Transcatheter Aortic Valve Replacement (TAVR)
NCVH - 2016 Update

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• Disclosures: none
Current State of TAVR - 2016

- ~350 US Centers performing TAVR
- WKHS currently only local institution performing TAVR (2 ICs, 2 cardiac surgeons)
- 2 valve options are currently FDA approved (Edwards, Medtronic)
- Numerous other valves in pipeline/approval process
Current FDA Approved Valves

» Edwards Sapien 3 - balloon expandable

» Medtronic Corevalve Evolut R - self-expanding

» Both are excellent valves!!! Both are reasonable options for the majority of patients.

» Advantages and disadvantages to each....we are still learning best way to individualize choice for each patient
Pre TAVR workup

» Meet the patient and family (discuss goals/expectations)

» CT

» RHC/LHC

» Assess risk (PFTs, frailty index, comorbidities, STS score, etc.)

» Surgical Consultation
Day of TAVR

» Team Approach - heart surgeon and interventional cardiologist work together on procedure, both scrubbed

» Lots of help and support!!! (cath lab RNs, rad techs, OR staff, perfusionist on standby, etc.)

» Typically ~ 1 hr, most still general anesthesia, extubate in OR
Post-op till Discharge

» Early ambulation
» Lines out quickly
» Avoidance of sedatives/narcotics
» Aspirin/Plavix
Cohesive, Multi-disciplinary Approach Embodies

- Optimal patient centric care
- Dedication across medical specialties
- Collaborative treatment decision

TAVR Heart Team Concept

National Coverage Determination\(^{18}\)
The patient (preoperatively and postoperatively) is under the care of a heart team
TAVR Evaluation Pathway

1. Pre-screening Review of Records
2. Clinical Evaluation
3. Gated CTA (Chest / Abdomen / Pelvis)
4. RHC / LHC Coronary Angiography
5. Functional Status Assessment (Cognitive Function, Frailty, etc.)
6. STS Score Calculation
7. Treatment Plan

Note: The above is a suggested flow for the patient screening process, however, the order in which screening tests are conducted varies depending on the patient’s profile and should be at the discretion of the Heart Team.
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

Alain Cribier: First Human Transcatheter Valve Replacement (2002)
What Causes Aortic Stenosis in Adults?

Less Common

- Congenital Abnormality
- Rheumatic Fever

More Common

- Age-Related Calcific Aortic Stenosis

Images courtesy of John Webb, MD at St. Paul’s Hospital and Renu Virmani, MD at the CVPath Institute
Population at Risk for Aortic Stenosis is Increasing

Approx. 2.5 Million People in the U.S. Over the Age of 75 suffer from this disease.¹

- Aortic Stenosis is estimated to be prevalent with **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
- 80% of adults with symptomatic aortic stenosis are male⁴
Symptoms of Aortic Stenosis

- Shortness of breath
- Angina
- Fatigue
- Syncope or Presyncope
- Other
  - Rapid or irregular heartbeat
  - Palpitations

The symptoms of aortic disease are commonly misunderstood by patients as ‘normal’ signs of aging. Many patients initially appear asymptomatic, but on closer examination up to 37% exhibit symptoms.
Severe Aortic Stenosis is Life Threatening and Treatment is Critical

After the onset of symptoms, patients with severe aortic stenosis have a survival rate as low as 50% at 2 years and 20% at 5 years without aortic valve replacement.

50% of patients died within 1 year without valve replacement. Per the Inoperable Cohort of the PARTNER Trial
Worse Prognosis than Many Metastatic Cancers

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

Survival, %

Breast Cancer: 23%
Lung Cancer: 4%
Colorectal Cancer: 12%
Prostate Cancer: 30%
Ovarian Cancer: 28%
Severe Inoperable AS*: 3%

In the absence of serious comorbid conditions, aortic valve replacement (AVR) is indicated in the majority of symptomatic patients with severe aortic stenosis.

Consultation with or referral to a Heart Valve Center of Excellence is reasonable when discussing treatment options for:

- Asymptomatic patients with severe valvular heart disease
- Patients with multiple comorbidities for whom valve intervention is considered

Because of the risk of sudden death, replacing the aortic valve should be performed promptly after the onset of symptoms.

Age is not a contraindication to surgery.
## Definition of Severe Aortic Stenosis

Patients with severe aortic stenosis typically have an aortic valve area ≤ 1.0 cm²

<table>
<thead>
<tr>
<th>Definition</th>
<th>Valve Hemodynamics</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-gradient severe aortic stenosis</td>
<td>- Aortic jet velocity ≥ 4 m/s or mean gradient ≥ 40 mmHg</td>
</tr>
<tr>
<td></td>
<td>- Or aortic valve area index ≤ 0.6 cm²/m²</td>
</tr>
<tr>
<td>Low-flow/low-gradient with reduced left ventricular ejection fraction</td>
<td>- Resting aortic jet velocity &lt; 4 m/s or mean gradient &lt; 40 mmHg</td>
</tr>
<tr>
<td></td>
<td>- Dobutamine stress echocardiography shows aortic valve area ≤ 1.0 cm² with aortic jet velocity ≥ 4 m/s at any flow rate</td>
</tr>
<tr>
<td></td>
<td>- Left ventricular ejection fraction &lt; 50%</td>
</tr>
<tr>
<td>Low-gradient with normal left ventricular ejection fraction or paradoxical low-flow</td>
<td>- Aortic jet velocity &lt; 4 m/s or mean gradient &lt; 40 mmHg</td>
</tr>
<tr>
<td></td>
<td>- Indexed aortic valve area ≤ 0.6 cm²/m²</td>
</tr>
<tr>
<td></td>
<td>- Stroke volume index &lt; 35 mL/m² measured when patient is normotensive (systolic blood pressure &lt; 140 mmHg)</td>
</tr>
<tr>
<td></td>
<td>- Left ventricular ejection fraction ≥ 50%</td>
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</tbody>
</table>

Symptoms:
Dyspnea or decreased exercise tolerance, heart failure, angina, syncope and presyncope.
Dobutamine stress echocardiography can be used to differentiate between true and pseudo severe aortic stenosis

- Better define the severity of the aortic stenosis
- Accurately assess contractile / pump reserve

Some patients with severe aortic stenosis based on valve area have a lower than expected gradient (e.g. mean gradient < 30 mmHg) despite preserved LV ejection fraction (e.g. EF > 50%)

- **Up to 35% of patients with severe aortic stenosis present with low flow, low gradient**
- These low gradients often lead to an underestimation of the severity of the disease, so many of these patients do not undergo surgical aortic valve replacement

Dobutamine stress in low gradient, low ejection fraction
AS Chambers, Heart. 2006 April; 92(4): 554–558
At Least 40% of Patients Who Need Valve Replacement Do Not Get Treatment

Studies show that patients with severe aortic stenosis are under-diagnosed and under-treated.
Medical Management and BAV are Inadequate Therapies for Inoperable Patients

- Despite frequent BAV, **standard therapy did not alter the dismal course of disease for inoperable patients** in the PARTNER Trial
  - 51% 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%.
### Severe Aortic Stenosis is Defined as:
Valve Area < 1.0 cm²
Mean Gradient > 40 mmHg OR Jet Velocity > 4.0 m/s

<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>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Open-Heart Surgery (AVR)</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
</tbody>
</table>

**High Risk Patients Defined by STS Risk Score > 8%**
For relief of aortic stenosis in patients with

- Symptomatic heart disease due to severe native calcific aortic stenosis
- Have native anatomy appropriate for the valve delivery system
- Evaluated by a Heart Team, including a cardiac surgeon, to be at high or greater risk for open surgical therapy

Society of Thoracic Surgeons operative risk score

≥ 8% OR at a ≥ 15% risk of mortality (at 30 days)
COREVALVE® EVOLUT® R CE STUDY
UNPARALLELED SURVIVAL AT 1 YEAR

93.3%*

Extreme and High Risk Patients
COREVALVE EVOLUT R CE STUDY
KEY TAKEAWAYS

Exceptional Outcomes

- High Survival
- Low Stroke Rate
- Low Pacemaker Rate
STRONG HEMODYNAMIC PERFORMANCE

7.5 mmHg
Single Digit Gradients

0%
Severe PVL

4.3%
Moderate PVL

Manoharan, G; Clinical Outcomes at 1 Year with a
TAVR is Better than Medical Management for Inoperable Patients

Edwards SAPIEN Valves Significantly Improve Survival
TAVR is Better than Medical Management for Inoperable Patients

Edwards SAPIEN is superior to medical management in inoperable patients

TAVR with Edwards SAPIEN valves is a reasonable alternative to surgery

Edwards SAPIEN 3 valve: Transformational design

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Edwards SAPIEN Valves Significantly Improve Survival
Standard Therapy is an Ineffective Treatment for Severe Aortic Stenosis Patients

Without treatment, 94% of patients in the standard therapy group died within 5 years.

21.8% absolute reduction in mortality at 5 years.

All-Cause Mortality (%)

Inoperable Cohort

Standard Rx (n = 179)  TAVR (n = 179)

50.7%  30.7%  71.8%  93.6%

HR [95% CI] = 0.50 [0.39, 0.65]
p (log rank) < 0.0001
87.3% of patients with standard therapy were rehospitalized for cardiac issues.

39.7% absolute reduction of rehospitalization at 5 years.
TAVR with Edwards SAPIEN Valves is Equivalent to Surgery

With the Benefits of a Less Invasive Procedure
TAVR with Edwards SAPIEN Valves is Equivalent to Surgery

TAVR is superior to medical management for inoperable patients.

Edwards SAPIEN valve is a reasonable alternative to surgery in high-risk patients.

Edwards SAPIEN 3 valve: Transformational design.

With the benefits of a less invasive procedure.
TAVR with Edwards SAPIEN Valves is Equivalent to Surgery

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TAVR with Edwards SAPIEN valves is a reasonable alternative to surgery

Edwards SAPIEN 3 valve: Transformational design

With the Benefits of a Less Invasive Procedure
TAVR is Equivalent to Surgery in High-Risk Patients

Per ACC / AHA Guidelines, **TAVR is a reasonable alternative to surgery** in patients who meet an indication for AVR and who have high surgical risk for surgical AVR.

**ALL CAUSE MORTALITY**

**At 5 Years**

Patients that had TAVR with the Edwards SAPIEN valve showed survival equivalent to SAVR.

Error Bars Represent 95% Confidence Limits

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

**p (log rank) = 0.76**

**No. at Risk**

<table>
<thead>
<tr>
<th></th>
<th>TAVR</th>
<th>SAVR</th>
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<tbody>
<tr>
<td>0</td>
<td>348</td>
<td>351</td>
</tr>
<tr>
<td>12</td>
<td>262</td>
<td>236</td>
</tr>
<tr>
<td>24</td>
<td>228</td>
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<td>36</td>
<td>191</td>
<td>174</td>
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<tr>
<td>48</td>
<td>154</td>
<td>131</td>
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</tbody>
</table>
| 60    | 61    | 64    

**ALL-CAUSE MORTALITY (%)**

- **SAVR**
  - 0%: 100%
  - 20%: 60%
  - 40%: 40%
  - 60%: 20%
  - 80%: 0%

- **TAVR**
  - 0%: 100%
  - 20%: 60%
  - 40%: 40%
  - 60%: 20%
  - 80%: 0%
At both 1 year and 5 year follow up, 85% of Patients treated with the Edwards SAPIEN valve were in NYHA Class I or II compared to only 6% at baseline.

<table>
<thead>
<tr>
<th></th>
<th>TAVR</th>
<th>SAVR</th>
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<th>SAVR</th>
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<th>SAVR</th>
<th>TAVR</th>
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<td>Baseline</td>
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<td>250</td>
<td>226</td>
<td>165</td>
<td>145</td>
<td>100</td>
<td>97</td>
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<td>1 Year</td>
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<td>3 Years</td>
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<td>5 Years</td>
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</tbody>
</table>

NYHA CLASS OVER TIME

- p = 0.64
- p = 0.91
- p = 0.35
- p = 0.93

Patients Continued to Show Improved Symptom Relief 5 Years After TAVR
Longest Follow-Up in Any TAVR Randomized Study

The PARTNER Trial 5-Year Results

**TAVR vs. Standard Therapy in Inoperable Patients**
- Significant mortality benefit
- Statistically significant reduction in hospitalization
- NNT is 5 patients to save a life

**TAVR vs. Surgical AVR in High-Risk Patients**
- Equivalent mortality benefit
- Persistent symptom relief

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**5 YEARS of PROVEN VALVE DURABILITY**
- Sustained hemodynamic performance
- No incidence of structural valve deterioration requiring surgical valve replacement
- Significant and sustained improvement in functional heart class
Now Approved: The Edwards SAPIEN 3 Valve
Now Approved: The Edwards SAPIEN 3 Valve

- TAVR is superior to medical management for inoperable patients
- TAVR is a reasonable alternative to surgery for high-risk patients
- Transformational advance in valve design: Edwards SAPIEN 3 Valve
Now Approved: The Edwards SAPIEN 3 Valve

- TAVR is superior to medical management for inoperable patients
- TAVR is a reasonable alternative to surgery for high-risk patients
- Edwards SAPIEN 3 valve: Transformational design

Unprecedented Clinical Outcomes
All-Cause Mortality of the 491 patients in the PARTNER II Trial was 1.6% at 30 days.

Cardiovascular Mortality was 1.0%
All-Cause Mortality Has Decreased Overall

ALL-CAUSE MORTALITY at 30 DAYS
PARTNER I Trial and PARTNER II Trial

SAPIEN Valve

PARTNER I B (TF) 175
PARTNER I A (All) 344
PARTNER I A (TF) 240
PARTNER II B (TF) 271

SAPIEN XT Valve

PARTNER II B (TF) 282

SAPIEN 3 Valve

PARTNER II HR (TF) 491

SAPIEN Valve

6% 5% 4% 5% 4% 2%
Of the 491 Patients in the PARTNER II Trial: Disabling Stroke was 0.8% at 30 days.
### Other Clinical Events at 30 Days (as Treated Patients)*

<table>
<thead>
<tr>
<th>Events</th>
<th>SAPIEN 3 Valve HR TF</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Events (%)</strong></td>
<td>(n = 491)</td>
</tr>
<tr>
<td>Major Vascular Comps.</td>
<td>5.3</td>
</tr>
<tr>
<td>Bleeding – Life Threatening</td>
<td>5.5</td>
</tr>
</tbody>
</table>
Femoral Case Example
Transapical Case Example
Where is all this going?

» Number and indication for procedure is growing

» Moving towards a “minimalist” approach

» Eventually, the great, great majority of these Aortic Stenosis cases will be done via TAVR (as opposed to traditional surgery)

» Therapies for Mitral and Tricuspid Valves is evolving quickly
Case Examples:
Valve in Valve with Corevalve Evolut R

» 86 yo male

» History of 23mm Medtronic Mosaic Valve ~ 15 years ago

» Now with bioprosthetic valve stenosis

» 3 recent CHF admits

» Mean gradient ~35, EF 15%
Edwards Sapien 3

» 88 yo WM
» NYHA Class III
» Good functional capacity