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openheart Predictors of clinical outcome following transcatheter aortic valve implantation: a prospective cohort study

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ABSTRACT

Objective In recent years, transcatheter aortic valve implantation (TAVI) has become the treatment of choice for patients with symptomatic aortic valve stenosis considered to be at increased or high surgical risk. The aim of this study was to identify predictors of postoperative adverse events in older adults undergoing TAVI.

Methods A prospective observational cohort study of patients who were referred to a geriatric outpatient clinic for a geriatric assessment prior to TAVI was conducted. The outcomes were mortality and hospital readmission within 3 months of TAVI and the occurrence of major postoperative complications during hospitalisation according to the Clavien-Dindo classification. These three outcomes were also combined to a composite outcome. Univariate and multivariate logistic regression analyses were performed to identify predictors of the outcomes and composite outcome of adverse events.

Results This cohort included 490 patients who underwent TAVI (mean age 80.7±6.2 years, 47.3% male). Within 3 months of TAVI, 19 (3.9%) patients died and 46 (9.4%) patients experienced a hospital readmission. A total of 177 (36.1%) patients experienced one or more major complications according to the Clavien-Dindo classification during hospitalisation and 193 patients (39.4%) experienced the composite outcome of adverse events. In multivariate analyses, cognitive impairment was identified as an independent predictor of major postoperative complications (OR 2.16; 95% CI 1.14 to 4.19) and the composite outcome of adverse events (OR 2.40; 95% CI 1.21 to 4.79). No association was found between the other variables and the separate outcomes and composite outcome.

Conclusion Cognitive impairment is associated with postoperative adverse events in older patients undergoing TAVI. Therefore, it is important to screen for cognitive impairment prior to TAVI and it is recommended to include this in current TAVI guidelines.

INTRODUCTION

Stenosis of the aortic valve is one of the most common cardiovascular diseases in the Western population.^{1–3} It is associated with ageing and affects one in eight individuals aged 75 years and above.^{1–3} In recent years, transcatheter aortic valve implantation

Key messages

What is already known about this subject?

- Stenosis of the aortic valve is one of the most common cardiovascular diseases in the Western population and associated with ageing.
- Common surgical risk scores to predict the risk of adverse events, such as the European System for Cardiac Operative Risk Evaluation and Society of Thoracic Surgeons score, do not include relevant risk factors that are specifically prevalent in the geriatric population.
- Previous studies on predictors of adverse outcomes in older patients undergoing transcatheter aortic valve implantation (TAVI) mainly focus on the occurrence of long-term mortality.
- There is a paucity of information about predictors of both (short-term) mortality and morbidity in these patients.

What does this study add?

- In this prospective cohort study on adverse outcomes in older patients, all patients underwent a Comprehensive Geriatric Assessment prior to TAVI and were given advice for appropriate treatment to prevent/reduce postoperative adverse outcomes. Cognitive impairment was found to be associated with postoperative morbidity and mortality. No association was found between other variables, like frailty, and the occurrence of adverse events.

How might this impact on clinical practice?

- Screening for cognitive impairment with a screening tool like the Mini-Mental State Examination or Montreal Cognitive Assessment could help identify patients who are at increased risk of adverse events following TAVI. Therefore, it is recommended to include screening for cognitive impairment in current TAVI guidelines.

(TAVI) has become the treatment of choice for patients with symptomatic aortic valve stenosis, considered to be at increased or high surgical risk.^{1–3} Common surgical risk scores, such as the European System for Cardiac Operative Risk Evaluation (EuroSCORE) and Society of Thoracic Surgeons score, are

widely used to guide treatment options based on the predicted risk of poor outcomes.³ These models were created and validated in a standard surgical risk population.^{3,4} Therefore, these models do not include relevant risk factors that are specifically prevalent in the geriatric population.¹⁻³ In recent years, the evidence has grown that frailty can help identify patients who are at increased risk of mortality after a TAVI procedure.^{3,4} Therefore, the European Society of Cardiology guidelines for the management of valvular heart disease and the guidelines of the American College of Cardiology (ACC) recommend to use frailty scores to determine a patients' suitability for TAVI.^{1,2} Previous studies aimed to identify preoperative factors predictive of postoperative adverse outcomes in older patients undergoing TAVI.^{3,4} Several predictors of 1-year mortality in older patients have been found, including the presence of frailty, a reduced gait speed and dependence in activities of daily living (ADL). With regard to predictors of short-term outcomes (eg, 30-day mortality), there have been conflicting results, in particular with respect to frailty.⁵⁻⁷

The majority of recently created prediction models in older patients focused on the occurrence of long-term mortality.⁸⁻¹⁰ Since the occurrence of postoperative complications results in substantial burden for patients and healthcare systems, it is necessary to focus both on postoperative mortality and morbidity and the overall occurrence of these negative outcomes.^{11,12}

In this study, we aimed to identify predictors of postoperative adverse events, including mortality, hospital readmissions, major postoperative complications and the composite of these outcomes in older patients undergoing TAVI.

METHODS

Study design and population

This prospective, single-centre cohort study was conducted at the University Medical Centre Utrecht, a tertiary hospital in the Netherlands. All consecutive patients who visited the geriatric outpatient clinic for a geriatric assessment prior to TAVI between January 2014 and June 2020 were included. Patients were excluded if (a) they were referred for a preoperative geriatric assessment prior to another operation than TAVI, (b) the TAVI operation was cancelled or (c) the 3-month follow-up appointment was planned after 30 June 2020. Data were collected from patients' electronic medical records during the outpatient clinic visit prior to TAVI, during the TAVI admission and 3 months post-TAVI.

TAVI-procedure

A multidisciplinary heart team consisting of at least one interventional cardiologist and one cardiac surgeon evaluated the patients' suitability for a TAVI-procedure according to current guidelines. A preoperative complete cardiac assessment was performed. The preferred access site was the transfemoral artery. Procedures were

performed under local or general anaesthesia. After the TAVI procedure, patients had to take 6 hours bed rest.

Preoperative geriatric assessment

The preoperative geriatric assessment was performed by a geriatric nurse practitioner under supervision of a geriatrician and involved a Comprehensive Geriatric Assessment (CGA) in which the following domains were assessed: somatic, psychological, social and functional. An anamnesis was performed and data were collected on medical history, medication use (in particular the presence of (hyper)polypharmacy), smoking status, alcohol use, living situation, dependence in (instrumental) activities of daily living ((i)ADL), nutritional status, the presence of a fall in the previous 6 months and the presence of a delirium in the past. With regard to the medical history, the Charlson Comorbidity Index (CCI) score was calculated.¹³ An adjusted CCI score without scoring points for age-category was used. A cut-off value of ≥ 3 was defined as multimorbidity. Polypharmacy was defined as the use of five or more medications, excluding food supplements without prescription, medication only taken when necessary, dermal creams and eye drops. Hyperpolypharmacy was defined as the use of 10 or more medications. With regard to alcohol use and smoking status, patients scored positive if they were current users, regardless of the amount. Patients lived dependent when they lived in a skilled nursing or assisted nursing facility. Patients lived independent when they lived in their own house, with or without homecare. To assess dependence in (i)ADL the KATZ-15 questionnaire was conducted.¹⁴ Dependence in (i)ADL was defined as a KATZ-15 score ≥ 2 . The nutritional status was assessed using the Malnutrition Universal Screening Tool (MUST).¹⁵ Malnutrition was suspected when the MUST score was ≥ 1 . In addition, the American Society of Anaesthesiologists score, determined by an anaesthesiologist, was obtained from the patients' electronic medical records.¹⁶

Furthermore, a psychical examination was performed, which consisted of measurement of vital signs, gait speed and handgrip strength and a neurological—and functional examination. A decreased gait speed was defined as a gait speed of ≤ 0.80 m/s and a decreased handgrip strength was defined as ≤ 20 kg for women and ≤ 30 kg for men.¹⁷ In addition, a Mini-Mental State Examination (MMSE) or Montreal Cognitive Assessment ($< 5\%$ of the cases, MoCA) was conducted to assess cognitive function.^{18,19} An MMSE score ≤ 24 or MoCA score < 26 was indicative for cognitive impairment. To assess the possible presence of a depression, the Geriatric Depression Scale (GDS) questionnaire was conducted. A GDS-15 score ≥ 6 was suggestive of a depression.²⁰

Frailty was assessed according to the Groningen Frailty Indicator (GFI).²¹ This is an internationally applied, validated frailty instrument which offers a multidomain view on the degree of frailty. The GFI questionnaire consists of 15 questions, covering all domains of the CGA. Frailty was present in case of a GFI score of ≥ 4 . Due to varying

standard instruments to determine frailty in recent years, the GFI score was not reported in all patients by the geriatric nurse practitioner. In these cases, the GFI score was determined by the authors based on information collected during the preoperative geriatric assessment. A few questions of the GFI could not be filled in retrospectively. Therefore, the answers to these questions were rated as missing and the total GFI score was calculated, excluding these questions. Based on the results of the CGA, advice was provided on perioperative delirium prevention including both non-pharmacological interventions and pharmacological interventions if indicated. Furthermore, advice was provided concerning fall-prevention, medication management, mobility, optimising nutritional status and reducing alcohol use and smoking. In some cases, it was recommended to cancel or postpone the TAVI procedure, for example, in case of multimorbidity or severe functional or cognitive impairment. Nonetheless, the cardiologist made the ultimate decision.

Postoperative geriatric involvement

One day after the TAVI procedure, a geriatric nurse practitioner visited the patient on the cardiac ward to assist in the prevention or treatment of complications prevalent in the geriatric population (eg, falls, delirium, stroke). Nurses from the cardiac ward observed the patients during the hospital stay and in case a postoperative delirium was suspected, the Delirium Observation Screening Scale (DOSS) was assessed three times a day. The DOSS is an early recognition tool for delirium, based on observations by nurses. A score of three and higher indicates a delirium.²² A postoperative delirium was confirmed by the geriatric consulting team, based on criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.²³ A postoperative delirium was treated by non-pharmacological interventions and if indicated, by pharmacological treatment like haloperidol.

Follow-up

Three months after the TAVI procedure there was a follow-up appointment with a geriatric nurse practitioner, mostly by phone. Patients were asked about their general well-being and physical complaints compared with the situation before the procedure. Data were collected on the occurrence of postoperative complications. Patients were also followed by their cardiologist 6 and 12 months after TAVI.

Outcomes

The outcomes were mortality and hospital readmissions within 3 months of TAVI and major postoperative complications during hospitalisation according to the Clavien-Dindo classification (online supplemental table 1).^{24 25} The Clavien-Dindo classification was already successfully implemented as outcome classification method in other surgical specialties (eg, non-cardiac thoracic surgery, colorectal surgery and urological surgery)^{26–30} and a

recent study proved that this classification adequately measures the quantity and severity of postoperative complications in adult cardiac surgery.³¹ The Clavien-Dindo classification consists of five categories, each category represents the type of therapy which was required to correct the complication. The need for pharmacological treatment is reflected in category I and II. Category III–IV range from a complication requiring a surgical, endoscopic or radiological intervention to a life-threatening complication requiring intensive care (unit) management. For example, an arrhythmia requiring the placement of a pacemaker is a Clavien-Dindo grade III complication. Category V reflects the death of a patient.^{24 25} A composite outcome was created in which the three outcomes were combined. A Clavien-Dindo grade of II and higher was considered a major postoperative complication. When a patient suffered from two or more complications in different grade categories, the highest grade was used in the analysis.

Statistical analysis

The prevalence of dichotomised baseline variables is presented as numbers and corresponding percentages. Continuous baseline variables are expressed as mean and SD. In case there were more than 10% missing values for a variable (which holds for the GDS), the Little's MCAR test was performed to determine whether missing values were completely at random or not. Since the results of the Little's MCAR test showed no significance ($p>0.05$), multiple imputation methods were not indicated. Univariate logistic regression analyses were performed to identify potential predictors of the outcomes and the composite outcome. Before entering continuous variables into the univariate logistic regression analysis, we first performed the Box-Tidwell procedure to assess whether the continuous variables were linearly related to the logit of the dependent variable.

All variables with p value ≤ 0.10 in univariate analyses were entered into a stepwise multivariate analysis. ORs with a 95% CI were calculated. Analyses were performed using IBM Statistical Package for the Social Sciences, V.25 (SPSS).

RESULTS

Patient inclusion and baseline characteristics

A total of 555 patients visited the geriatric outpatient clinic for a preoperative geriatric assessment between January 2014 and June 2020. 65 patients were excluded from this study. Reasons for exclusion were referral to the geriatric outpatient clinic because of a preoperative assessment for an intervention other than TAVI ($n=31$), no 3-month follow-up data available because the follow-up appointment was scheduled after 30 June 2020 ($n=20$), insufficient information collected during preoperative assessment ($n=10$) and cancellation of the TAVI procedure ($n=4$). Operations were mostly cancelled due to

Table 1 Baseline characteristics

		N	%
All patients		490	
Demographics			
Age	Years (mean±SD)	80.7±6.2	
	Age ≥80 years	319	65.1
Sex	Male	232	47.3
Smoking	Current smoker	31	6.3
	Ex-smoker	198	40.4
Alcohol use	Current alcohol user	241	49.2
Frailty			
GFI*	≥4	170	34.7
Somatic status			
ASA class†	≥3	456	93.1
CCI‡	≥3§	258	52.7
Medication use	Number (mean±SD)	8.4±4.5	
	Polypharmacy (≥5 medications)	408	83.3
	Hyperpolypharmacy (≥10 medications)	163	33.3
Cognitive and psychological status			
MMSE¶¶	(Mean±SD)	27.5±2.5	
	MMSE ≤24	47	9.6
MoCA¶¶	(Mean±SD)	26±3.4	
	MoCA <26	8	1.6
Impaired cognition	MMSE ≤24 or MoCA <26	55	11.2
GDS*	≥6	17	3.5
Delirium	In past	48	9.8
Social status			
Living situation	Dependent	22	4.5
Functional status			
Dependence in ADL**	KATZ6 ≥1	114	23.3
Dependence in iADL††	KATZ9 ≥1	287	60.5
Dependence in (i)ADL*	KATZ15 ≥2	225	45.9
(At risk of) malnutrition**	MUST ≥1	75	15.3
Gait speed	<0.8 m/s	98	20
Handgrip strength	≤20 kg female/≤30 kg male	246	50.2
Falls	≥1 in previous 6 months	93	19.1

*Score range from 0 to 15.

†Score range from 1 to 5.

‡Score range from 0 to 24.

§Points for age category not included.

¶Score range from 0 to 30.

**Score range from 0 to 6.

††Score range from 0 to 9.

ASA, American Society of Anaesthesiologists; CCI, Charlson Comorbidity Index; GDS, Geriatric Depression Scale; GFI, Groningen Frailty Indicator; (i)ADL, (instrumental) activities of daily living; MMSE, mini-mental state examination; MoCA, Montreal Cognitive Assessment; MUST, Malnutrition Universal Screening Tool.

severe comorbidities. Finally, 490 patients were included in the study.

The baseline characteristics of the study population are outlined in [table 1](#). Mean age was 80.7±6.2 years. Five per cent were between the age of 50 and 70 and

Table 2 Occurrence of outcome measures

	N	%
Mortality within 3 months of TAVI	19	3.9
Hospital readmission within 3 months of TAVI	46	9.4
Complications according to Clavien-Dindo during admission	177	36.1
Clavien-Dindo grade I	144	29.4
Clavien-Dindo grade II	69	14.1
Clavien-Dindo grade IIIa	66	13.5
Clavien-Dindo grade IIIb	15	3.1
Clavien-Dindo grade IVa	14	2.9
Clavien-Dindo grade IVb	2	0.4
Clavien-Dindo grade V	12	2.4
Composite outcome*	193	39.4

*Including mortality and hospital readmission within 3 months of TAVI and the occurrence of major postoperative complications (Clavien-Dindo grade≥II) during hospitalisation.

—TAVI, transcatheter aortic valve implantation.

28% 85 years or older. Two hundred and thirty-two patients (47.3%) were male. A total of 170 patients (34.7%) were frail. The mean logistic EuroSCORE was 14.8%.

Mortality and hospital readmissions within 3 months of TAVI

Occurrence of outcome measures is displayed in [table 2](#). Twelve patients (2.4%) died during hospital admission and 19 patients (3.9%) died within 3 months of TAVI. In total, there were 46 readmissions (9.4%), of which 22 (48%) were cardiac, 23 (50%) non-cardiac and for one readmission (2%) the reason could not be traced in the patient file. Cardiac reasons for readmission were often arrhythmias requiring pacemaker implantation or acute decompensated heart failure. Non-cardiac reasons were among others infections (requiring intravenous antibiotics) or cerebrovascular events. Due to the limited number of outcome events within 3 months of TAVI, logistic regression analyses to identify independent predictors were not feasible.

Occurrence of major postoperative complications during hospitalisation

A total of 177 (36.1%) patients experienced one or more major postoperative complications (Clavien-Dindo grade≥II) during hospital admission. Results of the univariate and multivariate analyses are displayed in [table 3](#). Univariate analysis showed that cognitive impairment (OR 2.30; 95% CI 1.30 to 4.07), dependence in (i) ADL (OR 1.57; 95% CI 1.08 to 2.30) and a decreased gait speed (OR 1.64; 95% CI 1.04 to 2.60) were significantly associated with a higher risk of a major postoperative complication during hospitalisation. Multivariate analysis showed that cognitive impairment was independently associated with a higher risk of a major postoperative complication during hospital admission (OR 2.16; 95% CI 1.14 to 4.19).

Table 3 Variables associated with major postoperative complications* during hospitalisation

Demographics	Univariate OR (95% CI)	P value	Multivariate OR (95% CI)	P value
Age	1.00 (0.97 to 1.03)	0.91		
Sex (male)	1.37 (0.94 to 1.98)	0.10	0.91 (0.59 to 1.40)	0.66
Current smoker	1.12 (0.53 to 2.37)	0.76		
Alcohol user	0.62 (0.42 to 0.89)	0.01	0.78 (0.50 to 1.21)	0.26
Frailty				
GFI ≥ 4 §	1.43 (0.96 to 2.13)	0.08	0.73 (0.42 to 1.24)	0.24
Somatic status				
ASA class ≥ 3 ¶	0.91 (0.44 to 1.86)	0.79		
CCI ≥ 3 †**	1.37 (0.94 to 1.98)	0.10	1.22 (0.80 to 1.87)	0.35
Polypharmacy	1.11 (0.67 to 1.83)	0.68		
Hyperpolypharmacy	1.27 (0.86 to 1.88)	0.22		
Cognitive and psychological status				
MMSE ≤ 24 or MoCA < 26 ††	2.30 (1.30 to 4.07)	< 0.01	2.16 (1.14 to 4.19)	0.02
GDS ≥ 6 §	0.57 (0.18 to 1.77)	0.33		
Delirium in past	1.06 (0.57 to 1.96)	0.85		
Social status				
Living dependent	2.20 (0.93 to 5.21)	0.07	1.59 (0.60 to 4.23)	0.35
Functional status				
Katz15 ≥ 2 §	1.57 (1.08 to 2.30)	0.02	1.20 (0.73 to 1.97)	0.47
MUST ≥ 1 ††	1.06 (0.64 to 1.77)	0.81		
Gait speed < 0.8 m/s	1.64 (1.04 to 2.60)	0.03	1.47 (0.85 to 2.55)	0.17
Handgrip strength ≤ 20 kg/ ≤ 30 kg‡	1.00 (0.68 to 1.47)	> 0.99		
Falls in previous 6 months	1.37 (0.86 to 2.17)	0.18		

*Clavien-Dindo grade \geq II.

†Points for age category not included.

‡ ≤ 20 kg female / ≤ 30 kg male.

§Score range from 0 to 15.

¶Score range from 1 to 5.

**Score range from 0 to 24.

††Score range from 0 to 30.

‡‡Score range from 0 to 6.

ASA, American Society of Anaesthesiologists; CCI, Charlson Comorbidity Index; GDS, Geriatric Depression Scale; GFI, Groningen Frailty Indicator; MMSE, minimal state examination; MoCA, Montreal Cognitive Assessment; MUST, Malnutrition Universal Screening Tool.

Composite outcome of adverse events

A total of 193 (39.4%) patients experienced the composite outcome consisting of mortality or hospital readmission within 3 months of TAVI and occurrence of major postoperative complications (Clavien-Dindo grade \geq II) during hospitalisation. Results from the univariate and multivariate analyses of the composite outcome are presented in [table 4](#). Cognitive impairment was statistically significant associated with an increased risk of the composite outcome in both univariate (OR 2.56; 95% CI 1.41 to 4.65) and multivariate analysis (OR 2.40; 95% CI 1.21 to 4.79). Univariate analysis showed that current alcohol use was associated with a lower risk (OR 0.62; 95% CI 0.43 to 0.90) and living dependently (OR 2.49; 95% CI 1.01 to 6.13), dependence in (i)ADL (OR 1.74; 95% CI 1.20 to 2.54) and a decreased gait speed (OR 1.62; 95% CI 1.02 to 2.56) with a higher risk of the composite outcome. In the multivariate analysis, these factors were not identified as independent predictors of the composite outcome.

DISCUSSION

The aim of this study was to identify predictors of postoperative adverse outcomes in older patients undergoing TAVI. Cognitive impairment was identified as an independent predictor of major postoperative complications during hospitalisation and the composite outcome of major complications, hospital readmissions and mortality. No association was found between the other variables and the composite and separate outcomes.

The finding of cognitive impairment as an independent predictor of worse outcomes in older patients is in line with previous studies conducted in patients undergoing TAVI. Yanagisawa *et al* evaluated if the presence of preoperative cognitive impairment was associated with postoperative adverse outcomes, in particular 1-year cumulative mortality.³² They included TAVI patients aged 70 or higher, whose cognitive performance was assessed using the MMSE. They found that patients with cognitive impairment had more in-hospital adverse outcomes (major bleeding, vascular complications,

Table 4 Variables associated with the composite outcome consisting of mortality or hospital readmission within 3 months of transcatheter aortic valve implantation and occurrence of major postoperative complications (Clavien-Dindo grade \geq II) during hospitalisation

Composite outcome: postoperative adverse events	Univariate OR (95% CI)	P value	Multivariate OR (95% CI)	P value
Demographics				
Age	1.01 (0.98 to 1.04)	0.51		
Sex (male)	0.87 (0.60 to 1.25)	0.45		
Current smoker	1.13 (0.54 to 2.38)	0.75		
Alcohol user	0.62 (0.43 to 0.90)	0.01	0.77 (0.50 to 1.19)	0.23
Frailty				
GFI \geq 4**	1.47 (0.99 to 2.19)	0.06	0.67 (0.39 to 1.15)	0.14
Somatic status				
ASA class \geq 3*	1.11 (0.54 to 2.27)	0.78		
CCI \geq 3†‡	1.38 (0.96 to 2.00)	0.09	1.23 (0.81 to 1.86)	0.34
Polypharmacy	1.18 (0.72 to 1.95)	0.52		
Hyperpolypharmacy	1.27 (0.86 to 1.87)	0.23		
Cognitive and psychological status				
MMSE \leq 24 or MoCA $<$ 26§	2.56 (1.41 to 4.65)	$<$ 0.01	2.40 (1.21 to 4.79)	0.01
GDS \geq 6**	0.46 (0.15 to 1.45)	0.19		
Delirium in past	1.20 (0.66 to 2.21)	0.55		
Social status				
Living dependent	2.49 (1.01 to 6.13)	0.05	1.85 (0.66 to 5.19)	0.24
Functional status				
Katz15 \geq 2**	1.74 (1.20 to 2.54)	$<$ 0.01	1.42 (0.87 to 2.31)	0.16
MUST \geq 1¶	1.03 (0.62 to 1.71)	0.90		
Gait speed $<$ 0.8 m/s	1.62 (1.02 to 2.56)	0.04	1.32 (0.76 to 2.28)	0.32
Handgrip strength \leq 20 kg/ \leq 30 kg††	1.11 (0.76 to 1.63)	0.58		
Falls in previous 6 months	1.39 (0.88 to 2.19)	0.16		

*Score range from 1 to 5.

†Points for age category not included.

‡Score from range 0 to 24.

§Score range from 0 to 30.

¶Score range from 0 to 6.

**Score range from 0 to 15.

††20 kg female/ \leq 30 kg male.

ASA, American Society of Anaesthesiologists; CCI, Charlson Comorbidity Index; GDS, Geriatric Depression Scale; GFI, Groningen Frailty Indicator; MMSE, mini-mental state examination; MoCA, Montreal Cognitive Assessment; MUST, Malnutrition Universal Screening Tool.

acute kidney injury, prolonged hospital stay) and that cognitive impairment was an independent predictor of 1-year all-cause mortality.³²

Khan *et al* included TAVI patients who were screened on the presence of geriatric risk factors.³³ They found that the presence of cognitive deficits (according to the Mini-Cog test) was associated with the occurrence of a postoperative delirium and 30-day mortality.³³

A possible explanation for this finding could be that patients with cognitive impairment are more prone to develop a postoperative delirium and that this is reflected in our outcome 'major postoperative complications during hospitalisation according to the Clavien-Dindo classification' and the composite outcome. However,

only a minority (11.3%) of all patients with a Clavien-Dindo grade II complication experienced a delirium for which pharmacological treatment was necessary. Another explanation, as stated by Yanagisawa *et al*, could be that a part of the patients with cognitive deficits are known to suffer from vascular cognitive impairment caused by systemic vascular risk factors.³² The presence of these vascular risk factors might explain the increased risk of postoperative morbidity in patients with cognitive impairment. In contrast to previous studies conducted in TAVI patients,^{3 4} we did not find an association between other variables, like frailty, and postoperative adverse outcomes. A possible explanation for this finding could be that all TAVI patients included in our study had a

preoperative CGA. Based on the results of the CGA, an extensive advice was given with regard to identified risk factors. Therefore, our study population differs from the study population in previous studies, since all patients in our study had a preoperative intervention consisting of a CGA and the subsequent advice for appropriate treatment to prevent/reduce postoperative adverse outcomes.

This study has several strengths. The study design was prospective and a relatively large number of patients was included. Whereas previous studies mostly focused on separate outcomes, in particular mortality, this study also assessed a composite outcome, including mortality and hospital readmission within 3 months of TAVI and the occurrence of major postoperative complications during hospitalisation, assessing both postoperative mortality and morbidity. Therefore, an advantage of this composite outcome is that it reflects the overall course following TAVI. Furthermore, we included a wide variety of potential preoperative predictive factors, covering all the different domains of the CGA. In this study, frailty was assessed by a validated frailty instrument that includes all domains of the CGA and therefore it offers a broad assessment of frailty in comparison to other frailty instruments that cover less domains of the CGA.²¹

This study has some limitations. Due to the limited number of events for mortality and hospital readmission within 3 months of TAVI, planned logistic regression analyses were not feasible. Furthermore, during the study period, the local guidelines regarding frailty instruments were changing. Therefore, for a number of patients, the GFI score was not reported by the geriatric nurse practitioner and had to be calculated by the authors. However, some questions of the GFI are subjective and could not be filled in retrospectively. The answers for these questions were rated as missing, and the total GFI score was calculated, excluding these questions. This might have resulted in an underestimation of the number of frail patients. However, the frailty prevalence in this study corresponded to the prevalence range (29%–63%) of frailty in patients undergoing TAVI that was found in a recent meta-analysis.³⁴ Finally, during the 3-month follow-up appointment with the geriatric nurse practitioner, patients were often not explicitly asked if they had been readmitted to a hospital within 3 months of TAVI. This may lead to an underestimation of the number of participants with a readmission if a patient was admitted to a hospital other than the University Medical Centre Utrecht.

Clinical implications

The results of this study have some important clinical implications. We found cognitive impairment to be independently associated with a higher risk of postoperative adverse events. Screening for cognitive impairment with a screening tool like the MMSE or MoCA could help identify patients who are at increased risk of unfavourable outcomes and will provide additional information on the potential risks of TAVI, which improves shared-decision making. Therefore, we advise to include screening for cognitive impairment in the current local and international guidelines.¹ The 2017 ACC expert

consensus on a decision pathway for TAVI in the management of adults with aortic stenosis, is innovative by advising to assess cognition by means of the MMSE, however, cognitive function is not yet included in their four proposed risk categories.² In addition, if a patient is suspected of cognitive decline or impairment after screening for cognitive impairment, he or she could be monitored more closely during admission and afterwards, especially by a geriatric team in order to detect and anticipate on problems in an early stage.

CONCLUSION

This study identified cognitive impairment as an independent predictor of postoperative adverse events in older patients undergoing TAVI. Therefore, it is important to screen for cognitive impairment prior to TAVI, as this can identify patients who are at increased risk to develop a postoperative adverse event. It is recommended to include screening for cognitive impairment in current TAVI guidelines.

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REFERENCES

- Falk V, Baumgartner H, Bax JJ, *et al.* 2017 ESC/EACTS guidelines for the management of valvular heart disease. *Eur J cardio-thoracic Surg* 2017;52:616–64.
- Otto CM, Kumbhani DJ, Alexander KP, *et al.* 2017 ACC expert consensus decision pathway for transcatheter aortic valve replacement in the management of adults with aortic stenosis: a report of the American college of cardiology task force on clinical expert consensus documents. *J Am Coll Cardiol* 2017;69:1313–46.
- Anand A, Harley C, Visvanathan A, *et al.* The relationship between preoperative frailty and outcomes following transcatheter aortic valve implantation: a systematic review and meta-analysis. *Eur Heart J Qual Care Clin Outcomes* 2017;3:123–32.
- van Mourik MS, Velu JF, Lanting VR, *et al.* Preoperative frailty parameters as predictors for outcomes after transcatheter aortic valve implantation: a systematic review and meta-analysis. *Neth Heart J* 2020;28:280–92.
- Green P, Arnold SV, Cohen DJ, *et al.* Relation of frailty to outcomes after transcatheter aortic valve replacement (from the partner trial). *Am J Cardiol* 2015;116:264–9.

- 6 Green P, Woglom AE, Genereux P, *et al.* The impact of frailty status on survival after transcatheter aortic valve replacement in older adults with severe aortic stenosis: a single-center experience. *JACC Cardiovasc Interv* 2012;5:974–81.
- 7 Assmann P, Kievit P, van der Wulp K, *et al.* Frailty is associated with delirium and mortality after transcatheter aortic valve implantation. *Open Heart* 2016;3:e000478.
- 8 Skaar E, Eide LSP, Norekvål TM, *et al.* A novel geriatric assessment frailty score predicts 2-year mortality after transcatheter aortic valve implantation. *Eur Hear J - Qual Care Clin Outcomes* 2019;5:153–60.
- 9 Goudzwaard JA, de Ronde-Tillmans MJAG, El Faquir N, *et al.* The erasmus frailty score is associated with delirium and 1-year mortality after transcatheter aortic valve implantation in older patients. the tavi care & cure program. *Int J Cardiol* 2019;276:48–52.
- 10 Rogers T, Alraies MC, Moussa Pacha H, *et al.* Clinical frailty as an outcome predictor after transcatheter aortic valve implantation. *Am J Cardiol* 2018;121:850–5.
- 11 Sieber FE, Barnett SR. Preventing postoperative complications in the elderly. *Anesthesiol Clin* 2011;29:83–97.
- 12 Karakoc D. Surgery of the elderly patient. *Int Surg* 2016;101:161–6.
- 13 Charlson ME, Pompei P, Ales KL, *et al.* A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373–83.
- 14 Laan W, Zuihoff NPA, Drubbel I, *et al.* Validity and reliability of the Katz-15 scale to measure unfavorable health outcomes in community-dwelling older people. *J Nutr Health Aging* 2014;18:848–54.
- 15 Elia M. Nutritional screening of adults: a multidisciplinary responsibility. development and use of the 'malnutrition universal screening tool' ('must') for adults; 2003: 127.
- 16 Doyle D, Goyal A, Bansal P. *American society of anesthesiologists classification (ASA class)*. StatPearls Treasure, 2020.
- 17 Reiss J, Iglseider B, Alzner R, *et al.* Sarcopenia and osteoporosis are interrelated in geriatric inpatients. *Z Gerontol Geriatr* 2019;52:688–93.
- 18 Folstein MF, Folstein SE, McHugh PR. "Mini-mental state": a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189–98.
- 19 Nasreddine ZS, Phillips NA, Bä@dirian Val@rie, *et al.* The Montreal cognitive assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc* 2005;53:695–9.
- 20 Yesavage JA, Brink TL, Rose TL, *et al.* Development and validation of a geriatric depression screening scale: a preliminary report. *J Psychiatr Res* 1982;17:37–49.
- 21 Stevernik N, Slaets JPL, Schuurmans H. Measuring frailty: development and testing the GFI (Groningen frailty indicator). *Gerontologist* 2001;41:236–7.
- 22 Schuurmans MJ, Shortridge-Baggett LM, Duursma SA. The delirium observation screening scale: a screening instrument for delirium. *Res Theory Nurs Pract* 2003;17:31–50.
- 23 American Psychiatric Association. *Diagnostic and statistical manual of mental disorders*. 5 edn, 2013.
- 24 Dindo D, Demartines N, Clavien P-A. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004;240:205–13.
- 25 Clavien PA, Barkun J, de Oliveira ML, *et al.* The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg* 2009;250:187–96.
- 26 Seely AJE, Ivanovic J, Threader J, *et al.* Systematic classification of morbidity and mortality after thoracic surgery. *Ann Thorac Surg* 2010;90:936–42.
- 27 Bosma E, Pullens MJJ, de Vries J, *et al.* The impact of complications on quality of life following colorectal surgery: a prospective cohort study to evaluate the Clavien-Dindo classification system. *Colorectal Dis* 2016;18:594–602.
- 28 Geskin AA, Westney OL, Graber WJ, *et al.* Complications of peri-operative ureteral catheter placement: experience at a major cancer center. *Urology* 2021:S0090–4295.
- 29 Wakita N, Hinata N, Suzuki K. Comparison of robot-assisted partial nephrectomy for complex (RENAL scores ≥ 10) and non-complex renal tumors: a single-center experience. *Int J Urol*.
- 30 Winter R, Haug I, Lebo P, *et al.* Standardizing the complication rate after breast reduction using the Clavien-Dindo classification. *Surgery* 2017;161:1430–5.
- 31 Hébert M, Cartier R, Dagenais F, *et al.* Standardizing postoperative complications-validating the Clavien-Dindo complications classification in cardiac surgery. *Semin Thorac Cardiovasc Surg* 2021;33:443–51.
- 32 Yanagisawa R, Tanaka M, Yashima F, *et al.* Frequency and consequences of cognitive impairment in patients underwent transcatheter aortic valve implantation. *Am J Cardiol* 2018;122:844–50.
- 33 Khan MM, Lanctôt KL, Fremes SE, *et al.* The value of screening for cognition, depression, and frailty in patients referred for TAVI. *Clin Interv Aging* 2019;14:841–8.
- 34 Piankova P, Afilalo J. Prevalence and prognostic implications of frailty in transcatheter aortic valve replacement. *Cardiol Clin* 2020;38:75–87.