Transcatheter Aortic Valve Replacement: Is it ready for prime time

Peter S. Fail, MD, FACC, FACP FSCAI
Director of the Cardiac Catheterization Laboratories and Interventional Research
Cardiovascular Institute of the South
Disclosures

Speaker’s Bureau:
• Amgen

Medical/Scientific Boards:
• CardioSolutions
• Toshiba

Stockholder:
• CardioSolutions

Grant/Research Support:
• Medtronic
• Direct Flow
• Abbott
• CardioKinetix
• Sunshine Heart
• Insert Company Name
Aortic Stenosis

• Scope of the Problem
• Issues with current treatment Strategies
• Alternatives
  – Short term and Long term results
• New Problems
• Next Generation Devices
  – New Ideas on access
Aortic Stenosis
From a Surgeons Point of View
Incidence and Prevalence

• Aortic stenosis is the most common acquired valvular disorder found in developed countries
  • Affects approximately 5 out of every 10,000 people in the United States

• Mild to severe AS present in up to 9% of adults over age 65 years

• The prevalence of calcific aortic stenosis increases with age and is expected to double in the next 20 years*

Symptomatic Patients with Severe AS Require Urgent Attention

Valvular Aortic Stenosis In Adults
(Average Course)

Latent Period
Increasing Obstruction Myocardial Overload

Onset Severe Symptoms
- Angina
- Syncope
- CHF

Surgical intervention should be performed promptly
even once minor symptoms occur.

Prevalence of Aortic Stenosis in Patients Age 65 and Over

U.S. Prevalence of Aortic Stenosis

- U.S. Population > 65: 40M (U.S. Census, 2010)
- Prevalence Rate: 4% (Cardiovascular Health Study)
- Prevalence: 1.6M (Calculation)
- Operable AS (%): 20% (L.E.K. Consulting Estimate)

Annual AVR Patients: 60K

Addressable Patients: 320K

19% of those who would benefit from AVR actually get it.
Treatment of Severe Aortic Stenosis (AS)

• SAVR is the gold standard for treatment of severe AS\(^1\)
• However, 33% of all patients $\geq$75 years of age with severe AS are declined for surgery\(^2\)
  – Of these patients who ultimately undergo SAVR, a portion are at high risk for morbidity/mortality from the procedure
  – Of the 100 patients who underwent SAVR during the study period, 5% died during the postoperative period (30 days)

SAVR=surgical aortic valve replacement.
Surgery is Safer than Ever

Unadjusted Aortic Valve Operative Mortality
Yearly Over Last 10 Years

Percentage of Patients

2001 2010

0% 4%

1% 3%

2% 2%

3% 1%

4%


Cardiovascular Institute
OF THE SOUTH
Characteristics of an Inoperable Patient Cohort B

TAVR patients may present with some of the following:

- Severe, symptomatic native aortic valve stenosis
- Old age
- Frailty
- History of stroke/CVA
- History of syncope
- Reduced EF
- Heavily calcified aorta
- Prior CABG
- Prior chest radiation
- History of AFib
- History of CAD
- Prior open chest surgery
- History of COPD
- Fatigue, slow gait
- History of renal insufficiency
- Peripheral vascular disease
- Diabetes and hypertension
Dividing the Pie of patients with Critical AS

Conventional Risk Patients
STS > 5
No Incidentals
Passing the “eyeball” test-

High Risk patients

Surgery
High Risk Surgery
PABV
TAVI
Conclusions— Nonsurgical implantation of a prosthetic heart valve can be successfully achieved with immediate and midterm hemodynamic and clinical improvement.
WHAT HAVE WE LEARNED SINCE 2002?
PARTNERS 1 Trial Data

- “Inoperable” patients had a reduced mortality compared to standard medical therapy.
- Patients deemed “High-risk” for surgical AVR that underwent TAVR had similar mortality to their surgical AVR counterparts.

The NEW ENGLAND JOURNAL of MEDICINE

COHORT B
Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

COHORT A
Transcatheter versus Surgical Aortic-Valve Replacement in High-Risk Patients
Effective and Lasting Drop in Gradient
COHORT A
Paravalvular Leak

Conduction Disturbance

Stroke

Coronary Occlusion

Embolization

Complications
All Stroke (ITT) SAPIEN

Numbers at Risk

<table>
<thead>
<tr>
<th></th>
<th>TAVR</th>
<th>Standard Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 yr</td>
<td>179</td>
<td>179</td>
</tr>
<tr>
<td>1 yr</td>
<td>128</td>
<td>118</td>
</tr>
<tr>
<td>2 yr</td>
<td>116</td>
<td>84</td>
</tr>
<tr>
<td>2 yr</td>
<td>105</td>
<td>62</td>
</tr>
<tr>
<td>3 yr</td>
<td>79</td>
<td>42</td>
</tr>
</tbody>
</table>

Incidence (%)

- Δ at 1 yr = 5.7%
- Δ at 2 yr = 8.3%

HR [95% CI] = 2.79 [1.25, 6.22]
p (log rank) = 0.009
Strokes (ITT) SAPEIN

HR [95% CI] = 1.09 [0.62, 1.91]

p (log rank) = 0.763
## All Stroke; CoreValve US Clinical Trial

### Graph

#### No. at Risk

<table>
<thead>
<tr>
<th>Group</th>
<th>Months Post-Procedure</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical</td>
<td></td>
<td>357</td>
<td>322</td>
<td>322</td>
<td>322</td>
<td>322</td>
<td>322</td>
<td>322</td>
<td>322</td>
<td>322</td>
<td>274</td>
<td>274</td>
<td>274</td>
<td>274</td>
<td>249</td>
</tr>
<tr>
<td>Transcatheter</td>
<td></td>
<td>390</td>
<td>363</td>
<td>363</td>
<td>363</td>
<td>363</td>
<td>363</td>
<td>363</td>
<td>363</td>
<td>363</td>
<td>334</td>
<td>334</td>
<td>334</td>
<td>334</td>
<td>314</td>
</tr>
</tbody>
</table>

#### Log-rank P=0.10

### Graph Details

- **Surgical**
- **Transcatheter**

- **All Stroke (%)**
  - Surgical: 4.9%, 6.2%, 8.8%, 12.6%
  - Transcatheter: 4.9%, 6.2%, 8.8%, 12.6%

- **Months Post-Procedure**
  - 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12
Paravalvular Leak
Sapien vs. CoreValve

Sapien

CoreValve

> Mild PVL Increase Mortality

> Moderate PVL Increase Mortality
Impact of Total AR on Mortality (AT)

TAVR Patients: Sapien

None - Trace
Mild
Moderate - Severe

No. at Risk

None-Tr 131
Mild 171
Mod-Sev 34

Months post Procedure

0 6 12 18 24 30 36

0% 10% 20% 30% 40% 50% 60% 70%

Mortality

38.2% 26.0% 12.3%

53.7% 32.5% 25.6%

60.8% 44.6% 35.3%
Impact of PVL on Late Mortality
CoreValve

Log rank P Value <0.0001

Extreme Risk Study | Iliofemoral Pivotal

All-Cause Mortality (%) vs Months Post Procedure

- None/Trivial N=208: 87.5%
- Mild N=180: 23.9%
- Moderate N=54: 22.2%
- Severe N=8: 17.8%

Impact of PVL on Late Mortality
CoreValve

Log rank P Value <0.0001

Extreme Risk Study | Iliofemoral Pivotal

All-Cause Mortality (%) vs Months Post Procedure

- None/Trivial N=208: 87.5%
- Mild N=180: 23.9%
- Moderate N=54: 22.2%
- Severe N=8: 17.8%

Impact of PVL on Late Mortality
CoreValve

Log rank P Value <0.0001

Extreme Risk Study | Iliofemoral Pivotal

All-Cause Mortality (%) vs Months Post Procedure

- None/Trivial N=208: 87.5%
- Mild N=180: 23.9%
- Moderate N=54: 22.2%
- Severe N=8: 17.8%

Impact of PVL on Late Mortality
CoreValve

Log rank P Value <0.0001

Extreme Risk Study | Iliofemoral Pivotal

All-Cause Mortality (%) vs Months Post Procedure

- None/Trivial N=208: 87.5%
- Mild N=180: 23.9%
- Moderate N=54: 22.2%
- Severe N=8: 17.8%

Impact of PVL on Late Mortality
CoreValve

Log rank P Value <0.0001

Extreme Risk Study | Iliofemoral Pivotal

All-Cause Mortality (%) vs Months Post Procedure

- None/Trivial N=208: 87.5%
- Mild N=180: 23.9%
- Moderate N=54: 22.2%
- Severe N=8: 17.8%
US Pivotal Extreme Risk – PVL Paired Analysis

Improvement in Moderate PVL Discharge to 1 Year

Patients with echos at both discharge and 1 Year

- Discharge
  - ≤ Mild
  - Moderate

- 1 Year
  - 29
  - 24

83% Improve

Discharge N=440

- 9.1%
- 40.7%
- 48.6%
- 1.6%
All-Cause Mortality (ITT): Cohort A High Risk Patients

Edwards Sapien

HR [95% CI] = 0.93 [0.74, 1.15]
p (log rank) = 0.483
2-Year All-cause Mortality
CoreValve

- Surgical
- Transcatheter

<table>
<thead>
<tr>
<th>Months Post-Procedure</th>
<th>No. at Risk</th>
<th>Surgical</th>
<th>Transcatheter</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>357</td>
<td>341</td>
<td>274</td>
</tr>
<tr>
<td>6</td>
<td>390</td>
<td>377</td>
<td>329</td>
</tr>
</tbody>
</table>

- 19.1% at 2 years
- 14.2% at 2 years
- 4.5% at 0 months
- 3.3% at 0 months
YEARS OF PROVEN VALVE DURABILITY

LOW AND STABLE AORTIC VALVE GRADIENT

Error Bars = ±SD
P < 0.0001

The PARTNER Trial

<table>
<thead>
<tr>
<th>MEAN GRADIENT, mm Hg</th>
<th>Baseline</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
<th>Year 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edwards THV</td>
<td>310</td>
<td>219</td>
<td>156</td>
<td>106</td>
<td>79</td>
<td>56</td>
</tr>
<tr>
<td>SAVR</td>
<td>299</td>
<td>158</td>
<td>123</td>
<td>86</td>
<td>61</td>
<td>48</td>
</tr>
</tbody>
</table>
## 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>4.0</td>
<td>7.0</td>
</tr>
<tr>
<td>Major, %</td>
<td>2.3</td>
<td>4.3</td>
</tr>
<tr>
<td>Myocardial Infarction, %</td>
<td>1.2</td>
<td>2.0</td>
</tr>
<tr>
<td>Reintervention, %</td>
<td>1.1</td>
<td>1.8</td>
</tr>
<tr>
<td>VARC Major or Life Threatening Bleeding, %</td>
<td>36.7</td>
<td>42.8</td>
</tr>
<tr>
<td>Life Threatening or Disabling, %</td>
<td>12.7</td>
<td>17.6</td>
</tr>
<tr>
<td>Major, %</td>
<td>24.9</td>
<td>28.5</td>
</tr>
<tr>
<td>Major Vascular Complications, %</td>
<td>8.2</td>
<td>8.4</td>
</tr>
<tr>
<td>Permanent Pacemaker Implant, %</td>
<td>21.6</td>
<td>26.2</td>
</tr>
<tr>
<td>Per ACC Guidelines, %</td>
<td>17.1</td>
<td>19.2</td>
</tr>
</tbody>
</table>

* Percentages obtained from Kaplan Meier estimates
No mortality differences between those patients receiving a new pacemaker and those without a new pacemaker out to 6-months.

P-value (log rank) 0.799
Change in LVEF?

Hoffmann, et al. JACC: Cardiovascular Intervention 2012 5:12; 1257
Long Term Effect of PPM Following TAVR
Balance of the Evidence

Mortality

Houthuizen (N=697)
Pereira (N=58)

TOTAL N= 755

No Δ
Mortality

Testa (N=879)
DeCarlo (N=275)
Wenaweser (N=508)
Franzoni (N=238)
Urena (N=668)
Nazif (N=1151)

TOTAL N=3719
COST

- Valve currently cost $30-32,500
  - Literally 6-7 times their surgical counterpart
  - Hospital reimbursement $52-85,000
Cost-Effectiveness of TAVR vs. Control Patients not Suitable for AVR

Lifetime Results

$100,000 per LY

ΔCost = $79,837
Δ LE = 1.59 years
ICER = $50,212/LYG

$50,000 per LY
Summary of Findings

• TAVR was associated with index admission costs of ~$78,000, including estimated physician fees

• Although follow-up costs were ~$23,000/pt lower with TAVR vs. standard care (mainly due to reduced CV hospitalizations), overall 1-year costs remained substantially higher with TAVR

• Based on observed data from PARTNER, we project that TAVR will result in an increased life expectancy of ~1.9 years compared with standard care and an iCER of $50,200 per life-year gained

• Results were minimally impacted by major sensitivity analyses
For patients with severe aortic stenosis who are unsuitable for surgical AVR, TAVR significantly increases life expectancy at an incremental cost per life year gained well within accepted values for commonly used cardiovascular technologies.
Conclusion

- Transcatheter Valve Replacement/Implantation has been the single biggest disruptive technology in the cardiovascular arena since Andreas Grüntzig placed a balloon in Dolf Bachman’s LAD
- Extreme and High–Risk patients benefit continues for 5 years
- Balloon expandable and Self Expanding valves have their own unique set of “side effects”
- Cost remains a significant obstacle for hospitals
- Intermediate risk patients are currently being studied
Is it Ready for Prime Time?

YES
Thank You