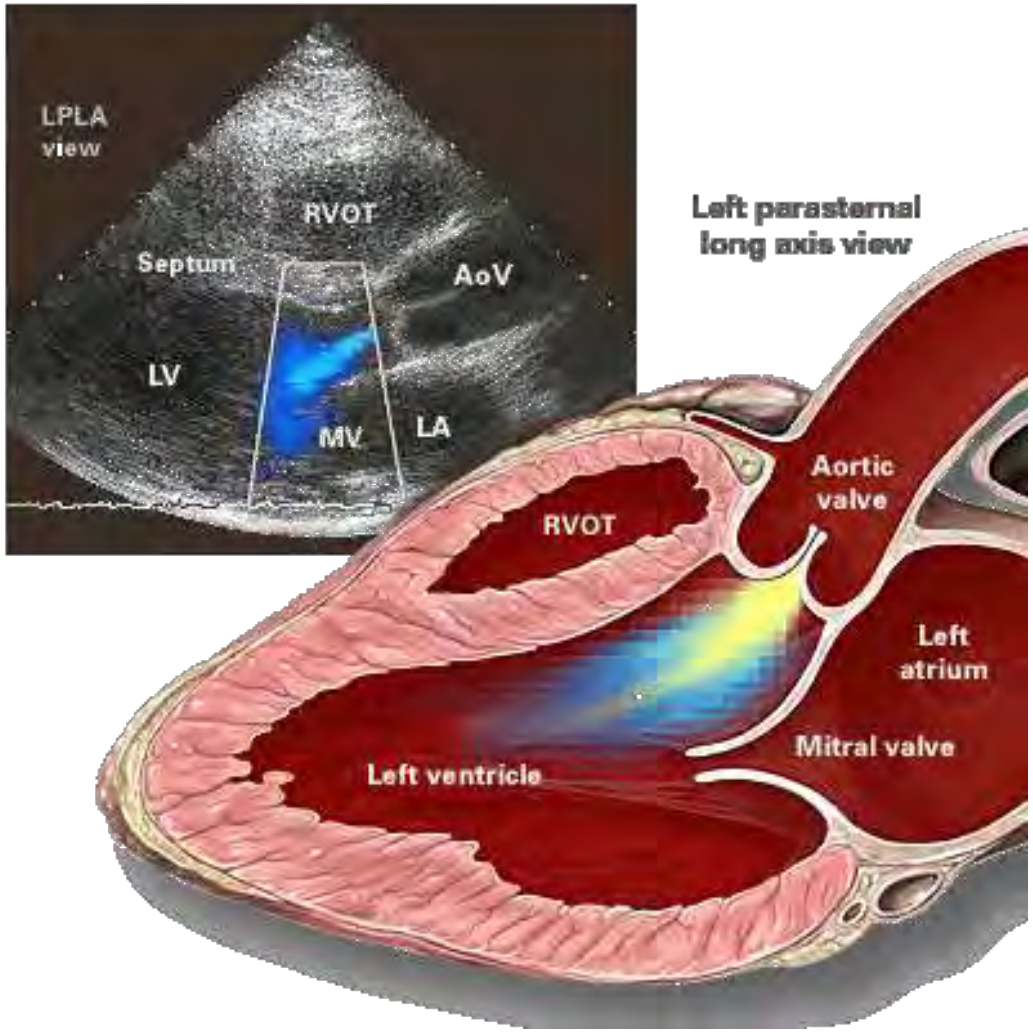


Coughlan J et al. Vascular & Endovascular Review 2019;2(1):23–7

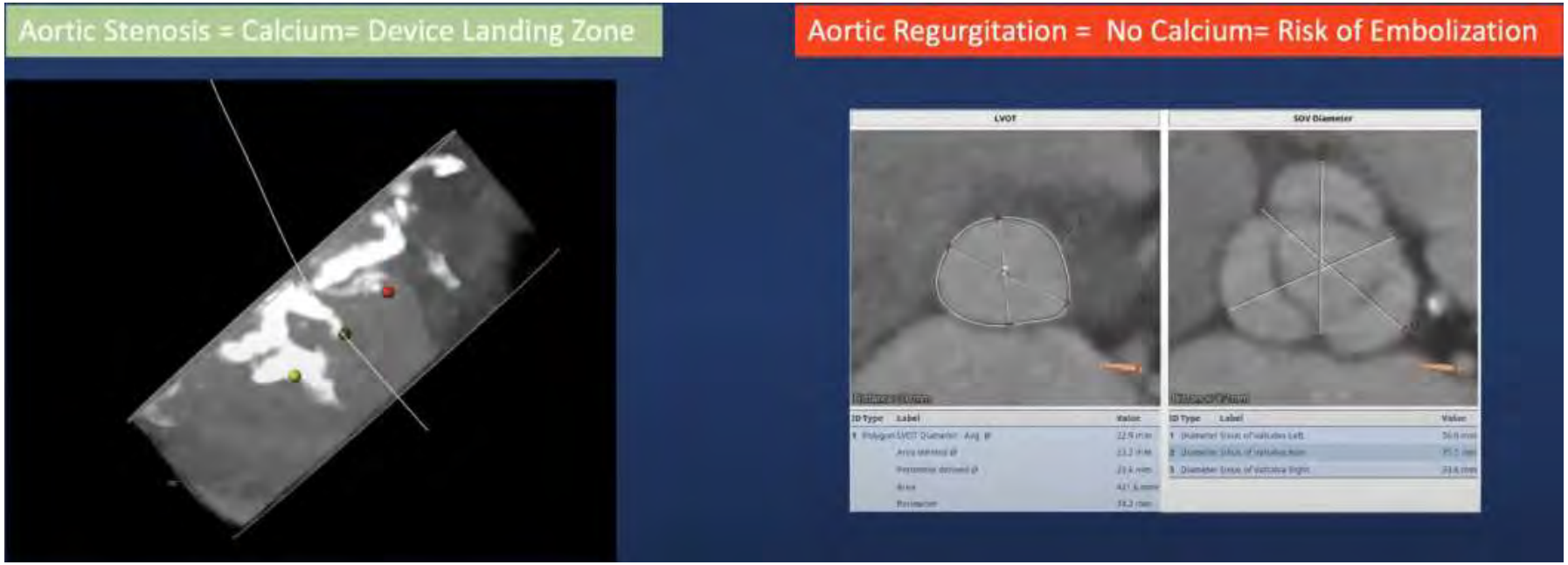
Alternative Access TAVR via the Carotid Artery

Room setup: L

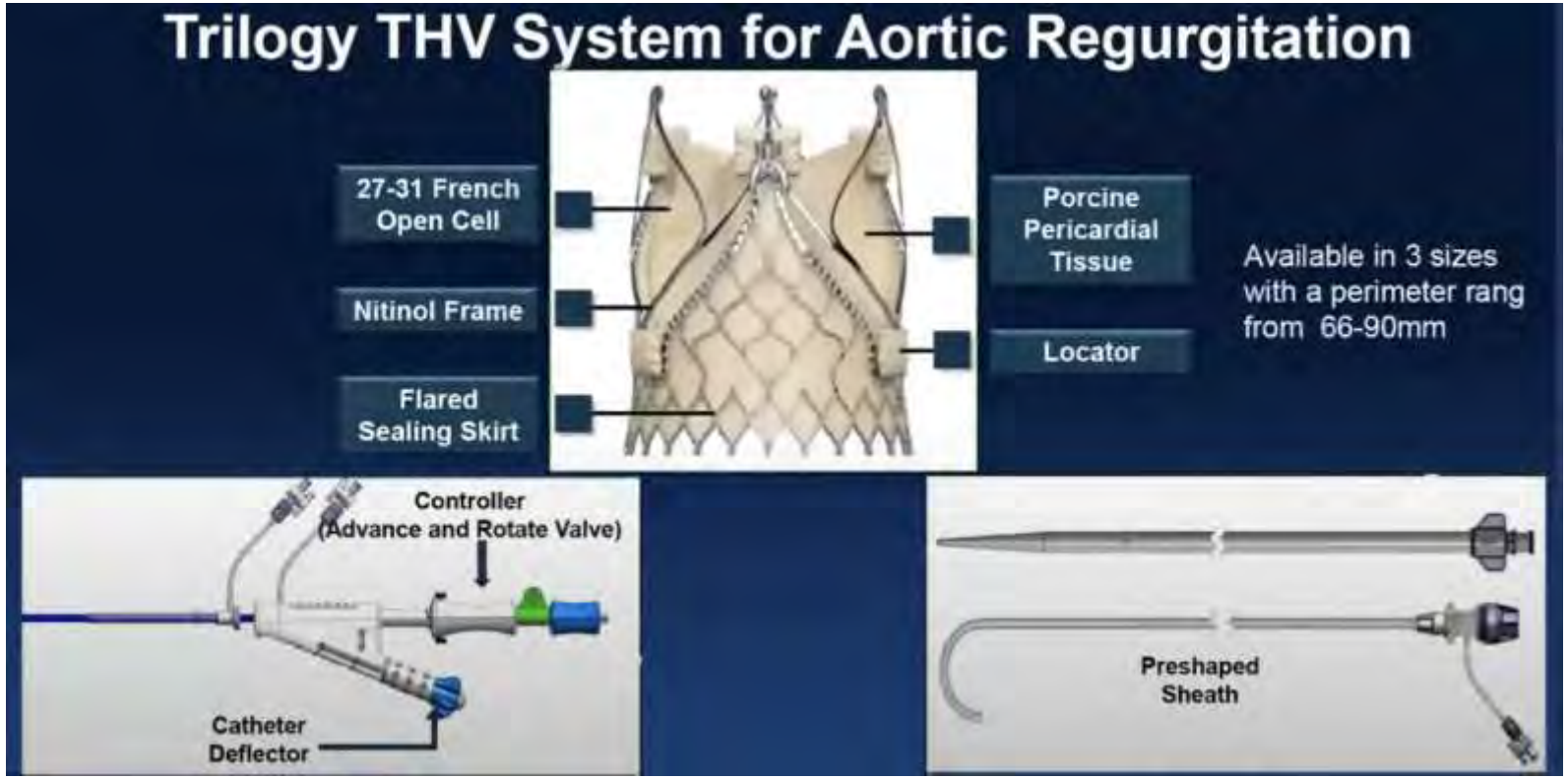
Aortic Regurgitation



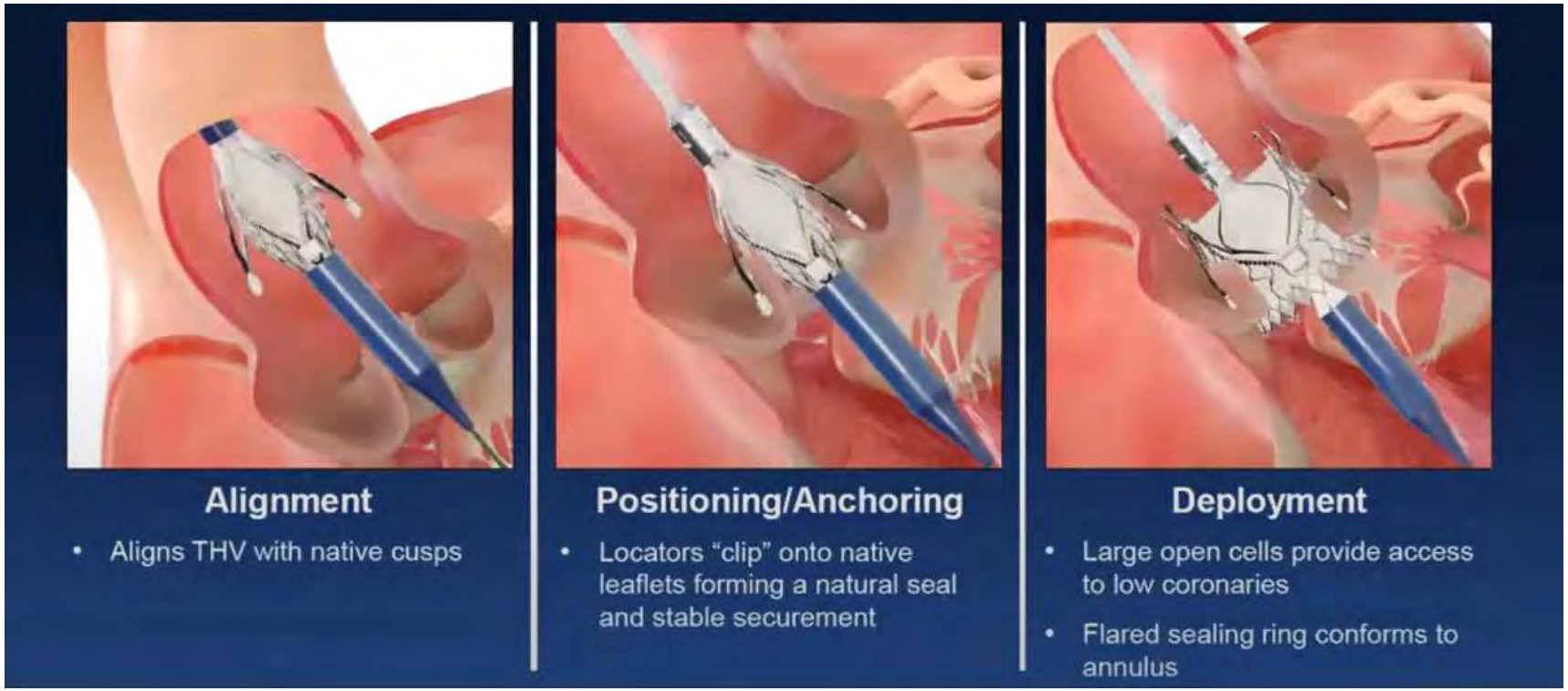
Why Do We Need Dedicated THVs for Aortic Regurgitation



JenaValve


Trilogy THV System for Aortic Regurgitation
27-31 French Open Cell
Nitinol Frame
Flared Sealing Skirt
Porcine Pericardial Tissue
Locator
Available in 3 sizes with a perimeter rang from 66-90mm
Controller (Advance and Rotate Valve)
Catheter Deflector
Preshaped Sheath

JenaValve Trilogy TAVR System



JenaValve Trilogy TAVR System

Procedural Outcomes

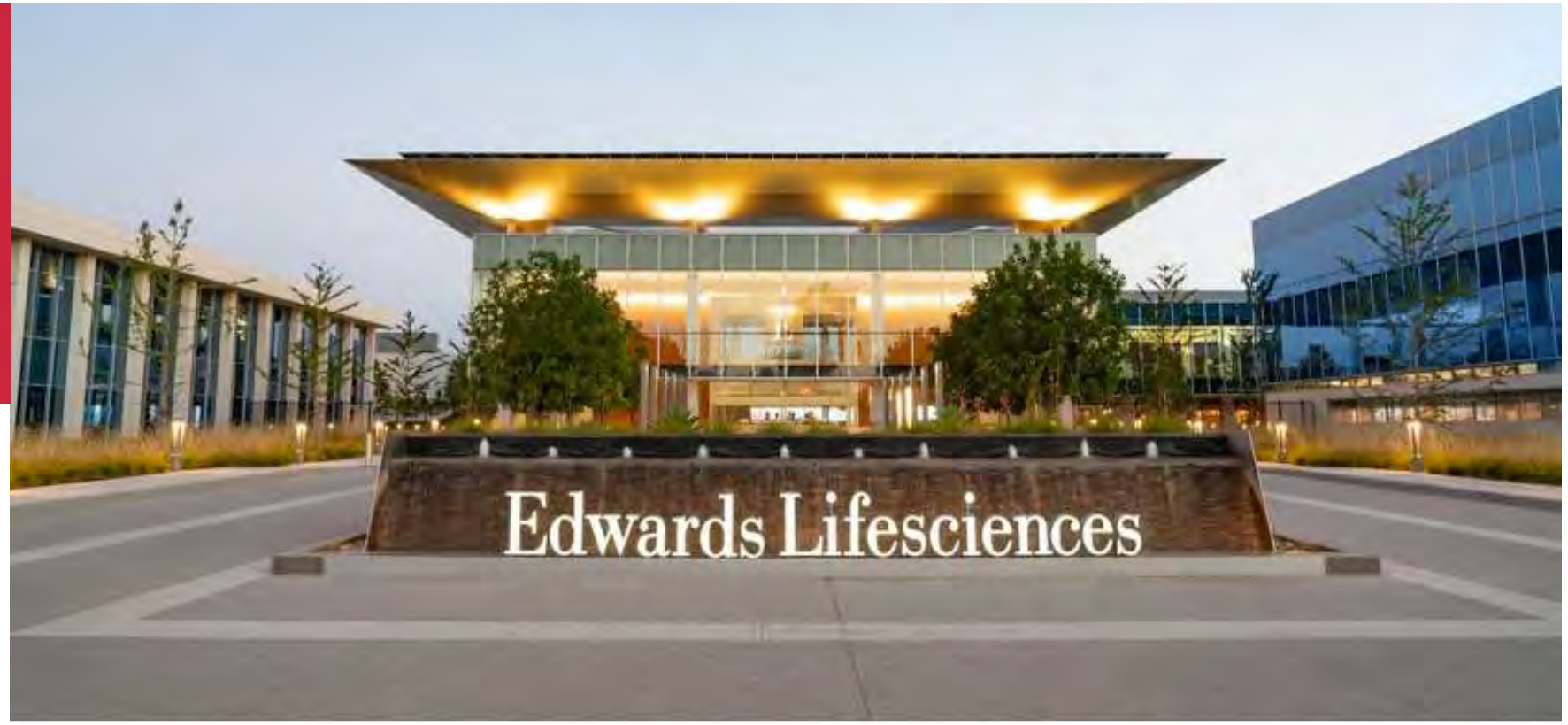
Outcome	% (n)
In-procedural Death	0
Annular Rupture	0
Ventricular Perforation	0
Coronary Obstruction	0
Valve Embolization	2.2% (4)
Aortic Dissection	0.6% (1)
Femoral Access Site Intervention	2.2% (4)
Success Technical Success Device Success Procedure Success	 95.0% (171) 96.7% (174) 92.8% (167)

Primary Safety Endpoint at 30 Days

Variable	% (n)
All Cause Mortality	2.2% (4)
Cardiovascular Mortality	2.2% (4)
Any Stroke Disabling Stroke Nondisabling Stroke	2.2% (4) 1.1% (2) 1.1% (2)
Major/Life Threatening Bleeding	4.4% (8)
Major Vascular Complication	3.9% (7)
Acute Kidney Injury Stage 2 or 3 or Dialysis (7 Days)	1.1% (2)
Surgery/Intervention Related to the Device	2.8% (5)
New Pacemaker Implantation Pre-existing PPM	24.0% (36) 16.7% (30)
≥ Moderate Paravalvular Regurgitation	0.6% (1)
Total	26.7% (48)

JenaValve

Press releases



Edwards Lifesciences reported its second-quarter earnings results this week, with growth coming in below expectations for its mainstay transcatheter aortic valve replacement business. (Edwards Lifesciences)

Edwards Lifesciences is dropping about $1.6 billion on a pair of acquisitions to bolster its structural heart portfolio.

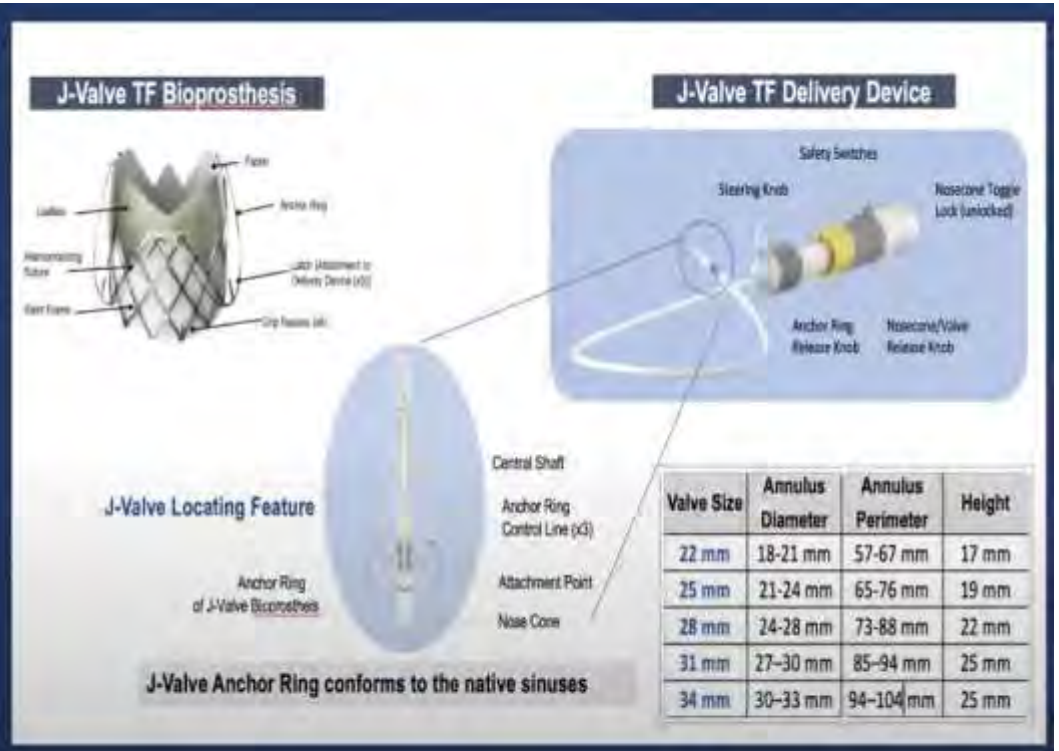
J-Valve

Bioprosthesis: self-expanding nitinol frame, bovine pericardial leaflets

Delivery System: steerable, flexible catheter, designed for TF access (18, 21 Fr)

Locating Feature: 3 anchor rings designed to conform to the native anatomy

Size matrix: 5 sizes, can treat wide range of anatomies (perimeters 57-104)

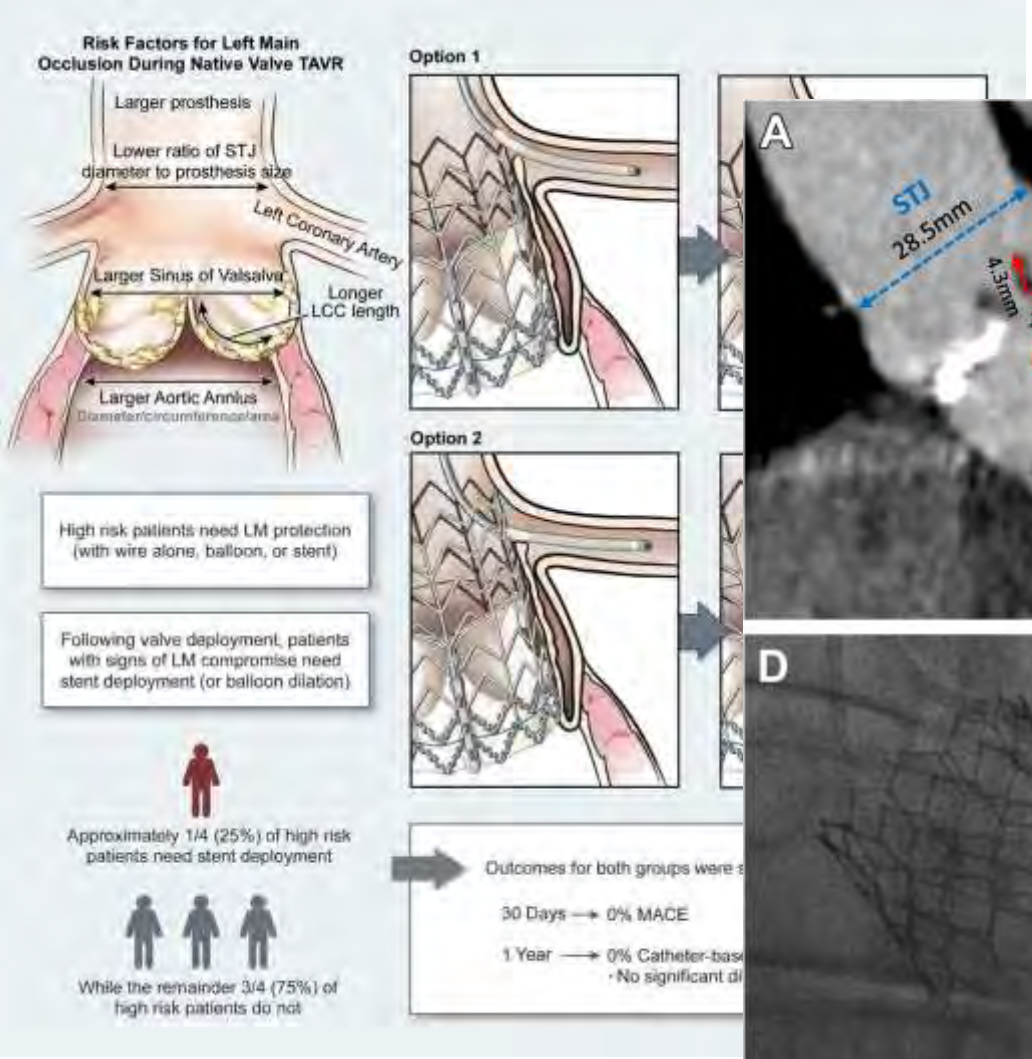


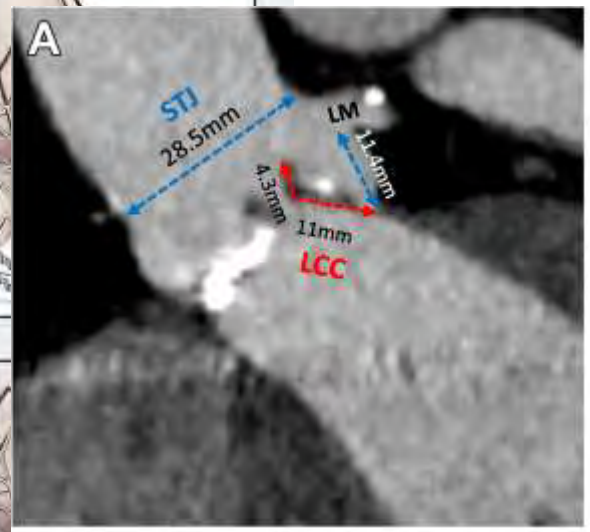
Valve Size	Annulus Diameter	Annulus Perimeter	Height
22 mm	18-21 mm	57-67 mm	17 mm
25 mm	21-24 mm	65-76 mm	19 mm
28 mm	24-28 mm	73-88 mm	22 mm
31 mm	27–30 mm	85–94 mm	25 mm
34 mm	30–33 mm	94–104 mm	25 mm

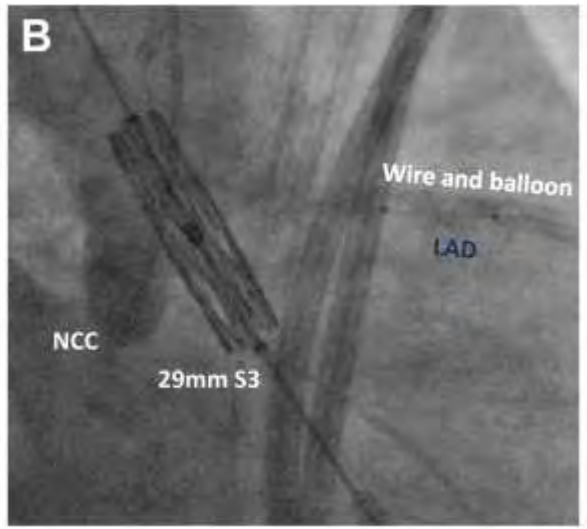
J-valve, JC Medical, Burlingame, CA

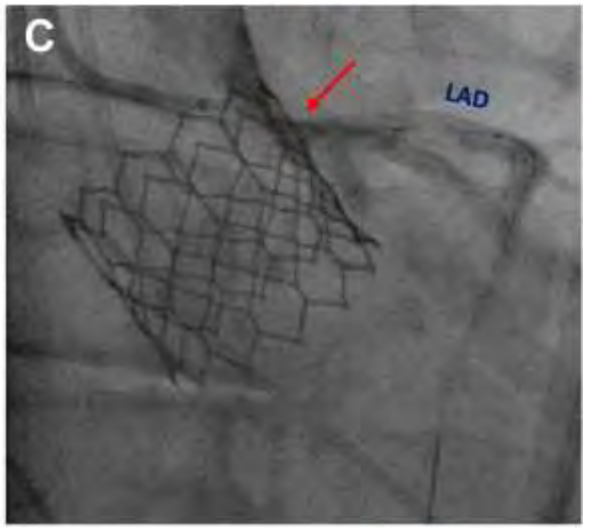
LM Protection During TAVR

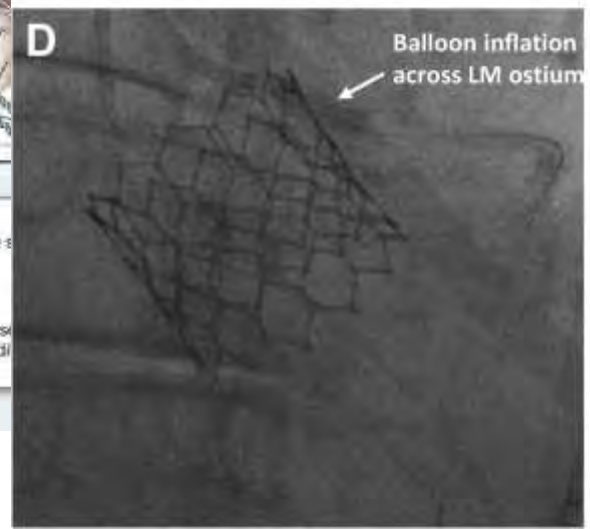
Left Main Protection During Transcatheter Aortic Valve Replacement With a Balloon-Expandable Valve
Hsiung, Ingrid et al.
Journal of the Society for Cardiovascular Angiography & Interventions, Volume 1, Issue 4, 100339

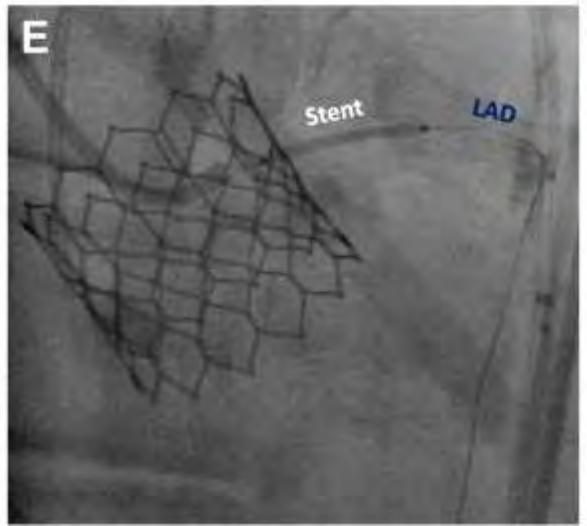


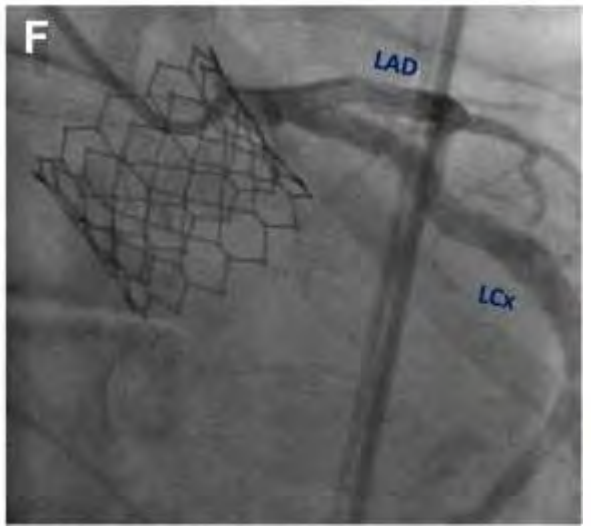




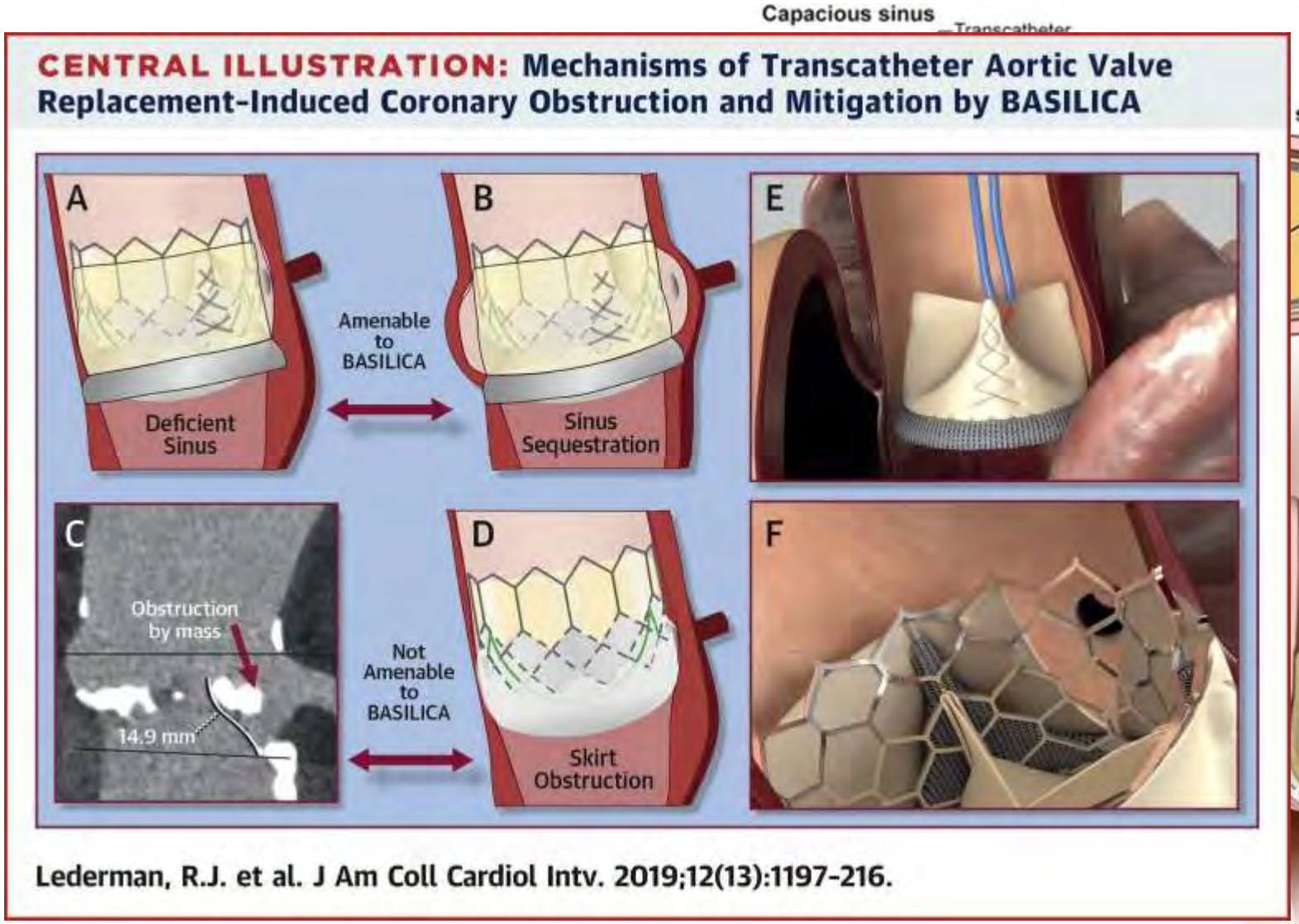


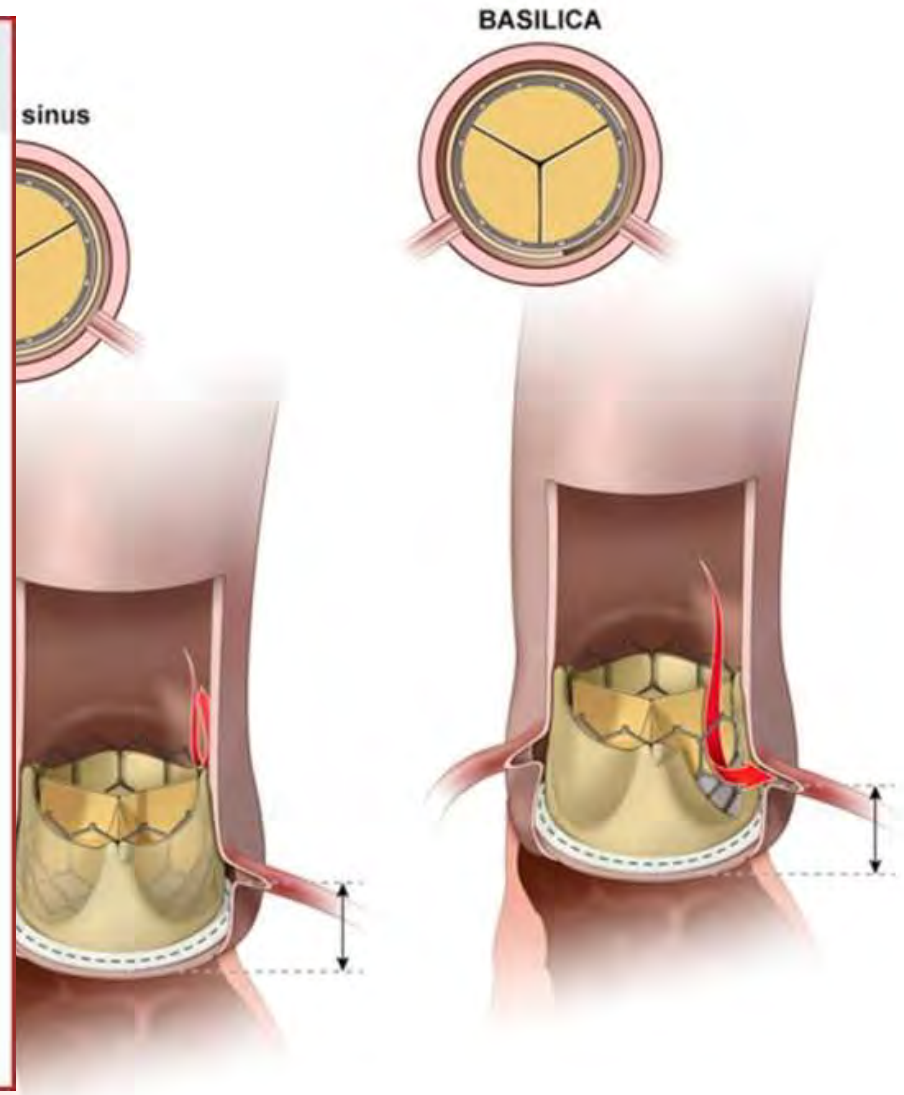






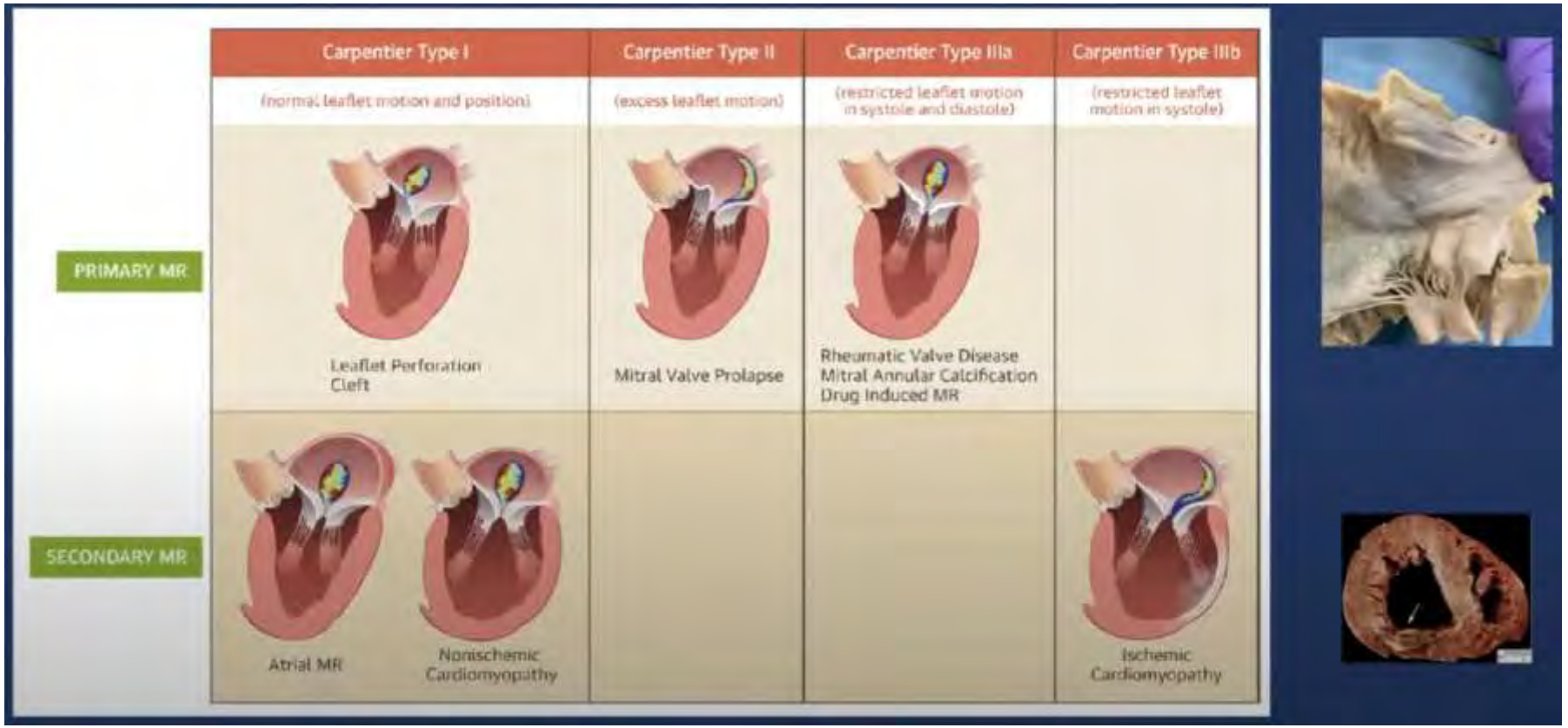
BASILICA (Bioprosthetic or native Aortic Scallop Intentional Laceration to prevent Iatrogenic Coronary Artery obstruction)



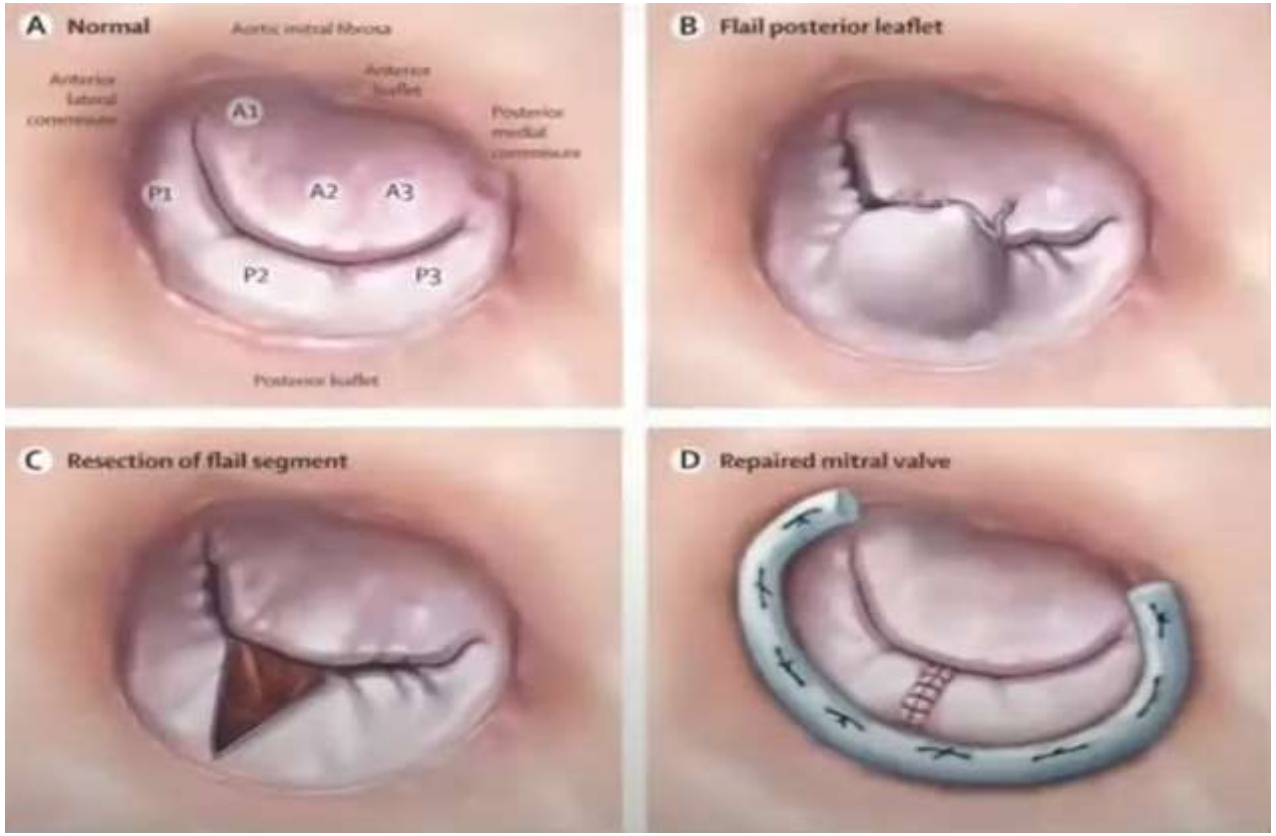


Mitral Valve

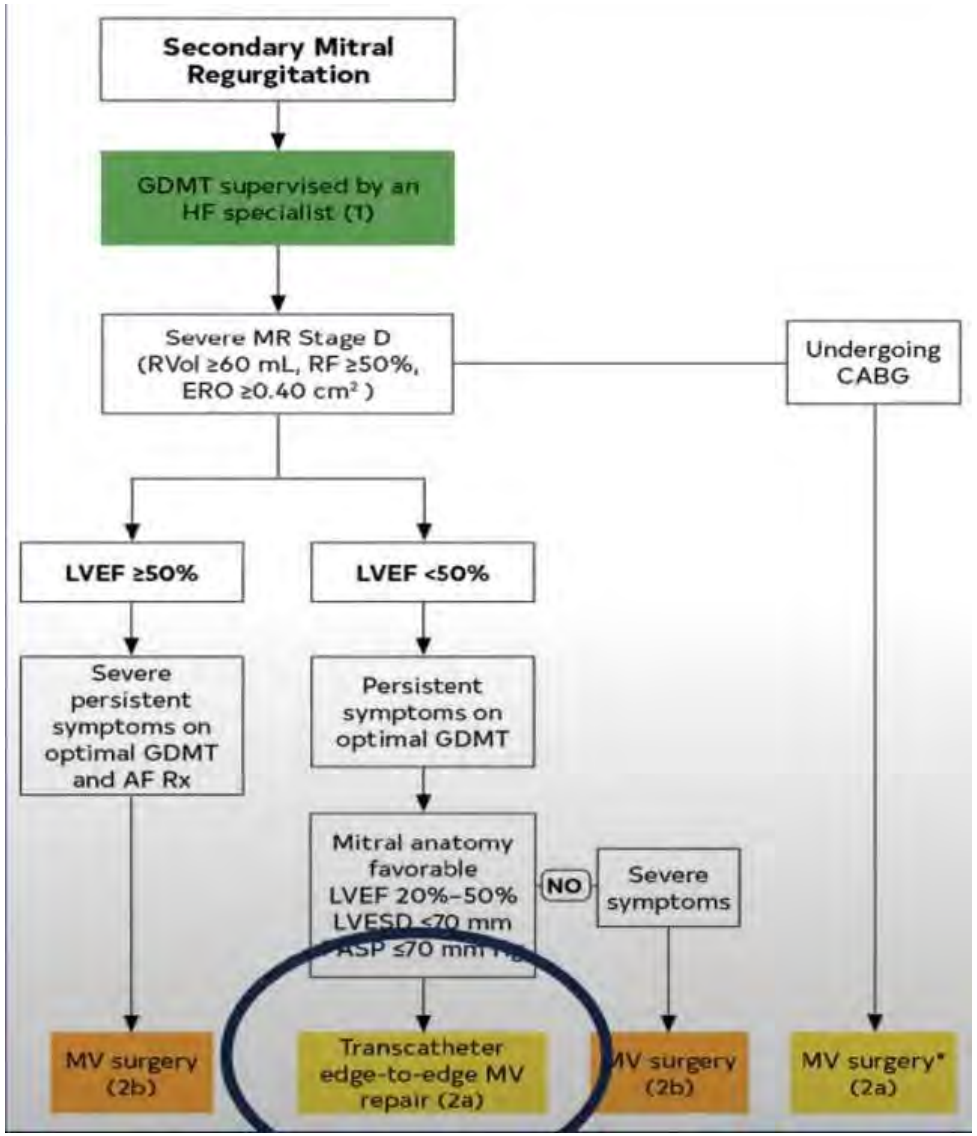
Classification of MR



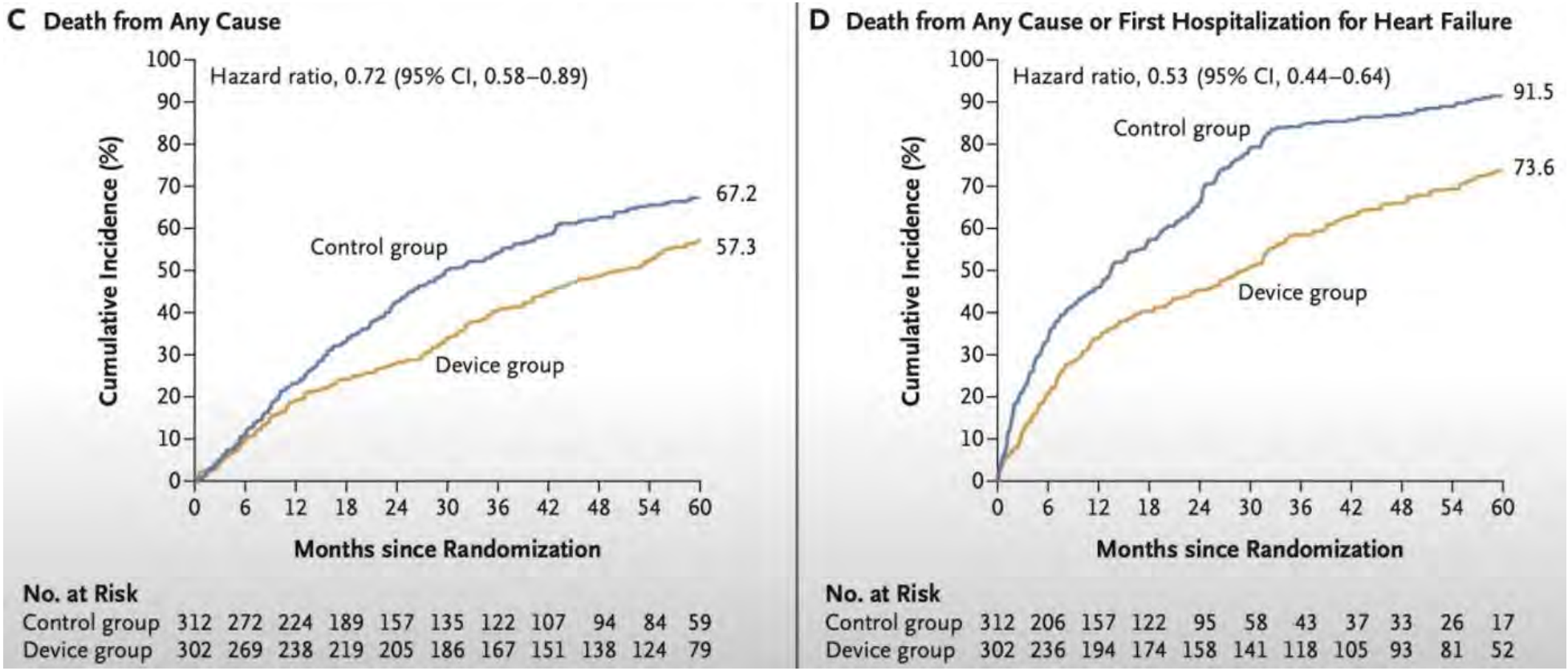
Standard of Care for Primary MR with Acceptable Surgical Risk



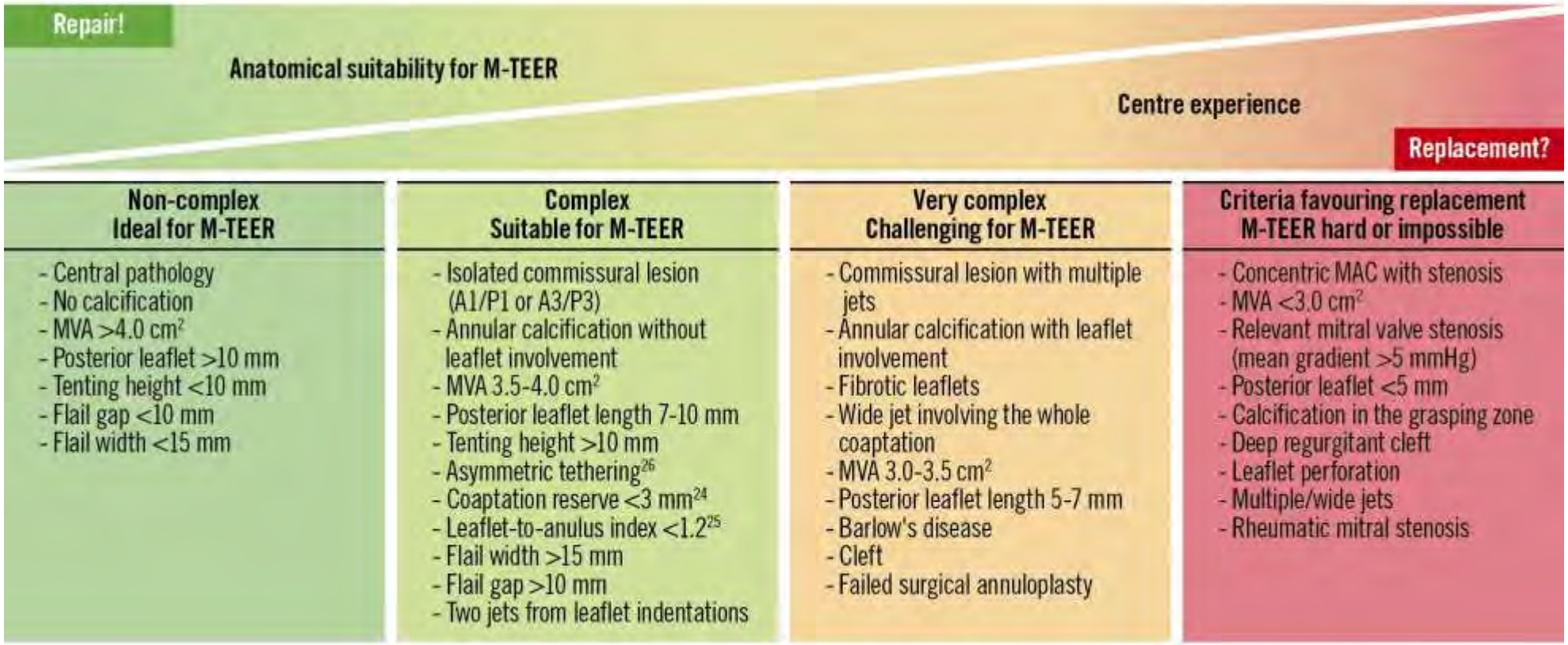
Guidelines


Secondary Mitral Regurgitation
GDMT supervised by an HF specialist (1)
Severe MR Stage D (RVol ≥60 mL, RF ≥50%, ERO ≥0.40 cm²)
Undergoing CABG
LVEF ≥50%
LVEF <50%
Severe persistent symptoms on optimal GDMT and AF Rx
Persistent symptoms on optimal GDMT
Mitral anatomy favorable
LVEF 20%–50%
LVESD ≤70 mm
NO
Severe symptoms
MV surgery (2b)
Transcatheter edge-to-edge MV repair (2a)
MV surgery (2b)
MV surgery* (2a)

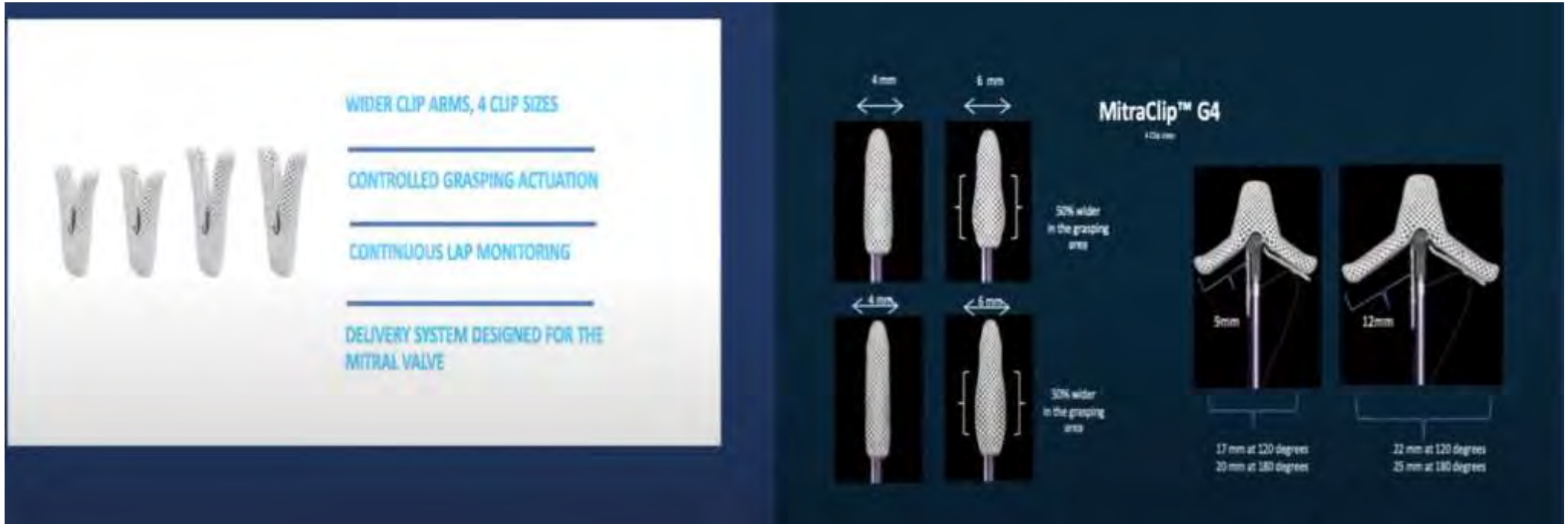
COAPT Trial 5-year Outcomes



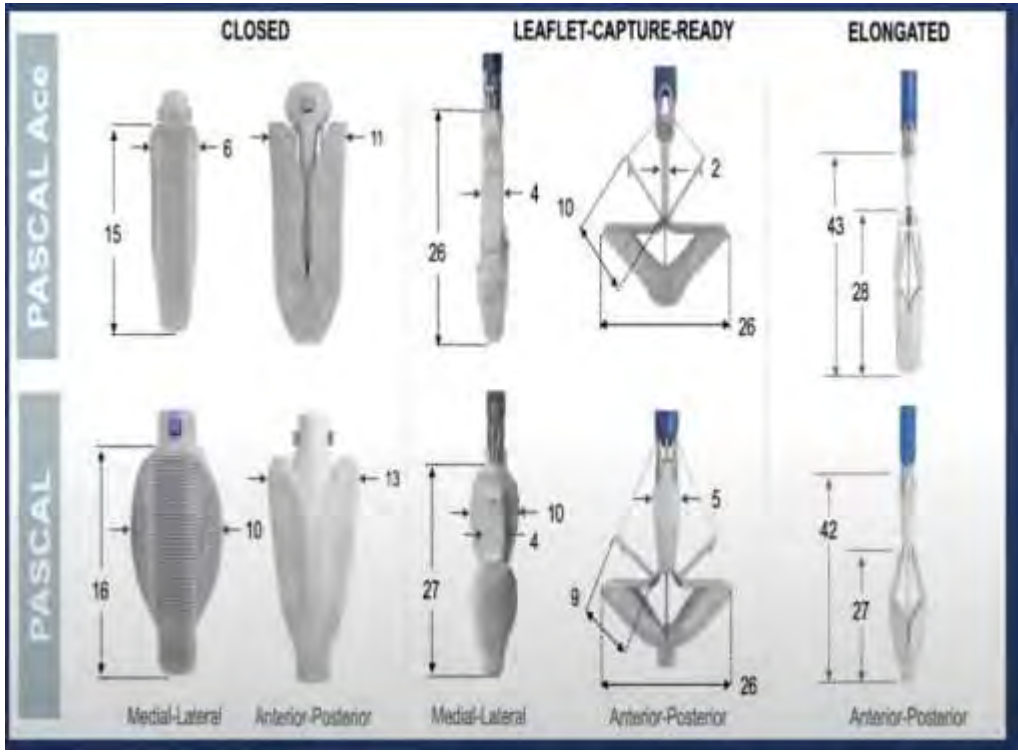
M-TEER Suitability Stratification

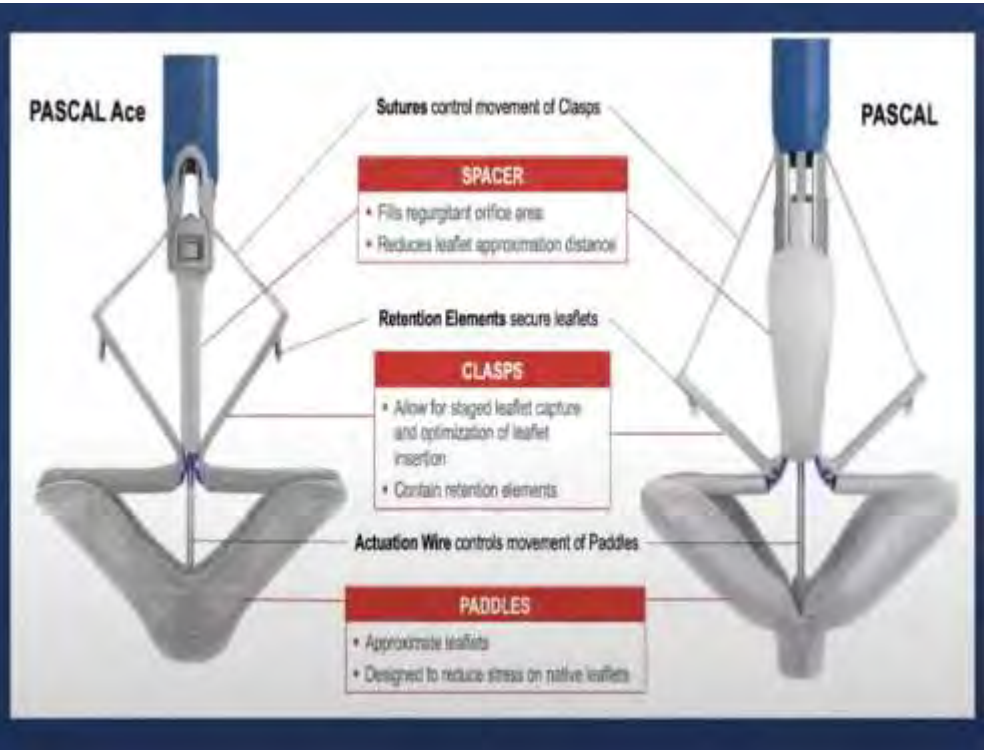


4th Generation MitraClip



PASCAL

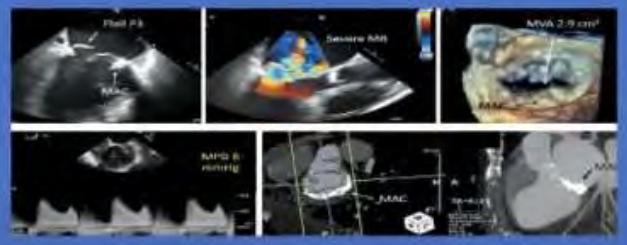

CLOSED
LEAFLET-CAPTURE-READY
ELONGATED
PASCAL Ace
PASCAL
6
11
15
4
26
10
2
26
43
28
10
13
16
10
4
27
5
9
26
42
27
Medial-Lateral
Anterior-Posterior
Medial-Lateral
Anterior-Posterior
Anterior-Posterior


PASCAL Ace
Sutures control movement of Clasps
PASCAL
SPACER
• Fills regurgitant orifice area
• Reduces leaflet approximation distance
Retention Elements secure leaflets
CLASPS
• Allow for staged leaflet capture and optimization of leaflet insertion
• Contain retention elements
Actuation Wire controls movement of Paddles
PADDLES
• Approximate leaflets
• Designed to reduce stress on native leaflets

Anatomies Unsuitable for M-TEER

1. Anatomic classification associated with mitral **stenosis** following TEER (Carpentier Class IIIA)

Rheumatic disease, radiation, MAC, rings, small mitral valve area



2. Anatomic classification associated with **inadequate reduction in MR**

Perforation, active endocarditis, severe Barlow's, short or restricted posterior leaflet < 5 mm, clefts

3. Patient Factors associated with **inability to perform TEER**

Inability to perform TEE, inadequate grasping views, insufficient height, hostile IAS

4. Clinical Factors Associated with **Futility**

Limited life expectancy, insufficient MR, intotropic dependency

Enter - TMVR

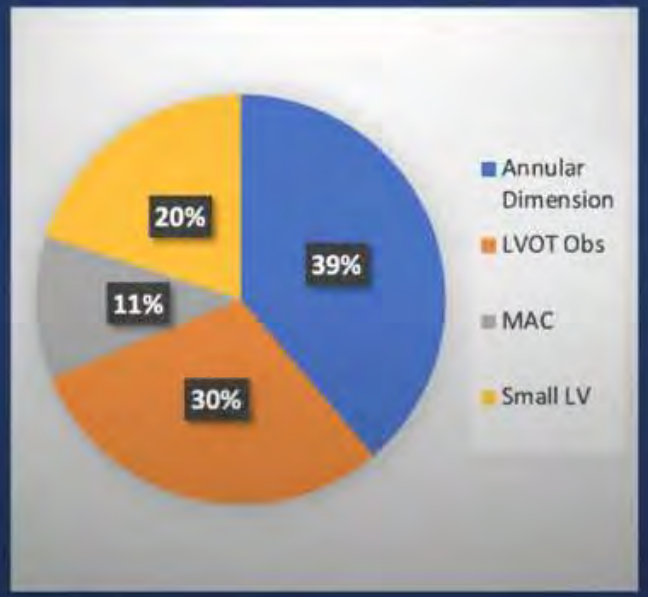
Challenges

- Dynamic
- Asymmetrical
- Heterogeneous
- Saddle-shaped annulus
- Complex sub-valvular apparatus

Potential solutions

- Leaflet and septal modification
- Better LVOTO risk prediction
- Broader size matrix
- PVL mitigation
- Lower profile, TF approach

Anatomical Exclusions

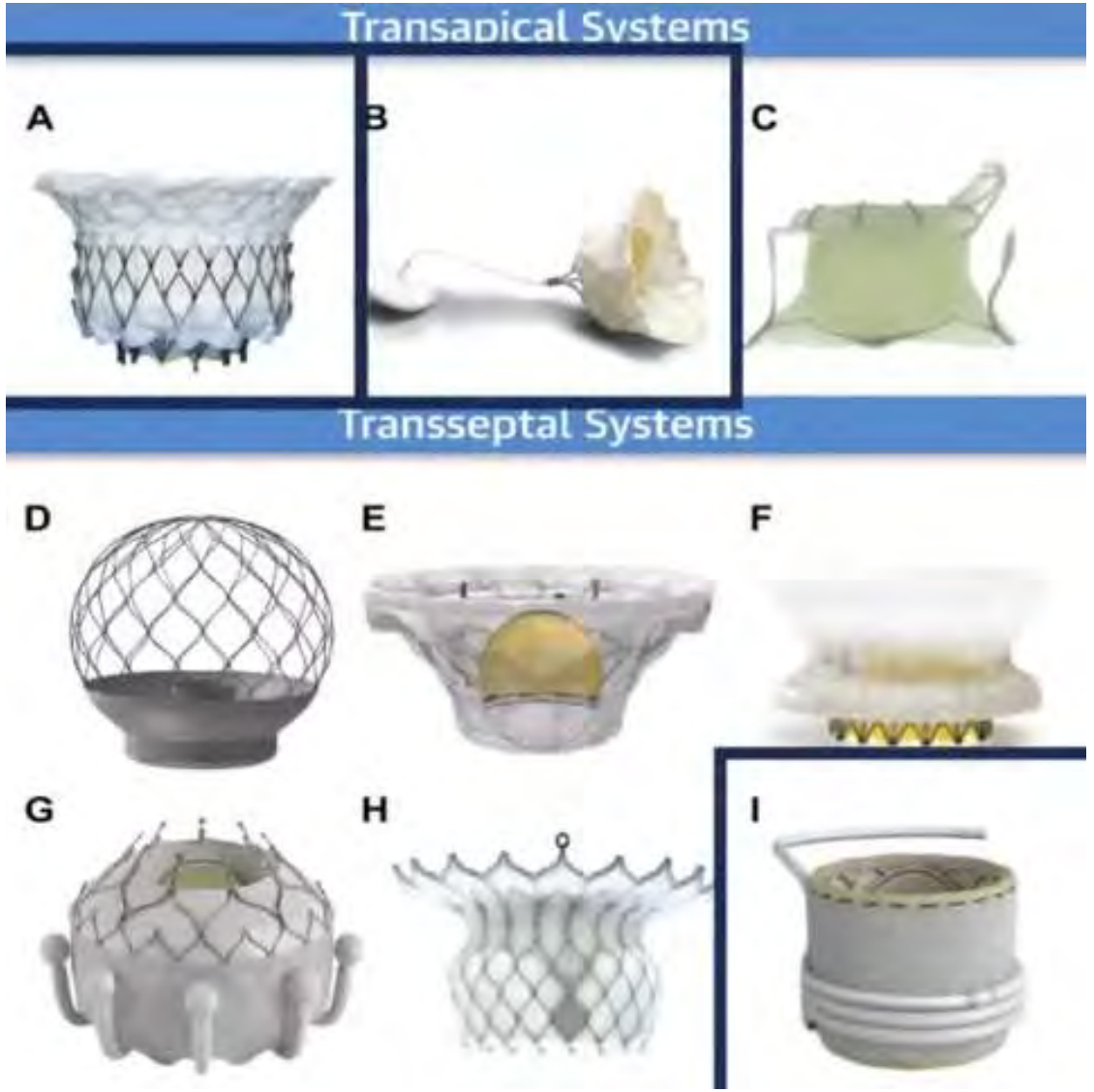


80% Screen Failure in Pivotal RCTs

Mostly due to anatomical limitations

LVOTO after TMVR

Current TMVR Device Landscape



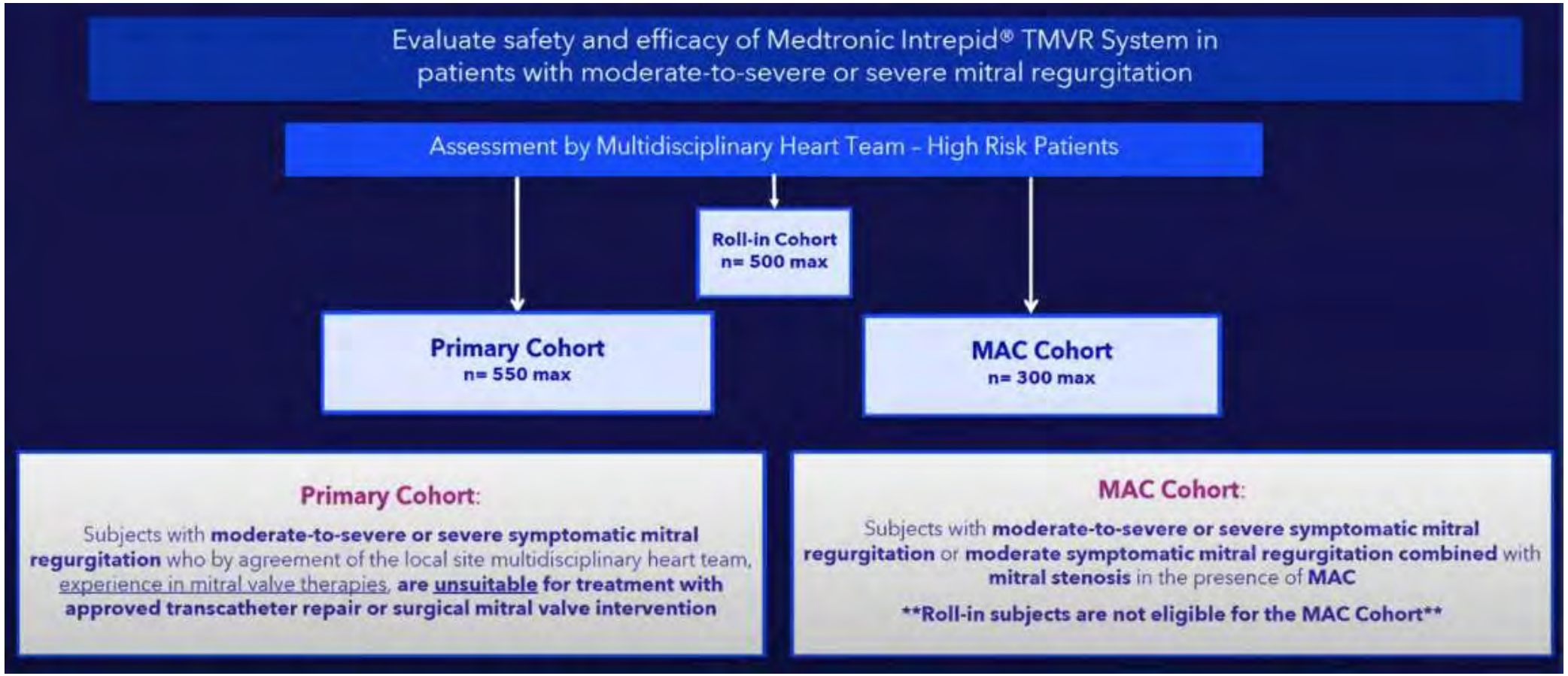
Intrepid TMVR

Device Size (mm)	Perimeter (mm)	Diameter (mm)	Annulus Area (cm^2)
42	99 - 117	28 - 39	7.3 - 10.4
48	114 - 134	29 - 45	9.6 - 13.8

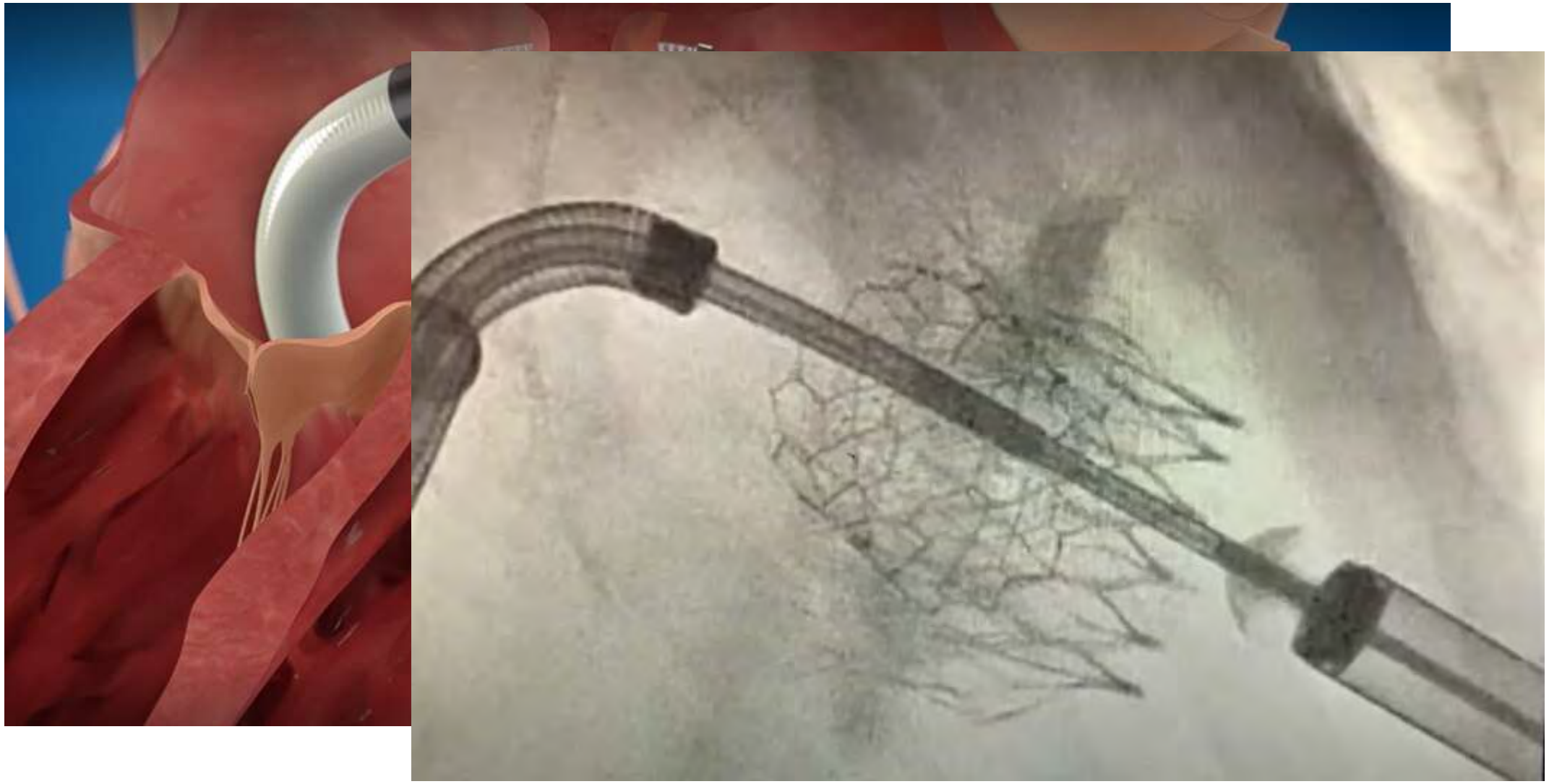
- Dual-stent, self-expanding nitinol
- Bovine pericardium valve (27 mm)
- Fixation: cork effect, small cleats
- 35 Fr system

- Started as a transapical system but is now evolving to a TF system to allow for a TS approach
- Plan to bring down catheter size to 29 F thereby limiting iatrogenic ASD creation

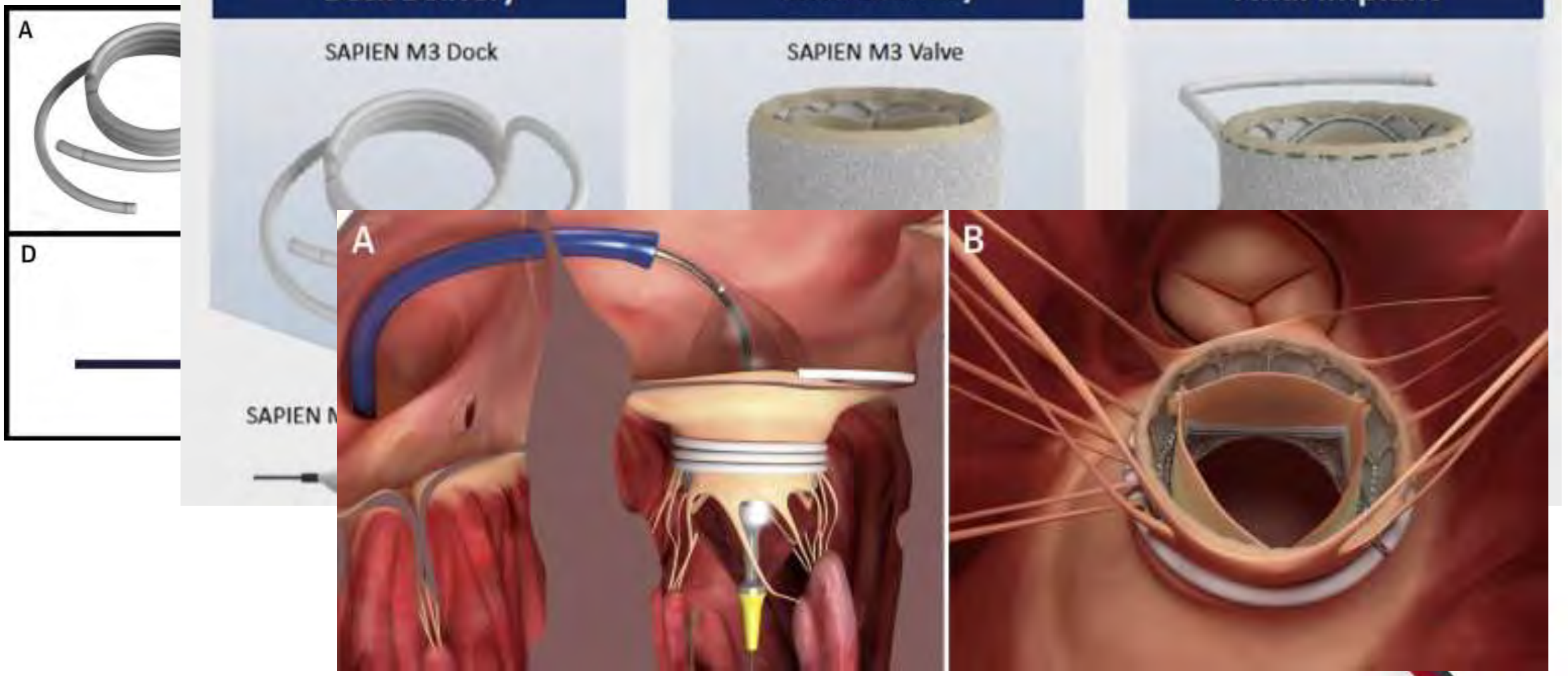
Intrepid TMVR – APOLLO Trial



Intrepid TMVR



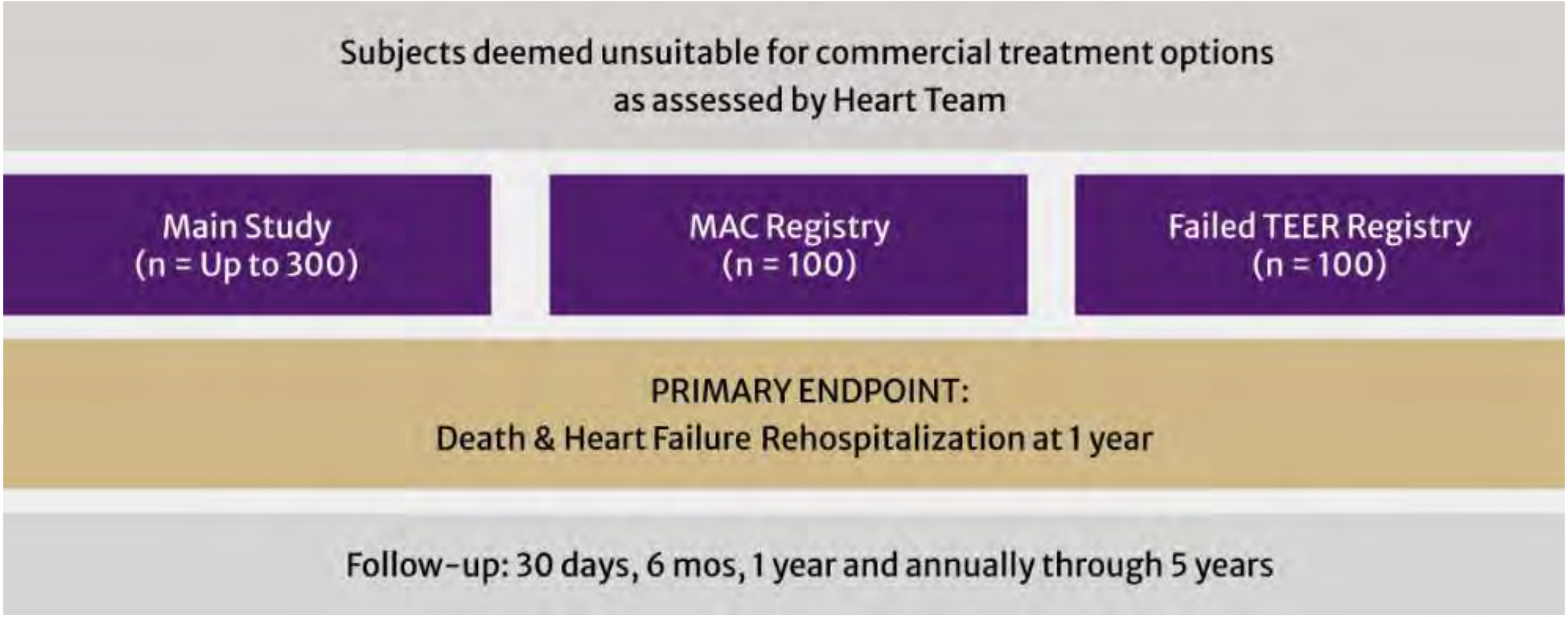
Sapien M3 TMVR System (Edwards Lifesciences)



Sapien M3 TMVR System

Essentially mimicking a ‘valve-in-ring’ implant

ENCIRCLE Trial



Tendyne TMVR (Abbott)

UNIQUE VALVE-TETHER-PAD DESIGN

- Repositionable
- Fully retrievable
- No need for CPB or rapid ventricular pacing

APICAL PAD

- Placed over ventricular access site

TETHER DESIGN

- Separates sealing from securement
- Enables full retrievability

VALVE DESIGN

- Tri-leaflet, bioprosthetic valve
- Outer frame contoured to mitral annulus
- Variety of valve sizes and profiles to address broad range of patient anatomies

Tendyne TMVR (Abbott)

Valve

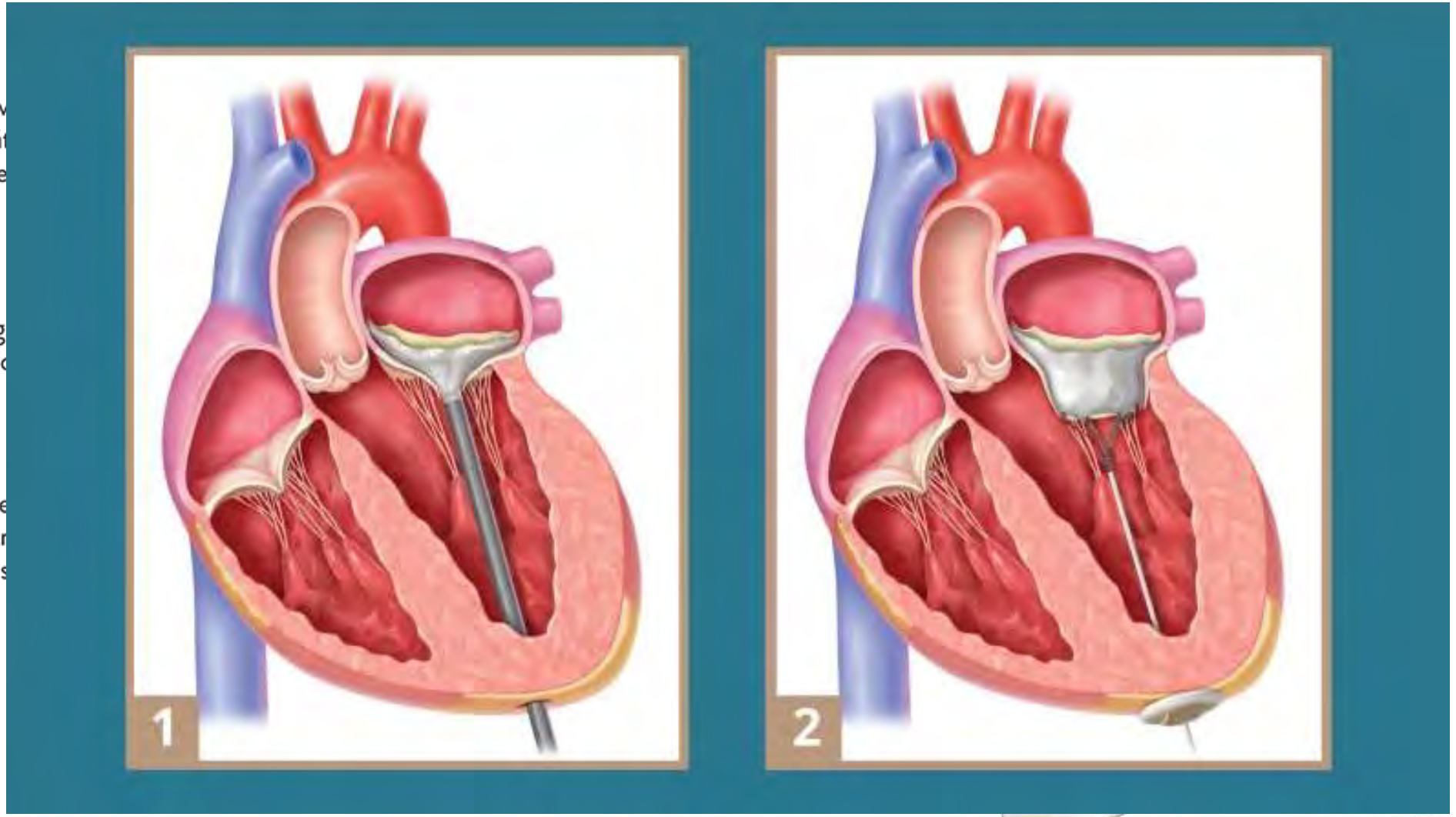
Dual-frame design prov
customized anatomic fi
stable hemodynamic pe

Inner frame

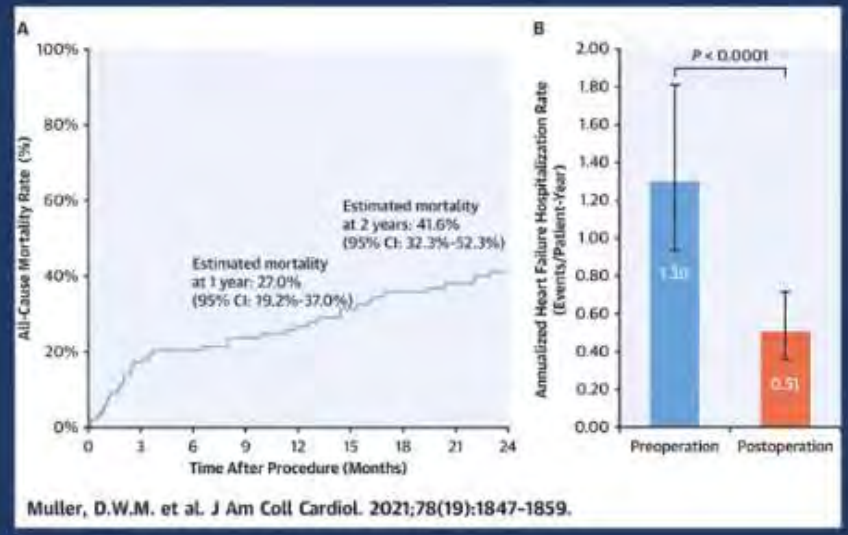
Circular self-expanding
tri-leaflet, bioprosthetic

Outer frame

Contoured design respe
shape of the native mitr
for secure fixation and s



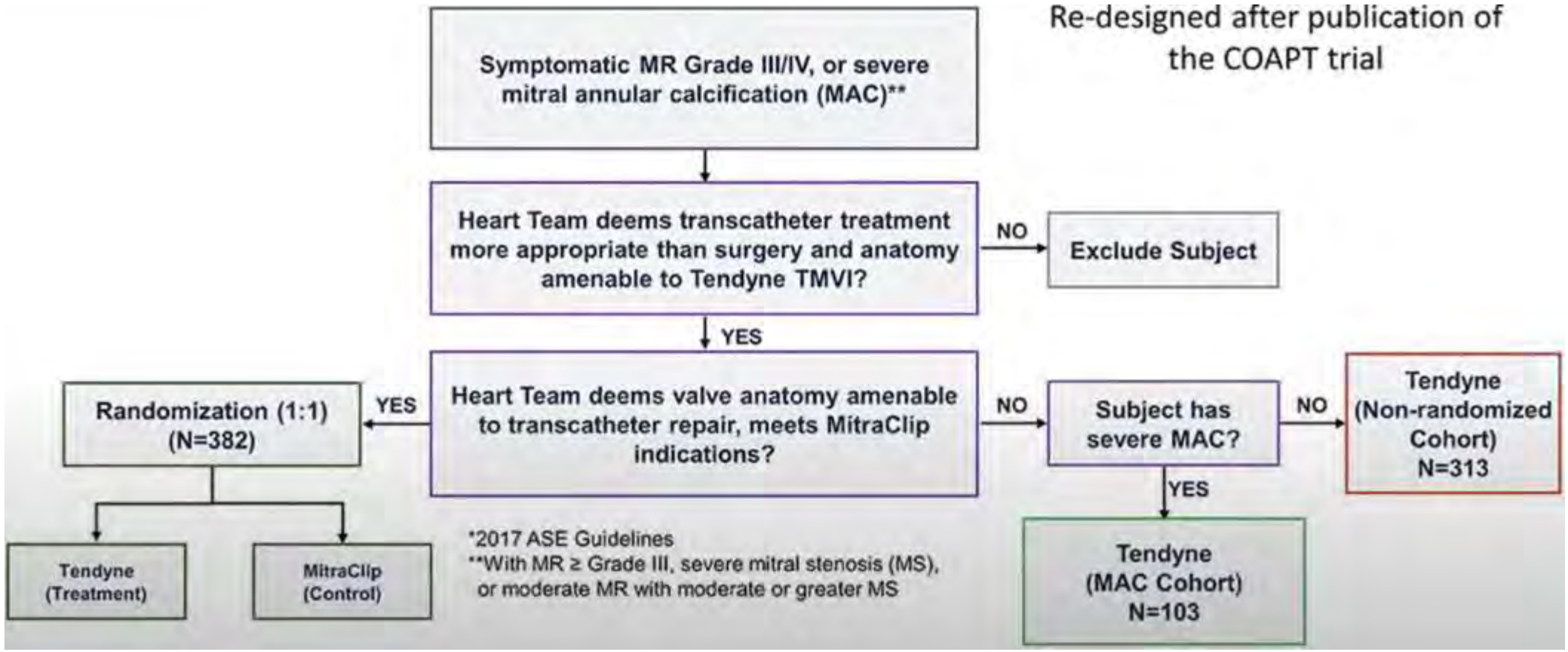
Tendyne TMVR



Muller, D.W.M. et al. J Am Coll Cardiol. 2021;78(19):1847-1859.

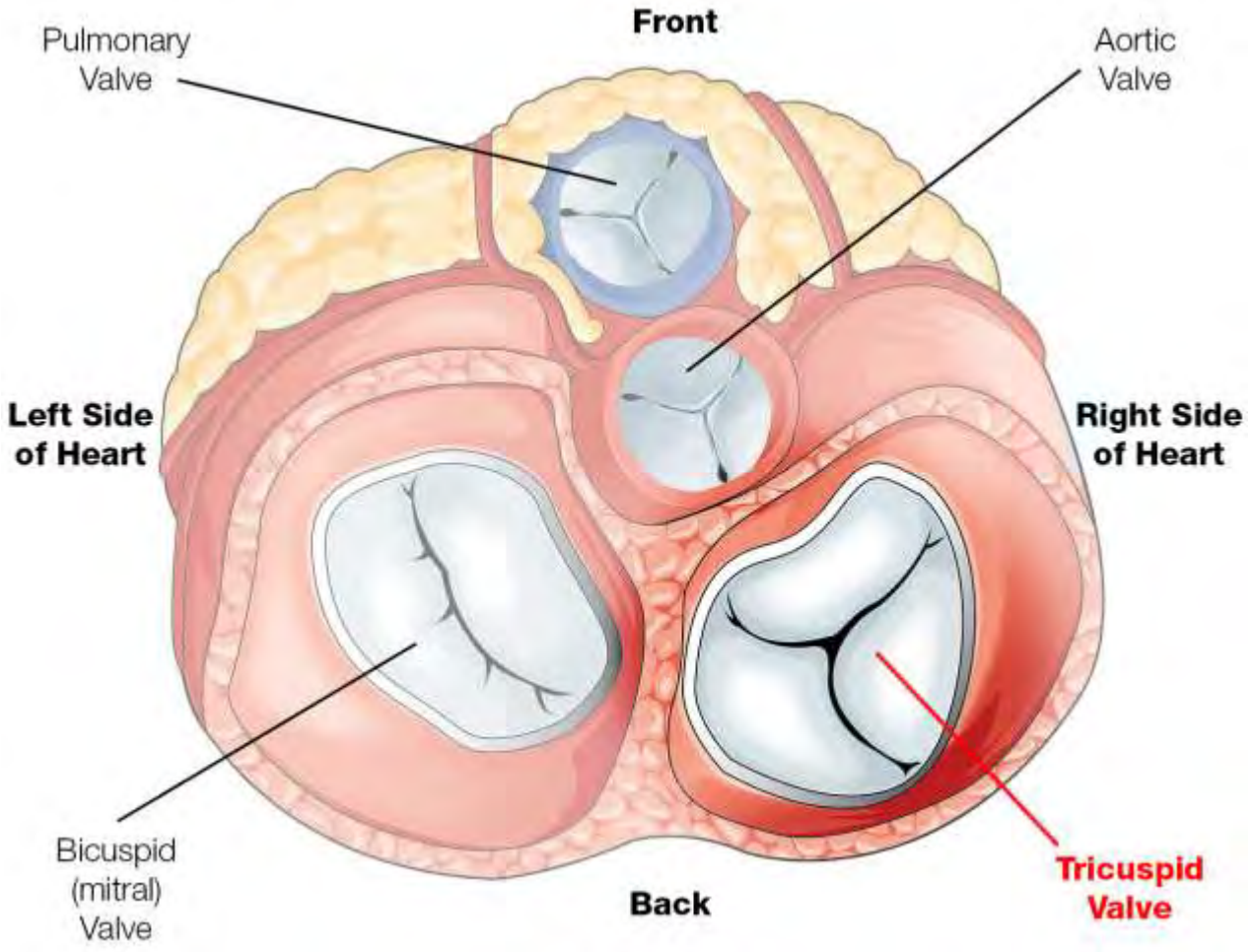
J Am Coll Cardiol. 2021

SUMMIT Trial

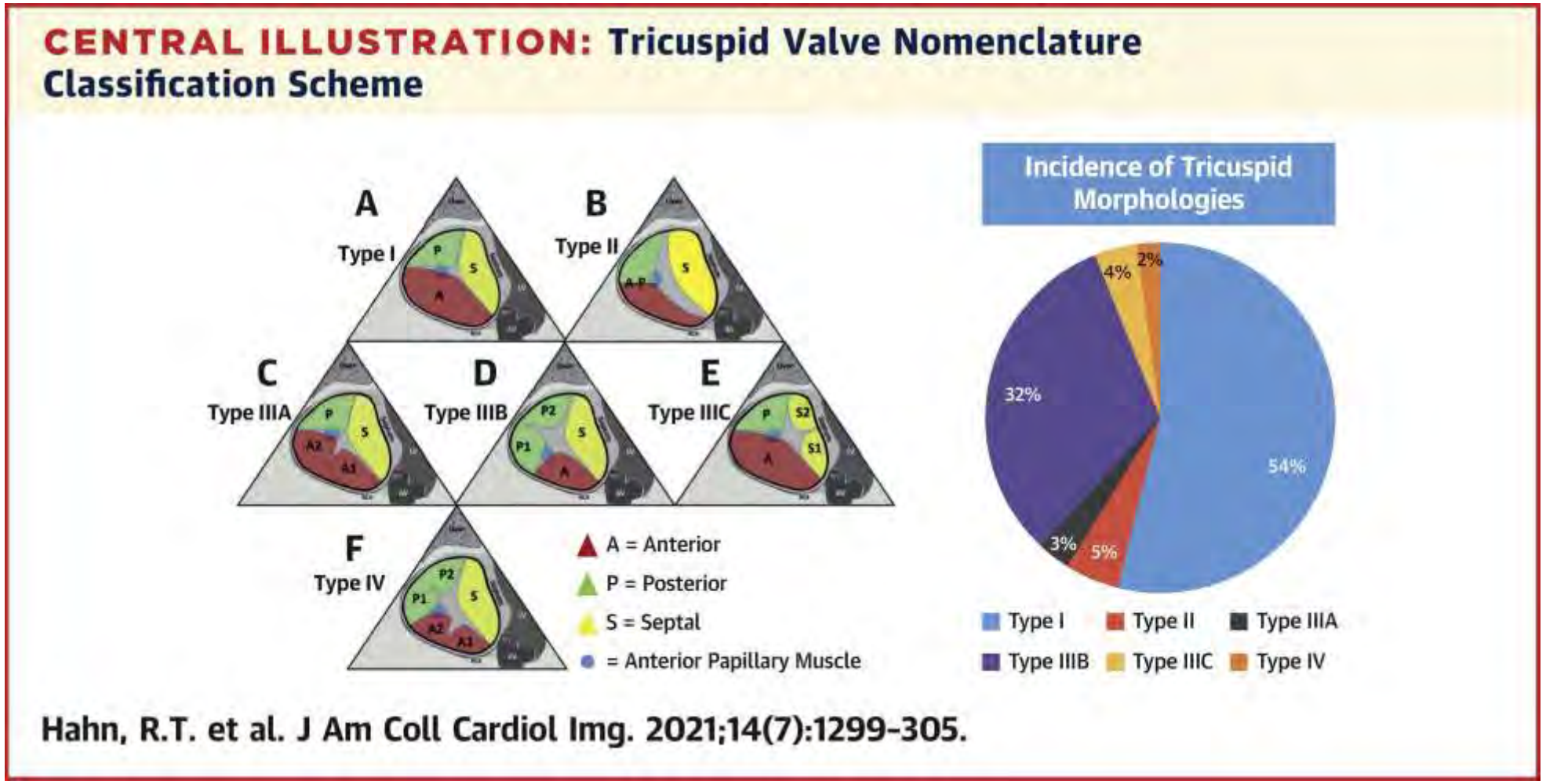


Tricuspid Valve

The “Forgotten” Valve



Not Often Tricuspid



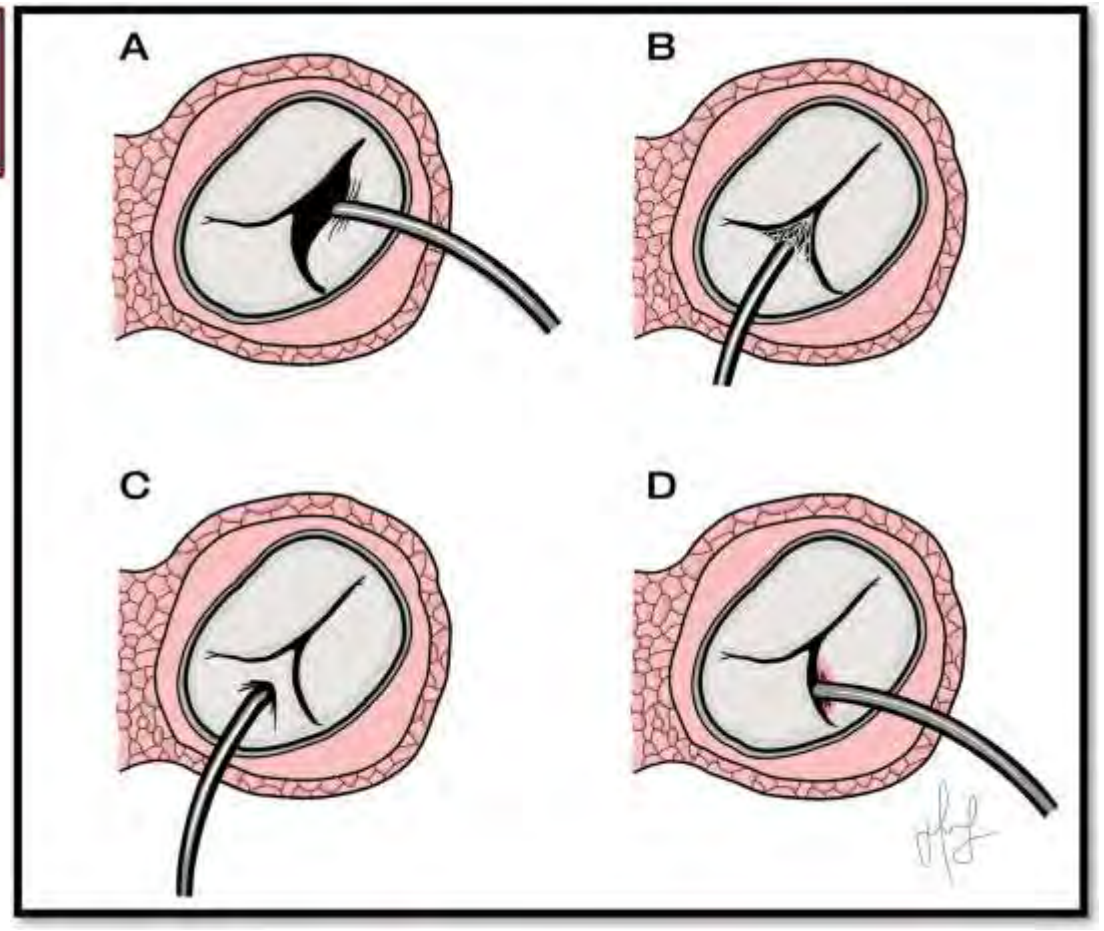
Approx only 54% of Tricuspid Valves are actually tricuspid

Tricuspid Regurgitation Causes

Causes of Primary and Secondary Tricuspid Regurgitation

- **Primary causes (25%)**
  - Rheumatic
  - Myxomatous
  - Ebstein anomaly
  - Endomyocardial fibrosis
  - Endocarditis
  - Carcinoid disease
  - Traumatic (blunt chest injury, laceration)
  - Iatrogenic (pacemaker/defibrillator lead, RV biopsy)
- **Secondary (Functional) causes (75%)**
  - Left heart disease (LV dysfunction or valve disease) resulting in pulmonary hypertension
  - Any cause of pulmonary hypertension (chronic lung disease, pulmonary thromboembolism, left to right shunt)
  - Any cause of RV dysfunction (myocardial disease, RV ischemia/infarction)

CIED Related TR



(A) Lead impingement causing mechanical interference on leaflet mobility and coaptation.
(B) Lead entanglement in the subvalvular apparatus, even with chordal entrapment.
(C) TV leaflet perforation during implantation.
(D) Lead adherence or leaflet laceration causing scarring and fibrosis, with or without leaflet tethering

Tricuspid Regurgitation Related to Cardiac Implantable Electronic Devices: An Integrative Review

Tricuspid Regurgitation Evaluation Pathway

Welle, G, Hahn, R, Lindenfeld, J. et al. New Approaches to Assessment and Management of Tricuspid Regurgitation Before Intervention. J Am Coll Cardiol Intv. 2024 Apr, 17 (7) 837–858. https://doi.org/10.1016/j.jcin.2024.02.034

Landscape

Tricuspid Regurgitation: Available Devices for the Interventionalist

Transcatheter Edge to Edge Repair

- Devices: TriClip, PASCAL
- Favorable Indications

1. Small leaflet coaptation gap (<7 mm)
2. "True" tricuspid (3 leaflets) morphology
3. Confined prolapse or flail of any leaflet
4. Jet location: Anteroseptal


TriClip


PASCAL

Tricuspid Valve Replacement

- Devices: Evoque, LuxValve, GATE
- Favorable Indications

1. Greater leaflet coaptation gap (>8.5 mm)
2. Valve tethering (more than moderate)
3. Previous Tricuspid Valve Replacement (ViV)
4. Thickened leaflets (heavily calcified)


LuxValve


Evoque


GATE

Annuloplasty

- Devices: Cardioband
- Favorable Indications

1. Dilated tricuspid annulus as the key pathophysiological mechanism
2. Valve tethering preferably mild
3. Jet location: Central


Cardioband

Heterotopic Caval Valve Implantation

- Devices: Tricento, TricValve
- Favorable Indications

1. Venous congestion – significant backflow in caval veins
2. Not suitable for orthotopic valve implantation
3. Appropriate cava anatomy-size


TricValve


Tricento

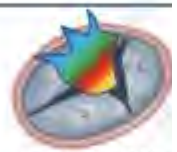
T-TEER

ACC.23 TOGETHER WITH WCC

Prospective

Populatio

- 350 patients enrolle sites in the US, C Europe
- Symptomatic, sever and at intermedia greater risk for TV sur
- 175 pts randomized 1 T-TEER (TriClip™ G4) c medical therapy (GDM



Patients with symptomatic sever

TRILUMINATE at

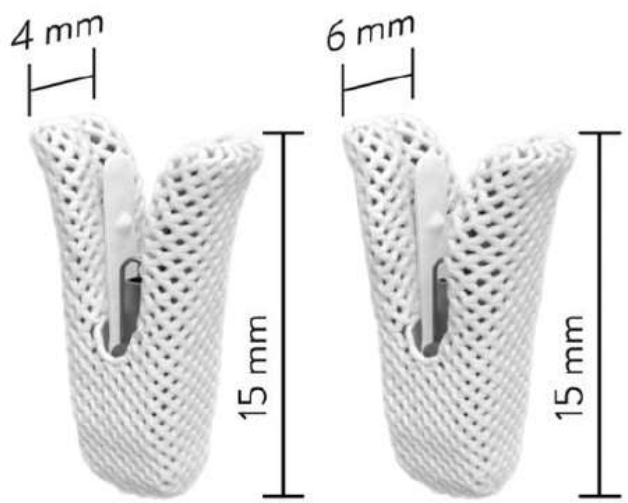
TRICLIP SYSTEM STEERING FUNCTIONALITY

Guide Handle:
Septal/ Lateral movement; Height above valve

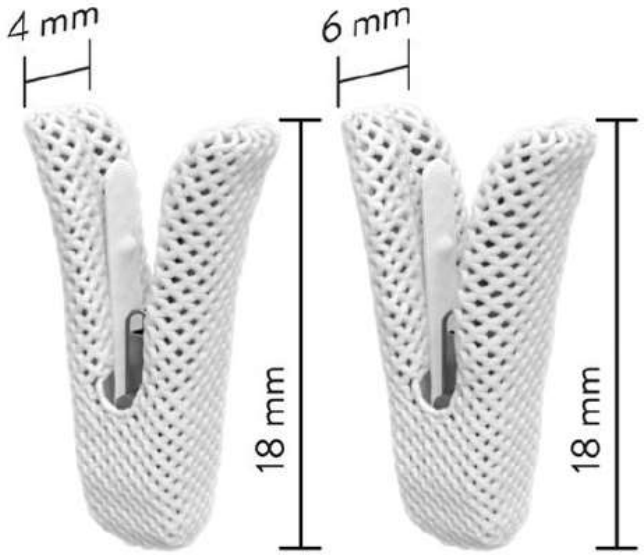
Guide Torque:
Septal/Lateral

Aor

Note: TriClip System in the non-planar Tri

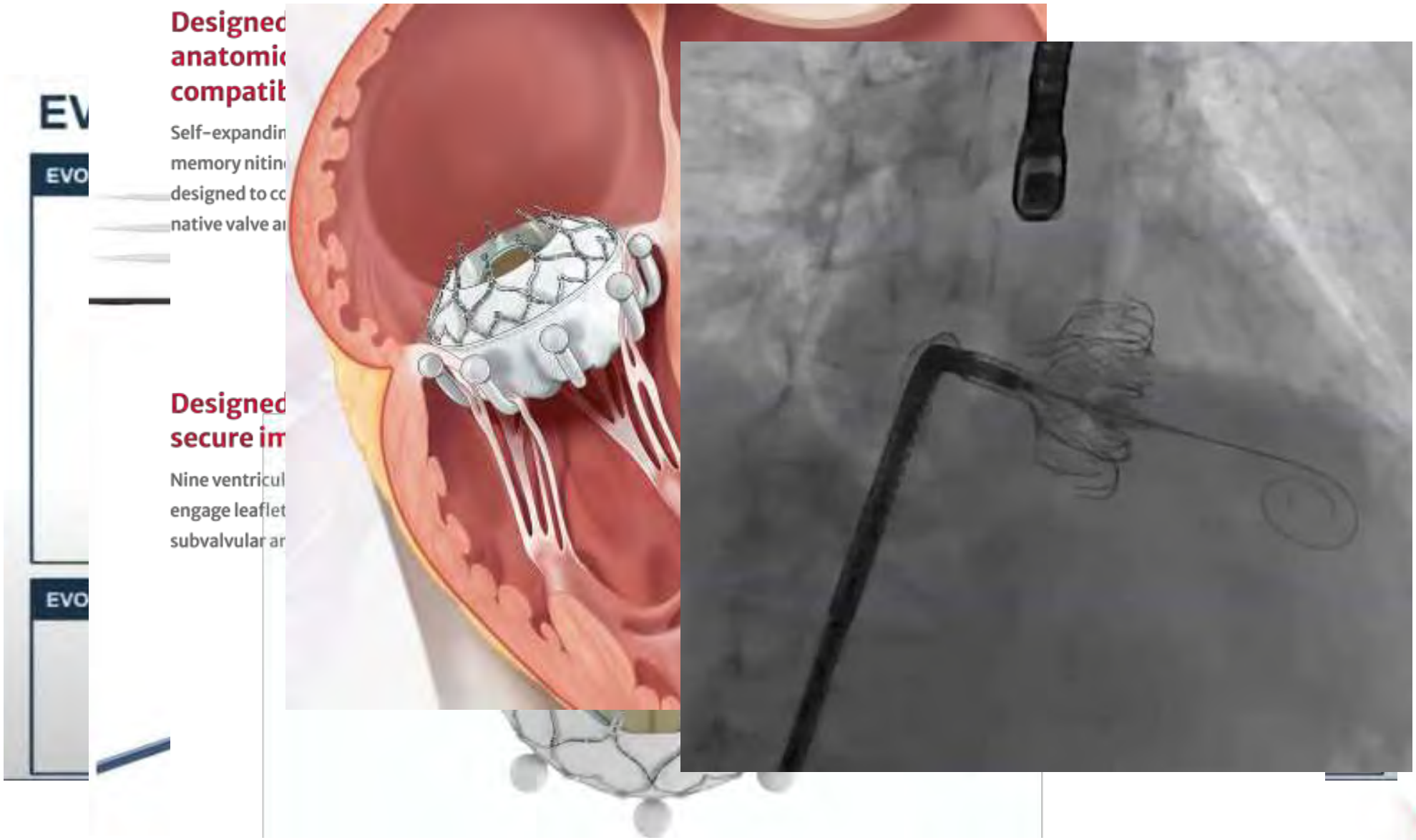


G4 NT **G4 NTW**



G4 XT **G4 XTW**

TTVR


Designed
anatomic
compatib
Self-expandin
memory nitin
designed to co
native valve a
Designed
secure im
Nine ventricul
engage leaflet
subvalvular ar
EVO
EVO

EVOQUE TTVR

TRISCEND II Trial Design

TRISCEND II: Two-Part Study Design Based on the Breakthrough Designation

'First 150'
First 150 patients randomized and treated

Total Cohort
N = 400
All-randomized patients
Enrolled, follow-up ongoing

Primary Endpoints	First 150	Total Cohort
Safety (30 Days)		
• Composite MAE rate	✓	✓
Effectiveness (6 Months)		
• TR grade reduction	✓	✓
• Hierarchical composite of KCCQ, NYHA and 6MWD		
Hierarchical Composite (1 Year)		
1. All-cause mortality		✓
2. RVAD implant or heart transplant		
3. TV surgery or intervention		
4. Annualized heart failure hospitalization		
5. KCCQ, NYHA, 6MWD		

✓ Prespecified analysis

- Median length of stay: 3 days (0.35)
- Composite of MAEs: 18.5%
- Severe bleeding: 17.7%
- Bleeding related to the main procedure: 1.6%
- New permanent pacemaker: 10.5%
- Stroke: 0%
- Myocardial infarction: 0%

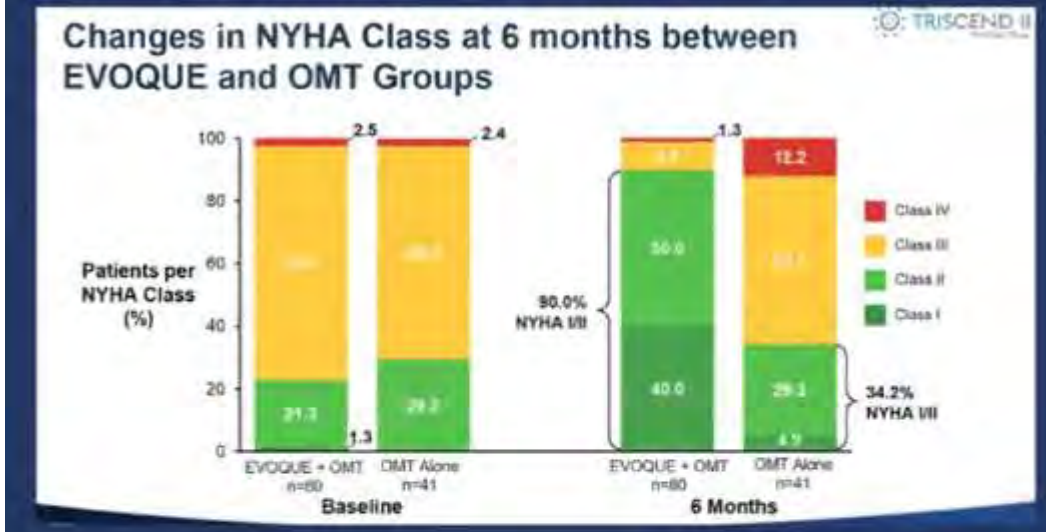
96±2%

- KM Freedom from HF Hospitalization @6m: 94±2%
- KM composite MAEs: 20±4%

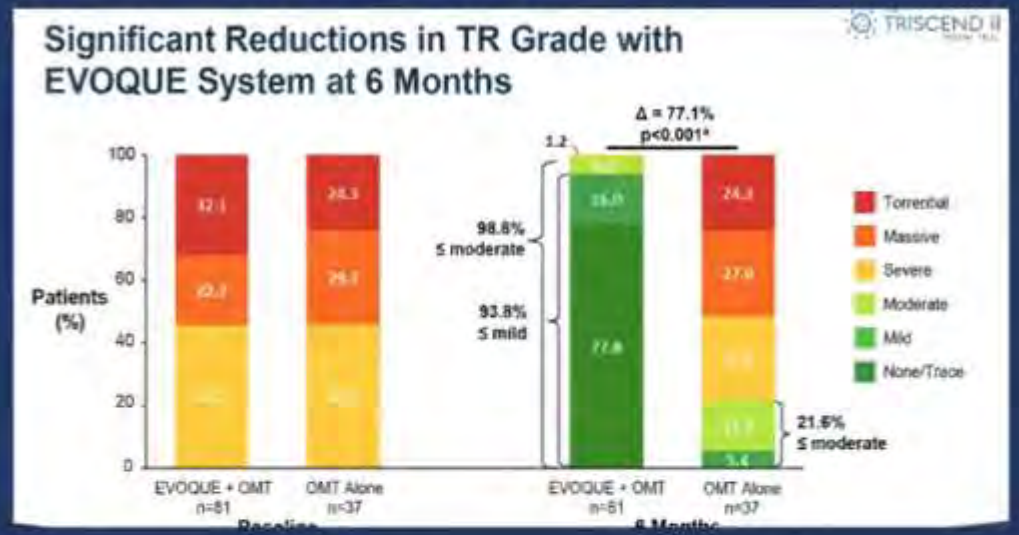
TTVR using the EVOQUE system demonstrated favorable 30-day outcomes sustained at 6-months showing significant TR reduction, 96% of survival, 94% of freedom from HF hospitalization, improvements in NYHA class, KCCQ score and 6MWD

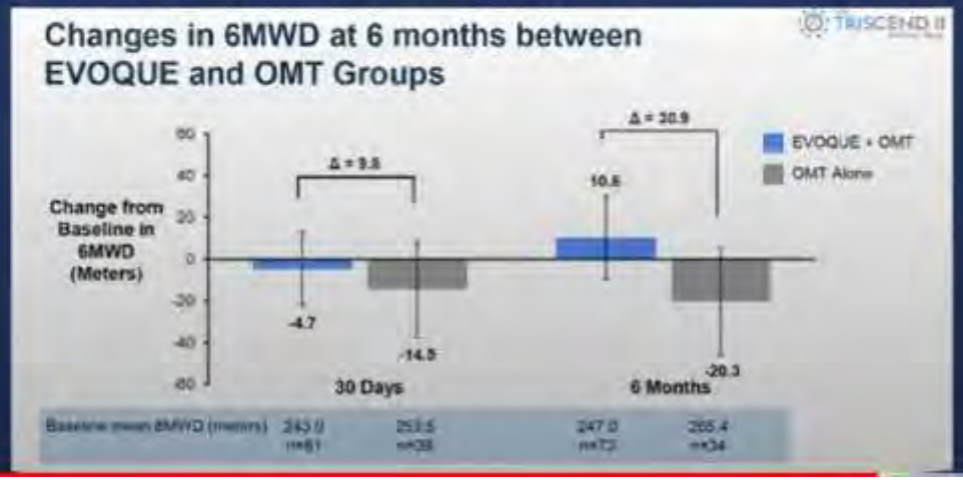
TRISCEND II: 150 Patients, 6-month Data

90 % NYHA FC I-II



93.8 % Mild or no TR



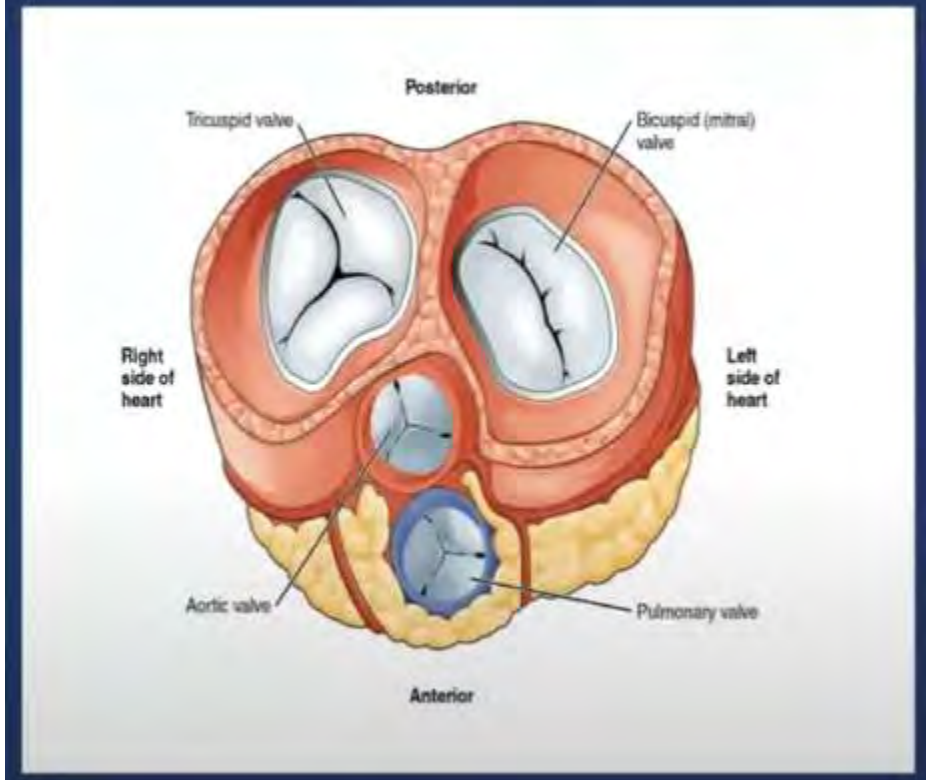


Walking distance
+ Delta 30 mts vs OMT

Pulmonic Valve

(Call ACHD …)

Conclusion



----- Approved ---- In Phase 3 clinical trial

Aortic

Replacement AS

Replacement AR

Mitral

Repair (M-TEER)

Replacement (TMVR)

Pulmonic

Replacement

Tricuspid

Repair (T-TEER)

Replacement (EVOQUE)

Thank You