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


“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

Aortic Stenosis

Severe Symptomatic Aortic Stenosis: 50% 2-year Mortality

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
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 2019

<table>
<thead>
<tr>
<th>STS 0-3</th>
<th>STS 4-8</th>
<th>STS &gt; 8</th>
</tr>
</thead>
<tbody>
<tr>
<td>EuroScore 0-2</td>
<td>EuroScore 3-5</td>
<td>EuroScore &gt; 6</td>
</tr>
</tbody>
</table>

- **LOW**
  - < 70 yo, no comorbidities

- **INTERMED**
  - 80 years old, 1-2 comorbidities

- **HIGH**
  - 80 years old

- **INOPERABLE**
  - Prior sternotomy

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TAVR: Determining Risk

<table>
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<th>STS 0-3</th>
<th>STS 4-8</th>
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- **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**

<table>
<thead>
<tr>
<th>STS &gt; 8</th>
<th>STS &gt; 15</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Commercial</strong></td>
<td><strong>PARTNER I</strong></td>
</tr>
<tr>
<td>52%</td>
<td>66%</td>
</tr>
<tr>
<td>10%</td>
<td>15%</td>
</tr>
</tbody>
</table>

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
- 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

Adapted from Kron et al, Circ 2013, 127(12):1580-1588; TAVR trials; Hanrath et al, Circ 2012, 126(20)
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≤1cm² AND max velocity ≥5m/sec or mean gradient ≥60mmHg
  - AVA≤1cm² AND mean gradient ≥40mmHg or max velocity ≥4m/sec AND positive exercise tolerance test
  - AVA≤1cm² AND mean gradient ≥40mmHg or max velocity ≥4m/sec AND LVEF ≤50%
## TAVR Candidacy in 2019

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

### Low Risk Trials

- **Partner II**
- **Sutured**
- **US Pivotal**

### SAPIEN

- **SAPIEN**
- **US Pivotal**

### SAVR

- **Low Risk**
- **Sutured**
- **US Pivotal**

Low Risk TAVR, Reported March 2019

Low Risk TAVR Trials Reported March 2019

<table>
<thead>
<tr>
<th>Transcatheter versus Surgical Outcomes in Low Risk Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcome</td>
</tr>
<tr>
<td>Death</td>
</tr>
<tr>
<td>Stroke</td>
</tr>
<tr>
<td>Bleeding</td>
</tr>
<tr>
<td>Vascular Complication</td>
</tr>
<tr>
<td>Kidney Injury</td>
</tr>
<tr>
<td>New Atrial Fibrillation</td>
</tr>
<tr>
<td>Pacemaker</td>
</tr>
<tr>
<td>Rehospitalization</td>
</tr>
<tr>
<td>Length of Stay</td>
</tr>
<tr>
<td>KCCQ/QOL Improvement</td>
</tr>
<tr>
<td>Discharged Home</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Extreme, High Risk</th>
<th>Intermediate Risk</th>
<th>Low Surgical Risk</th>
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</thead>
<tbody>
<tr>
<td>Procedural Stroke</td>
<td>Hemodynamics</td>
<td>Procedural Mortality</td>
</tr>
<tr>
<td>Vascular, Bleeding Complications</td>
<td>Durability</td>
<td>Hemodynamic Support</td>
</tr>
<tr>
<td>Procedural Mortality</td>
<td>Pacemaker Rate</td>
<td>Access to Coronaries</td>
</tr>
</tbody>
</table>

Bicuspid Aortic Stenosis | Aortic Regurgitation | Moderate 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
**Paravalvular Leak Tends to Remain Stable or Regress over Time**

<table>
<thead>
<tr>
<th>Post Procedure</th>
<th>None</th>
<th>Trace</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>27</td>
<td>12</td>
<td>24</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>Trace</td>
<td>24</td>
<td>12</td>
<td>12</td>
<td>17</td>
<td>0</td>
</tr>
<tr>
<td>Mild</td>
<td>3</td>
<td>10</td>
<td>23</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Moderate</td>
<td>2</td>
<td>1</td>
<td>5</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Severe</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

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

Kodali et al., 2012 NEJM

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

Blackmon et al., 2019 JACC

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

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

**Mean Gradient (mm Hg)**

**Aortic Valve Area (cm²)**

EOA

Mean Gradient

Makkar TCT 2011
**Imaging, Simulation, and TAVR Success**  
**Might Valve Durability and Cerebroembolism Share a Substrate?**

Subclinical leaflet thrombosis in surgical and transcatheter bioprosthetic aortic valves: an observational study  
Tayseh Chaharmahali, Ben Setyodihardjo, Taha Youssef, John Fielder, Deilin Quinones, Thomas Shiller, Tugay Akin, Jonathan Purnell, Tonya Simms, Steffen Senges, Gregory KontAhead, Martha de Faria, Andreas Gatzoulis, Patrick J. Serruys, Jr., Alfredo Teo, Deepak K. Bhatt, Martin E. Evans, Jr., Richard B. Chakravarti, on behalf of the RE-SOVIT and implant investigators  
Lancet 2018 (389) 2385-2392.

A meta-analysis of reduced leaflet motion for surgical and transcatheter aortic valves: Relationship to cerebrovascular events and valve degeneration  
Nader Malak 1, Satya Shresthovac 2, Dean Hricik 1, Scott Lilly 1

Cardiovasc Revasc Med 2018 (19) 88-97

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

With self-expandable Medtronic Evolut

With balloon-expandable Edwards SAPIEN
Imaging, Simulation, and TAVR Success
Collaboration Between Physicians and Scientists

Transcatheter Aortic Valve Replacement

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 cm²
- 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), Area (4.72 cm²), Sinus of Valsalva (26.5 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

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
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

Cohort
Coronary height < 12 mm
SOV width < 30 mm

49 TAVR Candidates

Predicted Occlusion
(n = 24; 38%)

High Risk
 (< 50% Stenosis)
(n = 7; 16%)

Intermediate Risk
(< 50% Stenosis)
(n = 17; 38%)

Outcomes
SAVR
(n = 8; 18%)

BAVI/Palliation
(n = 1; 2%)

TAVR with Coronary Protection
1 Rescue, No Occlusion

TAVR without Coronary Protection
No 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

<table>
<thead>
<tr>
<th>Patient</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>Surgical aortic valve replacement</td>
</tr>
<tr>
<td>Patient 2</td>
<td>Repeat testing in 6 months</td>
</tr>
<tr>
<td>Patient 3</td>
<td>TAVR</td>
</tr>
<tr>
<td>Patient 4</td>
<td>Transcatheter mitral valve replacement</td>
</tr>
<tr>
<td>Patient 5</td>
<td>TAVR</td>
</tr>
<tr>
<td>Patient 6</td>
<td>Surgical aortic valve replacement</td>
</tr>
<tr>
<td>Patient 7</td>
<td>Surgical aortic valve replacement</td>
</tr>
</tbody>
</table>

[Diagram of Heart Clinic team members]
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.