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Cerebral Ischemia after Transcatheter Aortic Valve Implantation

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TAVI is increasingly embraced as a viable treatment option for high-risk patients with aortic stenosis.

TAVI seems prone to embolic stroke:
- direct manipulation of the calcified aortic valve
- guiding of large-bore catheters
- passage of the stiff aorta, aortic arch
- prior balloon valvuloplasty
- prosthesis induced crushing of calcified leaflets

Periprocedural stroke rates: 2.9 - 10%

Clinically apparent versus silent cerebral ischemia

Omran et al. Lancet 2003
Potential Sources of Embolism
Findings on Cerebral MRI

Example of an 82-year-old patient 2 days after transfemoral TAVI
Aim of the Study: to assess clinically apparent and silent cerebral ischemia in patients undergoing transfemoral TAVI using clinical examination, neurological testing and serial diffusion-weighted magnetic resonance imaging before and after TAVI as well as at 3-month follow-up.
Methods

- 51 consecutive TAVI patients between 09/2007 and 03/2009

- exclusion of 19 patients
  - contraindication to MRI (n=9)
  - refusal to participate (n=2)
  - early death after the procedure precluding follow-up MRI (n=3)
  - new third-degree AV block requiring PM implantation (n=5)

- Group 1 \(\rightarrow\) balloon-expandable prosthesis (n=22)

- Group 2 \(\rightarrow\) self-expandable prosthesis (n=10)

- Group 3 \(\rightarrow\) historical control group of patients undergoing isolated surgical aortic valve replacement

Kahlert et al. *Circulation* 2010
Methods

NeuroCognitive Assessment

National Institute of Health Stroke Scale (NIHSS) and Mini Mental State Examination (MMSE) at baseline, post TAVI & at 3 months, Modified Rankin Scale (mRS) at 3-month FU

Serial Cerebral Magnetic Resonance Imaging
1.5 T Avanto® whole body imaging system (Siemens, Erlangen, Germany) transversal FLAIR and DW images, calculation of ADC maps volumetric quantification using dedicated scanner software time points of DW MRI: baseline, post TAVI, at 3-month follow-up

Assessment of Potential Sources of Embolism (at baseline) history, ECG, carotid Duplex ultrasound, transthoracic & transesophageal echo
Patient Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Edwards SAPIEN THV (n=22)</th>
<th>CoreValve (n=10)</th>
<th>Surgical AVR (n=21)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (95% CI)</td>
<td>78.3 (76.4-80.2)</td>
<td>83.8 (79.2-88.4)</td>
<td>67.4 (63.9-70.8)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Female gender, n (%)</td>
<td>14 (64)</td>
<td>4 (40)</td>
<td>8 (38)</td>
<td>0.201</td>
</tr>
<tr>
<td>Logistic EuroSCORE, % (95% CI)</td>
<td>22.8 (16.5-29.2)</td>
<td>17.9 (12.0-23.7)</td>
<td>2.5 (1.8-3.2)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

TAVI patients were older than surgical patients

TAVI patients had more comorbidities

TAVI patient had a higher operative risk

Ejection fraction, % (95% CI)  
- Edwards SAPIEN THV: 52.5 (46.5-58.6)  
- CoreValve: 48.3 (37.3-59.3)  
- Surgical AVR: 55.4 (48.0-62.8)  
- p = 0.47

Renal dysfunction, n (%)  
- Edwards SAPIEN THV: 7 (32)  
- CoreValve: 1 (10)  
- Surgical AVR: 0 (0)  
- p = 0.013

Prior cerebral ischemic event, n (%)  
- Edwards SAPIEN THV: 2 (9)  
- CoreValve: 0 (0)  
- Surgical AVR: 0 (0)  
- p = 0.231

Kahlert et al. Circulation 2010
Procedural Data

- Successful TAVI in all patients
- AVA after TAVI: 1.81 (1.62-2.00) cm²
- $\Delta p_{\text{mean}}$ after TAVI: 11.2 (7.8-14.6) mm Hg
- Hemodynamic stability during the entire procedure in all but 2 patients
- Complications:
  - Cardiac tamponade $\rightarrow$ surgical repair (n=1)
  - Defibrillation with short-term CPR (n=2)
  - Vascular access site complications (n=8) $\rightarrow$ endovascular / surgical repair

Kahlert et al. Circulation 2010
Findings on Diffusion-Weighted MRI

Group 1: 89 new DWI lesion in 19 of 22 patients (86%)

Group 2: 26 new DWI lesions in 8 of 10 patients (80%)

Group 3: 33 new DWI lesions in 10 of 21 patients (48%)

Lesion size was significantly smaller in TAVI than surgical patients.

<table>
<thead>
<tr>
<th>Lesion size, mm² (95% CI)</th>
<th>Group 1 (96-100)</th>
<th>Group 2 (91-95)</th>
<th>Group 3 (81-83)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periprocedural neurological deficits, n (%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (5)</td>
<td>0.460</td>
</tr>
<tr>
<td>Time of postprocedural DW MRI, days (95% CI)</td>
<td>3.5 (2.4-4.9)</td>
<td>3.2 (2.0-4.4)</td>
<td>4.2 (3.5-4.8)</td>
<td>0.54</td>
</tr>
</tbody>
</table>
Clinical Findings after TAVI

National Institute of Health Stroke Scale

at baseline: 0 in all but 1 patient (score of 3 due to pre-existing anopia)
post TAVI: unchanged
at 3 months: unchanged

Mini Mental State Examination

at baseline: 28.4 (27.4-29.3)
post TAVI: 28.2 (27.3-29.1) p=ns
at 3 months: 28.3 (27.3-29.4) p=ns

Modified Rankin Scale at 3 months post TAVI

0 in all patients (→ no functional impairment during daily activities)
TF-TAVI

In 16 (73%) of 22 transfemoral TAVI patients 75 new cerebral lesions were detected.
In 17 (68%) of 25 transapical TAVI patients new cerebral lesions were detected.
## Transfemoral vs Transapical TAVI

<table>
<thead>
<tr>
<th>Variables</th>
<th>All Patients (n = 60)</th>
<th>Transfemoral (n = 29)</th>
<th>Transapical (n = 31)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with new lesions</td>
<td>41 (68)</td>
<td>19 (66)</td>
<td>22 (71)</td>
<td>0.78</td>
</tr>
<tr>
<td>Total number of lesions</td>
<td>251</td>
<td>83</td>
<td>168</td>
<td></td>
</tr>
<tr>
<td>Lesions per patient</td>
<td>3 (2–8)</td>
<td>3 (1–7)</td>
<td>4 (2–9)</td>
<td>0.38</td>
</tr>
<tr>
<td>Patients with single lesion</td>
<td>10 (24)</td>
<td>5 (26)</td>
<td>5 (23)</td>
<td>1.00</td>
</tr>
<tr>
<td>Patients with multiple lesions</td>
<td>31 (76)</td>
<td>14 (74)</td>
<td>17 (77)</td>
<td></td>
</tr>
<tr>
<td>Lesion Left hemisphere</td>
<td>4 (10)</td>
<td>1 (5)</td>
<td>3 (14)</td>
<td></td>
</tr>
<tr>
<td>Lesions Bilateral</td>
<td>30 (73)</td>
<td>14 (74)</td>
<td>16 (73)</td>
<td></td>
</tr>
<tr>
<td>Anterior circulation territory</td>
<td>9 (22)</td>
<td>5 (26)</td>
<td>4 (18)</td>
<td>0.58</td>
</tr>
<tr>
<td>Posterior circulation territory</td>
<td>5 (12)</td>
<td>3 (16)</td>
<td>2 (9)</td>
<td></td>
</tr>
<tr>
<td>Anterior and posterior circulation territories</td>
<td>27 (66)</td>
<td>11 (58)</td>
<td>16 (73)</td>
<td></td>
</tr>
<tr>
<td>Lesion size, cm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;1</td>
<td>229 (91)</td>
<td>76 (92)</td>
<td>153 (91)</td>
<td>1.00</td>
</tr>
<tr>
<td>1-5</td>
<td>22 (9)</td>
<td>7 (8)</td>
<td>15 (9)</td>
<td>1.00</td>
</tr>
<tr>
<td>&gt;5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Time of post-procedural DW-MRI, days</td>
<td>4 (2–6)</td>
<td>4 (2–6)</td>
<td>5 (3–6)</td>
<td>0.37</td>
</tr>
</tbody>
</table>

Pts with new lesions: TF 66%  TA 71%
Cerebral Ischemia after Transcatheter Aortic Valve Implantation

Detection of Source of Emboli
- intraprocedural monitoring of both MCAs (temporal window)
- DWL Multi-Dop® $T^{digital}$ with PW 2 MHz monitoring probes
- adjustable DiaMon® probe fixation system
- dedicated software (QL, version 2.5) Compumedics Germany GmbH
- insonation depth: 50-55 mm, sample volume size: 8-16 mm, pulse repetition frequency: 1.5 kHz (probe specific)
- multigate Doppler M-mode spectogram (32 gates)
- intensity threshold for HITS detection: 9 dB
- automated HITS detection software and 2 human observers who attended all examinations directly watching the patient

## Patient Demographics and Procedure Details

<table>
<thead>
<tr>
<th></th>
<th>TF - CoreValve</th>
<th>TF - Edwards</th>
<th>TA-Edwards</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=32</td>
<td>n=15</td>
<td>n=16</td>
<td></td>
</tr>
<tr>
<td>Age [years]</td>
<td>80±7</td>
<td>84±4</td>
<td>81±4</td>
<td>0.119</td>
</tr>
<tr>
<td>Male Gender [n, %]</td>
<td>21 (38%)</td>
<td>5 (40%)</td>
<td>9 (54%)</td>
<td>0.103</td>
</tr>
<tr>
<td>BMI [kg/m²]</td>
<td>25.4 ± 3.7</td>
<td>27.3 ± 5.3</td>
<td>28.3 ± 4.9</td>
<td>0.096</td>
</tr>
<tr>
<td>ΔP\text{mean} [mm Hg]</td>
<td>51.4 ± 19.5</td>
<td>49.6 ± 9.5</td>
<td>58.6 ± 27.6</td>
<td>0.504</td>
</tr>
<tr>
<td>Aortic Valve Area</td>
<td>0.65 ± 0.19</td>
<td>0.59 ± 0.15</td>
<td>0.65 ± 0.21</td>
<td>0.571</td>
</tr>
<tr>
<td>LV EF [%]</td>
<td>49.9 ± 12.4</td>
<td>56.5 ± 3.7</td>
<td>50.8 ± 7.5</td>
<td>0.136</td>
</tr>
<tr>
<td>log. EuroSCORE [%]</td>
<td>17.3 ± 12.2</td>
<td>14.6 ± 8.6</td>
<td>29.9 ± 9.9</td>
<td>&lt;0.00</td>
</tr>
</tbody>
</table>

Procedural Success       100 100 100 -

ΔP\text{mean} [mm Hg]    9.9 ± 2.5 11.1 ± 7.6 10.7 ± 5.9 0.687

Aortic Valve Area [cm²]  1.62 ± 0.26 1.59 ± 0.29 1.76 ± 0.51 0.485

Kahlert et al. AHA 2010
Transcranial Doppler detected HITS

- Medtronic CoreValve
- Edwards Sapien - TF
- Edwards Sapien - TA

Valve Passage
Stiff Wire
BAV Balloon
BAV
Delivery System
Positioning
Implant
Total
## Transcranial Doppler Findings

### Number of HITS

<table>
<thead>
<tr>
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<tr>
<td><strong>n=32</strong></td>
<td><strong>n=15</strong></td>
<td><strong>n=16</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Aortic Valve Passage</strong></td>
<td>29.7 ± 48.5</td>
<td>24.7 ± 28.3</td>
<td>32.3 ± 32.5</td>
<td>0.869</td>
</tr>
<tr>
<td><strong>Introduction/Propagation of the Stiff</strong></td>
<td>30.3 ± 30.1</td>
<td>33.7 ± 29.1</td>
<td>25.1 ± 28.0</td>
<td>0.630</td>
</tr>
<tr>
<td><strong>Introduction/Propagation of the Balloon for BAV</strong></td>
<td>19.9 ± 24.0</td>
<td>19.1 ± 17.0</td>
<td>27.3 ± 17.2</td>
<td>0.453</td>
</tr>
<tr>
<td><strong>Balloon Aortic Valvuloplasty</strong></td>
<td>35.0 ± 39.3</td>
<td>27.8 ± 42.9</td>
<td>37.2 ± 18.3</td>
<td>0.746</td>
</tr>
<tr>
<td><strong>Propagation of the Delivery System / Valve</strong></td>
<td>16.1 ± 22.9</td>
<td>23.9 ± 25.5</td>
<td>19.8 ± 25.7</td>
<td>0.580</td>
</tr>
<tr>
<td><strong>Valve Positioning</strong></td>
<td>66.3 ± 139.0</td>
<td>226.3 ± 154.2</td>
<td>232.2 ± 111.4</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td><strong>Valve Implantation</strong></td>
<td>413.1 ± 264.5</td>
<td>97.6 ± 41.0</td>
<td>96.5 ± 66.0</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td><strong>Total HITS</strong></td>
<td>613.6±302.64</td>
<td>452.1±185.3</td>
<td>465.6±191.9</td>
<td>0.061</td>
</tr>
</tbody>
</table>

Equal distribution of HITS between right and left side.
Neurocognitive Testing: TF vs TA

<table>
<thead>
<tr>
<th></th>
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<th>TA-Edwards</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=32</td>
<td>n=15</td>
<td>n=16</td>
<td></td>
</tr>
<tr>
<td>MMSE before TAVI</td>
<td>27.9 ± 1.6</td>
<td>27.1 ± 3.4</td>
<td>27.6 ± 3.1</td>
<td>0.659</td>
</tr>
<tr>
<td>MMSE after TAVI</td>
<td>27.9 ± 1.6</td>
<td>25.8 ± 5.2</td>
<td>28.0 ± 1.4</td>
<td>0.514</td>
</tr>
<tr>
<td>NIHSS before TAVI *</td>
<td>0 (0-3)</td>
<td>0</td>
<td>0 (0-1)</td>
<td>0.817</td>
</tr>
<tr>
<td>NIHSS after TAVI *</td>
<td>0 (0-3)</td>
<td>0 (0-8)</td>
<td>0 (0-1)</td>
<td>0.383</td>
</tr>
</tbody>
</table>

* median (range)

1 patient in group 2 had a stroke with moderate left-sided hemiparesis.
1 patient in group 1 experienced a transitory ischemic attack.
What can we do?
What should we do?
Embolic Protection – The Solution?
Embolic Protection – The Solution?
Results: Correct placement of the embolic protection device was achieved without difficulty in all patients. Continuous brachiocephalic and aortic pressure monitoring documented equal pressures without evidence of obstruction to cerebral perfusion. Additional procedural time due to the use of the device was 13 min (interquartile range: 12 to 16 min). There were no procedural complications. Pre-discharge cerebral magnetic resonance imaging found no new defects in any of 3 patients undergoing transcatheter aortic valve implantation and a new 5-mm acute cortical infarct in 1 asymptomatic patient after balloon valvuloplasty alone. No patient developed new neurological symptoms or clinical findings of stroke.

Conclusions: Embolic protection during transcatheter aortic valve intervention seems feasible and might have the potential to reduce the risk of cerebral embolism and stroke. (J Am Coll Cardiol Intv 2010;3:1133–8) © 2010 by the American College of Cardiology Foundation

"... seems feasible and might have the potential to reduce the risk of cerebral embolism and stroke".
Conclusions

- cerebral microemboli detected by TCD in almost all patients
- main origin of these emboli was the calcified aortic valve
- manipulation of the sclerotic and calcified leaflets during valve positioning and implantation of the metallic stent frame into the aortic annulus was associated with the highest amount of HITS

- TA-TAVI was not associated with a lower rate of HITS, but TF-TAVI using the CoreValve device with a higher rate
Summary of the Findings

- prospective examination of 32 TAVI patients
- 115 new DWI lesions in 27 of 32 TAVI patients (84%)
- 10 of 21 surgical patients had DWI lesions (48%)
- lesions in TAVI patients were significantly smaller
- no neurological or neurocognitive deficits in the TAVI patients
- one stroke in the lower-risk surgical group
- no detectable scar formation on 3-month follow-up DW MRI
Conclusion

- Clinically silent new foci of restricted diffusion on cerebral MRI were detected in almost all (84%) patients undergoing TAVI.

- These foci were not associated with apparent neurological events or measurable deterioration of neurocognitive function during 3-month follow-up.

- Further work needs to be done to determine the exact origin of these foci and their clinical significance.
Cerebral Embolization during Transcatheter Aortic Valve Implantation: A Transcranial Doppler Study.

Philipp Kahlert¹, Philipp Doettger¹, Kathrine Mori¹, Fadi Al-Rashid¹, Matthias Thielmann², Daniel Wendt², Marc Schlamann³, Heinz Jakob², Raimund Erbel¹ and Holger Eggebrecht¹

West-German Heart Center Essen, Essen, Germany
Department of Cardiology¹, Department of Thoracic and Cardiovascular Surgery²
Institute of Diagnostic and Interventional (Neuro)Radiology³
Aim of the Study

- to assess the origin of cerebral emboli during TAVI (transfemoral and transapical) using transcranial Doppler
- to evaluate each step of the procedure regarding occurrence of microembolic signals
- to clarify whether transapical TAVI is associated with a lower rate of cerebral embolization as currently suggested
Patient Characteristics

- 63 out of 175 consecutive TAVI patients since 08/2009
  (exclusion of 99 patients due to poor acoustic windows and 13 due to refusal)

- **Group 1:** TF-TAVI using the CoreValve® prosthesis (n=32)

- **Group 2:** TF-TAVI using the Edwards Sapien/Sapien XT stent-valve (n=15)

- **Group 3:** TA-TAVI using the Edwards Sapien/Sapien XT prosthesis (n=16)