Original Research

CARDIOLOGY

Early cognitive and quality of life changes after transfemoral transcatheter aortic valve replacement

Mihnea Istrate[1,2,†], Mihaela Ioana Dregoesc[1,2,†], Victor Stefan Buiga[1,2], Julien Redfern[1], Adrian Corneliu Iancu[1,2]

1) Department of Cardiology, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

2) "Niculae Stancioiu" Heart Institute, Cluj-Napoca, Romania

† Equal contribution

Abstract

Background and aims. Cognitive impairment has been associated with the presence of severe aortic stenosis (AS). Our study evaluated the early changes in cognitive function and quality of life in patients with severe AS who underwent transfemoral transcatheter aortic valve replacement (TAVR).

Methods. The cognitive function and quality of life of patients with severe symptomatic AS who underwent transfemoral TAVR were assessed with the Montreal Cognitive Assessment (MoCA) and the EQ-5D-3L questionnaire, respectively. The tests were performed at the time of admission and at 48 to 72 h after TAVR.

Results. The study group included 37 patients with a mean age of 78 years. Cognitive improvement was observed in 72.9% of patients. A higher MoCA score at baseline was correlated with a better functional outcome after TAVR (r=0.49, p=0.02). Patients with an early post-procedural increase in MoCA scores had a smaller aortic valve area at baseline as compared to patients without cognitive improvement (0.5±0.2 vs. 0.7±0.1 sq.cm, p=0.02). The baseline aortic valve area was associated with an increase in MoCA scores at an optimal cutoff value ≤0.65 sq.cm (AUC 0.739; p=0.005). A significant increase in median EQ-5D-3L scores was observed between baseline and follow-up (60 (51-70) vs. 73 (65-80) points, p<0.001). The lack of improvement in functional status was associated with a prolonged stay in the Intensive Care Unit (ICU) (r=-0.46, p=0.02).

Conclusions. In patients with severe symptomatic AS, a smaller aortic valve area at baseline was associated with an early cognitive improvement after transfemoral TAVR. Baseline cognition and the length of stay in the ICU influenced the early functional outcomes.

Keywords: aortic stenosis, transcatheter aortic valve replacement, cognitive function, quality of life

DOI: 10.15386/mpr-2885

Manuscript received: 09.04.2025
Received in revised form: 25.04.2025
Accepted: 23.05.2025

Address for correspondence:
Adrian Corneliu Iancu
adrianiancu56@gmail.com

Introduction

Cognitive impairment occurs in one third of patients with severe aortic stenosis (AS) and is associated with functional disability [1-5]. While dementia shares common atherosclerotic risk factors with cardiovascular disease [6-7], cognitive decline is also the consequence of decreased cardiac output and subsequent cerebral hypoperfusion [3,8]. This is especially true in the setting of severe AS.

Pre-existing cognitive impairment is considered a risk factor for adverse postprocedural outcomes, delirium, and further cognitive decline [9]. However, in patients with severe AS, cognitive impairment is also the result of outflow obstruction [10] and might therefore represent a therapeutic target.

Literature data are inconclusive regarding the effect of transcatheter aortic valve replacement (TAVR) on the cognitive function of patients with severe

AS. Although apparent strokes are rare [11,12], magnetic resonance imaging (MRI) studies identified silent cerebral ischemic lesions in approximately three quarters of the patients who underwent TAVR [2,13]. However, less than 30% of these lesions were still visible as white matter hyperintensities after 3 – 5 months and were associated with postprocedural cognitive decline and lack of improvement at follow-up [2,14]. While the high incidence of silent cerebral ischemia raised concerns on the potentially negative neurocognitive impact of the procedure, several small studies showed an improvement in cognitive function in up to 40% of patients who underwent TAVR [15-17].

In addition to increased survival, the preservation or improvement in quality of life represents one of the main goals of any cardiovascular intervention. This desideratum is even more relevant for the elderly TAVR population. In this context, the aim of this study was to evaluate the early changes in cognition and functional status in a contemporary cohort of patients who underwent transfemoral TAVR for the treatment of severe symptomatic AS.

Methods

This was a single-center, prospective, observational study. Patients with severe AS who underwent transfemoral TAVR in a tertiary cardiovascular disease center were screened for inclusion. Patients who agreed to undergo cognitive and quality of life assessment both before and after the intervention were included in the analysis. The occurrence of a clinically apparent acute cerebrovascular event at anytime during hospitalization represented an exclusion criterion. All patients gave written informed consent for the procedure and for the anonymous processing of personal data. The study was approved by the local ethics committee and all procedures were conducted in accordance with the ethical standards outlined in the Declaration of Helsinki.

TAVR was performed according to current standards using either the balloon-expandable SAPIEN™ 3 Transcatheter Heart Valve system (Edwards Lifesciences, Irvine, CA, USA), the self-expandable Evolut™ R Transcatheter Aortic Heart Valve (Medtronic, Minneapolis, MN, USA), or the self-expandable Navitor™ Transcatheter Aortic Heart Valve System (St Jude Medical, St Paul, MN, USA). All procedures were performed under conscious sedation. Cerebral protection devices were not used for any of the procedures.

Cognitive function was evaluated with the Montreal Cognitive Assessment (MoCA) version 7.1 paper-based test (MoCA Cognition, Greenfield Park, Québec, Canada), translated into Romanian. The test was applied to all patients at baseline and at 48-72 hours after TAVR. The quality of life assessment was performed using the EQ-5D-3L questionnaire (EuroQol Group, Rotterdam, The Netherlands). Similarly to the MoCA test, the EQ-5D-3L questionnaire was applied both before and at 48-72 h after TAVR. Each test was administered by a trained healthcare professional and was scored according to current recommendations [18-21].

The echocardiographic assessment was performed on a Vivid™ E95 Cardiac Ultrasound Machine (GE HealthCare, Chicago, IL, USA). All measurements were performed according to current guidelines [22-24]. The aortic valve area was calculated in all patients based on the continuity equation.

Statistical analysis

Data distribution was assessed using Kolmogorov-Smirnov and D'Agostino tests. Quantitative continuous data were summarized as mean ± standard deviation (SD) whenever data proved normally distributed. Otherwise, the median and interquartile range (Q1–Q3, where Q1 = first quartile and Q3 = third quartile) were used. Groups were compared with Student t-test or Mann-Whitney U-test, as appropriate. Categorical data were presented as counts and proportions and compared with Fisher's exact test.

Receiver-operating characteristic (ROC) curves were built to evaluate the association between aortic valve area and the postprocedural changes in cognitive function. The area under the curve (AUC) was determined as a scalar measure of performance and the Youden index was used to identify the optimal cutoff values from the ROC curves.

Statistical analysis was performed with GraphPad Prism version 10.4.0 for Windows (GraphPad Software, CA, USA) and MedCalc (v 20.019, MedCalc Software, Ostend, Belgium). A two-sided p-value < 0.05 was considered statistically significant.

Results

Baseline and procedural characteristics

A cohort of 37 patients with a mean age of 77.9±5.1 years and a mean STS score of 4.4±1.6 was recruited. Males represented 45.9% of the population. A history of atrial fibrillation or atrial flutter was present in 32.4% of the patients, and 29.7% were on oral anticoagulant therapy. A diagnosis of diabetes mellitus was present in 43.2% of the patients. The mean aortic valve area was 0.6 ± 0.2 cm^2 and the mean LVEF was 57.5±11.7%. The baseline characteristics of the cohort are presented in table I.

Balloon-expandable devices were implanted in 62.2% of the patients. Periprocedural complications were recorded in three patients, as follows: one patient required dialysis for contrast-induced nephropathy, and two patients developed an access site hematoma. The rate of new pacemaker implantation was 31.6%. After the procedure, atrial fibrillation or atrial flutter was recorded in 35.1% of patients, and the use of oral anticoagulants increased to 48.6%. The postprocedural mean LVEF increased to 61.7±7.7% (p=0.07). The procedural characteristics of the cohort are presented in table II.

Table I. Baseline characteristics of the cohort.

PARAMETER	n=37
CLINICAL DATA	
Age (years), mean±SD	78±5.1
Males, n (%)	17 (45.9)
BMI (kg/m2), mean±SD	28.9±6
Hypertension, n (%)	34 (91.9)
Diabetes, n (%)	16 (43.2)
Coronary artery disease, n (%)	14 (37.8)
Carotid artery disease, (%)	1 (2.7)
Ischemic stroke, n (%)	1 (2.7)
Peripheral artery disease, n (%)	2 (5.4)
Chronic kidney disease, n (%)	10 (26.3)
COPD, n (%)	10 (27)
STS Score, mean±SD	4.4±1.6
EuroScore II, mean±SD	4.7±2.3
Baseline MoCA score, mean±SD	19±4.5
ECG, n (%)	
- Atrial fibrillation/atrial flutter	12 (32.4)
- Pre-existent LBBB	3 (8.1)
- Pre-existent 1st degree AV block	3 (8.1)
- Pre-existent pacemaker	2 (5.4)
ECHOCARDIOGRAPHIC DATA	
Aortic valve	
- Vmax (m/s), mean±SD	4.8±0.6
- Mean gradient (mmHg), mean±SD	58.6±14.7
- Aortic valve area (cm^2), mean±SD	0.6±0.2
- More than mild aortic regurgitation, n (%)	12 (32.4)
LVEF (%), mean±SD	57.4±11.8
LV end-diastolic diameter (mm), mean±SD	45.7±8.3
Interventricular septum (mm), mean±SD	17.2±2.2
Pulmonary hypertension, n (%)	28 (75.7)
Pericardial effusion, n (%)	10 (27)
CARDIAC COMPUTED TOMOGRAPHY DATA	
Calcium score, mean±SD	3310±1381
Aortic annulus minimum diameter (mm), mean±SD	21±2
LABORATORY DATA	
Baseline hemoglobin (g/dl), mean±SD	12.9±1.3
WBC ($x10^3/mm^3$), mean±SD	7.6±2.6
Platelets ($x10^3/mm^3$), mean±SD	214±86.6
Baseline creatinine (mg/dl), median (Q1 – Q3)	1.0±0.3
Baseline eGFR (ml/min/1.73m^2), mean±SD	66.4±20.4
MEDICATION	
Oral anticoagulation, n (%)	11 (29.7)
Aspirin, n (%)	25 (67.6)
P2Y12 inhibitor, n (%)	5 (13.5)
Betablocker, n (%)	10 (27)
ACEI/ARB, n (%)	29 (78.4)
Statin, n (%)	36 (97.3)

*ACEI=angiotensin converting enzyme inhibitor; ARB=angiotensin receptor blocker; AV=atrio-ventricular; BMI=body mass index; COPD=chronic obstructive pulmonary disease; ECG=electrocardiography; eGFR=estimated glomerular filtration rate; EuroSCORE II=European System for Cardiac Operative Risk Evaluation II; LBBB=left bundle branch block; LV=left ventricle; LVEF=left ventricular ejection fraction; MoCA=Montreal Cognitive Assessment; n=number; Q1=1st quartile; Q3=3rd quartile; SD=standard deviation; STS=Society of Thoracic Surgeons; Vmax=maximum velocity; WBC=white blood cells.

Table II. Procedural characteristics of the cohort.

PARAMETER	n=37
Right femoral access, n (%)	31 (83.8)
Type of device	
- Balloon-expandable, n (%)	23 (62.2)
- Self-expandable, n (%)	14 (37.8)
Predilation, n (%)	34 (91.9)
Postdilation, n (%)	2 (5.4)
Periprocedural complications, n (%)	3 (8.1)
New pacemaker, n (%)	11 (31.4)
Post-TAVI atrial fibrillation/atrial flutter	13 (35.1)
Echocardiographic data	
- Vmax (m/s), mean±SD	2.3±0.3
- Mean gradient (mmHg), mean±SD	11.4±4.1
- More than mild aortic regurgitation, n (%)	4 (10.8)
- LVEF (%), mean±SD	61.7±7.8
Laboratory data	
- 48h post-TAVI Hb (g/dl), mean±SD	11.5±1.4
- 48h post-TAVI creatinine value (mg/dl), mean±SD	1.2±0.8
- 48h post-TAVI eGFR (ml/min/1.73 m^2), mean±SD	64±24.5
Contrast-induced nephropathy, n (%)	5 (13.5)
Dialysis, n (%)	1 (2.7)
Medication	
- Oral anticoagulant, n (%)	18 (48.6)
- Aspirin, n (%)	16 (43.2)
- P2Y12 inhibitor, n (%)	12 (32.4)
- Betablocker, n (%)	10 (27)
- ACEI/ARB, n (%)	31 (83.8)
- Statin, n (%)	36 (97.3)

*ACEI=angiotensin converting enzyme inhibitor; ARB=angiotensin receptor blocker; eGFR=estimated glomerular filtration rate; Hb=hemoglobin; LVEF=left ventricular ejection fraction; n=number; SD=standard deviation; TAVI=transcatheter aortic valve implantation; Vmax= maximum velocity.

Factors associated with an early change in cognitive function

All patients underwent cognitive function assessment. Throughout the cohort, cognitive improvement was observed in 72.9% of patients. The median MoCA test scores increased from baseline to follow-up from 19 (16–22) to 22 (18–24) points (p=0.08) (figure 1A). A very strong positive correlation was observed between the baseline and the post-procedural MoCA test scores (r=0.93, p<0.001) (figure 1B).

Patients with an early post-procedural increase in the MoCA test score had a smaller aortic valve area at baseline as compared to patients who did not experience an immediate improvement in cognitive function (0.5±0.2 vs. 0.7 ± 0.1 cm^2, p=0.02). A baseline aortic valve area ≤ 0.65 cm^2 predicted an improvement in post-procedural MoCA test scores with a sensitivity of 81.5% and a specificity of 60% (AUC 0.739; 95%CI 0.569 – 0.869; p=0.005) (figure 2).

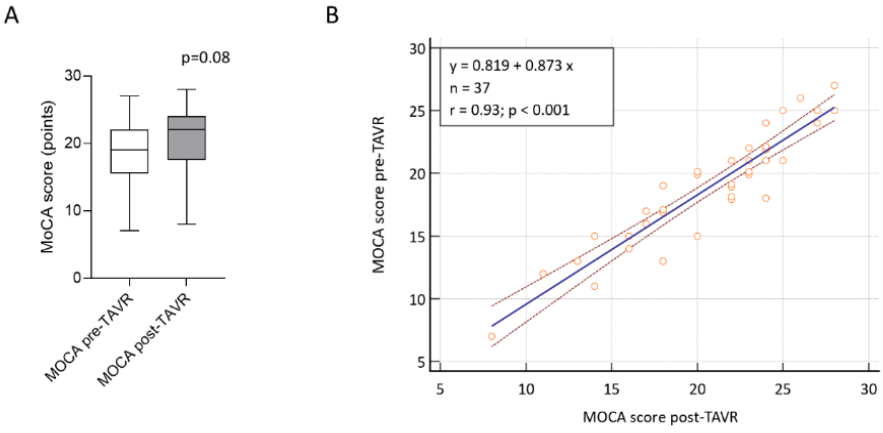

Figure 1. Cognitive function assessment before and after TAVR. MoCA=Montreal Cognitive Assessment; TAVR=transcatheter aortic valve replacement.

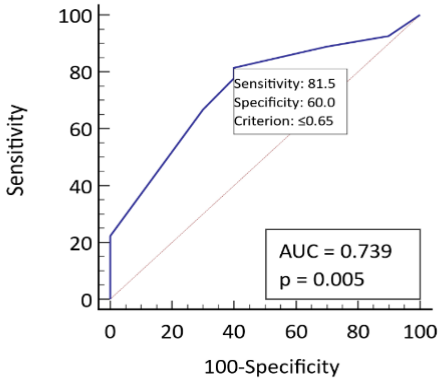

Figure 2. ROC curve analysis. The baseline aortic valve area was associated with an improvement in MoCA test scores at an optimal cutoff value ≤0.65 cm^2. AUC=area under the curve; MoCA=Montreal Cognitive Assessment; ROC=receiver operating curves.

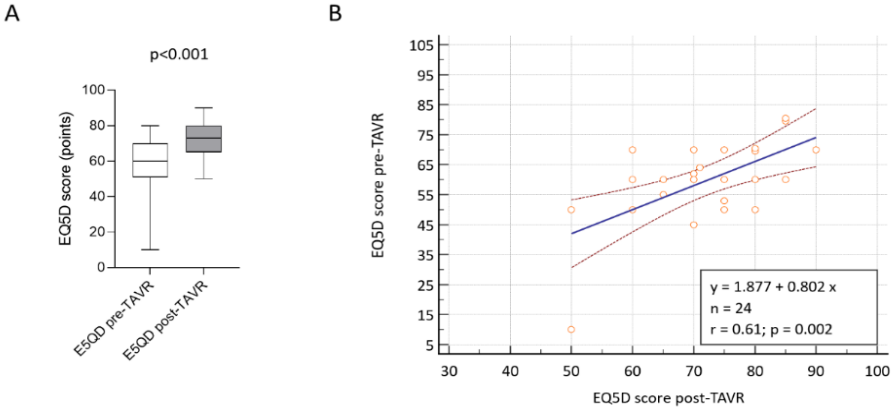

Figure 3. Quality of life assessment before and after TAVR. TAVR=transcatheter aortic valve replacement.

Table III. Factors associated with cognitive improvement.

	Improvement of cognitive function		
	Yes (n=27)	No (n=10)	p-value
CLINICAL CHARACTERISTICS			
Age (years)	78.0±5.3	77.6±4.8	0.98
Male sex, n (%)	11 (40.7)	6 (60)	0.46
BMI	30.1±6.5	25.6±2.5	0.04
STS Score	4.4±1.7	4.5±1.3	0.96
Hypertension, n (%)	24 (88.9)	10 (100)	0.54
Diabetes mellitus, n (%)	12 (44.4)	4 (40)	0.81
Carotid artery disease, n (%)	0 (0)	1 (10)	0.10
History of ischemic stroke, n (%)	1 (3.7)	0 (0)	0.55
Peripheral artery disease, n (%)	0 (0)	2 (20)	0.01
Chronic kidney disease, n (%)	7 (25.9)	3 (30)	0.81
History of atrial fibrillation/atrial flutter, n (%)	9 (33.3)	3 (30)	0.85
COPD, n (%)	9 (33.3)	2 (20)	0.44
ECHOCARDIOGRAPHIC DATA			
Aortic valve			
- Vmax (m/s)	4.9±0.6	4.6±0.5	0.26
- Mean gradient (mmHg)	60.3±15.1	54.2±13.5	0.41
- Aortic valve area (cm^2)	0.6±0.2	0.7±0.1	0.02
LVEF (%)	57.1±12.2	58.4±11.3	0.83
LV end-diastolic diameter (mm)	46.1±9.4	44.6±4.8	0.61
Interventricular septum (mm)	17.3±2.1	17.2±2.2	0.59
Pulmonary hypertension, n (%)	20 (74.1)	8 (80)	0.72
Pericardial effusion, n (%)	6 (22.2)	4 (40)	0.29
Pre-existent pacemaker, n (%)	1 (3.7)	1 (10)	0.45
CARDIAC COMPUTED TOMOGRAPHY DATA			
Calcium score	3407±1282	3047±1664	0.45
Aortic annulus minimum diameter (mm)	21±2.3	21±1.7	0.97
LABORATORY DATA			
Baseline hemoglobin (g/dl)	12.9±1.3	12.9±1.2	>0.99
WBC ($x10^3/mm^3$)	7.4±2.2	8.3±3.7	0.67
Platelets ($x10^3/mm^3$)	198±39.3	258±150.4	0.33
Baseline creatinine (mg/dl)	0.9±0.3	1.1±0.4	0.27
Baseline eGFR ($ml/min/1.73m^2$)	66.8±18.6	65.1±25.7	0.82
MEDICATION			
Oral anticoagulation, n (%)	9 (33.3)	2 (20)	0.44
Aspirin, n (%)	16 (59.3)	9 (90)	0.08
P2Y12 inhibitor, n (%)	4 (14.8)	1 (10)	0.71
Betablocker, n (%)	6 (22.2)	4 (40)	0.29
ACEI/ARB, n (%)	20 (74.1)	9 (90)	0.31
Statin, n (%)	26 (96.3)	10 (100)	0.55
PROCEDURAL CHARACTERISTICS			
Right femoral access, n (%)	24 (88.9)	7 (70)	0.17
Balloon-expandable prosthesis, n (%)	16 (59.3)	7 (70)	0.56
Prosthesis dimension	26±2.9	26±1.9	0.75
Predilation, n (%)	25 (92.5)	9 (90)	0.80
Postdilation, n (%)	2 (7.4)	0 (0)	0.39
Periprocedural complications, n (%)	3 (11.1)	0 (0)	0.28
New pacemaker, n (%)	7 (26.9)	4 (40)	0.34
Post-TAVI atrial fibrillation/atrial flutter	10 (37)	3 (30)	0.70
Echocardiographic data			
- Vmax (m/s)	2.2±0.3	2.4±0.3	0.11
- Mean gradient (mmHg)	9.3±3.4	12.1±4.2	0.07
- More than mild aortic regurgitation, n (%)	14.8	0 (0)	0.21
- LVEF (%)	61±7.8	63.6±8	0.39
Post-TAVI laboratory data			
- 48h post-TAVI Hb (g/dl)	11.3±1.3	12±1.6	0.18
- 48h post-TAVI creatinine value (mg/dl)	1.2±0.9	1.1±0.4	0.53
Post-TAVI medication			
- Oral anticoagulant, n (%)	15 (55.5)	3 (30)	0.18
- Aspirin, n (%)	10 (37)	6 (60)	0.22
- P2Y12 inhibitor, n (%)	9 (33.3)	3 (30)	0.85
- Betablocker, n (%)	6 (22.2)	4 (40)	0.29
- ACEI/ARB, n (%)	23 (85.2)	8 (80)	0.71
- Statin, n (%)	26 (96.3)	10 (100)	0.55

*values are presented as mean±SD, unless otherwise stated; ACEI=angiotensin converting enzyme inhibitor; ARB=angiotensin receptor blocker; BMI=body mass index; COPD=chronic obstructive pulmonary disease; eGFR=estimated glomerular filtration rate; Hb=hemoglobin; LV=left ventricle; LVEF=left ventricular ejection fraction; n=number; SD=standard deviation; STS=Society of Thoracic Surgeons; TAVI=transcatheter aortic valve implantation; Vmax=maximum velocity; WBC=white blood cells.

Among the baseline characteristics, a lower body mass index (BMI) (25.6±2.5 vs. 30.1±6.5, p=0.04) and the presence of peripheral artery disease (PAD) (20 vs. 0%, p=0.01) were associated with a lack of improvement in post-procedural MoCA test scores (Table III).

Factors associated with an early change in the quality of life

Quality of life testing was performed in 24 out of the 37 patients. A significant improvement in median EQ-5D-3L scores occurred between baseline and follow-up (60 (51 - 70) vs. 73 (65 - 80) points, p<0.001), with a moderate correlation observed between the two assessments (r=0.61, p=0.002) (Figure 3). A prolonged Intensive Care Unit (ICU) stay was associated with a lack of improvement in EQ-5D-3L scores (r=-0.46, p=0.02), while a positive correlation was noticed between postprocedural hematocrit and an early improvement in functional status (r=0.47, p=0.02). Patients who scored higher on postprocedural EQ-5D-3L testing were more likely to receive angiotensin-converting enzyme inhibitor/angiotensin receptor blocker (ACEI/ARB) or betablocker therapy (r=0.7, p<0.001 and r=0.44, p=0.03, respectively). A high baseline MoCA score was moderately correlated with a better functional outcome after TAVR (r=0.49, p=0.02) (Figure 4).

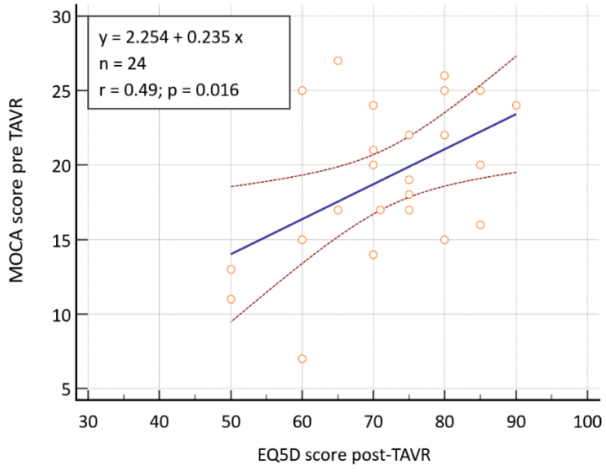

Figure 4. Preprocedural MoCA score was positively correlated with the early functional status after TAVR; MoCA=Montreal Cognitive Assessment; TAVR=transcatheter aortic valve replacement.

Discussion

In a group of patients with severe AS and a mean STS score of 4.4%, an early post-procedural increase in MoCA scores was associated with a smaller aortic valve area at baseline and with a higher preprocedural BMI. Native aortic valve area predicted an early postoperative improvement in cognitive function at an optimal cutoff value ≤ 0.65 cm^2. A higher baseline MoCA score was correlated with a better functional outcome after TAVR as evaluated by the EQ-5D-3L questionnaire. A significant increase in median EQ-5D-3L scores was observed between baseline and follow-up, but a longer ICU stay was associated with a lack of improvement in functional status.

A decrease in cardiac output leads to a subsequent alteration of cerebral perfusion [8]. In the setting of severe AS, several autoregulatory mechanisms, like PaCO2-induced vasoconstriction, or the presence of endothelial dysfunction contribute to the decrease in cerebral blood flow [25,26]. In this regard, a relief in left ventricular outflow obstruction following TAVR might be associated with an improvement in cerebral perfusion and cognition [27,28]. In the immediate postprocedural course, the sudden afterload reduction and the increase in systemic blood pressure also contribute to an increase in brain perfusion [29].

Recently, using arterial spin labelling MRI, the CAPITA study demonstrated for the first time that cerebral blood flow increased three months after TAVR, while cognitive function was not only preserved, but also improved in a subset of patient [5]. Furthermore, the greatest improvement in cognitive function was observed in patients with low baseline cognitive performance [5]. In our cohort, a baseline aortic valve area ≤ 0.65 cm^2 was associated with an immediate improvement in cognition. In accordance with the previously described pathophysiological mechanisms, this result suggests that the more severe the baseline obstruction, and the alteration in cerebral blood flow, the greater the potential improvement in cognitive function. The same relation between small baseline aortic valve area and cognitive improvement was demonstrated six months after the procedure [28]. Interestingly, our results suggest that the impact of improved cerebral blood flow might positively affect cognition even in the immediate postprocedural phases.

While cognitive dysfunction has emerged as a possible therapeutic target in patients with severe AS, the high rates of silent cerebral infarcts that accompany the procedure in approximately 75% of the cases [2,13] have previously raised concerns about the potential cognitive harm of transcatheter therapies. Recent reports, however, showed that only around 25% of these lesions evolved into gliotic scars at imaging follow-up [2] and might therefore have a negative impact on cognition [5]. Two previous meta-analyses reported rates of cognitive decline between 7 and 26% either immediately or at six months after the procedure [13,17]. On the contrary, smaller studies showed some degree of cognitive improvement in up to 40% of patients who underwent TAVR [15,16]. In our study cohort of intermediate-risk patients with severe AS, the observed rate of cognitive improvement reached 73% in the first three days after TAVR. This percentage might have been overestimated by the early postoperative cognitive

assessment, in the setting of brisk afterload reduction, with a subsequent increase in systemic blood pressure. Nevertheless, the uniform use of conscious sedation, instead of general anesthesia could also explain the better cognitive outcomes as compared to other reports.

In accordance with the existing data, our study did not identify any differences in the dynamics of cognitive function in relation to procedural characteristics such as femoral access side, valve design, or dimensions [17,27,30]. The association between peripheral artery disease and the absence of cognitive improvement was also consistent with literature data [31,32] and might reflect a high-risk patient category with generalized atherosclerosis [33]. In this regard, the role of intensive hypolipemic therapies on the neurocognitive outcomes of patients with diffuse atherosclerosis who undergo transfemoral TAVR may warrant investigation in larger cohort studies. Several studies have shown that patients with a lower BMI have higher mortality rates after TAVR [34-36] and severe AS patients with cognitive impairment frequently have a low BMI [37]. Our study observed an interesting association between a low baseline BMI and a lack of immediate improvement in cognition after TAVR. Whether this association is dependent on patient sex or degree of frailty remains to be further investigated in adequately powered studies.

Cognitive impairment has been associated with low quality of daily life and decreased mental well-being [38,39]. Accordingly, in our study, patients with a higher baseline cognitive capacity had a significantly better functional status following TAVR. This observation raises awareness on the importance of preprocedural cognitive assessment, as a risk factor for prolonged hospitalization and poor functional recovery. The timely detection of cognitive impairment in patients with AS may prompt enrolment in assisted postoperative care programs, which may subsequently lead to improved treatment compliance and better patient outcomes [40]. While both this study and others showed an improvement in the quality of life following TAVR [41-44], a prolonged ICU stay negatively influences functional status. In this regard, the development of dedicated in-hospital cardiac rehabilitation programs is essential in achieving the desired postprocedural functional benefit.

The main limitation of this study consists in the low sample size, which led to a decrease in statistical power when dividing the cohort according to outcomes. Furthermore, the absence of quality of life assessment in some of the patients led to incomplete data analysis when evaluating the association between cognition and functional status. While common to many previously published reports, the absence of a complete neuropsychological assessment must also be acknowledged among the limitations of this study. Nevertheless, the multiple cognitive domains assessed by the MoCA test allowed for an accurate diagnosis of even mild cognitive impairment [3,5,18,45]. Finally, a mid- and long-term follow-up evaluation would have offered an important perspective on the dynamic changes in cognitive function following intervention.

While hypothesis-generating, our results underline the importance of cognitive assessment as part of a multidisciplinary approach in patients undergoing transfemoral TAVR for the treatment of severe AS. The early diagnosis of cognitive impairment may guide treatment optimization, through more intensive secondary prevention and neuroprotective measures. Also, the presence of preprocedural cognitive dysfunction may raise awareness of the risk of prolonged hospitalization and protracted functional recovery. Finally, the association between low native aortic valve areas and an immediate postoperative improvement in cognition brings additional evidence on the potential and less explored benefits of invasive procedures even in the setting of advanced-stage structural heart disease.

Conclusions

In patients with severe symptomatic AS, a smaller native aortic valve area was associated with early cognitive improvement after transfemoral TAVR. Baseline cognition and the length of stay in the ICU influenced the early functional outcomes. Our results emphasize the importance of preprocedural cognitive assessment both as a potential therapeutic target and as a risk factor for worse immediate functional status and protracted recovery.

References

1. Lazar RM, Pavol MA, Bormann T, Dwyer MG, Kraemer C, White R, et al. Neurocognition and Cerebral Lesion Burden in High-Risk Patients Before Undergoing Transcatheter Aortic Valve Replacement: Insights From the SENTINEL Trial. JACC Cardiovasc Interv. 2018;11:384-392.
2. De Carlo M, Liga R, Migaleddu G, Scatturin M, Spaccarotella C, Fiorina C, et al. Evolution, Predictors, and Neurocognitive Effects of Silent Cerebral Embolism During Transcatheter Aortic Valve Replacement. JACC Cardiovasc Interv. 2020;13:1291-1300.
3. van Nieuwkerk AC, Delewi R, Wolters FJ, Muller M, Daemen M, Biessels GJ; Heart-Brain Connection Consortium. Cognitive Impairment in Patients With Cardiac Disease: Implications for Clinical Practice. Stroke. 2023;54:2181-2191.
4. Ghanem A, Kocurek J, Sinning JM, Wagner M, Becker BV, Vogel M, et al. Cognitive trajectory after transcatheter aortic valve implantation. Circ Cardiovasc Interv. 2013;6:615-624.
5. van Nieuwkerk AC, Hemelrijk KI, Aarts HM, et al. Cerebral blood flow and cognitive functioning in patients undergoing transcatheter aortic valve implantation. EClinicalMedicine. 2025;81:103092.

6. Livingston G, Huntley J, Sommerlad A, Ames D, Ballard C, Banerjee S, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. Lancet. 2020;396:413-446.
7. Tsao CW, Aday AW, Almarzooq ZI, Alonso A, Beaton AZ, Bittencourt MS, et al. Heart Disease and Stroke Statistics-2022 Update: A Report From the American Heart Association. Circulation. 2022;145:e153-e639.
8. Meng L, Hou W, Chui J, Han R, Gelb AW. Cardiac Output and Cerebral Blood Flow: The Integrated Regulation of Brain Perfusion in Adult Humans. Anesthesiology. 2015;123:1198-208.
9. Sim JJL, Ling RR, Neo VSQ, Tan FL, Djohan AH, Yeo LLL, et al. The Impact of Cognitive Impairment on Clinical Outcomes After Transcatheter Aortic Valve Implantation (from a Systematic Review and Meta-Analysis). Am J Cardiol. 2022;185:63-70.
10. Vlastra W, van Nieuwkerk AC, Bronzwaer AGT, Versteeg A, Bron EE, Niessen WJ, et al. Cerebral Blood Flow in Patients with Severe Aortic Valve Stenosis Undergoing Transcatheter Aortic Valve Implantation. J Am Geriatr Soc. 2021;69:494-499.
11. Kahlert P, Knipp SC, Schlamann M, Thielmann M, Al-Rashid F, Weber M, et al. Silent and apparent cerebral ischemia after percutaneous transfemoral aortic valve implantation: a diffusion-weighted magnetic resonance imaging study. Circulation. 2010;121:870-878.
12. Kahlert P, Al-Rashid F, Döttger P, Mori K, Plicht B, Wendt D, et al. Cerebral embolization during transcatheter aortic valve implantation: a transcranial Doppler study. Circulation. 2012;126:1245-1255.
13. Woldendorp K, Indja B, Bannon PG, Fanning JP, Plunkett BT, Grieve SM. Silent brain infarcts and early cognitive outcomes after transcatheter aortic valve implantation: a systematic review and meta-analysis. Eur Heart J. 2021;42:1004-1015.
14. Ghanem A, Dörner J, Schulze-Hagen L, Müller A, Wilsing M, Sinning JM, et al. Subacute Subclinical Brain Infarctions after Transcatheter Aortic Valve Implantation Negatively Impact Cognitive Function in Long-Term Follow-Up. PLoS One. 2017;12:e0168852.
15. Khan MM, Herrmann N, Gallagher D, et al. Cognitive Outcomes After Transcatheter Aortic Valve Implantation: A Metaanalysis. J Am Geriatr Soc. 2018;66:254-262.
16. Potluri S, Szerlip M, Al-Azizi K, Harrington K, Kodali S, Kapadia S, et al. Neurocognitive Function Change in Low-Risk Patients Undergoing TAVR Versus SAVR: Insights From PARTNER-3. JACC Cardiovasc Interv. 2020;13:2713-2714.
17. Ghezzi ES, Ross TJ, Davis D, Psaltis PJ, Loetscher T, Keage HAD. Meta-Analysis of Prevalence and Risk Factors for Cognitive Decline and Improvement After Transcatheter Aortic Valve Implantation. Am J Cardiol. 2020;127:105-112.
18. Nasreddine ZS, Phillips NA, Bédirian V, Charbonneau S, Whitehead V, Collin I, et al. The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. J Am Geriatr Soc. 2005;53:695-699.
19. Greiner W, Weijnen T, Nieuwenhuizen M, Oppe S, Badia X, Busschbach J, et al. A single European currency for EQ-5D health states. Results from a six-country study. Eur J Health Econ. 2003;4:222-231.
20. Rabin R, de Charro F. EQ-5D: a measure of health status from the EuroQol Group. Ann Med. 2001;33:337-343.
21. Devlin NJ, Brooks R. EQ-5D and the EuroQol Group: Past, Present and Future. Appl Health Econ Health Policy. 2017;15:127-137.
22. Dweck MR, Loganath K, Bing R, Treibel TA, McCann GP, Newby DE, et al. Multi-modality imaging in aortic stenosis: an EACVI clinical consensus document. Eur Heart J Cardiovasc Imaging. 2023;24:1430-1443.
23. Agricola E, Ancona F, Bartel T, Brochet E, Dweck M, Faletra F, et al. Multimodality imaging for patient selection, procedural guidance, and follow-up of transcatheter interventions for structural heart disease: a consensus document of the EACVI Task Force on Interventional Cardiovascular Imaging: part 1: access routes, transcatheter aortic valve implantation, and transcatheter mitral valve interventions. Eur Heart J Cardiovasc Imaging. 2023;24:e209-e268.
24. Galderisi M, Cosyns B, Edvardsen T, Cardim N, Delgado V, Di Salvo G, et al. Standardization of adult transthoracic echocardiography reporting in agreement with recent chamber quantification, diastolic function, and heart valve disease recommendations: an expert consensus document of the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging. 2017;18:1301-1310.
25. Clement P, Mutsaerts HJ, Václavů L, Ghariq E, Pizzini FB, Smits M, et al. Variability of physiological brain perfusion in healthy subjects - A systematic review of modifiers. Considerations for multi-center ASL studies. J Cereb Blood Flow Metab. 2018;38:1418-1437.
26. Claassen JAHR, Thijssen DHJ, Panerai RB, Faraci FM. Regulation of cerebral blood flow in humans: physiology and clinical implications of autoregulation. Physiol Rev. 2021;101:1487-1559.
27. Tsuchiya S, Matsumoto Y, Suzuki H, Takanami K, Kikuchi Y, Takahashi J, et al. Transcatheter aortic valve implantation and cognitive function in elderly patients with severe aortic stenosis. EuroIntervention. 2020;15:e1580-e1587.
28. Schoenenberger AW, Zuber C, Moser A, Zwahlen M, Wenaweser P, Windecker S, et al. Evolution of Cognitive Function After Transcatheter Aortic Valve Implantation. Circ Cardiovasc Interv. 2016;9:e003590.
29. Michail M, Hughes AD, Comella A, et al. Acute Effects of Transcatheter Aortic Valve Replacement on Central Aortic Hemodynamics in Patients With Severe Aortic Stenosis. Hypertension. 2020;75:1557-1564.
30. Auffret V, Campelo-Parada F, Regueiro A, Del Trigo M, Chiche O, Chamandi C, et al. Serial Changes in Cognitive Function Following Transcatheter Aortic Valve Replacement. J Am Coll Cardiol. 2016;68:2129-2141.
31. Gardner AW, Montgomery PS, Wang M, Shen B, Casanegra AI, Silva-Palacios F, et al. Cognitive decrement in older adults with symptomatic peripheral artery disease. Geroscience. 2021;43:2455-2465.

32. Stefanidis KB, Askew CD, Greaves K, Summers MJ. The Effect of Non-Stroke Cardiovascular Disease States on Risk for Cognitive Decline and Dementia: A Systematic and Meta-Analytic Review. Neuropsychol Rev. 2018;28:1-15.
33. Armijo G, Nombela-Franco L, Tirado-Conte G. Cerebrovascular Events After Transcatheter Aortic Valve Implantation. Front Cardiovasc Med. 2018;5:104.
34. Gupta R, Mahmoudi E, Behnoush AH, Khalaji A, Malik AH, Sood A, et al. Effect of BMI on patients undergoing transcatheter aortic valve implantation: A systematic review and meta-analysis. Prog Cardiovasc Dis. 2023;78:58-66.
35. van Nieuwkerk AC, Santos RB, Sartori S, Regueiro A, Tchétché D, Mehran R, et al. Impact of body mass index on outcomes in patients undergoing transfemoral transcatheter aortic valve implantation. JTCVS Open. 2021;6:26-36.
36. Abawi M, Rozemeijer R, Agostoni P, van Jaarsveld RC, van Dongen CS, Voskuil M, et al. Effect of body mass index on clinical outcome and all-cause mortality in patients undergoing transcatheter aortic valve implantation. Neth Heart J. 2017;25:498-509.
37. Miyawaki N, Ishizu K, Shirai S, Miyahara K, Yamamoto K, Suenaga T, et al. Impact of Cognitive Impairment on Long-Term Outcomes After Transcatheter Aortic Valve Implantation. Circ Rep. 2024;6:357-365.
38. Stites SD, Harkins K, Rubright JD, Karlawish J. Relationships Between Cognitive Complaints and Quality of Life in Older Adults With Mild Cognitive Impairment, Mild Alzheimer Disease Dementia, and Normal Cognition. Alzheimer Dis Assoc Disord. 2018;32:276-283.
39. Gopalakrishnan P, Tiwari S, Nagaraja R, Krishnan G. Quality of life in persons with mild cognitive impairment: a systematic review and meta-analysis. Dement Neuropsychol. 2024;18:e20230093.
40. Wiersinga JHI, Rhodius-Meester HFM, Kleipool EEF, Handoko L, van Rossum AC, Liem SS, et al. Managing older patients with heart failure calls for a holistic approach. ESC Heart Fail. 2021;8:2111-2119.
41. Lauck SB, Yu M, Ding L, Hardiman S, Wong D, Sathananthan J, et al. Quality-of-Life Outcomes After Transcatheter Aortic Valve Implantation in a "Real World" Population: Insights From a Prospective Canadian Database. CJC Open. 2021;3:1033-1042.
42. Lauck SB, Arnold SV, Borregaard B, et al. Very Early Changes in Quality of Life After Transcatheter Aortic Valve Replacement: Results From the 3M TAVR Trial. Cardiovasc Revasc Med. 2020;21:1573-1578.
43. Zelis JM, van 't Veer M, Houterman S, Pijls NHJ, Tonino PAL; Netherlands Heart Registration Transcatheter Heart valve Implantation Registration Committee. Survival and quality of life after transcatheter aortic valve implantation relative to the general population. Int J Cardiol Heart Vasc. 2020;28:100536.
44. Ussia GP, Barbanti M, Cammalleri V, Scarabelli M, Mulè M, Aruta P, et al. Quality-of-life in elderly patients one year after transcatheter aortic valve implantation for severe aortic stenosis. EuroIntervention. 2011;7:573-579.
45. Malek-Ahmadi M, Nikkhahmanesh N. Meta-analysis of Montreal cognitive assessment diagnostic accuracy in amnestic mild cognitive impairment. Front Psychol. 2024;15:1369766.