Transcatheter Aortic Valve Replacement in 2019: Revolution Completed

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BSWH.md/CardiologyUpdate
Disclosure

Minor financial interest: I have served as a proctor for Edwards LifeScience
Case Study

90 year old woman with symptomatic severe AS:

– Chronic LV diastolic dysfunction
– COPD (FEV1 = 0.75 L 50% predicted)
– s/p pacer
– HTN, DM

– Mildly frail, although still active as a volunteer at her church, other civic groups and lives alone

• STS PROM 9.5%
Decision Making/Follow Up

• Consultation in multidisciplinary valve clinic
  – Interventional cardiologist
  – CT surgeons
  – Radiology, cardiac imaging specialist, cardiac anesthesiologist

• Underwent TF TAVR by open cut down
  – Op date: 11/30/2012
  – Last seen, early 2016, age 95
  – Still living alone, emails each of her 3 kids daily
Rationale for the Development of Transcatheter Aortic Valve Replacement

1. Unmet clinical need
   – Inoperable
   – Unacceptably high risk patients

2. Less invasive therapy
Standard Therapies are Inadequate

- Standard therapy did not alter the dismal course of disease for inoperable patients
  - 50% died within 1 year
  - 94% died within 5 years

* In an age and gender matched US population without comorbidities, the mortality at 5 years is 40.5%.

**THE PARTNER TRIAL**

- Control Group (Med Rx and BAV) (n = 179)

  - HR [95% CI] = 0.50 [0.39, 0.65]
  - p (log rank) < 0.0001

- All-Cause Mortality (%)
  - 0%  50.8%
  - 12%  68.0%
  - 24%  80.9%
  - 36%  87.5%
  - 48%  93.6%
  - 60%  93.6%
Landmark Early Trials
PARTNER 1B

Inoperable Patients: TAVR vs. “Medical Therapy”

20% absolute risk reduction in death
NNT: 5

Median survival:
31 vs. 11 months

Severe, symptomatic aortic stenosis

- Low risk: STS < 4, Surgery
- Moderate Risk: STS 4 - 8, Surgery
- High Risk for Surgery: STS 8 - 12, High risk Surgery
- Inoperable: STS > 12, No therapy, TAVR

November 2, 2011

FDA approves the first TAVR system in the US for use in inoperable patients with severe aortic stenosis
Case Example #2

• 77 y/o man from B/CS with prior CABG, now presenting with symptomatic severe AS
• Works 20+ years as usher at Kyle field
• STS 1.5%
• No functional issues
• CXR, then CT show extensive aortic calcification
CTA Thoracic Aorta

CTA showing heavy calcification of the ascending aorta ("porcelain aorta")
Follow Up

- Underwent TF TAVR on Friday, 8/21/15
- Dismissed early morning on Monday, Aug 24\textsuperscript{th}
- Began cardiac rehab 1 week later
- Follow up echo
  - AVA 1.7 cm\textsuperscript{2}
  - Mean gradient: 7 mm Hg
- Returned to work for 1\textsuperscript{st} home game on Sept 5\textsuperscript{th}
  (an Aggie victory against Arizona State)
“High Risk Patients”

**Partner 1A**

- **Death from Any Cause, All Patients**
  - Hazard ratio, 0.93 (95% CI, 0.71–1.22)
  - P=0.62
  - No. at Risk
    - Transcatheter: 348 298 260 147 67
    - Surgical: 351 252 236 139 65

**CoreValve High Risk**

- No. at Risk
  - TAVR: 390 377 353 329
  - Surgical replacement: 357 341 297 274

- Trend to lower stroke with TAVR
- SAVR  Stroke, Vasc comp
- TAVR  Bleeding, AKI, A fib
- TAVR  PPM, Vasc comp

**References**

- Smith CR. N Eng J Med. 2011;364: 2187f
Severe, symptomatic aortic stenosis

- Low risk: STS < 4 → Surgery
- Moderate Risk: STS 4 - 8 → Surgery
- High Risk for Surgery: STS 8 - 12 → TAVR > SAVR
- Inoperable: STS > 12 → TAVR

October 19, 2012
FDA approves the first TAVR system in the US for use in high risk patients with severe aortic stenosis
From 2012-2016

• Heart team solidified
• Valve iterations, addressing:
  – Access size, regurgitation
• Pre-procedural CT
  – Vascular access, annular sizing, aortic assessment
• Technique: lower PPM, lower vascular complications
**TAVR vs. SAVR -- Intermediate Risk Patients**

**Partner 2a. SURTAVI**

2,032 intermediate risk pts
Primary end: *Death/disabling stroke* at 2 yrs

1,746 intermediate risk pts
Primary end: *Death/disabling stroke* at 2 yrs

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**Leon et al. NEJM 2016; 374: 1609-20.**

**Reardon et al. NEJM 2017; 376: 1321-31.**
Partner 2 S3i Arm
TAVR Trial Results

- Single arm (historical comparison) trial
- n= 1,077
- Intermediate risk patients (avg STS 5.3%)

State-of-the-Art (End 2016-Summer 2019)

Severe, symptomatic aortic stenosis

- Low risk
  - STS < 4
  - Surgery (TAVR only in clinical trials)
  - SAVR

- Moderate Risk
  - STS 4 - 8
  - TF TAVR → Surgery

- High Risk for Surgery
  - STS 8 - 12
  - TAVR → SAVR

- Inoperable
  - STS > 12
  - TAVR

Partner III CoreValve Low Risk

November 2, 2011  TAVR approved in the US for inoperable patients
October 19, 2012  TAVR approved in the US for high risk patients
August 18, 2016  TAVR approved in the US for intermediate risk patients
Aortic Stenosis by Risk Category

Patient Risk

- Low: 80%
- Intermediate: 14%
- High: 6%

Now FDA approved in **ALL** risk categories
But what about me?…

• 70 year old man
  – Presents with DOE, limiting
• Works as agricultural extension agent (biologist) and bee keeper
• No significant co-morbidities
• STS 2%

He inquires, if TAVR an option for him…
TAVR in Low Risk Patients
(Two separate RCTs)

**Partner III**

*46% reduction* in endpoint
Death, stroke, re-hosp

**CoreValve Low Risk**

Noninferior; trend favors TAVR
TAVR superior: disabling stroke, bleeding, AKI, atrial fib.
TAVR inferior: AI, PPM

Mack et al.  NEJM 2019; 380: 1965f
State-of-the-Art (December 2019)

Severe, symptomatic aortic stenosis

- Low risk
  - STS < 4: TAVR → Surgery
  - STS 4 - 8: TF TAVR → Surgery

- Moderate Risk
  - STS 8 - 12: TAVR → SAVR

- High Risk for Surgery
  - STS > 12: TAVR

- Inoperable

- November 2, 2011: TAVR approved in the US for inoperable patients
- October 19, 2012: TAVR approved in the US for high risk patients
- August 18, 2016: TAVR approved in the US for intermediate risk patients
- August 16, 2019: TAVR approved in the US for low risk patients
Which way to choose?
## Compare TAVR vs. SAVR

*(Low risk patients—Partner III data)*

<table>
<thead>
<tr>
<th></th>
<th>Vascular complications</th>
<th>=</th>
<th>=</th>
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<tbody>
<tr>
<td>2.</td>
<td>Bleeding</td>
<td></td>
<td>7 x ↑</td>
</tr>
<tr>
<td>3.</td>
<td>Atrial Fibrillation</td>
<td></td>
<td>8 x ↑</td>
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<tr>
<td>4.</td>
<td>Stroke</td>
<td></td>
<td>3-4 x ↑</td>
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<tr>
<td>5.</td>
<td>PVL (mod/severe)</td>
<td>=</td>
<td>=</td>
</tr>
<tr>
<td>6.</td>
<td>Pacemaker</td>
<td>=</td>
<td>=</td>
</tr>
<tr>
<td>7.</td>
<td>LBBB</td>
<td>3 x ↑</td>
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Compare TAVR vs. SAVR
(Low risk patients)

1. Length of stay
2. Discharge to home
3. QOL up to 1 year
4. Durability

<table>
<thead>
<tr>
<th></th>
<th>TAVR</th>
<th>SAVR</th>
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<tbody>
<tr>
<td>Length of stay</td>
<td>↓</td>
<td>↑</td>
</tr>
<tr>
<td>Discharge to home</td>
<td>↑</td>
<td>= / ↑</td>
</tr>
<tr>
<td>QOL up to 1 year</td>
<td>= / ↑</td>
<td>???</td>
</tr>
</tbody>
</table>
Durability

- *Mechanical* valves have superior durability
- Bio-prosthetic surgical valves are ever-evolving
- Definitions/follow up of surgical valves has not been overly rigorous
- New SOC allows better definitions of durability
### 4-5 year Valve Durability
Based on Partner 2a and S3i, n > 3,000 pts

<table>
<thead>
<tr>
<th></th>
<th>BVF</th>
<th>SVD or BVF</th>
<th>p value</th>
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</thead>
<tbody>
<tr>
<td>Sapien XT</td>
<td>3.7%</td>
<td>9.5%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Surgical valves (various)</td>
<td>0.5%</td>
<td>3.5%</td>
<td></td>
</tr>
<tr>
<td>Sapien 3</td>
<td>0.6%</td>
<td>2.7%</td>
<td>0.74</td>
</tr>
</tbody>
</table>
Incidence Stroke in AVR

**Surgical AVR**
- 7% (STS database)
- 17% (neuro evaluation)
- 54% (MRI)

Messe et al.  Circulation 2014; 129: 2253-61
Primer: Follow Up of TAVR Patients

- 1 day hospital stay
- Full activity after 1 week
- DAPT x 3-6 months; followed by ASA mono
- Annual echo and ECG
- Endocarditis prophylaxis
- No MRI restrictions
History of TAVR at Scott & White

- 5/4/12: 1st TF Implant
- 12/7/12: 1st CoreValve Implant
- 4/30/13: 1st transapical Implant
- 3/7/14: 1st Sapien S3 implant
- 6/13/14: 1st concious sedation
- 11/28/14: 1st Subclavian Implant
- 4/03/15: 1st Same day discharge
- 9/18/15: 100th Implant
- 5/13/16: 1st Sapien S3 implant
- 12/28/16: 200th Implant
- 3/24/17: 300th Implant
- 5/4/18: 500th Implant
- 7/26/19: 700th Implant
- 8/16/19: Approved for low risk pts
- 8/23/19: 1st Lotus Implant
Summary/Aortic Stenosis Therapy

1. TAVR superior in inoperable/high risk patients; extends life and improves QOL
2. TAVR equal or superior to SAVR in low and intermediate risk patients
3. Ultimate TAVR durability > 5 years unknown
4. Role of TAVR in bicuspid valve unclear
5. TAVR associated with:
   - Shorter LOS, quicker recovery
   - Less bleeding, AKI, a. fib, vascular complic, CVA