Predictors, incidence and outcomes of patients undergoing transcatheter aortic valve implantation complicated by stroke

From the CENTER-Collaboration

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University of Amsterdam, The Netherlands
On behalf of the CENTER-collaborators
Disclosure Statement of Financial Interest

I, Wieneke Vlastra 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

TAVI

• **TAVI** is a life-saving and minimally invasive treatment in patients with severe aortic valve stenosis
  - The TAVI population has rapidly expanded from inoperable to intermediate-risk patients

• **Stroke remains one of the most detrimental complications of TAVI**
  - Stroke in TAVI patients increases mortality but also decreases the patient’s quality of life
Background
Pathophysiology of stroke during TAVI

Vlastra et al, *J Thorac Dis* 2017
Background
Debris captured in cerebral protection devices

Kapadia et al, JACC 2017
Background

Debris captured in cerebral protection devices

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Debris captured in cerebral protection devices

Kapadia et al, JACC 2017
Background
Cerebral infarctions after TAVI

- Cerebral diffusion weighted magnetic resonance imaging (DW-MRI)
  - 78% of patients (95% CI 72-83%) have new ischemic lesions after the TAVI procedure

Pagnesi et al, Int J Cardiol, 2016
Hassell et al, Nature Reviews Cardiology, 2013
Background
TAVI and stroke

• Incidence of stroke
  - Reported rates vary from 1.3% to 21.0% despite development of the Valve Academic Research Consortium (VARC) criteria to promote uniformity

• Limited data assessing patients at risk and determining clinical outcomes in patients with stroke
  - Data from large-scale, patient-level, real-world studies is needed
Study Aim
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• Determine the incidence and timeframe of 30-day stroke in TAVI patients
• Identify predictors of stroke
• Assess the impact of stroke on mortality and other clinical outcomes

In a large-scale, real-world & international patient population
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Study selection

• Inclusion criteria for studies: including patients undergoing transfemoral TAVI with either Edwards SAPIEN valves or Medtronic CoreValves and reporting 30 day stroke outcomes
Study selection

903 potentially eligible individual studies on patients undergoing TAVI and stroke were identified.

- No Original data N=359
- Less than 50 patients treated with ESV and/or MCV† N=385
- No primary procedures performed N=73
- Only bicuspid valves treated N=2
- No transfemoral TAVI performed N=7

77 studies included the intended study population

- 30-day stroke was not reported N=36
- Stroke was not defined according to VARC or equivalent definitions N = 10
- Overlapping patient populations N= 3

28 studies eligible for inclusion in the CENTER-trial

- No participation in collaboration N=18

10 studies included in the current collaboration
Study selection

903 potentially eligible individual studies on patients undergoing TAVI and stroke were identified.

Screening of title and abstract

77 studies included the intended study population

Screening in full

28 studies eligible for inclusion in the CENTER-trial

P1’s approached for participation in collaborative analysis.

10 studies included in the current collaboration

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## CENTER-Collaboration
### Included patient populations (2007-2018)

<table>
<thead>
<tr>
<th>Study</th>
<th>Study design</th>
<th>(n = 12,381)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brazil</td>
<td>National registry</td>
<td>768</td>
</tr>
<tr>
<td>France-2</td>
<td>National registry</td>
<td>2,347</td>
</tr>
<tr>
<td>Milano</td>
<td>Single-centre registry</td>
<td>515</td>
</tr>
<tr>
<td>Verona</td>
<td>Single-centre registry</td>
<td>346</td>
</tr>
<tr>
<td>OBSERVANT</td>
<td>Multi-centre registry</td>
<td>577</td>
</tr>
<tr>
<td>Rabin</td>
<td>Single-centre registry (subset from multi-centre study)</td>
<td>544</td>
</tr>
<tr>
<td>Padova</td>
<td>Single-centre registry</td>
<td>447</td>
</tr>
<tr>
<td>Spain</td>
<td>National registry</td>
<td>5,320</td>
</tr>
<tr>
<td>BRAVO-3</td>
<td>Randomized controlled trial</td>
<td>732</td>
</tr>
<tr>
<td>WIN-TAVI</td>
<td>Multi-centre registry</td>
<td>785</td>
</tr>
</tbody>
</table>
Primary and secondary endpoints
CENTER-Collaboration

• Primary endpoint
  ▪ Incidence and timeframe of 30-day stroke according to the VARC criteria

• Secondary endpoints
  ▪ Predictors of stroke
  ▪ Clinical outcomes in patients with stroke
## Baseline Patient Demographics
### CENTER-Population (N=12,381)

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>81.6 ± 6.8</td>
</tr>
<tr>
<td>Female gender</td>
<td>7,109 (58%)</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>27.1 ± 5.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Risk scores (%)</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Logistic EuroSCORE</td>
<td>14.4 (9.0-23.0)</td>
</tr>
<tr>
<td>EuroSCORE II</td>
<td>4.0 (2.4-6.9)</td>
</tr>
<tr>
<td>STS-PROM</td>
<td>6.4 (4.0-13.0)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Echocardiographic characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic max gradient (mmHg)</td>
<td>79 ± 23</td>
</tr>
<tr>
<td>Mean gradient (mmHg)</td>
<td>49 ± 16</td>
</tr>
<tr>
<td>Aortic valve area (cm²)</td>
<td>0.7 ± 0.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Medical history</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous CVA or TIA</td>
<td>1,246 (10%)</td>
</tr>
<tr>
<td>Previous ACS</td>
<td>1,599 (14%)</td>
</tr>
<tr>
<td>Previous PCI</td>
<td>1,946 (22%)</td>
</tr>
<tr>
<td>Previous CABG</td>
<td>1,375 (12%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>3,550 (31%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>8,603 (79%)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>5,526 (55%)</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>1,698 (15%)</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>4,493 (43%)</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>3,029 (27%)</td>
</tr>
<tr>
<td>GFR &lt; 30 ml/min/1.73m²</td>
<td>1,136 (13%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Valve-types</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edwards SAPIEN valve</td>
<td>6,239 (50%)</td>
</tr>
<tr>
<td>Medtronic CoreValve</td>
<td>6,142 (50%)</td>
</tr>
</tbody>
</table>
Stroke after TAVI
Incidence and timeframe

• The 30-day incidence of stroke was 2.4%
Stroke after TAVI
Incidence and timeframe

• The 30-day incidence of stroke was 2.4%

• The incidence of stroke was equal in the early years and late years of TAVI (p = 1.0)
  ▪ 2007-2012: 2.4%
  ▪ 2013-2018: 2.4%
Timing of Stroke after TAVI

![Graph showing number of strokes per day after TAVI procedure.](image-url)
Study Aim
Timing of stroke after TAVI

- Median time between TAVI and stroke was 1 day (IQR 0-6 days)
Study Aim
Timing of stroke after TAVI

- Median time between TAVI and stroke was 1 day (IQR 0-6 days)
- 80% occurred within the first week
Cerebrovascular events after TAVI

- Stroke was defined as major stroke in 75%

- The incidence of TIA at 30 days was 0.6%

- The cumulative stroke rate increased from 2.4% at 30 days to 5% at 1 year
Stroke after TAVI
Predictors

• Predictors of 30-day stroke in multivariate regression analysis
  - Previous cerebrovascular events OR 2.1 (95%CI 1.4-3.3) p=0.001
  - GFR of less than 30 ml/min/1.73m2 OR 1.6 (95% CI 1.0-2.5) p=0.03

<table>
<thead>
<tr>
<th></th>
<th>No stroke at 30 days (n = 10,721)</th>
<th>Stroke at 30 days (n = 261)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous CVA or TIA</td>
<td>1057 (10%)</td>
<td>43 (17%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GFR &lt; 30 ml/min/1.73m²</td>
<td>1013 (13%)</td>
<td>33 (19%)</td>
<td>0.03</td>
</tr>
</tbody>
</table>
30-day clinical outcomes (%)
In patients with and without stroke
30-day clinical outcomes (%) 
In patients with and without stroke

• **Six-fold increase in mortality**
  OR 6.0, 95% CI 4.4-8.1, p<0.001
30-day clinical outcomes (%) 
In patients with and without stroke

- **Six-fold increase in mortality**
  OR 6.0, 95% CI 4.4-8.1, p<0.001

- **Two-fold increase in major or life-threatening bleeding**
  OR 1.9, 95% CI 1.3-3.0, p=0.003
30-day clinical outcomes (%)  
In patients with and without stroke

- Six-fold increase in mortality  
  OR 6.0, 95% CI 4.4-8.1, p<0.001

- Two-fold increase in major or life-threatening bleeding  
  OR 1.9, 95% CI 1.3-3.0, p=0.003

- Five-fold more frequent new-onset atrial fibrillation  
  OR 5.2, 95% CI 1.9-14.1, p=0.001
Conclusions
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• The 30-day incidence of stroke after TAVI was 2.4%, this was consistent over time
• 80% of the strokes occurred during the first week after TAVI
• Patients with prior cerebrovascular events or a low GFR were at higher risk for stroke
• There was a strong association between new-onset atrial fibrillation and stroke
• Stroke was associated with a six-fold increase of 30-day mortality and a two-fold higher risk of major or life-threatening bleedings
Discussion
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• **Study design**
  - Heterogeneous studies
  - Not all studies had independent adjudication of clinical events
  - Newest valve types were used in a minimum amount of patients
Discussion
CENTER-Collaboration

• Study design
  ▪ Heterogeneous studies
  ▪ Not all studies had independent adjudication of clinical events
  ▪ Newest valve types were used in a minimum amount of patients

• Reflection of current practice of TAVI during the past decade (across the globe)
Need to reduce stroke

• Incidence over time – poor outcomes
• The majority of strokes are directly post-procedure
  - Patient/device selection (?)
  - Cerebral protection devices (?)
  - NOAC (?)

Days since TAVI

Number of strokes

0 1 2 3 4 5 6 7

tct2018
CENTER-trial Collaborators

• Spanish TAVI registry
  - Pilar Jimenez-Quevedo
  - Jose M de la Torre
  - Rosana Hernandez-Antolin

• FRANCE-2
  - Didier Tchétché
  - Nicolas Dumonteil
  - Thomas Modine

• BRAVO-3 & WIN-TAVI
  - Jaya Chandrasekhar
  - Samantha Sartori
  - Roxana Mehran

• National Brazilian TAVI registry
  - Fabio S. de Brito
  - Rogério Sarmento-Leite

• OBSERVANT
  - Marco Barbanti
  - Paola D’Errigo

• Rabin medical centre
  - Ran Kornowski
  - Katia Orvin

• Milano
  - Azeem Latib
  - Matteo Pagnesi

• Padova
  - Augusto D’Onofrio
  - Chiara Fraccaro

• Verona
  - Flavio Ribichini
  - Mattia Lunardi

• Amsterdam UMC
  - Jan Baan
  - Jan Tijssen
  - Jan Piek
  - Ronak Delewi
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