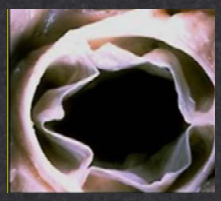
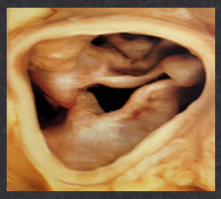
Transcatheter Aortic Valve Replacement

Scott M. Lilly, MD, PhD
Associate Professor - Clinical
Division of Cardiovascular Medicine
The Ohio State University Wexner Medical Center

Outline

- Aortic Stenosis
- Advent of TAVR
- TAVR Candidacy
- Long-term Success

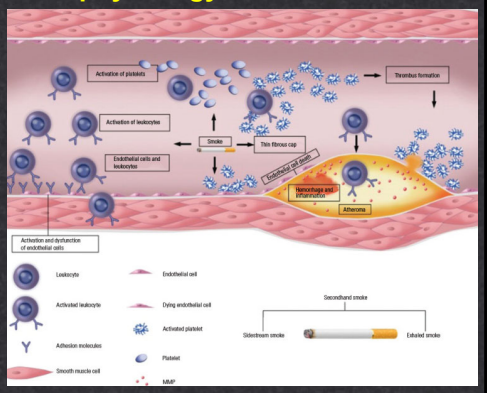




Aortic Stenosis Pathophysiology

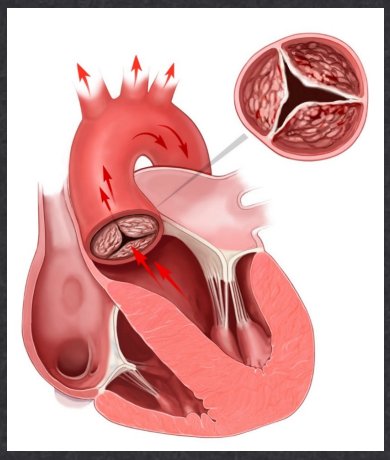
- Pathophysiology for degenerative AS is similar to atherosclerosis.
- Involves inflammation/immune system activation, fibrosis and calcifications, etc
- Risk factors are shared, HTN, hyperlipidemia, tobacco use, sex
- Medical therapy that is shown to be effective for atherosclerosis is not effective for valve sclerosis

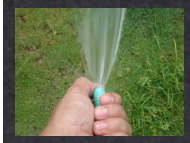
Pathophysiology of atherosclerosis

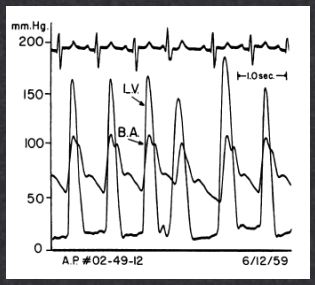


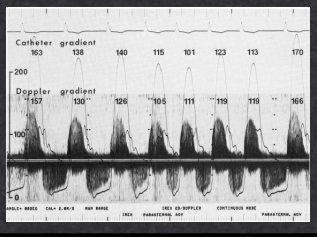
Aortic Stenosis

"In every patient the presence of aortic stenosis was confirmed by the demonstration of a systolic pressure gradient between the left ventricle and brachial artery at the time of left heart catheterization"





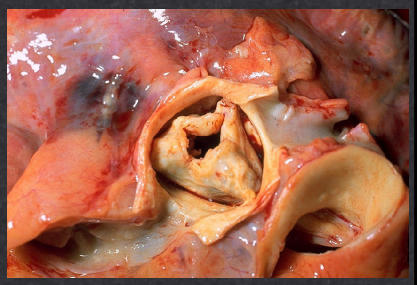




Morrow et al. 1963, Ann Surgery; Brockenbrough et al. 1961, Circulation; Curie 1985

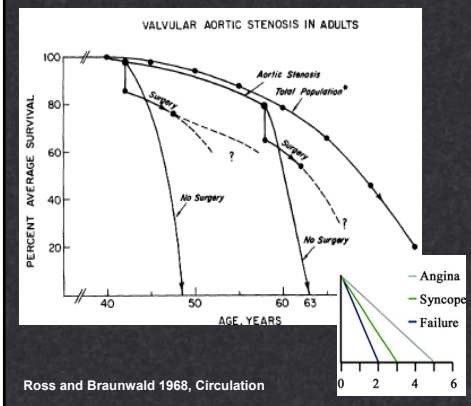
Aortic Stenosis Pathophysiology

- Changes in the LV result from increased afterload
- Initially LV hypertrophies, but overtime remodeling occurs leading to fibrosis and dilation, eventually decreased LVEF and heart failure
- Subendocardial ischemia due to transmural pressure gradient, exacerbated by concomitant CAD
- Increased LVEDP/filling pressures, pulmonary hypertension/edema, RV overload



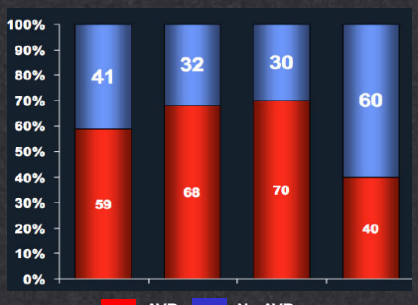
Aortic Stenosis

Severe Symptomatic Aortic Stenosis: 50% 2-year Mortality



Ross and Braunwald 1968, Circulation

Severe Symptomatic Aortic Stenosis: Percent Treated

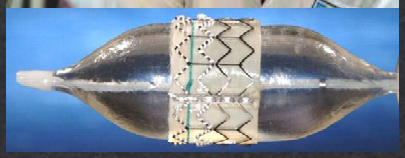


- Bouma B J et al. Heart 1999;82:143-148
- Iung B et al. European Heart Journal 2003;24:1231-1243
- Pellikka, Sarano et al. Circulation 2005
- Charlson E et al. J Heart Valve Dis 2006;15:312-321

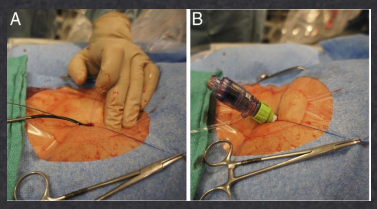
Untreated Symptomatic Severe Aortic Stenosis: 50% Mortality at 2 years

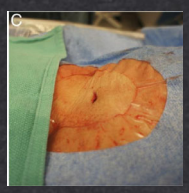
A Novel Approach…

Transcatheter Aortic Valve Replacement

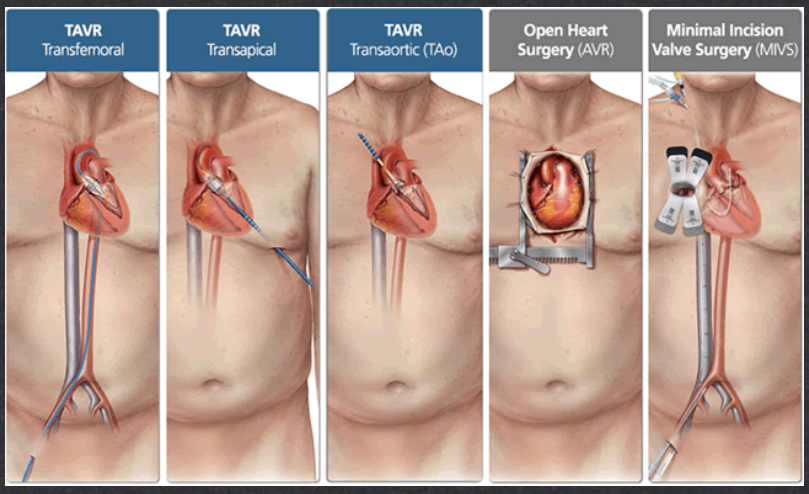


Transcatheter Aortic Valve Replacement





Transcatheter Aortic Valve Replacement



Source: www.cvtsc.com

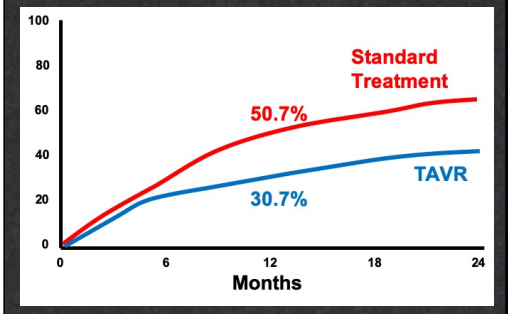
TAVR Candidacy in (November) 2015

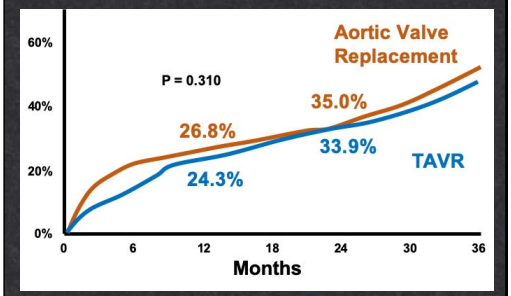
SAPIEN VALVE

- Inoperable
  - Superior to Standard Therapy
  - Approved November, 2011
- High Risk:
  - Non-inferior to SAVR
  - Approved October, 2012

CoreValve

- Inoperable
  - Superior to Expected Mortality
  - Approved January, 2014
- High Risk:
  - Superior to SAVR (ACC.14)
  - Approved 2014





TAVR Candidacy in 2019

	STS 0-3 EuroScore 0-2	STS 4-8 EuroScore 3-5	STS > 8 EuroScore > 6	
	LOW	INTERMED	HIGH	INOPERABLE
	< 70 yo, no comorbidities	80 years old, 1-2 comorbidities	80 years old Prior sternotomy	
SAPIEN	*Low Risk Trials*	PARTNER II	PARTNER I	PARTNER I
CORE		SURTAVI	US PIVOTAL	US PIVOTAL
SAVR				

TAVR: Determining Risk

STS 0-3 EuroScore 0-2	STS 4-8 EuroScore 3-5	STS > 8 EuroScore > 6	
LOW	INTERMED	HIGH	INOPERABLE

Risk of death or serious irreversible morbidity of AVR as assessed by cardiologist and two surgeons must exceed 50%

Surgeons must agree and attest that before PARTNER these patients would not have received AVR treatment

Mean STS Score in Inoperable Patients

	Commercial	PARTNER I
STS > 8	52%	66%
STS > 15	10%	15%

From Pendyala et al. 2014, Am J Cardiol 113: 342-347.

What Risk Scores Miss…

Variable	EuroSCORE II	STS Score
Age	X	X
Gender	X	X
Height		
Weight		
Body mass index		
Diabetes mellitus		
Chronic lung/pulm disease		
Mild/moderate/s		
Extracardiac arteri		
Peripheral vascular		
Neurologic dysfun		
Cerebrovascular ac		
Poor mobility		
Previous cardiac su		
Number of previ operations		
Previous coronary		
Previous valve sur		
Renal failure/impa		
Dialysis-dependent failure		
Serum creatinine/cle		
Hypertension		
Active endocarditis	X	X
Immunosuppressive therapy		X
Arrhythmia		X

Variable	EuroSCORE II	STS Score
	X	X
Recent myocardial infarction		X
Timing		X
		X
		X
		X
		X
		X
		X
Procedural status/urgency		
Weight of intervention	X	X
Single noncoronary bypass/2 or 3 procedures	X	X

Clinical Features
- **Severity of pulmonary hypertension**
- **Degree of coronary or peripheral arterial disease**
- **Liver disease**
- **Dementia**

Procedural Considerations
- **Porcelin aorta, chest radiation, LIMA course**
- **Access Route**
- **Peri-procedural Support**

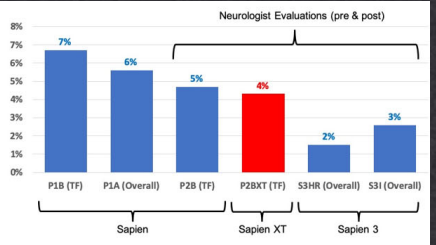
Composite Indices
- **Frailty**

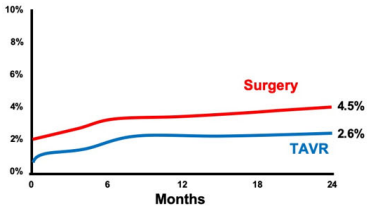
Fewer Procedural Complications

STROKE
- Initially 5-7% incidence at 30d
- 95% Ischemic, Higher mortality
- Now 2-3%, comparable to SAVR
  - Positioning, Deployment

EARLY (< 1 Day; 54%)
Experience
Diabetes
Balloon-dilation
New atrial fibrillation

LATE (30 Days; 46%)
Chronic Atrial fibrillation
Peripheral arterial disease
Cerebrovascular disease
Anticoagulation





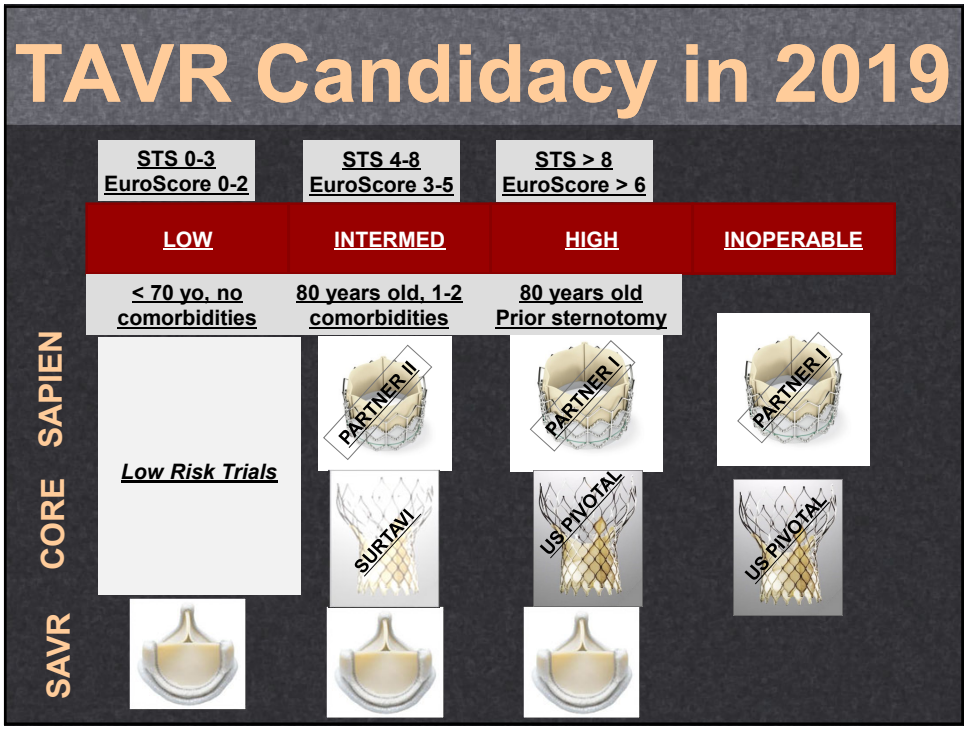
Reardon et al., NEJM 2017, 37(6);
Vahl et al., JACC 2016, 67(12); Nombela-Franco et al. Circ 2012 26(25)

PARTNER 3 Low Risk Trial

- Randomized trial (n=1328) comparing Edwards SAPIEN 3 vs. SAVR
- Symptomatic, severe, calcific AS
- Heart Team agrees patient has STS risk of mortality <4%
- Primary outcome: all cause mortality, all stroke, re-hospitalization
- Patient follow-up at 30 days, 6 months, and annually through 10 years

EVOLUT R Low Risk Trial

- Randomized trial (n=1200) comparing Medtronic Evolut vs. SAVR
- Severe symptomatic or asymptomatic AS
  - Very severe AS: AVA≤1cm^2 AND max velocity ≥5m/sec or mean gradient ≥60mmHg
  - AVA≤1cm^2 AND mean gradient ≥40mmHg or max velocity ≥4m/sec AND positive exercise tolerance test
  - AVA≤1cm^2 AND mean gradient ≥40mmHg or max velocity ≥4m/sec AND LVEF ≤50%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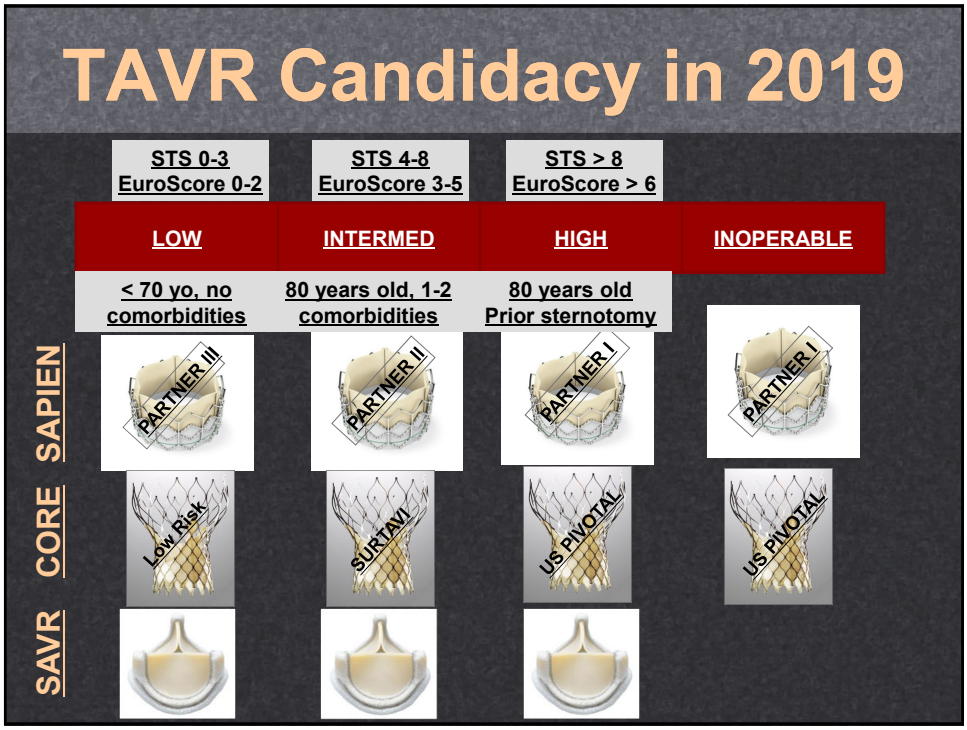
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SAPIEN
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PARTNER III
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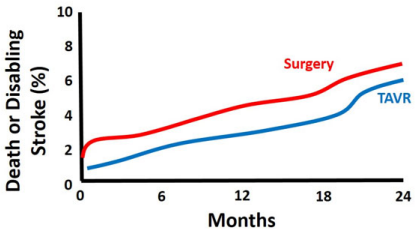
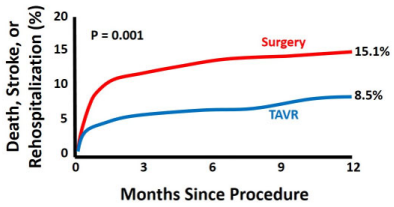
Low Risk
SURTAVI
US PIVOTAL
US PIVOTAL

Low Risk TAVR, Reported March 2019

Self-Expanding

Balloon-Expandable





TAVR non-inferior (CoreValve) or superior (SAPIEN) to surgery in low-risk surgical patients

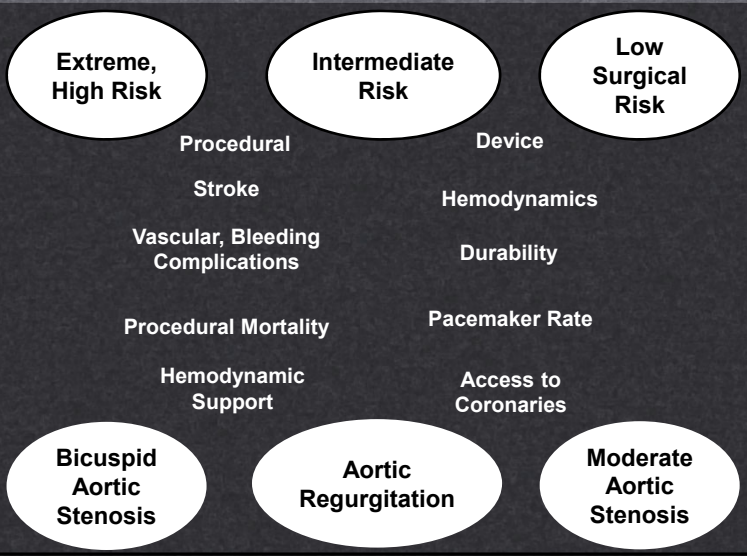
Low Risk TAVR Trials Reported March 2019

Transcatheter versus Surgical Outcomes in Low Risk Trials

Outcome	CoreValve	SAPIEN Valve
Death	Similar	Lower
Stroke	Lower*	Lower
Bleeding	Lower*	Lower*
Vascular Complication	Similar	Similar
Kidney Injury	Lower*	Similar
New Atrial Fibrillation	Lower*	Lower*
Pacemaker	Higher*	Similar
Rehospitalization	Lower*	Lower
Length of Stay	Shorter*	Shorter*
KCCQ/QOL Improvement	Higher* (30-d)	Higher*
Discharged Home		Higher*

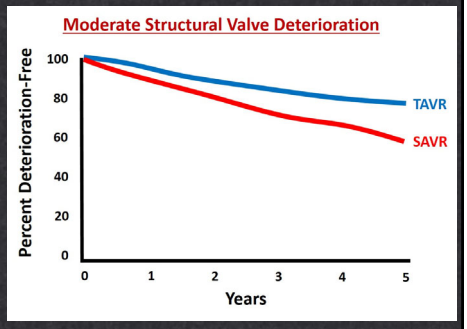
Combined 12-month stroke and mortality was LOWER with TAVR compared to Surgical Valve Replacement

Evolving Populations, Considerations



What is "Long-Term Success"?

1. Prosthetic Valve Durability
   - -Comparable to, better than SAVR?
   - -Different Mechanisms of Failure
2. Absence of Stroke
   - -Primary Endpoint in Low-risk trials
   - -Protection devices, new standard
3. Avoidance of Pacemaker



Imaging, Simulation, and TAVR Success: Valve Durability
The Leak? Or the Gradient? Or something else?

Paravalvular Leak Tends to Remain Stable or Regress over Time

2 year

	2 Year				
Post Procedure	None	Trace	Mild	Moderate	Severe
None	17	8	6	1	0
Trace	24	12	11	1	0
Mild	3	10	34	5	0
Moderate	2	1	5	3	0
Severe	0	0	0	0	0

Related to…
Sizing, LVOT – Aortic Angle, depth, valve type

Kodali et al., 2012 NEJM

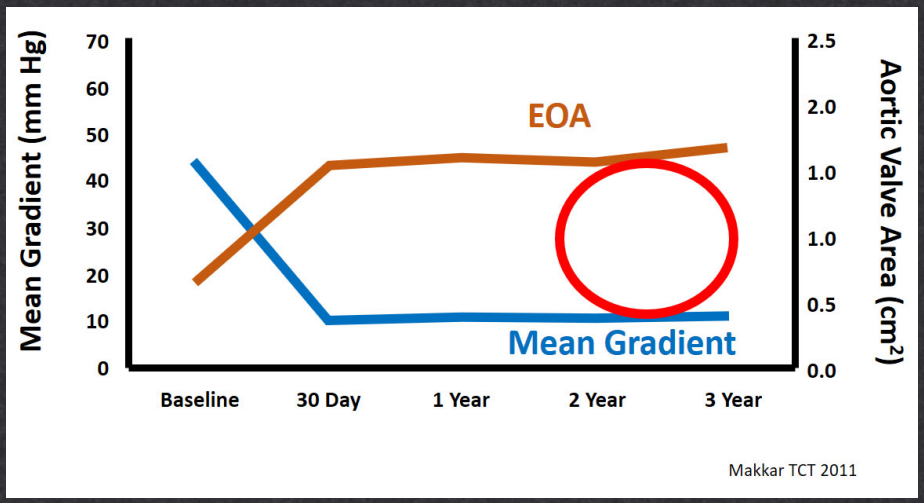
4 Year

	Baseline	Follow-Up	p Value
Peak gradient*	19.1 (18.0-20.2)	17.1 (15.9-18.4)	0.002
Aortic regurgitation†			<0.01
None/trivial	73/221 (33.0)	105/221 (47.5)	
Mild	126/221 (57.0)	94/221 (42.5)	
Moderate	22/221 (10.0)	21/221 (9.5)	
Severe	0/221 (0.0)	1/221 (0.5)	

PVL Incidence Decreasing…
Earliest TAVR RCT ~ 10%
Most recent ~ 4%

Blackmon et al., 2019 JACC

Imaging, Simulation, and TAVR Success: Valve Durability
The Leak? Or the Gradient? Or something else?



Makkar TCT 2011

Imaging, Simulation, and TAVR Success Might Valve Durability and Cerebro-embolism Share a Substrate?

Subclinical leaflet thrombosis in surgical and transcatheter bioprosthetic aortic valves: an observational study

Tarun Chakravarty, Lars Søndergaard, John Friedman, Ole De Backer, Daniel Berman, Klaus F Kofoed, Hasan Jilaihawi, Takahiro Shiota, Yigal Abramowitz, Troels H Jørgensen, Tanya Rami, Sharjeel Israr, Gregory Fontana, Martina de Knegt, Andreas Fuchs, Patrick Lyden, Alfredo Trento, Deepak L Bhatt, Martin B Leon, Raj R Makkar, on behalf of the RESOLVE and SAVORY Investigators*

Lancet 2018 (389) 2383-2392

A meta-analysis of reduced leaflet motion for surgical and transcatheter aortic valves: Relationship to cerebrovascular events and valve degeneration☆

Nader Makki [a], Satya Shreenivas [b], Dean Kereiakes [b], Scott Lilly [a,*]

Cardiovasc Revasc Med 2018 (19) 868-873

Less common with anticoagulation
Can resolve with anticoagulation

Precedes significant increase in gradient

May precede valve degeneration and/or correlate with cerebroembolism

Imaging, Simulation, and TAVR Success Avoiding Coronary Obstruction

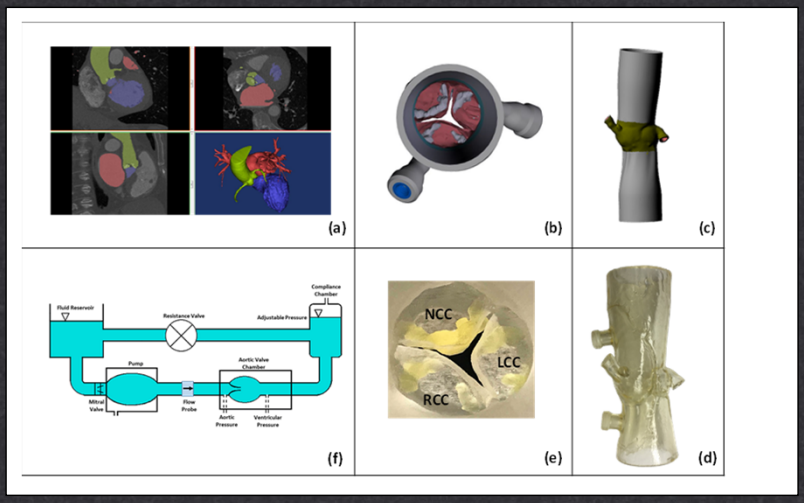
Risk of Coronary obstruction if:

- **Coronary height < 10 -12 mm**
- **Sinus of Valsalva diameter (SOVd) < 30 - 32 mm**

26 % of TAVR cases were excluded

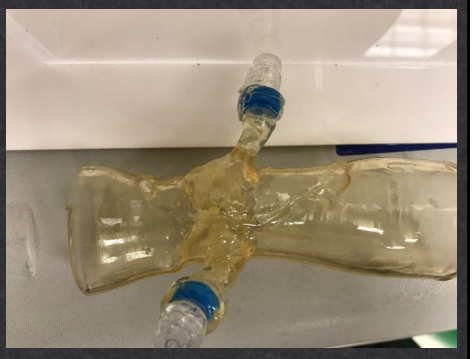
(Ribeiro et al, 2013)

Imaging, Simulation, and TAVR Success
Collaboration Between Physicians and Scientists



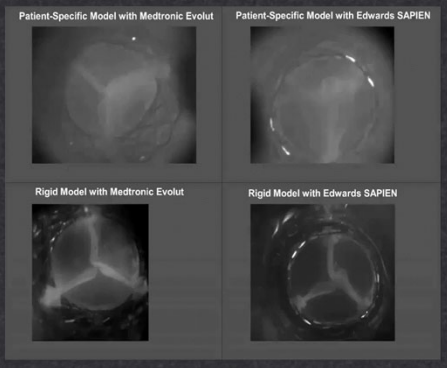
Imaging, Simulation, and TAVR Success
Collaboration Between Physicians and Scientists

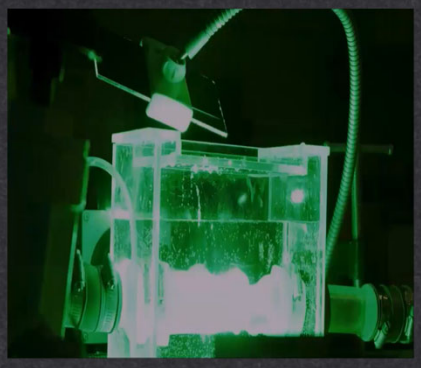
With self-expandable Medtronic Evolut



With balloon-expandable Edwards SAPIEN

Imaging, Simulation, and TAVR Success
Collaboration Between Physicians and Scientists





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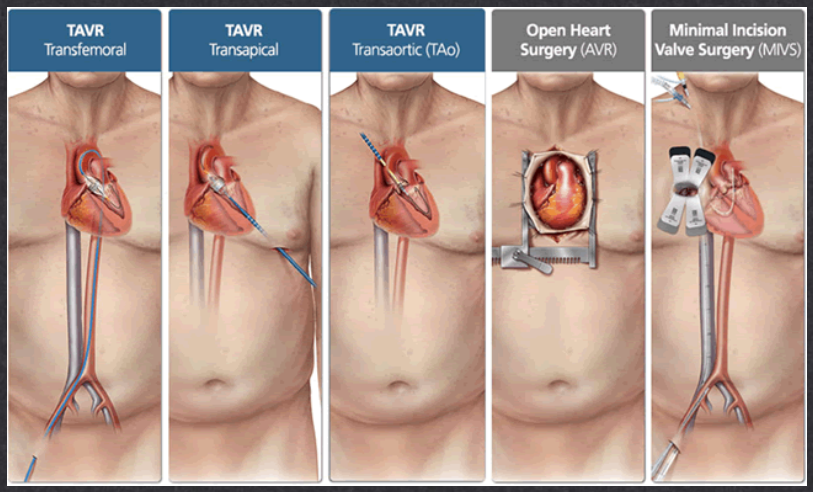


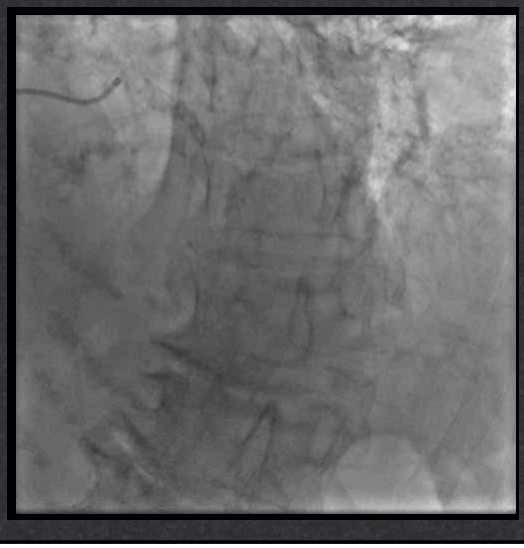
www.cvtsc.com

Case Presentation

89 year old female, severe symptomatic aortic stenosis

- Mean gradient 48 mm Hg, Vmax 4.4 m/s, AVA0.84 cm^2
- Stage III CKD, COPD, insulin-dependent diabetes, prior CVA
- STS 9%, TAVR 30-d predicted mortality 4.5%

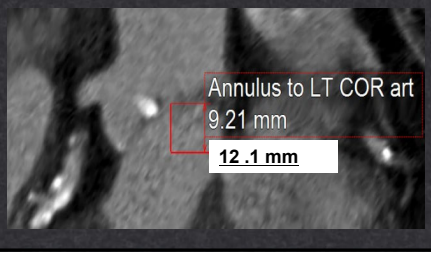
Pre-TAVR Coronary Angiogram

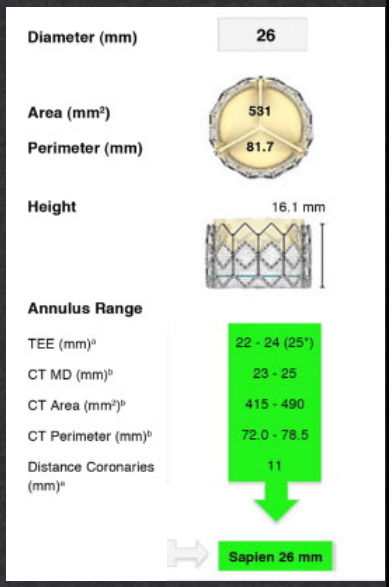


89 year old female, severe symptomatic aortic stenosis

Initial CT-derived measurements suggested low-lying coronary arteries

Mean annulus diameter (24.3 mm), And area (4.72 cm$^{2)}$ Sinus of Valsalva (26.5mm)

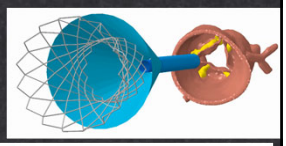




Simulation

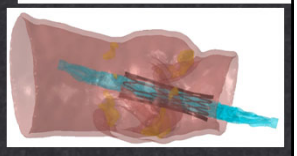
Self-Expandable (SE)

- Crimping TAV
- Delivering TAV to prescribed position
- Releasing TAV by gradually removing sheath

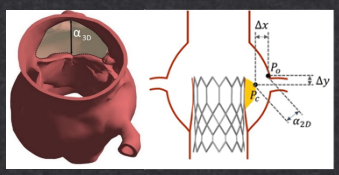


Balloon-Expanding (BE)

- TAV and balloon are already crimped and positioned in prescribed location.
- Balloon is gradually inflated, expanding TAV and pushing away native leaflets.

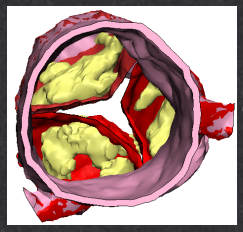


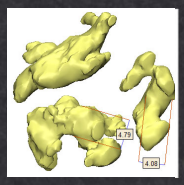
Goal: To estimate the final Distance between native/bioprosthetic Leaflet and Coronary ostium (DLC) and Area available for Coronay Flow (ACF) after TAVR

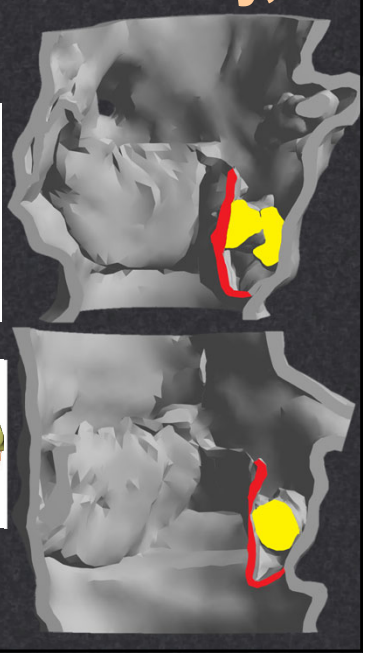


Anatomical Leaflet, Coronary, Sinus Modeling

Left Coronary Artery	
Ostium diameter	5.1 mm
Vessel height	12.3 mm
Leaflet length	14.2 mm
Nodule thickness	4.0 mm
Sinus width	1.8 mm







Reconstructions

-2-dimensional

- ***CT-derived measurements***

-3-dimensional

- ***To predict apposition of leaflets***

Balloon Valvuloplasty and Aortography

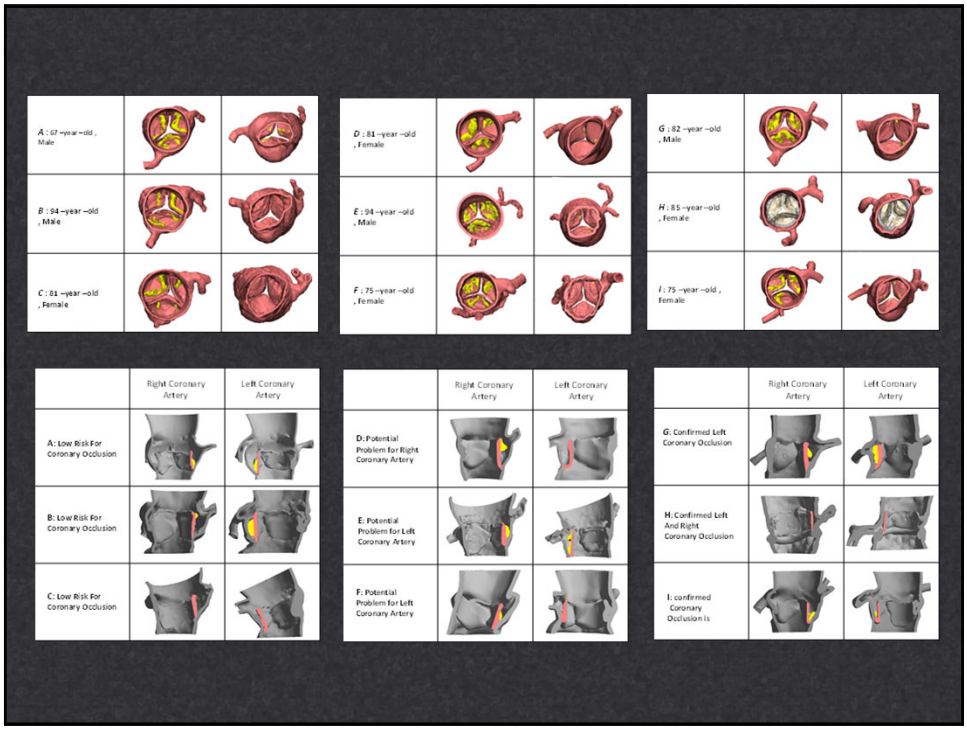
SAPIEN Valve Deployment

Post-Deployment Aortogram

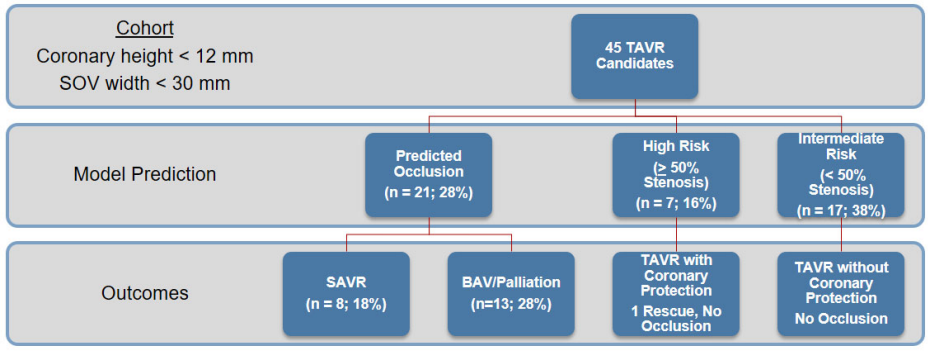
Post-Deployment Angiogram

Now 15 months post-TAVR…

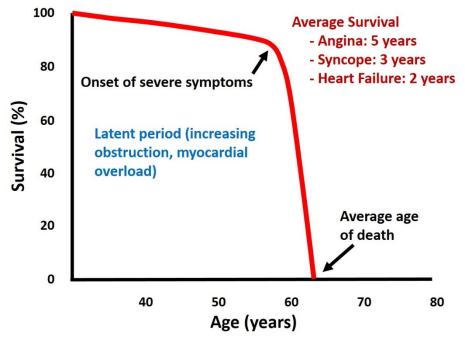
- Not re-hospitalized
- NYHA II
- Valve remains well-seated, trivial aortic regurgitation
- Mean gradient 10 mmHg, calculated AVA 1.8 cm^2
- Ejection fraction is 65-70%



Reconstructive Modeling to Identify Patients At-Risk for Coronary Occlusion



Why Coordination is important…



From onset of symptoms the average patient with aortic stenosis survives 2 years.

Prior to TAVR, patients need

- Echocardiogram
- Coronary angiogram
- CT Scan
- Functional status assessment
- Quality of life assessment
- Carotid ultrasound
- Pulmonary function tests
- ECG
- Visit with cardiologist, 1 surgeon

One Structural Heart Clinic in August…

65% of patients travel > 1 hr to the Ross

	Recommendation
Patient 1	Surgical aortic valve replacement
Patient 2	Repeat testing in 6 months
Patient 3	TAVR
Patient 4	Transcatheter mitral valve replacement
Patient 5	TAVR
Patient 6	Surgical aortic valve replacement
Patient 7	Surgical aortic valve replacement

Imaging Specialist

Cardiothoracic Surgeon

Heart Failure physician

SHD Coordinator

Nurse Practitioner

Interventional Cardiologist

Nurse

Research Staff

Conclusions

- TAVR is here to stay, more common than surgical approach in U.S.
- Procedural and device developments will continue to provide improvements in outcomes
- Patient-specific models and simulation can inform therapy
- These therapies rely on multidisciplinary care

Acknowledgements

The National Institutes of Health (NIH), the American Heart Association (AHA), OSU Trifit challenge award and OSU presidential fellowship.