Brain diffusion tensor imaging in patients with transcatheter aortic valve implantation: early results of the RETORIC study

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Aims and objectives

Chronic cerebral hypoperfusion due to severe aortic valve stenosis impairs neural function, potentially causing alterations in white matter (WM) integrity, that can be measured using diffusion tensor imaging (DTI). These patients can be treated with transcatheter aortic valve implantation (TAVI) and, in this study, we hypothesized that WM microstructural integrity improves significantly after TAVI, together with cognitive function.

DTI provides information on the anisotropic diffusion of water molecules. By measuring the fractional anisotropy (FA) and apparent diffusion coefficient (ADC), it is possible to detect changes at the level of cellular microarchitecture, as well as to show changes in normal appearing WM (NAWM) that are not visible on plain MR.

FA reflects the directionality and coherence of water selfdiffusion:

- highly regular WM fibers have high anisotropy;
- less regular WM fibers demonstrate low anisotropy.

The ADC is an indicator of the average diffusion of a water molecule within a given voxel and it is independent of the directionality. Tissues such as WM exhibit low ADC because of cellular barriers to diffusion.

There are some studies using diffusion weighted MRI (DWI-MRI) in patients undergoing TAVI, reporting periprocedural new embolic lesions in 61-90% of patients [1-6], with a minority developing focal neurological deficit [1-5] and a great majority with preserved cognitive performance after 3 months [6] or 2 years after TAVI [7]. To the best of our knowledge, this is the first report focusing on DTI in relation to cognitive function in TAVI patients.
Methods and materials

**Study population**
Following IRB approval, we selected all TAVI patients from the prospective arm of the Rule out Transcatheter Aortic Valve Thrombosis with Post-implantation Computed Tomography (RETORIC) study (NCT02826200) with complete imaging data. The study was performed in accordance with institutional guidelines and all patients signed a written informed consent before participation in the examination.

**MRI protocol**
All patients underwent MRI-DTI one week and 6-9 months after TAVI (discharge and follow up). All examinations were performed on a 1.5-T MR scanner (Achieva1.5, Philips Medical Systems, Best, The Netherlands) using a 8-channel head coil. The imaging protocol included: axial Fluid-Attenuated Inversion Recovery (FLAIR) T2-weighted, T2*-Gradient Echo (GRE), sagittal 3D T1-weighted sequences.

**Diffusion tensor imaging**
DTI studies were performed using a single shot Spin Echo Echo-Planar Imaging (SE EPI) sequence in 32 coding directions with the following parameters:

- Repetition time (TR): 14-19 ms
- Echo time (TE): 62 ms
- Flip angle (FA): 90°
- EPI Factor: 59
- Turbo Factor: 59
- matrix: 112 x 128
- Field of view (FOV): 24 x 24 cm
- number of excitations 1
- b values 0 and 1000 s/mm².

**ERRATUM: the last bullet point above should read as follows:**

- b values 0 and 800 s/mm²

Axial 2 mm-thick slices with no spacing were obtained. The total **acquisition time was 7 min 30 s - 8 min 30 s.**

DTI data were post-processed on a commercial workstation (Extended MR WorkSpace 2.6.3.5, Philips Medical Systems, Best, The Netherlands) using the Fiber Tracking software to generate **color-coded and parametric maps** of FA and ADC.
measurements were obtained on axial slices using ROIs of 20 mm² within the selected 16 WM tracts, which were defined using available anatomy atlases and publications [8-9].

The association fibers included

- the right and left inferior longitudinal fasciculi (ILFs) at the level of midbrain Fig. 1 on page 5;
- the inferior fronto-occipital fasciculi (IFOFs) at the level of inferior aspect of the thalami Fig. 2 on page 5
- the superior longitudinal fasciculi (SLFs) at the level of superior aspect of lateral ventricles Fig. 3 on page 6;
- the cingulate gyrus (CG) fibers above the body of the corpus callosum Fig. 4 on page 7;
- the lateral parts of the arcuate fascicle (AF) above the temporal stem posterior to the Sylvian fissure Fig. 5 on page 8.

The assessed commissural tracts included the genu (GCC) and the splenium (SCC) of the corpus callosum at the level of basal ganglia Fig. 6 on page 9.

The examined projection tracts included the posterior limbs of internal capsules (PLICs) Fig. 7 on page 10 and the middle cerebellar peduncles (MCPs) Fig. 8 on page 11.

Only WM tracts with normal signal intensity were included in our study.

**Neurologic evaluation**

Cognitive function was tested in a subgroup of 14 patients within one week and 6-9 months following the TAVI procedure. Global cognitive function was assessed using the Mini Mental State Examination (MMSE); specific cognitive domains were investigated using the Addenbrooke's cognitive examination (ACE). ACE is a brief cognitive test that assesses five cognitive domains, namely attention/orientation, memory, verbal fluency, language and visuospatial abilities (the total score is 100).

**Statistical Analysis**

Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables as counts and percentages. Intra-individual changes between the discharge and follow up examinations were assessed using the Wilcoxon test for paired data. All statistical calculations were performed using SPS software (SPSS v.23; IBM Corp., Armonk, NY).
Images for this section:

Fig. 1

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Fig. 2

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Fig. 3

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Fig. 8

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Results

Out of 77 consecutive patients of the RETORIC study, we included 23 subjects (8 males, age 77±7 years, range 63-91 years) in our analysis. The remaining 54 patients had:

- missing baseline DTI (n=5)
- not yet/not performed follow up DTI (n=44)
- poor DTI image quality (n=5)

We found improved directionality and coherence of water diffusion in the NAWM of all fiber tracts, reflected by increased FA and decreased ADC.

Apart from the left middle cerebellar peduncle and right arcuate fascicle (AF), all other fiber tracts showed significant increase in FA (p<0.022), from 4% to 13%.

Apart from the right posterior limb of internal capsule, the left AF and the left superior longitudinal fascicle, the other fibers showed significant decrease in ADC (p<0.016), from 3% to 9%. Table 1.

Table 1.

<table>
<thead>
<tr>
<th>Fiber Tract</th>
<th>Average FA (SD) x 1000</th>
<th>ADC (SD) x 10^-6 mm^2/s</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Discharge (FU)</td>
<td>Change (%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Discharge (FU)</td>
</tr>
<tr>
<td>Rt ILF</td>
<td>612 (64)</td>
<td>686 (61)</td>
</tr>
<tr>
<td>Lt ILF</td>
<td>620 (66)</td>
<td>682 (62)</td>
</tr>
<tr>
<td>Rt IFOF</td>
<td>596 (66)</td>
<td>659 (61)</td>
</tr>
<tr>
<td>Lt IFOF</td>
<td>616 (60)</td>
<td>677 (66)</td>
</tr>
<tr>
<td>Rt SLF</td>
<td>605 (68)</td>
<td>647 (66)</td>
</tr>
<tr>
<td>Lt SLF</td>
<td>603 (76)</td>
<td>655 (66)</td>
</tr>
</tbody>
</table>
**Significant improvement** was found in verbal fluency (p=0.039) and language (p=0.034), whereas the total ACE and MMSE scores did not change significantly (p=0.310 and p=0.066, respectively). Table 2.

Variations in cognitive function were minimal, preventing correlation with DTI findings.

Table 2.
<table>
<thead>
<tr>
<th></th>
<th>26</th>
<th>21</th>
<th>27</th>
<th>27</th>
<th>24</th>
<th>28</th>
<th>0.034</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Language</strong></td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>3</td>
<td>5</td>
<td>0.914</td>
<td></td>
</tr>
<tr>
<td><strong>Visuospatial abilities</strong></td>
<td>66</td>
<td>57</td>
<td>78</td>
<td>67</td>
<td>62</td>
<td>78</td>
<td>0.310</td>
</tr>
<tr>
<td><strong>ACE (total)</strong></td>
<td>24</td>
<td>28</td>
<td>27</td>
<td>21</td>
<td>28</td>
<td>0.066</td>
<td></td>
</tr>
</tbody>
</table>
Conclusion

Our preliminary data show microstructural improvement after TAVI in the measured WM tracts of patients with aortic valve stenosis. Furthermore we found improvement in some cognitive function domains. The RETORIC study might reveal important implications regarding the effect of TAVI on neural function.
References


White%20Matter%20Tract%20Anatomy/DTI%20tutorial%201.html