TRANSCATHETER VALVE REPLACEMENT: MOVING BEYOND HIGH RISK AND INOPERABLE PATIENTS (A SURGEON’S VIEW)

Mark J Russo, MD, MS

Director, Aortic Center
Director, Cardiac Surgery Research
Barnabas Heart Hospital/NJ

Assistant Professor of Surgery
Rutgers-New Jersey Medical School

Disclosures

Site Principle Investigator
• PARTNER II Trial (Edwards Lifesciences)
• SURTAVI (Medtronic)
• PORTICO (St. Jude)

Case Review Board
• PARTNER II Trial (Edwards Lifesciences)

Speakers Panel and Case Proctor
• Edwards Lifesciences

I Will Discuss Off-Label and/or Experimental Therapies
1. TAVR is not a “new” or “novel” procedure
   – 250,000+ TAVRs performed worldwide
   – 5 FDA-approved valves
   – 5 primary New England Journal of Medicine articles

2. Isolated Surgical AVR (SAVR) will become a historic operation (eg open AAA repairs)... soon
   – Today, TAVR remains complementary to SAVR
   – However, TAVR is a disruptive technology
   – In the near-term, TAVR will cannibalize SAVR

3. Surgeons need to evolve or...

THANK YOU!!

ANY QUESTIONS?
NOT ONLY IS TAVR NOT NEW. . .

TAVR IS A MATURE TECHNOLOGY

An Explosive Growth Trajectory

Estimated Global TAVR Procedures

<table>
<thead>
<tr>
<th>Year</th>
<th>Global TAVR Units</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>32,000</td>
</tr>
<tr>
<td>2013</td>
<td>41,000</td>
</tr>
<tr>
<td>2014</td>
<td>56,000</td>
</tr>
</tbody>
</table>

YoY Global Growth

- 2012-2013: 41%
- 2013-2014: 28%
- 2014: 36%
In the Next 10 Years, TAVR will Increase 4X

Estimated Global TAVR Procedures

5 FDA-Approved Devices

Sapien - 2012
Sapien XT – 2014
Corevalve - 2013
Sapien 3 – 2015
Evolute-R - 2015
Overwhelming Evidence to Support Its Use

Transcatheter Aortic-Valve Replacement with a Self-Expanding Prosthesis

Transcatheter Aortic-Valve Replacement for Inoperable Severe Aortic Stenosis

Two-Year Outcomes after Transcatheter or Surgical Aortic-Valve Replacement

TAVR AS A COMPLEMENTARY TECHNOLOGY TO SURGICAL AVR
Barnabas – TAVR Volume by Year

600% increase in TAVR volume in 2 years

NBI - Valves vs. CABGs

CABG Volume 33%; Cath volume 20%
Valve Procedures are 200%
Valve:CABG; 1:1 -> 3:1
Surgical Valve Volume 25%
Overall Cardiac Surgery Volume 25%
TAVR Increased SAVR Volume Nationally


Greater % TAVR Positively Impacts Cardiac Volume

- NJ programs where TAVR constituted >9% of all cases, cardiac surgery volume from ’13 -> ’14
- NJ programs where TAVR constituted <9% of all cases, cardiac surgery volume from ’13 -> ’14

*There were 3 exceptions
Improved SAVR Outcomes in the Post-TAVR ERA


THE IMPENDING SHIFT:
TAVR AS A DISRUPTIVE TECHNOLOGY

**TAVR is a Disruptive Technology**

In the end, the new product or idea completely redefines the industry. Eventually it moves upstream (eg high/intermediate risk) disrupting an existing market, displacing an earlier technology. Typically formed in a niche market that may appear unattractive or inconsequential to industry incumbents (eg inoperable).
Unattractive or Inconsequential – Extreme/High Risk

All-Cause Mortality (ITT)
Crossover Patients Censored at Crossover

Moving Upstream – Displacing an Existing Market

PARTNER Studies: 30-day survival
Moderate / Severe PVL at 30 Days
Edwards SAPIEN Valves

<table>
<thead>
<tr>
<th>Valve Type</th>
<th>0%</th>
<th>10%</th>
<th>20%</th>
<th>30%</th>
<th>40%</th>
<th>50%</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1B (TF)</td>
<td>179</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P1A (Overall)</td>
<td>344</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P2B (TF)</td>
<td>276</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P2B XT (TF)</td>
<td>284</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S3HR (Overall)</td>
<td>583</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>S3i (Overall)</td>
<td>1076</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Freedom From All-Cause Mortality

1 Year KM Freedom from All-Cause Mortality
TF Populations
Low Risk TAVR: NOTION Trial

Randomized 280 lower-risk patients – TAVR vs SAVR
3 European centers - Dec 2009 and Apr 2013
• Avg Age: 79 years
• Avg STS score: 3.0%
• STS Score < 4: 80%

<table>
<thead>
<tr>
<th></th>
<th>Surgery (n = 135)</th>
<th>TAVR (n = 145)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-Cause Mortality</td>
<td>9.8%</td>
<td>8.0%</td>
<td>.54</td>
</tr>
<tr>
<td>CV Mortality</td>
<td>9.1%</td>
<td>6.5%</td>
<td>.40</td>
</tr>
<tr>
<td>Stroke</td>
<td>5.4%</td>
<td>3.6%</td>
<td>.45</td>
</tr>
<tr>
<td>MI</td>
<td>6.0%</td>
<td>5.1%</td>
<td>.69</td>
</tr>
<tr>
<td>A. fib</td>
<td>60.2%</td>
<td>22.7%</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Pacemaker</td>
<td>4.2%</td>
<td>41.3%</td>
<td>&lt; .001</td>
</tr>
</tbody>
</table>


Redefining the Industry
This Shift Will NOT Be Limited to AS

• TAVR: From 2006-2011, 3 companies paid a combined $1.1B for 3 startups
  • w 3000+ human implants

  In 2006, Edwards paid $125M for PVT
  • 100+ human implants
  • On going studies in Europe and Canada

  In 2009, Medtronic paid $700M for CoreValve
  • 2500+ implants
  • Completed Feasibility study in Europe; CE Mark granted in 2010

  In 2011, Boston Scientific paid $197M for Lotus
  • 100+ implants
  • Completed Feasibility Study in Europe

• Mitrals: In a 45 day period, 3 companies paid a combined $1.1B for 3 startups
  with 19 human implants; 1 incs have 0 implants and no sales

  10 Jul, Edwards paid $400M for CardiAC
  • 9 human implants

  3 Aug, Abbott paid $250M for Tendyne
  • 10 human implants

  27 Aug, Medtronic paid $458 for Twelve
  • 0 human implants
THE SURGEON

Admiral James Stockdale/The Stockdale Paradox

• United States Navy vice admiral
• He is one of the most decorated Navy officers
  – Medal of Honor
  – Navy Distinguished Service Medal (3)
  – Silver Star Medal (4)
  – Legion of Merit with Combat "V"
  – Distinguished Flying Cross (2)
  – Bronze Star (2) with Combat "V"
  – Purple Heart Medal (2)
• In the Vietnam War where he was a prisoner of war for over seven years.

“You must maintain unwavering faith that you can and will prevail in the end, regardless of the difficulties, . . . AND at the same time have the discipline to confront the most brutal facts of your current reality, whatever they might be.”

— Jim Collins, Good to Great: Why Some Companies Make the Leap . . . And Others Don’t
Surgeons Perspective: Brutal Facts

• Previous generation of TAVR valves were technically inferior to SAVR, but will not be true in the future (now)
  – TAVR outcomes may already be better than SAVR across all risk strata
  – Soon, TAVR will make isolated SAVR a historic procedure

• Remaining Role for Surgeons
  – Be one of 2 surgeon to sign off on TAVR for high-risk/inoperable patients (NCD)
    = Giving away (sharing) your practice
  – Back up for catastrophes - CBP for hemodynamic compromise; Root rupture; Perforations
    = Doing salvage procedures on high risk and inoperable patients
  – Chest access cases
    • With current generation > 90% of cases will be TF
      – 100 TAVRs / year → 15 chest cases / 2 surgeons
      → 1 case / surgeon / 2 months
    • TF is generally superior to a chest approach = Relegated to another inferior procedure

Surgeons Perspective: Brutal Facts

• Surgeons need to learn TF/catheter-based procedures to be relevant
  – Don’t relive past mistakes – PCI, BiP, AICDs, TEVAR

EVOLVE
DIE
My Singular Motivation

$130,428

Fall 2029 - Spring 2030
Surgeons Perspective: Good News

- TF TAVR more suited to ICs skill set
  - However, valve on a catheter ≠ IC is a valve expert
    - What is the ICs replacement experience with valve replacement
    - What is your CVS colleague’s experience

- TAVR – not technically difficult
  - TAVR – 21 steps and 76 moves
    - SAVR – 28 steps and 253 moves
  - 50–100 cases to teach TF-TAVR to the average CTS (my estimate)
    - How many cases would it take to teach a non-surgeon to do a SAVR?

More Good News

- 90% of TAVR success is about planning
  - Quantifying Risks/ Risk Stratification
    - STS Score
    - Extreme Risk Characteristics (eg Porcelain Aorta, Adverse Anatomy, PHTN, Liver Dz)
    - Functional Status Assessment - Cognitive Function/Frailty
    - PFTs, Carotids/PVD, Renal
  - Understanding anatomy and imaging
    - 90% of TAVR success is about planning...
      and 90% of the planning is in the imaging

- Understand advantages / disadvantages of surgical therapies
  - Even if TAVR is better for all risk strata, w/concomitant disease (severe, MR, severe TR, Ao aneurysm, and complex CAD) TAVR alone will often be insufficient
More Good News

- In low / intermediate risk (STS) patients, decisions about TAVR vs SAVR will be based on:
  - Root dimensions (SoV, STJ, LM / RCA heights)
  - Calcification (LVOT, leaflets, annular)
  - Annular morphology
  - LVOT / LV cavity dimensions
  - Conduction abnormalities
  - Frailty
  - Peripheral Access
  - Concomitant disease

  → Learn / understand imaging correlate with anatomy
  → Patients may be low / intermediate risk for SAVR and high risk adverse event with TAVR

It Gets Better For Surgeons

- Leverage advantage of being less threatening to referring
  - Surgeons will not “steal” their patients
  - Move closer to the patient and not wait for the patient to be referred to them
    • Apply the same model for heart failure or aneurysm centers
    • Follow patients before they meet treatment criteria (eg AVA < 1.2)

- Patient centered
  - Surgeons can offer the full spectrum of treatments SAVR, TF, TA, Tao
  - Removes bias / avoid “I’m a hammer you’re a nail” approach
National Coverage Decision (NCD)

- Covered under Coverage with Evidence Development (CED) for all FDA-approved indications when:
  - Valve system approved by FDA for specific indication
  - 2 cardiac surgeons independently examine (“face-to-face”) and document suitability for SAVR
  - Heart team provides pre-, intra-, and post-op care
  - Provided by hospitals and heart teams with specific qualifications (separate for “with” and “without” TAVR experience)
  - IC and surgeon jointly participate in intraoperative aspects of procedure
  - Hospital and heart team participate in audited registry that enrolls consecutive patients and tracks specific outcomes

Under the NCD, Surgeons Are the Gatekeepers

- Covered under Coverage with Evidence Development (CED) for all FDA approved indications when:
  - Valve system approved by FDA for specific indication
  - 2 cardiac surgeons independently examine (“face-to-face”) and document suitability for SAVR
  - Heart team provides pre-, intra-, and post-op care
  - Provided by hospitals and heart teams with specific qualifications (separate for “with” and “without” TAVR experience)
  - IC and surgeon jointly participate in intraoperative aspects of procedure
  - Hospital and heart team participate in audited registry that enrolls consecutive patients and tracks specific outcomes

Even if you don’t subscribe to the heart team concept... Payers are increasing barriers to costly therapies... not eliminating them
Case Study - EVAR

Retrospective analysis using the Nationwide Inpatient Sample (1998 to 2009) of 28,094 EVARs.

In EVAR Surgeons are Better than Interventionalists

Retrospective analysis using the Nationwide Inpatient Sample (1998 to 2009) of 28,094 EVARs.
In EVAR Surgeons are Better . . .
Regardless of Experience

Retrospective analysis using the Nationwide Inpatient Sample (1998 to 2009) of 28,094 EVARs.


In EVAR Surgeons are Better . . .
Across Every Subgroup

In EVAR Surgeons’…
Patients are in the Hospital for Less Time

Retrospective analysis using the Nationwide Inpatient Sample (1998 to 2009) of 28,094 EVARs.

For ICs – Finding a Partner

- Partner with the “right” CVS
  - Has a long-term view; collaborative; open to new technology
  - Willing to learn catheter-based skills
    - However… surgeons need to be willing to embarrass themselves
    - You will NOT differentiate yourself based on technical skills (at least initially)
      - Your goal should be to make them the busiest

- Share cases – look for opportunities to involve team members
  - Multiple members of team active in each case
  - Let the ICs does the “CTS part” and let the CTS does the “IC part”
Interdisciplinary Training

- Opportunity to learn new skills
  - Echo / CT interpretation
  - Hemodynamics
  - Wire skills
  - Valve deployment
  - Peripheral vascular skills
  - Surgical strategies
  - PCI strategies

If Successful

- Involving CVS will drive volume
  - Won’t be competing for cases
    - Particularly important with intermediate risk indication
  - Provides another referral source
  - Evolution of your program requires CVS engagement – AI, MR, TR
Other Opportunities to Collaborate

• Coronary disease
• Aortic disease
• Other valvular disease (e.g., mitral, pulmonic)
• Peripheral vascular disease
• Heart failure
• Arrhythmia

Final Points

1. TAVR will soon be the standard for all risk strata

2. Surgeons need to evolve

3. Surgeons have natural advantages in TAVR
   – EVAR provides a natural case study

4. It’s in the ICs interest to engage their CVS
TRANSCATHETER VALVE REPLACEMENT: MOVING BEYOND HIGH RISK AND INOPERABLE PATIENTS (A SURGEON’S VIEW)

Mark J Russo, MD, MS

Director, Aortic Center
Director, Cardiac Surgery Research
Barnabas Heart Hospital/NJ

Assistant Professor of Surgery
Rutgers-New Jersey Medical School

Other Opportunities to Collaborate
To the CTS....You Can Get ON the Bus

...Or...You Can Get UNDER It