Transcatheter Aortic Valve Replacement (TAVR): The Future

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Outline

1. Severe Aortic Stenosis and Concept of “Operability”
2. Review Data for TAVR in Inoperable and High Risk Patients
3. Vascular Complication Avoidance
4. Stroke Prevention Strategies
5. Novel Applications: Bicuspid, Prior AVR, Aortic Regurgitation
6. Lower risk populations
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Aortic Stenosis is Life Threatening and Progresses Rapidly

Valvular Aortic Stenosis in Adults (Average Course)

- Survival after onset of symptoms 50% at 2 yrs, 20% at 5 yrs
- Surgical intervention should be performed promptly once even minor symptoms occur


Aortic Valve Replacement Improves Survival

A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on Valvular Heart Disease

KEYWORDS
Valvular heart disease;
Echocardiography;
Cardiac surgery

Aim: To identify the characteristics, treatment, and outcomes of contemporary patients with valvular heart disease (VHD) in Europe, and to examine adherence to guidelines.

Methods and results: The Euro Heart Survey on VHD was conducted from April to July 2001 in 92 centres from 25 countries; it included prospectively 5001 adults with moderate to severe native VHD, infective endocarditis, or previous valve intervention. VHD was native in 71.9% of patients and 28.1% had had a previous intervention. Mean age was 64.14 years. Degenerative aetiology were the most frequent in aortic VHD and mitral.

31.8% did not undergo intervention, most frequently because of comorbidities.
Aortic Stenosis Undertreatment is Profound

At least 40% of patients with severe aortic stenosis do not have an AVR
Mortality with standard therapy is worse than with certain metastatic cancers.

### 5-Year Survival Rates

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

Percutaneous Aortic Valve Development

- Professor Alain Cribier (Rouen, France) First described percutaneous aortic valve interventions in 1985

- Proved that a stent could be deployed without removing the diseased native valve

- Implanted first percutaneous aortic valve on a patient on April 16, 2002
Edwards SAPIEN Transcatheter Valve

Bovine pericardial tissue

Stainless steel frame

PET skirt

The Carpentier-Edwards ThermaFix process* is intended to minimize the risk of calcification, helping preserve valve performance.
Edwards SAPIEN

Edwards SAPIEN THV
23 and 26 mm valves

RetroFlex
22 and 24 F sheaths
Self Expanding Technology: CoreValve (Medtronic)

2007 CE Mark
2014 Jan FDA Approval Extreme Risk
2014 Jun FDA Approval High Risk
TAVR Access

1. Transfemoral
2. Direct Aortic
3. Subclavian
4. Transapical
TAVR Patient Evaluation

STS Score

- <4 Low Risk
- 4-8 Intermediate Risk
- >8 High Risk
- Inoperable: >50% death or serious irreversible condition

Agarwal S et al. Heart 2015;101:169-177
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TAVR For Inoperable Patients

1. Edwards Sapien Valve
2. Medtronic Corevalve
TAVR For Inoperable Patients

1. Edwards Sapien Valve
2. Medtronic Corevalve
Cohort B

Transcatheter Aortic-Valve Implantation for Aortic Stenosis in Patients Who Cannot Undergo Surgery

Martin B. Leon, M.D., Craig R. Smith, M.D., Michael Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., David L. Brown, M.D., Peter C. Block, M.D., Robert A. Guyton, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Pamela S. Douglas, M.D., John L. Petersen, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart Pocock, Ph.D., for the PARTNER Trial Investigators*
TAVR Results: Mean Gradient & Valve Area
PARTNER Cohort B
Primary Endpoint

HR [95% CI] = 0.56 [0.43, 0.73]
P (log rank) < .0001

All-Cause Mortality, %

Δ at 1 yr = 20.0%
NNT = 5.0 pts

Δ at 2 yrs = 24.7%
NNT = 4.0 pts

Numbers at Risk

<table>
<thead>
<tr>
<th></th>
<th>Edwards SAPIEN THV</th>
<th>Standard Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers at Risk</td>
<td>179</td>
<td>179</td>
</tr>
<tr>
<td>1 yr</td>
<td>138</td>
<td>124</td>
</tr>
<tr>
<td>2 yr</td>
<td>124</td>
<td>110</td>
</tr>
<tr>
<td>3 yr</td>
<td>110</td>
<td>83</td>
</tr>
<tr>
<td>4 yr</td>
<td>83</td>
<td>62</td>
</tr>
<tr>
<td>5 yr</td>
<td>62</td>
<td>42</td>
</tr>
</tbody>
</table>
All Cause Mortality (ITT): 5 year Follow up

*In an age and gender matched US population without comorbidities, the mortality at 5 years is 40.5%.

HR [95% CI] = 0.50 [0.39, 0.65]
\( p \text{ (log rank)} < 0.0001 \)

Median Survival

Standard Therapy: 11.1 Months
TAVR: 29.7 Months

Kapadia TCT Sept 2014
Repeat Hospitalization: TAVR vs. Standard Treatment

Kapadia TCT Sept 2014
PARTNER B Mean Gradient and Valve Area at 5 years

Kapadia TCT Sept 2014
Stroke following TAVR: Inoperable cohort

**Stroke at 30 Days, 1 Year, and 2 Years**

- **Edwards SAPIEN THV (n = 179)**
  - 30 Days: 7.3%
  - 1 Year: 11.2%
  - 2 Years: 13.8%

- **Standard Therapy (n = 179)**
  - 30 Days: 1.7%
  - 1 Year: 5.5%
  - 2 Years: 5.5%

*P = .01 for Edwards SAPIEN THV vs. Standard Therapy*
Mortality Stratified by Stroke (ITT)
Vascular Complications: TAVR vs. Standard Treatment

For 30 Days:
- Edwards SAPIEN THV: 16.8%
- Standard Therapy: 1.1%

For 1 Year:
- Edwards SAPIEN THV: 17.4%
- Standard Therapy: 2.8%

For 2 Years:
- Edwards SAPIEN THV: 17.4%
- Standard Therapy: 2.8%

All differences are statistically significant at p < .0001.
TAVR For Inoperable Patients

1. Edwards Sapien Valve
2. Medtronic Corevalve
Transcatheter Aortic Valve Replacement Using a Self-Expanding Bioprosthesis in Patients With Severe Aortic Stenosis at Extreme Risk for Surgery

Jeffrey J. Popma, MD,* David H. Adams, MD, † Michael J. Reardon, MD, ‡ Steven J. Yakubov, MD, § Neal S. Kleiman, MD, ‡ David Heimansohn, MD, †|| James Hermiller, Jr, MD, ‡|| G. Chad Hughes, MD, ¶ J. Kevin Harrison, MD, ¶ Joseph Coselli, MD, # Jose Diez, MD, # Ali Kafi, MD, ** Theodore Schreiber, MD, *** Thomas G. Gleason, MD, †† John Conte, MD, ††† Maurice Buchbinder, MD, §§ G. Michael Deeb, MD, ‡‡ Blasé Carabello, MD, ¶¶ Patrick W. Serruys, MD, PriD, ## Sharla Chenoweth, MS, *** Jae K. Oh, MD, ††† for the CoreValve United States Clinical Investigators

Boston, Massachusetts; New York, New York; Houston, Texas; Columbus, Ohio; Indianapolis, Indiana; Durham, North Carolina; Detroit and Ann Arbor, Michigan; Pittsburgh, Pennsylvania; Baltimore, Maryland; Palo Alto, California; Rotterdam, the Netherlands; and Minneapolis and Rochester, Minnesota

JACC 2014;63:1972-81
CoreValve Extreme Risk Clinical Outcomes at 1 and 12 Months

<table>
<thead>
<tr>
<th>Outcome</th>
<th>30 Days (N = 489)</th>
<th>12 Months (N = 489)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death from any cause or major stroke</td>
<td>48 (9.8)</td>
<td>127 (26.0)</td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>From any cause</td>
<td>41 (8.4)</td>
<td>119 (24.3)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>41 (8.4)</td>
<td>88 (18.3)</td>
</tr>
<tr>
<td>Stroke</td>
<td>19 (4.0)</td>
<td>31 (7.0)</td>
</tr>
<tr>
<td>Major</td>
<td>11 (2.3)</td>
<td>19 (4.3)</td>
</tr>
<tr>
<td>Minor</td>
<td>9 (1.9)</td>
<td>14 (3.2)</td>
</tr>
<tr>
<td>TIA</td>
<td>3 (0.6)</td>
<td>5 (1.1)</td>
</tr>
<tr>
<td>MAODE</td>
<td>60 (12.3)</td>
<td>143 (29.2)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>6 (1.2)</td>
<td>9 (2.0)</td>
</tr>
<tr>
<td>Periprocedural</td>
<td>6 (1.2)</td>
<td>6 (1.2)</td>
</tr>
<tr>
<td>Spontaneous</td>
<td>0 (0)</td>
<td>3 (0.7)</td>
</tr>
<tr>
<td>Rhinotilization</td>
<td>5 (1.1)</td>
<td>8 (1.8)</td>
</tr>
<tr>
<td>Major or life-threatening bleeding</td>
<td>179 (36.7)</td>
<td>206 (42.8)</td>
</tr>
<tr>
<td>Life-threatening or disabling</td>
<td>62 (12.7)</td>
<td>83 (17.6)</td>
</tr>
<tr>
<td>Major</td>
<td>121 (24.9)</td>
<td>136 (28.5)</td>
</tr>
<tr>
<td>Major vascular complications</td>
<td>40 (8.2)</td>
<td>41 (8.4)</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>57 (11.8)</td>
<td>57 (11.8)</td>
</tr>
<tr>
<td>Cardiogenic shock</td>
<td>13 (2.7)</td>
<td>13 (2.7)</td>
</tr>
<tr>
<td>Cardiac perforation</td>
<td>9 (1.8)</td>
<td>9 (1.8)</td>
</tr>
<tr>
<td>Device migration</td>
<td>0</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Device embolization</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

P<0.0001

Performance Goal=43%

[26.0% [22.1, 29.9]]

JACC 2014;63:1972-81
CoreValve Hemodynamics and Functional Improvement

JACC 2014;63:1972-81
CoreValve Extreme Risk 2 year Outcomes

![Graph showing All-Cause Mortality and Cardiovascular Mortality](image1)

**Events**, %

<table>
<thead>
<tr>
<th>Event</th>
<th>1 Year</th>
<th>2 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any stroke</td>
<td>7.0</td>
<td>8.7</td>
</tr>
<tr>
<td>Major</td>
<td>4.3</td>
<td>5.1</td>
</tr>
<tr>
<td>Minor</td>
<td>3.2</td>
<td>4.1</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>2.0</td>
<td>2.8</td>
</tr>
<tr>
<td>Reintervention</td>
<td>1.8</td>
<td>1.8</td>
</tr>
<tr>
<td>VARC bleeding</td>
<td>42.8</td>
<td>45.3</td>
</tr>
<tr>
<td>Life threatening or disabling</td>
<td>18.0</td>
<td>20.8</td>
</tr>
<tr>
<td>Major</td>
<td>28.3</td>
<td>29.1</td>
</tr>
<tr>
<td>Major vascular complications</td>
<td>8.4</td>
<td>8.4</td>
</tr>
<tr>
<td>Permanent pacemaker implant</td>
<td>26.4</td>
<td>28.9</td>
</tr>
<tr>
<td>Per ACC guidelines</td>
<td>19.5</td>
<td>22.0</td>
</tr>
</tbody>
</table>

* Percentages obtained from Kaplan Meier estimates
High Risk Operable:
TAVR vs. Surgical Aortic Valve Replacement (SAVR)

1. Edwards Sapien TAVR vs. SAVR
2. Medtronic Corevalve TAVR vs. SAVR
High Risk Operable:
TAVR vs. Surgical Aortic Valve Replacement (SAVR)

1. Edwards Sapien TAVR vs. SAVR
2. Medtronic Corevalve TAVR vs. SAVR
Transcatheter versus Surgical Aortic-Valve Replacement in High-Risk Patients

Craig R. Smith, M.D., Martin B. Leon, M.D., Michael J. Mack, M.D., D. Craig Miller, M.D., Jeffrey W. Moses, M.D., Lars G. Svensson, M.D., Ph.D., E. Murat Tuzcu, M.D., John G. Webb, M.D., Gregory P. Fontana, M.D., Raj R. Makkar, M.D., Mathew Williams, M.D., Todd Dewey, M.D., Samir Kapadia, M.D., Vasilis Bablagiros, M.D., Vinod H. Thourani, M.D., Paul Corso, M.D., Augusto D. Pichard, M.D., Joseph E. Bavaria, M.D., Howard C. Herrmann, M.D., Jodi J. Akin, M.S., William N. Anderson, Ph.D., Duolao Wang, Ph.D., and Stuart J. Pocock, Ph.D., for the PARTNER Trial Investigators*
Echo Aortic Valve Gradients: Sapien TAVR vs. SAVR
PARTNER A Primary Endpoint:
1 Year All-Cause Mortality TAVR vs SAVR

HR [95\% CI] = 0.93 [0.71, 1.22]
P (log rank) = 0.62
Cohort A Quality of Life: TAVR vs. SAVR

![Graph showing quality of life outcomes for TAVR vs. SAVR at baseline, 30 days, 6 months, and 1 year.](image)

- **P-values:**
  - Baseline: P=1.00
  - 30 Days: P<0.001
  - 6 Months: P=0.05
  - 1 Year: P=0.74

- **NYHA Levels:**
  - Dead
  - IV
  - III
  - II
  - I
# High Risk: TAVR vs SAVR

## Table 2. Clinical Outcomes at 30 Days and 1 Year in the Intention-to-Treat Population

<table>
<thead>
<tr>
<th>Outcome</th>
<th>30 Days</th>
<th>1 Year</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Transcatheter Replacement (N = 348)</td>
<td>Surgical Replacement (N = 351)</td>
</tr>
<tr>
<td></td>
<td>no. of patients (%)</td>
<td>no. of patients (%)</td>
</tr>
<tr>
<td><strong>Death</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>From any cause</td>
<td>12 (3.4)</td>
<td>22 (6.5)</td>
</tr>
<tr>
<td>From cardiac causes</td>
<td>11 (3.2)</td>
<td>10 (3.0)</td>
</tr>
<tr>
<td>Repeat hospitalization</td>
<td>25 (4.4)</td>
<td>12 (3.7)</td>
</tr>
<tr>
<td>Death or repeat hospitalization</td>
<td>25 (7.2)</td>
<td>33 (9.7)</td>
</tr>
<tr>
<td><strong>Stroke or transient ischemic attack</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Either</td>
<td>19 (5.5)</td>
<td>8 (2.4)</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>3 (0.9)</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minor</td>
<td>3 (0.9)</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Major</td>
<td>13 (3.8)</td>
<td>7 (2.1)</td>
</tr>
<tr>
<td>Death from any cause or major stroke</td>
<td>24 (6.9)</td>
<td>28 (8.2)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0</td>
<td>2 (0.6)</td>
</tr>
<tr>
<td><strong>Vascular complication</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any</td>
<td>59 (17.0)</td>
<td>13 (3.8)</td>
</tr>
<tr>
<td>Major</td>
<td>38 (11.0)</td>
<td>11 (3.2)</td>
</tr>
<tr>
<td><strong>Acute kidney injury</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine &gt;3 mg/dl (265 μmol/liter)</td>
<td>4 (1.2)</td>
<td>4 (1.2)</td>
</tr>
<tr>
<td>Renal-replacement therapy</td>
<td>10 (2.9)</td>
<td>10 (3.0)</td>
</tr>
<tr>
<td><strong>Major bleeding</strong></td>
<td>32 (9.3)</td>
<td>67 (19.5)</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>0</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>New-onset atrial fibrillation†</td>
<td>30 (8.6)</td>
<td>56 (16.0)</td>
</tr>
<tr>
<td>New pacemaker</td>
<td>13 (3.8)</td>
<td>12 (3.6)</td>
</tr>
</tbody>
</table>

*All percentages are Kaplan–Meier estimates at the specific time point and thus do not equal the number of patients divided by the total number in the study group.
† The presence of new-onset atrial fibrillation was determined in an electrocardiography core laboratory.
Paravalvular Aortic Regurgitation: Sapient TAVR vs. SAVR
CV Mortality Stratified by PV Leak (ITT)

- Moderate or Severe
- None to Mild

Δ at 1 yr = 14.4%
NNT = 6.9 pts

Δ at 2 yr = 9.7%
NNT = 10.3 pts

p (log rank) = 0.381

Numbers at Risk

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>6</th>
<th>12</th>
<th>18</th>
<th>24</th>
</tr>
</thead>
<tbody>
<tr>
<td>None to Mild</td>
<td>147</td>
<td>118</td>
<td>107</td>
<td>95</td>
<td>72</td>
</tr>
<tr>
<td>Moderate or Severe</td>
<td>17</td>
<td>12</td>
<td>11</td>
<td>10</td>
<td>8</td>
</tr>
</tbody>
</table>

Determination of first PV Leak starts with the discharge echo
High Risk Operable:
TAVR vs. Surgical Aortic Valve Replacement (SAVR)

1. Edwards Sapien TAVR vs. SAVR
2. Medtronic Corevalve TAVR vs. SAVR
Primary Endpoint: 1 Year All-cause Mortality

Surgical: 3.3% to 19.1%
Transcatheter: 4.5% to 14.2%

P = 0.04 for superiority

No. at Risk:
- Surgical: 357, 341, 297, 274
- Transcatheter: 390, 377, 353, 329

Adams ACC 2014
All Stroke

Log-rank P=0.10

No. at Risk

Surgical | 357 | 322 | 274 | 249
Transcatheter | 390 | 363 | 334 | 314

Adams ACC 2014
<table>
<thead>
<tr>
<th>Events</th>
<th>1 Month</th>
<th></th>
<th></th>
<th>1 Year</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TAVR</td>
<td>SAVR</td>
<td>P Value</td>
<td>TAVR</td>
<td>SAVR</td>
<td>P Value</td>
</tr>
<tr>
<td>Vascular complications (major), %</td>
<td>5.9</td>
<td>1.7</td>
<td>0.003</td>
<td>6.2</td>
<td>2.0</td>
<td>0.004</td>
</tr>
<tr>
<td>Pacemaker implant, %</td>
<td>19.8</td>
<td>7.1</td>
<td>&lt;0.001</td>
<td>22.3</td>
<td>11.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Bleeding (life threatening or disabling), %</td>
<td>13.6</td>
<td>35.0</td>
<td>&lt;0.001</td>
<td>16.6</td>
<td>38.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>New onset or worsening atrial fibrillation, %</td>
<td>11.7</td>
<td>30.5</td>
<td>&lt;0.001</td>
<td>15.9</td>
<td>32.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Acute kidney injury, %</td>
<td>6.0</td>
<td>15.1</td>
<td>&lt;0.001</td>
<td>6.0</td>
<td>15.1</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

* Percentages reported are Kaplan-Meier estimates and log-rank P values.
Echocardiographic Findings

Post implant, there were significant differences (P < 0.001) between TAVR and SAVR at each time point for both EOA and mean gradient.

Adams ACC 2014
There was significantly lower PVL with SAVR over TAVR at each time point (P<0.001).
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5. Novel Applications: Bicuspid, Prior AVR, Aortic Regurgitation
6. Lower risk populations
Vascular Safety: Get Smaller

Terumo Solopath:
15f insertion, balloon expandable to 19f.
Corevalve compatible
“Original” Edwards SAPIEN Sheaths

22F RetroFlex 3 Sheath
(compatible with 23mm SAPIEN valve)
- Requires a minimum vessel diameter of ≥ 7 mm
- 8.4 mm
- 35 cm

24F RetroFlex 3 Sheath
(compatible with 26mm SAPIEN valve)
- Requires a minimum vessel diameter of ≥ 8 mm
- 9.2 mm
- 35 cm
Edwards SAPIEN vs SAPIEN XT

<table>
<thead>
<tr>
<th>Valve</th>
<th>Valve Size</th>
<th>Sheath ID</th>
<th>Sheath OD</th>
<th>Minimum Vessel Diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAPIEN THV</td>
<td>23mm</td>
<td>22F</td>
<td>25F (8.4mm)</td>
<td>7.0mm</td>
</tr>
<tr>
<td>SAPIEN XT THV</td>
<td>23mm</td>
<td>18F</td>
<td>22F (7.2mm)</td>
<td>6.0mm</td>
</tr>
<tr>
<td>SAPIEN THV</td>
<td>26mm</td>
<td>24F</td>
<td>28F (9.2mm)</td>
<td>8.0mm</td>
</tr>
<tr>
<td>SAPIEN XT THV</td>
<td>26mm</td>
<td>19F</td>
<td>23F (7.5mm)</td>
<td>6.5mm</td>
</tr>
</tbody>
</table>

33% reduction in CSA

**NEW FRAME GEOMETRY**
- Less metal content
- Lower crimp profile

**NEW FRAME MATERIAL**
- Cobalt-chromium
- Greater tensile and yield strength

**NEW LEAFLET GEOMETRY**
- Partially closed
PARTNER II Study Design

Symptomatic Severe Aortic Stenosis

Operable (STS ≥4)

ASSESSMENT: Transcatheter Access

n = 2000 Randomized Patients

Yes

Transcatheter (TF)

1:1 Randomization

Primary Endpoint: All-Cause Mortality + Disabling Stroke at Two Years (Non-inferiority)

TF TAVR SAPIEN XT vs Surgical AVR

No

Transapical (TA) TransAortic (TAo)

1:1 Randomization

Two Parallel Randomized Trials +6 Nested Registries

Inoperable

n = 560 Randomized Patients

ASSESSMENT: Transcatheter Access

Yes

TF TAVR SAPIEN XT vs TF TAVR SAPIEN

Primary Endpoint: All-Cause Mortality + Disabling Stroke + Repeat Hospitalization at One Year (Non-inferiority)

6 Nested Registries

<table>
<thead>
<tr>
<th>Sample Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>NR1 (Sm Vessel) 100</td>
</tr>
<tr>
<td>NR2 (Transapical) 100</td>
</tr>
<tr>
<td>NR3 (ViV) 100</td>
</tr>
<tr>
<td>NR4 (TAo) 100</td>
</tr>
<tr>
<td>NR5 (29 mm TF) 50</td>
</tr>
<tr>
<td>NR6 (29 mm TA) 50</td>
</tr>
</tbody>
</table>
PARTNER II Inoperable Cohort

**Symptomatic Severe Aortic Stenosis**

**ASSESSMENT by Heart Valve Team**

**Inoperable**

**ASSESSMENT: Transfemoral Access**

1:1 Randomization

- TF TAVR SAPIEN XT
- TF TAVR SAPIEN

Primary Endpoint: All-Cause Mortality + Disabling Stroke + Repeat Hospitalization at One Year (Non-inferiority)

n = 560 Randomized Patients

Leon ACC 2013
PARTNER II Mortality and Stroke

HR [95% CI] = 0.93 [0.66, 1.33]
p (log rank) = 0.706

HR [95% CI] = 0.96 [0.43, 2.14]
p (log rank) = 0.926
PARTNER II: Comparison of Valve Function
## PARTNER II: Comparison Vascular Complications

<table>
<thead>
<tr>
<th>Events</th>
<th>SAPIEN (n=271)</th>
<th>SAPIEN XT (n=282)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td><strong>Vascular:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major</td>
<td>42</td>
<td>15.5</td>
<td>27</td>
</tr>
<tr>
<td>Minor</td>
<td>20</td>
<td>7.4</td>
<td>14</td>
</tr>
<tr>
<td><strong>Bleeding:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disabling</td>
<td>34</td>
<td>12.6</td>
<td>22</td>
</tr>
<tr>
<td>Major</td>
<td>44</td>
<td>16.4</td>
<td>44</td>
</tr>
<tr>
<td>Patients with transfusions</td>
<td>80</td>
<td>29.5</td>
<td>73</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Events</th>
<th>SAPIEN (n=271)</th>
<th>SAPIEN XT (n=282)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Perforation</td>
<td>13</td>
<td>4.8</td>
<td>2</td>
</tr>
<tr>
<td>Dissection</td>
<td>25</td>
<td>9.2</td>
<td>12</td>
</tr>
<tr>
<td>Hematoma</td>
<td>16</td>
<td>5.9</td>
<td>10</td>
</tr>
</tbody>
</table>
Outline

1. Severe Aortic Stenosis and Concept of “Operability”
2. Review Data for TAVR in Inoperable and High Risk Patients
3. Vascular Complication Avoidance
4. Stroke Prevention Strategies
5. Novel Applications: Bicuspid, Prior AVR, Aortic Regurgitation
6. Lower risk populations
Cerebral Emboli During TAVR and SAVR Using Transcranial Doppler

TAVR, N=85

SAVR, N=42

1 patient in each arm suffered a stroke at 30 day follow up
Cerebral Ischemia Following TAVR

32 TAVR procedures. Day 3 MRI evidence of emboli in 84%.

...BUT 0 clinical strokes, 80% of cerebral lesions resolved at 3 months...

...AND no cognitive decline

# TAVR Real World Outcomes

Nov ‘12 – Aug ‘14 (N=86)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>GHS (N=86)</th>
<th>TVT Registry (N=7710)</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-day mortality</td>
<td>8.1%</td>
<td>7.8%</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.2%</td>
<td>2.8%</td>
</tr>
<tr>
<td>Death or Stroke</td>
<td>9.3%</td>
<td>10.1%</td>
</tr>
<tr>
<td>30-day aortic valve re-intervention</td>
<td>0%</td>
<td>0.5%</td>
</tr>
<tr>
<td>30-day new dialysis-dependent renal failure</td>
<td>0%</td>
<td>2.5%</td>
</tr>
<tr>
<td>1-year mortality (n=44)</td>
<td>20.5%</td>
<td>22.1%</td>
</tr>
</tbody>
</table>
Protection of cerebral events during TAVR

**Embrella Embolic Deflector**  
(Edwards Lifesciences)

**Triguard**  
(Keystone Heart, Herzliya Pituach, Israel)

Freeman et al. CCI 2014;84(6):885-896
Protection of cerebral events during TAVR

Claret Montage
(Claret Medical, CA)
Protection of cerebral events during TAVR

Embol-X (Edwards Lifesciences)
Outline

1. Severe Aortic Stenosis and Concept of “Operability”
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5. Novel Applications: Bicuspid, Prior AVR, Aortic Regurgitation
6. Lower risk populations
Novel Applications: Bicuspid Aortic Valve

Performance of transcatheter aortic valve implantation in patients with bicuspid aortic valve: Systematic review

Altayyeb Yousef a,1, Trevor Simard a,1, Ali Pourdjabbar a, John Webb b, Derek So a, Aun-Yeong Chong a, Christopher Glover a, Michel Le May a, Benjamin Hibbert a, Marino Labianza a,*

a Division of Cardiology, University of Ottawa Heart Institute, Ottawa, Ontario, Canada
b Division of Cardiology, St. Paul’s Hospital, University of British Columbia, Vancouver, British Columbia, Canada

Post TAVI outcomes.

<table>
<thead>
<tr>
<th>Sample size</th>
<th>Hyashida</th>
<th>Himbert</th>
<th>Bauer</th>
<th>Wijesinghe</th>
<th>Seger</th>
<th>Chiam</th>
<th>Maluenda</th>
<th>Delgado</th>
<th>Jilaihawi</th>
<th>Raja</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary Endpoints 30 day Mortality</td>
<td>1 (4.8)</td>
<td>1 (4.7)</td>
<td>4 (10.5)</td>
<td>2 (18)</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

One notable finding is that para-valvular leak was reported in almost two thirds of the published cases. The majority of these was graded as mild but 31% were reported to be of moderate or greater severity. This proportion of aortic regurgitation is greater than the 11.2% rate reported in PARTNER-B. Moreover, both clinical trials and
Valve in Valve Implantation

Transcatheter Aortic Valve Implantation in Failed Bioprosthetic Surgical Valves

Danny Dvir, MD; John G. Webb, MD; Sabine Bleiziffer, MD; Miralem Pasic, MD, PhD; Ron Waksman, MD; Susheel Kodali, MD; Marco Barbanti, MD; Azeem Latib, MD; Ulrich Schaefer, MD; Josep Rodès-Cabau, MD; Hendrik Treede, MD; Nicolo Piazza, MD, PhD; David Hillick-Smith, MD; Dominique Himbert, MD; Thomas Walther, MD; Christian Hengstenberg, MD; Henrik Nissen, MD, PhD; Raffi Bekeriedjian, MD; Patrizia Presbitero, MD; Enrico Ferrari, MD; Amit Segev, MD; Arend de Weger, MD; Stephan Windecker, MD; Neil E. Moat, FRCS; Massimo Napodano, MD; Manuel Wilbring, MD; Alfredo G. Cerillo, MD; Stephen Brecker, MD; Didier Tchetche, MD; Thierry Lefèvre, MD; Federico De Marco, MD; Claudia Fiorina, MD; Anna Sonia Petronio, MD; Rui C. Teles, MD; Luca Testa, MD; Jean-Claude Laborde, MD; Martin B. Leon, MD; Ran Kornowski, MD; for the Valve-in-Valve International Data Registry Investigators

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>All (n = 459)</th>
<th>Stenosis (n = 181)</th>
<th>Regurgitation (n = 139)</th>
<th>Combined (n = 139)</th>
<th>P Value</th>
<th>Self-Expandable (n = 213)</th>
<th>Balloon-Expandable (n = 246)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of hospital stay, median (IQR), d</td>
<td>8 (5-12)</td>
<td>7 (5-11)</td>
<td>7 (5-12)</td>
<td>8 (6-13)</td>
<td>.21</td>
<td>7 (5-12)</td>
<td>8 (6-13)</td>
<td>.07</td>
</tr>
<tr>
<td>Thirty-day outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death, No. (%)</td>
<td>35 (7.6)</td>
<td>19 (10.5)</td>
<td>6 (4.3)</td>
<td>10 (7.2)</td>
<td>.04</td>
<td>15 (7)</td>
<td>20 (8.1)</td>
<td>.66</td>
</tr>
<tr>
<td>One-year outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death, No. (%)</td>
<td>62 (16.8)</td>
<td>34 (23.4)</td>
<td>10 (8.8)</td>
<td>18 (16.1)</td>
<td>.01</td>
<td>25 (15)</td>
<td>37 (18.7)</td>
<td>.44</td>
</tr>
</tbody>
</table>

JAMA 2014; 312(2):162-70
Edwards evolution of valve design

SAPIEN

SAPIEN XT

SAPIEN 3
Valves Under Development

(A) Lotus (Boston Scientific Inc., Natick, Massachusetts), (B) Direct Flow (Direct Flow Medical Inc., Santa Rosa, California), (C) HLT (Bracco Inc., Princeton, New Jersey), (D) Portico (St. Jude Medical Inc., St. Paul, Minnesota), (E) Enlarge (Medtronic Inc., Minneapolis Minnesota), (F) JenaClip (JenaValve Inc., Munich, Germany), (G) Acutar valve (Symetis Inc., Ecublens, Switzerland), and (H) Inovare (Braile Biomedica Inc., São José do Rio Preto, Brazil) valves.
Expanding the Limits

Transapical Transcatheter Aortic Valve for Severe Aortic Regurgitation

Daniel Wendt, MD, PhD, Philipp Kahlert, MD, PhD, Susanne Pasa, MD, Karim El-Chilali, MD, Fadi Al-Rashid, MD, Konstantinos Tsagakis, MD, Daniel Sebastian Dohle, MD, Raimund Erbel, MD, PhD, Heinz Jakob, MD, PhD, Matthias Thielmann, MD, PhD

**TABLE 4 3- to 6-Month Echocardiographic Follow-up**

<table>
<thead>
<tr>
<th>Patient</th>
<th>LV Function, %</th>
<th>Prosp vs. 3-6 Months, %</th>
<th>Preop min Hg</th>
<th>Postop min Hg</th>
<th>AHA cm²</th>
<th>Vmax m/s</th>
<th>AR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>55</td>
<td>0</td>
<td>16</td>
<td>19</td>
<td>1.9</td>
<td>2.0</td>
<td>1</td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>-10</td>
<td>15</td>
<td>19</td>
<td>1.4</td>
<td>1.9</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>55</td>
<td>+2</td>
<td>18</td>
<td>20</td>
<td>1.5</td>
<td>2.1</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>40</td>
<td>-10</td>
<td>19</td>
<td>11</td>
<td>1.6</td>
<td>1.6</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>50</td>
<td>-1</td>
<td>28</td>
<td>17</td>
<td>N/A</td>
<td>2.1</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>55</td>
<td>+10</td>
<td>15</td>
<td>19</td>
<td>1.8</td>
<td>1.9</td>
<td>0</td>
</tr>
<tr>
<td>7</td>
<td>35</td>
<td>-7</td>
<td>18</td>
<td>10</td>
<td>N/A</td>
<td>1.6</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>35</td>
<td>+10</td>
<td>18</td>
<td>10</td>
<td>N/A</td>
<td>1.6</td>
<td>0</td>
</tr>
</tbody>
</table>

**Mortality**

| 30-day all cause | 0 (0) |
| 30-day cardiovascular | 0 (0) |
| 12-month all cause | 0 (0) |
| 12-month cardiovascular | 0 (0) |
| Stroke/TIA 30-day | 0 (0) |
| Minor bleeding | 0 (0) |
| Major bleeding | 0 (0) |
| Blood transfusion | 0 (0) |
| Acute kidney injury | 1 (20.0) |
| Pacemaker implantation | 0 (0) |
| Myocardial infarction | 0 (0) |
| VARC-2 procedure success | 8 (100) |
| Access site complications | 0 (0) |

Self-expandable ACURATE TA bioprosthesis (Symetis SA, Ecublens, Switzerland).

Characteristics of new-generation transcatheter aortic valves

Table 2  Salient characteristics of the new-generation transcatheter aortic valves

<table>
<thead>
<tr>
<th>Valve</th>
<th>Stent material</th>
<th>Sizes (mm)</th>
<th>Access</th>
<th>Access size (Fr)</th>
<th>Expansion</th>
<th>Repositionable</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edwards SAPIEN 3 (Edwards Lifesciences, California, USA)</td>
<td>Cobalt chromium</td>
<td>20, 23, 26, 29</td>
<td>TF, TA, TAO</td>
<td>14 e sheath</td>
<td>Balloon expandable</td>
<td>No</td>
</tr>
<tr>
<td>Edwards CENTERA (Edwards Lifesciences, California, USA)</td>
<td>Nitinol</td>
<td>23, 26</td>
<td>TF</td>
<td>14 e sheath</td>
<td>Self-expandable</td>
<td>Yes</td>
</tr>
<tr>
<td>Direct Flow Medical (Direct Flow, Medical, California, USA)</td>
<td>No stent (polyester Fabric cuff)</td>
<td>23, 25, 27, 29</td>
<td>TF, Subclavian</td>
<td>18</td>
<td>Inflation of ring balloons by a polymer</td>
<td>Yes</td>
</tr>
<tr>
<td>Heart Leaflet Technologies (Heart Leaflet Technologies, Minnesota, USA)</td>
<td>Nitinol</td>
<td>21, 23</td>
<td>TF</td>
<td>18</td>
<td>Self-expandable</td>
<td>Yes</td>
</tr>
<tr>
<td>Innova (Brail Biomedical, Brazil)</td>
<td>Stainless steel</td>
<td>20, 22, 24, 26, 28</td>
<td>TA</td>
<td>20 (for 20, 22, 24 mm)</td>
<td>Balloon-expandable</td>
<td>No</td>
</tr>
<tr>
<td>Portico (St. Jude Medical, Minnesota, USA)</td>
<td>Nitinol</td>
<td>23, 25</td>
<td>TF</td>
<td>18</td>
<td>Self-expandable</td>
<td>Yes</td>
</tr>
<tr>
<td>JenaValve (JenaValve Technology, Germany)</td>
<td>Nitinol</td>
<td>23, 25, 27</td>
<td>TA</td>
<td>32</td>
<td>Self-expandable</td>
<td>Yes</td>
</tr>
<tr>
<td>Sadra Lotus Medical (Boston Scientific, Minnesota, USA)</td>
<td>Nitinol</td>
<td>23, 27</td>
<td>TF</td>
<td>18</td>
<td>Self-expandable</td>
<td>Yes</td>
</tr>
<tr>
<td>Symetis Accurate (Symetis, Ecublens, Switzerland)</td>
<td>Nitinol</td>
<td>23, 25, 27</td>
<td>TF, TA</td>
<td>18 (TF) 28 (TA)</td>
<td>Self-expandable</td>
<td>Yes</td>
</tr>
<tr>
<td>Engager (Medtronic, Minnesota, USA)</td>
<td>Nitinol</td>
<td>23, 26</td>
<td>TA</td>
<td>28</td>
<td>Self-expandable</td>
<td>Yes</td>
</tr>
<tr>
<td>CoreValve Evolut R (Medtronic, Minnesota, USA)</td>
<td>Nitinol</td>
<td>23, 26, 29, 31</td>
<td>TF, TAO, Subclavian</td>
<td>18</td>
<td>Self-expandable</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Fr, French; TAO, transaortic; TA, transapical; TF, transfemoral.

Agarwal S et al. Heart 2015;101:169-177
Minimalist Approach TAVR: Single Center, High Volume

Babaliaros V et al. JACC Int 2014;7(8):898-904
Patient-Focused Multidisciplinary Heart Team Approach

• Multidisciplinary in all aspects:
  – Patient selection
  – Procedure Planning
  – Patient Treatment
  – Post Operative care
CTA: Critical for determining Access
Valve Sizing: TEE
Valve Sizing: CT
Advanced Real Time Imaging for TAVR

Agarwal S et al. Heart 2015;101:169-177
Bern TAVI Registry: The European Experience with less than high risk patients

LOW VS. HIGH: RR (95% CI) = 0.27 (0.09–0.77)
INTERMEDIATE VS. HIGH: RR (95% CI) = 0.41 (0.24–0.67)
P < 0.001

NUMBER AT RISK

HIGH  94  81  66  64  64  62  62  51  46  44  43  42  41
INTERMEDIATE  254  244  213  208  203  202  195  172  165  164  158  156  154
LOW  41  40  39  36  35  35  34  32  32  32  32  28

Active Intermediate Risk Trials:

TAVR vs. SAVR

Corevalve

- OUS
  - STS mortality risk ≥4% and ≤10%

- Corevalve Sapien XT
  - US
    - STS mortality risk ≥4% and ≤10%

  - Heart Team Evaluation
    - including assessment for significant CAD with determination of need for revascularization

  - Randomization
    - with 5 year follow up

    - Presence of significant CAD with intended revascularization
    - TAVI + PCI
    - SAVR + CABG
    - TAVI
    - SAVR

    - No intended revascularization

Sapien XT

- Operable
  - (STS ≥4)

  - Assessment: Transfemoral Access

    - Yes
      - Transfemoral (TF)
        - 1:1 Randomization
          - TF TAVR SAPIEN XT
          - Surgical AVR
          - TAVR: TA / TAo SAPIEN XT
          - Surgical AVR

    - No
      - Transapical (TA) / TransAortic (TAo)
        - 1:1 Randomization

  - Primary Endpoint: All-Cause Mortality + Disabling Stroke at Two Years (Non-inferiority)
Conclusions

1. TAVR (TAVI) is the current standard of care for inoperable patients with severe AS
2. TAVR is an acceptable option for high risk operable patients
3. TAVR may soon be an option for intermediate risk patients
4. Technology advancements: smaller sheaths, AI prevention, stroke prevention