



Brigham and Women's Hospital
Founding Member, Mass General Brigham

Percutaneous Approaches to Valve Disease

Pinak B. Shah, MD

Director, Interventional Cardiology

Mass General Brigham

Associate Professor of Medicine

Harvard Medical School



Pinak Shah, MD



- University of Pennsylvania School of Medicine
- Medicine Residency @ BWH
- Cardiovascular Medicine Fellowship @ BWH
- Interventional Cardiology Fellowship @BWH
- Clinical Focus
 - Percutaneous Coronary Intervention
 - Trans-catheter Valve Therapies

Disclosures

- Proctor- Edwards LifeSciences
- Educational Grants- Abbott, Medtronic, Edwards
- Advisory Board- Xenter

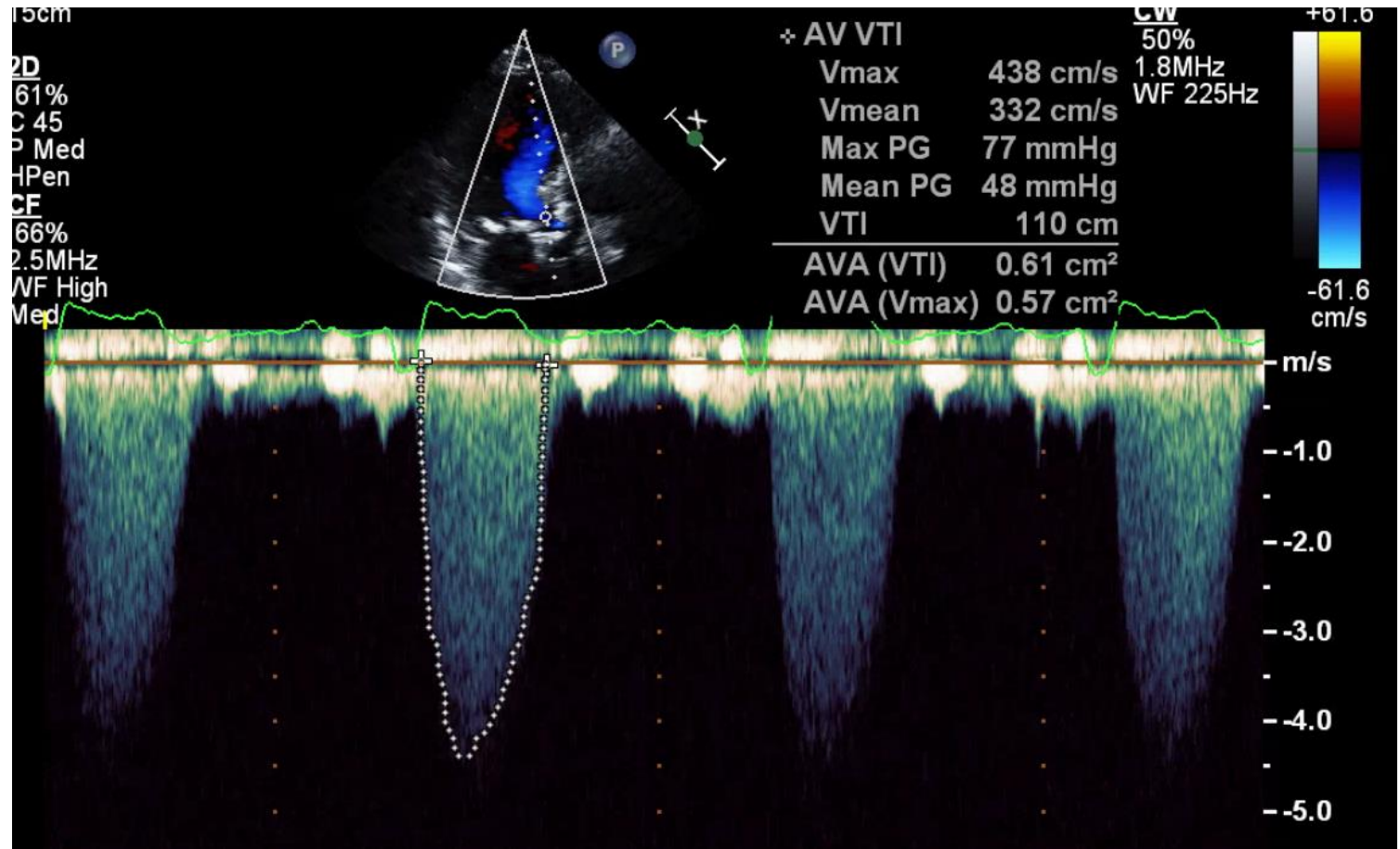
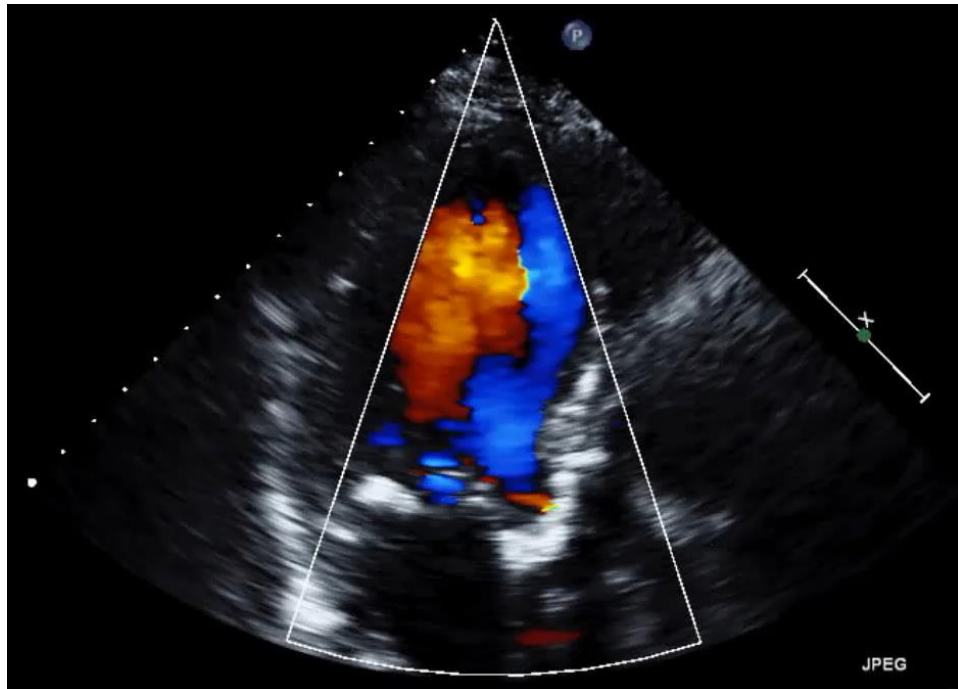
Objectives

- Use 3 case vignettes to:
 - Highlight trans-catheter options for the management of common valvular heart conditions
 - Review investigational devices that may have a future role in broadening the management armamentarium for patients with valvular heart disease

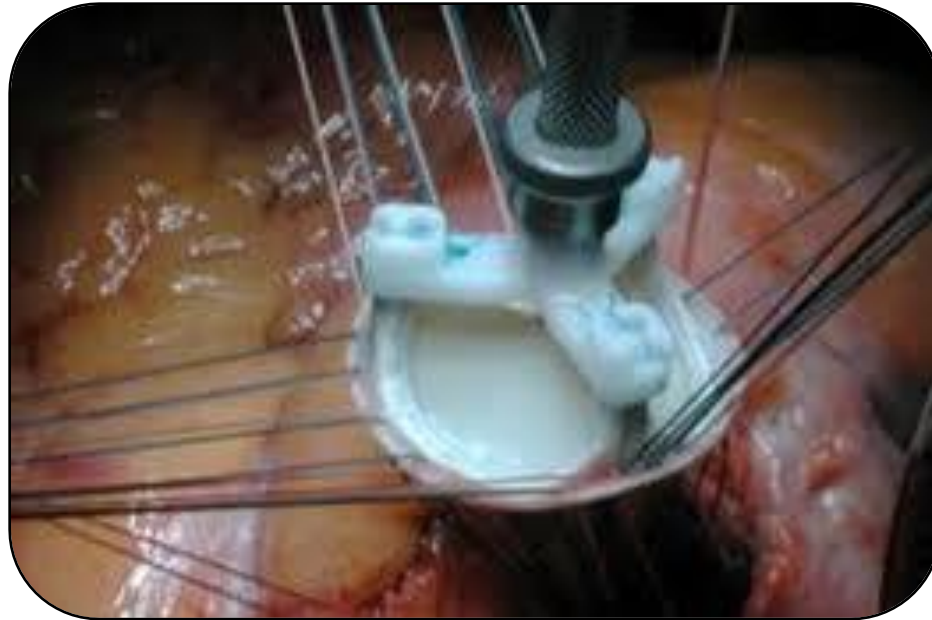
Case 1

- 85 year old man with progressive dyspnea on exertion
- Exam notable for a loud systolic ejection murmur at the right upper sternal border
- Carotid upstrokes noted to be diminished
- ECHO: severe aortic stenosis with V_{\max} 4.5 m/s, mean gradient 54 mmHg, aortic valve area 0.6 cm².
- Referred for treatment considerations
- STS score 3.5%

Case 1- Echo



Surgical Aortic Valve Replacement (SAVR)



Historical Gold Standard for Aortic Valve Replacement

Trans-catheter Aortic Valve Replacement (TAVR)

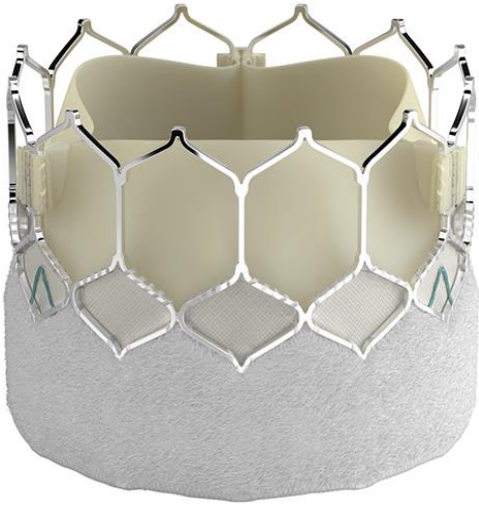


Catheter based delivery
and implantation of an
aortic valve

SAVR vs TAVR

	SAVR	TAVR
Access	Sternotomy	Vascular
Cardiopulmonary Bypass	Yes	No
General Anesthesia	Yes	No
Hospitalization	5-7 Days	1 Day
Recovery	4-6 weeks	< 1 week
Valve Types	mechanical/biological	biological

FDA Approved TAVR Valves in the United States



Sapien 3 Ultra
4th Generation
Edwards LifeSciences




Evolut FX+
5th Generation
Medtronic



Navitor
Abbott Vascular
*high surgical risk patients only

Assessing Surgical Risk: STS Score

**Online STS Risk Calculator**Dataset: 2.73DefinitionsSupport

Help[More about Risk Calculator](#)NewPrint**Calculations**

Today's Date 4/19/2013

Procedure
Coronary Artery Bypass ☐ Yes ☐ No ☒ Missing
Valve Surgery ☐ Yes ☐ No ☒ Missing
VAD Implanted or Removed ☐ No
☐ Yes, implanted
☐ Yes, explanted
☐ Yes, implanted and explanted
☒ Missing
Other Non-Cardiac Procedure ☐ Yes ☐ No ☒ Missing
Unplanned Procedure ☐ No
☐ Yes, unsuspected patient disease or anatomy
☐ Yes, surgical complication
☒ Missing
Other Cardiac Procedure ☐ Yes ☐ No ☒ Missing

Procedure Name
Risk of Mortality
Morbidity or Mortality
Long Length of Stay
Short Length of Stay
Permanent Stroke
Prolonged Ventilation
DSW Infection
Renal Failure
Reoperation



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	Low Risk (Must Meet ALL Criteria in This Column)	Intermediate Risk (Any 1 Criterion in This Column)	High Risk (Any 1 Criterion in This Column)	Prohibitive Risk (Any 1 Criterion in This Column)
STS PROM [*]	<4% AND	4%–8% OR	>8% OR	Predicted risk with surgery of death or major morbidity (all-cause) >50% at 1 y OR
Frailty [†]	None AND	1 Index (mild) OR	≥2 Indices (moderate to severe) OR	
Major organ system compromise not to be improved postoperatively [‡]	None AND	1 Organ system OR	No more than 2 organ systems OR	≥3 Organ systems OR
Procedure-specific impediment [§]	None	Possible procedure-specific impediment	Possible procedure-specific impediment	Severe procedure-specific impediment

2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease

 CrossMark

*Developed in Collaboration With the American Association for Thoracic Surgery,
American Society of Echocardiography, Society for Cardiovascular Angiography and Interventions,
Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons*

TAVR Clinical Trials (>10,000 Patients)

Trial	Year	Device	Risk	Result
PARTNER B	2010	Sapien	Inop	TAVR > Medical Therapy
PARTNER A	2011	Sapien	High	TAVR non-inf to SAVR
Corevalve XR	2014	Corevalve	Inop	TAVR > Performance Goal
Corevalve HR	2014	Corevalve	High	TAVR non-inf to SAVR, possibly superior
PARTNER 2	2016	Sapien XT	Intermed	TAVR > SAVR for TF candidates
Sapien 3 HR	2016	Sapien 3	High/Inop	Low Event Rates for SAVR
Sapien 3 IR	2016	Sapien 3	Intermed	TAVR > SAVR
SURTA VI	2017	Corevalve & Evolut R	Intermed	TAVR non-inf to SAVR
PARTNER 3	2019	Sapien 3	Low	TAVR > SAVR
Evolut Low Risk	2019	Corevalve Evolut R	Low	TAVR non-inf to SAVR

TAVR Candidacy and Surgical Risk

“Inoperable” or “Extreme Risk”

- Patients in whom two cardiac surgeons feels the risk of mortality from sAVR is likely > 50%

FDA APPROVED FOR TAVR

“High Risk”-

- Patients with a Society of Thoracic Surgeons Risk Score (STS) of $\geq 8\%$
- Patients with STS Risk Score < 8% but in whom the estimated risk of mortality from sAVR is $\geq 15\%$ by two surgical assessments

“Intermediate Risk”

- Patients with STS score between $\geq 4\%$ but < 8%
- Patients with STS score < 4% but in whom estimate risk of mortality is between 4-8% by surgical assessment

“Low Risk”

- Patients with STS < 4%

FDA APPROVED FOR TAVR
August 2019

TAVR Specific Concerns c/w SAVR

- *Stroke/Cerebral Emboli*
- *Paravalvular Regurgitation*
- *Need for Permanent Pacemaker*
- *Leaflet Thrombosis*
- *Durability*
- *Coronary Access*
- *Bicuspid Valves*

Sources of Debris Leading to CVA During TAVR



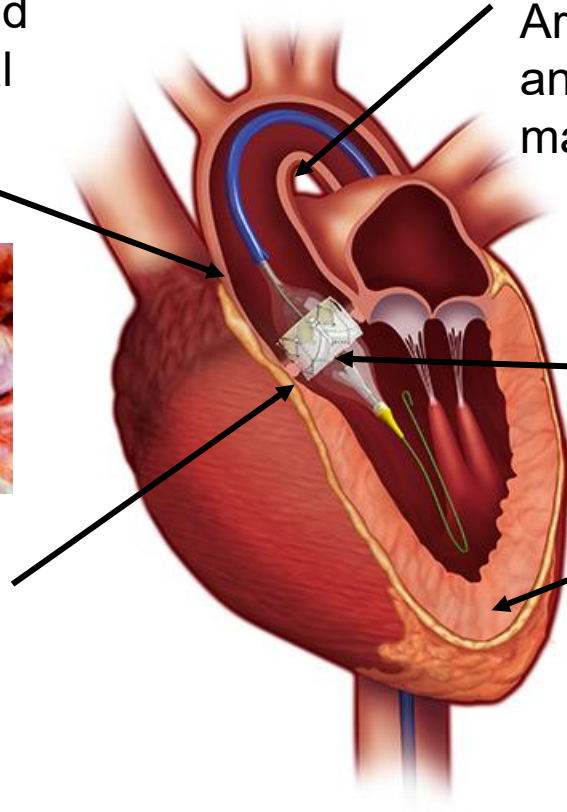
ASCENDING ARCH

Arterial wall, calcific and atherosclerotic material



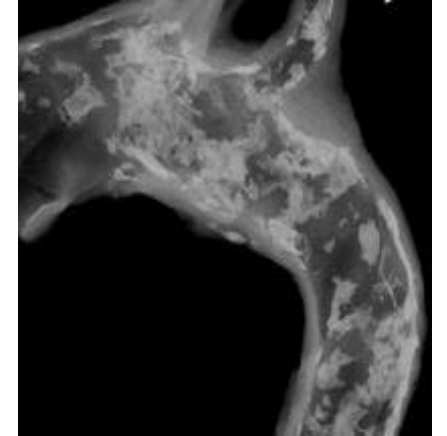
STENOTIC VALVE

Leaflet tissue and calcific deposits



TRANSVERSE ARCH

Arterial wall, calcific and atherosclerotic material



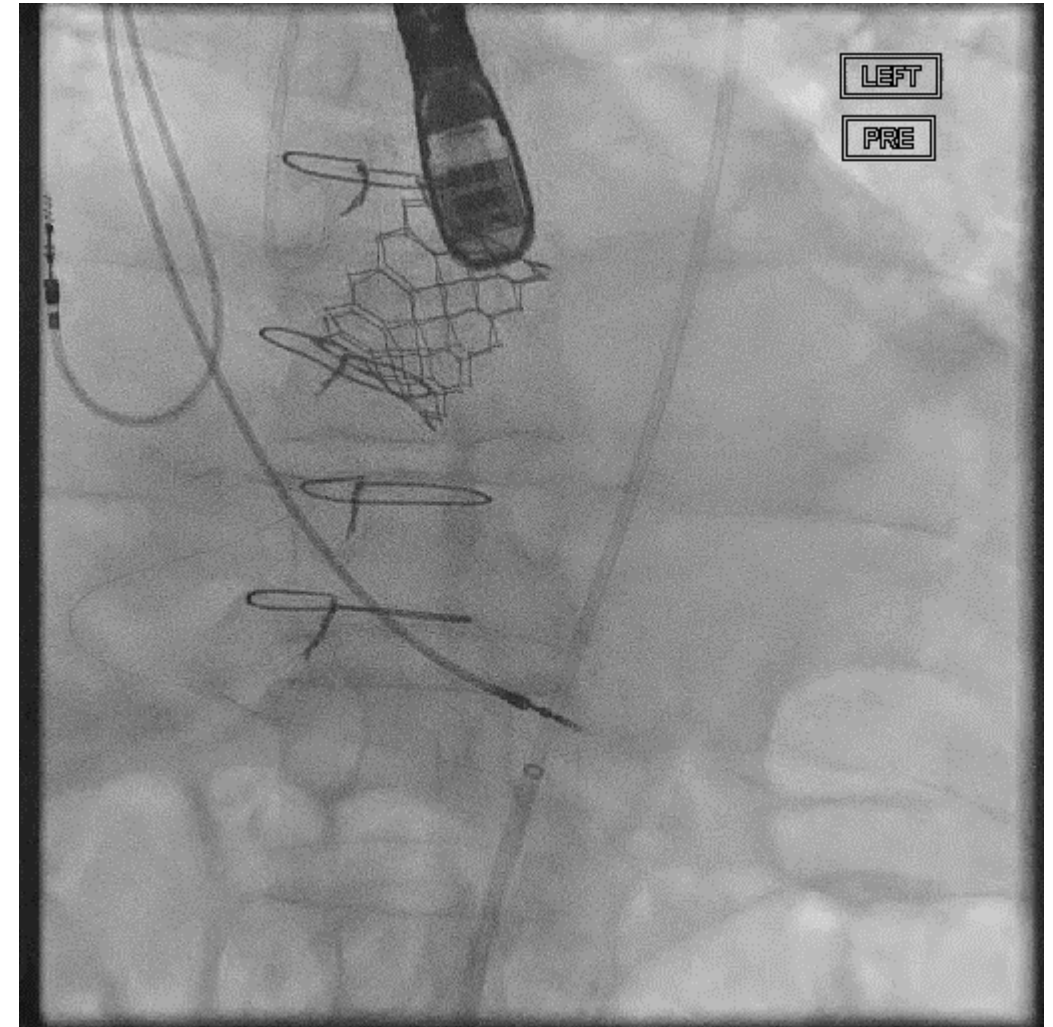
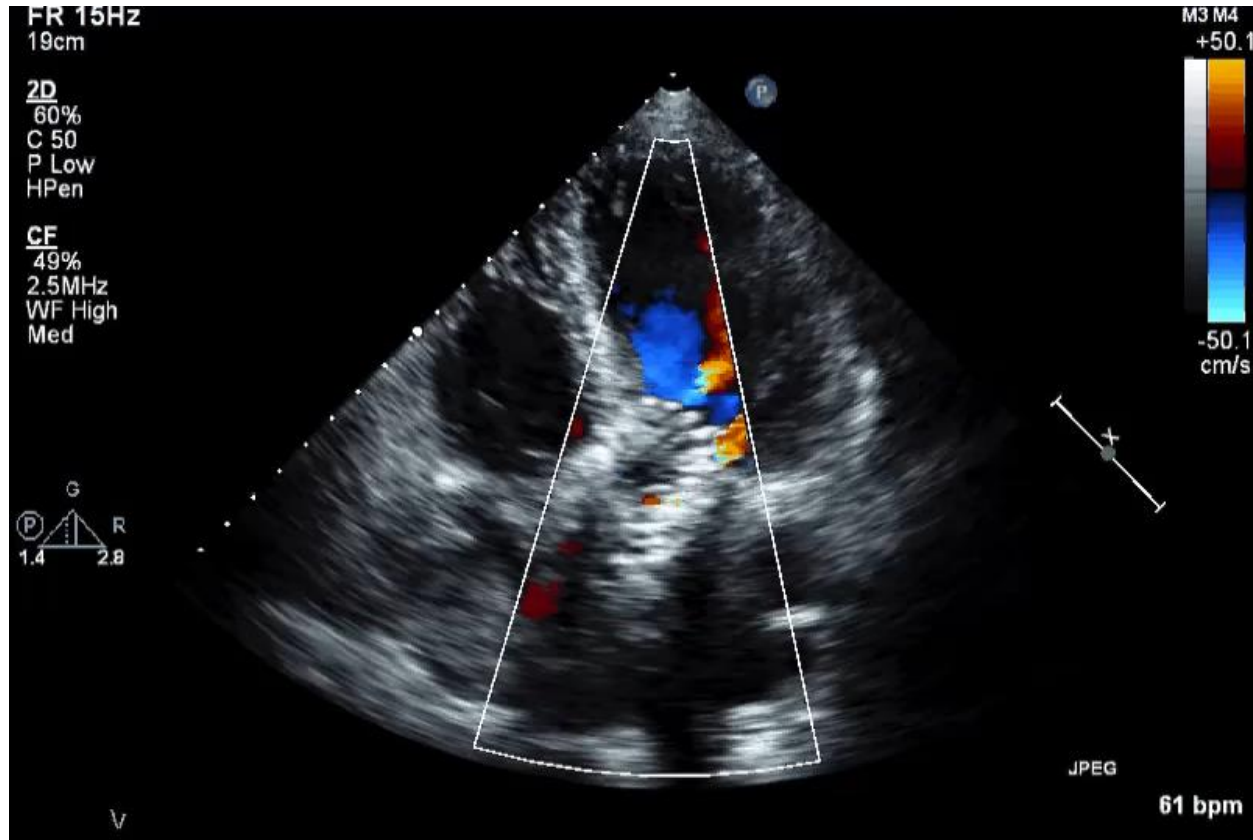
TAVI DEVICES

Foreign material, thrombus

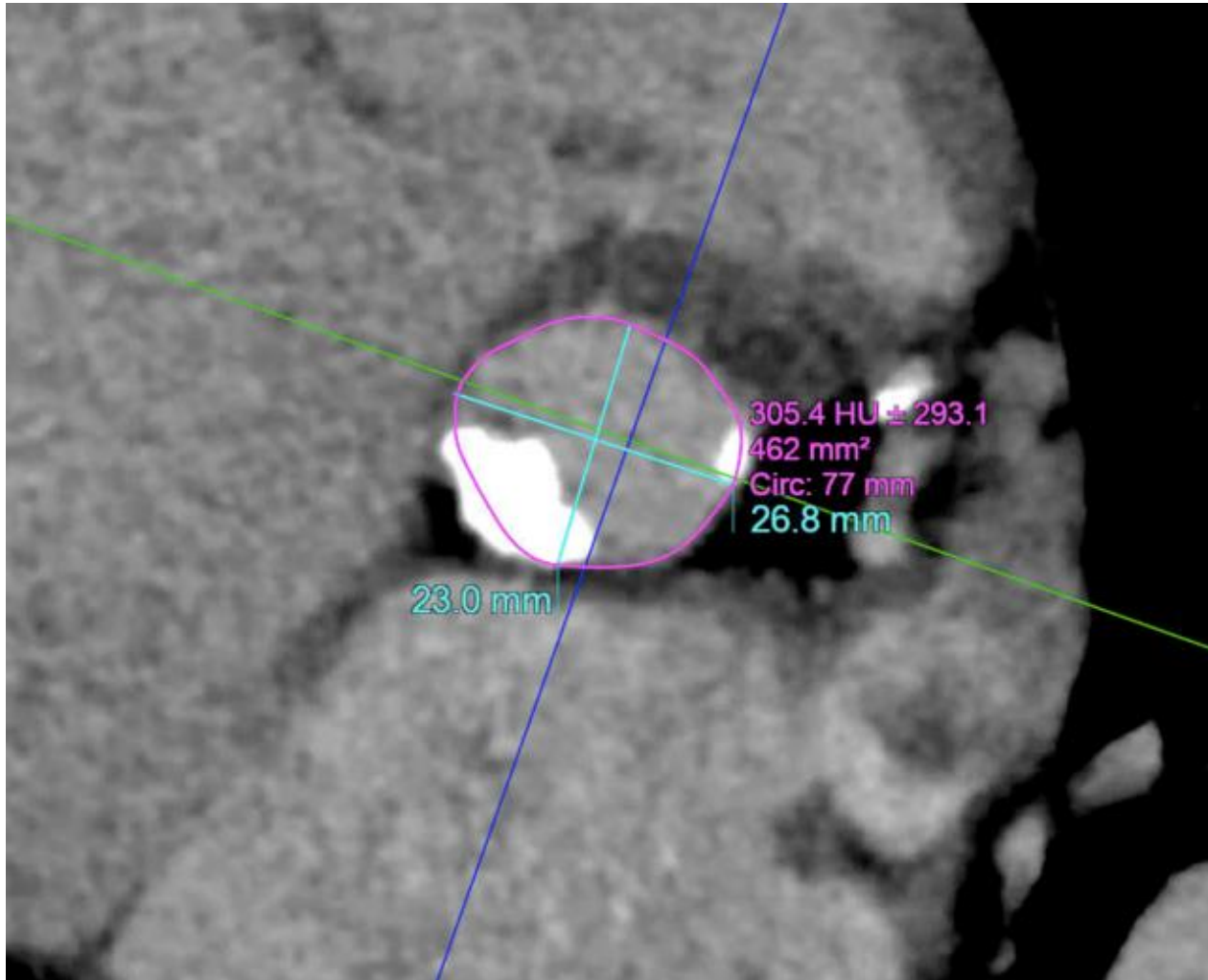
NATIVE HEART

Myocardium

Paravalvular Leak (PVL)



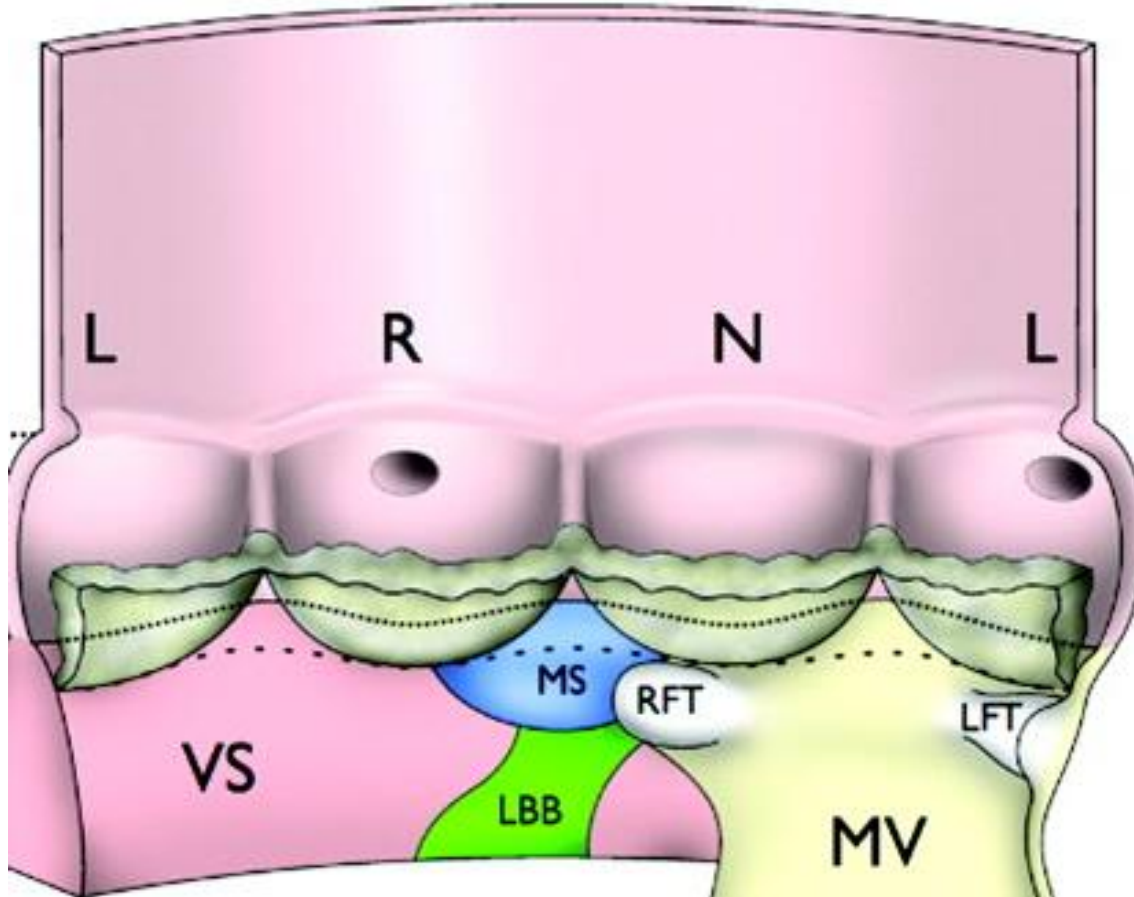
Paravalvular Leak (PVL)



Risk Factors

- Undersized prosthesis
- Hi/Low THV positioning
- Severe LVOT/annular calcium
- Irregularly shaped annulus

Pacemaker after TAVR



- Trauma to conduction system
- Higher risk with baseline conduction disease
- Higher risk with lower implants
- PPM rates and PVL rates are inversely proportional

TAVR Clinical Trials

Trial	Year	Device	Risk	Death (1yr)	Stroke (30d)	Mod/Sev PVL (30d)	PPM (30d)
PARTNER B	2010	Sapien	Inop	30.7	6.7	10.5	3.4
PARTNER A	2011	Sapien	High	24.2	5.5	12.2	3.8
Corevalve XR	2014	Corevalve	Inop	26.0	4.0	11.4	21.6
Corevalve HR	2014	Corevalve	High	14.2	4.9	9.0	19.8
PARTNER 2	2016	Sapien XT	Intermed	14.5	6.4	3.7	8.5
Sapien 3 HR	2016	Sapien 3	High/Inop	14.4	2.4	2.5	16.9
Sapien 3 IR	2016	Sapien 3	Intermed	7.4	2.4	1.5	10.2
SURTAVI	2017	Corevalve & Evolut R	Intermed	8.1	5.4	5.3	25.9
PARTNER 3	2019	Sapien 3	Low	1.0	0.6	0.8	6.5
CoreValve LR	2019	Evolut R	Low	2.3	3.4	3.5	17.4

TAVR Specific Concerns c/w SAVR

- *Stroke/Cerebral Emboli*
- *Paravalvular Regurgitation*
- *Need for Permanent Pacemaker*
- ***Leaflet Thrombosis***
- ***Durability***
- ***Coronary Access***
- ***Bicuspid Valves***

TAVR Clinical Trials: What Have We Learned?

- TAVR improves mortality in inoperable patients.
- TAVR is at least as effective at reducing mortality in high, intermediate, **and low** surgical candidates.
- TAVR highly effective at improving symptoms/functional class
- Durability of TAVR valves appears to be excellent out to 7-10 years

FDA/CMS Indication for TAVR

Severe Native Aortic Stenosis in a Tri-leaflet Aortic Valve
Life expectancy >12 months

Heart Team Evaluation

- Interventional Cardiologist
- Cardiac Surgery

Intermediate or High Risk or Inoperable

- Two cardiac surgeon evaluation
- STS > 3.0% OR
- Surgical assessment deems patient intermediate risk

Severe Aortic Stenosis in a Failed Surgically Implanted Bioprosthetic Valve in High Risk Patients

Cardiac Surgeon and Interventional Cardiologist must be present for procedure

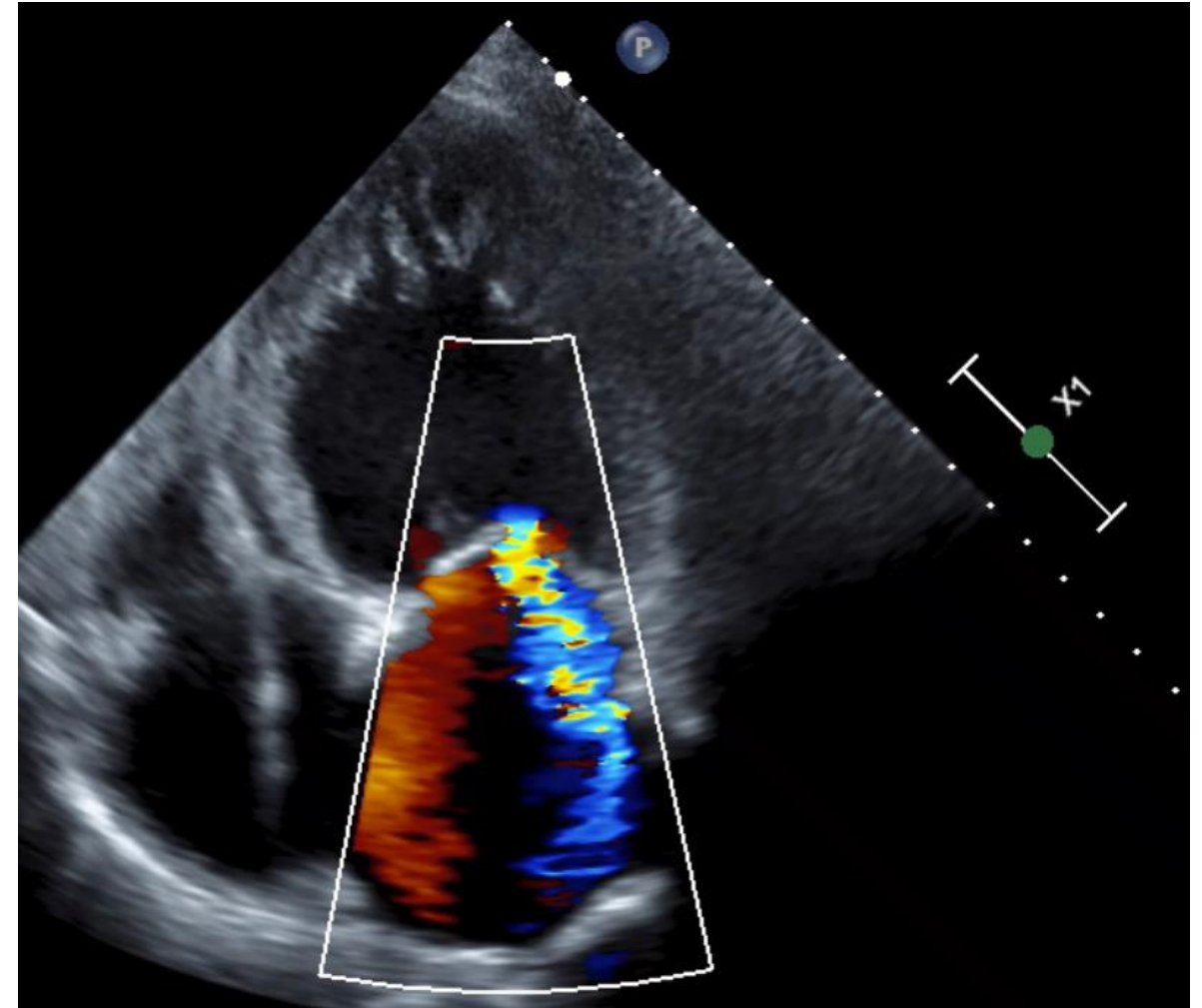
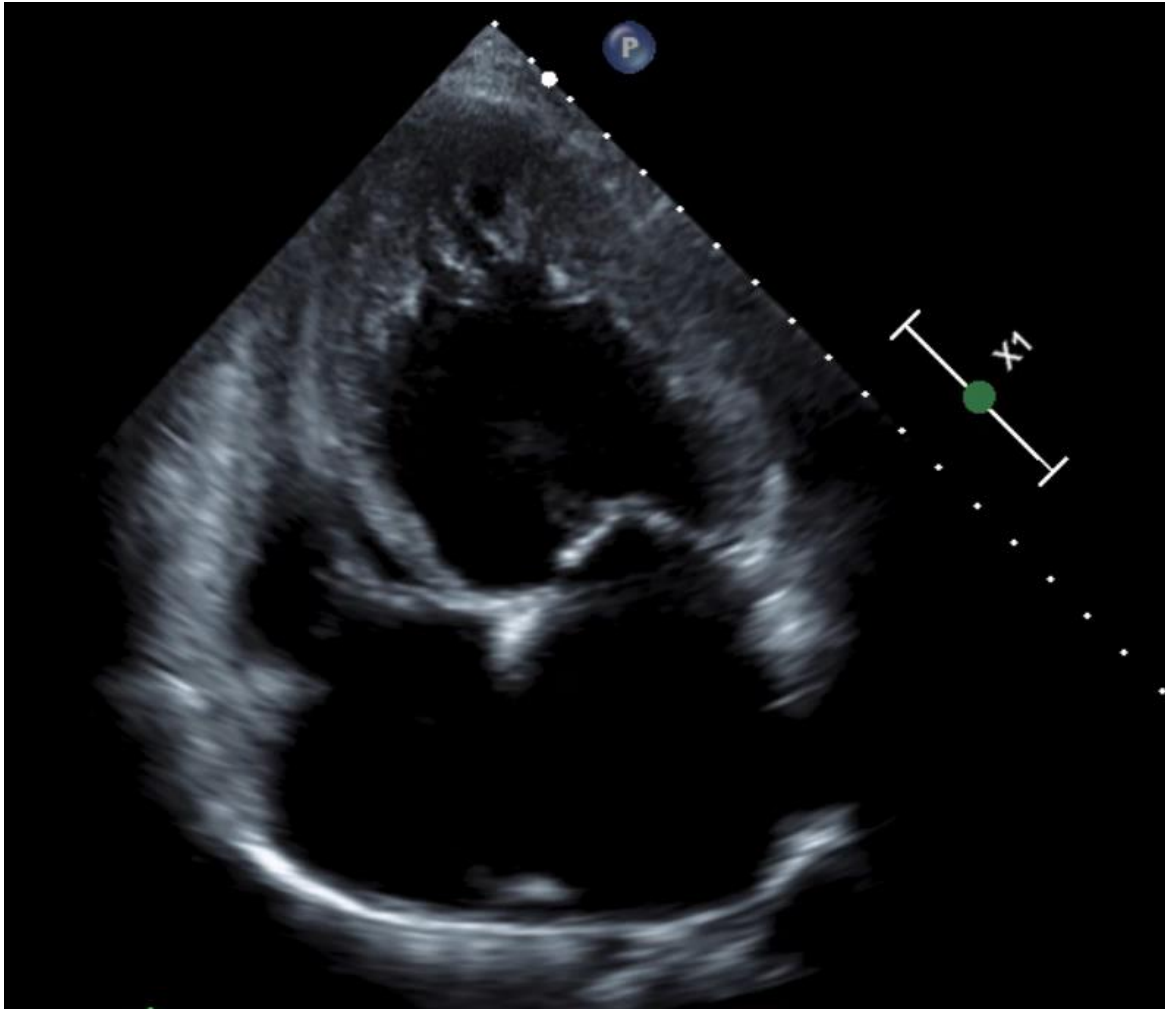
TAVR: The Future

- **Device improvements**
 - Reduce PVL
 - Reduce PPM
 - Smaller device profiles
- **Optimal anticoagulant/antithrombin regimens**
 - Several on-going trials
- **Reducing stroke risk**
 - Shields
 - Filters
- **Formal assessment of durability**
 - 10 year f/u in PARTNER 3 and Evolut Low Risk
- **Bicuspid valves**
- **Defining optimal timing of treatment of AS**
 - EARLY TAVR
 - PROGRESS

Case 2

- 82 yo F presents with severe shortness of breath waking her up while asleep
 - Non-ischemic (familial) cardiomyopathy (LVEF 20%, LVEDD 65 mm)
 - Left-bundle s/p CRT-D
 - Atrial fibrillation (on warfarin)
 - Moderate-severe MR
 - Type 2 DM
- BP 120/68| P 91| 80 % on RA
- Exam: Laterally displaced PMI, harsh HSM @ apex, +S3; crackles throughout

Case 2



LVEDD 65 mm; LVESD 61 mm

Degenerative vs. Functional MR



Normal mitral valve



**Degenerative MR
caused by mitral
valve prolapse**



**Degenerative MR
caused by flail leaflet**



Functional MR

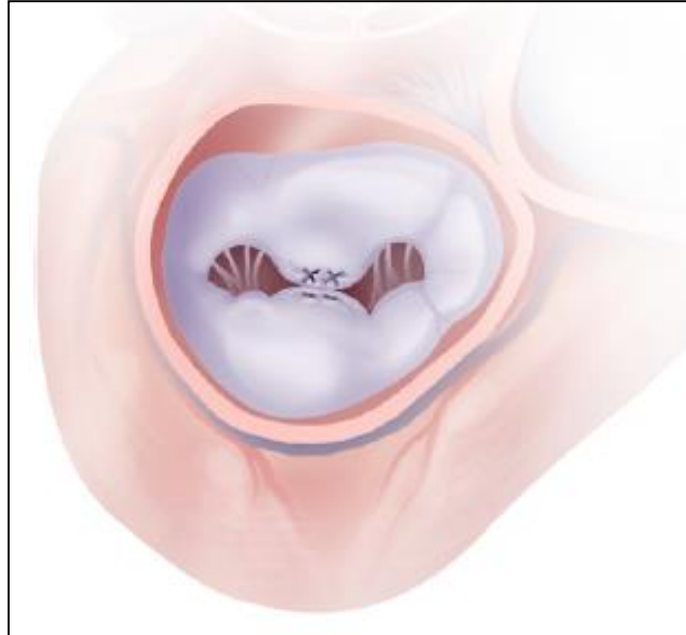
Photo source: Abbott Vascular

Edge-to-Edge Trans-catheter Mitral Valve Repair

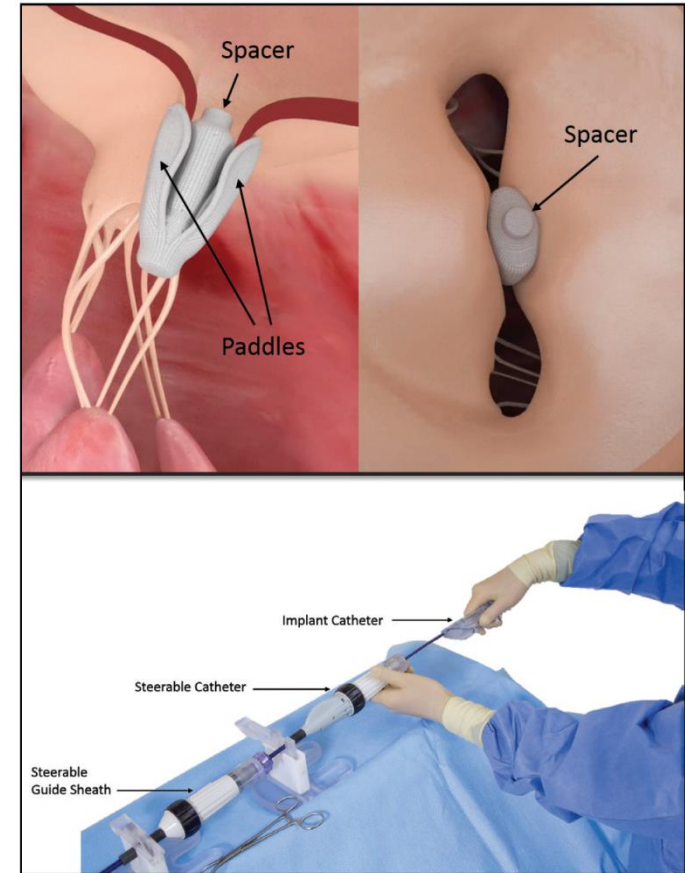


MitraClip (Abbott)

FDA Approved for Primary and Secondary MR



Alfieri Stitch



Pascal (Edwards)

FDA approved for Primary MR

MitraClip: Early Clinical Trials

Trial	Year	Comparator	Risk	No. Patients	Result
EVEREST 1	2006	Single Arm	Operable	107	MC feasible and safe
EVEREST 2	2011	MV Repair	Operable	178 MC 80 MV Repair	MV repair > MC
EVEREST 2 HR	2012	Single Arm	High	78	MC > Performance Goal
EVEREST 2 HR REALISM	2014	Single Arm	High Non-High	628 271	Improved MR, NYHA, and reduced readmissions

Based on these data, MitraClip presently approved for patients with degenerative MR who are too high risk for surgery.

MitraClip for Functional MR

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Percutaneous Repair or Medical Treatment for Secondary Mitral Regurgitation

J.-F. Obadia, D. Messika-Zeitoun, G. Leurent, B. Iung, G. Bonnet, N. Piriou, T. Lefèvre, C. Piot, F. Rouleau, D. Carrié, M. Nejjari, P. Ohlmann, F. Leclercq, C. Saint Etienne, E. Teiger, L. Leroux, N. Karam, N. Michel, M. Gilard, E. Donal, J.-N. Trochu, B. Cormier, X. Armoiry, F. Boutitie, D. Maucort-Boulch, C. Banel, G. Samson, P. Guerin, A. Vahanian, and N. Mewton, for the MITRA-FR Investigators*

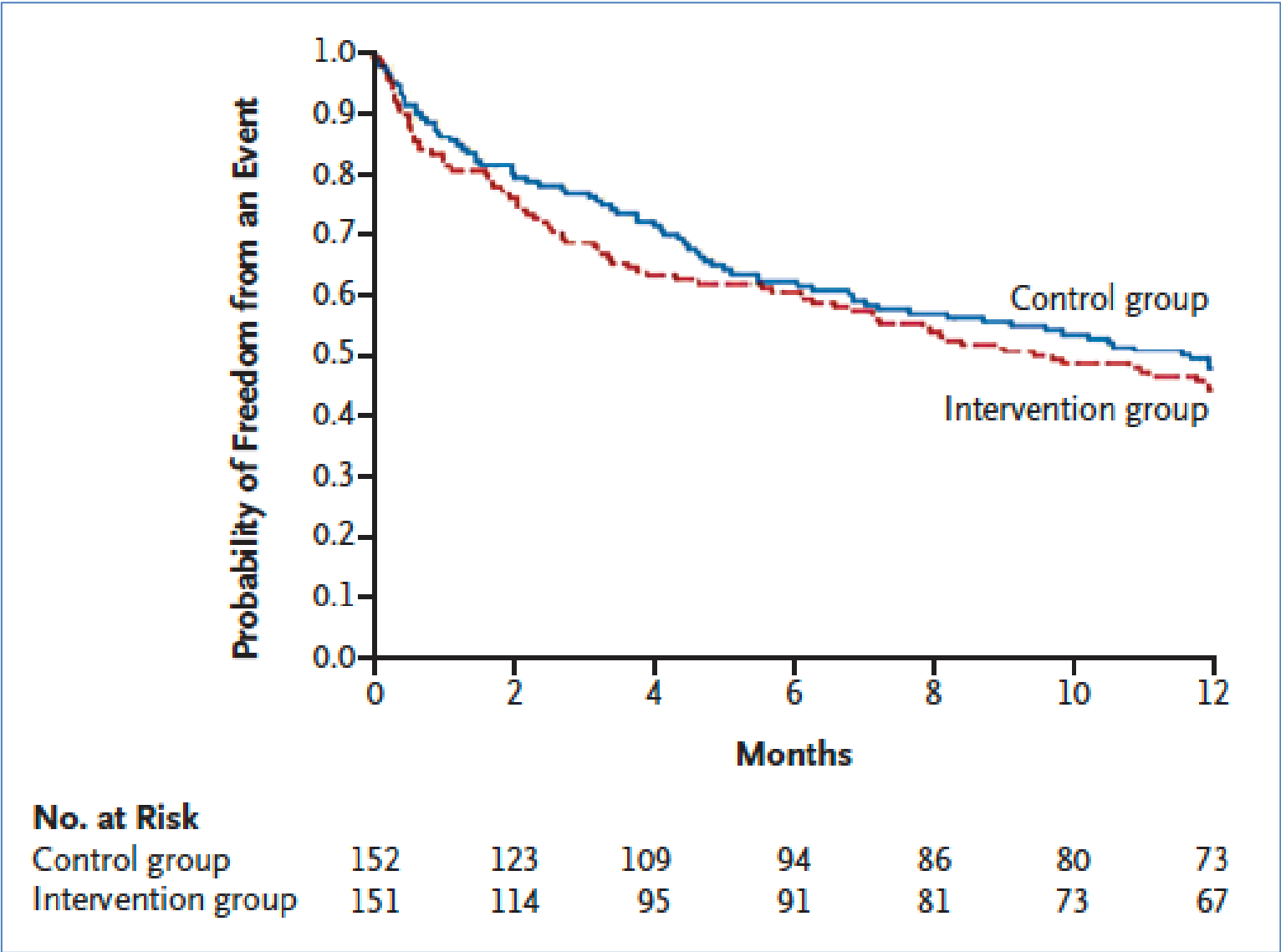
ORIGINAL ARTICLE

Transcatheter Mitral-Valve Repair in Patients with Heart Failure

G.W. Stone, J.A. Lindenfeld, W.T. Abraham, S. Kar, D.S. Lim, J.M. Mishell, B. Whisenant, P.A. Grayburn, M. Rinaldi, S.R. Kapadia, V. Rajagopal, I.J. Sarembock, A. Brieke, S.O. Marx, D.J. Cohen, N.J. Weissman, and M.J. Mack, for the COAPT Investigators*



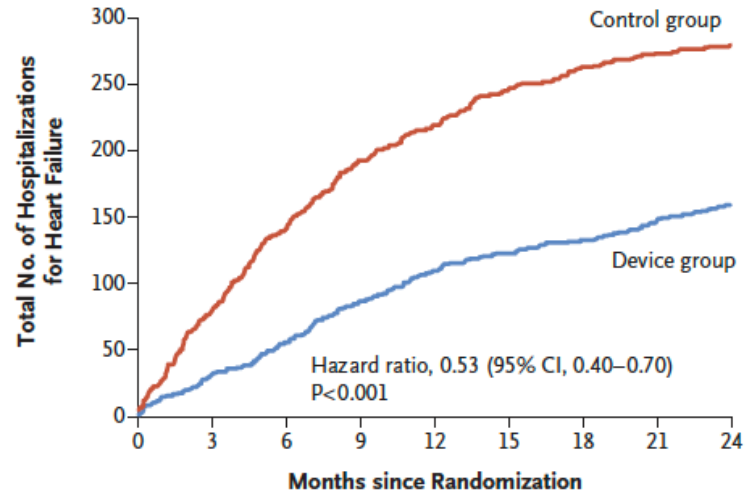
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**Primary End Point:
Death or Unplanned
Hospitalization at 12
Months**

COAPT

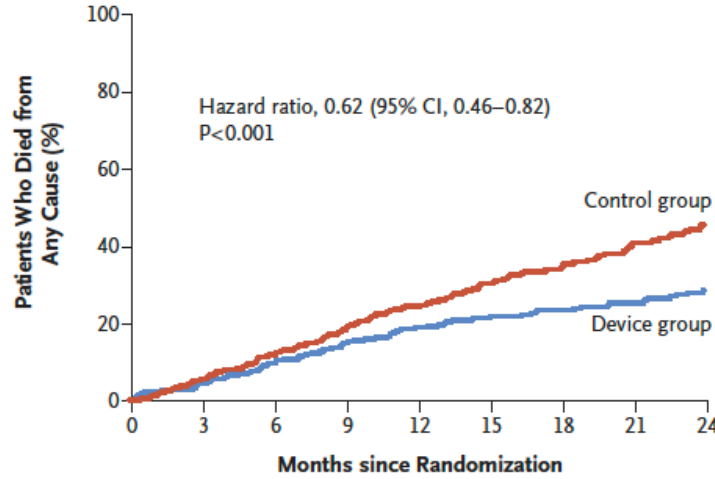
A Hospitalization for Heart Failure



No. at Risk

Control group	312	294	271	245	219	176	145	121	88
Device group	302	286	269	253	236	191	178	161	124

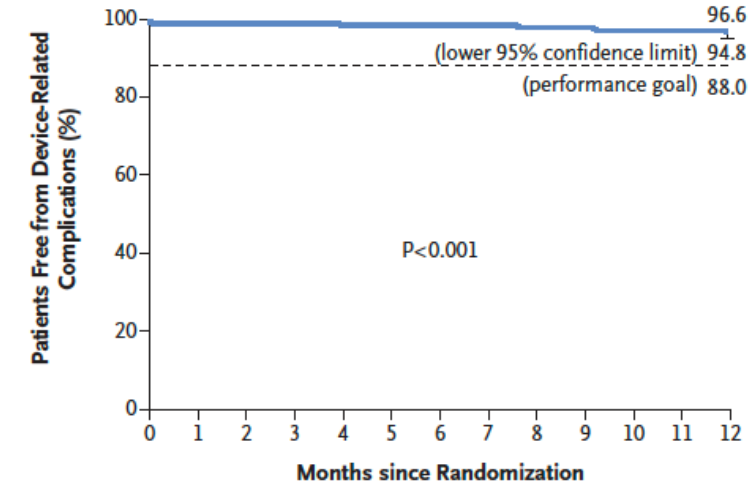
C Death from Any Cause



No. at Risk

Control group	312	294	271	245	219	176	145	121	88
Device group	302	286	269	253	236	191	178	161	124

B Freedom from Device-Related Complications



No. at Risk

Device group	293	283	282	277	272	269	261	258	251	245	241	236	221
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NEJM 2018; 379: 2307-2318

Clinical Trials of MitraClip for Functional MR

TABLE 5 Comparison of Ongoing Randomized Trials of the MitraClip in Patients With Heart Failure and Secondary Mitral Regurgitation			
	COAPT	RESHAPE-HF	MITRA-FR
Number of patients and sites	430 patients at 75 U.S. and Canadian sites	800 patients at 50 E.U. sites	288 patients at 18 French sites
Secondary MR grade (core laboratory verified)	$\geq 3+$ (EROA ≥ 30 mm ² and/or Rvol > 45 ml)	$\geq 3+$ (EROA ≥ 30 mm ² and/or Rvol > 45 ml)	Severe (EROA > 20 mm ² + Rvol > 30 ml)
NYHA functional class	II, III, or ambulatory IV	III or ambulatory IV	II-IV
LVEF	$\geq 20\%$ to $\leq 50\%$	$\geq 15\%$ to $\leq 40\%$	$\geq 15\%$ to $\leq 40\%$
Surgical criteria	Not appropriate for mitral valve surgery (heart team)	None	None
Left ventricular volume entry criterion	LV end-systolic dimension ≤ 70 mm	LV end-diastolic dimension ≥ 55 mm	None
Control arm	Guideline-directed medical therapy (+CRT, if indicated)	Guideline-directed medical therapy (+CRT, if indicated)	Guideline-directed medical therapy (+CRT, if indicated)
Primary efficacy endpoint (superiority)	Heart failure rehospitalizations at 1 yr	Death or heart failure hospitalization at 1 yr	Death or recurrent heart failure hospitalization at 1 yr
Primary safety endpoint (noninferiority)	The composite of: SLDA; device embolization; endocarditis requiring surgery; echocardiography core laboratory-confirmed mitral stenosis requiring surgery; LVAD implant; heart transplant; or any device-related complications requiring nonelective cardiovascular surgery at 12 months	None	None
Health economics	Assessed	Assessed	None
Follow-up, yrs	5	2	

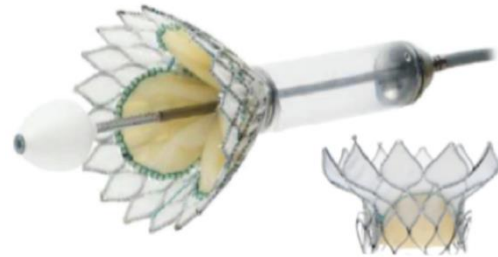
TMVR: Challenges to TMVR Development

- Access to MV more difficult
 - Trans-apical access
 - Trans-septal access
- MV annulus very large
 - Larger device sizes
- MV annulus not rigid
 - Requirement for active fixation
- Proximity to LVOT
 - LVOT obstruction
- MV complex structure
 - Chords, papillary muscles

TMVR Devices

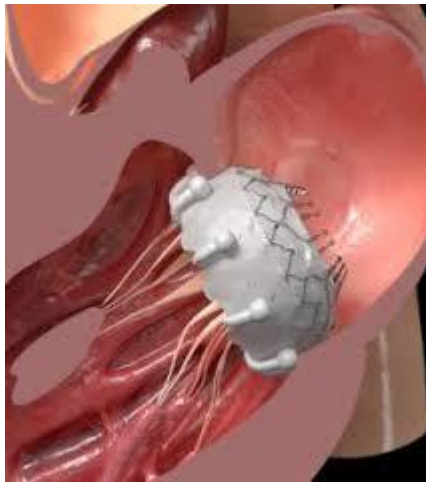


Intrepid (Medtronic)



Tendyne (Abbott)*

*FDA Approved 2025



Evoque (Edwards)



M3 (Edwards)*

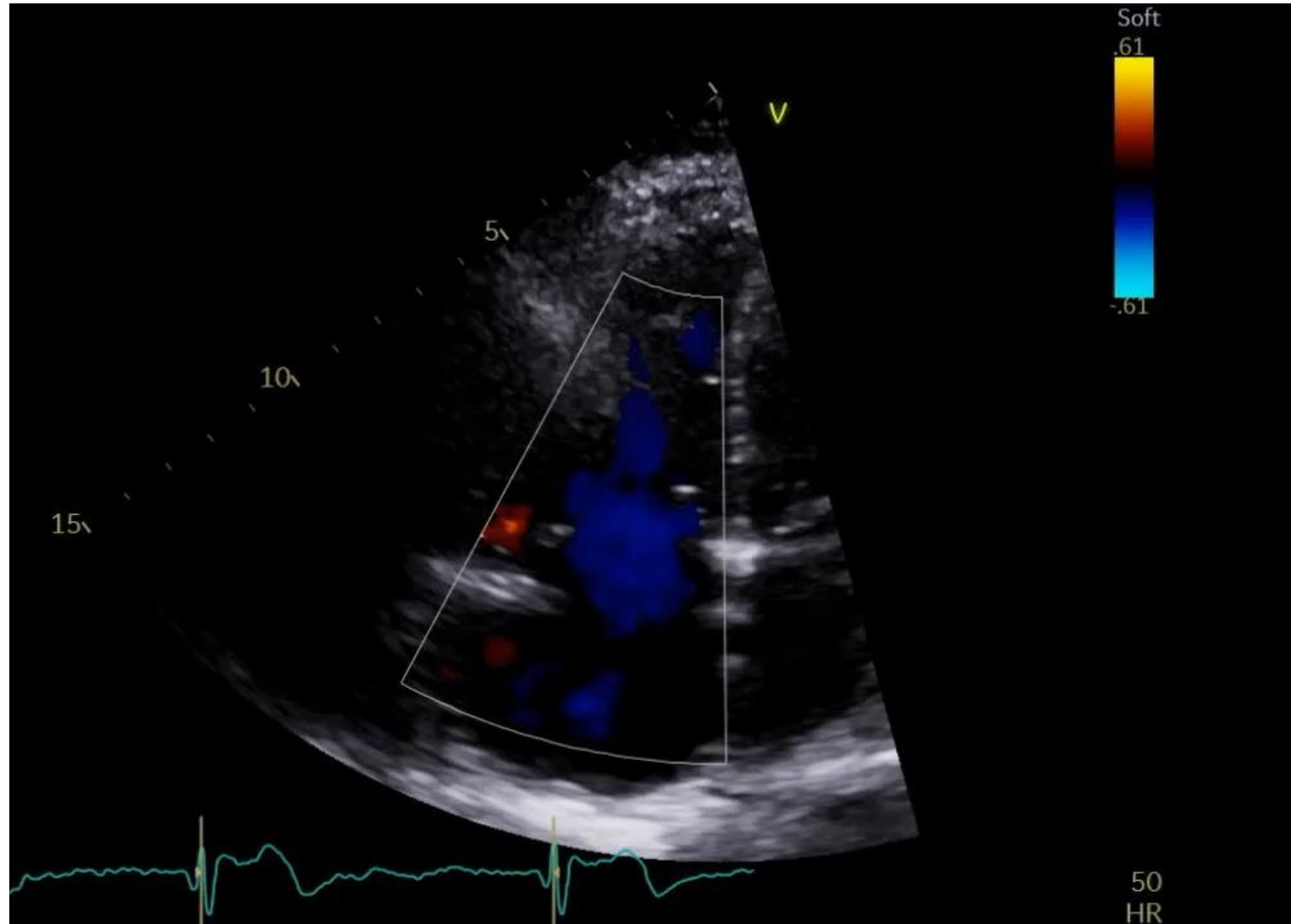
Trans-Catheter Mitral Valve Therapies: Conclusions

- Important to understand mechanism of MR: primary (degenerative) or secondary (functional)
- TEER indicated for high-surgical risk primary MR patients appropriately selected secondary MR patients
- Many TMVR and TMVr devices in clinical trials at this time.
- Critical for patients to be assessed in a multidisciplinary fashion to determine best treatment options
- Imagers, heart failure MDs, interventional cardiologists, and surgeons

Case 3

- 83 year-old woman with worsening shortness of breath, lower extremity edema
- Initially responsive to diuretics but now requiring increasing doses
- Trans-thoracic echo notable for severe tricuspid regurgitation with slight increase in RV size
- Felt to be a poor candidate for surgery

Case 3- Echocardiogram



- The TV is often called the “forgotten valve”
- Slow progression, rarely acutely fatal, no great treatment options outside of diuretics and surgery
- As a results, patients are often referred late for consideration of therapies
- Etiologies: primary (degenerative) and secondary (functional)
- At the present time, all percutaneous treatment options are investigational

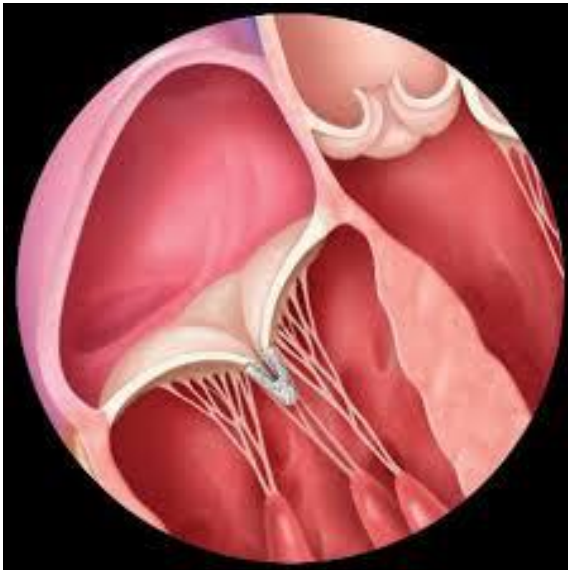
Tricuspid Repair Devices- Investigational

Tricuspid Trans-catheter Edge to Edge Repair



Tri-Clip

TRILUMINATE Trial-FDA approved April 2024

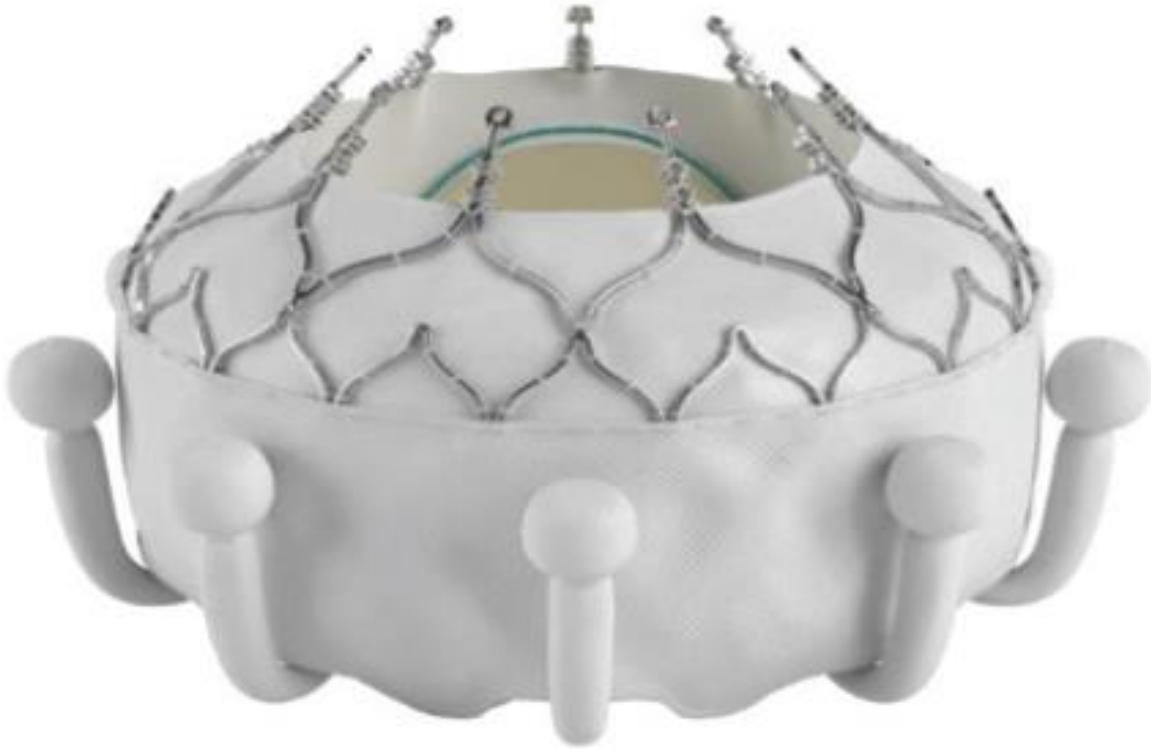


Pascal

TRICLASP Trial



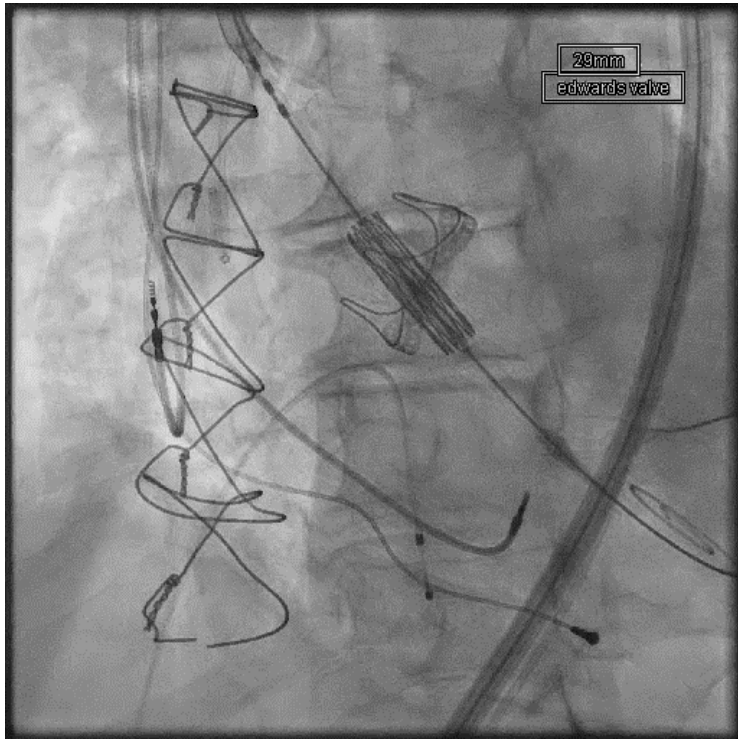
Tricuspid Replacement Devices



Evoque (Tricuspid)
TRISCEND II Trial

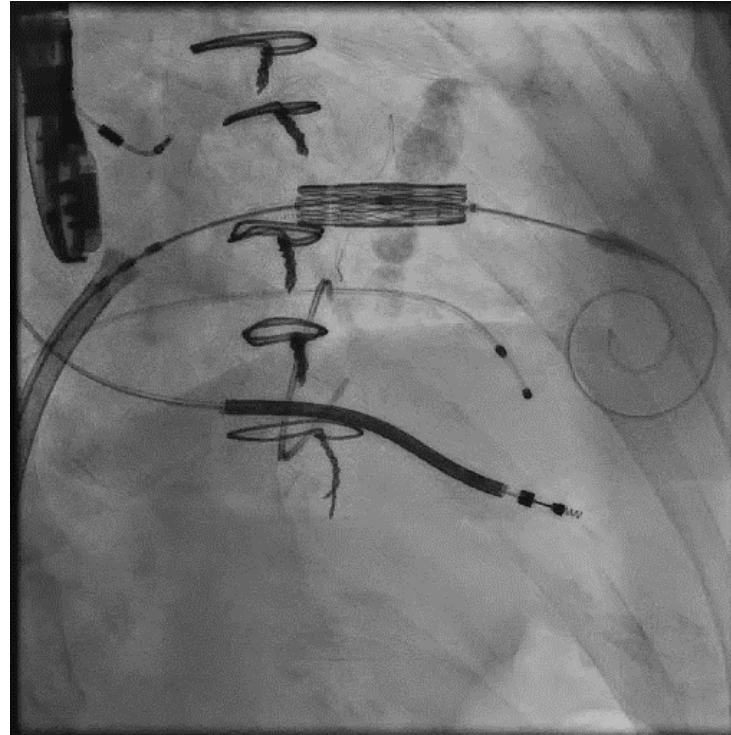
FDA Approved March 2024

Valve-in-Valve Procedures



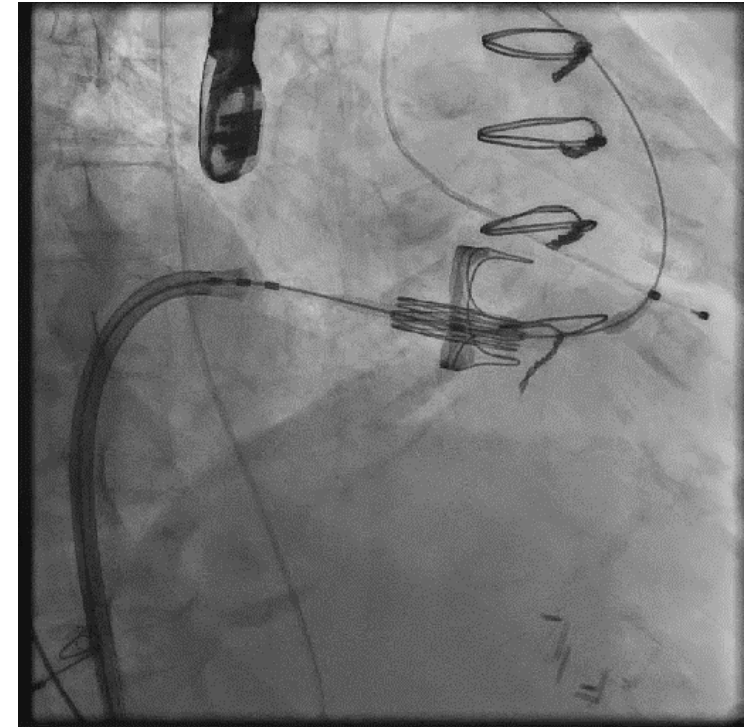
Aortic Valve-in-Valve

- Approved for high-risk
- Ongoing studies of intermediate and low risk



Mitral Valve-in-Valve

- Approved for high-risk
- Ongoing studies of intermediate and low risk



Tricuspid Valve-in-Valve

- Not FDA approved

Conclusions

- TAVR is standard of care (compared to surgical AVR) in patients who are deemed inoperable or high risk for surgical AVR and is an acceptable treatment for patients independent of surgical risk for AVR.
- Trans-catheter edge-to-edge procedure can be considered in patients high risk for surgical MVR with severe symptomatic MR due to degenerative mitral valve disease.
- Trans-catheter edge-to-edge procedure has shown favorable results in patients with functional MR who have been maximized on guideline directed medical therapy and remain symptomatic
- Intense investigation ongoing evaluating novel percutaneous devices for mitral valve and tricuspid valve repair and replacement.

Conclusions (2)

- For any patient with valvular heart disease, early referral to cardiology paramount to ensure greatest access to therapies or investigational protocols that may improve long-term outcomes

Thank You

pbshah@bwh.harvard.edu

X: @PinakShahMD

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The PARTNER Trial. NEJM 2011: 2187-2198.

The CoreValve Extreme Risk Study. JACC 2014: 1972-1981.

The PARTNER 2 Trial. NEJM 2016: 1609-1620.

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The EVEREST II Trial. NEJM 2011: 1395-1406.

The MITRA FR Trial. NEJM 2018: 2297-2306.

The COAPT Trial. NEJM 2018: 2307-2318.

The PARTNER 3 Trial. NEJM 2019: ePublication March 2019

The CoreValve Evolut Low Risk Trial. NEJM 2019: ePublication March 2019