Stroke after Surgical vs. Transfemoral Transcatheter Aortic Valve Replacement: In Depth Analysis from the PARTNER Trial

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Disclosure Statement of Financial Interest

I, Chetan Huded, DO NOT have a financial interest/arrangement or affiliation with one or more organizations that could be perceived as a real or apparent conflict of interest in the context of the subject of this presentation.
Background

• Stroke is an important complication of aortic valve replacement procedures.

• In contemporary practice, >90% of TAVR is performed from a transfemoral (TF) approach.

• The risk of stroke in TF-TAVR vs. SAVR is unknown.
Stroke is Associated with a Major Reduction in 1-Year Survival after TAVR


1-Year Survival Following TAVR

- Transfemoral:
  - Stroke: 47%
  - No Stroke: 82%
  - 43% reduction in survival

- Transapical:
  - Stroke: 53%
  - No Stroke: 80%
  - 34% reduction in survival
PARTNER 1A Raised Concern of Increased Neurologic Risk of TAVR

Objective

To study the risk of neurologic events and relationship to quality of life in a large prospective cohort of SAVR vs. TF-TAVR in a pooled analysis of the PARTNER Trials.
Methods

PARTNER 1 (N=3159)
1A (High Risk)
TAVR vs SAVR
1B (Inoperable)
TAVR vs Medical Tx

PARTNER 2 (N=2805)
2A (Intermediate Risk)
TAVR vs SAVR
2B (Inoperable)
Sapien vs Sapien XT

PARTNER 2 S3 (N=1661)
≥ Intermediate Risk TAVR Registry
Sapien 3

Final Propensity Matched Study Population

Methods

April 2007 – October 2015

1:1 Propensity Matching
TF-TAVR vs. SAVR
Matching caliper 0.1
96% SAVR cases matched

Excluded 1988 (26%)
1. Medical therapy arm
2. Non-femoral TAVR
3. Cross-over between TAVR/SAVR
4. Died prior to AVR

TF-TAVR: 4389
SAVR: 1248

As Treated

<table>
<thead>
<tr>
<th></th>
<th>PARTNER 1</th>
<th>PARTNER 2</th>
<th>S3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>TF-TAVR</td>
<td>406</td>
<td>602</td>
<td>196</td>
<td>1204</td>
</tr>
<tr>
<td>SAVR</td>
<td>306</td>
<td>898</td>
<td>0</td>
<td>1204</td>
</tr>
</tbody>
</table>

Final Propensity Matched Study Population

TF-TAVR: 4389
SAVR: 1248

TF-TAVR: 1.5 years
SAVR: 2 years

Median Follow-up
TF-TAVR: 1.5 years
SAVR: 2 years
TF-TAVR Devices in the Propensity Matched Study Population

- SAPIEN: 43%
- SAPIEN XT: 41%
- SAPIEN 3: 16%
## Study Outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. <strong>30-Day</strong> Neurologic Events</td>
<td>Chi square test</td>
</tr>
<tr>
<td>2. <strong>Early and Late-Phase</strong> Neurologic Risk</td>
<td>Multiphase non-proportional hazards model&lt;br&gt;Competing risk methodology</td>
</tr>
<tr>
<td>3. Relationship of Post-op AV Gradients and Stroke</td>
<td>Time-related hazard model of stroke with post-procedure AV gradient</td>
</tr>
<tr>
<td>4. Relationship of Stroke with <strong>1 Year Quality of Life</strong></td>
<td>1 Year KCCQ overall summary score&lt;br&gt;Linear regression</td>
</tr>
</tbody>
</table>
Stroke Event Adjudication

<table>
<thead>
<tr>
<th>Score</th>
<th>Symptoms / Disability</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No symptoms</td>
</tr>
<tr>
<td>1</td>
<td>Symptoms with no significant disability</td>
</tr>
<tr>
<td>2</td>
<td>Slight disability</td>
</tr>
<tr>
<td>3</td>
<td>Moderate disability</td>
</tr>
<tr>
<td>4</td>
<td>Moderately severe disability</td>
</tr>
<tr>
<td>5</td>
<td>Severe disability / bedridden</td>
</tr>
<tr>
<td>6</td>
<td>Death</td>
</tr>
</tbody>
</table>

**Minor stroke** = 90 day modified Rankin score < 2

**Major stroke** = 90 day modified Rankin score ≥ 2

- Independent clinical events committee reviewed all neurologic events.
- Mandated postoperative neurologic assessment in PARTNER 2 and PARTNER S3 (70% of study population)
Results
## Baseline Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>SAVR (n = 1204)</th>
<th>TF-TAVR (n=1204)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age - yrs</td>
<td>82 ± 6.7</td>
<td>82 ± 7.9</td>
<td>0.10</td>
</tr>
<tr>
<td>Female</td>
<td>45%</td>
<td>44%</td>
<td>0.9</td>
</tr>
<tr>
<td>CAD - %</td>
<td>69%</td>
<td>70%</td>
<td>0.6</td>
</tr>
<tr>
<td>Previous MI - %</td>
<td>20%</td>
<td>20%</td>
<td>0.8</td>
</tr>
<tr>
<td>Prior PCI - %</td>
<td>28%</td>
<td>28%</td>
<td>&gt;0.9</td>
</tr>
<tr>
<td>Prior CABG - %</td>
<td>30%</td>
<td>31%</td>
<td>0.6</td>
</tr>
<tr>
<td>Prior BAV - %</td>
<td>6.4%</td>
<td>3.6%</td>
<td>0.003</td>
</tr>
<tr>
<td>Cerebrovascular Disease - %</td>
<td>31%</td>
<td>33%</td>
<td>0.4</td>
</tr>
<tr>
<td>Prior Stroke - %</td>
<td>12%</td>
<td>12%</td>
<td>0.8</td>
</tr>
<tr>
<td>Peripheral Vascular Disease - %</td>
<td>43%</td>
<td>45%</td>
<td>0.4</td>
</tr>
</tbody>
</table>
30-Day Neurologic Events

- TIA: 0.4% (SAVR), 0.6% (TF-TAVR) (P=0.6)
- Minor stroke: 1.2% (SAVR), 1.4% (TF-TAVR) (P=0.6)
- Major stroke: 3.9% (SAVR) vs. 2.2% (TF-TAVR) (P=0.018)
- Any stroke: 4.2% vs. 3.7% (P=0.09)
- Stroke or TIA: 5.4% vs. 4.2% (P=0.18)
Early Phase Risk (<7 Days)

Instantaneous Risk Modeling

**Stroke**

- SAVR
- TF-TAVR

\[ P = 0.15 \]

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**Stroke or TIA**

- SAVR
- TF-TAVR

\[ P = 0.2 \]
Late Phase Risk (4 Years)

**Instantaneous Risk Modeling**

**Stroke**

- SAVR
- TF-TAVR

**P = 0.6**

#/100 Patient months

0.0 0.3 0.6 0.9 1.2 1.5

0 6 12 18 24 30 36 42 48

**Months**

**Stroke or TIA**

- SAVR
- TF-TAVR

**P = 0.6**

#/#100 Patient months

0.0 0.3 0.6 0.9 1.2 1.5

0 6 12 18 24 30 36 42 48

**Months**

SHDS2018
Cumulative Incidence of Events
Adjusted for Competing Risk of Mortality

**Stroke**
- SAVR: 5.5%, 6.7%, 8.3%, 9.1%
- TF-TAVR: 6.4%, 7.4%, 8.3%, 9.1%
- P = 0.5

**Stroke or TIA**
- SAVR: 7.1%, 8.8%, 9.1%, 10.6%
- TF-TAVR: 7.8%, 9.1%, 10.6%, 10.9%
- P = 0.8
Association of Postoperative AV Gradients and Late Stroke Risk

• Increasing post-procedure mean trans-AV gradient was not associated with risk of stroke (P>0.7).
• No interaction of AV gradient and procedure type with risk of stroke (P interaction >0.2).
Association of Stroke and 1 Year Quality of Life

**KCCQ Overall Summary Score**

- **Any Stroke**
  - SAVR: 79, 67; TF-TAVR: 78, 75; *P*=0.01, *P*=0.5

- **Major Stroke**
  - SAVR: 79, 64; TF-TAVR: 78, 60; *P*=0.03, *P*=0.04

- **Minor Stroke**
  - SAVR: 79, 74; TF-TAVR: 78, 85; *P*=0.2, *P*=0.5
Association of Stroke and 1 Year Quality of Life

### Any Stroke

<table>
<thead>
<tr>
<th></th>
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<th>TF-TAVR</th>
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</thead>
<tbody>
<tr>
<td>No Stroke</td>
<td>79</td>
<td>67</td>
</tr>
<tr>
<td>Stroke</td>
<td>78</td>
<td>75</td>
</tr>
</tbody>
</table>

P = 0.01
P = 0.5

### Major Stroke

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>No Major Stroke</td>
<td>79</td>
<td>64</td>
</tr>
<tr>
<td>Major Stroke</td>
<td>78</td>
<td>60</td>
</tr>
</tbody>
</table>

P = 0.03
P = 0.04

### Minor Stroke

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>No Stroke</td>
<td>79</td>
<td>74</td>
</tr>
<tr>
<td>Minor Stroke</td>
<td>78</td>
<td>85</td>
</tr>
</tbody>
</table>

P = 0.2
P = 0.5
Principal Findings

1. 30-day major stroke risk lower in TF-TAVR.
2. Similar pattern of early-peaking (<24 hours) and nearly constant late neurologic risk between SAVR and TF-TAVR.
3. No association with increasing valve gradients and late-phase stroke risk.
4. Major, but not minor, strokes are associated with lower QOL at 1-year.
Limitations

• Non-randomized trial of SAVR vs. TF-TAVR.
• PARTNER 1 no mandated neurologic assessment.
• Changes in TF-TAVR devices over time.
• Hospital and operator-level characteristics not assessed.
Conclusions

• The risk of early major stroke is significantly higher after SAVR vs. TF-TAVR in similar-risk patients.

• Major stroke is associated with a significantly lower quality of life at 1 year post-AVR.

• Peri-procedural strategies to mitigate stroke risk offer the potential to improve the safety of aortic valve procedures in the coming years.