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

Percutaneous Approaches to Valve Disease

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HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

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

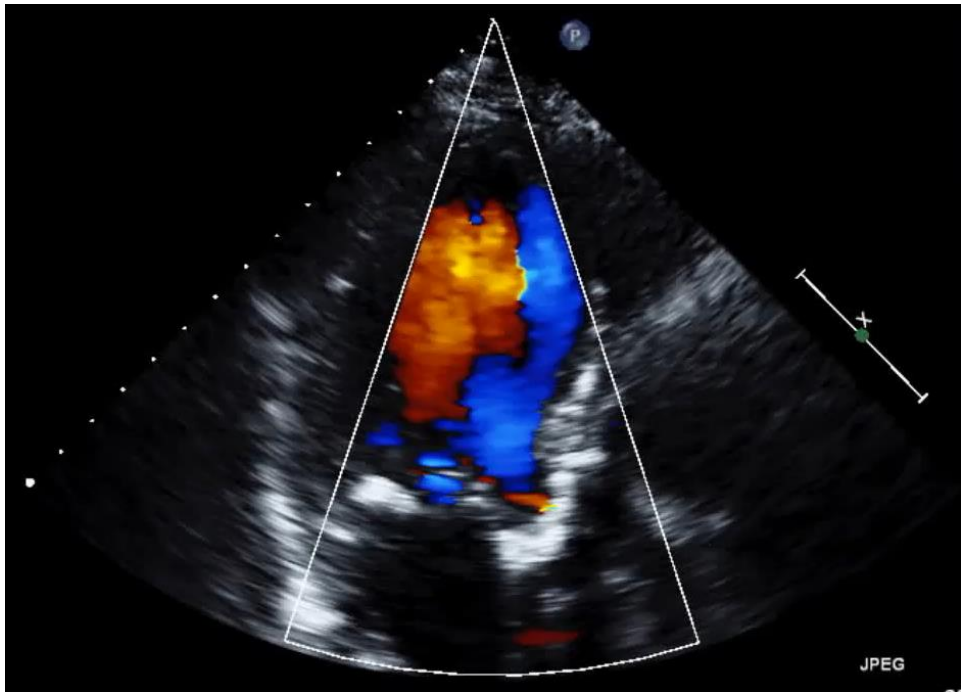
Objectives

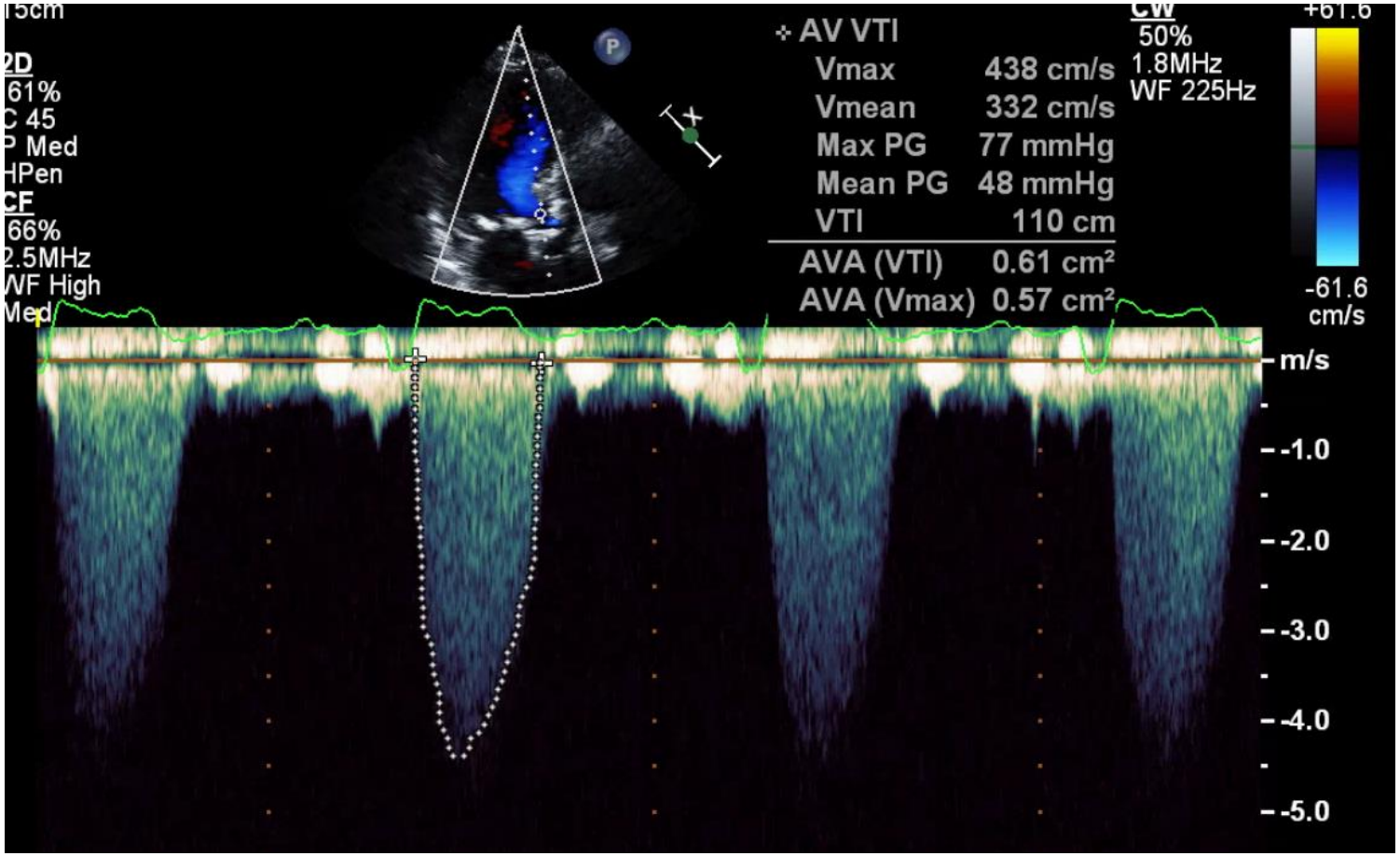
- Use 3 case vignettes to:
  - Highlight trans-catheter options for the management of common valvular heart conditions
  - Review investigational devices that may have a future role in broadening the management armamentarium for patients with valvular heart disease

Case 1

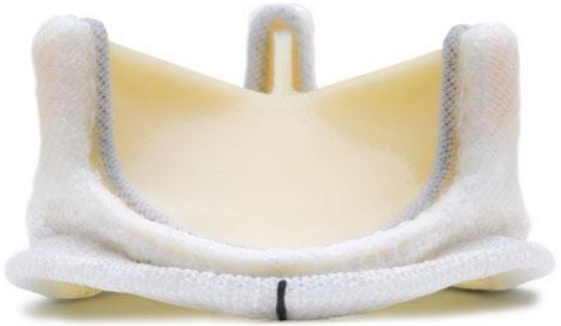
- 85 year old man with progressive dyspnea on exertion
- Exam notable for a loud systolic ejection murmur at the right upper sternal border
- Carotid upstrokes noted to be diminished
- ECHO: severe aortic stenosis with V_{max} 4.5 m/s, mean gradient 54 mmHg, aortic valve area 0.6 cm^2.
- Referred for treatment considerations
- STS score 3.5%

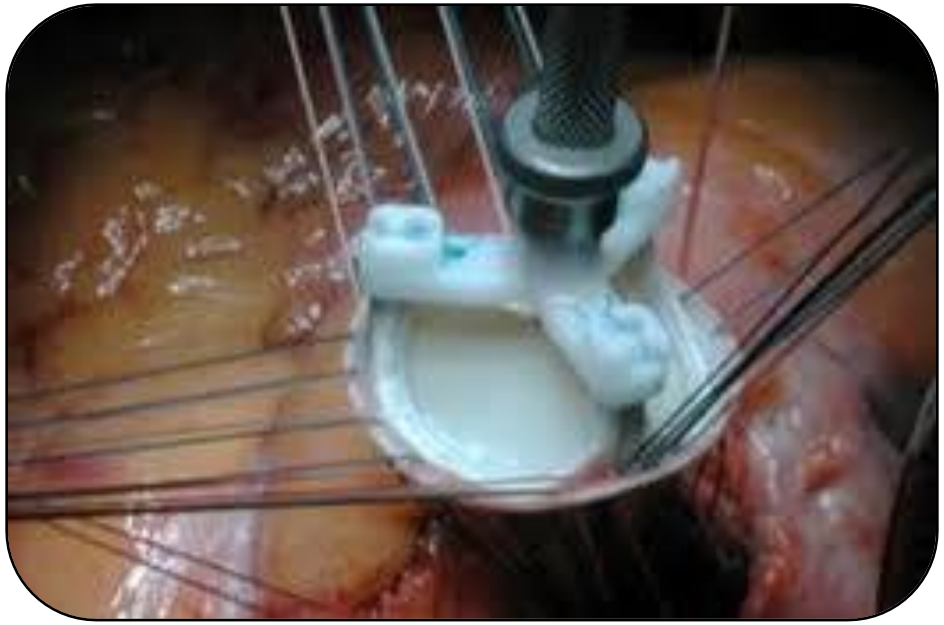
Case 1- Echo


JPEG


AV VTI
Vmax 438 cm/s
Vmean 332 cm/s
Max PG 77 mmHg
Mean PG 48 mmHg
VTI 110 cm
AVA (VTI) 0.61 cm²
AVA (Vmax) 0.57 cm²
CW
50%
1.8MHz
WF 225Hz
+61.6
-61.6
cm/s
m/s
-1.0
-2.0
-3.0
-4.0
-5.0

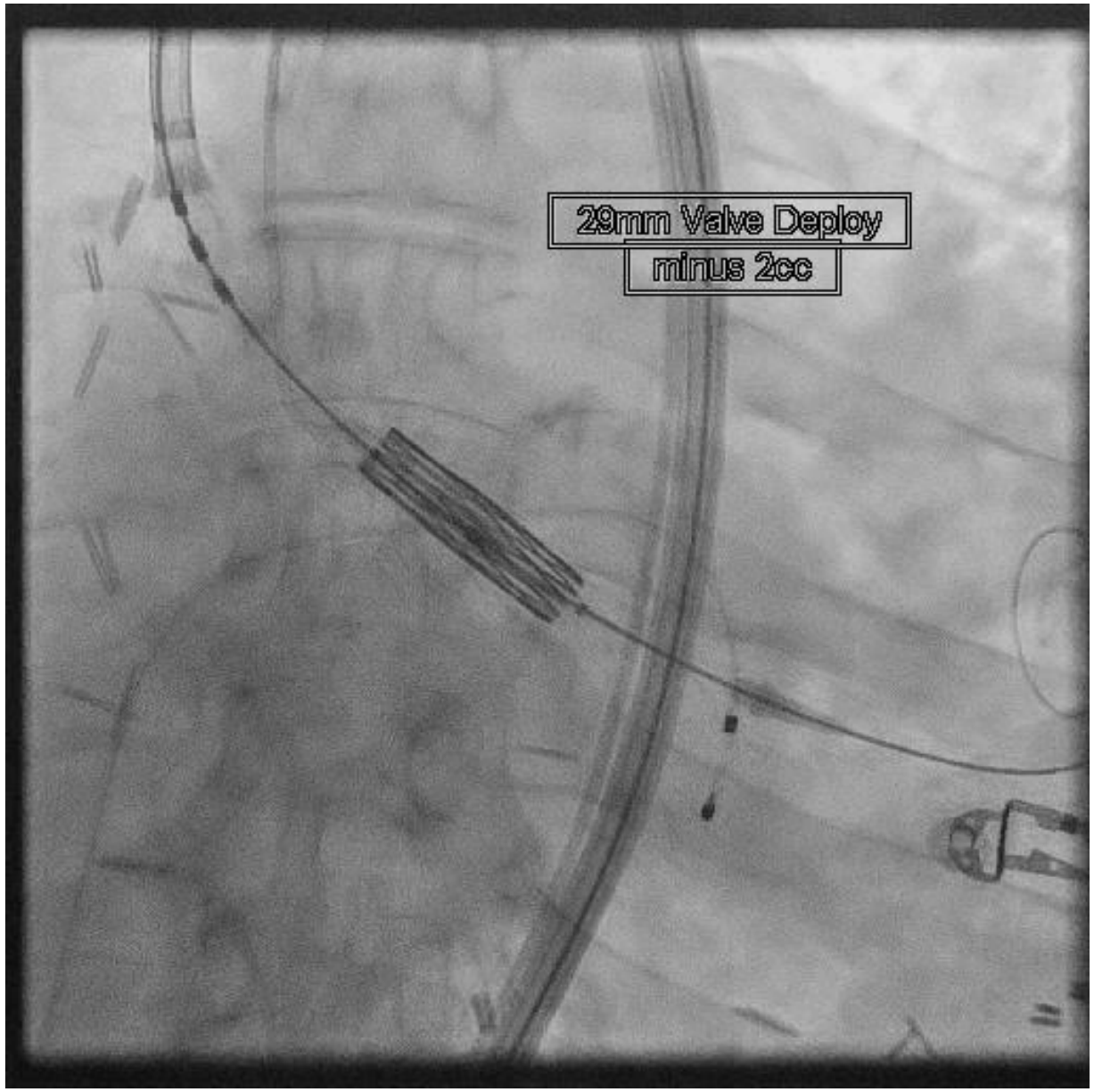
Surgical Aortic Valve Replacement (SAVR)





Historical Gold Standard for Aortic Valve Replacement

Trans-catheter Aortic Valve Replacement (TAVR)



Catheter based delivery and implantation of an aortic valve

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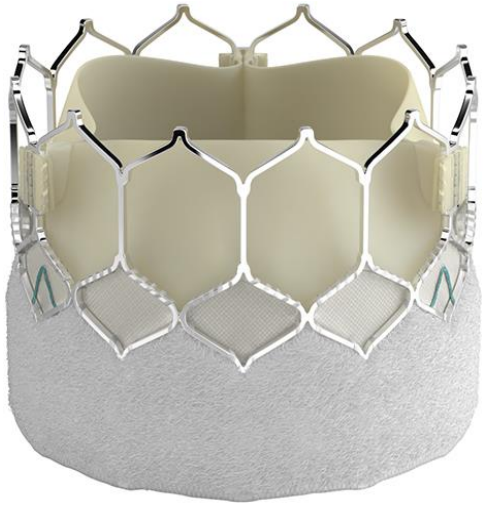
SAVR vs TAVR

	SAVR	TAVR
Access	Sternotomy	Vascular
Cardiopulmonary Bypass	Yes	No
General Anesthesia	Yes	No
Hospitalization	5-7 Days	1-3 Days
Recovery	4-6 weeks	< 1 week
Valve Types	mechanical/biological	biological

TAVR 2025

- Location: CCL vs. Hybrid OR
- Anesthesia: GA vs. IVCS
- Access Points:
  - Venous (IJ or femoral): temporary pacer
  - 5-6Fr Arterial (radial or femoral): pigtail for aortography
  - 14Fr Arterial (femoral): delivery sheath
- Large Sheath Closure
  - Suture mediate closure devices: Perclose
- Post-procedure recovery
  - CCU vs. floor
- Procedure time: ~60 minutes
- D/C 24 hours, normal activity 72 hours

FDA Approved TAVR Valves in the United States

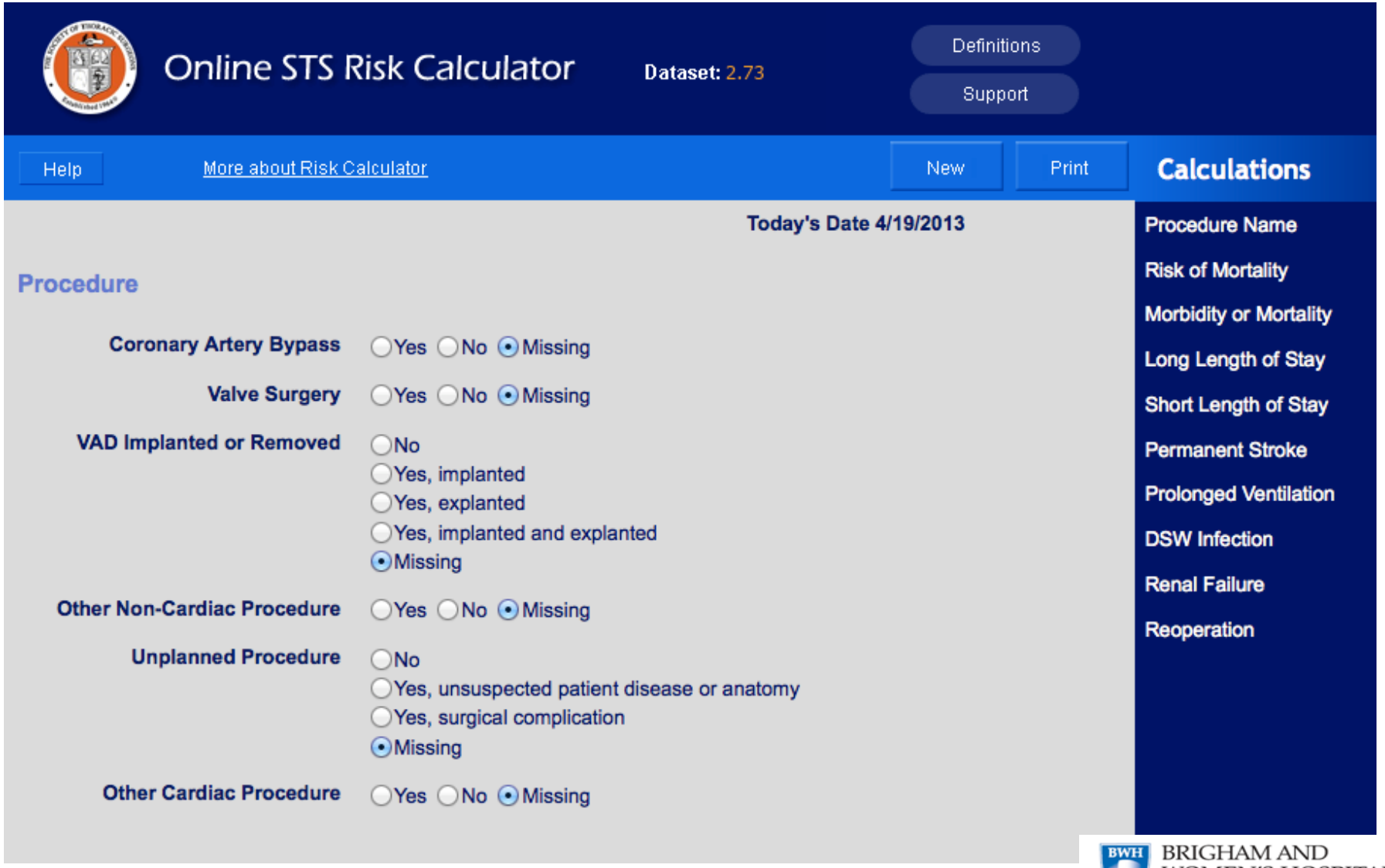


Sapien 3 Ultra/Resilia
4th Generation
Edwards LifeSciences

Evolut FX
5th Generation
Medtronic

Navitor
Abbott Vascular
*high surgical risk patients only

Assessing Surgical Risk: STS Score



http://riskcalc.sts.org/STSWebRiskCalc273/

Assessing Surgical Risk

Table 7. Risk Assessment Combining STS Risk Estimate, Frailty, Major Organ System Dysfunction, and Procedure-Specific Impediments

	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

PRACTICE GUIDELINE

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

A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

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

CrossMark

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TAVR Clinical Trials (>10,000 Patients)

Trial	Year	TAVR Device	Risk	N	Result	Follow-Up
PARTNER B	2010	Sapien	Inop	358	TAVR > Medical Therapy	1 year
PARTNER A	2011	Sapien	High	699	TAVR non-inf to SAVR	1 year
Corevalve XR	2014	Corevalve	Inop	506	TAVR > Performance Goal	1 year
Corevalve HR	2014	Corevalve	High	795	TAVR non-inf to SAVR, possibly superior	1 year
NOTION	2015	Corevalve	Low	280	No Difference between TAVR and SAVR	10 years
PARTNER 2	2016	Sapien XT	Intermed	2032	TAVR > SAVR for TF candidates	5 years
SURTAVI	2017	Corevalve/ Evolut R	Intermed	1746	TAVR non-inf to SAVR	5 years
PARTNER 3	2019	Sapien 3	Low	1000	TAVR > SAVR	5 years (10)
Evolut Low Risk	2019	Evolut R	Low	1468	TAVR non-inf to SAVR	4 years (10)
DEDICATE	2024	All Devices	Low	1414	TAVR non-inf to SAVR	1 year

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 ≥ 8%
- Patients with STS Risk Score < 8% but in whom the estimated risk of mortality from sAVR is ≥ 15% by two surgical assessments

"Intermediate Risk"

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

"Low Risk"

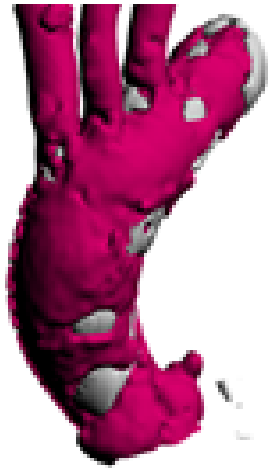
- Patients with STS < 4%

FDA APPROVED FOR TAVR
August 2019

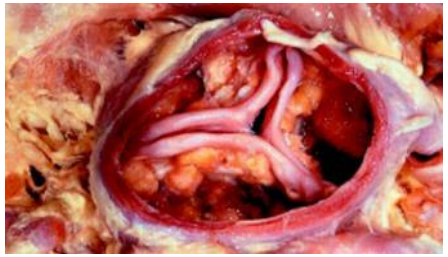
TAVR Specific Concerns c/w SAVR

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

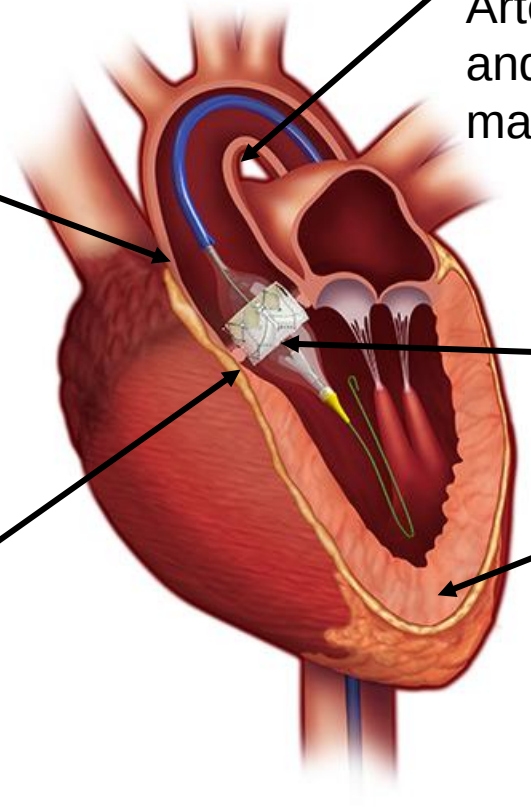
Sources of Debris Leading to CVA During TAVR



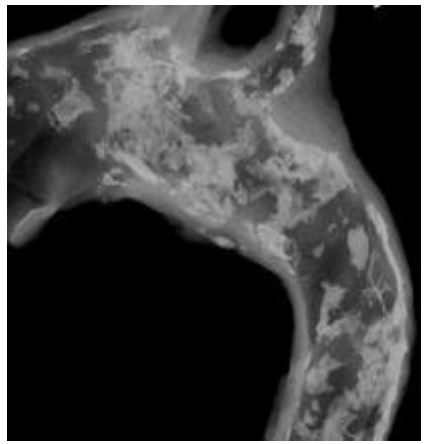
ASCENDING ARCH
Arterial wall, calcific and atherosclerotic material



STENOTIC VALVE
Leaflet tissue and calcific deposits



TRANSVERSE ARCH
Arterial wall, calcific and atherosclerotic material



TAVI DEVICES
Foreign material, thrombus

NATIVE HEART
Myocardium

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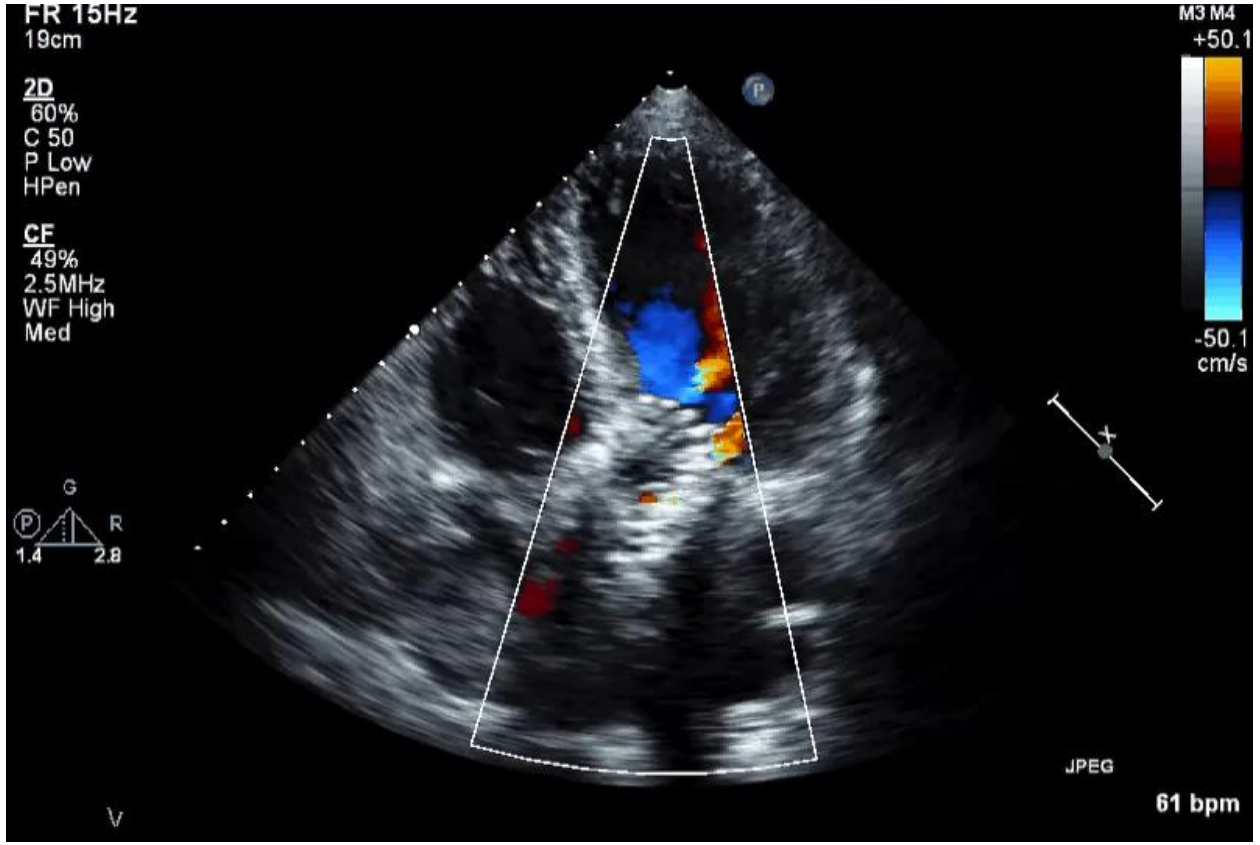
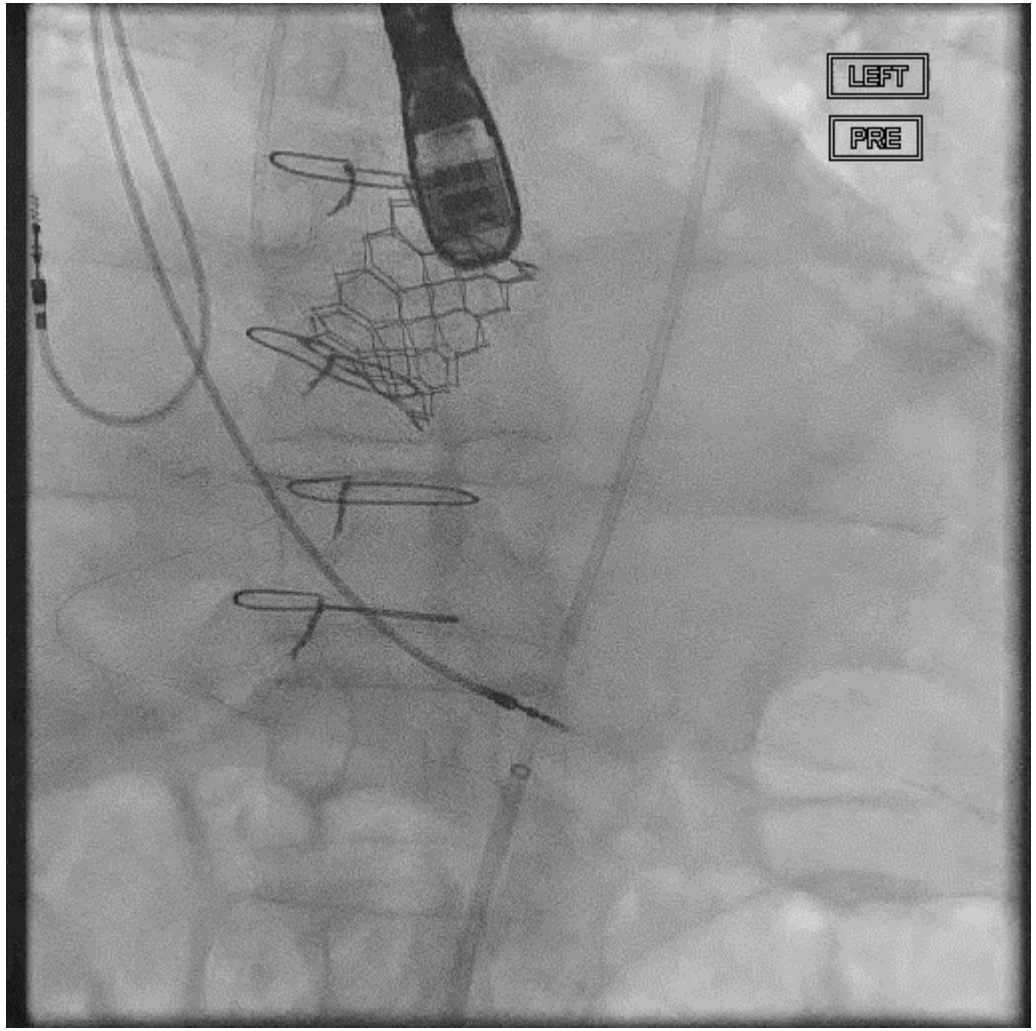
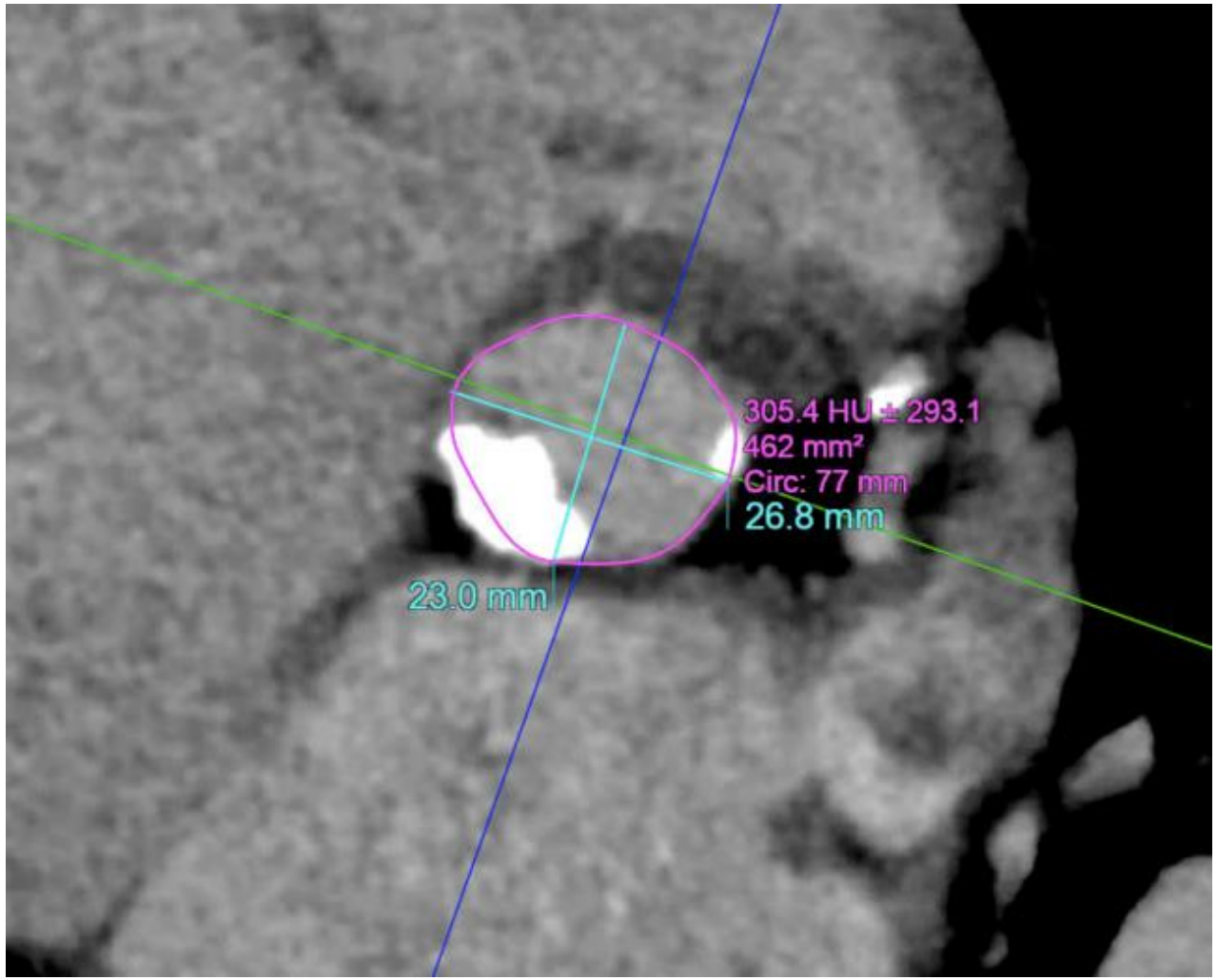
Paravalvular Leak (PVL)





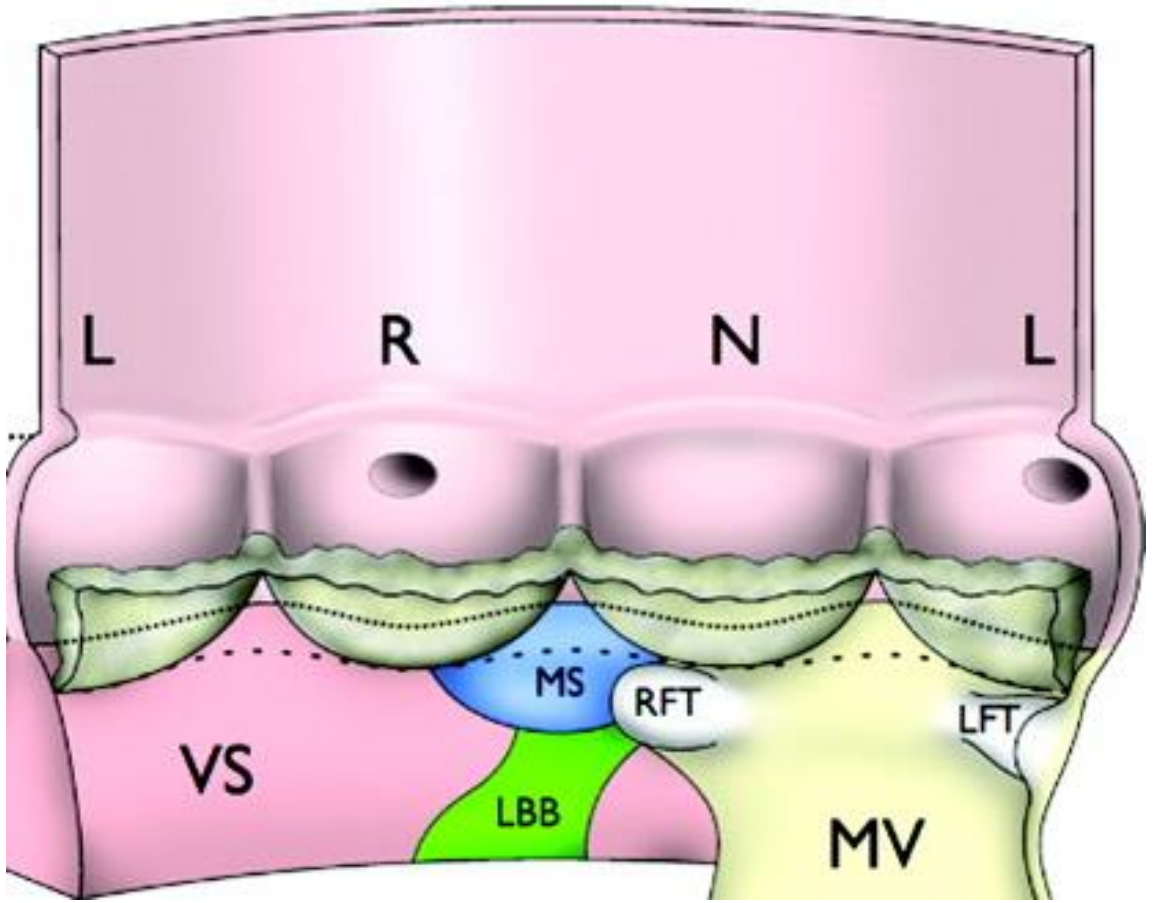
Paravalvular Leak (PVL)



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 5 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

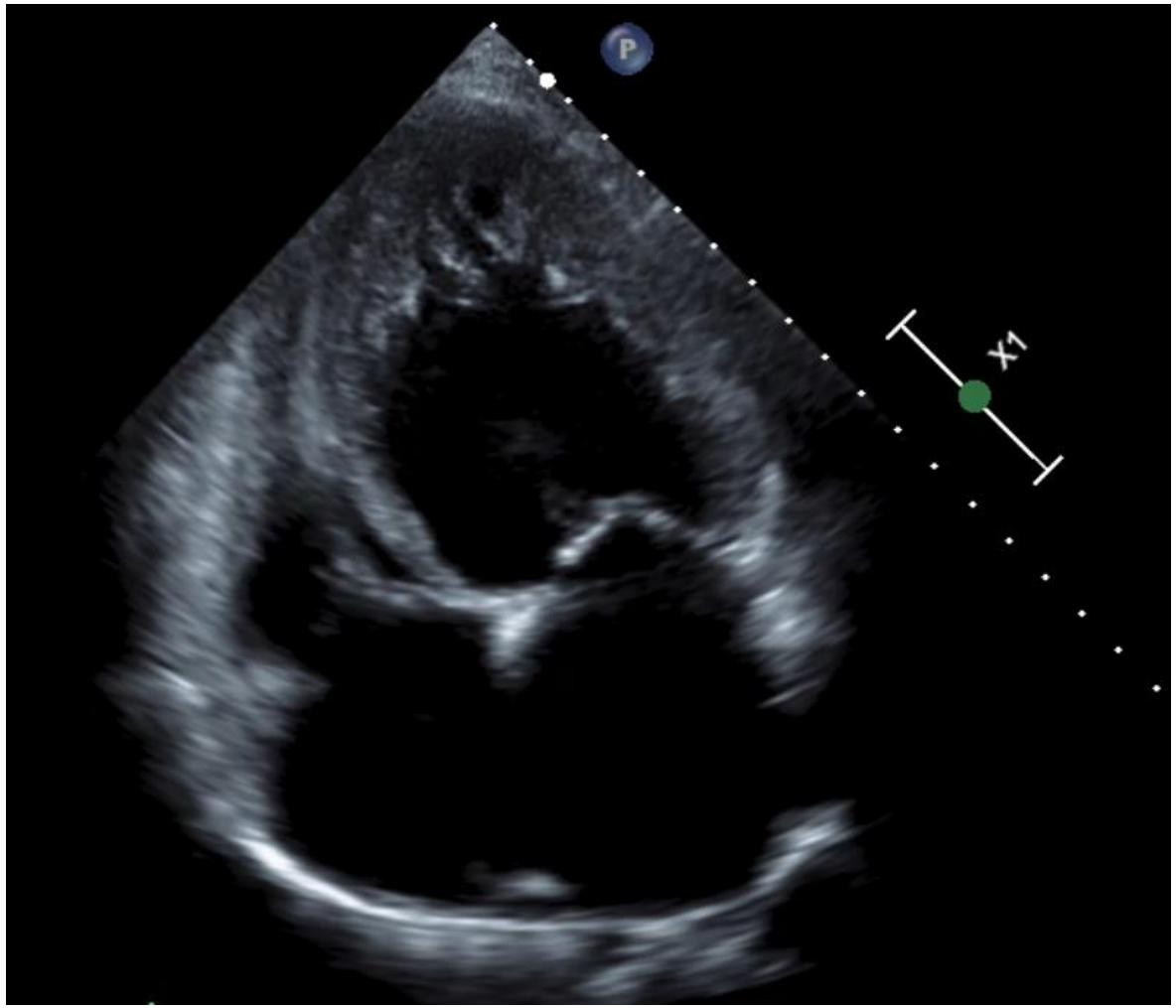
TAVR: The Future

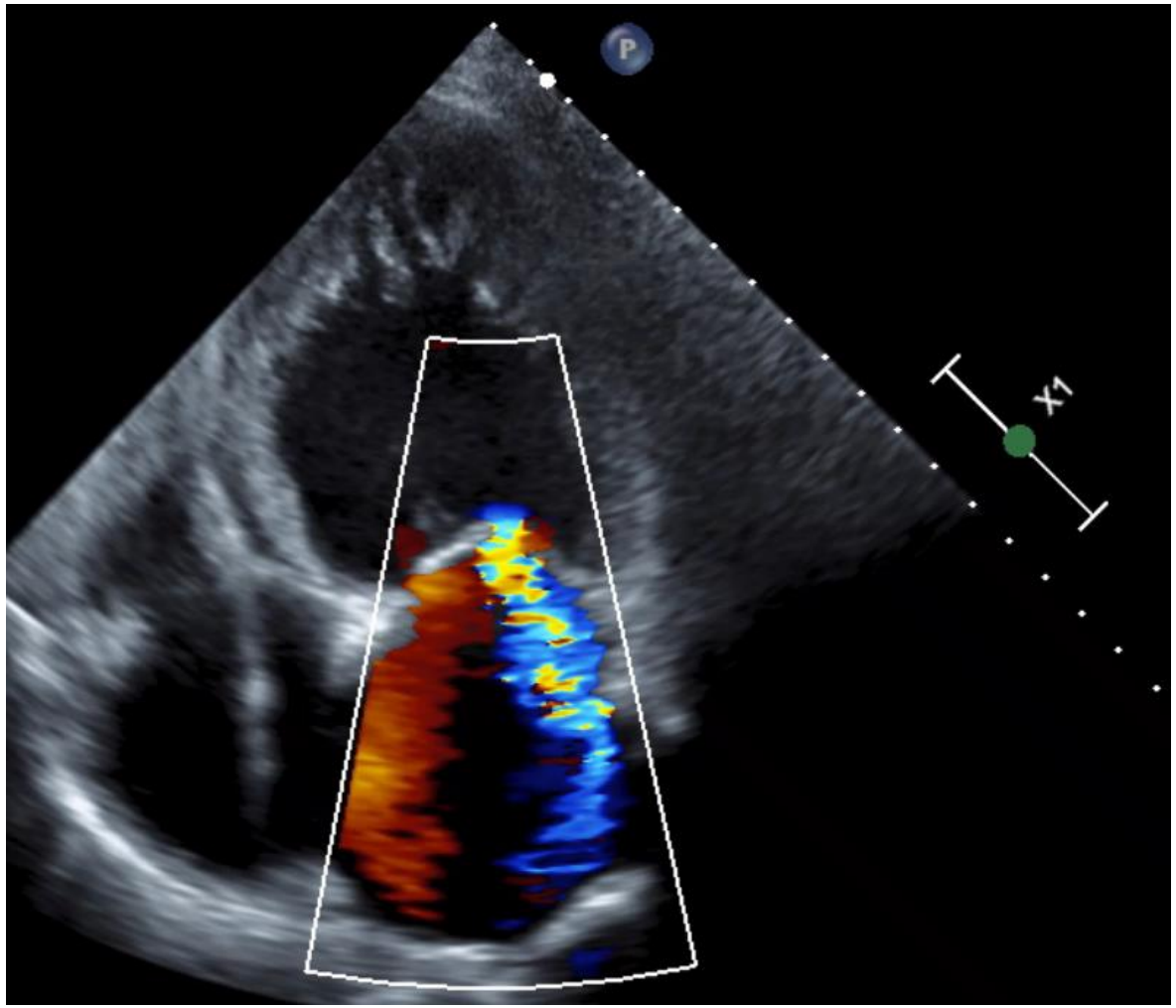
- **Device improvements**
  - Reduce PVL
  - Reduce PPM
  - Smaller device profiles
- **Optimal anticoagulant/antithrombin regimens**
  - Several on-going trials
- **Reducing stroke risk**
  - Shields
  - Filters
- **Formal assessment of durability**
  - 10 year f/u in PARTNER 3 and Evolut Low Risk
-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

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

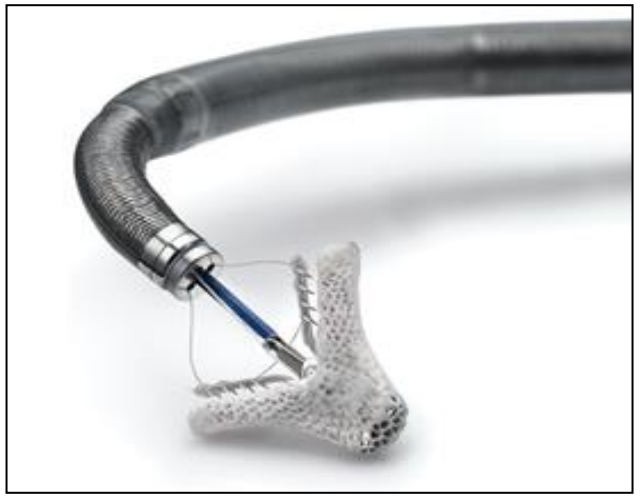
Degenerative MR caused by mitral valve prolapse

Degenerative MR caused by flail leaflet

Functional MR

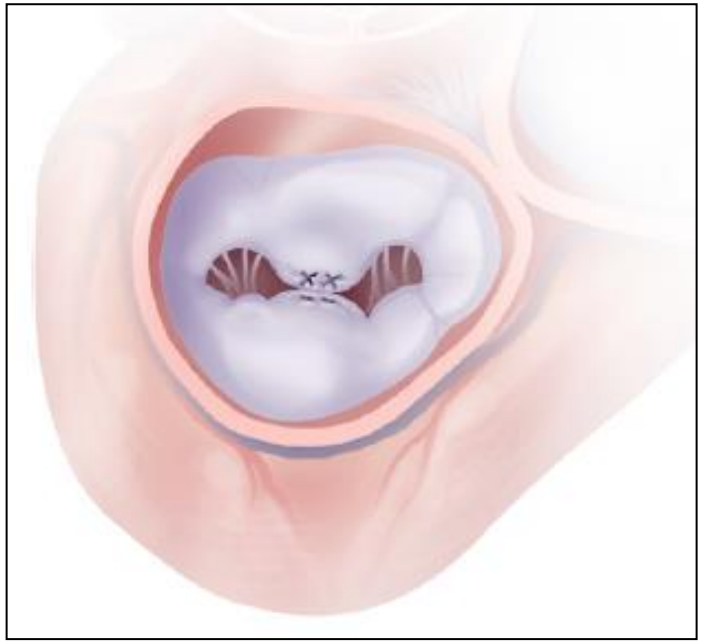
Photo source: Abbott Vascular

Edge-to-Edge Trans-catheter Mitral Valve Repair

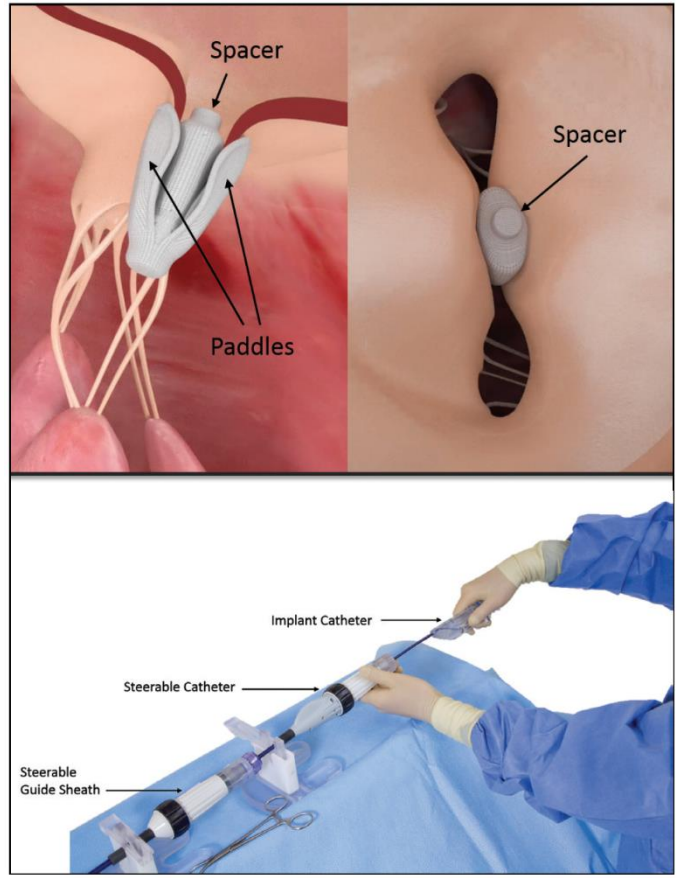


MitraClip (Abbott)

FDA Approved for Primary and Secondary MR



Alfieri Stitch



Pascal (Edwards)

FDA approved for Primary MR

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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.

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)	≥3+ (EROA ≥30 mm^2 and/or Rvol >45 ml)	≥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	≥20% to ≤50%	≥15% to ≤40%	≥15% to ≤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	

Asgar et al. JACC, 2015.

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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 in Clinical Trials

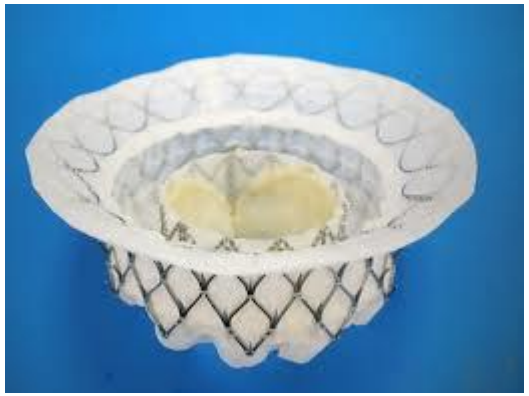
Continued Access

M3-Edwards

Tendyne- Abbott

Pivotal Trials

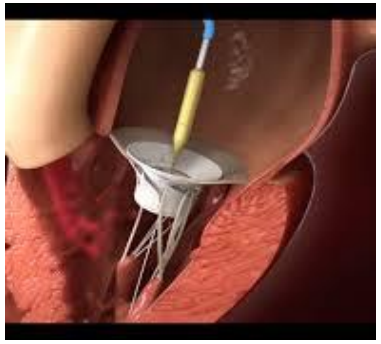
AltaValve- 4C



Intrepid- Medtronic

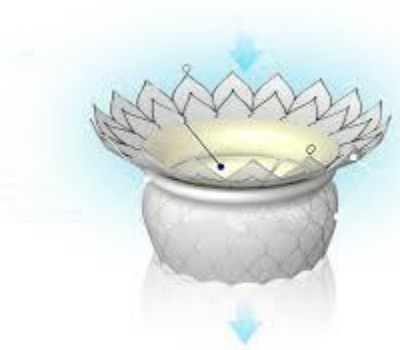
EFS

Evoque-Edwards



Twist- Edwards

Cephea- Abbott



High Life- High Life

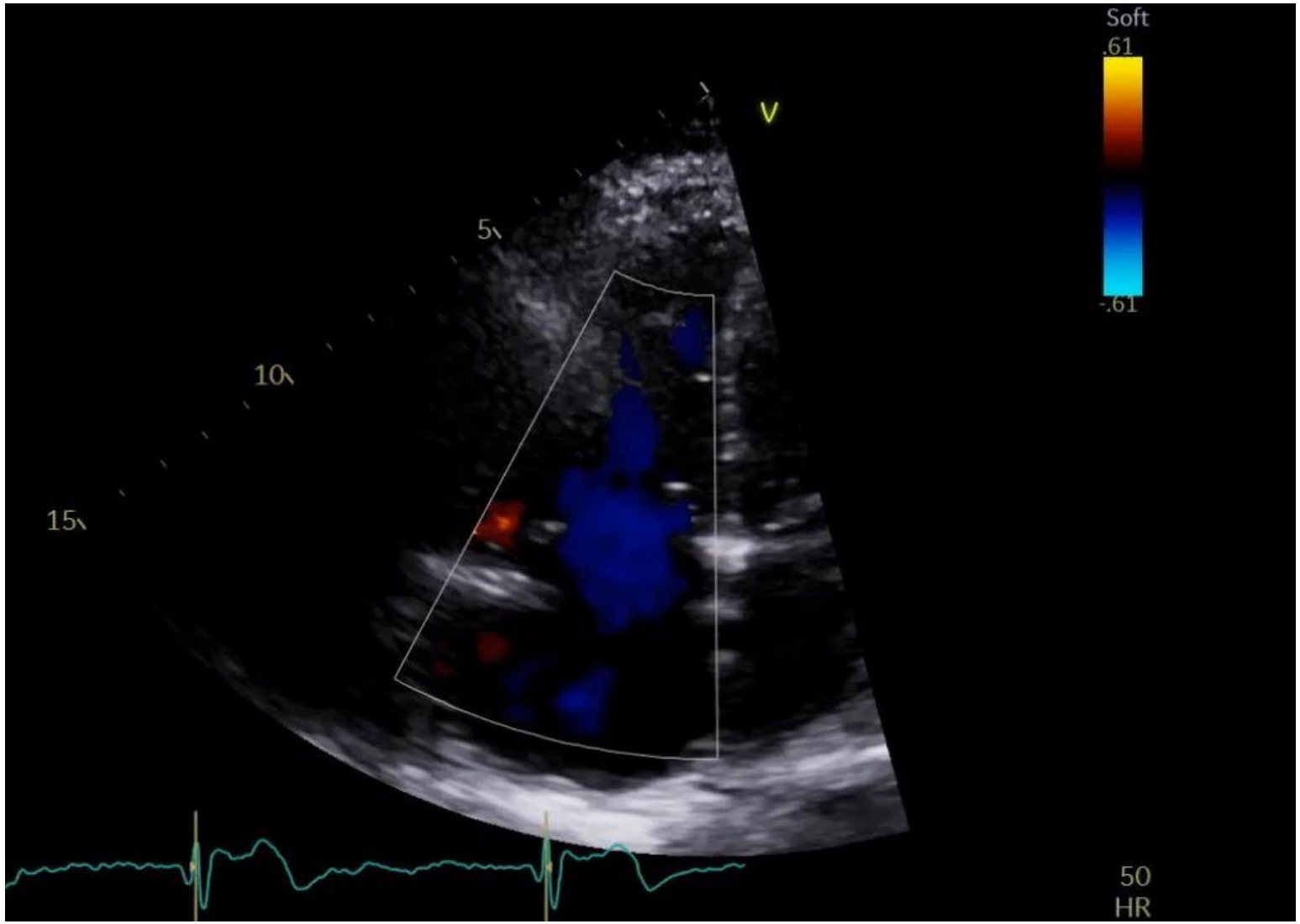
Trans-Catheter Mitral Valve Therapies: Conclusions

- 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 triscupid regurgitation with slight increase in RV size
- Felt to be a poor candidate for surgery

Case 3- Echocardiogram



Tricuspid Valve Regurgitation

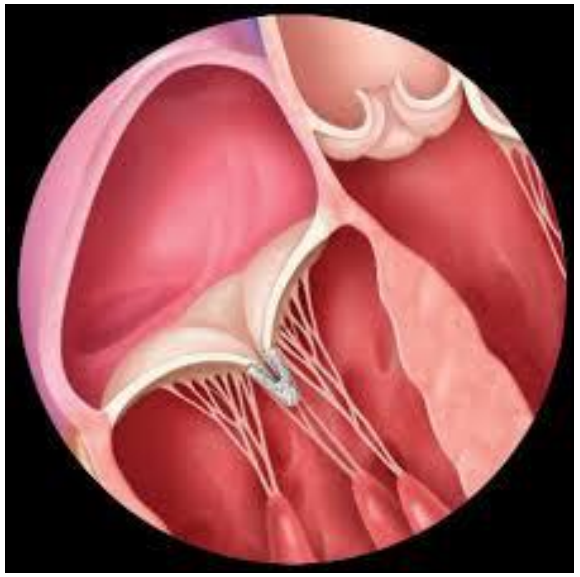
- The TV is often called the “forgotten valve”
- Slow progression, rarely acutely fatal, no great treatment options outside of diuretics and surgery
- As a results, patients are often referred late for consideration of therapies
- Etiologies: primary (degenerative) and secondary (functional)
- At the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

Tricuspid Repair Devices

Tricuspid Trans-catheter Edge to Edge Repair

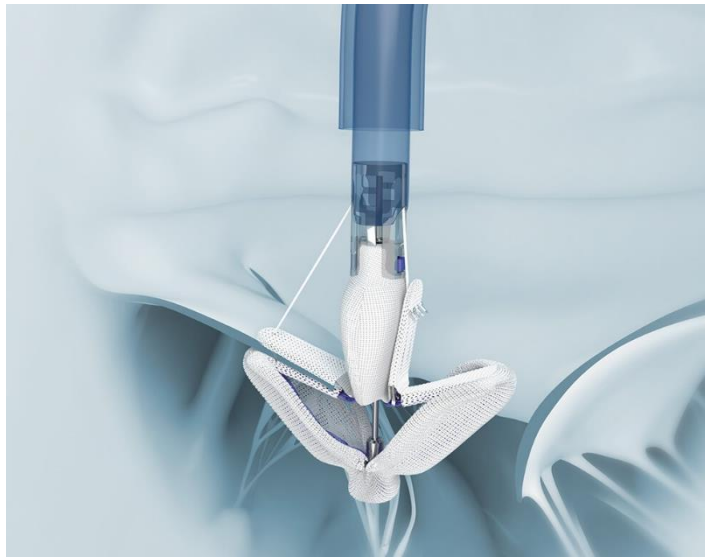
Tri-Clip

TRILUMINATE Trial-FDA approved April 2024

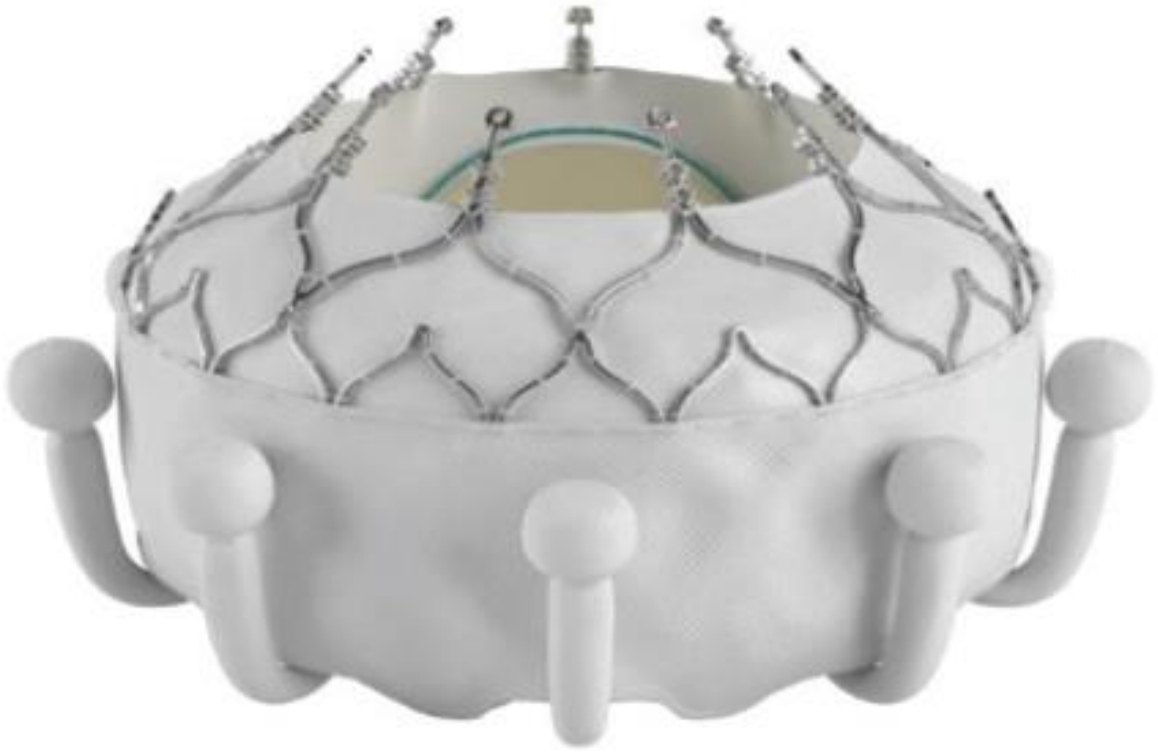


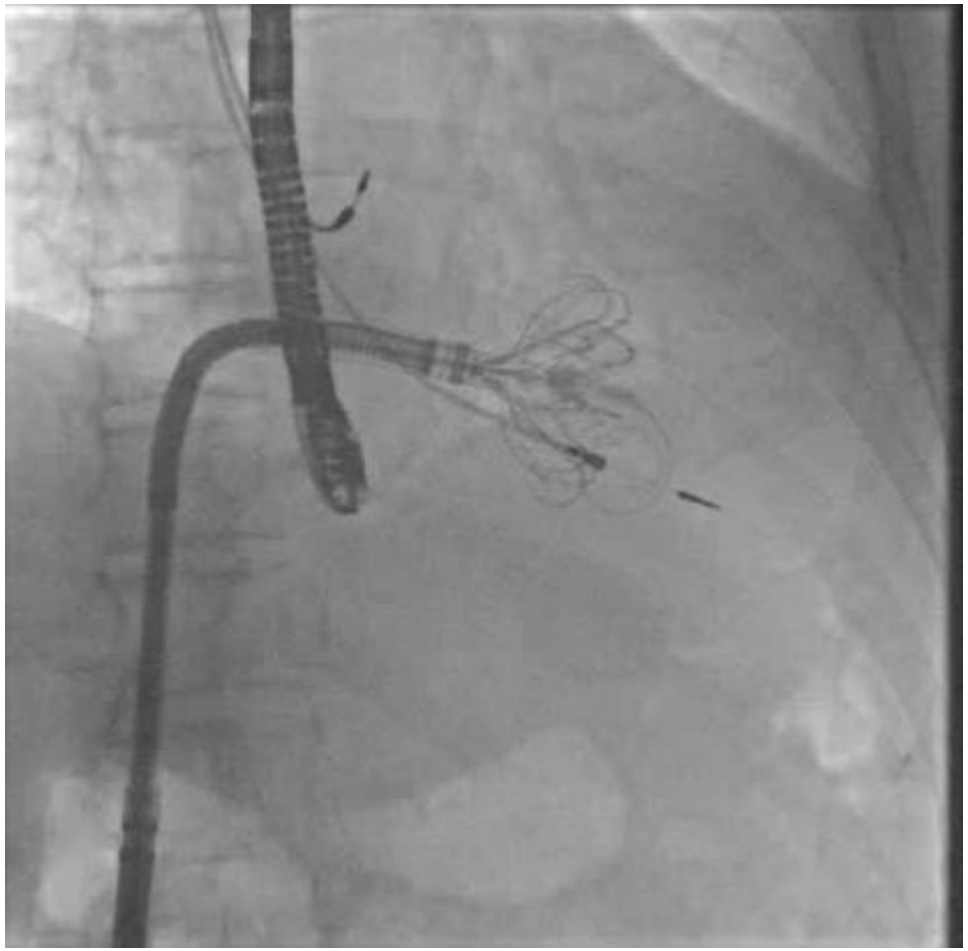
Pascal

TRICLASP Trial



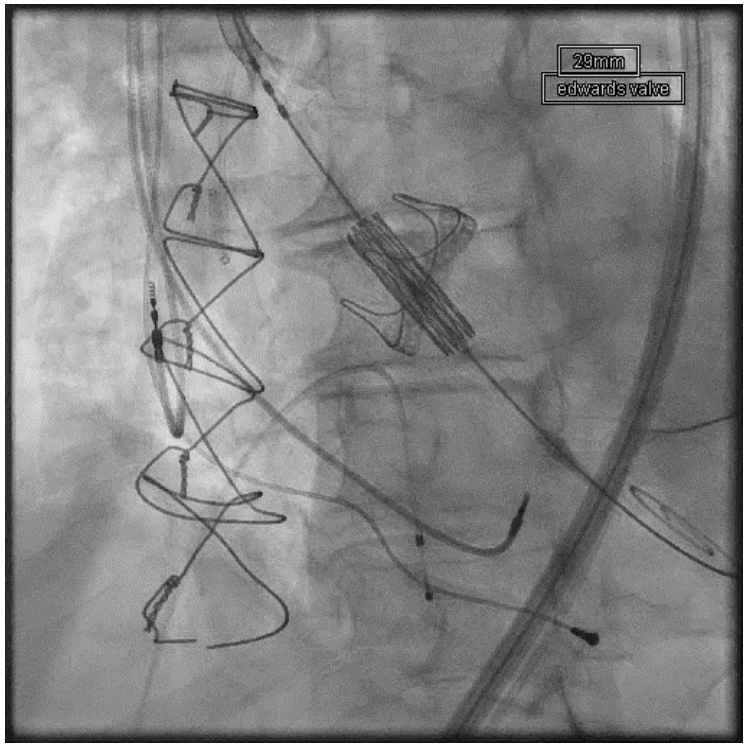
Tricuspid Replacement Devices





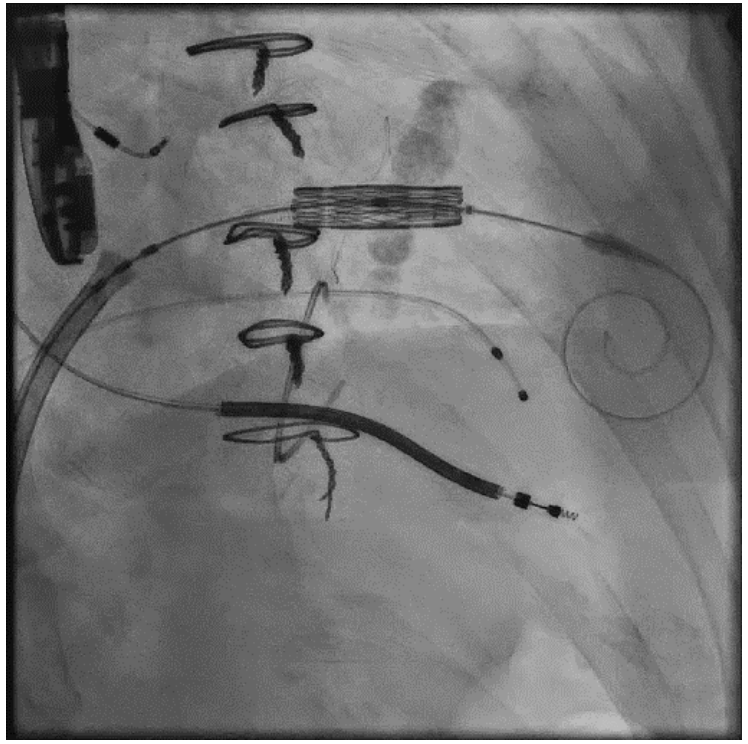
Evoque (Tricuspid)
TRISCEND II Trial
FDA Approved March 2024

Valve-in-Valve Procedures



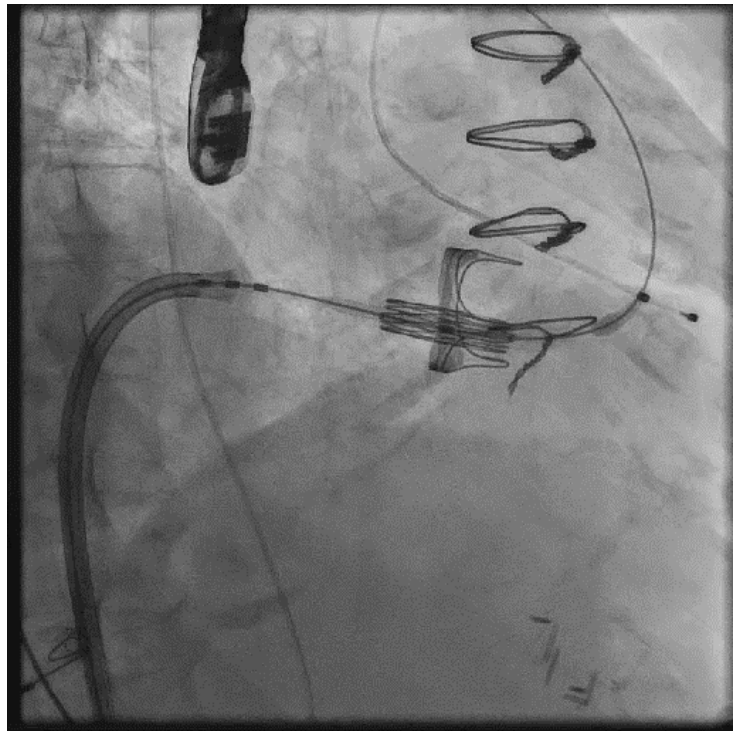
Aortic Valve-in-Valve

- 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

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