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

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

"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"
**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

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**Aortic Stenosis**

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

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

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**A Novel Approach…**

Transcatheter Aortic Valve Replacement

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**Transcatheter Aortic Valve Replacement**
### Transcatheter Aortic Valve Replacement

- **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 (November) 2015

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### TAVR Candidacy in 2019

<table>
<thead>
<tr>
<th>STS Score</th>
<th>EuroScore</th>
<th>Low Risk</th>
<th>INTERMED</th>
<th>HIGH</th>
<th>INOPERABLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 70 yo, no comorbidities</td>
<td>STS 0-3 EuroScore 0-2</td>
<td>Low Risk Trials</td>
<td>INTERMED</td>
<td>HIGH</td>
<td>INOPERABLE</td>
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<tr>
<td>80 years old, 1-2 comorbidities</td>
<td>STS 4-8 EuroScore 3-5</td>
<td></td>
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<tr>
<td>80 years old, Prior sternotomy</td>
<td>STS &gt; 8 EuroScore &gt; 6</td>
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</table>

### TAVR: Determining Risk

**Mean STS Score in Inoperable Patients**

<table>
<thead>
<tr>
<th>STS Score</th>
<th>EuroScore</th>
<th>Commercial</th>
<th>PARTNER I</th>
</tr>
</thead>
<tbody>
<tr>
<td>STS 8</td>
<td>52%</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>STS 15</td>
<td>10%</td>
<td>15%</td>
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What Risk Scores Miss…

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

Procedural Considerations
- Porcelain aorta, chest radiation, LIMA course
- Access Route
- Periprocedural Support

Composite Indices
- Frailty

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

Fewer Procedural Complications

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: AVAS1cm AND max velocity ≥25m/sec or mean gradient ≥80mmHg
  - AVAS≤1cm AND mean gradient ≥40mmHg or max velocity ≥24m/sec AND positive exercise tolerance test
  - AVAS≤1cm AND mean gradient ≥40mmHg or max velocity ≥24m/sec AND LVEF ≤50%
### TAVR Candidacy in 2019

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**SAVR**

**SAPIEN**

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### Low Risk TAVR, Reported March 2019

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

### Low Risk TAVR Trials Reported March 2019

<table>
<thead>
<tr>
<th>Outcome</th>
<th>CoreValve</th>
<th>SAPIEN Valve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>Similar</td>
<td>Lower</td>
</tr>
<tr>
<td>Stroke</td>
<td>Lower*</td>
<td>Lower</td>
</tr>
<tr>
<td>Bleeding</td>
<td>Lower*</td>
<td>Lower*</td>
</tr>
<tr>
<td>Vascular Complication</td>
<td>Similar</td>
<td>Similar</td>
</tr>
<tr>
<td>Kidney Injury</td>
<td>Lower*</td>
<td>Similar</td>
</tr>
<tr>
<td>New Atrial Fibrillation</td>
<td>Lower*</td>
<td>Lower*</td>
</tr>
<tr>
<td>Pacemaker</td>
<td>Higher*</td>
<td>Similar</td>
</tr>
<tr>
<td>Rehospitalization</td>
<td>Lower*</td>
<td>Lower</td>
</tr>
<tr>
<td>Length of Stay</td>
<td>Shorter*</td>
<td>Shorter*</td>
</tr>
<tr>
<td>KCCQ/QOL Improvement</td>
<td>Higher* (30-d)</td>
<td>Higher*</td>
</tr>
<tr>
<td>Discharged Home</td>
<td>Higher*</td>
<td></td>
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**Transcatheter versus Surgical Outcomes in Low Risk Trials**

**CoreValve**

**SAPIEN Valve**
### Evolving Populations, Considerations

- **Low Surgical Risk**
  - Procedural
  - Hemodynamics
  - Pacemaker Rate
  - Access to Coronaries

- **Intermediate Risk**
  - Procedural Mortality
  - Hemodynamic Support

- **Extreme, High Risk**
  - Stroke
  - Vascular, Bleeding Complications

### Bicuspid Aortic Stenosis

#### 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 vs 4 Year

- **PVL Incidence**
  - Earliest TAVR RCT ~ 10%
  - Most recent ~ 4%

- **Related to...**
  - Sizing, LVOT – Aortic Angle, depth, valve type

### What is “Long-Term Success”? (Graph)

- **Moderate Structural Valve Deterioration**
- **Percent Deterioration**

### Imaging, Simulation, and TAVR Success: Valve Durability

**The Leak? Or the Gradient? Or something else?**

- **Mean Gradient**
  - Baseline: 40-60 mm Hg
  - 1 Year: 20-40 mm Hg
  - 5 Year: ~10 mm Hg

- **EOA**

- **Aortic Valve Area**
  - Baseline: 1.0-1.5 cm²
  - 1 Year: 0.75-1.0 cm²
  - 5 Year: ~0.5 cm²

### Related References

- Kodali et al., 2012 NEJM
- Blackmon et al., 2019 JACC
- 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

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

Ribeiro et al, 2013

Precedes significant increase in gradient
May precede valve degeneration and/or correlate with cerebroembolism

Less common with anticoagulation
Can resolve with anticoagulation

(Ribeiro et al, 2013)

**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

**Collaboration Between Physicians and Scientists**

With self-expandable Medtronic Evolut
With balloon-expandable Edwards SAPIEN
Case Presentation

89 year old female, severe symptomatic aortic stenosis

- Mean gradient 48 mm Hg, Vmax 4.4 m/s, AVA 0.84 cm²
- Stage III CKD, COPD, insulin-dependent diabetes, prior CVA
  - STS 9%, TAVR 30-d predicted mortality 4.5%
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 cm²).
Sinus of Valsalva (25.5 mm).

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 Coronary Flow (ACF) after TAVR.

Anatomical Leaflet, Coronary, Sinus Modeling

-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 cm²
- Ejection fraction is 65-70%
Reconstructive Modeling to Identify Patients At-Risk for Coronary Occlusion

Why Coordination is important...

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

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

One Structural Heart Clinic in August...

65% of patients travel > 1 hr to the Ross

65% of patients travel > 1 hr to the Ross
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.