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# Serial Changes in Cognitive Function Following Transcatheter Aortic Valve Replacement

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## ABSTRACT

**BACKGROUND** Data regarding the mid- to long-term cognitive trajectory of transcatheter aortic valve (TAVR) recipients are scarce.

**OBJECTIVES** Changes in global cognition and specific cognitive domains up to 1 year post-TAVR were evaluated.

**METHODS** Fifty-one patients (median age 80.0 [interquartile range: 72.0 to 85.0] years; 37% women) underwent TAVR and prospective assessment of cognitive function using the Montreal Cognitive Assessment (MoCA) at baseline, short-term (30 days), and 1 year post-TAVR. Processing speed and executive cognitive functions were further evaluated with the digit-symbol substitution test (DSST), Trail Making Tests (TMT), and verbal fluency tests at the same time points. Cognitive decline (CD) was determined by changes in mean scores and as a rate using practice-corrected reliable change index (RCI).

**RESULTS** The baseline mean total MoCA score was 22.71 ± 3.84. Twenty patients (39.2%) were considered cognitively impaired using a cutoff of <23 of 30 points. Mean total MoCA score improved at short-term post-TAVR and remained stable at 1 year ($p = 0.022$). On the basis of the RCI of total MoCA score, 4 patients (7.8%) presented with short-term CD, which persisted at 1 year in 1 patient (2.0%). Four patients (7.8%) exhibited cognitive improvement at 1 year, increasing to 15% among those with baseline cognitive impairment. No significant changes were observed over time in the mean DSST, TMT, and verbal fluency test scores. On the basis of the RCI, 10 of 40 patients (25%) presented with a reduction in performance of at least 1 test at 30 days that persisted at 1 year in 4 patients (10%).

**CONCLUSIONS** TAVR was associated with global improvement in cognitive status, more pronounced among those with cognitive impairment pre-TAVR. However, early decline in some complex cognitive functions was observed in one-quarter of TAVR recipients, persisting at 1 year in 10% of patients. (J Am Coll Cardiol 2016;■:■–■)
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Clinically apparent stroke occurs in ~4% (1.5% to 5%) of patients undergoing transcatheter aortic valve replacement (TAVR), and is associated with increased short- and mid-term mortality (1-3). However, new ischemic brain lesions on diffusion-weighted magnetic resonance imaging (DW-MRI) are found in ≈75% of patients (4), and cerebral embolization is almost ubiquitous in studies

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**ABBREVIATIONS AND ACRONYMS**

**CD** = cognitive decline

**DSST** = digit-symbol substitution test

**DW-MRI** = diffusion-weighted magnetic resonance imaging

**MoCA** = Montréal Cognitive Assessment

**RCI** = reliable change index

**TAVR** = transcatheter aortic valve replacement

**TMT** = Trail Making Test

that used dual carotid filters (5) or transcranial Doppler (6). Although the cognitive impact of these findings post-TAVR remains controversial, subclinical cerebral lesions were previously linked to a >2-fold risk of subsequent dementia in other settings (7). Few studies have specifically assessed the cognitive trajectory of TAVR recipients, and most have focused on memory during a short follow-up period (6,8-19). However, cognitive impairment in patients undergoing TAVR may predominantly be of vascular origin, primarily affecting executive functioning and necessitating specific evaluation (20). Furthermore, there has been a high variability across studies in the methodology used to determine significant changes in cognitive status, and no study to date has used the practice-adjusted reliable change index (RCI) (21,22), a well-known tool that takes into account possible measurement errors and practice effects in the evaluation of cognitive status changes over time.

This study evaluated 1-year changes in global cognition and specific cognitive domains among TAVR recipients using a standardized battery of neuropsychological tests, including complex cognitive status evaluation tests.

**TABLE 1 Baseline Characteristics of Included and Excluded Patients**

| | Included Patients (n = 51) | Excluded Patients (n = 50) | p Value |
|---|---|---|---|
| Age, yrs | 80.0 (72.0-85.0) | 82.0 (76.0-86.0) | 0.278 |
| Female | 19 (37.3) | 23 (46.0) | 0.490 |
| Body mass index, kg/m$^2$ | 27.2 ± 5.2 | 27.4 ± 5.0 | 0.845 |
| Hypertension | 43 (84.3) | 42 (84.0) | 1.000 |
| Diabetes mellitus | 19 (37.3) | 22 (44.0) | 0.626 |
| Atrial fibrillation | 12 (23.5) | 19 (38.0) | 0.174 |
| New York Heart Association functional class III or IV | 28 (54.9) | 35 (70.0) | 0.174 |
| Coronary artery disease | 30 (58.8) | 29 (58.0) | 1.000 |
| Previous myocardial infarction | 12 (23.5) | 11 (22.0) | 1.000 |
| Previous stroke/transient ischemic attack | 8 (15.7) | 7 (14.0) | 0.967 |
| Peripheral vascular disease | 13 (25.5) | 16 (32.0) | 0.659 |
| Chronic obstructive pulmonary disease | 15 (29.4) | 19 (38.0) | 0.437 |
| Chronic kidney disease | 27 (52.9) | 28 (56.0) | 0.913 |
| Logistic EuroSCORE I (%) | 19.6 ± 10.8 | 19.6 ± 14.4 | 0.444 |
| STS-PROM (%) | 6.5 ± 4.4 | 8.0 ± 5.7 | 0.189 |
| Echocardiographic characteristics | | | |
| Left ventricular ejection fraction (%) | 53.8 ± 12.6 | 50.4 ± 16.0 | 0.196 |
| Aortic valve area, cm$^2$ | 0.78 ± 0.40 | 0.64 ± 0.23 | 0.116 |
| Aortic mean gradient, mm Hg | 38.9 ± 18.9 | 41.7 ± 14.6 | 0.421 |

Values are median (interquartile range), n (%), or mean ± SD.

EuroSCORE = European System for Cardiac Operative Risk Evaluation; STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality.

## METHODS

**STUDY POPULATION AND TAVR PROCEDURES.** A total of 101 TAVR candidates underwent cognitive assessment at baseline. Of these, 50 patients did not complete the serial cognitive assessment post-TAVR, either because of unsuccessful TAVR with no valve implantation or periprocedural death (n = 3), death within the year following TAVR (n = 12), patient's refusal of an on-site follow-up (n = 7), patient's refusal of the neurocognitive tests (n = 2), or logistic reasons (n = 26). The final study population consisted of 51 patients.

All baseline, procedural, and follow-up data were prospectively gathered within a dedicated database. The study protocol was in accordance with the institutional ethics committee and all patients provided written informed consent for the procedures. The local heart team determined TAVR indications, approach, and the type of transcatheter valves used. Details of TAVR procedures were reported elsewhere (23).

Follow-up was obtained by clinical outpatient visit at 30 days and 1 year post-TAVR. Periprocedural events were defined according to the Valve Academic Research Consortium (VARC)-2 criteria (24). Functional status was assessed with the use of the Duke Activity status index (Online Figure 1). Quality of life was measured with the EQ-5D-3LTM questionnaire (Online Figure 2), using both index scores and the visual analog scale. As no general Canadian population survey was available for the calculation of index scores, they were calculated with data from the U.S. and European population.

**COGNITIVE ASSESSMENT.** All subjects underwent a standardized cognitive assessment using the Montreal Cognitive Assessment (MoCA), performed by a trained, dedicated staff at baseline, at short-term (30 days), and at 1 year post-TAVR. Additionally, the digit-symbol substitution test (DSST), Trail Making Tests (TMT) Parts A and B, the word fluency test, and the animal naming test were also performed to further assess specific cognitive domains. The MoCA test was administered first, followed by the DSST, TMT, and word fluency/animal naming tests. All patients completed the MoCA test at all time points, but 11 patients refused to complete at least 1 of the other cognitive tests. A description of these cognitive tests is provided in the Online Appendix.

To measure the cognitive change during follow-up, while taking into account measurement errors and practice effects, we used the practice-adjusted