# Transcatheter Aortic Valve Replacement

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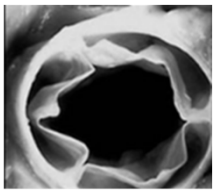
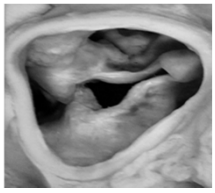
# Outline

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

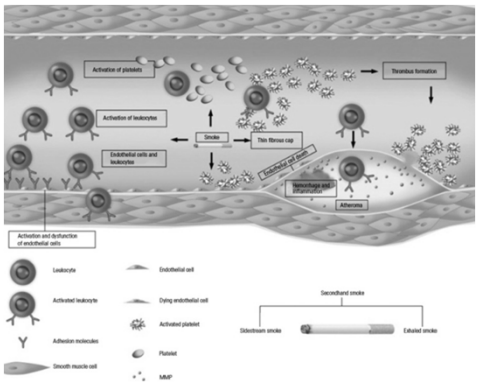




# Aortic Stenosis Pathophysiology

- 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

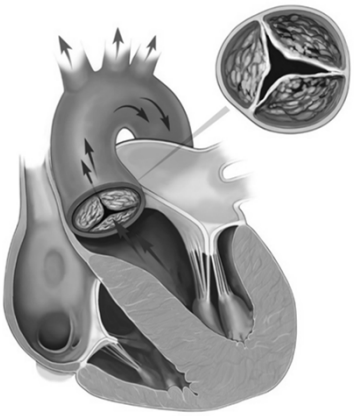
**Pathophysiology of atherosclerosis**

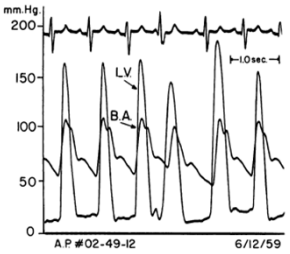


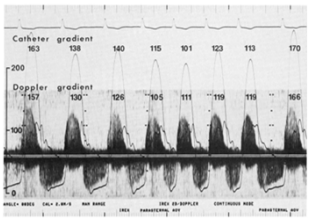



# Aortic Stenosis

***"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"***





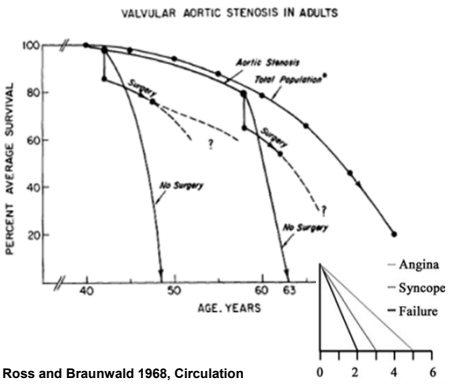

*Morrow et al. 1963, Ann Surgery; Brockenbrough et al. 1961, Circulation; Curie 1985*

# 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**

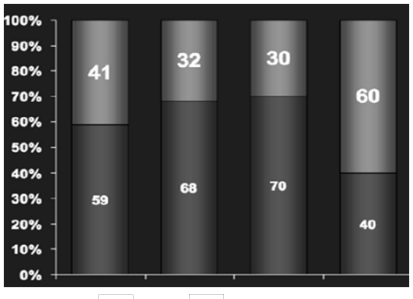
# Aortic Stenosis

***Severe Symptomatic Aortic Stenosis: 50% 2-year Mortality***




Ross and Braunwald 1968, Circulation

***Severe Symptomatic Aortic Stenosis: Percent Treated***

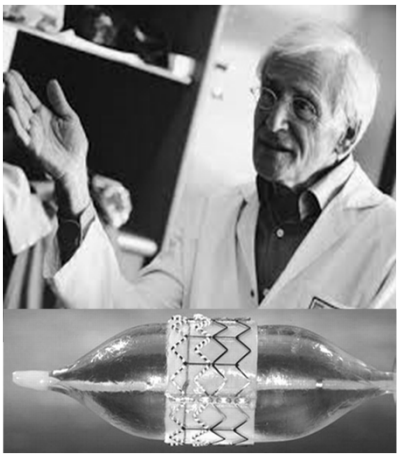



- Bouma B J et al. Heart 1999;82:143-148
- Iung B et al. European Heart Journal 2003;24:1231-1243
- Pellikka, Sarano et al. Circulation 2005
- Charlson E et al. J Heart Valve Dis 2006;15:312-321

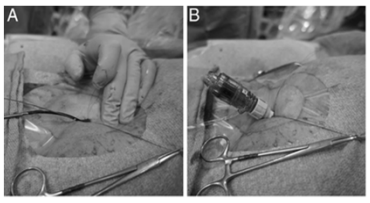
**Untreated Symptomatic Severe Aortic Stenosis: 50% Mortality at 2 years**

# A Novel Approach…

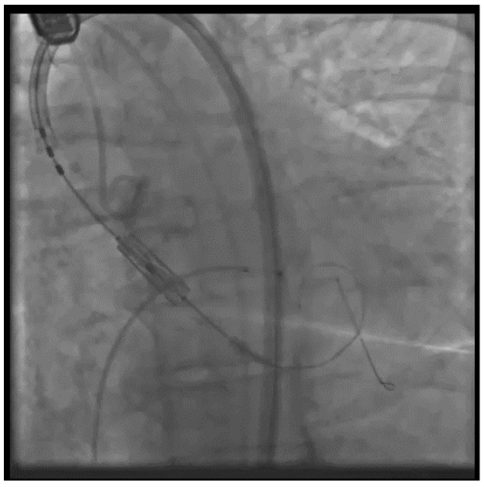
**Transcatheter Aortic Valve Replacement**



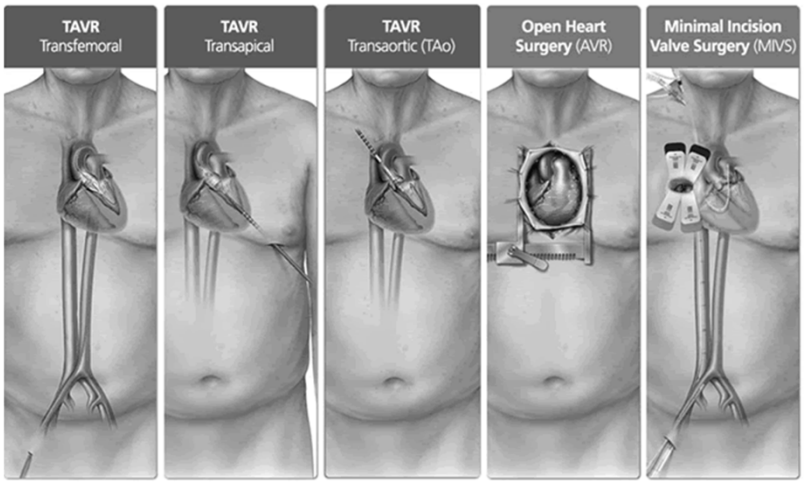
# Transcatheter Aortic Valve Replacement







# Transcatheter Aortic Valve Replacement




Source: www.cvtsc.com

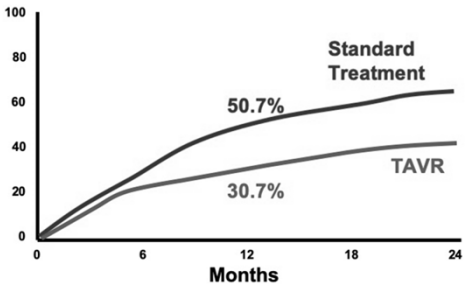
# TAVR Candidacy in (November) 2015

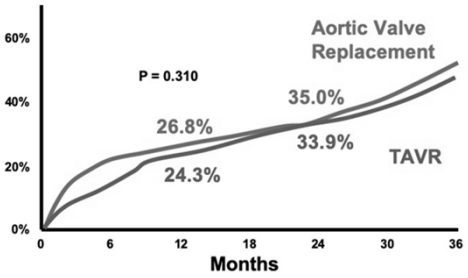
**SAPIEN VALVE**

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

# TAVR: Determining Risk

| STS 0-3<br>EuroScore 0-2 | STS 4-8<br>EuroScore 3-5 | STS > 8<br>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 vascula | | |
| Neurologic dysfun | | |
| Cerebrovascular ac | | |
| Poor mobility | | |
| Previous cardiac s | | |
| 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 |
| | | X |
| | | X |
| | | X |
| | | X |
| | | X |
| | | X |
| | | X |
| | | X |
| Weight of intervention | X | X |
| Single noncoronary bypass/2 or 3 procedures | 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**

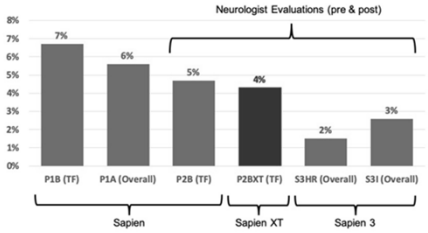
*Adapted from Durand 2013, Am J Cardiol 111:891-897*

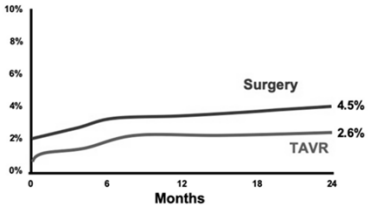
# Fewer Procedural Complications

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

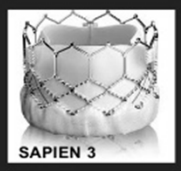
LATE (30 Days; 46%)
Chronic Atrial fibrillation
Peripheral arterial disease
Cerebrovascular disease
Anticoagulation




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

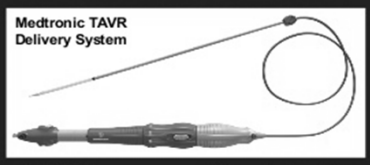
## PARTNER 3 Low Risk Trial





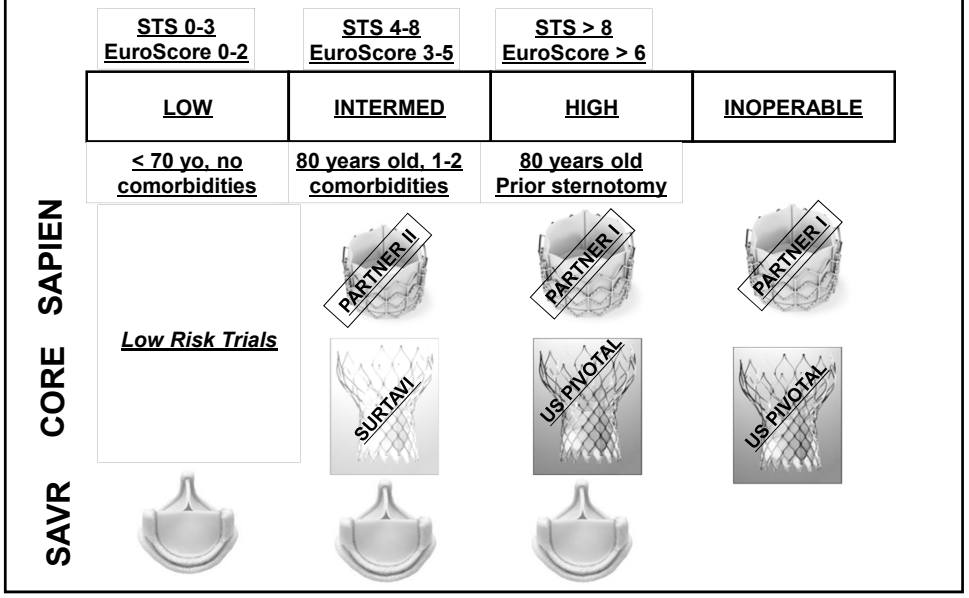
- Randomized trial (n=1328) comparing Edwards SAPIEN 3 vs. SAVR
- Symptomatic, severe, calcific AS
- Heart Team agrees patient has STS risk of mortality <4%
- Primary outcome: all cause mortality, all stroke, re-hospitalization
- Patient follow-up at 30 days, 6 months, and annually through 10 years

## EVOLUT R Low Risk Trial

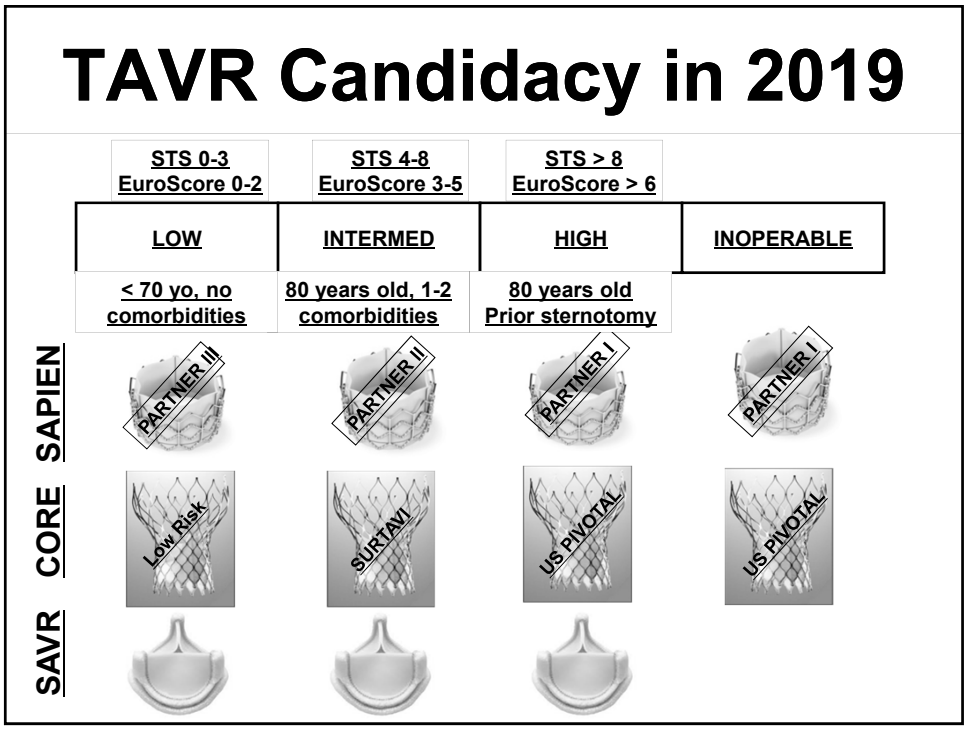



- Randomized trial (n=1200) comparing Medtronic Evolut vs. SAVR
- Severe symptomatic or asymptomatic AS
  - Very severe AS: AVA≤1cm$^2$ AND max velocity ≥5m/sec or mean gradient ≥60mmHg
  - AVA≤1cm$^2$ AND mean gradient ≥40mmHg or max velocity ≥4m/sec AND positive exercise tolerance test
  - AVA≤1cm$^2$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

# TAVR Candidacy in 2019



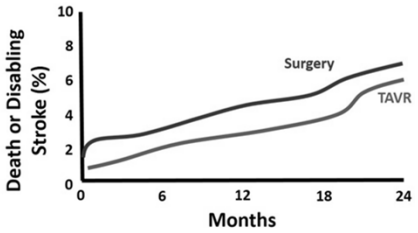

# TAVR Candidacy in 2019

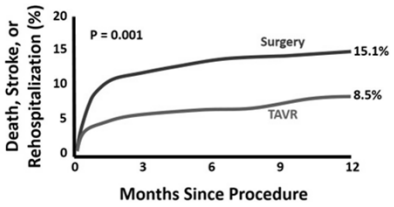


# Low Risk TAVR, Reported March 2019

Self-Expanding

Balloon-Expandable




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

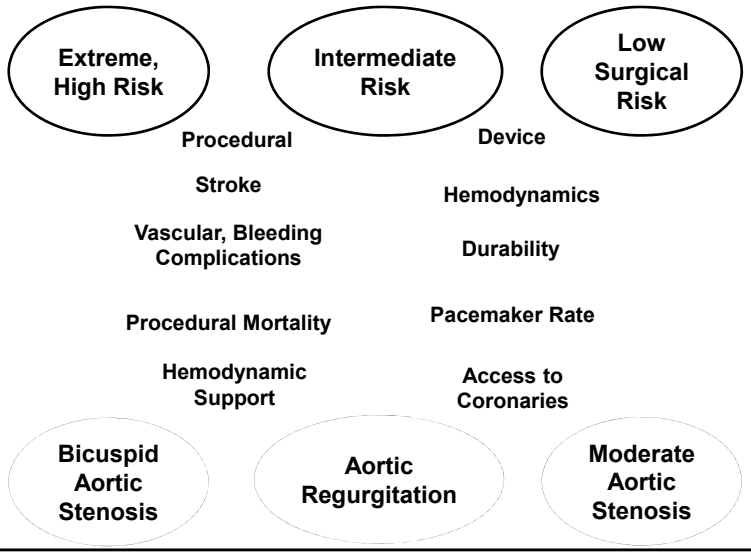
# Low Risk TAVR Trials Reported March 2019

***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* |

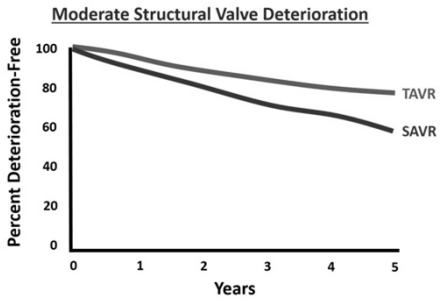
**Combined 12-month stroke and mortality was LOWER with TAVR compared to Surgical Valve Replacement**

# 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

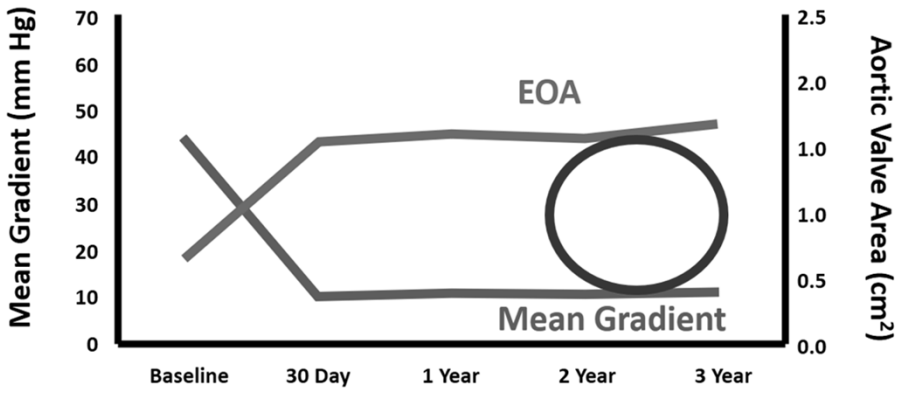
**4 Year**

| | 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

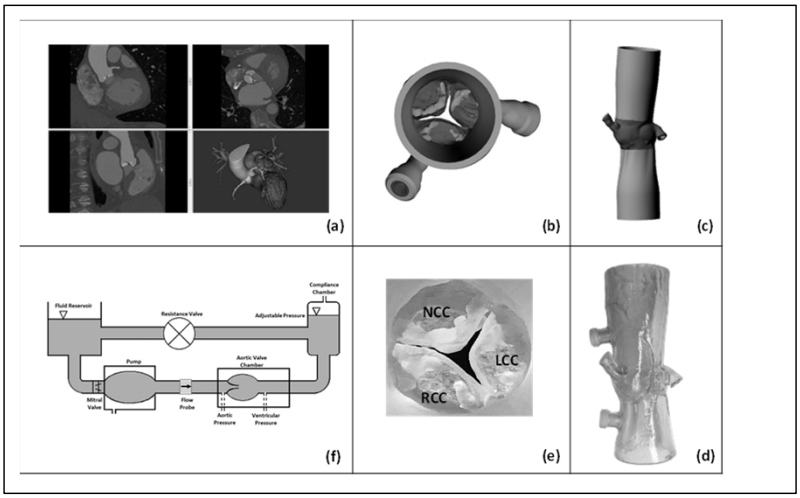
**Risk of Coronary obstruction if:**

- **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*

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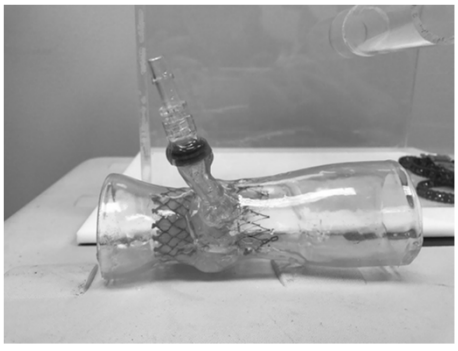
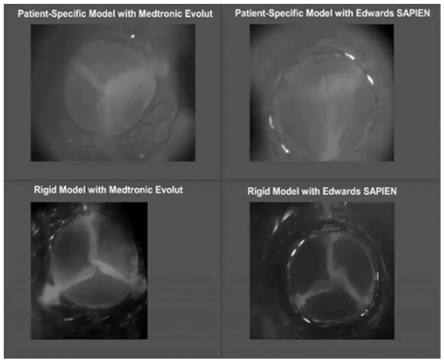
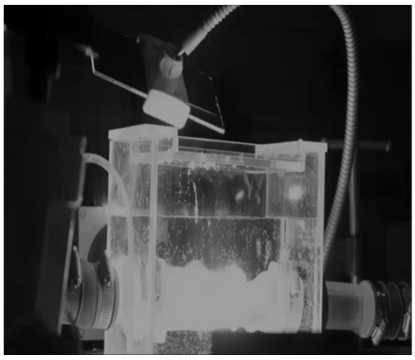


**With self-expandable Medtronic Evolut**

**With balloon-expandable Edwards SAPIEN**

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



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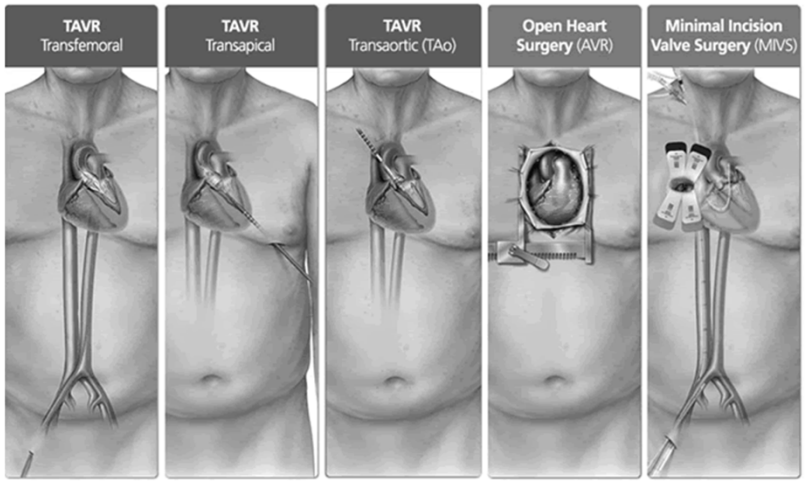


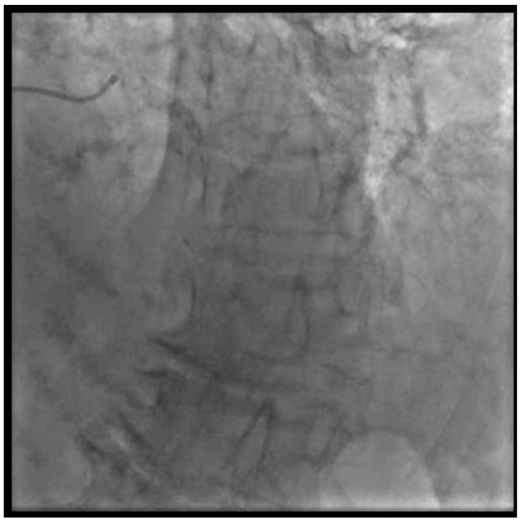

www.cvtsc.com

# 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%

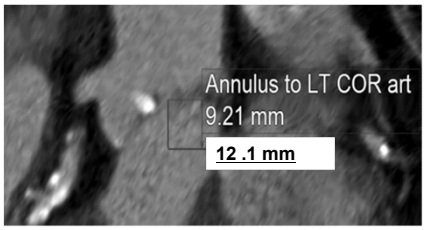
# Pre-TAVR Coronary Angiogram

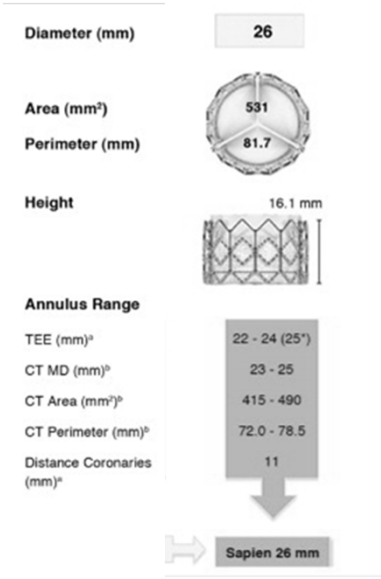


## 89 year old female, severe symptomatic aortic stenosis

**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)**

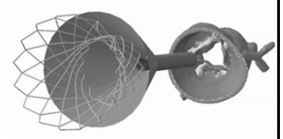



# Simulation

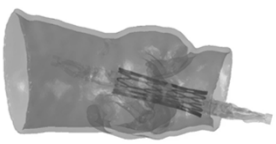
**Self-Expandable (SE)**

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

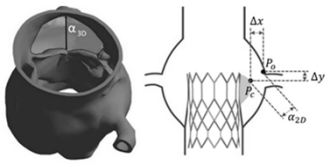


**Balloon-Expanding (BE)**

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

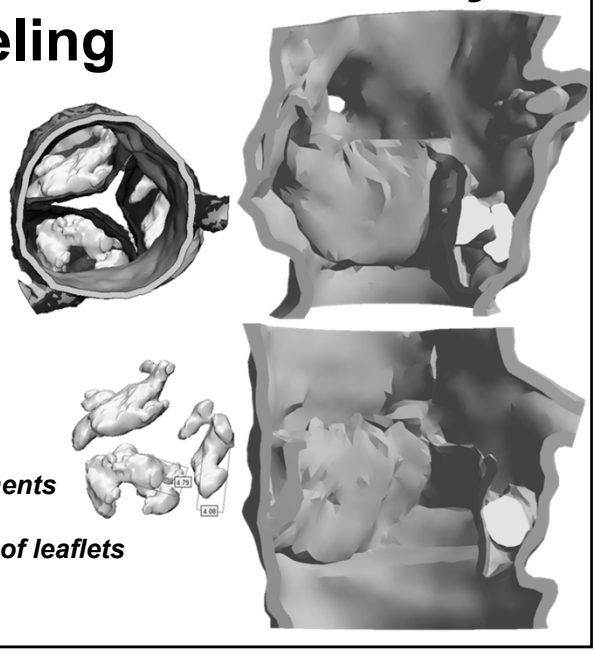


Goal: To estimate the final Distance between native/bioprosthetic Leaflet and Coronary ostium (DLC) and Area available for Coronay Flow (ACF) after TAVR



# 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***

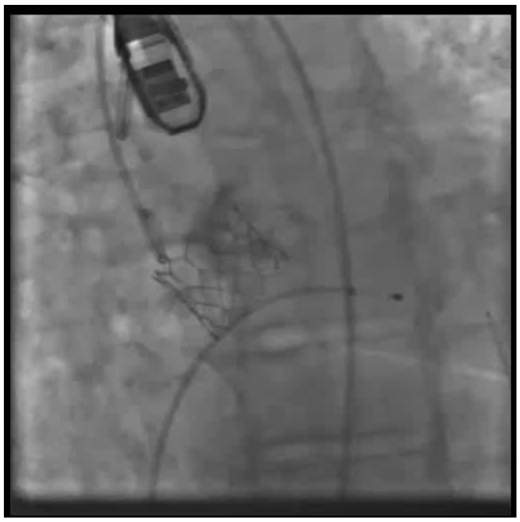
***-3-dimensional***

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

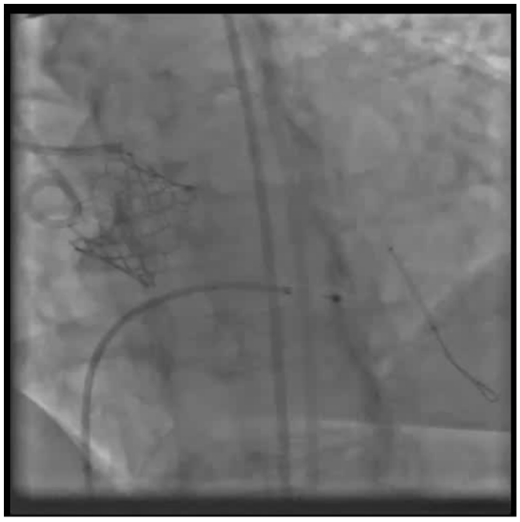
# Balloon Valvuloplasty and Aortography

## SAPIEN Valve Deployment

## Post-Deployment Aortogram

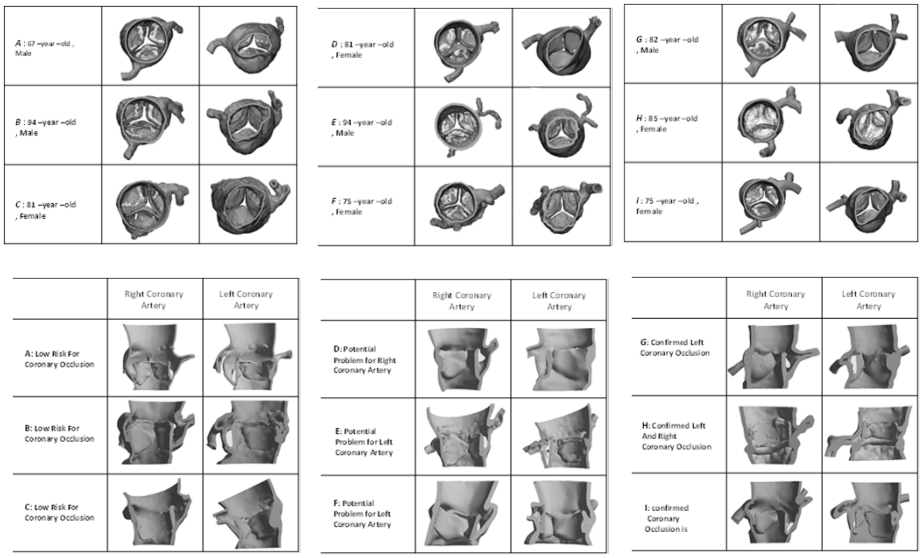


# Post-Deployment Angiogram

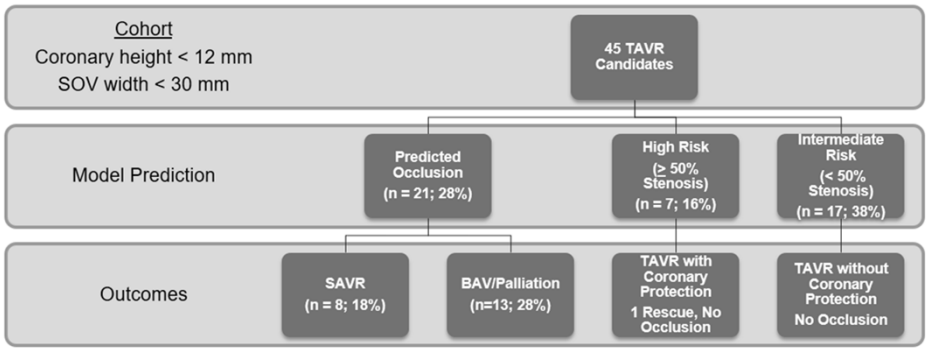


# Now 15 months post-TAVR…

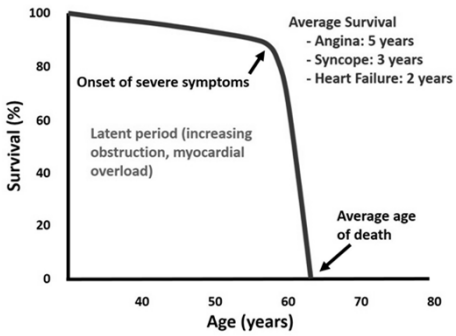
- **Not re-hospitalized**
- **NYHA II**
- **Valve remains well-seated, trivial aortic regurgitation**
- **Mean gradient 10 mmHg, calculated AVA 1.8 $cm^2$**
- **Ejection fraction is 65-70%**




# 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

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