Endovascular Approaches for Treatment of Valvular Disease: The Time is Now!

Paul Mahoney, MD, FACC

Director

Structural Heart Program, Sentara Heart Hospital
## Disclosures

<table>
<thead>
<tr>
<th>Disclosure</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research</td>
<td>Medtronic, Edwards, Boston Scientific, Abbott/St Jude, Direct Flo Medical, Keystone Medical</td>
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<td>Consultant/Advisory Board</td>
<td>Medtronic, Edwards, Boston Scientific</td>
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<td>Physician Proctor</td>
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<tr>
<td>Stock</td>
<td>None</td>
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<td>Equity</td>
<td>None</td>
</tr>
</tbody>
</table>
Greetings from Norfolk, Virginia
The Problem:
Aortic Stenosis
AS Survival: High Mortality with Symptom onset

- 3 cardinal symptoms:
  - Angina, Syncope, Dyspnea
Aortic Stenosis: Worse Prognosis than Many Metastatic Cancers

5-YEAR SURVIVAL (Distant Metastasis)\(^8\)

<table>
<thead>
<tr>
<th>Condition</th>
<th>Survival, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast Cancer</td>
<td>23</td>
</tr>
<tr>
<td>Lung Cancer</td>
<td>4</td>
</tr>
<tr>
<td>Colorectal Cancer</td>
<td>12</td>
</tr>
<tr>
<td>Prostate Cancer</td>
<td>30</td>
</tr>
<tr>
<td>Ovarian Cancer</td>
<td>28</td>
</tr>
<tr>
<td>Severe Inoperable AS(^4)</td>
<td>3</td>
</tr>
</tbody>
</table>
Population at Risk for Aortic Stenosis is Increasing

- Aortic Stenosis is estimated to be prevalent in **12.4% of the population over the age of 75**.²
- The elderly population will more than double between now and the year 2050, to 80 million.³
What is TAVR?

- **Transcatheter Aortic Valve Replacement**

- Catheter based approach for valve replacement

- Initially: treating the untreatable

- Rapid adoption of this new technology
Alain Cribier: First Human Transcatheter Valve Replacement (2002)
Inoperable Patients:

> 30% Absolute Reduction in CV Mortality

CARDIOVASCULAR MORTALITY AT 1 YEAR AND 2 YEARS

HR [95% CI] = 0.44 [0.32, 0.60]
P (log rank) < .0001

Edwards SAPIEN THV
Standard Therapy

Numbers at Risk

<table>
<thead>
<tr>
<th></th>
<th>1 yr</th>
<th>2 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edwards SAPIEN THV</td>
<td>138</td>
<td>124</td>
</tr>
<tr>
<td>Standard Therapy</td>
<td>121</td>
<td>85</td>
</tr>
</tbody>
</table>

Δ at 1 yr = 24.1%
NNT = 4.1 pts

Δ at 2 yrs = 31.4%
NNT = 3.2 pts
TAVR is Equivalent to Surgery in High-Risk Patients

---

**ALL CAUSE MORTALITY**

At 5 Years

HR [95% CI] = 1.04 [0.86, 1.24]

p (log rank) = 0.76

---

**Partner 1 High Risk Trial**

![Graph showing all-cause mortality rates over time for TAVR and SAVR, with details on event rates and statistical significance.]
Primary Endpoint: 1 Year All-cause Mortality

Corevalve High Risk Trial

- Surgical: 19.1%
- Transcatheter: 14.2%

P = 0.04 for superiority

No. at Risk
- Surgical: 357, 341, 297, 274
- Transcatheter: 390, 377, 353, 329

Months Post-Procedure: 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12
All Stroke

CoreValve High Risk Trial

Surgical
Transcatheter

All Stroke (%)
0 5 10 15 20

Months Post-Procedure
0 1 2 3 4 5 6 7 8 9 10 11 12

No. at Risk
Surgical 357 322 274 249
Transcatheter 390 363 334 314

Log-rank P=0.10

6.2% 4.9% 12.6% 8.8%
# SAPIEN Platforms in PARTNER

## Device Evolution

<table>
<thead>
<tr>
<th>Valve Technology</th>
<th>SAPIEN</th>
<th>SAPIEN XT</th>
<th>SAPIEN 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><img src="image1" alt="SAPIEN" /></td>
<td><img src="image2" alt="SAPIEN XT" /></td>
<td><img src="image3" alt="SAPIEN 3" /></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Sheath Compatibility</th>
<th>22-24F</th>
<th>16-20F</th>
<th>14-16F</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image4" alt="Sheath 22-24F" /></td>
<td><img src="image5" alt="Sheath 16-20F" /></td>
<td><img src="image6" alt="Sheath 14-16F" /></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Available Valve Sizes</th>
<th>23 mm</th>
<th>26 mm</th>
<th>23 mm</th>
<th>26 mm</th>
<th>29 mm</th>
<th>20 mm</th>
<th>23 mm</th>
<th>26 mm</th>
<th>29 mm</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image7" alt="Valve Sizes 23 mm" /></td>
<td><img src="image8" alt="Valve Sizes 26 mm" /></td>
<td><img src="image9" alt="Valve Sizes 23 mm" /></td>
<td><img src="image10" alt="Valve Sizes 26 mm" /></td>
<td><img src="image11" alt="Valve Sizes 29 mm" /></td>
<td><img src="image12" alt="Valve Sizes 20 mm" /></td>
<td><img src="image13" alt="Valve Sizes 23 mm" /></td>
<td><img src="image14" alt="Valve Sizes 26 mm" /></td>
<td><img src="image15" alt="Valve Sizes 29 mm" /></td>
<td></td>
</tr>
</tbody>
</table>
All-Cause Mortality at 1 Year
Edwards SAPIEN Valves (As Treated Patients)

PARTNER I and II Trials
TF Patients

- High-Risk
- Inoperable

<table>
<thead>
<tr>
<th>Valve Type</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>P1B (TF)</td>
<td>175</td>
</tr>
<tr>
<td>P1A (TF)</td>
<td>240</td>
</tr>
<tr>
<td>P2B (TF)</td>
<td>271</td>
</tr>
<tr>
<td>P2B XT (TF)</td>
<td>282</td>
</tr>
<tr>
<td>S3 Inop (TF)</td>
<td>101</td>
</tr>
<tr>
<td>S3HR (TF)</td>
<td>324</td>
</tr>
<tr>
<td>S3 CE HR (TF)</td>
<td>96</td>
</tr>
</tbody>
</table>

Mortality rates:
- P1B (TF): 30.7%
- P1A (TF): 21.4%
- P2B (TF): 23.7%
- P2B XT (TF): 22.5%
- S3 Inop (TF): 15.7%
- S3HR (TF): 10.7%
- S3 CE HR (TF): 8.4%
2017: Deciding who gets TAVR today (and tomorrow)

• Lets look at a recent case.... It’s not 2012 anymore!
Case Presentation

[Patient LE]

Patient Evaluation
Structural Heart Program

Sentara Heart Hospital
Norfolk, VA

Interv. Cardiology:
P. Mahoney, MD
D. Talreja, MD
N. Mistry, MD

Cardiac Surgery:
J. Newton, MD
J. Philpott, MD
G. Dimeling, MD
C. Kemp, MD

TAVR Coordinators:
L. Morris, PA-C
M. Sukholutsky, PA-C
E. Willette, NP
A. Kanter, RN
## Clinical History

- **69 years old**
- **STS 2.6%**
- **NYHA Class II**
- **BSA / BMI: 1.7 / 22**
- **Creatinine: 0.8**
- **Hb: 14.3**
- **PLT: 178**
- **Team: PDM**
- **Ht: 165cm**
- **Wt: 61kg**

### Clinical History

**Severe aortic stenosis and moderate aortic insufficiency**
- **Echo 2/21/17 (Riverside)** -- AVA 1.0cm², peak 104mmHg, mean 55mmHg, Vmax 501cm/s, 2+ AI
- **TEE 4/14/17** – moderate AI
- **Cath 4/14/17** – AVA 0.9 cm², mean 48mmHg

**Non-obstructive CAD**

**Normal LV function, EF 55%**

**COPD and Asthma -- on inhalers**
- Ongoing tobacco abuse
- **PFT's 4/6/17** -- FEV1 2.32, 97% predicted, DLCO 74

**Multiple sclerosis - uses cane or wheelchair outside the house**

**Carotid PVL 4/4/17** - <50% stenosis bilaterally

Edentulous
STS Risk Score / Frailty:

- **STS risk score:**

  Procedure: AV Replacement  
  Risk of Mortality: 2.578%  
  Morbidity or Mortality: 15.774%  
  Long Length of Stay: 6.451%  
  Short Length of Stay: 35.949%  
  Permanent Stroke: 1.54%  
  Prolonged Ventilation: 9.522%  
  DSW Infection: 0.17%  
  Renal Failure: 2.459%  
  Reoperation: 7.635%

<table>
<thead>
<tr>
<th>STS Risk Drivers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild lung disease</td>
</tr>
<tr>
<td>PAD</td>
</tr>
<tr>
<td>HTN</td>
</tr>
</tbody>
</table>

**Frailty Assessment: 1/4**

- Grip strength: [normal]  
- Katz ADL: [6/6]  
- 5 meter walk: [abnormal]  
- Albumin: [normal]
Coronary Angiography

Summary: LM patent, LAD 20-30% stenosis, LCx patent, RCA patent

Plans for Revascularization: medical therapy
Echocardiography

Annulus = 19mm
Aortic valve assessment by CT

Distance: 23.8 mm x 16.4 mm
Area: 3.32 cm²
Avg. Diameter: 20.6 mm
Perimeter: 68.1 mm

Sinus-N
29.6 mm
Sinus-L
30.6 mm
Sinus-R
26.7 mm
RC Ht
13.9 mm
7.83 mm
Peripheral assessment
CT

Common iliacs

External iliacs

Common femorals
IVUS

<table>
<thead>
<tr>
<th></th>
<th>Right</th>
<th>Left</th>
</tr>
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<tbody>
<tr>
<td>Common Iliac</td>
<td>8.2mm</td>
<td>xxx</td>
</tr>
<tr>
<td>External Iliac</td>
<td>7.5mm</td>
<td>xxx</td>
</tr>
<tr>
<td>Common Femoral</td>
<td>7.5mm</td>
<td>xxx</td>
</tr>
</tbody>
</table>
Procedural Plan:

• Judgement of Heart Team:
  – Patient is at INTERMEDIATE risk for planned AVR given STS score and comorbidities.

• Bailout → OPEN

• Fast Track Protocol

<table>
<thead>
<tr>
<th>Annulus Diameter and Area Measurements</th>
<th>THV Valve Size Proposed</th>
<th>Access</th>
<th>Smallest Vessel Diameter Measurement in accessed vessel</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annulus = 19mm Area = 332mm Perimeter = 68.1mm</td>
<td>[23] S3</td>
<td>RFA (high bifurcation)</td>
<td>7.5mm Right EI and CF</td>
</tr>
</tbody>
</table>
Post deployment
Vascular Access - Completion angiography
Vascular Access: Percutaneous Approach

• 14 Fr Arterial Sheath

• Perclose sutures placed percutaneously
Hospital Course

• Uncomplicated TAVR
• Procedure time: 31 minutes, skin to skin

• Minimalist approach, fast track
  – Conscious sedation
  – No TEE, No PA catheter
  – 4 hour ICU stay; ambulating at 4 hours
  – POD #1: Discharged to home
TAVR Trials: Intermediate Risk Patients

- 2 surgeons agree on risk
- 2 year follow up
- Major endpoints: Death, stroke
Superiority Achieved

Weighted Difference: -9.2%
Upper 2-sided 95.0% CI: -5.4%

Superiority Testing:
p-value < 0.001

Favors TAVR

Favors Surgery

Superiority Achieved
Superiority Analysis
Components of Primary Endpoint (VI)

**Mortality**
- Weighted Difference: -5.2%
- Upper 2-sided 95% CI: -2.4%
- Superiority Testing: p-value < 0.001

**Stroke**
- Weighted Difference: -3.5%
- Upper 2-sided 95% CI: -1.1%
- Superiority Testing: p-value = 0.004

**AR \geq** Moderate
- Weighted Difference: +1.2%
- Lower 2-sided 95% CI: +0.2%
- Superiority Testing: p-value = 0.0149
Unadjusted Time-to-Event Analysis
All-Cause Mortality (AT)

Number at risk:
P2A Surgery 944 859 836 808 795
S3 TAVR 1077 1043 1017 991 963

All-Cause Mortality (%)

0 10 20 30 40

Months from Procedure

P2A Surgery
SAPIEN 3 TAVR
Unadjusted Time-to-Event Analysis
All Stroke (AT)

Number at risk:
P2A Surgery 944
S3 TAVR 1077

Months from Procedure

<table>
<thead>
<tr>
<th>Months</th>
<th>P2A Surgery</th>
<th>SAPIEN 3 TAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>6.1%</td>
<td>2.7%</td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>8.2%</td>
<td>4.6%</td>
</tr>
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</table>
Unadjusted Time-to-Event Analysis
All-Cause Mortality and All Stroke (AT)

- P2A Surgery
- SAPIEN 3 TAVR

Number at risk:
- P2A Surgery: 944
- S3 TAVR: 1077

<table>
<thead>
<tr>
<th>Months from Procedure</th>
<th>P2A Surgery</th>
<th>SAPIEN 3 TAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>3.7%</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>9.7%</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>10.8%</td>
</tr>
<tr>
<td>12</td>
<td>18.8%</td>
<td></td>
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</table>

3.7%
Other Unadjusted Clinical Outcomes
At 30 Days and 1 Year (AT)

<table>
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<tr>
<th>Events (%)</th>
<th>30 Days</th>
<th>1 Year</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>TAVR (n = 1077)</td>
<td>Surgery (n = 944)</td>
</tr>
<tr>
<td>Re-hospitalization</td>
<td>4.6</td>
<td>6.8</td>
</tr>
<tr>
<td>MI</td>
<td>0.3</td>
<td>1.9</td>
</tr>
<tr>
<td>Major Vascular Complication</td>
<td>6.1</td>
<td>5.4</td>
</tr>
<tr>
<td>AKI (Stage III)</td>
<td>0.5</td>
<td>3.3</td>
</tr>
<tr>
<td>Life-Threatening/Disabling Bleeding</td>
<td>4.6</td>
<td>46.7</td>
</tr>
<tr>
<td>New Atrial Fibrillation</td>
<td>5.0</td>
<td>28.3</td>
</tr>
<tr>
<td>New Permanent Pacemaker</td>
<td>10.2</td>
<td>7.3</td>
</tr>
<tr>
<td>Re-intervention</td>
<td>0.1</td>
<td>0.0</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>0.2</td>
<td>0.0</td>
</tr>
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</table>
The conclusions from the PARTNER 2A randomized trial and this propensity score analysis provide strong evidence that in intermediate-risk patients with severe aortic stenosis, SAPIEN 3 TAVR compared with surgery improves clinical outcomes and is the preferred therapy.

75% reduction in death vs surgery
75% reduction in stroke vs surgery
## Options for Aortic Valve Replacement per Guidelines

### Indications for Severe Symptomatic Aortic Stenosis

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Low- to Moderate-Risk</th>
<th>High Risk</th>
<th>Greater Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transcatheter Aortic Valve Replacement (TAVR)</td>
<td>X (interm)</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>Open-Heart Surgery (AVR)</td>
<td>X</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>
Expanding TAVR Clinical Indications

• Low risk patients (all comers?)
• Severe asymptomatic AS
• Low flow, low gradient AS
• Bicuspid AV disease
• AS + concomitant disease (CAD, MR, AF)
• Bioprosthetic valve failure (aortic and mitral)
• Moderate AS + CHF
• High risk AR
The PARTNER 3 Trial
Study Design

Symptomatic Severe Calcific Aortic Stenosis

Low Risk ASSESSMENT by Heart Team
(STS < 4%, TF only)

1:1 Randomization
(n=1,228)

TF - TAVR
(SAPIEN 3)

CT Imaging Sub-Study (n=200)
Actigraphy/QoL Sub-Study

Surgery
(Bioprosthetic Valve)

CT Imaging Sub-Study (n=200)
Actigraphy/QoL Sub-Study

PARTNER 3 Registries

Alternative Access
(n=100)
(TA/TAo/Subclavian)

Bicuspid Valves
(n=50)

SAVR or TAVR ViV
(n=100/25)

Mitral ViV or ViR
(n=50/50)

PRIMARY ENDPOINT:
Composite of all-cause mortality, all strokes, or re-hospitalization at 1 year post-procedure

Follow-up: 30 days, 6 mos, 1 year and annually through 10 years
EARLY TAVR Trial
Study Flow

Asymptomatic Severe AS and 2D-TTE (PV ≥4m/s or AVA ≤1 cm²)
Exclusion if patient is symptomatic, EF<50%, concomitant surgical indications, bicuspid valve, or STS >8

Treadmill Stress-Test

- Stress-Test Normal
  - CTA and Angiography
  - TF- TAVR eligibility
  - Early-TAVR Randomized Trial

- Stress-Test Abnormal
  - Early TAVR Registry

Randomization 1:1
Stratified by STS (<3 vs ≥3)

- TF- TAVR
- Clinical Surveillance

Primary Endpoint (superiority): 2-year composite of all-cause mortality, all strokes, and repeat hospitalizations (CV)
TAVR: Transition to standard of care

- Increasing volume
- Decreasing acuity of illness of patients
- Expanding indications (intermediate risk, valve in valve)
- Improving outcomes
- Transition to mostly transfemoral
- Better patient selection
  - Frailty
    - Better identification of Risk (beyond STS) by CT surgeons
- Improved post operative protocols
TAVR: As volume rises, “minimalist” approach helpful

- Why a minimalist approach?
  - Reduce complexity, cost, improve outcome and programmatic efficiencies

- KISS model
  - Percutaneous Access
  - No Foley catheters (men)
  - No routine PA catheter
  - No TEE
  - Conscious sedation protocols
    - Reduce ICU and overall LOS
    - Fast track ICU protocols: goal 4-6 hours in ICU
Same time, expanding high risk capabilities

- Alternate access
  - Subclavian/Axillary
  - Direct aortic
  - Transcarotid
  - Transcaval
  - transapical
Transcaval
1. Cross with wire

2. Exchange for stiffer wire

3. Bring sheath from RFV to aorta

4. Close aorta with Amplatz device
Limitations of TAVR

• Durability
  - *No real “in vivo” data past 10 years*
  - *8-10 years - minimal valve failure*
  - *Rx for failed TAVR is… repeat TAVR*

• AS plus other anatomy
  - Aortic pathology
  - CAD
  - Polyvalvular disease
The Trifecta
Case Presentation

[Patient CC]

Patient Evaluation
Structural Heart Program

Sentara Heart Hospital
Norfolk, VA
Summary – Clinical History:

- 68 years old
- STS 2.1% AVR
- NYHA Class II
- BSA / BMI: 1.93 / 26
- Creatinine: 0.6
- Hb: 13.7
- PLT: 182
- Team: PDM
- Ht: 173 cm
- Wt: 78 kg

Clinical history

Bioprosthetic aortic valve stenosis and AI
- H/o severe AS with root enlargement s/p aortic root replacement with #23 Medronic freestyle graft, and #26 Gelweave graft as ascending aortic interposition graft by Dr. B on 6/17/2004
- 2D Echo 11/10/16 -- AVA 1cm2, peak gradient 44mmHG, mean gradient 22mmHG, Vmax 330cm/s with moderate AI
- LHC 3/9/17 – AVA 0.96cm2, mean gradient 17 mmHg, severe AI by aortography

2D Echo 11/10/16 -- EF 60%
TEE 3/9/17 – moderate MR

Normal Coronary arteries by LHC 3/9/17

CTA 3/7/17 – as shown

Hyperlipidemia, Hypothyroidism, Urinary frequency

Panorex – cleared by Primary dentist (in EPIC)

Carotid PVL 3/3/17 - < 50% stenosis bilaterally

PFT’s 3/3/17 – FEV1 2.19, 81% predicted, DLCO 67
Annulus = 23mm

Echocardiography
Plan: SURGERY – REDO AVR with root and ascending aorta repair
What does a Valve clinic look like in 2017?

• The Heart Team
Developing TAVR Program at Sentara Heart

• First implant: Dec 2011
  ▪ >800 TAVR procedures to date; > 300 pred in 2017
  ▪ > 100 MitraClip
  ▪ > 200 Watchman
  ▪ >200 CHIP cases

• Structural Heart Service
  ▪ IC, CTS, Imaging
  ▪ 4 PA’s, 2 RN’s, 1 MA
  ▪ Busy in-patient service
  ▪ daily full office schedule
Research

- PORTICO – High risk TAVR, novel valve
- SURTAVI – Intermediate Risk, Evolut
- Partner 3 – Low risk TAVR 1:1 surgery
- Early TAVR - Asymptomatic AS

- Transcatheter Mitral Valve Replacement Trials – coming this summer!