The Transcatheter Aortic Valve Replacement (TAVR) Program at Southcoast Health

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Disclosures

- Edwards Lifesciences: speaking honorarium
Outline

• Prevalence, Pathophysiology, and Prognosis for Severe Aortic Stenosis
• Transcatheter Aortic Valve Replacement (TAVR) and patient selection
• Recent Evidence and Future Direction for TAVR
• The Southcoast TAVR Program
Prevalence of Valve Disease by Age

Prevalence of Aortic Stenosis

- Aortic stenosis is estimated to be prevalent in up to 7% of the population over the age of 65.¹
- This prevalence increases with each decade of life after 65.

Echocardiographic Guidelines are the Gold Standard in Assessing Severe Aortic Stenosis

According to the 2008 ACC/AHA guidelines, severe aortic stenosis is defined as:

- Aortic valve area (AVA) less than 1.0 cm²
- Mean gradient greater than 40 mmHg or jet velocity greater than 4.0 m/s

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
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<tbody>
<tr>
<td>Jet velocity (m/s)</td>
<td>&lt; 3.0</td>
<td>3.0 - 4.0</td>
<td>&gt; 4.0</td>
</tr>
<tr>
<td>Mean gradient (mmHg)</td>
<td>&lt; 25</td>
<td>25 - 40</td>
<td>&gt; 40</td>
</tr>
<tr>
<td>Valve area (cm²)</td>
<td>&gt; 1.5</td>
<td>1.0 – 1.5</td>
<td>&lt; 1.0</td>
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<tr>
<td>Valve area index (cm²/m²)</td>
<td>N/A</td>
<td>N/A</td>
<td>&lt; 0.6</td>
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</tbody>
</table>

*Doppler-Echocardiographic measurements
Calcific Aortic Stenosis: Mechanisms

- Calcific aortic stenosis is a biologically active process
- Lipid accumulation
  - LDL accumulation and oxidation
- Inflammation
  - T-cells, monocytes, inflammatory mediators, cytokines
- Calcification
  - Osteoblast expression, bone formation
Do Statins Slow the Progression of Aortic Stenosis?

- Six retrospective studies had found statin therapy was associated with a reduced rate of AS progression
- However, three prospective randomized trials have failed to show a decrease in hemodynamic progression of AS or a delay in AVR...

Helske S, Otto CM. Circulation 2009;119:2653-2655
Randomized Trials of Statin Therapy and Progression of Aortic Stenosis


Pathophysiology Aortic Stenosis

Aortic Stenosis

LV outflow obstruction

↑ LVSP

↑ LV Mass

LV dysfunction

↓ LV failure

↑ LVET

↑ LVDP

↓ Aortic P

↑ Myocardial O2 consumption

Myocardial ischemia

↓ Diastolic time

↓ Myocardial O2 supply
Prognosis

Survival after onset of symptoms is 50% at 2 years and 20% at 5 years.
Rationale for Treadmill Testing in the “Asymptomatic” Patient with Severe Aortic Stenosis

• Quantitative evaluation of exercise capacity
• Assessment of blood pressure response with exertion
• Evaluate left ventricular function with exercise
• Assess RVSP with activity
Sobering Perspective

5-Year Survival

5 year survival of breast cancer, lung cancer, prostate cancer, ovarian cancer and severe inoperable aortic stenosis

*Using constant hazard ratio. Data on file, Edwards Lifesciences LLC. Analysis courtesy of Murat Tuczu, MD, Cleveland Clinic
• As seen previously, survival after onset of symptoms in patients with aortic stenosis is 50% at 2 years\(^1\)
• The PARTNER Trial showed that in inoperable patients with severe aortic stenosis who did not receive a valve replacement, 50% died within 1 year
• Despite the frequent utilization of BAV, standard therapy did not do much to alter the dismal course of disease for inoperable patients with severe aortic stenosis

Leon et al, NEJM 2010; 363:1597-1607
Aortic Valve Replacement Greatly Improves Survival

- Study data demonstrate that early and late outcomes were similarly good in both symptomatic and asymptomatic patients.

- It is important to note that among asymptomatic patients with SAS, omission of surgical treatment was the most important risk factor for late mortality.
Frequently not treated
Transcatheter Aortic Valve Replacement (TAVR)

- Bovine pericardial tissue
- Leaflets matched for thickness and elasticity
- Stainless steel frame
- PET skirt

Approach
PARTNER Study Design

Symptomatic Severe Aortic Stenosis

ASSESSMENT: High-Risk AVR Candidate
3,105 Total Patients Screened

Total = 1,057 patients

High Risk

Inoperable

ASSESSMENT: Transfemoral Access

Yes

1:1 Randomization

TF TAVR

VS

No

Not In Study

Standard Therapy

Primary Endpoint: All-Cause Mortality Over Length of Trial (Superiority)
Co-Primary Endpoint: Composite of All-Cause Mortality and Repeat Hospitalization (Superiority)
Edwards SAPIEN THV Improved Survival

\[ P \text{ (log rank)} < 0.0001 \]
\[ \Delta \text{ at 2 yrs} = 24.7\% \]
\[ \text{NNT} = 4.0 \text{ pts} \]

All-Cause Mortality, %

- Standard Therapy: 68.0%
- Edwards SAPIEN THV: 43.3%
- 12 Months: 50.7%
- 24 Months: 30.7%

Numbers at Risk:
- Edwards SAPIEN THV: 179
- Standard Therapy: 179

THE PARTNER TRIAL COHORT B

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Treatment for Inoperable Aortic Stenosis

FDA Approves Transcatheter Valve for Patients with Inoperable AS

Cardiology Today Intervention, January/February 2012

The Sapien transcatheter heart valve has been approved by the FDA for the treatment of patients with severe aortic stenosis who are ineligible for surgery. The approval makes the device the first artificial heart valve available in the United States that can replace an aortic heart valve without surgery.
PARTNER Study Design

Symptomatic Severe Aortic Stenosis

ASSESSMENT: High-Risk AVR Candidate
3,105 Total Patients Screened

Total = 1,057 patients

High Risk

Yes

ASSESSMENT: Transfemoral Access

TF TAVR

VS

Primary Endpoint: All-Cause Mortality at 1 yr (Non-inferiority)

No

Transapical (TA)

1:1 Randomization

1:1 Randomization

Transfemoral (TF)

AVR

TA TAVR

AVR

Inoperable

Yes

ASSESSMENT: Transfemoral Access

1:1 Randomization

TF TAVR

VS

Standard Therapy

No

Not In Study

Primary Endpoint: All-Cause Mortality Over Length of Trial (Superiority)
Co-Primary Endpoint: Composite of All-Cause Mortality and Repeat Hospitalization (Superiority)
All-Cause Mortality

**ITT Population**

ALL-CAUSE MORTALITY AT 1 YEAR AND 2 YEARS

- HR [95% CI] = 0.88 [0.70, 1.12]
- \( P \) (log rank) = 0.31

- Edwards SAPIEN THV
- AVR

Number at Risk

<table>
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<tr>
<th></th>
<th>0</th>
<th>3</th>
<th>6</th>
<th>9</th>
<th>12</th>
<th>15</th>
<th>18</th>
<th>21</th>
<th>24</th>
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<tbody>
<tr>
<td>Edwards SAPIEN THV</td>
<td>348</td>
<td>312</td>
<td>298</td>
<td>269</td>
<td>260</td>
<td>247</td>
<td>234</td>
<td>222</td>
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<tr>
<td>AVR</td>
<td>351</td>
<td>274</td>
<td>252</td>
<td>245</td>
<td>236</td>
<td>225</td>
<td>217</td>
<td>208</td>
<td>165</td>
</tr>
</tbody>
</table>

THE PARTNER TRIAL COHORT A
All Strokes

AT Population

STROKE AT 1 YEAR AND 2 YEARS

HR [95% CI] = 1.23 [0.66, 2.31]
P (log rank) = 0.51

THE PARTNER TRIAL COHORT A
Major Vascular Complications

AT Population

MAJOR VASCULAR COMPLICATIONS
AT 30 DAYS, 1 YEAR, AND 2 YEARS

Edwards SAPIEN THV
AVR

30 Days
11.1
3.8

1 Year
11.1
3.8

2 Years
11.4
3.8

p < 0.001
p < 0.001
p < 0.001

Kaplan-Meier estimates.

THE PARTNER TRIAL COHORT A

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Major Bleeding

MAJOR BLEEDING COMPLICATIONS AT 30 DAYS, 1 YEAR, AND 2 YEARS*

Kaplan-Meier estimates. *Major bleeding is defined as any episode of major internal or external bleeding that caused death, hospitalization or permanent injury (e.g., vision loss) or necessitated transfusion of greater than 3 units PRBCs within a 24-hour period, pericardiocentesis, open and/or endovascular procedure for repair or hemostasis.

THE PARTNER TRIAL COHORT A
October 19, 2012

FDA Approves The Sapien Transcatheter Heart Valve For High Risk Patients

by Larry Husten • Interventional Cardiology & Surgery • Tags: Sapien, TAVI, TAVR, transcatheter aortic valve replacement

The FDA today approved an expanded indication for Edwards Lifesciences’ Sapien transcatheter heart valve (THV). The device can now be implanted in patients who are eligible for aortic valve replacement surgery but at high risk for serious surgical complications or death. Previously the Sapien valve was approved only for use in patients who were not eligible for surgery.
The PARTNER II Trial with the SAPIEN 3 Valve Study Design

Symptomatic Severe Aortic Stenosis

ASSESSMENT by Heart Valve Team

Intermediate-Risk Operable* (n = 1076 Patients)
- ASSESSMENT: Optimal Valve Delivery Access
  - Transfemoral (TF)
    - TF TAVR SAPIEN 3

SAPIEN 3 (n = 583 Patients)
- 2 Single Arm Non-Randomized Historical-Controlled Studies
  - PARNER II A Trial
    - SAVR
  - PARNER IA Trial
    - SAPIEN

High-Risk Operable / Inoperable (HR)
- ASSESSMENT: Optimal Valve Delivery Access
  - Transfemoral (TF)
    - TF TAVR SAPIEN 3
  - Transapical / Transaortic (TA/TAo)
    - TAA TAVR SAPIEN 3

*The SAPIEN 3 valve is only indicated for patients at high or greater risk.
Clinical Outcomes Improve as Therapy Evolves

Low Mortality and Stroke Rates
Patient selection, procedural techniques, device evolution

Improved Vascular Access
Lower profile devices expands treatment possibilities

Increased Treatment Range
Larger and smaller valves

*only used with 20,23,26 valve sizes

RetroFlex 3 Delivery System
NovaFlex+ Delivery System
Edwards Commander Delivery System

RetroFlex 3 Introducer Sheath
Edwards eSheath Introducer Set
Edwards eSheath Introducer Set*

SAPIEN Valve
23 and 26 mm

SAPIEN XT Valve
23, 26, 29 mm

SAPIEN 3 Valve
20, 23, 26, 29 mm
Low Profile Demonstrates > 50% Reduction in Major Vascular Complications*

<table>
<thead>
<tr>
<th>SAPIEN 3 Valve Size</th>
<th>20 mm</th>
<th>23 mm</th>
<th>26 mm</th>
<th>29 mm</th>
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<tbody>
<tr>
<td>Edwards eSheath Introducer Set</td>
<td>14F</td>
<td>14F</td>
<td>14F</td>
<td>16F</td>
</tr>
<tr>
<td>Minimum Access Vessel Diameter</td>
<td>5.5 mm</td>
<td>5.5 mm</td>
<td>5.5 mm</td>
<td>6.0 mm</td>
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</tbody>
</table>

*PARTNER II Trial high-risk TF SAPIEN 3 valve cohort (VARC II) versus SAPIEN XT valve cohort (VARC I) 30-day results.
Baseline Patient Characteristics
SAPIEN 3 Valve HR Patients

Average STS = 8.6%
(Median 8.4%)

Average Age = 82.6yrs

N = 583

- Female 42%
- Male 58%

- TF, 84%
- TA / TAo, 16%

- 20 mm
- 23 mm
- 26 mm
- 29 mm

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Mortality at 30 Days (As Treated Patients)

- Mortality: 1.6%
- Cardiovascular: 1.0%

Transfemoral n=491
Stroke at 30 Days (As Treated Patients)

- **All Stroke**: 1.4%
- **Disabling Stroke**: 0.8%

Transfemoral n=491
All-Cause Mortality at 30 Days (As Treated Patients)

PARTNER I Trial and PARTNER II Trial
Overall and TF Patients

- PARTNER I B (TF): 6.3%
- PARTNER I A (All): 5.2%
- PARTNER I A (TF): 3.7%
- PARTNER II B (TF): 4.5%
- PARTNER II B (TF): 3.5%
- PARTNER II HR (TF): 1.6%

Sample sizes:
- SAPIEN Valve: 175
- SAPIEN XT Valve: 344
- SAPIEN 3 Valve: 240
- SAPIEN XT Valve: 271
- SAPIEN 3 Valve: 282
- SAPIEN 3 Valve: 491
All Strokes at 30 Days

PARTNER I Trial and PARTNER II Trial

Neurologist Evaluations (Pre- and Post)

PARTNER I B (TF) 7.3%
PARTNER I A (Overall) 4.4%
PARTNER II B (TF) 4.1%
PARTNER II B (TF) 4.3%
PARTNER II HR (TF) 1.4%

179 344 271 282 491
SAPIEN Valve SAPIEN XT Valve SAPIEN 3 Valve

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Paravalvular Leak
(At 30 Days - Transfemoral Cohort)

- None/Trace: 2.5%
- Mild: 36.4%
- Moderate: 61.1%
- Severe: 0.0%

30 Day
1 Year MACCE

Major Cardiovascular and Cerebrovascular Event (%)

- Surgical
- Transcatheter

No. at Risk:
- Surgical: 357, 320, 273, 247
- Transcatheter: 390, 360, 329, 361

Months Post-Procedure:

log rank P=0.03

27.3% at 12 months
20.4% at 12 months
10.4% at 12 months
7.7% at 12 months
CoreValve Evolut R

- 14F Delivery system
- Nitinol self expanding valve
- Full recapture is possible
- Ease of use
- Initial valve in valve indication
- Larger annular sizes
Transfemoral TAVR
Development of the Transcatheter Aortic Valve Replacement Program at Southcoast Health
The Surgical Program at Southcoast

• Since joining Southcoast in 2012 Dr. James Fingleton has performed over 50 mitral valve repairs.
• Average 20/yr which is an important marker
• Dr. Iraklis Gerogiannis and Dr. Fingleton have performed several complex aorta surgeries (valve sparing root, Bentall, aneurysm, dissections)
• Over 60 minimally invasive aortic valve replacements
Valve Imaging Program

Through the tremendous efforts of Dr. Abadi and Dr. Schneider we have a superb advanced valve imaging program—**invasive echocardiography**

Dr. John Mungovan, chief of radiology and Liz Przeszlo we have excellent CT imaging
The Heart Valve Team at Southcoast
The Goal of the Southcoast Valve Clinic

- To provide a comprehensive evaluation by the cardiologists and cardiac surgeon.
- Provide an expeditious and coordinated evaluation (CT, echo, etc.).
- Offer the best path to a diverse range of therapies: traditional surgery, minimally invasive surgery, transcatheter valve therapy, or balloon valvuloplasty. decided upon by a multidisciplinary team.
- Provide clear and accessible follow up communication with the referring physician.
Southcoast Future Direction

- A shift towards more trans-femoral access = quicker recovery
- Percutaneous access
- Conscious sedation
- Shorter Hospitalizations
- A “paired down” TAVR procedure and work up?
- Reduced costs of product
- Diversify Procedures

A NEW SPACE!!!!!
Conclusion

• Severe symptomatic aortic stenosis is common.
• Symptoms can be subtle, but when present and assoc with comorbidities = poor prognosis.
• TAVR has emerged as a viable treatment approach in high risk surgical patients ?moderate.
• The TAVR program has had tremendous results here at Southcoast.
Thank You