

App-based assessment of neurocognitive changes in patients undergoing transcatheter aortic valve implantation - a prospective cohort study

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ABSTRACT

Background Transcatheter aortic valve implantation (TAVI) has emerged as an established treatment for severe aortic stenosis in elderly patients. Periprocedural cerebral embolic events are common and may contribute to subtle neurocognitive changes. Conventional neurocognitive assessments are time-consuming and resource-intensive, limiting their routine use. Digitalized, app-based testing with AI-assisted recording may offer a feasible alternative. This study aimed to evaluate the use of app-based cognitive screening with AI-assisted recording in elderly TAVI patients and, building on prior pilot findings, to provide a more comprehensive, norm-referenced evaluation of cognitive function across multiple domains.

Methods Neurocognitive assessments were performed before and after TAVI. Seven validated tests were administered and recorded using the “Delta-App” on a tablet. Patient performance was compared with normative data.

Results Between October 2020 and March 2022, 141 patients (mean age 81 ± 6 years; 57.5% male) were enrolled, of whom 112 (79%) completed post-TAVI testing. Memory performance improved significantly (Word List Learning + 2.13 (± 3.22) words; $P < 0.001$; Word List Recall + 1 word; $P < 0.001$), while executive function, attention and processing speed remained stable. Overall, 37.7% were cognitively impaired pre-TAVI vs. 31.6% post-TAVI, with 59.6% remaining stable. Compared with normative data, performance was reduced but unchanged post-procedure. The app-based assessment proved well applicable in this elderly population.

Conclusion In this single-center study, TAVI was not associated with a consistent decline in global cognitive performance during the early postoperative period. App-based neurocognitive testing proved to be readily applicable and may represent a valuable tool for routine clinical monitoring, supporting systematic assessment and early detection of cognitive changes to optimize rehabilitation outcomes.

Degenerative aortic valve stenosis is one of the most common heart valve diseases, particularly affecting the elderly.^[1] When the stenosis becomes severe and symptomatic, valve replace-

ment becomes necessary. Operative therapies include surgical aortic valve replacement (SAVR) or minimal invasive transcatheter aortic valve implantation (TAVI).^[2]

TAVI is predominantly performed in patients at high

surgical risk, often elderly individuals with multiple comorbidities.^[3] Prior to TAVI, this population already shows reduced memory function relative to age-matched controls.^[4] Additionally, they are at high risk of both intraoperative and postoperative complications such as postoperative neurocognitive impairments including delirium, postoperative cognitive dysfunction, and stroke-related cognitive decline.^[5,6] Besides the more prominent strokes, which are often recognized and treated, even smaller strokes, which often go unnoticed, can have significant effects on cognition.^[7]

These cognitive changes can significantly impact the overall success of the procedure. In elderly patients, cognitive outcomes are crucial for recovery. Postoperative cognitive decline can delay physical rehabilitation, reduce quality of life, and impair the ability to live independently.^[8,9] It is therefore essential to determine the extent of cognitive changes following TAVI and assess how they might affect postoperative recovery.

Currently, there is no standardized method for assessing cognitive changes in areas such as memory, attention, cognitive flexibility, and inhibitory control. Although cognitive function has been investigated in numerous studies following TAVI,^[10-13] the assessment methods used have been highly heterogeneous. None of these approaches, however, has gained widespread adoption in routine clinical practice outside of research settings. Standardized, time-intensive cognitive testing requires trained personnel and has not been integrated into clinical protocols.

Reliable and objective cognitive assessments could play a key role in personalized postoperative rehabilitation planning, yet the implementation of such assessments in routine clinical practice remains challenging. A promising approach involves the use of app-based, standardized digital test batteries with AI-assisted scoring. These systems have the potential to objectively evaluate cognitive performance based on normative data,^[14] enabling scalable and accessible assessment in both clinical and research contexts.

This study aimed to evaluate the use of app-based cognitive screening with AI-assisted speech recognition in elderly TAVI patients and to explore its potential to detect subtle individual cognitive changes, expanding upon earlier pilot work^[4] by including a broader neurocognitive test battery, domain-specific normative comparisons, and standardized, STROBE-compliant methodology.

METHODS

This study represents an extension of the previously published pilot study,^[4] which focused primarily on memory function and attention, employing only the CERAD Word List and Digit Span Test to demonstrate a significant short-term improvement in memory performance after TAVI, with reference to a single normative dataset. Here, we expanded the cognitive assessment to seven validated cognitive tests across multiple domains—memory, executive function, processing speed, and verbal fluency—and introduced detailed comparisons with age-, sex-, and education-adjusted normative reference values. This comprehensive approach allowed for a multidimensional classification of cognitive trajectories.

Patients

Included were patients scheduled for TAVI at the University Hospital Heart Center Brandenburg between October 2020 and March 2022. Patients aged ≥ 18 years with severe symptomatic aortic stenosis scheduled for elective TAVI were included if classified as high surgical risk according to European Society of Cardiology (ESC) guidelines.^[15] All patients were initially evaluated in an interdisciplinary Heart Team including interventional cardiologists, cardiothoracic surgeons and cardiovascular anesthesiologists.

Exclusion criteria included emergency procedures, dialysis patients, patients (or their legal representatives) unable to provide written informed consent for study participation, and conditions that precluded neurocognitive testing.

Procedures were performed under conscious sedation (CS) or general anesthesia (GA). Depth of anesthesia was monitored in all patients using bispectral index (BIS) monitoring, with target ranges of 40–60 for general anesthesia and >70 for conscious sedation.

In addition, intraoperative cerebral oxygenation was continuously monitored in all patients using near-infrared spectroscopy (NIRS), as part of the standard monitoring protocol. The study was approved by the local ethics committee (E-01-20191006). The study was registered with the German Clinical Trial Register (DRKS00020813). Reporting of results adhered to STROBE recommendation.^[16]

Data Collection

For neurocognitive testing, the “Delta-App” (version



1.2.1, ki elements UG) was used on a third-generation iPad Air (Apple, iPadOS 14.4) in combination with an Apple Pencil (first generation). Interactions, both via touchscreen and voice recognition, were automatically recorded. Reaction times, as well as correct and incorrect touchscreen responses, were automatically captured by the app. In selected tests, standardized scores (e.g., Z-scores, Efficiency scores) were calculated based on pre-defined algorithms. AI-assisted speech recognition was used for the automated capture and processing of verbal responses (e.g., in word generation tasks). All automated analyses were cross-checked by a trained psychologist, who manually compared the outputs with the raw data to ensure accuracy and validity. Deidentified test data were then extracted for further analysis.

Preoperative tests were conducted upon admission. Postoperative tests were performed after patients had been transferred from the intensive care or recovery unit back to the general ward. Demographic and clinical data were collected via the app to enable definition of the normative sample subgroups. Additional clinical data was obtained from the electronic medical record. Postoperative delirium screening was conducted in all patients using the "Confusion Assessment Method for the Intensive Care Unit" (CAM-ICU).^[17]

Neurocognitive Tests

A battery of seven neurocognitive tests was administered to assess cognitive function before and after the TAVI. Table 1 provides an overview of the neurocognitive tests.

CERAD Word List Learning and Recall Test

The CERAD Word List Memory Test consists of two parts: the Word List Learning (WL-W) and the Word List Recall (WL-A) subtests. In the WL-W, patients were presented with a list of 10 words, which were read aloud to them three times consecutively.

After each presentation, patients were asked to verbally recall as many words as they could remember. The number of correctly recalled words was recorded. At the end of our cognitive test battery, patients were asked to retrieve the same 10 words from the WL-W test, which was referred to as the Word List Recall Test (WL-A). The Z-score provides a standardized measure of test performance relative to the CERAD normative cohort. The values were automatically generated by the AI-based scoring system. A Z-score of "0" indicates no impairment, "1" mild cognitive impairment, "2" moderate impairment and "3" severe cognitive impairment.^[18]

Trail Making Test A/B

Within the Trail Making Test A (TMT-A), patients were instructed to connect numbers with the Apple Pencil on the display in ascending order as quickly as possible (1, 2, 3, 4, etc.). Both the total time taken to complete the sequence and the number of errors (including errors of skipping (= error of commission) or omitting (= error of omission)) were recorded. For the Trail Making Test B (TMT-B), patients were required to alternate between numbers and letters in ascending order (e.g., 1-A-2-B-3-C, etc.). Again, the time to completion and the number of errors were documented.^[19] The Efficiency Score is a per-

Table 1 Overview of neurocognitive tests.

Test	Cognitive Domains	Description	Outcome
CERAD Word List Learning (WL-W)	Short-term memory, learning	10-word list presented 3×, immediate recall after each presentation	Number of correctly recalled words
CERAD Word List Recall (WL-A)	Long-term memory, retrieval	Recall of same 10 words after delay (end of test battery)	Number of correctly recalled words
Trail Making Test A (TMT-A)	Processing speed, visual attention	Connect numbers in ascending order	Completion time, number of errors
Trail Making Test B (TMT-B)	Cognitive flexibility, divided attention	Connect alternate numbers and letters in ascending order	Completion time, number of errors
Digit Span Test (DST)	Working memory, attention span	Repeat increasingly long digit sequences	Maximum correctly recalled span length
Victoria Stroop Test (VST)	Inhibitory control, processing speed	Name color of dots, neutral words, incongruent color words	Correct responses, reaction time
Phonemic Fluency Test (PFT)	Executive function, speech production	Generate words starting with letter "A" (pre-TAVI) or "F" (post-TAVI) in 60s	Total number of correct words

Overview of the neurocognitive tests, corresponding domains, and outcomes. TAVI: transcatheter aortic valve implantation.



formance index derived from the ratio of processing speed to error rate. Lower scores indicate impaired efficiency in cognitive task execution.^[20]

The Digit Span Test

During the Digit Span Test (DST), patients were presented with a sequence of digits, starting with two digits and increasing by one digit per successful repetition. Patients were asked to repeat the digits in the same order immediately after presentation. The test was discontinued after the patient failed to reproduce the correct sequence in two consecutive attempts of the same length. The maximum span length (i.e., the highest number of digits correctly recalled) was recorded for each patient.^[21]

Victoria Stroop Test

When performing the Victoria Stroop Test (VST), patients were asked to name the color of the presented stimulus (dot, word or inked word), rather than reading the stimulus itself.

The test consists of three phases of increasing difficulty. In the first phase patients were asked to name the color of a colored dot (e.g., red, blue, yellow). In the second phase, they are shown color-neutral words (e.g., “hello,” “sun,” “around”). In the third phase, color words (e.g., “red”) are shown printed in an incongruent ink color (e.g., “red” printed in blue ink). Participants must name only the ink color while ignoring the word meaning.

For each repetition, the number of correct and incorrect responses as well as the total time to completion were recorded.^[22]

Phonemic Fluency Test

At the beginning of the Phonemic Fluency Test (PFT), participants were presented with a single letter and instructed to orally produce as many words as possible, beginning with that letter within 60 seconds. The letter “A” was administered in the pre-TAVI assessment, while the letter “F” was used in the post-TAVI assessment. The total number of produced words was recorded.^[23]

Cognitive Change

A cutoff of 1.5 standard deviation (SD) from the normative mean was applied, representing a widely used and well-established threshold in neuropsychological and mild cognitive impairment (MCI) research.^[24,25] Cog-

nitive impairment was defined as a test score ≥ 1.5 SD below the normative mean for accuracy-based measures (e.g., number of correct responses), or ≥ 1.5 SD above the mean for time-based measures (e.g., task completion time).

Conversely, scores in the opposite direction (≥ 1.5 SD above the mean for accuracy-based measures or ≤ 1.5 SD below the mean for time-based measures) were classified as above-average performance. For multi-variable tests, a patient was considered “impaired” (or “above-average”) if at least one variable met the respective threshold.

The term “cognitive decline” is used when patients newly meet the criteria for cognitive impairment within a given domain compared to baseline. Note that a patient could simultaneously be categorized as “impaired” in one test and “above-average” in another, which could lead to double-counting. Cognitive trajectories were then analyzed by comparing pre- and post-TAVI status, allowing identification of patients who remained stable, improved, or developed new cognitive impairment after TAVI. To ensure accurate assessment of changes over time, the analysis included only those patients who underwent testing both before and after the intervention.

Reference samples

Validated normative samples were used for each cognitive assessment. Normative values for WL-W, WL-A, TMT-A, TMT-B and PFT were obtained from the CERAD reference sample.^[18] For the DST, normative data from a study by H. J. Choi^[26] was used. The VST was evaluated using normative values from a cohort of 272 healthy, community-dwelling adults age 18 to 94 in Canada.^[22]

Statistical Analysis

For baseline characteristics, continuous variables are presented as median with interquartile range (IQR) and mean with standard deviation (SD) and categorical variables as absolute numbers with percentages. Normality was tested using Shapiro-Wilk analysis. Continuous variables with dependent observations were compared using paired Student’s *t*-tests for normally distributed data or Wilcoxon signed-rank test for non-normally distributed data. Differences in the number of patients showing improvement versus decline were assessed using McNemar’s test. For comparison with the reference sample, the cohort was divided into age-, gender-, and education-specific groups, respectively. A *p*-value of less



than 0.05 was considered statistically significant. Data analysis was performed using R software (Version 2023.12.1+402 (2023.12.1+402)). The following packages were used: qwraps2,^[27] naniar,^[28] table1,^[29] ggplot2,^[30] comorbidity,^[31] dplyr,^[32] tidyr^[33] and patchwork^[34]

RESULTS

Patient Characteristics and Outcome

A total of 141 patients (57.5% men) were included in the analysis with a mean age of 81 ± 6 years (range 57–94 years). Of 141 enrolled patients, 112 (79%) successfully completed both pre- and post-procedure cognitive testing. Patient flow is shown in Figure 1. Baseline characteristics overall and by age group are shown in Table 2. A total of 30 patients underwent conscious sedation, whereas 110 patients received general anesthesia (0.71% missing values). The mean time from baseline cognitive assessment to TAVI was 2.0 ± 5.2 days. On average, the follow-up cognitive assessment was performed 5.0 ± 3.1 days after the procedure. Following TAVI implantation, 7 patients (5.2%) required admission to the intensive care unit. Six patients (4.3%) developed delirium. One patient (0.7%) died during the hospital stay. The median length of hospital stay was 10.0 (8.0–13.0 days) days. Within three months, 23 patients (16.3%) required rehospitalization. Three patients (2.1%) died within three month and 5 patients (3.5%) within six months. Follow-up data are presented in Table 2.

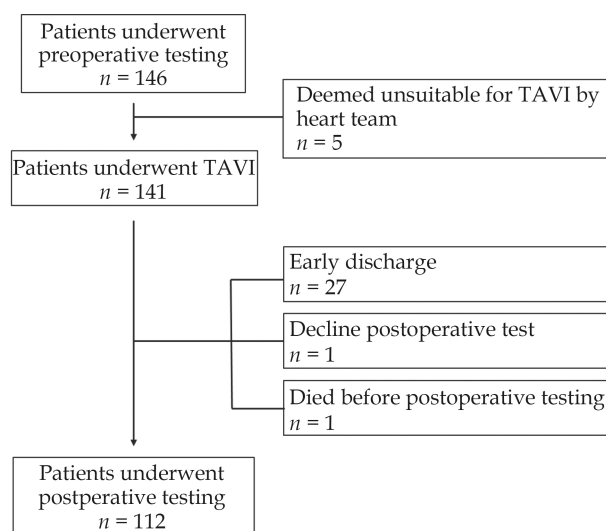


Figure 1 Patient flow through the study. Flow chart. TAVI = Transcatheter aortic-valve implantation.

The use of the tablet and Apple Pencil was not associated with major difficulties. Only minor technical issues (occasional touchscreen or speech-recognition interruptions) occurred, without relevant data loss or patient exclusion.

CERAD Word List Learning and Recall Test

A total of 141 patients completed the WL-W prior to TAVI, and 112 underwent follow up assessment after TAVI. 76 patients (68%) showed improvement in recalled words, with a mean increase of $2.13 (\pm 3.22)$ words ($P < 0.001$; Table 3, Table S1 and Figure 2).

In the WL-A, 141 patients completed the assessment pre-TAVI, and 111 underwent testing post-TAVI. The median number of recalled words increased from 2 [0, 4] pre-TAVI to 3 [1,5] post-TAVI ($p < 0.001$; Table 2, Table S1 and Figure 3).

Trail Making Test A/B

A total of 141 patients completed the TMT-A and TMT-B before undergoing TAVI, and 103 patients repeated the TMT-A test as well as 102 patients the TMT-B test after the procedure. In both the TMT-A and TMT-B, there was no significant change in the number of errors or the time needed to complete the test (see Table 3, Table S1 and Figure 4 and 5).

The Digit Span Test

Of the 141 patients who completed the DST prior to TAVI, 112 patients completed the test after the procedure. No improvement in the mean number of correctly recalled digits was observed (see Table 3 and Figure 6).

Victoria Stroop Test

A total of 141 patients completed the VST prior to TAVI, 120 underwent follow-up assessment after TAVI. Neither the number of errors nor the time required showed significant changes in the color-naming of colored dots (24 [24,24] vs. 24 [24,24], $P = 0.51$) or color words (23 [22,24] vs. 24 [22,24], $P = 0.37$) (see Table 3 and Figure 7).

Although medians were identical, paired comparison indicated a small but statistically significant improvement in the median number of correctly read neutral words, increasing from 24 [24,24] prior TAVI to 24 [24,24] after TAVI ($P = 0.04$).



Table 2 Comparison of patient characteristics between age groups.

Patient Characteristics	< 69 yrs n = 8	69-79 yrs n = 38	> 79 yrs n = 95	Overall n = 141
Age, yrs	65 ± 4	76 ± 3	84 ± 3	81 ± 6
Men	6 (75.0%)	21 (55.3%)	54 (56.8%)	81 (57.5%)
Formal education, yrs	13.0 [13.0, 15.3]	10.0 [8.0, 10.0]	9.0 [8.0, 13.5]	10.0 [8.0, 13.0]
Length of stay	12.0 [10.8, 17.0]	10.5 [8.0, 12.0]	9.0 [8.0, 13.0]	10.0 [8.0, 13.0]
Comorbidities				
Diabetes type I	0 (0%)	1 (2.6%)	0 (0%)	1 (0.7%)
Diabetes type II (insulin)	4 (50.0%)	11 (28.9%)	18 (18.9%)	33 (23.4%)
Hyperlipoproteinemia	4 (50.0%)	20 (52.6%)	39 (41.1%)	63 (44.7%)
Smoker	3 (37.5%)	3 (7.9%)	10 (10.5%)	16 (11.3%)
COPD	0 (0%)	5 (13.2%)	9 (9.5%)	14 (9.9%)
Asthma	0 (0%)	0 (0%)	6 (6.3%)	6 (4.3%)
NYHA-Classification				
NYHA I	0 (0%)	0 (0%)	0 (0%)	0 (0%)
NYHA II	2 (25.0%)	8 (21.1%)	18 (19.0%)	28 (19.9%)
NYHA III	5 (62.5%)	25 (65.8%)	65 (68.4%)	95 (67.4%)
NYHA IV	1 (12.5%)	0 (0%)	6 (6.3%)	7 (5.0%)
Arterial hypertension	6 (75.0%)	31 (81.6%)	77 (81.1%)	114 (80.9%)
Coronary heart disease	5 (62.5%)	25 (65.8%)	61 (64.2%)	91 (64.5%)
Previous CABG	2 (25.0%)	6 (15.8%)	6 (6.3%)	14 (9.9%)
Previous PTCA	2 (25.0%)	13 (34.2%)	38 (40.0%)	53 (37.6%)
Previous myocardial infarction	1 (12.5%)	3 (7.9%)	9 (9.5%)	13 (9.2%)
Stroke	0 (0%)	2 (5.3%)	7 (7.4%)	9 (6.4%)
Atrial fibrillation	0 (0%)	7 (18.4%)	41 (43.2%)	48 (34.0%)
Hypertensive heart disease	0 (0%)	8 (21.1%)	10 (10.5%)	18 (12.8%)
Peripheral vascular disease	2 (25.0%)	3 (7.9%)	6 (6.3%)	11 (7.8%)
Cardiac device	0 (0%)	1 (2.6%)	15 (15.8%)	16 (11.3%)
Echocardiographic parameter				
LVEF (%)	50.0 [40.5, 58.8]	52.5 [42.0, 60.0]	54.5 [40.0, 60.0]	54.5 [40.0, 60.0]
TAPSE, mm	21 (5%)	20 (6%)	20 (5%)	20 (5%)
Procedural characteristics				
Sedation strategies				
Conscious sedation	0 (0%)	9 (24.3%)	21 (22.1%)	30 (21.4%)
General anesthesia	8 (100%)	28 (75.7%)	74 (77.9%)	110 (78.6%)
Fluoroscopy time, s	772 [601, 924]	587 [464, 759]	699 [527, 875]	686 [513, 861]
Valve size, mm	29.0 [29.0, 34.0]	28.0 [26.0, 29.0]	29.0 [29.0, 34.0]	29.0 [26.5, 34.0]
Self-expanding valve	4 (50.0%)	25 (65.8%)	82 (86.3%)	111 (78.7%)
Pre-dilatation	7 (87.5%)	25 (65.8%)	64 (67.4%)	96 (68.1%)
Post-dilatation	2 (25.0%)	7 (18.4%)	20 (21.1%)	29 (20.6%)
Valve-in-valve	1 (12.5%)	1 (2.6%)	4 (4.2%)	6 (4.3%)
Complications				
Cardiac decompensation	1 (12.5%)	0 (0%)	4 (4.2%)	5 (3.5%)
Septic shock	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Infection	1 (12.5%)	3 (7.9%)	4 (4.2%)	8 (5.7%)
Delirium	1 (12.5%)	2 (5.3%)	3 (3.2%)	6 (4.3%)
Stroke	0 (0%)	1 (2.6%)	3 (3.2%)	4 (2.8%)
ICU admission	3 (37.5%)	3 (7.9%)	1 (1.1%)	7 (5.0%)

Continued

Patient Characteristics	< 69 yrs n = 8	69-79 yrs n = 38	> 79 yrs n = 95	Overall n = 141
Died during hospital	0 (0%)	0 (0%)	1 (1.1%)	1 (0.7%)
Follow-up				
Died within 3 months	0 (0%)	0 (0%)	3 (3.2%)	3 (2.1%)
Rehospitalization within 3 months	1 (12.5%)	6 (15.8%)	16 (16.8%)	23 (16.3%)
Died within 6 months	1 (12.5%)	0 (0%)	4 (4.2%)	5 (3.5%)
Rehospitalization within 6 months	2 (25.0%)	5 (13.2%)	10 (10.5%)	17 (12.1%)

Values are displayed as *n* (%), mean $\pm$ SD or median [interquartile range]. Sedation strategies: 0.71% missing values. CABG: coronary artery bypass graft; COPD: chronic obstructive pulmonary disease; ICU: intensive care unit; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; PTCA: percutaneous transluminal coronary angioplasty.

Table 3 Change (Δ) from pre- to post-TAVI.

	Overall Pre-TAVI: N = 141 Post-TAVI: N = *	P-value
CERAD Word List Learning Test: *n = 112		
Number of correct words	2.1 $\pm$ 3.2	< 0.001
CERAD Word List Recall Test: *n = 112		
Number of correct words	0 [0, 2]	< 0.001
Trail Making Test A: *n = 103		
Error of commission	0 [-1, 0]	0.332
Error of omission	0 [0, 0]	0.777
Duration, s	-2.8 [-13.2, 6]	0.158
Efficiency Score	-0.1 [-0.6, 0.4]	0.299
Trail Making Test B: *n = 102		
Error of commission	0 [-1, 0]	0.184
Error of omission	0 [0, 0]	0.065
Duration, s	1.4 [-26.6, 41.7]	0.500
Efficiency Score	-0.1 [-1.4, 2.4]	0.918
Digit Span Test: *n = 112		
Number of correct digits	0 [0, 0]	0.954
Victoria Stroop Test: *n = 120		
Number of correct dots	0 [0, 0]	0.507
Number of correct words	0 [0, 0]	0.037
Number of correct color words	0 [0, 1]	0.367
Reaction time dots, s	-0.2 [-1.6, 1.6]	0.904
Reaction time words, s	-0.7 [-3.1, 1.7]	0.060
Reaction time color words, s	-0.7 [-6.4, 4.9]	0.361
Phonemic Fluency Test: *n = 96		
Number of words	1 [-1, 3]	0.019
Cognitive trajectory of the patients ¹		
Number of patients who improved ²	30 (26.3%)	0.689
Number of patients who declined ²	26 (22.8%)	0.689
Number of patients who did not change	68 (59.6%)	0.689

Values are displayed as *n* (%), mean $\pm$ SD or median [interquartile range]. ¹Note: Cumulative patient counts may exceed the total cohort size because individual patients can improve in one test while declining in another, leading to double counting. ²Note: "improved" and "declined" performance were defined as a deviation of 1.5 standard deviations below and above the normative mean.



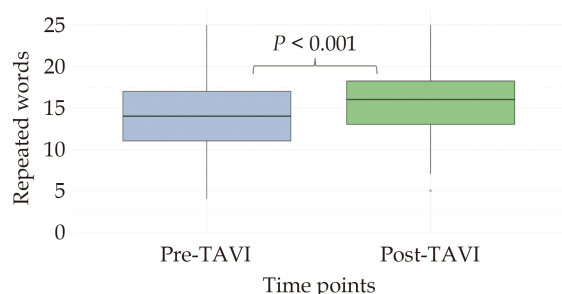


Figure 2 CERAD WL-W before and after TAVI. Change in CERAD Word List Learning Test scores before (Pre-TAVI: 14 repeated words) and after (Post-TAVI: 16.1 repeated words) TAVI. Performance improved significantly after TAVI ($P < 0.001$). TAVI: transcatheter aortic valve implantation; WL-W: word list learning test.

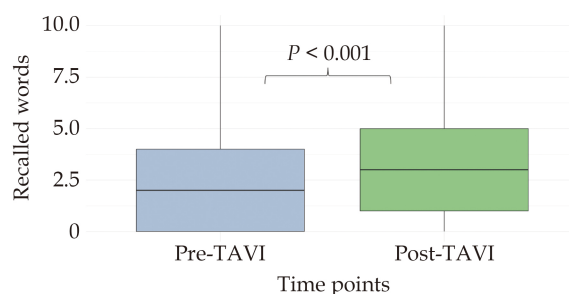


Figure 3 CERAD WL-A before and after TAVI. Change in CERAD Word List Recall Test scores before (Pre-TAVI: 2.1 repeated words) and after (Post-TAVI: 2.9 repeated words) TAVI. Performance improved significantly after TAVI ($P < 0.001$). TAVI: transcatheter aortic valve implantation; WL-A: word list recall test.

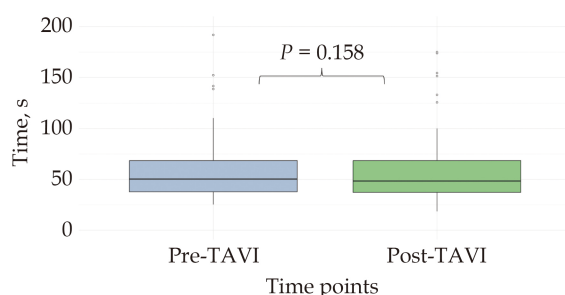


Figure 4 TMT-A before and after TAVI. Change in Trail Making Test A scores before (Pre-TAVI: 50.4 seconds) and after (Post-TAVI: 48.5 seconds) TAVI. Performance improved not significantly after TAVI ($P = 0.158$). TAVI: transcatheter aortic valve implantation; TMT-A: trail making test A.

Phonemic Fluency Test

A total of 141 patients completed the PFT prior to TAVI, and 96 underwent follow-up assessment after TAVI implantation. 53 patients (37.6%) showed improvement in the number of words, with a median increase of 1 [-1, 3] words ($P < 0.02$; see Table 3 and Figure 8).

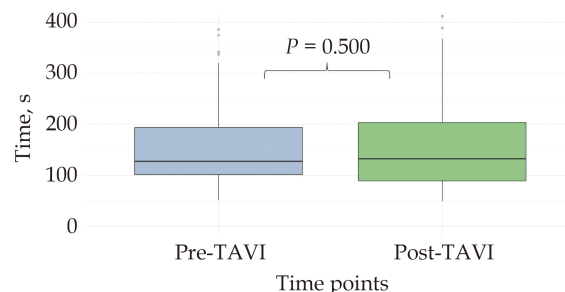


Figure 5 TMT-B before and after TAVI. Change in Trail Making Test B scores before (Pre-TAVI: 156 seconds) and after (Post-TAVI: 164 seconds) TAVI. Performance improved not significantly after TAVI ($P = 0.500$). TAVI: transcatheter aortic valve implantation; TMT-B: Trail Making Test B.

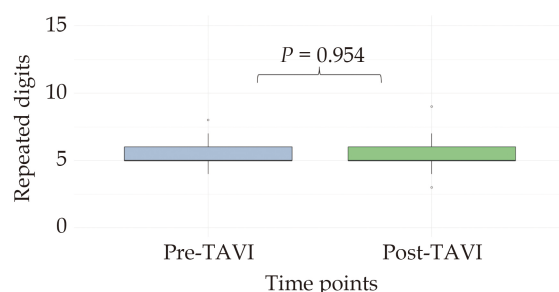


Figure 6 DST before and after TAVI. Change in Digit Span Test scores before (Pre-TAVI: 5 repeated digits) and after (Post-TAVI: 5 repeated digits) TAVI. Performance improved not significantly after TAVI ($P = 0.954$). DST: digit span test; TAVI: transcatheter aortic valve implantation.

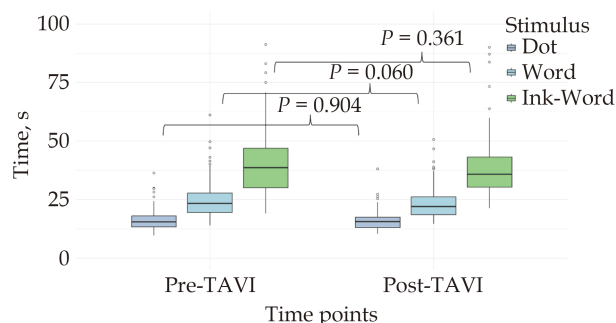


Figure 7 VST before and after TAVI. Change in Victoria Stroop Test scores before (Pre-TAVI: 15.5 seconds (Dot), 23.4 seconds (Word), 38.6 seconds (Ink-Word)) and after (Post-TAVI: 15.6 seconds (Dot), 22 seconds (Word), 35.8 seconds (Ink-Word)) TAVI. Performance improved not significantly ($P = 0.904$ (Dot), $P = 0.361$ (Ink-Word)) and significantly ($P = 0.060$ (Word)) after TAVI. TAVI: transcatheter aortic valve implantation; VST: Victoria Stroop Test.

Cognitive Change

Prior to TAVI, 37.7% of patients ($n = 43$) were classified as impaired in at least one cognitive test compared to their peers. After TAVI, 31.6% ($n = 36$) were classified

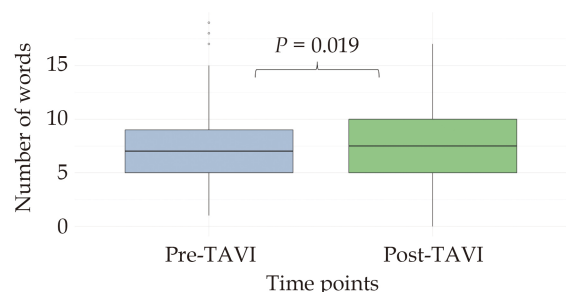


Figure 8 PFT before and after TAVI. Change in Phonemic Fluency Test scores before (Pre-TAVI: 7 repeated words) and after (Post-TAVI: 7.5 repeated words) TAVI. Performance improved significantly after TAVI ($P = 0.019$). PFT: phonemic fluency test; TAVI: transcatheter aortic valve implantation.

as impaired. The majority of patients remained in the same cognitive category before and after the procedure ($n = 68, 59.6\%$). 11.4% ($n = 13$) were newly classified as impaired post-TAVI, and 17.5% ($n = 20$) transitioned from impaired to average. In addition, 28.1% ($n = 32$) demonstrated above-average cognitive performance prior to TAVI and 25.4% ($n = 29$) after the procedure. The distribution of cognitive trajectories is shown in Table S1 and Figure 9.

Reference samples

Compared to the sex-, age-, and education-adjusted normative samples, the TAVI cohort demonstrated

lower performance across all cognitive tests both before and after the procedure (see Figures S1- S7).

DISCUSSION

Key Findings

This study represents the first comprehensive, prospective analysis using a digital, app-based neurocognitive assessment with AI-assisted speech recognition in elderly patients undergoing TAVI. Building on prior pilot work,^[4] the present study demonstrates good acceptance in a frail, elderly population. This suggests that app-based cognitive testing can overcome common limitations of traditional neuropsychological evaluations in this population.

Compared with age-, sex-, and education-adjusted normative data, TAVI patients showed lower performance across all cognitive domains prior to the intervention – indicating baseline vulnerability but not severe impairment. Thus, the cohort still had measurable cognitive reserve and was at risk of cognitive loss through treatment.

The study found no evidence of systematic or procedure-related cognitive decline after TAVI. Across seven validated neurocognitive tests, the vast majority of pa-

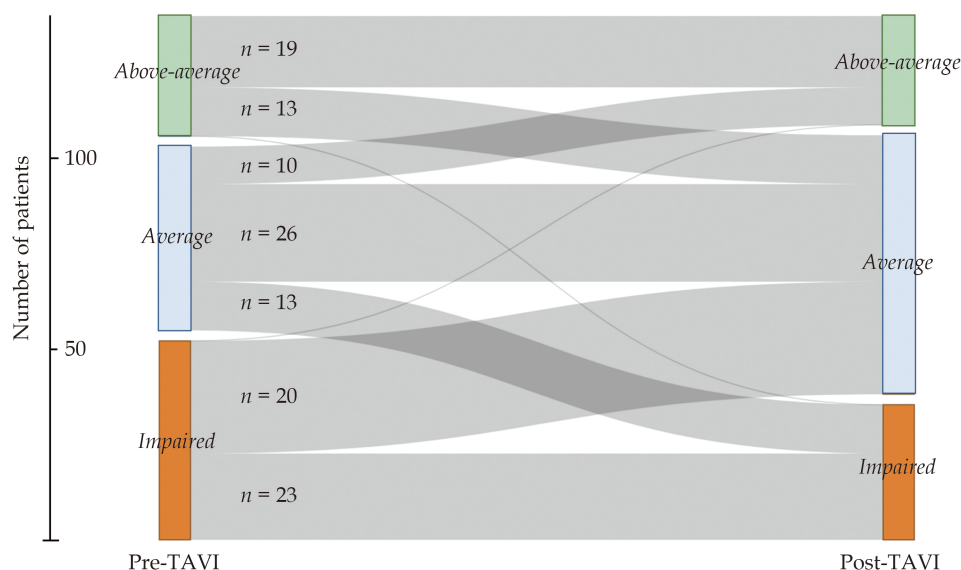


Figure 9 Sankey diagram illustrating the cognitive trajectories of patients. Sankey diagram illustrating the cognitive trajectories of patients from before TAVI to after TAVI. Cognitive performance was categorized into “Impaired”, “Average” and “Above-average”, “Impaired” and “above-average” performance were defined as a deviation of 1.5 SD below and above the normative mean, respectively. The diagram shows how individual cognitive status changed following TAVI. Only patients who underwent cognitive testing both before and after TAVI were included. Note: Cumulative patient counts may exceed the total cohort size because individual patients can improve in one test while deteriorating in another, leading to double counting. TAVI: transcatheter aortic valve implantation.



tients remained cognitively stable, while a subset even showed improvements, particularly in memory-related domains. Other domains such as executive function, attention, and inhibitory control remained largely unchanged. Among patients classified as cognitively declined, changes were typically limited to a single test parameter rather than observed across multiple domains, arguing against a consistent or global cognitive decline.

Relationship to Previous Studies

Our findings are consistent with several prior studies indicating that cognitive function in most patients remains stable after TAVI.^[11,13,35,36] It is important to highlight the methodological differences across existing studies. While some analyses assess only mean group-level changes before and after TAVI (e.g., Khan, *et al.*^[13]), others examine individual patient trajectories. In our cohort, group-level cognitive performance remained stable, and the proportion of patients showing apparent decline (22.8%) was within the expected range of test-retest variability reported in similar populations. A meta-analysis by Ghezzi, *et al.*^[35] reported a cognitive decline in 7% of patients at one month and 14% within six months after TAVI. Similarly, Schoenenberger, *et al.*^[11] found a decline of more than 3 points in the Mini Mental Test in 12.7% of patients after TAVI.

While these studies do not contradict the overall pattern of cognitive stability, they underline the importance of identifying patients at risk for adverse cognitive outcomes. In the present study, regression analyses to identify predictors of cognitive decline were not performed due to the limited number of patients showing cognitive decline and the exploratory design. Future larger-scale studies with extended follow-up will be needed to identify clinical or procedural predictors of cognitive decline.

One of the main limitations in both clinical workflows and previous studies has been the time- and personnel-intensive nature of traditional cognitive testing, which typically requires administration by trained neuropsychologists so that clinical adoption remains lacking. Consistent with previous findings showing equivalent outcomes but greater efficiency of digital over paper-and-pen-based assessments,^[37] our study demonstrates the applicability of app-based cognitive testing, which combines automated scoring with validated test components to yield results comparable to conventional neuropsychy-

chological measures. Completion rates for digital neurocognitive assessments in older adults have been reported in only a few studies, ranging from 61-82%. The 79% completion rate observed in the present study aligns with these limited data, but overall, feasibility and completion rates of app-based cognitive testing in elderly clinical populations remain underexplored.^[38]

Still, there is currently no standardized protocol for the administration and interpretation of these traditional pen-and-paper cognitive tests,^[39] which substantially limits the comparability of findings across studies.

Strengths and Limitations of the Study

To the best of our knowledge, this is the first prospective trial investigating the use of a digital, app-based cognitive assessment with automated data recording, speech recognition, and scoring based on normative references. This approach ensured a standardized, and efficient application for neurocognitive monitoring in clinical routine. Each patient completed the same set of tests in the same order and under the same conditions, enhancing the reliability. This approach reduces variability due to examiner differences and manual scoring errors, which are common in traditional paper-and-pencil assessments. The app-based assessment facilitates the integration of meaningful cognitive testing into everyday clinical practice. This approach enables the assessment of patient populations (such as elderly TAVI patients) who are potentially underrepresented or overlooked in traditional normative samples, thereby broadening the clinical relevance of cognitive screening.

One of the main strengths of our study was the comprehensive coverage of cognitive domains achieved through the use of established and standardized neuropsychological tests with longstanding validation. Our cognitive test battery assessed short-term memory (WL-W, DST;^[18,26]), long-term memory (WL-A;^[18]), cognitive flexibility and inhibitory control (VST;^[22]), processing speed and divided attention (TMT-A/B;^[19]) and speech production and executive function (PFT;^[18]). Nevertheless, the field would benefit from the future development and adoption of a standardized test battery for TAVI patients to improve comparability across studies.

Interestingly, following TAVI, patients frequently demonstrate selective improvement in learning and memory, whereas other cognitive domains remain largely unchanged. Tsuchiya *et al.* (2020)^[40] observed an increase in cerebral perfusion in specific brain regions,



including the right hippocampus, after TAVI. As the hippocampus plays a key role in memory processing^[41] and is particularly sensitive to cerebral hypoperfusion,^[42] an improved cerebral blood flow following TAVI may directly enhance hippocampus-dependent memory function. In contrast, executive functions, which are less directly influenced by global perfusion changes, tend to remain stable.^[36,43,44] However, it should also be considered that the apparent domain-specific improvement may reflect differences in test sensitivity in this patient population or simply result from sample variability. Our study was not designed to disentangle these possibilities, and this question therefore remains open, representing an area for further investigation in future studies specifically addressing this issue.

There are also some limitations to our study. First, the study was single center and relatively small, which limits the generalizability of the results, especially with regard to subgroup analyses. However, the consistency of our findings aligns with previous studies supporting the validity of our results despite the small sample size.

Second, while nearly all patients completed the full cognitive test battery before TAVI, completion rates varied between tests in the postoperative assessment. This discrepancy primarily reflects differences in postoperative recovery and patient tolerance. Some patients experienced fatigue, reduced motivation, or time constraints during the hospital stay, leading to selective omission of more demanding or time-consuming tasks such as the Trail Making or Phonemic Fluency tests. Also, isolated technical issues with the Delta-App (e.g., interruptions in touchscreen or speech recognition input) occurred. In contrast, pre-TAVI testing was conducted under standardized, well-controlled conditions, accounting for the high completion rate at baseline.

Third, potential sensory impairments (e.g., visual or auditory deficits) and difficulties handling new technology, despite guidance, may have influenced performance in some cases. However, patients were asked before testing about any visual and hearing impairments and testing conditions were adjusted accordingly (e.g., increasing the volume of instructions). Nevertheless, such sensory challenges are generally unavoidable when testing older populations and must be considered and might therefore also be present in the age matched comparison group.

Fourth, it is well known that repeated administration of neurocognitive tests can lead to a natural improve-

ment in performance, known as the “practice effect”.^[45] For example, repeated administration of the Hopkins Verbal Learning Test demonstrated significant improvements in total and delayed recall after only one week (immediate recall improving by 0.8 words and delayed recall by 0.7 words based on a 12-word list).^[46] Similarly, another study demonstrated that repeated assessments over a three-month period were associated with an increase in learning and memory performance of up to $13.3 \pm 12.3\%$ relative to baseline. Also, this effect is particularly strong for completely novel tasks that participants have not encountered before. For more familiar tasks, such as TMT-A, which resemble activities already practiced in childhood (e.g., connecting numbers for paintings), practice effects are expected to be smaller.^[47] Given that these effects are particularly pronounced in verbal learning tests, the observed improvements in WL-W and WL-A may at least partially reflect retest-related gains rather than true cognitive improvement.

To minimize the practice effect, different test versions were used (e.g., for PFT test, one time using the letter A and another time the letter F). Those “practicing effects” likely influences all patients undergoing repeated testing, such that an overall improvement is expected simply due to repeated exposure. Thus, a pronounced practice effect could potentially mask subtle cognitive decline, leading to an underestimation of the true extent of cognitive decline.

Finally, it is well known that psychological factors can influence cognitive performance.^[48–49] Preoperative assessments may be affected by anxiety or apprehension related to the upcoming procedure, while postoperative testing could be influenced by relief or, conversely, by distraction due to postoperative complications, pain, or other confounders. To minimize acute influences, postoperative cognitive assessments in our study were conducted only after patients had returned to the general ward and were on a recovery trajectory towards discharge. The postoperative test was performed on day 5, on average; serious complications were rare. Nevertheless, this remains a potential confounder that may have influenced our results. Future studies should consider additional screening and adjustment for anxiety, depression, and pain levels to further address this limitation.

Implication and Future Direction

Our study shows that digital, app-based assessments



offer a practical and scalable tool for clinical workflows, reducing the need for time- and personnel-intensive traditional testing methods. Early detection of subtle impairments could enable personalized rehabilitation strategies and closer follow-up, improving recovery and long-term independence. Nevertheless, the clinical interpretation of early postoperative assessment requires careful consideration. Cognitive performance may be influenced by transient postoperative factors such as fatigue, residual effects of anesthesia, periinterventional stress or subclinical delirium, thereby limiting the ability to draw conclusions about stable or long-term neurocognitive outcomes.^[50] At the same time, it is precisely this early interval in which primary caregivers can detect emerging deficits, initiate targeted diagnostic workup, and implement timely interventions.

Establishing TAVI-specific normative datasets will further improve the accuracy and interpretation of digital cognitive assessments in this vulnerable patient population. Differences in age distribution, educational level and cultural context may limit the comparability between normative cohorts used in this study and the present TAVI population, potentially affecting the interpretation of standardized scores. However, normative data specifically derived from TAVI populations are currently not available, which represents a common limitation when studying highly selected patient groups with specific underlying conditions.

Moreover, future studies should consider additional screening and adjustment for anxiety, depression, and pain levels to further address this potential confounding.

In conclusion, in this single-center study, we observed no consistent or procedure-induced cognitive decline after TAVI during the early postoperative period. App-based cognitive testing proved to be well accepted among elderly TAVI patients, a population that generally shows lower cognitive performance compared to the healthy population. The integration of an app-based assessment combined with AI-supported scoring presents a promising step toward an accessible and standardized neurocognitive testing, enabling the early identification of patients with cognitive decline and allowing individualized cognitive support and rehabilitation. Still, further research and the development of normative data for this special cohort is needed for accurately interpreting the cognitive performance.

DISCLOSURE

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Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics committee of the Brandenburg Medical School (MHB) (E-01-20191006.) All patients provided written informed consent prior to study participation.

Consent for Publication

All participants provided written informed consent for the use of anonymized data for scientific publication purposes. No individual person's data (such as images, videos, or personal health information) are presented in this manuscript in a form that would require additional consent for publication.

Availability of Data and Materials

The dataset analyzed during the current study is not publicly available due to institutional and legal data protection regulations concerning patient privacy.

Competing Interests

None.

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Authors' Contributions

Conceptualization: JN, AHF; Methodology: AG, JN, AHF, CB, MH; Formal analysis and investigation: AG, JN; Writing—original draft preparation: AG, JN, AHF; Writing—review and editing: CB, MH, GF, FH; Funding acquisition and Resources: JN, AHF; Supervision: AHF, CB. All authors approved the final manuscript.



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