Structural Heart Disease
Transcatheter Aortic Valve Replacement (TAVR)

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Prevalence of Aortic Stenosis

- Aortic stenosis is estimated to be prevalent in up to 7% of the population over the age of 65\textsuperscript{1}

- It is more likely to affect men than women; 80% of adults with symptomatic aortic stenosis are male\textsuperscript{3}
Aortic Stenosis Demographics

- Aortic stenosis 2% US population >65yrs old
- Aortic sclerosis 29% US population >65 yrs old
- Aortic sclerosis 50% greater risk of mortality and myocardial infarction.
- Aortic sclerosis progresses to aortic stenosis in 9% over 5 years
What Causes Aortic Stenosis in Adults?

Aortic stenosis in patients over the age of 65 is usually caused by calcific (calcium) deposits associated with aging.

In some cases adults may develop aortic stenosis resulting from a congenital abnormality.

Adults who have had rheumatic fever may also be at risk for aortic stenosis.

**More Common**

- Age-Related Calcific Aortic Stenosis

**Less Common**

- Rheumatic Fever
- Congenital Abnormality
3 Major Etiologies for aortic stenosis
Major Risk Factors

Independent clinical factors associated with degenerative aortic valve disease include the following:

- Increasing age
- Male gender
- Hypertension
- Smoking
- Elevated lipoprotein A
- Elevated LDL cholesterol
Signs and Symptoms

- Heart Failure
- Angina
- Syncope

- Carotid Parvus et Tardus
- Laterally displaced PMI
- Soft A2
- Crescendo-Decrescendo systolic murmur
- Timing of peak murmur and NOT intensity predicts severity
Aortic Stenosis Is Life Threatening and Progresses Rapidly

- Survival after onset of symptoms is 50% at 2 years and 20% at 5 years\(^1\)
- Surgical intervention for severe aortic stenosis should be performed promptly once even minor symptoms occur\(^1\)
Sobering Perspective

5-Year Survival

Survival, %

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

*Using constant hazard ratio. Data on file, Edwards Lifesciences LLC. Analysis courtesy of Murat Tuczu, MD, Cleveland Clinic

5 year survival of breast cancer, lung cancer, prostate cancer, ovarian cancer and severe inoperable aortic stenosis
Echocardiographic Guidelines are the Gold Standard in Assessing Severe Aortic Stenosis

According to the 2014 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
Multiple Modalities May Be Used to Diagnose Severe Aortic Stenosis\textsuperscript{6}
Echocardiography:
Continuity Equation - Conservation of Mass

\[ A_1 \cdot V_1 = A_2 \cdot V_2 \]
Measurement of Aortic Stenosis Severity

LVOT diameter 1.9 cm

LVOT velocity 0.8 m/s

AS Jet 3.6 m/s

SV\textsubscript{LVOT} = SV\textsubscript{ASjet}

CSA\textsubscript{LVOT} \times VTI\textsubscript{LVOT} = AVA \times VTI\textsubscript{ASjet}

AVA = (VTI\textsubscript{LVOT} \times CSA\textsubscript{LVOT}) / VTI\textsubscript{ASjet}
Echocardiography:

3D Planimetry
Stages of aortic stenosis

Stage C - *Asymptomatic severe*
leaflet calcification
mean pressure gradient $\geq 40$ mm Hg
AVA $\leq 1.0$ cm$^2$

Stage D - *Symptomatic severe*
leaflet calcification
mean pressure gradient $\geq 40$ mm Hg
AVA $\leq 1.0$ cm$^2$
Gorlin Method of Calculation of Aortic Valve Area

\[
\text{AVA} = \frac{\text{CO/SEP}}{44.3 \times \sqrt{\text{LV-Aorta}}}
\]

AVA = aortic valve area; where
CO = cardiac output = 5000 cc/min;
HR = heart rate = 70 beats/min;
LVET = LV ejection time = 360 msec;
SEP = systolic ejection period = 70 x 360 msec = 25 sec;
LV - aorta = mean aortic gradient = 81 mm Hg

\[
\text{AVA (cm}^2) = \frac{5000/25}{44.3 \times \sqrt{81}}
\]

AVA (cm\(^2\)) = 0.5 cm\(^2\)
Not so classic aortic stenosis
1. Low Flow, Low Gradient Severe AS

2. Paradoxical Low Flow, Low Gradient Severe AS
Low Flow, Low Gradient AS

• Low gradient with a small calculated valve area in the setting of poor systolic function. This may result in lack of referral for AVR because of the low gradient.

• Dobutamine Stress Echo:
  – By increasing cardiac output, we can determine if the AS is severe by reassessing the gradient across the aortic valve (increases) AND the aortic valve area (decreases).
  – Assess myocardial contractile reserve
    • Does the cardiac output improve by 20% or more.
  – Critical for decision making regarding aortic valve replacement.
Paradoxical Low Flow and/or Low Gradient Severe Aortic Stenosis

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
### Stages of Valvular AS

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
<th>Valve Anatomy</th>
<th>Valve Hemodynamics</th>
<th>Hemodynamic Consequences</th>
<th>Symptoms</th>
</tr>
</thead>
</table>
| A     | At risk of AS  | • Bicuspid aortic valve (or other congenital valve anomaly)  
       |            | • Aortic valve sclerosis | • Aortic V<sub>max</sub> ≤2 m/s | None | None |
| B     | Progressive AS | • Mild-to-moderate leaflet calcification of a bicuspid or trileaflet valve with some reduction in systolic motion or  
       |          | • Rheumatic valve changes with commissural fusion | • Mild AS: Aortic V<sub>max</sub> 2.0–2.9 m/s or mean ΔP <20 mmHg  
       |          |  
       |          | • Moderate AS: Aortic V<sub>max</sub> 3.0–3.9 m/s or mean ΔP 20–38 mmHg | • Early LV diastolic dysfunction may be present | Normal LVEF | None |
| C     | Asymptomatic severe AS | • Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening | • Aortic V<sub>max</sub> ≥4 m/s or mean ΔP ≥40 mmHg  
       |            | • AVA typically ≤1.0 cm<sup>2</sup> (or AVAI ≤0.6 cm<sup>2</sup>/m<sup>2</sup>)  
       |            | • Very severe AS is an aortic V<sub>max</sub> ≥5 m/s or mean ΔP ≥60 mmHg | • LV diastolic dysfunction  
       |            | • Mild LV hypertrophy  
       |            | • Normal LVEF | None | Exercise testing is reasonable to confirm symptom status |
| C1    | Asymptomatic severe AS | • Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening | • Aortic V<sub>max</sub> ≥4 m/s or mean ΔP ≥40 mmHg  
       |            | • AVA typically ≤1.0 cm<sup>2</sup> (or AVAI ≤0.6 cm<sup>2</sup>/m<sup>2</sup>) | • LVEF <50% | None |
| C2    | Asymptomatic severe AS with LV dysfunction | • Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening | • Aortic V<sub>max</sub> ≥4 m/s or mean ΔP ≥40 mmHg  
       |            | • AVA typically ≤1.0 cm<sup>2</sup> (or AVAI ≤0.6 cm<sup>2</sup>/m<sup>2</sup>) | • LV diastolic dysfunction  
       |            | • Mild LV hypertrophy  
       |            | • Normal LVEF | None |
| D     | Symptomatic severe AS | • Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening | • Aortic V<sub>max</sub> ≥4 m/s or mean ΔP ≥40 mmHg  
       |            | • AVA typically ≥1.0 cm<sup>2</sup> (or AVAI ≥0.6 cm<sup>2</sup>/m<sup>2</sup>) but may be larger with mixed AS/AR | • LV diastolic dysfunction  
       |            | • LV hypertrophy  
       |            | • Pulmonary hypertension may be present | • Exertional dyspnea or decreased exercise tolerance  
       |            | • Exertional angina | • Exertional syncope or presyncope |
| D1    | Symptomatic severe high-gradient AS | • Severe leaflet calcification or congenital stenosis with severely reduced leaflet opening | • Aortic V<sub>max</sub> ≥4 m/s or mean ΔP ≥40 mmHg  
       |            | • AVA typically ≤1.0 cm<sup>2</sup> (or AVAI ≤0.6 cm<sup>2</sup>/m<sup>2</sup>) but may be larger with mixed AS/AR | • LV diastolic dysfunction  
       |            | • LV hypertrophy  
       |            | • LVEF <50% | • HF  
       |            | • Angina | • Syncope or presyncope |
| D2    | Symptomatic severe low-flow/low-gradient AS with reduced LVEF | • Severe leaflet calcification with severely reduced leaflet motion | • AVA ≤1.0 cm<sup>2</sup> with resting aortic V<sub>max</sub> <4 m/s or mean ΔP <40 mmHg  
       |            | • Dobutamine stress echocardiography shows AVA ≤1.0 cm<sup>2</sup> with V<sub>max</sub> ≥4 m/s at any flow rate | • LV diastolic dysfunction  
       |            | • LV hypertrophy  
       |            | • LVEF <50% | • HF  
       |            | • Angina | • Syncope or presyncope |
| D3    | Symptomatic severe low-gradient AS with normal LVEF or paradoxical low-flow severe AS | • Severe leaflet calcification with severely reduced leaflet motion | • AVA ≤1.0 cm<sup>2</sup> with aortic V<sub>max</sub> <4 m/s or mean ΔP <40 mmHg  
       |            | • Indexed AVA ≤0.6 cm<sup>2</sup>/m<sup>2</sup> and  
       |            | • Stroke volume index <35 mL/m<sup>2</sup>  
       |            | • Measured when patient is normotensive (systolic BP <140 mmHg) | • Increased LV relative wall thickness  
       |            | • Small LV chamber with low stroke volume  
       |            | • Restrictive diastolic filling LVEF <50% | • HF  
       |            | • Angina | • Syncope or presyncope |

AR indicates aortic regurgitation; AS, aortic stenosis; AVA, aortic valve area; AVAI, aortic valve area indexed to body surface area; BP, blood pressure; HF, heart failure; LV, left ventricular; LVEF, left ventricular ejection fraction; ΔP, pressure gradient; and V<sub>max</sub>, maximum aortic velocity.

ACC/AHA 2104 Valve Guidelines  
### Summary of Recommendations for AS: Timing of Intervention


<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVR is recommended for symptomatic patients with severe high-gradient AS who have symptoms by history or on exercise testing (stage D1)</td>
<td>I</td>
<td>B</td>
<td>9,91,134,135</td>
</tr>
<tr>
<td>AVR is recommended for asymptomatic patients with severe AS (stage C2) and LVEF &lt;50%</td>
<td>I</td>
<td>B</td>
<td>136,137</td>
</tr>
<tr>
<td>AVR is indicated for patients with severe AS (stage C or D) when undergoing other cardiac surgery</td>
<td>I</td>
<td>B</td>
<td>108,138</td>
</tr>
<tr>
<td>AVR is reasonable for asymptomatic patients with very severe AS (stage C1, aortic velocity ≥5.0 m/s) and low surgical risk</td>
<td>IIa</td>
<td>B</td>
<td>139,140</td>
</tr>
<tr>
<td>AVR is reasonable in asymptomatic patients (stage C1) with severe AS and decreased exercise tolerance or an exercise fall in BP</td>
<td>IIa</td>
<td>B</td>
<td>25,47</td>
</tr>
<tr>
<td>AVR is reasonable in symptomatic patients with low-flow/low-gradient severe AS with reduced LVEF (stage D2) with a low-dose dobutamine stress study that shows an aortic velocity ≥4.0 m/s (or mean pressure gradient ≥40 mm Hg) with a valve area ≤1.0 cm² at any dobutamine dose</td>
<td>IIa</td>
<td>B</td>
<td>43,141,142</td>
</tr>
<tr>
<td>AVR is reasonable in symptomatic patients who have low-flow/low-gradient severe AS (stage D3) who are normotensive and have an LVEF ≥50% if clinical, hemodynamic, and anatomic data support valve obstruction as the most likely cause of symptoms</td>
<td>IIa</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>AVR is reasonable for patients with moderate AS (stage B) (aortic velocity 3.0–3.9 m/s) who are undergoing other cardiac surgery</td>
<td>IIa</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>AVR may be considered for asymptomatic patients with severe AS (stage C1) and rapid disease progression and low surgical risk</td>
<td>IIb</td>
<td>C</td>
<td>N/A</td>
</tr>
</tbody>
</table>

AS indicates aortic stenosis; AVR, aortic valve replacement by either surgical or transcatheter approach; BP, blood pressure; COR, Class of Recommendation; LOE, Level of Evidence; LVEF, left ventricular ejection fraction; and N/A, not applicable.
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.
Options for Aortic Valve Replacement

Inoperable OR High Risk

- Transcatheter Aortic Valve Replacement (TAVR)

Patients Suitable for Open Chest Surgery

- Surgical Aortic Valve Replacement (sAVR)
- Minimal Incision Valve Surgery (MIVS)

Transfemoral Approach
# Prosthetic Heart Valves

## Types of Prosthetic Heart Valves

<table>
<thead>
<tr>
<th>Mechanical</th>
<th>Bioprosthetic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caged-ball</td>
<td>Heterograft (porcine or bovine)</td>
</tr>
<tr>
<td>Starr-Edwards</td>
<td>- Porcine aortic valve</td>
</tr>
<tr>
<td>Tilting-disc</td>
<td>Carpenter-Edwards</td>
</tr>
<tr>
<td>Single-tilting</td>
<td>Hancock</td>
</tr>
<tr>
<td>Medtronic-Hall</td>
<td>- Bovine pericardial</td>
</tr>
<tr>
<td>Omniscience</td>
<td>Carpenter-Edwards</td>
</tr>
<tr>
<td>Bjork-Shiley</td>
<td>- Stented valves (porcine)</td>
</tr>
<tr>
<td>Bileaflet-tilting</td>
<td>Carpenter-Edwards</td>
</tr>
<tr>
<td>St.Jude</td>
<td>Hancock</td>
</tr>
<tr>
<td></td>
<td>- Stentless valves (porcine)</td>
</tr>
<tr>
<td></td>
<td>Toronto SPV</td>
</tr>
<tr>
<td></td>
<td>Freestyle</td>
</tr>
<tr>
<td></td>
<td>CryoLife-O-Brian</td>
</tr>
<tr>
<td>Homograft</td>
<td>- Human cadaveric aortic valve</td>
</tr>
</tbody>
</table>
Tilting Disc Valve
Bio-prosthetic Valve
Low Percentage of Aortic Valve Surgery

- Studies show at least 40% of patients with severe AS are not treated with an AVR\(^9\)\(^-\)\(^{15}\)
<table>
<thead>
<tr>
<th>Recommendations</th>
<th>COR</th>
<th>LOE</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgical AVR is recommended in patients who meet an indication for AVR (Section 3.2.3) with low or intermediate surgical risk</td>
<td>I</td>
<td>A</td>
<td>74,148</td>
</tr>
<tr>
<td>For patients in whom TAVR or high-risk surgical AVR is being considered, members of a Heart Valve Team should collaborate to provide optimal patient care</td>
<td>I</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>TAVR is recommended in patients who meet an indication for AVR for AS who have a prohibitive surgical risk and a predicted post-TAVR survival &gt;12 mo</td>
<td>I</td>
<td>B</td>
<td>169,170</td>
</tr>
<tr>
<td>TAVR is a reasonable alternative to surgical AVR in patients who meet an indication for AVR (Section 3.2.3) and who have high surgical risk (Section 2.5)</td>
<td>IIa</td>
<td>B</td>
<td>171,172</td>
</tr>
<tr>
<td>Percutaneous aortic balloon dilation may be considered as a bridge to surgical or transcatheter AVR in severely symptomatic patients with severe AS</td>
<td>IIb</td>
<td>C</td>
<td>N/A</td>
</tr>
<tr>
<td>TAVR is not recommended in patients in whom existing comorbidities would preclude the expected benefit from correction of AS</td>
<td>III: No Benefit</td>
<td>B</td>
<td>169</td>
</tr>
</tbody>
</table>

AS indicates aortic stenosis; AVR, aortic valve replacement; COR, Class of Recommendation; LOE, Level of Evidence; N/A, not applicable; and TAVR, transcatheter aortic valve replacement.
What is TAVR - Transcatheter Aortic Valve Replacement?

- An aortic valve replacement as an alternative to traditional thoracotomy.
- Less invasive than traditional thoracotomy for patients considered too high risk for traditional surgery.
TAVR Multimodality imaging
Pre-procedural assessment

- **ECG**
  - Pre-existing conduction disturbances, consider/anticipate PPM

- **Transthoracic Echo**
  - TEE seldom needed

- **ECG-gated CTA**
  - Annular sizing, deployment angle, coronary heights, Cапattern, etc
  - Vascular Access anatomy
  - 3D analysis: local and by vendor

- **Coronary angiography**
  - Ao valve study only if echo diagnosis still uncertain
  - RHC only if otherwise indicated

- **Heart Team review**
  - Prior to scheduling
  - Again immediately prior to procedure
3D analysis: Annulus

Calcifications

Hockey Puck (MIP)

LAO: 20°
Caudal: 5°

RAO: 65°
Cranial: 42°

Series: 302
Slices: 257-512
Slice Spacing: 0.6 mm
3D analysis: Annulus

Annulus & Diameters

<table>
<thead>
<tr>
<th>ID Type</th>
<th>Label</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>Polygon Min. Ø</td>
<td>25.0 mm</td>
</tr>
<tr>
<td></td>
<td>Max. Ø</td>
<td>30.8 mm</td>
</tr>
<tr>
<td></td>
<td>Avg. Ø</td>
<td>27.9 mm</td>
</tr>
<tr>
<td></td>
<td>Area derived Ø</td>
<td>27.4 mm</td>
</tr>
<tr>
<td></td>
<td>Perimeter derived Ø</td>
<td>27.6 mm</td>
</tr>
<tr>
<td></td>
<td>Area</td>
<td>588.4 mm²</td>
</tr>
<tr>
<td></td>
<td>Perimeter</td>
<td>86.9 mm</td>
</tr>
</tbody>
</table>
3D analysis: Access
BEValve kit (SAPIEN3 Edwards)
TAVR Procedure

- Micropuncture bilateral femoral percutaneous access:
  - PreClose, ~18F sheath
  - Contralateral access for pigtail (aortogram)
- Place temp pacer, test threshold

Source: Edwards Lifesciences, Inc -- TAVR Intro ppt
TAVR Procedure (BE)
TAVR
Transfemoral AV Deployment

- 22 or 24 French sheath with surgical repair
- Preparatory BAV
- FlexCath to deliver valve around arch
- Rapid RV pacing

*Rapid pacing: 220/min*
Aortogram after Transfemoral TAVI
Preferred

Poor vascular access
Ao arch pathology (bulky atheroma or porcelain Ao)
Retrograde AV crossing difficulties
1) Small incision between the 5th & 6th ribs of the left chest wall

2) Introducer sheath placed through apex of the heart & balloon valvuloplasty performed

3) Valve deployed over a guidewire using balloon catheter into native aortic annulus

4) Valve fully deployed
TAVR COMPLICATIONS

• Major TAVI Complications
  • Annular rupture
  • Coronary obstruction
  • Aortic dissection and rupture
    • Stroke
  • Vascular access site complications
    • Paravalvular leak
  • AV block and pacemaker implantation
Two TAVR Options

The History

- Edwards Sapien Valve
  - Stainless Steel Frame
  - More Aortic Regurg, less AV block/PPM
  - Better for severe bulky calcification.

- Medtronic CoreValve
  - Nitinol Frame-self expanding
  - Less Aortic Regurg, More heart block/PPM
PARTNER Study Design

Symptomatic Severe Aortic Stenosis

Cohort A

N = 699

High Risk

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

Total = 1,057 patients

2 Parallel Trials: Individually Powered

ASSESSMENT: Transfemoral Access

Transfemoral (TF)

1:1 Randomization

N = 244

TF TAVR

VS

N = 248

AVR

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

Cohort B

Inoperable

N = 358

ASSESSMENT: Transfemoral Access

Yes

TF TAVR

N = 179

TA TAVR

VS

N = 104

N = 103

NYHA functional class

AVA and
Mean gradient
Peak jet velocity

Predicted operative mortality or irreversible morbidity

> 50%

≥ II

< 0.8 cm²

> 40 mmHg

> 4.0 m/s

Primary Endpoint: All-Cause Mortality at 1 yr
### Characteristics of an Inoperable Patient

#### Cohort B

TAVR patients may present with some of the following:

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe, symptomatic native aortic valve stenosis</td>
</tr>
<tr>
<td>Old age</td>
</tr>
<tr>
<td>Frailty</td>
</tr>
<tr>
<td>History of stroke/CVA</td>
</tr>
<tr>
<td>History of syncope</td>
</tr>
<tr>
<td>Reduced EF</td>
</tr>
<tr>
<td>Heavily calcified aorta</td>
</tr>
<tr>
<td>Prior CABG</td>
</tr>
<tr>
<td>Prior chest radiation</td>
</tr>
<tr>
<td>History of AFib</td>
</tr>
<tr>
<td>History of CAD</td>
</tr>
<tr>
<td>Prior open chest surgery</td>
</tr>
<tr>
<td>History of COPD</td>
</tr>
<tr>
<td>Fatigue, slow gait</td>
</tr>
<tr>
<td>History of renal insufficiency</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
</tr>
<tr>
<td>Diabetes and hypertension</td>
</tr>
</tbody>
</table>
Cohort B Survival

**ALL-CAUSE MORTALITY**

- $P$ (log rank) < .0001
- Δ at 2 yrs = 24.7%
- NNT = 4.0 pts

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

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

Months:
- 0
- 6
- 12
- 18
- 24

THE PARTNER TRIAL COHORT B
Cohort A: All-Cause Mortality

No. at Risk | TAVR | AVR
--- | --- | ---
26.8% | 348 | 351
24.3% | 298 | 252
26.8% | 261 | 236
23.2% | 239 | 223
33.7% | 222 | 202
44.8% | 187 | 174
44.2% | 149 | 142

HR [95% CI] = 0.93 [0.74, 1.15]
p (log rank) = 0.483
NYHA Class Survivors

90% of Patients Improved at Least 1 NYHA Class by 1 Year
60% of Patients Improved at Least 2 NYHA Classes by 1 Year

Percentage of Patients

<table>
<thead>
<tr>
<th>Time</th>
<th>NYHA IV</th>
<th>NYHA III</th>
<th>NYHA II</th>
<th>NYHA I</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>8.8%</td>
<td>64.7%</td>
<td>26.5%</td>
<td>0%</td>
</tr>
<tr>
<td>1 Month</td>
<td>35.1%</td>
<td>47.1%</td>
<td>17.1%</td>
<td>0.7%</td>
</tr>
<tr>
<td>6 Month</td>
<td>54.8%</td>
<td>8.5%</td>
<td>35.9%</td>
<td>0.8%</td>
</tr>
<tr>
<td>1 Year</td>
<td>58.8%</td>
<td>7.6%</td>
<td>32.0%</td>
<td>1.5%</td>
</tr>
</tbody>
</table>

TCT 2013 LBCT

Extreme Risk Study | Iliofemoral Pivotal
Primary Endpoint: 1 Year All-cause Mortality

- Surgical: 3.3% at 1 year with 357 at risk at baseline.
- Transcatheter: 4.5% at 1 year with 390 at risk at baseline.

P = 0.04 for superiority.

No. at Risk
- Surgical: 357 at baseline, 341 at 1 year.
- Transcatheter: 390 at baseline, 377 at 1 year.

ACC 2014
2-Year All-cause Mortality

Surgical

Transcatheter

No. at Risk

Surgical    357  341  274  28
Transcatheter  390  377  329  38

Months Post-Procedure

All-cause Mortality (%)
Patients at High Surgical Risk

Trials randomizing high risk patients to either TAVR or SAVR soon followed

US CoreValve Pivotal Trial
CoreValve, N=390, STS 7.3% vs. SAVR, N=357, STS 7.5%

PARTNER 1A
SAPIEN, N=348, STS 11.8% vs. SAVR, N=351, STS 11.7%
Patients at Intermediate Surgical Risk

Randomized trial data comparing TAVR to SAVR in lower-risk patients recently became available

SAPIEN XT and SAPIEN 3

CoreValve

Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

Two-Year Outcomes in Patients With Severe Aortic Valve Stenosis Randomized to Transcatheter Versus Surgical Aortic Valve Replacement

The All-Comers Nordic Aortic Valve Intervention Randomized Clinical Trial
Key Milestones for TAVR Technology in the United States

- **2011**: "Gen1" BE TAVR
- **2012**: "Gen2" BE TAVR
- **2013**: "Gen1" SE TAVR
- **2014**: "Gen3" BE TAVR
- **2015**: "Gen3" SE TAVR
- **2015**: Evolut R approved
- **2016**: "Gen3" SE TAVR
  - Evolut Pro approved
  - "Not-yet-FDA-approved" TAVR valves
  - "Not-yet-FDA-approved" TAVR valves
PATIENT BENEFIT

• **Females**: PARTNER A found high-risk females who underwent TAVI had better survival compared to SAVR.


• **Diabetics**: Diabetics in PARTNER trial (N=275) had significant benefit compared to SAVR (18% vs 27% at 2 years)

  (*Transcatheter Versus Surgical Aortic Valve Replacement in Patients With Diabetes and Severe Aortic Stenosis at High Risk for Surgery: An Analysis of the PARTNER Trial. JACC 2014*)

• **Renal dysfunction**: Poor outcomes in SAVR, not TAVI


• **Major Bleeding**: 13% in TAVI vs 35% in SAVR


• **O2 dependent COPD**: Better outcomes with TAVI

  (*Outcomes of patients with chronic lung disease and severe aortic stenosis treated with transcatheter versus surgical aortic valve replacement or standard therapy: insights from the PARTNER trial. J Am Coll Cardiol. 2014 Jan 28;63(3):269-79.*)

• **Mod-severe MR**: Increased 2 year mortality for SAVR, not TAVI

As TAVR is applied to younger patients, new strategies will be needed to manage inevitable clinical realities later in their lives.

**Failed TAVs**

Redo TAVR or surgical revision will be required for a subset of patients.

![SAPIEN XT at explant (1 year)](image)

**Coronary Artery Disease**

Strategies to manage CAD post TAVR will be needed.
Aortic Stenosis is prevalent with a high morbidity and mortality when symptomatic and aortic valve replacement is the only treatment associated with improved outcomes.

Asymptomatic low risk patients will benefit from surgical AVR.

Low gradient does not necessarily exclude severe aortic stenosis, even when the ejection fraction is normal!!

TAVR is an excellent alternative to traditional Aortic Valve Surgery but increased risk of stroke and vascular injury and the need for a permanent pacemaker.