Indication, Timing, Assessment and Update on TAVI

Swedish Heart and Vascular Institute

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Interventional Cardiology
Structure Heart Disease
Conflict of Interest

None
Mortality at 30 days (%)

- First-in-Human Transarterial (7): 11.1%
- SOURCE (8): 6.3%
- PARTNER I B (9)*: 5.0%
- PARTNER I B Sapien (10)*: 5.1%
- PARTNER I A (11): 3.7%
- SOURCE XT (12): 4.3%
- PARTNER I B Sapien XT (16): 3.5%
- CE Mark Sapien 3: 2.1%

Edwards Leadership and Expertise in Valve Innovation

- **Starr-Edwards** Mechanical Heart Valve
- **Carpentier-Edwards** PERIMOUNT Pericardial Heart Valve
- **Carpentier-Edwards** PERIMOUNT Magna Ease Pericardial Heart Valve
- **Cribier-Edwards** Transcatheter Heart Valve
- **Edwards SAPIEN** Transcatheter Heart Valve
- **Edwards SAPIEN XT** Transcatheter Heart Valve
- **Edwards SAPIEN 3** Transcatheter Heart Valve
Objective

- Current ACC/AHA guideline
- Evidence based management of TAVI
- Current registry and randomized trial
- Q&A
PRACTICE GUIDELINE

2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease
A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines

Developed in Collaboration With the American Association for Thoracic Surgery, American Society of Echocardiography, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons
Heart Valve Centers of Excellence

The Heart Team Approach

Stages of Heart Valve Disease

Evaluation of Surgical and Interventional Risk
A hospital with the appropriate infrastructure that includes but is not limited to:

- a. Cardiothoracic surgeons experienced in valvular surgery;
- b. Cardiac catheterization laboratory or hybrid operating room/catheterization laboratory;
- c. Non-invasive imaging expertise including transthoracic/transesophageal/3D echocardiography, vascular studies and cardiac CT studies;
- d. Sufficient space, in a sterile environment, to accommodate necessary equipment for cases with and without complications;
- e. Post-procedure intensive care facility with personnel experienced in managing patients who have undergone open-heart valve procedures;
- f. Adequate outpatient clinical care facilities;
The Heart Team Approach

- Evaluation of the suspected valvular heart disease
- Severity of Valve Disease
- Optimization of Medical Therapy
- Diagnostic Testing/subspecialty consultation
Purpose of intervention

- Improve symptoms and/or prolong survival,
- To minimize the risk of VHD-related complications

Indication for intervention

- Symptoms
- Severity of VHD
- The effect on the pulmonary or systemic circulation
- A change in heart rhythm.
## Stages of Progression of Valvular Heart Disease

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>At risk</td>
<td>Patients with risk factors for development of VHD</td>
</tr>
<tr>
<td>B</td>
<td>Progressive</td>
<td>Patients with progressive VHD (mild-to-moderate severity and asymptomatic)</td>
</tr>
<tr>
<td>C</td>
<td>Asymptomatic severe</td>
<td>Asymptomatic patients who have the criteria for severe VHD:</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C1: Asymptomatic patients with severe VHD in whom the left or right ventricle remains compensated</td>
</tr>
<tr>
<td></td>
<td></td>
<td>C2: Asymptomatic patients with severe VHD with decompensation of the left or right ventricle</td>
</tr>
<tr>
<td>D</td>
<td>Symptomatic severe</td>
<td>Patients who have developed symptoms as a result of VHD</td>
</tr>
</tbody>
</table>

VHD indicates valvular heart disease.
Intermediate Risk (Top 33% Surgical Risk)
STS ≥ 4

High Risk (Top 10% Surgical Risk)
STS ≥ 8

Extreme Risk
Inoperable

Cohort C
Do not treat

Low Risk SAVR

80% of patients in STS Database*

14%

6%

Aortic stenosis Patient Population

DISEASE PREVALENCE

Patients Treated in STS Database

- Low Risk: 80%
- Intermediate Risk: 14%
- High Risk: 6%

Disease Prevalence

- Low Risk: 29%
- Intermediate Risk: 27%
- High Risk: 35%
- Extr. Risk: 9%

Clinical Exclusions for TAVI Today:
- Concomitant surgical procedures (CABG, double/triple valve)
- Congenital bicuspid

Risk Assessment by STS Score

- Age
- Gender
- BSA
- Diabetes and hypertension
- Renal function
- Peripheral vascular disease and cerebrovascular disease
- COPD
- Immunosuppression
- Previous CABG
- Reoperation

- LV function
- Heart failure and NYHA class
- CAD
  - LM > 50%
- Arrhythmia
- Atrial fibrillation
- Status of procedure (urgency)
Futility, Benefit, and Transcatheter Aortic Valve Replacement

STS <5%
Hazard ratio, 0.37 (95% CI, 0.13–1.01)
P=0.04

STS 5–14.9%
Hazard ratio, 0.58 (95% CI, 0.41–0.81)
P=0.002

STS ≥15%
Hazard ratio, 0.77 (95% CI, 0.46–1.28)
P=0.31

(J Am Coll Cardiol Intv 2014;7:707–16)
Risk Assessment

- STS risk score provides a reasonable preliminary estimate of risk for the majority of patients.

- The STS score fails to account for certain factors:
  - Anatomic Factors: Porcelain aorta, prior sternotomy with IMA graft or RV immediately posterior to sternum, chest wall radiation or deformity (hostile chest)
  - Severe pulmonary disease (restrictive, ILD)
  - Severe liver disease
  - Severe pulmonary hypertension
  - Dementia and/or severe cerebrovascular disease
  - Frailty
  - Lack of motivation
Medical Comorbidities Outside of STS

- Low-Threshold for Subspecialty Consultation
- Formal Risk Assessment
  - **Pulmonary**: PFT’s (FEV1 < 1L or 40%, DLCO <30%, resting hypoxia or hypercarbia)
  - **Pulmonary Hypertension**: RHC
  - **Cirrhosis**: Child-Pugh and MELD Score
  - **Dementia**: neurocognitive testing, Clinical Dementia Rating Scale, imaging
  - **Frailty**: decreased physiologic reserve and increased vulnerability to stressors
    - “Eyeball test” vs formal assessment
# Evaluation of Surgical and Interventional Risk

Table 7. Risk Assessment Combining STS Risk Estimate, Frailty, Major Organ System Dysfunction, and Procedure-Specific Impediments

<table>
<thead>
<tr>
<th>Risk Category</th>
<th>Low Risk (Must Meet ALL Criteria in This Column)</th>
<th>Intermediate Risk (Any 1 Criterion in This Column)</th>
<th>High Risk (Any 1 Criterion in This Column)</th>
<th>Prohibitive Risk (Any 1 Criterion in This Column)</th>
</tr>
</thead>
<tbody>
<tr>
<td>STS PROM*</td>
<td>&lt;4% AND</td>
<td>4%–8% OR</td>
<td>&gt;8% OR</td>
<td>Predicted risk with surgery of death or major morbidity (all-cause) &gt;50% at 1 year OR</td>
</tr>
<tr>
<td>Frailty†</td>
<td>None AND</td>
<td>1 Index (mild) OR</td>
<td>≥2 Indices (moderate to severe) OR</td>
<td></td>
</tr>
<tr>
<td>Major organ system compromise not to be improved postoperatively‡</td>
<td>None AND</td>
<td>1 Organ system OR</td>
<td>No more than 2 organ systems OR</td>
<td>≥3 Organ systems OR</td>
</tr>
<tr>
<td>Procedure-specific impediment§</td>
<td>None</td>
<td>Possible procedure-specific impediment</td>
<td>Possible procedure-specific impediment</td>
<td>Severe procedure-specific impediment</td>
</tr>
</tbody>
</table>

*STS PROM: Society of Thoracic Surgeons Preoperative Risk Model
†Frailty: Aged ≥60 years
‡Major organ system compromise: Renal, hepatic, pulmonary, or neurologic failure requiring specific intervention or medications postoperatively
§Procedure-specific impediment: Any procedural-related risk exceeding standard surgical risk
Cumulative Records Entered into TVT Registry
May 2012-Feb 2014
(Does not represent all valves deployed)
The majority of patients from 2012 to 2013 and 2014 are from 80 to 90 years of age. Although there were significant differences over time, these differences were not clinically significant. TAVR = transcatheter aortic valve replacement.
**B**

Valve Sheath Access Site of Patients Undergoing TAVR

![Graph showing Valve Sheath Access Site of Patients Undergoing TAVR](image)

- **Femoral**
- **Transapical**
- **Other**

5-Year Outcome After Transcatheter Aortic Valve Implantation

Stefan Toggweiler, MD, Karin H. Humphries, DSc, May Lee, MSc, Ronald K. Binder, MD, Robert R. Moss, MD, Melanie Freeman, MBBS, Jian Ye, MD, Anson Cheung, MD, David A. Wood, MD, John G. Webb, MD

Vancouver, British Columbia, Canada

3 patients (3.4%) had moderate prosthetic valve dysfunction. Survival rates at 1 to 5 years were 83%, 74%, 53%, 42%, and 35%. Median survival time after TAVI was 3.4 years.
Comprehensive Analysis of Mortality Among Patients Undergoing TAVR

Results of the PARTNER Trial

Lars G. Svensson, MD, PhD,*† Eugene H. Blackstone, MD,*† Jeevanantham Rajeswaran, PhD,*† Nicholas Brozzi, MD,† Martin B. Leon, MD,†§ Craig R. Smith, MD,§ Michael Mack, MD,‖ D. Craig Miller, MD,¶ Jeffrey W. Moses, MD,§ E. Murat Tuzcu, MD,* John G. Webb, MD,# Samir Kapadia, MD,* Gregory P. Fontana, MD,** Raj R. Makkar, MD,** David L. Brown, MD,|| Peter C. Block, MD,‖ Robert A. Guyton, MD,‖ Vinod H. Thourani, MD,‖ Augusto D. Pichard, MD,‖ Joseph E. Bavaria, MD, §§ Howard C. Herrmann, MD, §§ Mathew R. Williams, MD,§ Vasilis Babaliaros, MD,‖ Philippe Généreux, MD,§ Jodi J. Akin, MSN,||| for the PARTNER Trial Investigators
### TABLE 1 Categorization of Deaths in PARTNER-A Patients

<table>
<thead>
<tr>
<th>Mode of Death</th>
<th>TF-TAVR</th>
<th>TA-TAVR</th>
<th>AVR</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>N N (%)</td>
<td>N n (%)</td>
<td>N n (%)</td>
<td>p Value</td>
</tr>
<tr>
<td>Heart failure</td>
<td>13 (39)</td>
<td>4 (40)</td>
<td>16 (35)</td>
<td>0.90</td>
</tr>
<tr>
<td>Sudden death</td>
<td>9 (27)</td>
<td>1 (10)</td>
<td>12 (26)</td>
<td>0.50</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>1 (3)</td>
<td>3 (30)</td>
<td>5 (11)</td>
<td>0.05</td>
</tr>
<tr>
<td>Stroke</td>
<td>5 (15)</td>
<td>0 (0)</td>
<td>7 (15)</td>
<td>0.40</td>
</tr>
<tr>
<td>Noncerebral hemorrhage</td>
<td>1 (3)</td>
<td>1 (10)</td>
<td>2 (4.3)</td>
<td>0.60</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1 (3)</td>
<td>0 (0)</td>
<td>1 (2.2)</td>
<td>0.80</td>
</tr>
<tr>
<td>Prosthetic valve endocarditis</td>
<td>0 (0)</td>
<td>1 (10)</td>
<td>1 (2.2)</td>
<td>0.20</td>
</tr>
<tr>
<td>Peripheral arterial disease or abdominal aortic aneurysm</td>
<td>1 (3)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0.40</td>
</tr>
<tr>
<td>Other</td>
<td>1 (3)</td>
<td>0 (0)</td>
<td>1 (2.2)</td>
<td>0.80</td>
</tr>
<tr>
<td>Unknown</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (2.2)</td>
<td>0.60</td>
</tr>
<tr>
<td>Noncardiovascular</td>
<td>39</td>
<td>19</td>
<td>60</td>
<td></td>
</tr>
<tr>
<td>Infection/sepsis</td>
<td>15 (38)</td>
<td>7 (37)</td>
<td>28 (47)</td>
<td>0.60</td>
</tr>
<tr>
<td>Renal disease</td>
<td>6 (15)</td>
<td>0 (0)</td>
<td>6 (10)</td>
<td>0.20</td>
</tr>
<tr>
<td>Malignancy</td>
<td>4 (10)</td>
<td>1 (5.3)</td>
<td>8 (13)</td>
<td>0.60</td>
</tr>
<tr>
<td>Accidental</td>
<td>3 (7.7)</td>
<td>0 (0)</td>
<td>1 (1.7)</td>
<td>0.20</td>
</tr>
<tr>
<td>Respiratory</td>
<td>3 (7.7)</td>
<td>7 (37)</td>
<td>9 (15)</td>
<td>0.02</td>
</tr>
<tr>
<td>Other</td>
<td>8 (20)</td>
<td>2 (10)</td>
<td>7 (12)</td>
<td>0.50</td>
</tr>
<tr>
<td>Unknown</td>
<td>0 (0)</td>
<td>2 (11)</td>
<td>1 (1.7)</td>
<td>0.05</td>
</tr>
<tr>
<td>Uncategorizable</td>
<td>18</td>
<td>17</td>
<td>33</td>
<td></td>
</tr>
</tbody>
</table>

### TABLE 2 Categorization of Deaths in PARTNER-B Patients

<table>
<thead>
<tr>
<th>Mode of Death</th>
<th>Standard Therapy</th>
<th>TF-TAVR</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>N n (%)</td>
<td>N n (%)</td>
<td>p Value</td>
</tr>
<tr>
<td>Heart failure</td>
<td>34 (51)</td>
<td>13 (33)</td>
<td>0.07</td>
</tr>
<tr>
<td>Sudden death</td>
<td>21 (31)</td>
<td>4 (10)</td>
<td>0.02</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>4 (6)</td>
<td>1 (2.5)</td>
<td>0.60</td>
</tr>
<tr>
<td>Stroke</td>
<td>4 (6)</td>
<td>7 (18)</td>
<td>0.10</td>
</tr>
<tr>
<td>Noncerebral hemorrhage</td>
<td>2 (3)</td>
<td>0 (0)</td>
<td>0.50</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0 (0)</td>
<td>2 (5)</td>
<td>0.14</td>
</tr>
<tr>
<td>Prosthetic valve endocarditis</td>
<td>0 (0)</td>
<td>2 (5)</td>
<td>0.14</td>
</tr>
<tr>
<td>Peripheral arterial disease or abdominal aortic aneurysm</td>
<td>0 (0)</td>
<td>1 (2.5)</td>
<td>0.40</td>
</tr>
<tr>
<td>Other</td>
<td>1 (1.5)</td>
<td>2 (5)</td>
<td>0.60</td>
</tr>
<tr>
<td>Unknown</td>
<td>1 (1.5)</td>
<td>5 (12)</td>
<td>0.02</td>
</tr>
<tr>
<td>Noncardiovascular</td>
<td>21</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>Infection/sepsis</td>
<td>7 (33)</td>
<td>10 (31)</td>
<td>&gt;0.90</td>
</tr>
<tr>
<td>Renal disease</td>
<td>3 (14)</td>
<td>3 (9.4)</td>
<td>0.70</td>
</tr>
<tr>
<td>Malignancy</td>
<td>4 (19)</td>
<td>4 (13)</td>
<td>0.70</td>
</tr>
<tr>
<td>Accidental</td>
<td>0 (0)</td>
<td>2 (6.3)</td>
<td>0.50</td>
</tr>
<tr>
<td>Respiratory</td>
<td>3 (14)</td>
<td>5 (16)</td>
<td>&gt;0.90</td>
</tr>
<tr>
<td>Other</td>
<td>1 (4.8)</td>
<td>6 (19)</td>
<td>0.20</td>
</tr>
<tr>
<td>Unknown</td>
<td>3 (14)</td>
<td>2 (6.3)</td>
<td>0.40</td>
</tr>
<tr>
<td>Uncategorizable</td>
<td>47</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>
Randomly assigned 2032 intermediate-risk patients

The primary hypothesis was that TAVR would not be inferior to surgical replacement.

The rate of death from any cause or disabling stroke was similar in the TAVR group and the surgery group.

At 2 years, the Kaplan–Meier event rates were 19.3% in the TAVR group and 21.1% in the surgery group.

TAVR resulted in larger aortic-valve areas and resulted in lower rates of acute kidney injury, severe bleeding, and new-onset atrial fibrillation.

Surgery resulted in fewer major vascular complications and less paravalvular aortic regurgitation.
EuroPCR: Degenerated TAVR Not Uncommon by 10 Years

The median time to valve degeneration was 61 months, although mean survival after TAVR was 51 months, Danny Dvir, MD, of St. Paul’s Hospital in Vancouver.

Freedom from transcatheter heart valve deterioration dropped to around 80% at year 6, then below 40% by year 8.

Baseline renal failure was a risk factor for valve deterioration (hazard ratio 3.22, 95% CI 1.45-7.15).

Dvir's study included 387 patients who underwent TAVR between 2002 and 2011 at two sites. Only two out of 387 patients (0.52%) survived 10 years after the intervention.
Sapien 3 Registry at ACC 2015

The registry included two arms:
(1) 583 high risk and inoperable patients with an average STS score of 8.6;
(2) 1076 intermediate risk patients with an average STS score of 5.3%.
(3) Fifteen percent of patients underwent TAVR with conscious sedation as opposed to general anesthesia.

In the high-risk cohort, 30-day all cause mortality rate was 2.2% with a disabling stroke rate of 0.9%.

The 30-day all-cause mortality of the intermediate risk patients was 1.1% with a disabling stroke rate of 1%.

The rate of permanent pacemaker placement was 13% in the high-risk cohort, and 10.1% in the intermediate risk patients.

The rates of aortic regurgitation were significantly lower than with prior generation devices: moderate aortic regurgitation was 3.7% and severe aortic regurgitation was 0.1%.
### Sapien 3 Intermediate Risk Registry at ACC 2016

#### Unadjusted 1-Year Outcomes: Propensity Score Analysis (as treated)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>TAVR</th>
<th>Surgery</th>
<th>Weighted Difference&lt;sup&gt;a&lt;/sup&gt;</th>
<th>P Value for Superiority</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>7.4%</td>
<td>13.0%</td>
<td>-5.2%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Stroke</td>
<td>4.6%</td>
<td>8.2%</td>
<td>-3.5%</td>
<td>0.0004</td>
</tr>
<tr>
<td>Aortic Regurgitation ≥ Moderate</td>
<td>1.5%</td>
<td>N/A</td>
<td>+1.2%</td>
<td>0.0149</td>
</tr>
</tbody>
</table>

<sup>a</sup> Weighted proportion differences were calculated using the average treatment effect on the treated methods with weights derived based on the sample size of the SAPIEN 3 cohort within each quintile.
We reserve the right to refuse service to anyone at anytime.
Open Issues in TAVR

1. The need for improved risk scores
2. The value of sophisticated, non-invasive imaging
3. Individual design of each prosthesis without the need of aggressive oversizing
4. TAVR for bicuspid valves
5. Low-flow low-gradient AS
6. Outcome for TAVR with pre-existent left ventricular (LV) dysfunction
7. Concomitant mitral regurgitation (MR), tricuspid regurgitation (TR)
8. Coronary artery disease (CAD)
9. Durability of transcatheter heart valves
10. TAVR for failing surgical bioprostheses
11. Expanding indications for aortic regurgitation
12. Lessons from transcatheter aortic valve implantation registries: results in clinical practice
13. Moderate risk for SURTAVI and PARTNER 2
14. A Pathway to Earlier Discharge Following TAVI: Assessment of Safety and Resource Utilization
1. How will this technology be regulated and by what authority?

2. Will the technology be available in all centers to all interested parties or will it be restricted to specialized centers?

3. What training will be required for interventional cardiologists and surgeons, and how will it be accomplished? What criteria will be utilized to grant procedural privileges?

4. What clinical, procedural, administrative, and follow-up data will be collected to ensure rigorous assessment of outcomes across centers and provide a framework for comparative effectiveness research and cost effectiveness assessment?

5. How will patient cohorts who are most and least likely to benefit from this technology be identified?

6. What mechanisms will exist to allow for the careful extension of this technology to the treatment of other groups of patients not included or studied in the initial, randomized clinical trials?

6. How will this technology be reimbursed? Will there be a national coverage determination?