TAVR IN INTERMEDIATE-RISK PATIENTS

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Interventional Cardiologist

Evangelismos General Hospital
The Burden of Valve Disease

Prevalence

Survival

Nkomo. Lancet 2006;368:1005-1011
NATURAL HISTORY OF AS

TAVR

- Standard treatment for severe AS in high risk or inoperable patients
- Expansion to intermediate and low risk patients
- More than 200,000 TAVRs implanted worldwide
- Remarkable increase in the number of centers
- Multiple areas were evidence and even expert consensus are lacking
**TAVR vs Medical Therapy**

**A**
- Death from any cause (%)
- Hazard ratio, 0.55 (95% CI, 0.40–0.74)
- $P < 0.001$
- No at risk:
  - TAVI: 179, 138, 122, 67, 26
  - Standard therapy: 179, 121, 83, 41, 12

**B**
- Death from cardiovascular cause (%)
- Hazard ratio, 0.39 (95% CI, 0.27–0.56)
- $P < 0.001$
- No at risk:
  - TAVI: 179, 138, 122, 67, 26
  - Standard therapy: 179, 121, 83, 41, 12

TAVR vs Medical Therapy

5 Year Mortality in Inoperable Patients

TAVR vs. AVR in EU (est. 2011)
TAVR 16.9% of all AVR procedures

TAVR Categories
(risk is a continuum)

Operable AS patients

Too Sick
Inoperable
Low-Intermediate Risk
High Risk

90%
10%
FDA Approval
2005 to 2015: 68,936 procedures, Previous year range 10 to 600 TAVR/year
HEART TEAM
2017 ESC/EACTS Guidelines for the management of valvular heart disease
Aspects to be considered by the Heart Team for the decision between SAVR and TAVI in patients at increased surgical risk

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Favours TAVI</th>
<th>Favours SAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>STS/EuroSCORE II &lt;4% (logistic EuroSCORE I&lt;10%)</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>STS/EuroSCORE II ≥4% (logistic EuroSCORE I ≥10%)</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Presence of severe comorbidity (not adequately reflected by scores)</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Age &lt;75 years</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Age ≥75 years</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Previous cardiac surgery</td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>
Aspects to be considered by the Heart Team for the decision between SAVR and TAVI in patients at increased surgical risk (continued)

<table>
<thead>
<tr>
<th>Clinical characteristics (continued)</th>
<th>Favours TAVI</th>
<th>Favours SAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frailty</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Restricted mobility and conditions that may affect the rehabilitation process after the procedure</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Suspicion of endocarditis</td>
<td></td>
<td>+</td>
</tr>
</tbody>
</table>

Anatomical and technical aspects

| Favourable access for transfemoral TAVI | +            |
| Unfavourable access (any) for TAVI    | +            |
Aspects to be considered by the Heart Team for the decision between SAVR and TAVI in patients at increased surgical risk

(continued)

<table>
<thead>
<tr>
<th>Anatomical and technical aspects (continued)</th>
<th>Favours TAVI</th>
<th>Favours SAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sequelae of chest radiation</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Porcelain aorta</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Presence of intact coronary bypass grafts at risk when sternotomy is performed</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Expected patient–prosthesis mismatch</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Severe chest deformation or scoliosis</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Short distance between coronary ostia and aortic valve annulus</td>
<td></td>
<td>+</td>
</tr>
</tbody>
</table>
Aspects to be considered by the Heart Team for the decision between SAVR and TAVI in patients at increased surgical risk (continued)

<table>
<thead>
<tr>
<th>Cardiac conditions in addition to aortic stenosis that require consideration for concomitant intervention (continued)</th>
<th>Favours TAVI</th>
<th>Favours SAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe primary mitral valve disease, which could be treated surgically</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Severe tricuspid valve disease</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Aneurysm of the ascending aorta</td>
<td></td>
<td>+</td>
</tr>
<tr>
<td>Septal hypertrophy requiring myectomy</td>
<td></td>
<td>+</td>
</tr>
</tbody>
</table>
TAVR was superior to standard therapy in patients with symptomatic severe aortic stenosis who were not candidates for surgery AND was equivalent to surgery in high-risk patients.
All-Cause Mortality (ITT)
All Patients

PARTNER 1A trial
TAVR non-inferior to SAVR

CoreValve US Pivotal trial
TAVR superior to SAVR

Popma et al, JACC 2013
Surgery:

- "Play of Chance": ~5%
- Extreme Risk: ~10%
- High Risk: ~10%
- Intermed. Risk: ~15%
- Low Risk: ~60%

TAVR:

- No
- Preferred
- OK
- SURTAVI Partner II

TAVR or AVR

Futile: ~5%
Transcatheter or Surgical Aortic-Valve Replacement in Intermediate-Risk Patients

Transcatheter or Surgical Aortic Valve Replacement in Intermediate Risk Patients with Aortic Stenosis:

Final Results from the PARTNER 2A Trial

Craig R. Smith, MD
on behalf of the PARTNER Trial Investigators

ACC 2016 | Chicago | April 2, 2016
The PARTNER 2A Trial
Study Design

Symptomatic Severe Aortic Stenosis

ASSESSMENT by Heart Valve Team
Operable (STS ≥ 4%)

Randomized Patients
n = 2032

ASSESSMENT:
Transfemoral Access

Yes

Transfemoral (TF)

1:1 Randomization (n = 1550)

TF TAVR (n = 775)

Surgical AVR (n = 775)

No

Transapical (TA) / TransAortic (TAo)

1:1 Randomization (n = 482)

TA/TAo TAVR (n = 236)

Surgical AVR (n = 246)

Primary Endpoint: All-Cause Mortality or Disabling Stroke at Two Years
Primary Endpoint (ITT)
All-Cause Mortality or Disabling Stroke

HR [95% CI] = 0.89 [0.73, 1.09]
p (log rank) = 0.253

Number at risk:

<table>
<thead>
<tr>
<th></th>
<th>Surgery</th>
<th>TAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1021</td>
<td>1011</td>
</tr>
<tr>
<td>3</td>
<td>838</td>
<td>918</td>
</tr>
<tr>
<td>6</td>
<td>812</td>
<td>901</td>
</tr>
<tr>
<td>9</td>
<td>783</td>
<td>870</td>
</tr>
<tr>
<td>12</td>
<td>770</td>
<td>842</td>
</tr>
<tr>
<td>15</td>
<td>747</td>
<td>825</td>
</tr>
<tr>
<td>18</td>
<td>735</td>
<td>811</td>
</tr>
<tr>
<td>21</td>
<td>717</td>
<td>801</td>
</tr>
<tr>
<td>24</td>
<td>695</td>
<td>774</td>
</tr>
</tbody>
</table>

All-Cause Mortality or Disabling Stroke (%) vs Months from Procedure.
Primary Endpoint (ITT)
All-cause Mortality or Disabling Stroke

TAVR
n = 1011
19.3%

SAVR
n = 1021
21.1%

Relative Risk Ratio 0.92
Upper 1-sided 97.5%CI 1.09

Non-Inferiority p-value = 0.001

Pre-specified non-inferiority margin = 1.2

Favors TAVR
Risk ratio (test/control)
Favors Surgery

Primary Non-Inferiority Endpoint Met
# Primary Endpoint Subgroup Analysis

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>TAVR (%)</th>
<th>AVR (%)</th>
<th>Hazard Ratio (95% CI)</th>
<th>HR (95% CI)</th>
<th>p-value for interaction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Overall</strong></td>
<td>19.3</td>
<td>21.1</td>
<td>0.89 [0.73-1.09]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 85</td>
<td>18.0</td>
<td>19.5</td>
<td>0.90 [0.69-1.17]</td>
<td>0.89 [0.65-1.20]</td>
<td>0.96</td>
</tr>
<tr>
<td>≥ 85</td>
<td>21.5</td>
<td>23.6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>16.9</td>
<td>20.3</td>
<td>0.81 [0.59-1.10]</td>
<td>0.96 [0.74-1.25]</td>
<td>0.37</td>
</tr>
<tr>
<td>Male</td>
<td>21.4</td>
<td>21.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>STS Score</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 5</td>
<td>15.8</td>
<td>18.4</td>
<td>0.84 [0.61-1.16]</td>
<td>0.94 [0.73-1.21]</td>
<td>0.60</td>
</tr>
<tr>
<td>&gt; 5</td>
<td>22.4</td>
<td>23.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LV Ejection Fraction</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 55</td>
<td>19.1</td>
<td>21.5</td>
<td>0.84 [0.56-1.25]</td>
<td>1.11 [0.81-1.53]</td>
<td>0.27</td>
</tr>
<tr>
<td>&gt; 55</td>
<td>20.1</td>
<td>18.0</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Mod or Severe Mitral Regurgitation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>17.8</td>
<td>20.3</td>
<td>0.85 [0.67-1.08]</td>
<td>1.00 [0.64-1.57]</td>
<td>0.53</td>
</tr>
<tr>
<td>Yes</td>
<td>25.9</td>
<td>24.4</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Previous CABG</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>20.6</td>
<td>22.2</td>
<td>0.91 [0.73-1.13]</td>
<td>0.82 [0.53-1.27]</td>
<td>0.69</td>
</tr>
<tr>
<td>Yes</td>
<td>15.3</td>
<td>18.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Peripheral Vascular Disease</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>18.2</td>
<td>20.7</td>
<td>0.85 [0.67-1.09]</td>
<td>0.99 [0.71-1.40]</td>
<td>0.47</td>
</tr>
<tr>
<td>Yes</td>
<td>22.3</td>
<td>22.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>15 Foot Walk Test</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>≤ 7 secs</td>
<td>17.7</td>
<td>20.9</td>
<td>0.82 [0.62-1.09]</td>
<td>0.97 [0.71-1.31]</td>
<td>0.43</td>
</tr>
<tr>
<td>&gt; 7 secs</td>
<td>20.7</td>
<td>20.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Access Route</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transfemoral</td>
<td>16.8</td>
<td>20.4</td>
<td>0.79 [0.62-1.00]</td>
<td>1.21 [0.84-1.74]</td>
<td>0.06</td>
</tr>
<tr>
<td>Transthoracic</td>
<td>27.7</td>
<td>23.4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Other Clinical Endpoints (ITT)  
At 30 Days and 2 Years

<table>
<thead>
<tr>
<th>Events (%)</th>
<th>30 Days</th>
<th>2 Years</th>
<th>p-value*</th>
<th>30 Days</th>
<th>2 Years</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rehospitalization</td>
<td>6.5 (TAVR)</td>
<td>6.5 (Surgery)</td>
<td>0.99</td>
<td>19.6 (TAVR)</td>
<td>17.3 (Surgery)</td>
<td>0.22</td>
</tr>
<tr>
<td>MI</td>
<td>1.2 (TAVR)</td>
<td>1.9 (Surgery)</td>
<td>0.22</td>
<td>3.6 (TAVR)</td>
<td>4.1 (Surgery)</td>
<td>0.56</td>
</tr>
<tr>
<td>Major Vascular Complications</td>
<td>7.9 (TAVR)</td>
<td>5.0 (Surgery)</td>
<td>0.008</td>
<td>8.6 (TAVR)</td>
<td>5.5 (Surgery)</td>
<td>0.006</td>
</tr>
<tr>
<td>Life-Threatening / Disabling Bleeding</td>
<td>10.4 (TAVR)</td>
<td>43.4 (Surgery)</td>
<td>&lt;0.001</td>
<td>17.3 (TAVR)</td>
<td>47.0 (Surgery)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AKI (Stage III)</td>
<td>1.3 (TAVR)</td>
<td>3.1 (Surgery)</td>
<td>0.006</td>
<td>3.8 (TAVR)</td>
<td>6.2 (Surgery)</td>
<td>0.02</td>
</tr>
<tr>
<td>New Atrial Fibrillation</td>
<td>9.1 (TAVR)</td>
<td>26.4 (Surgery)</td>
<td>&lt;0.001</td>
<td>11.3 (TAVR)</td>
<td>29.3 (Surgery)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>New Permanent Pacemaker</td>
<td>8.5 (TAVR)</td>
<td>6.9 (Surgery)</td>
<td>0.17</td>
<td>11.8 (TAVR)</td>
<td>10.3 (Surgery)</td>
<td>0.29</td>
</tr>
<tr>
<td>Re-intervention</td>
<td>0.4 (TAVR)</td>
<td>0.0 (Surgery)</td>
<td>0.05</td>
<td>1.4 (TAVR)</td>
<td>0.6 (Surgery)</td>
<td>0.09</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>0.0 (TAVR)</td>
<td>0.0 (Surgery)</td>
<td>NA</td>
<td>1.2 (TAVR)</td>
<td>0.7 (Surgery)</td>
<td>0.22</td>
</tr>
</tbody>
</table>

*Event rates are KM estimates, p-values are point in time
NYHA Class (ITT)  
All Patients

All $p < 0.001$ for change from baseline to each time point

<table>
<thead>
<tr>
<th></th>
<th>TAVR</th>
<th>Surgery</th>
<th>TAVR</th>
<th>Surgery</th>
<th>TAVR</th>
<th>Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>1011</td>
<td>1020</td>
<td>875</td>
<td>977</td>
<td>817</td>
<td>899</td>
</tr>
<tr>
<td>Number at risk</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$\text{p = 0.90}$  
$\text{p = 0.0013}$  
$\text{p = 0.97}$
**Echocardiography Findings (VI)**

**Aortic Valve Area**

<table>
<thead>
<tr>
<th>No. of Echos</th>
<th>Surgery</th>
<th>TAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Echos</td>
<td>861</td>
<td>899</td>
</tr>
<tr>
<td>30 Day</td>
<td>727</td>
<td>829</td>
</tr>
<tr>
<td>1 Year</td>
<td>590</td>
<td>695</td>
</tr>
<tr>
<td>2 Year</td>
<td>488</td>
<td>567</td>
</tr>
</tbody>
</table>

*p = NS*

Error bars represent ± Standard Deviation
Paravalvular Regurgitation (VI)
3-Class Grading Scheme

No. of echos

<table>
<thead>
<tr>
<th></th>
<th>30 Days</th>
<th>2 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAVR</td>
<td>872</td>
<td>600</td>
</tr>
<tr>
<td>Surgery</td>
<td>757</td>
<td>514</td>
</tr>
</tbody>
</table>

- P < 0.001
- ≥ Moderate 8.0%
- Mild 26.8%
- ≥ Moderate 0.6%
- Mild 3.5%
Severity of PVR at 30 Days and All-cause Mortality at 2 Years (VI)

Overall Log-Rank $p = 0.001$

Moderate/Severe (reference = None/Trace) $p (\text{Log-Rank}) < 0.001$

Mild (reference = None/Trace) $p (\text{Log-Rank}) = 0.82$

Number at risk:
- Moderate/Severe: 36, 32, 32, 26, 26, 24, 22, 22, 22, 21
- Mild: 219, 204, 199, 194, 188, 184, 182, 180, 175
- None/Trace: 701, 678, 664, 647, 628, 621, 612, 605, 585
In intermediate-risk patients with symptomatic severe aortic stenosis, results from the PARTNER 2A trial demonstrated that...

- TAVR using SAPIEN XT and surgery were similar (non-inferior) for the primary endpoint (all-cause mortality or disabling stroke) at 2 years.
- In the transfemoral subgroup (76% of patients), TAVR using SAPIEN XT significantly reduced all-cause mortality or disabling stroke vs. surgery (ITT: p = 0.05, AT: p = 0.04).
The PARTNER 2A Trial
Conclusions (2)

• Other clinical outcomes:
  – TAVR reduced AKI, severe bleeding, new AF, and LOS
  – Surgery reduced vascular complications and PVR

• The SAPIEN XT valve significantly increased echo AVA compared to surgery.

• In the SAPIEN XT TAVR cohort, moderate or severe PVR, but not mild PVR, was associated with increased mortality at 2 years.
SAPIEN 3 Transcatheter Aortic Valve Replacement Compared with Surgery in Intermediate-Risk Patients: A Propensity Score Analysis

Vinod H. Thourani, MD
on behalf of The PARTNER Trial Investigators
SAPIEN Platforms in PARTNER
Device Evolution

Valve Technology

SAPIEN

SAPIEN XT

SAPIEN 3

Sheath Compatibility

22-24F

16-20F

14-16F

Available Valve Sizes

23 mm

26 mm

23 mm

26 mm

29 mm

20 mm

23 mm

26 mm

29 mm
The PARTNER 2A and S3i Trials
Study Design

Intermediate Risk Symptomatic Severe Aortic Stenosis

Intermediate Risk ASSESSMENT by Heart Valve Team

P2 S3i
n = 1078

ASSESSMENT: Optimal Valve Delivery Access

Transfemoral (TF)

Transapical / Transaortic (TA/TAo)

TF TAVR SAPIEN 3

TA/TAo TAVR SAPIEN 3

P2A
n = 2032

ASSESSMENT: Transfemoral Access

Yes

Transfemoral (TF)

1:1 Randomization

TF TAVR SAPIEN XT VS Surgical AVR

No

Transapical / TransAortic (TA/TAo)

1:1 Randomization

TA/Tao TAVR SAPIEN 3 VS Surgical AVR

Primary Endpoint: All-Cause Mortality, All Stroke, or Mod/Sev AR at One Year (Non-inferiority Propensity Score Analysis)
Primary Endpoint - Non-inferiority Death, Stroke, or AR ≥ Mod at 1 Year (VI)

Weighted Difference  -9.2%
Upper 1-sided 95% CI  -6.0%
Non-Inferiority p-value < 0.001

Pre-specified non-inferiority margin = 7.5%

Primary Non-Inferiority Endpoint Met
Superiority Analysis
Components of Primary Endpoint (VI)

**Mortality**
- Favors TAVR
- Favors Surgery
- 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 > Moderate**
- Weighted Difference: +1.2%
- Lower 2-sided 95% CI: +0.2%
- Superiority Testing p-value = 0.0149
Paravalvular Regurgitation 3-Class Grading Scheme (VI)

No. of echos

<table>
<thead>
<tr>
<th>Procedure</th>
<th>30 Days</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>P2A Surgery</td>
<td>755</td>
<td>610</td>
</tr>
<tr>
<td>S3i TAVR</td>
<td>992</td>
<td>875</td>
</tr>
</tbody>
</table>

P < 0.001

- 100%  
- 80%  
- 60%  
- 40%  
- 20%  
- 0%  

TAVR  
Surgery

≥ Moderate
- 1.5%

Mild
- 39.8%

None/Trace

Severe

Moderate

Mild

No/Trace

P < 0.001
Primary Endpoint (ITT)
All-cause Mortality or Disabling Stroke

TAVR
n = 1011
19.3%

SAVR
n = 1021
21.1%

Relative Risk Ratio 0.92
Upper 1-sided 97.5% CI 1.09

Non-Inferiority p-value = 0.001

Pre-specified non-inferiority margin = 1.2

Risk ratio (test/control)

Primary Non-Inferiority Endpoint Met
Transcatheter aortic valve replacement versus surgical valve

Research in context

Evidence before this study
Before we did the PARTNER 2A and SAPIEN 3 studies, clinical trial evidence comparing transcatheter aortic valve replacement (TAVR) to surgery was mainly limited to patients at high risk of death during surgery. Data from large national registries have now indicated a global trend towards TAVR being used in lower-risk populations despite little rigorous clinical trial evidence for this practice. We searched MEDLINE on Jan 31, 2016, with the terms “transcatheter aortic valve implantation”, “transcatheter aortic valve implantation in low risk patients”, “transcatheter aortic valve implantation in intermediate risk patients”, “transcatheter aortic valve replacement in low risk patients”, “transcatheter aortic valve replacement in intermediate risk patients”, “transcatheter aortic valve replacement in intermediate risk patients”, “surgical aortic valve replacement”, and “surgical aortic valve replacement in intermediate risk patients” in English with no date limitations. The published studies include a small randomised trial and several non-adjudicated comparisons between TAVR and surgery in intermediate-risk patients. These studies did not use neurologists for stroke assessment, a clinical events committee to adjudicate outcomes, or core laboratories for analysis of imaging studies.

Added value of this study
We show TAVR with SAPIEN 3 to be superior to surgery at 1 year follow-up with lower rates of all-cause mortality, stroke, and the composite endpoint of mortality, stroke, and moderate or severe aortic regurgitation, but higher rates of moderate or severe regurgitation. Our analysis is the first rigorously designed and carried out clinical study to compare TAVR with the SAPIEN 3 device with surgery in intermediate-risk patients. The prespecified propensity analysis allows for meaningful comparisons between the two groups.

Implications of all the available evidence
TAVR should be considered as the preferred alternative to surgery in intermediate-risk patients and future should consider expanding the indications for TAVR.
Transcatheter Aortic Valve Replacement with a Self-Expanding Prosthesis or Surgical Aortic Valve Replacement in Intermediate-Risk Patients: First Results from the SURTAVI Clinical Trial

Michael J. Reardon, MD
For the SURTAVI Investigators
All-Cause Mortality or Disabling Stroke

24 Months

<table>
<thead>
<tr>
<th></th>
<th>TAVR</th>
<th>SAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.6%</td>
<td>14.0%</td>
<td></td>
</tr>
</tbody>
</table>

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>SAVR</th>
<th>TAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>796</td>
<td>864</td>
<td></td>
</tr>
<tr>
<td>674</td>
<td>755</td>
<td></td>
</tr>
<tr>
<td>555</td>
<td>612</td>
<td></td>
</tr>
<tr>
<td>407</td>
<td>456</td>
<td></td>
</tr>
<tr>
<td>241</td>
<td>272</td>
<td></td>
</tr>
</tbody>
</table>
Primary Endpoint

PP > 0.999 meets noninferiority

Difference in 24-month incidence
TAVR - SAVR

<table>
<thead>
<tr>
<th>TAVR (95% CI)</th>
<th>SAVR (95% CI)</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.6% (10.2%, 15.3%)</td>
<td>14.0% (11.4%, 17.0%)</td>
<td>-1.4% (-5.2%, 2.3%)</td>
</tr>
</tbody>
</table>
Disabling Stroke

24 Months

<table>
<thead>
<tr>
<th></th>
<th>TAVR</th>
<th>SAVR</th>
<th>95% CI for Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage</td>
<td>2.6%</td>
<td>4.5%</td>
<td>-4.0, 0.1</td>
</tr>
</tbody>
</table>

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>SAVR</th>
<th>TAVR</th>
</tr>
</thead>
<tbody>
<tr>
<td>24 Months Post-Procedure</td>
<td>796</td>
<td>864</td>
</tr>
<tr>
<td>6</td>
<td>674</td>
<td>755</td>
</tr>
<tr>
<td>12</td>
<td>555</td>
<td>612</td>
</tr>
<tr>
<td>18</td>
<td>407</td>
<td>456</td>
</tr>
<tr>
<td>24</td>
<td>241</td>
<td>272</td>
</tr>
</tbody>
</table>
## 30-Day Safety and Procedure-related Complications

<table>
<thead>
<tr>
<th></th>
<th>TAVR (N=864)</th>
<th>SAVR (N=796)</th>
<th>95% CI for Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality or disabling stroke</td>
<td>2.8</td>
<td>3.9</td>
<td>-2.8, 0.7</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>2.2</td>
<td>1.7</td>
<td>-0.9, 1.8</td>
</tr>
<tr>
<td>Disabling stroke</td>
<td>1.2</td>
<td>2.5</td>
<td>-2.6, 0.1</td>
</tr>
<tr>
<td>All stroke</td>
<td>3.4</td>
<td>5.6</td>
<td>-4.2, -0.2</td>
</tr>
<tr>
<td>Overt life-threatening or major bleeding</td>
<td>12.2</td>
<td>9.3</td>
<td>-0.1, 5.9</td>
</tr>
<tr>
<td>Transfusion of PRBCs* - n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 units</td>
<td>756 (87.5)</td>
<td>469 (58.9)</td>
<td>24.4, 32.5</td>
</tr>
<tr>
<td>2 – 4 units</td>
<td>48 (5.6)</td>
<td>136 (17.1)</td>
<td>-14.5, -8.5</td>
</tr>
<tr>
<td>≥ 4 units</td>
<td>31 (3.6)</td>
<td>101 (12.7)</td>
<td>-11.7, -6.5</td>
</tr>
<tr>
<td>Acute kidney injury, stage 2-3</td>
<td>1.7</td>
<td>4.4</td>
<td>-4.4, -1.0</td>
</tr>
<tr>
<td>Major vascular complication</td>
<td>6.0</td>
<td>1.1</td>
<td>3.2, 6.7</td>
</tr>
<tr>
<td>Cardiac perforation</td>
<td>1.7</td>
<td>0.9</td>
<td>-0.2, 2.0</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>1.1</td>
<td>3.8</td>
<td>-4.2, -1.1</td>
</tr>
<tr>
<td>Permanent pacemaker implant</td>
<td>25.9</td>
<td>6.6</td>
<td>15.9, 22.7</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>12.9</td>
<td>43.4</td>
<td>-34.7, -26.4</td>
</tr>
</tbody>
</table>
All-Cause Mortality by Pacemaker Implantation

P-value (log-rank) = 0.32

No. at Risk
PPI Prior 87 74 59 46 28
With New PPI 217 198 164 121 56
Without New PPI 559 491 400 300 197
Hemodynamics*

TAVR had significantly better valve performance over SAVR at all follow-up visits

<table>
<thead>
<tr>
<th></th>
<th>Aortic Valve Area, cm²</th>
<th>AV Mean Gradient, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>0.77</td>
<td>12.4</td>
</tr>
<tr>
<td>Discharge</td>
<td>47.2</td>
<td>8.9</td>
</tr>
<tr>
<td>6 Months</td>
<td>47.8</td>
<td>8.3</td>
</tr>
<tr>
<td>12 Months</td>
<td>11.1</td>
<td>8.3</td>
</tr>
<tr>
<td>24 Months</td>
<td>11.8</td>
<td>7.8</td>
</tr>
</tbody>
</table>

TAVR: Transcatheter Aortic Valve Replacement
SAVR: Surgical Aortic Valve Replacement
## Total Aortic Regurgitation*

<table>
<thead>
<tr>
<th></th>
<th>Discharge</th>
<th>12 Months</th>
<th>24 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TAVR</strong> (N=832)</td>
<td>3%</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td><strong>SAVR</strong> (N=707)</td>
<td>61%</td>
<td>93%</td>
<td>93%</td>
</tr>
<tr>
<td><strong>TAVR</strong> (N=599)</td>
<td>5%</td>
<td>9%</td>
<td>9%</td>
</tr>
<tr>
<td><strong>SAVR</strong> (N=506)</td>
<td>34%</td>
<td>90%</td>
<td>90%</td>
</tr>
<tr>
<td><strong>TAVR</strong> (N=299)</td>
<td>5%</td>
<td>5%</td>
<td>5%</td>
</tr>
<tr>
<td><strong>SAVR</strong> (N=244)</td>
<td>60%</td>
<td>60%</td>
<td>60%</td>
</tr>
</tbody>
</table>

*Severe, Moderate, Mild, None/trace
Summary

- TAVR had significantly less 30 day stroke, AKI, atrial fibrillation and transfusion use and a superior quality of life at 30 days.
- TAVR resulted in significantly improved AV hemodynamics with lower mean gradients and larger aortic valve areas than SAVR through 24 months.
- SAVR had less residual aortic regurgitation, major vascular complications and fewer new pacemakers.
- Need for a new pacemaker after TAVR was not associated with increased mortality.
In conclusion: in a comparison between TAVR and surgical replacement in patients with symptomatic, severe aortic stenosis at intermediate risk for surgery, TAVR was a statistically noninferior alternative to surgery with respect to death from any cause or disabling stroke at 24 months. However, each procedure had a different pattern of adverse events.

METHODS
We evaluated the clinical outcomes in intermediate-risk patients with severe, symptomatic aortic stenosis in a randomized trial comparing TAVR (performed with the use of a self-expanding prosthesis) with surgical aortic-valve replacement. The primary end point was a composite of death from any cause or disabling stroke at 24 months in patients undergoing attempted aortic-valve replacement. We used Bayesian analytical methods (with a margin of 0.07) to evaluate the noninferiority of TAVR as compared with surgical valve replacement.
2017 ACC/AHA Guidelines for the management of valvular heart disease

- **Severe AS Symptomatic (stage D)**
  - **Low surgical risk**
    - Surgical AVR (Class I)
  - **Intermediate surgical risk**
    - Surgical AVR (Class I)
    - TAVR (Class IIa)
  - **High surgical risk**
    - Surgical AVR or TAVR (Class I)
  - **Prohibitive surgical risk**
    - TAVR (Class I)

Class I
Class IIa
Class IIb
Major Problems of TAVR

• Paravalvular Regurgitation

• Periprocedural Stroke

• Vascular Complications

• Pacemaker Dependance

• Durability of TAVR devices?

• Subclinical leaflet thrombosis?
Very low pacemaker implantation

Published on 20 December 2021

Before TAVI

- SR, BBB 9%
- SR, BBB, AVB1 3%
- Pacemaker 8%

After TAVI

- SR, BBB, AVB1 14%
- SR, AVB1 10%
- SR 44%

- SR, BBB, AVB1 5%
- Afib 13%
- A fib, BBB 4%
- Pacemaker 10%

✓ ACURATE neo size selection based on perimeter-derived annular diameter
✓ Predilatation balloon 1-3 mm smaller than the perimeter-derived annular diameter
✓ If required, post-dilatation balloon 1-2 mm smaller than the perimeter-derived annular diameter

2.3% new permanent pacemaker rate
10.3% new left bundle branch block rate
Durability of devices: long-term results and clinical outcomes

Mani Arslan1,2 MD; Michael I. Mack3,4 MD

Conclusions

So far, no study demonstrating high rates of SVD in transcatheter valves has been published. However, reliable data are only available at five years of follow-up. Experience with several surgical bioprostheses has taught us that increasing rates of SVD may occur beyond this period. The reported durability of TAVI devices appears adequate for an elderly, high-risk cohort. Long-term studies, much greater than five years in duration, are necessary to prove non-inferior durability compared to surgical valves for younger, lower-risk patients. Because TAVI durability is only established in elderly and high-risk patients, much caution is necessary when considering TAVI in intermediate-risk and younger patients.
Subclinical leaflet thrombosis – a concern, but also an issue?

Published on 2 February 2018

Lars Søndergaard*, MD, DMSc

The Heart Centre, Bispehospitalet, University of Copenhagen, Copenhagen, Denmark

More recently, however, four-dimensional volume-rendered computed tomography (4DCT) has revealed the presence of subclinical leaflet thrombosis as a more common finding after both TAVI and SAVR[4,5,6,7]. Valve leaflet thickening and reduced leaflet motion have, with reference to their CT appearance, been referred to as hypoattenuating leaflet thickening (HALT) and the more severe

So how should the community act at the present time with regard to subclinical leaflet thrombosis? It has been suggested not to change clinical practice with regard to the choice of transcatheter or surgical bioprosthetic valve. TAVI has become an important and lifesaving treatment option for patients with aortic stenosis, and the current uncontrolled data do not justify a limitation in a potential expansion of this therapy. Similarly, there is no case for a change in antithrombotic therapy in favour of anticoagulation at the cost of a higher bleeding rate. Instead, it is recommended to await the ongoing randomised clinical trials between TAVI and SAVR, where a subset of the patients will undergo 4DCT (NCT02675114, NCT02701283), as well as the trial between different antithrombotic regimes (ARTE NCT01559298, AUREA NCT01642134, POPULAR-TAVI NCT02247128, GALILEO NCT02556203, ATLANTIS NCT02664649, AVATAR NCT02735902).

Routine 4DCT to check for subclinical leaflet thrombosis should not be performed outside clinical studies, since this will expose the patients to radiation and contrast without any evidence that a positive silent finding is an indication for anticoagulation therapy. However, patients who after TAVI or SAVR present with a new stroke/TIA or an increased transvalvular gradient may be considered for 4DCT and anticoagulation in case of a leaflet thrombosis.
Updates From NOTION: The First All-Comer TAVR Trial

Lars Sondergaard, MD, DMSc
Professor of Cardiology
Rigshospitalet
Copenhagen, Denmark
### Nordic Aortic Valve Intervention Trial

**The NOTION Trial**

<table>
<thead>
<tr>
<th><strong>Objective:</strong></th>
<th>Compare TAVR vs. SAVR in patients &gt;70 years eligible for surgery (all-comers population)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome:</strong></td>
<td>Composite rate of death from any cause, stroke or myocardial infarction at 1 year (VARC II-defined)</td>
</tr>
<tr>
<td><strong>Secondary outcomes:</strong></td>
<td>Safety and efficacy (NYHA), echocardiographic outcomes (VARC II-defined)</td>
</tr>
<tr>
<td><strong>Design:</strong></td>
<td>Prospective, multicenter, non-blinded, randomized trial</td>
</tr>
<tr>
<td><strong>Enrollment period:</strong></td>
<td>December 2009 - April 2013</td>
</tr>
</tbody>
</table>
All-cause mortality, Stroke or MI

Patients with STS <4%

Functional Class

Aortic Valve Regurgitation

All-cause mortality in TAVR patients according to PVL rate

Conclusions (I)

• The NOTION trial was the first all-comers trial to randomize lower-risk patients to TAVR or SAVR

• TAVR was safe and effective, and comparable to SAVR regarding the composite rate of death from any cause, stroke or myocardial infarction after 2 years
Conclusions (II)

- TAVR resulted in larger EOA and lower gradients, but higher rate of moderate PVL than SAVR.
- These two year data support the safety and effectiveness of TAVR in lower risk patients.
- Longer term data on durability and more randomized clinical trials in lower risk patients are necessary.
Transcatheter aortic valve implantation versus surgical aortic valve replacement for severe aortic stenosis: Results from an intermediate risk propensity-matched population of the Italian OBSERVANT study

Paola D’Errigo a, Marco Barbanti b,c,* , Marco Ranucci d, Francesco Onorati e, Remo Daniel Covello f, Stefano Rosato a, Corrado Tamburino b,c, Francesco Santini e, Gennaro Santoro g, Fulvia Seccareccia a and on behalf of the OBSERVANT Research Group

METHODS:
- 101 Italian centers; unadjusted enrollment = 1383 SAVR and 725 TAVI
  AS pts; propensity matched low-risk population of 266 pts (133 each group, log ES 9.4% for SAVR and 8.9% for TAVI)

RESULTS:
- 30-day mortality was 3.8% for both SAVR and TAVI; similar MI and strokes; increased bleeding with SAVR; increased vasc complications and permanent pacemakers with TAVR
TAVR vs. SAVR in low to intermediate risk patients: A meta-analysis of randomized and observational studies

Conclusions: Comparing with SAVR in patients at low to intermediate surgical risk, TAVR has:

Similar mortality rate and MACCE,
Lower incidence of acute kidney injury and new-onset atrial fibrillation,
Higher major vascular complications and permanent pacemaker implantation.

Zhou Y et al. Int J Cardiol. 2017 Feb 1;228:723-728
TAVI vs SAVR: Low risk RCTs

- **PARTNER 3** (n=1228) 1:1 STS≤4, 10yr FU
- **Evolut R** (n=1256) 1:1 STS≤3, 10yr FU
- **NOTION** 2 (n=992) 1:1 STS≤4, age ≤75yrs

**PARTNER 3 Registries**

- Bicuspid valve (n=100)
- Valve in Valve (n=100)
- Alternate access (n=100)
Conclusions

• TAVR is feasible and safe and more effective in intermediate risk pts

• TAVR is equal or even better than surgery in lower risk pts

• Several questions need to be resolved in this population