Transcatheter Aortic Valve Replacement: Update on Patient Selection and Valve Prostheses

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Disclosure:

- Consulting/Employment: Consulting for Edwards Lifesciences
- Other Relationships: Advisory Board: Phillips Imaging and Steering Committee of Partner 2 Clinical Trial
Outline

- Introduction
- Factors influencing patient outcomes and selection
  - Sex
  - Coronary disease
  - Diabetes
  - Coronary obstruction
  - Aortic insufficiency
  - Chronic lung disease
- Futility
- New prostheses
Introduction

Edwards SAPIEN valve  Edwards SAPIEN XT valve  CoreValve Revalving system
Sex Differences in Mortality after TAVR

- Women 51.3%
  - Frail
  - Smaller AVA
  - Lower GFR
- Similar procedural success
- Procedural Complications
  - Vascular complications 12% vs. 5% (p=0.003)
  - Blood transfusion: 9.5% vs. 3.6% (p=0.005)
  - 30 day mortality: 6.5% vs. 11.2% (p=0.05)
- In PARTNER Cohort A
  - TAVR mortality: 18.4% vs. 28.4% p=0.03
  - SAVR mortality: 27.2% vs. 24.2% p=0.54
- Mechanism
  - Less fibrosis?
  - LV hypertrophy regression

J Am Coll Cardiol 2012;60:882
J Am Coll Cardiol 2012;59:566
TAVR and Coronary Artery Disease (CAD)

- Presence of CAD affects survival in patients undergoing TAVR and AVR.
- Concomitant revascularization increases surgical risk and survival.
- Multidisciplinary discussion is key to patient selection
  - Type of revascularization
  - Timing
  - Data

TAVR and Paravalvular AI

- **Moderate AI**
  - 7-24% of patients
  - mortality and heart failure

- **Aortic annulus measurement**
  - 2D vs. 3D
  - TTE vs. TEE
  - Role of MSCT
  - Perimeter vs. Area

- **Quantification**

- **Factors:**
  - Cover Index
  - Annular size
  - Annular eccentricity
  - Leaflet calcification
  - Malposition

Int J Cardiol (2010), doi:10.1016/j.ijcard.2010.03.004
TEE vs. TTE
MSCT and Annulus sizing

- Allows for multiplanar reconstruction
- Gated to 25-35% RR interval
- Area and Perimeter
- Ellipse vs. Circular
TAVR and Chronic Lung Disease

- **Mortality**
  - Cohort B: 52% vs. 69% \( p = 0.04 \)
  - Cohort A: 64.8% vs. 66.4% \( p = 0.92 \)
  - No difference between TA vs. TF

- **All TAVR patients (Continued access + RCT)**
  - 1 Yr mortality: 23.4% vs. 19.6% \( p = 0.02 \)
  - Oxygen dependence: 29.7% vs. 21.4% \( p = 0.004 \)

- **Factors associated with mortality**

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 minute walk &lt; 50 m</td>
<td>1.67</td>
</tr>
<tr>
<td>( O_2 ) dependence</td>
<td>1.44</td>
</tr>
<tr>
<td>BMI</td>
<td>0.97</td>
</tr>
<tr>
<td>Cr &gt; 2mg/dl</td>
<td>1.43</td>
</tr>
<tr>
<td>mPAP</td>
<td>1.26</td>
</tr>
</tbody>
</table>

J Am Coll Cardiol DOI: 10.1016/j.jacc.2013.09.024
Coronary Obstruction

- Incidence: 0.66%
- Procedural death: 16%
- 30 day mortality: 40%

Risk factors:
- Women
- Without CABG
- Valve in Valve
- Smaller Sinus of Valsalva < 30 mm
- Low coronary ostia < 12 mm
- Small aortic annulus
- Balloon expandable prosthesis
Aortic Root and Annular Rupture

- Incidence: 1%
- 48% in hospital mortality rate
- Seen during valve deployment or post-dilation
- Recognized by refractory hypotension or bleeding
- Risk Factors
  - LVOT or subannular calcification
    - Agatson score 181 vs 22 (p<0.001)
  - >20% oversizing (annular area)
    - 79% vs. 29% (p<0.001)
  - Postdilation
    - 22% vs. 0% (p<0.005)

Circulation 2013;128:244-253
Circ Cardiovasc Interv 212;5:424
What is treatment futility in TAVR?

### Quality of life
- SF-12 MCS
- Mean gradient
- Mod-Severe MR
- BMI
- 6MWT distance
- O2-dependent COPD
- Creatinine
- Diabetes
- Mod-Severe AR
- KCCQ
- Arrhythmia
- Age

### Early mortality
- Decreasing BMI
- Coagulopathy
- Liver disease
- Lower BMI
- Decreasing MMSE
- Renal disease
- IABP during procedure
- Non-fata major complications

US COREVALVE Trial
Pivotal Trial Design

CoreValve US Pivotal Trials

Extreme Risk
- Iliofemoral Access > 18 Fr Sheath
  - Yes
    - CoreValve Iliofemoral
      - N=487
  - No
    - CoreValve Non-Iliofemoral
      - N=147

High Risk
- Randomization 1:1
  - Versus
    - CoreValve
    - SAVR

N=487 N=147

TCT 2013 LBCT
### Baseline Demographics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N=471</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>83.1 ± 8.6</td>
</tr>
<tr>
<td>Men, %</td>
<td>49.0</td>
</tr>
<tr>
<td>STS Predicted Risk of Mortality, %</td>
<td>10.3 ± 5.6</td>
</tr>
<tr>
<td>Logistic EuroSCORE, %</td>
<td>22.7 ± 17.4</td>
</tr>
<tr>
<td>New York Heart Association (NYHA)</td>
<td></td>
</tr>
<tr>
<td>NYHA Class III/IV, %</td>
<td>91.9</td>
</tr>
<tr>
<td>Diabetes Mellitus, %</td>
<td>42.5</td>
</tr>
<tr>
<td>Insulin Requiring Diabetes, %</td>
<td>19.1</td>
</tr>
<tr>
<td>Prior Stroke, %</td>
<td>13.8</td>
</tr>
<tr>
<td>Modified Rankin 0 or 1, %</td>
<td>71.9</td>
</tr>
<tr>
<td>Modified Rankin &gt; 1, %</td>
<td>28.1</td>
</tr>
<tr>
<td>Co-Morbidity Assessment</td>
<td>N=471</td>
</tr>
<tr>
<td>-------------------------------------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>Any Chronic Lung Disease (STS Criteria), %</td>
<td>58.8</td>
</tr>
<tr>
<td>Moderate, %</td>
<td>15.3</td>
</tr>
<tr>
<td>Severe*, %</td>
<td>24.0</td>
</tr>
<tr>
<td>Home Oxygen, %</td>
<td>30.4</td>
</tr>
<tr>
<td>FEV1 ≤ 1000 cc, %</td>
<td>23.1</td>
</tr>
<tr>
<td>Diffusion Capacity &lt; 50%, %</td>
<td>22.3</td>
</tr>
<tr>
<td>Charlson Co-Morbidity Score**, %</td>
<td>5.3 ± 2.3</td>
</tr>
<tr>
<td>Moderate (3, 4), %</td>
<td>32.9</td>
</tr>
<tr>
<td>Severe (&gt; 5), %</td>
<td>58.6</td>
</tr>
</tbody>
</table>

*STS Criteria: Severe = FEV1 < 50% predicted and/or RA pO2 < 60 or pCO2 > 50

*Charlson Score: = 1 MI, CHF, PVD, CVD, dementia, chronic lung disease, connective tissue disease, ulcer, mild liver disease, DM; = 2 hemiplegia, mod-severe kidney disease, diabetes with end organ damage, leukemia, lymphoma; = 3 moderate or severe liver disease; = 6 metastatic solid tumor, AIDS
# Frailty Assessment

<table>
<thead>
<tr>
<th>Frailty Characteristic</th>
<th>N=471</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anemia With Prior Transfusion, %</td>
<td>22.9</td>
</tr>
<tr>
<td>BMI &lt; 21 kg/m², %</td>
<td>7.6</td>
</tr>
<tr>
<td>Albumin &lt; 3.3 g/dL, %</td>
<td>18.5</td>
</tr>
<tr>
<td>Unplanned Weight Loss &gt; 10 pounds, %</td>
<td>16.9</td>
</tr>
<tr>
<td>Falls in Past 6 Months, %</td>
<td>17.8</td>
</tr>
<tr>
<td>5 Meter Gait Speed &gt; 6 secs, %</td>
<td>84.2</td>
</tr>
<tr>
<td>Grip Strength &lt; Threshold, %</td>
<td>67.6</td>
</tr>
</tbody>
</table>
Echocardiographic Findings

- Effective orifice area: 0.73 cm² at Screening, 1.82 cm² at Discharge, 1.88 cm² at 1 Month, 1.90 cm² at 6 Month, 1.89 cm² at 1 Year.
- Mean gradient: 47.4 mm Hg at Screening, 9.4 mm Hg at Discharge, 8.5 mm Hg at 1 Month, 9.0 mm Hg at 6 Month, 8.8 mm Hg at 1 Year.

Screening: N=470
Discharge: N=445
1 Month: N=418
6 Month: N=363
1 Year: N=323
# Secondary Endpoints

<table>
<thead>
<tr>
<th>Events*</th>
<th>1 Month</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Stroke, %</td>
<td>3.9</td>
<td>6.7</td>
</tr>
<tr>
<td>Major, %</td>
<td>2.4</td>
<td>4.1</td>
</tr>
<tr>
<td>Minor, %</td>
<td>1.7</td>
<td>3.1</td>
</tr>
<tr>
<td>Myocardial Infarction, %</td>
<td>1.3</td>
<td>2.0</td>
</tr>
<tr>
<td>Reintervention, %</td>
<td>1.3</td>
<td>2.0</td>
</tr>
<tr>
<td>VARC Bleeding, %</td>
<td>35.1</td>
<td>41.4</td>
</tr>
<tr>
<td>Life Threatening or Disabling, %</td>
<td>11.7</td>
<td>16.6</td>
</tr>
<tr>
<td>Major, %</td>
<td>24.1</td>
<td>27.6</td>
</tr>
<tr>
<td>Major Vascular Complications, %</td>
<td>8.3</td>
<td>8.5</td>
</tr>
<tr>
<td>Permanent Pacemaker Implant, %</td>
<td>22.2</td>
<td>27.1</td>
</tr>
<tr>
<td>Per ACC Guidelines, %</td>
<td>17.4</td>
<td>19.9</td>
</tr>
</tbody>
</table>

* Percentages obtained from Kaplan Meier estimates
NYHA Class Survivors

90% of Patients Improved at Least 1 NYHA Class by 1 Year

60% of Patients Improved at Least 2 NYHA Classes by 1 Year

Percentage of Patients

Baseline N=468

1 Month N=416

6 Month N=365

1 Year N=328

90% of Patients Improved at Least 1 NYHA Class by 1 Year
60% of Patients Improved at Least 2 NYHA Classes by 1 Year
Paravalvular Regurgitation

Percentage of Patients

<table>
<thead>
<tr>
<th>Category</th>
<th>Discharge</th>
<th>1 Month</th>
<th>6 Month</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>445</td>
<td>418</td>
<td>363</td>
<td>323</td>
</tr>
<tr>
<td>Severe</td>
<td>1.6%</td>
<td>0.5%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Moderate</td>
<td>8.9%</td>
<td>11.0%</td>
<td>8.5%</td>
<td>4.1%</td>
</tr>
<tr>
<td>Mild</td>
<td>40.7%</td>
<td>41.6%</td>
<td>32.7%</td>
<td>28.8%</td>
</tr>
<tr>
<td>None/Trivial</td>
<td>48.7%</td>
<td>46.9%</td>
<td>58.8%</td>
<td>67.1%</td>
</tr>
</tbody>
</table>

TCT 2013 LBCT
Extreme Risk Study | Iliofemoral Pivotal
Newer Prostheses
St Jude’s Portico Valve

- Self Expanding
- Bovine pericardial leaflets
- Porcine pericardial cuff
- Available in 2 sizes
- Delivery
  - Transfemoral, Subclavian
  - Transapical
- Fully retrievable
- Lower rate of pacemaker or LBBB
- US Trial starting soon
DirectFlow Medical

- Trileaflet
- Bovine pericardium
- 18 Fr delivery system
- No metal
- Retreivable and repositionable
- Can be aligned manually
- Epoxy resin allows fixation

Size
- 25 mm (19-24 mm)
- 27 mm (24-26.5 mm)
Direct Flow Medical
Discover Trial

- N=100
- High risk or extreme high risk
- 6 month follow
  - 96% survival
  - Mean gradient: 12mmHg
  - VARC success: 93%
  - Vascular complications: 2.5%
  - CVA: 4%
  - 90% NYHA @ 6 months
Lotus Valve

- 18 Fr Delivery system
- Flexible
- Predictable and accurate placement
- Repositionable
- Resheathable
- Adaptive seal
- Automated deployment
- Reprise trials
Reprise II Trial

- N=120
- Age: 84 yrs
- High Risk
  - STS plus: 11.8%
  - NYHA III/IV=75%
- AVA=0.7 ±0.2 cm²
- Mean Grad: 46±15 mmHg

Post Procedure:
- Procedural success: 100%
- Valve retrieval: 6 pts
- No embolization
- Mean gradient: 11.5 mmHg
- AVA: 1.7 cm²
- AI:
  - None: 61%
  - Trace: 20.8%
  - Mild: 16.8%
  - Moderate: 1%
- All cause mortality: 4.2%
- Stroke: 5.9%
How do you treat?

- 72 y/o male
- Severe symptomatic AS
  - AVA: 0.7 cm²
  - Mean gradient 45 mmHg
- Porcelain aorta
Options

- **TAVR**
  - Undersize a balloon expandable prosthesis?
  - Utilize a self expanding prosthesis?
  - Utilize a inflatable prosthesis?

- **SAVR**
  - Circulatory arrest?
Conclusions

- TAVR continues to be a promising procedure.
- Special emphasis will be placed on patient selection to improve procedural outcomes and long term survival.
- New prostheses will provide different treatment options, tailored to specific patient characteristics.