Severe Aortic Valve Disease: TAVR in Four Ages and Four Etiologies

Age 25 y/o Congenital, 50 y/o Bicuspid, 75 y/o Rheumatic, 100 y/o Degenerative

Samin K. Sharma, MD, FACC, FSCAI
Director Clinical & Interventional Cardiology
President Mount Sinai Heart Network
Dean, International Clinical Affiliations
Anandi Lal Sharma Professor of Medicine (Cardiology)

Cardiovascular Institute
Mount Sinai Hospital, New York

COI: No relationship to disclose for this presentation
Aortic Stenosis

Aortic valve area: Normal 3-4 cm²
AS:
- mild >1.5 cm²
- moderate 1.0-1.5 cm²
- severe <1.0 cm²
- critical <0.7 cm²

Etiology:
Congenital: unicuspid (25 y/o)
bicuspid (50 y/o)
tricuspid

Acquired: rheumatic (75 y/o)
calcific deg (100 y/o)
↑cholesterolemia
rheumatoid

Treatment Choices for AS:

- SAVR
- TAVR: Sapien, CoreValve
- BAV
## Procedure

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Yes</th>
<th>No</th>
<th>Missing</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Coronary Artery Bypass</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Valve Surgery</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>VAD Implanted or Removed</strong></td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes, implanted</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes, explanted</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes, implanted and explanted</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Missing</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other Non-Cardiac Procedure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Unplanned Procedure</strong></td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes, unsuspected patient disease or anatomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes, surgical complication</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Missing</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other Cardiac Procedure</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Transcatheter Aortic Valves Intervention: TAVR vs SAVR

Surgical risk is a continuum (STS risk score)

Operable AS pts

<table>
<thead>
<tr>
<th>STS Risk Score</th>
<th>Low-risk (STS &lt; 3-4%)</th>
<th>Intermediate-risk (3-4 to 8-10%)</th>
<th>High-risk (10-15%)</th>
<th>Extreme-risk (15%)</th>
<th>Too-sick (&gt;50%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>%</td>
<td>~30%</td>
<td>~20%</td>
<td>~20%</td>
<td>~20%</td>
<td>~10%</td>
</tr>
</tbody>
</table>
PARTNER Trial: Aortic Mean Gradient & Valve Area

Mean Gradient (mmHg)

EOA

Mean Gradient

Error bars = ± 1 Std Dev

Valve Area (cm²)

<table>
<thead>
<tr>
<th>Year</th>
<th>Valve Area (cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>159</td>
</tr>
<tr>
<td>1 Year</td>
<td>163</td>
</tr>
<tr>
<td>2 Years</td>
<td>44</td>
</tr>
<tr>
<td>3 Years</td>
<td>31</td>
</tr>
<tr>
<td>4 Years</td>
<td>15</td>
</tr>
<tr>
<td>5 Years</td>
<td>15</td>
</tr>
</tbody>
</table>

N =
PARTNER Trial Cohort B: Inoperable Extreme Risk
Rate of Death (N=358)

Hazard ratio, 0.56 (95% CI 0.43–0.73)
P<0.001

CoreValve Extreme Risk: No Randomization
1 Year Mortality (N=487)

Makkar et al., NEJM 2012;366:1696
Popma et al, JACC 2014;63:1972
PARTNER Trial Cohort A: Primary Endpoints at 3-Yr

Death from Any Cause

- Major drawback: ES TAVR had 2x the Stroke rates vs. SAVR

CoreValve Trial High Risk: Primary Endpoints at 3-Yr

Death from Any Cause

Kodali et al., NEJM 2012;366:1686

Deeb et al., JACC 2016;67:2565
PARTNER 2A Trial: Clinical Endpoints (ITT) at 2 Years

Death/stroke
- TAVR (n=1011): 19.3%
- SAVR (n=1021): 21.1%
  \( p=0.33 \)

Death
- TAVR (n=1011): 16.7%
- SAVR (n=1021): 18.0%
  \( p=0.45 \)

All stroke
- TAVR (n=1011): 9.5%
- SAVR (n=1021): 8.9%
  \( p=0.67 \)

Disabling stroke
- TAVR (n=1011): 6.2%
- SAVR (n=1021): 6.4%
  \( p=0.83 \)

Major vasc compl
- TAVR (n=1011): 8.6%
- SAVR (n=1021): 5.5%
  \( p=0.005 \)

PPM
- TAVR (n=1011): 11.8%
- SAVR (n=1021): 10.3%
  \( p=0.29 \)

AKI
- TAVR (n=1011): 3.8%
- SAVR (n=1021): 6.2%
  \( p=0.02 \)

SURTAVI Trial: Clinical Outcomes

TAVR (n=864)  Surgery (n=796)

Primary endpoint: 12.6% (TAVR) vs 14.0% (Surgery)

Death: 11.4% (TAVR) vs 11.6% (Surgery)

Stroke: 6.2% (TAVR) vs 8.4% (Surgery)

Disabling stroke: 2.6% (TAVR) vs 4.5% (Surgery)

MACCE: 18.6% (TAVR) vs 18.6% (Surgery)

24 Months

Reardon et al., N Engl J Med 2017;376:1321
TAVR for Low Risk AS patients

STS mortality risk of <3%

One Trial OUS: Notion Trial (Completed)- CoreValve

Two Trials in US have started:
- PARTNER-3 of Sapien-3 vs SAVR (n=1228)
- Evolut-R CoreValve vs SAVR (n=1200)

Trials
NOTION Trial: Clinical Outcomes at 4-5 Years

280 patients with severe AS at low surgical risk for SAVR or TAVR with self-expanding CoreValve

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>TAVR (n=145)</th>
<th>SAVR (n=135)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Endpoint</td>
<td>29.1%</td>
<td>30.2%</td>
<td>0.56</td>
</tr>
<tr>
<td>Death</td>
<td>20.0%</td>
<td>23.0%</td>
<td>0.85</td>
</tr>
<tr>
<td>Stroke</td>
<td>6.8%</td>
<td>7.3%</td>
<td>0.87</td>
</tr>
<tr>
<td>MI</td>
<td>7.7%</td>
<td>7.8%</td>
<td></td>
</tr>
<tr>
<td>PPM Implantation</td>
<td>43.7%</td>
<td>9.0%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Valve Endocarditis</td>
<td>4.3%</td>
<td>5.9%</td>
<td>0.47</td>
</tr>
</tbody>
</table>

Sondergaard, ePCR, ESC 2017
The PARTNER 3 Trial: Study Design

Symptomatic Severe Calcific Aortic Stenosis
Age <65yrs

Low Risk ASSESSMENT by Heart Team (STS ≤ 3%, TF only)

1:1 Randomization (n=1228)

TF - TAVR (SAPIEN 3)
CT Imaging Sub-Study (n=200)
Actigraphy/QoL Sub-Study (n=100)

Surgery (Bioprosthetic Valve)
CT Imaging Sub-Study (n=200)
Actigraphy/QoL Sub-Study (n=100)

PARTNER 3 Registries

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

Bicuspid Valves (n=100)

ViV (AV and MV) (n=100)

PARTNER 3 Registries

CT Imaging Sub-Study (n=200)
Actigraphy/QoL Sub-Study (n=100)

ACTIVITY 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
Medtronic TAVR in Low Risk Patients

Trial Design & leaflet Sub-study

- **Patient Population: Low Risk Cohort**
  - Determined by Heart Team to be low surgical risk

- **Primary Endpoint:**
  - Safety: Death, all stroke, life-threatening bleed, major vascular complications or AKI at 30 days
  - Efficacy: Death or major stroke at 2 yrs

- **Sample Size:** ~1200 Subjects

- **Follow-up Evaluations:**
  - 30-days, 6-month, 18-month, and 1 through for 5 years

- **Number of Sites:** Up to 80 sites
Transcatheter Aortic Valves Replacement (TAVR)

**Current Indications:** Symptomatic AS

<table>
<thead>
<tr>
<th>Operable AS pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAVR vs TAVR</td>
</tr>
<tr>
<td>TAVR (PARTNER IIA, SURTAVI)</td>
</tr>
<tr>
<td>TAVR/SAVR</td>
</tr>
<tr>
<td>TAVR</td>
</tr>
<tr>
<td>FUTILE ?BAV</td>
</tr>
</tbody>
</table>

**Low-risk**
- STS: <3%
- ~30%

**Intermediate-risk**
- 3-4 to 8-10%
- ~20%

**High-risk**
- 10-15%
- ~20%

**Extreme-risk**
- 15-50%
- ~20%

**Too-sick**
- >50%
- ~10%

Pt with prohibitive surgical risk are appropriate for TAVR even with low STS risk:
- hostile mediastinum, egg-shell aorta, RT
- prior CABG with IM stuck to mediastinum
- severe COPD, extreme frailty

FDA approved two RCT of low risk AS for both Sapien-3 and Evolut-R vs SAVR are ongoing.
### Recommendations for Choice of Interventions in AS

<table>
<thead>
<tr>
<th>COR</th>
<th>LOE</th>
<th>RECOMMENDATIONS</th>
<th>COMMENT/RATIONALE</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>C</td>
<td>For patients in whom TAVR or high-risk surgical AVR is being considered, a heart valve team consisting of an integrated, multidisciplinary group of healthcare professionals with expertise in VHD, cardiac imaging, interventional cardiology, cardiac anesthesia, and cardiac surgery should collaborate to provide optimal patient care.</td>
<td>2014 recommendation remains current.</td>
</tr>
<tr>
<td>I</td>
<td>B-NR</td>
<td>Surgical AR is recommended for symptomatic patients with severe AS (Stage D) and asymptomatic patients with severe AS (Stage C) who meet an indication for AVR when surgical risk is low or intermediate.</td>
<td>MODIFIED: LOE updated from A to B-NR. Prior recommendations for intervention choice did not specify patient symptoms. The patient population recommended for surgical AVR encompasses both symptomatic and asymptomatic patients who meet an indication for AVR with low-to-intermediate surgical risk. This is opposed to the patient population recommended for TAVR, in whom symptoms are required to be present. Thus, all recommendations for type of intervention now specify the asymptomatic status of the patient.</td>
</tr>
<tr>
<td>I</td>
<td>A</td>
<td>Surgical AVR or TAVR is recommended for symptomatic patients with severe AS (Stage D) and high risk for surgical AVR, depending on patient-specific procedural risks, values, and preferences.</td>
<td>MODIFIED: COR updated from IIa to I, LOE updated from B to A. Longer-term follow-up and additional RCTs have demonstrated that TAVR is equivalent to surgical AVR for severe symptomatic AS when surgical risk is high.</td>
</tr>
<tr>
<td>I</td>
<td>A</td>
<td>TAVR is recommended for symptomatic patients with severe AS (Stage D) and a prohibitive risk for surgical AVR who have a predicted post-TAVR survival greater than 12 months.</td>
<td>MODIFIED: LOE updated from B to A. Longer-term follow-up from RCTs and additional observational studies has demonstrated the benefit of TAVR in patients with a prohibitive surgical risk.</td>
</tr>
<tr>
<td>I</td>
<td>B-R</td>
<td>TAVR is a reasonable alternative to surgical AVR for symptomatic patients with severe AS (Stage D) and an intermediate surgical risk, depending on patient-specific procedural risks, values, and preferences.</td>
<td>NEW: New RCT showed noninferiority of TAVR to surgical AVR in symptomatic patients with severe AS at intermediate surgical risk.</td>
</tr>
<tr>
<td>IIb</td>
<td>C</td>
<td>Percutaneous aortic balloon dilation may be considered as a bridge to surgical AVR or TAVR for symptomatic patients with severe AS.</td>
<td>2014 recommendation remains current.</td>
</tr>
<tr>
<td>III: No Benefit</td>
<td>B</td>
<td>TAVR is not recommended in patients in whom existing comorbidities would preclude the expected benefit from correction of AS.</td>
<td>2014 recommendation remains current.</td>
</tr>
</tbody>
</table>

_Nishimura et al., J Am Coll Cardiol 2017;70:252_
TAVR in Bicuspid Aortic Valve Disease
Clinical Outcomes

Mylotte et al., J Am Coll Cardiol 2014;63:2330
TAVR in Evolution (2017+)
Future Clinical Indications

- Valve-in-valve for bio-prosthetic AV failure
- Predominant Aortic regurgitation (AR, AI)
- Bicuspid aortic valve stenosis
- Low flow-low gradient AS
- Asymptomatic severe AS *(Early TAVR)*
- Moderate AS with CHF Class III-IV *(Unload TAVR)*