


# openheart Association between perioperative statin treatment and short-term clinical outcomes following transcatheter aortic valve implantation: a retrospective cohort study

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## ABSTRACT

**Background** Studies have found statin treatment to be associated with improved 1-year survival after transcatheter aortic valve implantation (TAVI), suggesting pleiotropic effects of statins on preventing perioperative complications. Statin treatment is not associated with postoperative cardiovascular complications or mortality; however, other postoperative complications have not been investigated.

**Aim** To explore whether preoperative statin treatment is associated with a lower short-term risk of mortality, readmission and major postoperative complications in older patients undergoing TAVI.

**Methods** A retrospective cohort study including patients aged 65 years and older who had undergone a comprehensive geriatric assessment prior to TAVI between January 2014 and January 2021. The primary outcomes were 90-day mortality, 90-day readmissions and major postoperative complications according to the Clavien-Dindo classification. Multivariable logistic regression was performed with adjustment for potential confounders, namely age, gender, comorbidity, body mass index, smoking, diminished renal function, alcohol use and falls.

**Results** This study included 584 patients, of whom 324 (55.5%) were treated with a statin. In the statin treated group, 15 (4.6%) patients died within 90 days of TAVI compared with 10 (3.8%) patients in the non statin group (adjusted OR 1.17; 95% CI 0.51 to 2.70). The number of 90-day readmissions was 39 (12.0%) and 34 (13.1%) (adjusted OR 0.91; 95% CI 0.54 to 1.52), respectively. In the statin treated group, 115 (35.5%) patients experienced a major complication compared with 98 (37.7%) in the non-statin group (adjusted OR 0.95; 95% CI 0.67 to 1.37).

**Conclusion** Preoperative statin treatment is not associated with improved short-term outcomes after TAVI. A randomised controlled trial with different statin doses may be warranted to investigate whether initiating statin treatment before TAVI improves both postoperative outcomes and long-term survival.

## WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Some studies found that statin treatment is associated with improved long-term outcomes after transcatheter aortic valve implantation (TAVI). Recent literature suggests that perioperative pleiotropic effects of statin treatment during and direct after TAVI might in part explain the improved long-term outcomes after TAVI.

## WHAT THIS STUDY ADDS

⇒ We found no association between continued statin treatment and postoperative complications after TAVI, including mortality, rehospitalisation and postoperative major complications according to the Clavien-Dindo classification.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Initiation of statin treatment is not advised specifically to improve short-term outcomes after TAVI.

## INTRODUCTION

Aortic valve stenosis is the most common valvular heart disease in developed countries and becomes more prevalent with age. In people aged 75 years and older, the prevalence is 12.4%.<sup>1</sup> Due to the poor prognosis of untreated symptomatic aortic valve stenosis, even in the absence of severe comorbidities, early treatment is recommended. Transcatheter aortic valve implantation (TAVI) is recommended in patients who are unsuitable for surgical aortic valve replacement. The criteria for TAVI include increased surgical risk, age  $\geq 75$  years and frailty.<sup>2</sup> Although TAVI is a well-established therapy in older patients, especially in more frail patients, the 5-year survival rate after TAVI is only 48%.<sup>3</sup>

Periprocedural statin treatment, among other treatments, has been the subject of

investigations to improve patients' survival after TAVI. In a meta-analysis of observational studies on statin treatment at the time of TAVI, statin treatment was found to be associated with reduced all-cause mortality 2 years after TAVI.<sup>4</sup> Since this meta-analysis, three more observational studies have been published, the results of which were in line with the original meta-analysis.<sup>5-7</sup> In two of these studies, the observed association was strongest in patients without coronary artery disease and within the first months after TAVI.<sup>5,7</sup> One could discuss whether this association was caused by residual confounding or by direct, pleiotropic effects of statin treatment on post-TAVI complications. Suggested pleiotropic effects include anti-inflammatory effects, the inhibition of cytokine-mediated induction of proadhesive and procoagulant substances, the reduction of neointimal thickening and the induction of endothelial nitric oxide synthase leading to improved vascular remodelling.<sup>8-10</sup> However in studies on short-term cardiovascular outcomes after TAVI, no association has been found between statin treatment and periprocedural cardiovascular outcomes or 30-day mortality.<sup>11,12</sup> This finding is in line with two randomised controlled trials (RCTs) that have indicated no effect of statin treatment in preventing perioperative myocardial injury in cardiothoracic surgery.<sup>13,14</sup> Furthermore, the available studies on short-term outcomes have focused on cardiovascular outcomes and mortality, not on other postoperative complications. Therefore, in this study, we aimed to determine whether statin treatment is associated with a short-term risk of mortality and readmissions, as well as with major postoperative complications in older patients undergoing TAVI.

## METHODS

### Study design

This retrospective cohort study was conducted at the University Medical Center Utrecht, a tertiary teaching hospital in the Netherlands. All patients aged 65 years and older who had undergone a comprehensive geriatric assessment (CGA) within 90 days prior to TAVI between January 2014 and January 2021 were included. Patients were excluded if no CGA was performed or if they declined permission for their healthcare data to be reused for research.

### Data collection

#### Baseline

Patients visited the geriatric outpatient clinic for a CGA prior to TAVI. During this visit, the patients' somatic, psychological, functional and social domains were assessed as described in an earlier study.<sup>15</sup> After the CGA had been performed, the patients were advised regarding the feasibility of TAVI, how to optimise their health prior to the intervention, and how to reduce the risk of complications. Data from the CGA (online supplemental table 1) were collected from electronic medical charts. The Charlson Comorbidity Index at baseline was calculated

for each patient. A score of 3 or higher was defined as multimorbid. Moreover, statin treatment was determined based on structured medication reconciliation at hospital admission and actual statin treatment at hospital admission before and after TAVI. Furthermore, the intensity of statin treatment was divided into low-to-moderate intensity statin (LMIS) and high intensity statin (HIS) therapy.<sup>16</sup> HIS therapy was defined as daily dosage of atorvastatin  $\geq 40$  mg or rosuvastatin  $\geq 20$  mg. Lower daily doses of these medications and the use of other types of statins were defined as LMIS therapy.

### Follow-up

During hospitalisation for TAVI (index hospitalisation), a geriatric nurse practitioner performed patient follow-up to diagnose and treat geriatric complications such as falls, delirium, functional decline and stroke. During a follow-up appointment 3 months after TAVI, a geriatric nurse practitioner checked whether rehospitalisation had occurred. This practitioner was supervised by a geriatrician.

### Outcomes

The primary outcomes were 90-day mortality, 90-day readmissions and major postoperative complications during hospitalisation. The Clavien-Dindo classification system was used to classify postoperative complications through reviewing patient charts of all patients.<sup>17,18</sup> All complications that occurred during index hospitalisation were collected and classified according to the treatment needed for the complication. Grades I complications require no intervention or mainly basic pharmacological treatment; grade II complications require more advanced pharmacological treatment; grade III complications require surgical, endoscopic or radiological intervention; grade IV complications require intensive care and grade V indicates death. This study considered a Clavien-Dindo grade II complications or higher to be major postoperative complications (online supplemental table 2). For secondary outcomes, we divided these major postoperative complications, into cardiovascular complications, respiratory complications, neurologic complications, renal complications and complications with other organ systems. Cardiovascular complications encompassed various conditions such as arrhythmia requiring medication or pacemaker insertion, tamponade, myocardial infarction and resuscitation; pulmonary complications were mainly pneumonia; neurological complications included delirium, transient ischaemic attacks and stroke; renal complications primarily consisted of urinary tract infections; and other complications included post-procedural bleeding or anaemia requiring transfusion. Furthermore, acute kidney injury (AKI) was evaluated as a postoperative complication, as it is often only a Clavien-Dindo Grade I complication according to the Clavien-Dindo classification. AKI was defined as an increase in serum creatinine of  $\geq 26.5$   $\mu\text{mol/L}$  from baseline or to  $\geq 1.5$  times the baseline value.<sup>19</sup>

## Statistical analysis

Categorical baseline variables were expressed as numbers and corresponding percentages. Continuous baseline variables were presented as means and SDs. Between-group differences for categorical variables were determined using Pearson's  $\chi^2$  and Fisher's exact test where appropriate. For continuous variables, an independent two-sample t-test was used to test for group differences. In the case of more than 10% missing values for a variable, we performed Little's missing completely at random test to determine whether the missing values were missing completely at random. Since no variables were missing in more than 10% of patients, multiple imputation methods were not indicated. Furthermore, we performed a logistic regression analysis to assess the association between statin treatment and the various outcomes. For the multivariate analysis, the number of independent variables included was limited to 1 per 10 outcomes. The selected variables were age, gender, a Charlson Comorbidity Index 3 or higher, body mass index (BMI)  $\geq 30$  kg/m<sup>2</sup>, smoking, estimated glomerular filtration rate  $< 60$ , alcohol use and falls in the previous 6 months. ORs with 95% CIs were calculated. Additional analyses were performed to assess for effect modification by LMIS or HIS therapy, and age ( $< 80$  years and  $\geq 80$  years). All analyses were performed using the IBM SPSS software V.26.0 (SPSS).

## RESULTS

### Patient inclusion and baseline characteristics

During the study period, 620 patients underwent TAVI. Seven patients did not permit their data to be reused for clinical research, while 29 patients did not receive a CGA prior to TAVI. A total of 584 patients were included in this study, of whom 324 were treated with a statin before TAVI (55.5%). Moreover, 65 patients were treated with HIS (20% of the statin users). [Table 1](#) presents the patients' baseline characteristics. Compared with non-users, statin users were younger (79.8 vs 81.7 years); were more often male (53.7% vs 38.5%); had a higher BMI (27.1 vs 26.3); were more often multimorbid (51.2% vs 35.8%) including prior stroke (21.9% vs 13.1%), prior myocardial infarction (18.8% vs 6.9%) and diabetes (29.6% vs 12.3%); used more medications (10.6 vs 7.5), and were less often at risk of malnutrition (14.8% vs 21.9%). The statin treatment status did not change for any patient during their hospital stay.

### Primary outcomes

Statin treatment was found not to be associated with a decreased short-term risk of mortality, readmissions or major complications ([table 2](#)). The 90-day mortality rate was 4.6% among statin users compared with 3.8% among non-users (adjusted OR 1.17; 95% CI 0.51 to 2.70). Furthermore, readmission risks at 90 days were 12.0% (39) in statin users and 13.1% (34) in non-users (adj. OR 0.91; 95% CI 0.54 to 1.52). Of the statin users, 35.5% experienced a major complication compared with

37.7% of non-users (adjusted OR 0.95; 95% CI 0.67 to 1.37). The effect of statin use on the short-term risks of mortality, readmissions or postoperative complications was not significantly modified by the intensity of statin treatment (ie, LMIS or HIS) or age ([table 3](#)).

### Secondary outcomes

No significant associations were observed between statin treatment and the risk of postoperative complications in any specific organ system, including major cardiac or neurological complications or AKI ([table 2](#)). The rate of cardiovascular complications was 18.2% among statin users compared with 19.6% among non-users (adjusted OR 0.95; 95% CI 0.62 to 1.45). Pulmonary complications occurred in 2.5% of statin users and 3.1% in non-users (adjusted OR 0.84; 95% CI 0.30 to 2.32), while neurological complications were found in 7.1% of statin users compared with 7.7% in non-users (adjusted OR 1.05; 95% CI 0.56 to 2.00). Renal complications were seen in 3.7% of statin users compared with 2.3% of non-users (adjusted OR 1.54; 95% CI 0.56 to 4.23) and other complications occurred in 15.1% of statin users compared with 18.8% of non-users (adjusted OR 1.05; 95% CI 0.65 to 1.68). AKI occurred in 5.9% of statin users and 3.5% of non-users (adjusted OR 0.88; 95% CI 0.40 to 1.85).

## DISCUSSION

This study found no association between statin treatment before TAVI and a decreased risk of negative short-term outcomes, including 90-day mortality, 90-day readmissions and major postoperative complications. Although several studies have suggested a direct pleiotropic effect of statins during the postoperative period after TAVI, we found no association between statin treatment and any postoperative complications.

The difference between our study and the two previous studies that have suggested a direct pleiotropic effect directly after TAVI is that they were propensity score matched.<sup>5 7</sup> In the first study, which included 3956 patients, a total of 626 matched pairs were formed, accounting for 31% of the initial cohort.<sup>5</sup> In the second study which included 2588 patients, 936 matched pairs were created, accounting for 72% of the initial study population.<sup>7</sup> In both studies, 40% of patients who were not using statins could not be successfully matched. It is important to consider that propensity score matching might have led to the exclusion of patients without an indication for statin treatment while including patients with a high cardiovascular risk who were not using statin treatment. This could have led to higher mortality risks in the included non-users compared with the included users. This could have potentially accounted for the observed positive effect of statin use on mortality in these two studies, as matching was performed based on variables such as prior cardiovascular events, cholesterol levels and other coexisting medical conditions.

**Table 1** Baseline characteristics

		Statin	No statin	P value
		(n=324)	(n=260)	
Demographics				
Age	Years (mean±SD)	79.8±6.2	81.7±5.9	<0.001
	Age ≥80 years	187 (57.7%)	190 (73.1%)	<0.001
Gender	Male	174 (53.7%)	100 (38.5%)	<0.001
BMI	kg/m <sup>2</sup> (mean±SD)	27.1±4.8	26.3±4.8	0.05
Smoking	Current smoker	28 (8.6%)	17 (6.5%)	0.38
	Missing	4 (1.2%)	8 (3.1%)	
Alcohol use	Current alcohol user	163 (50.3%)	128 (49.2%)	0.99
	Missing	4 (1.2%)	9 (3.5%)	
Frailty				
EFS* or GFI†	≥6 or ≥4, respectively	81 (25.0%)	64 (24.6%)	0.936
	Missing	20 (6.2%)	17 (6.5%)	
Somatic status				
CCI‡	≥3	166 (51.2%)	93 (35.8%)	<0.001
Diabetes	n (%)	96 (29.6%)	32 (12.3%)	<0.001
Stroke	n (%)	70 (21.9%)	34 (13.3%)	0.008
Myocardial infarction	n (%)	61 (18.8%)	18 (6.9%)	<0.001
Any malignancy	n (%)	41 (12.7%)	29 (11.2%)	0.58
Medication use	No (mean±SD)	10.6±4.2	7.5±4.0	<0.001
	Polypharmacy (≥5 medications)	312 (96.3%)	196 (75.4%)	<0.001
	Hyper polypharmacy (≥10 medications)	175 (54.0%)	73 (28.1%)	<0.001
eGFR	<60 mL/min/1.73 m <sup>2</sup>	109 (33.6%)	78 (30.0%)	0.35
Cognitive and psychological status				
Impaired cognition	MMSE¶ ≤24, MOCA¶ <26, 6-CIT≥8**	5 (1.5%)	3 (1.2%)	0.68
	Missing	33 (10%)	24 (9.2%)	
GDS-15†	≥6	14 (4.3%)	10 (3.8%)	0.77
Delirium in past		41 (12.7%)	23 (8.8%)	0.14
	Missing	3 (0.9%)	2 (0.8%)	
Functional status				
Dependence in (i)ADL	KATZ-15† ≥2	154 (47.5%)	122 (46.9%)	0.81
	Missing	21 (6.5%)	15 (5.8%)	
At risk of malnutrition	MNA†† ≤11, MUST‡‡ <sup>h</sup> ≥1	48 (14.8%)	57 (21.9%)	0.03
	Missing	7 (2.2%)	5 (1.9%)	
Falls	≥1 in previous 6 months	63 (19.4%)	45 (17.3%)	0.55
	Missing	10 (3.1%)	11 (4.2%)	
Social status				
Living situation	Living dependent	15 (4.6%)	8 (3.1%)	0.37
	Missing	27 (8.3%)	28 (10.8%)	

\*Score range from 0 to 17.

†Score range from 0 to 15.

‡Score range from 0 to 33.

§Not adjusted for age.

¶Score range from 0 to 30.

\*\*Score range from 0 to 28.

††Score range from 0 to 14.

‡‡Score range from 0 to 6.

BMI, body mass index; CCI, Charlson Comorbidity Index; 6-CIT, six-item cognitive impairment test; EFS, Edmonton Frail Scale; eGFR, estimated glomerular filtration rate; GDS, Geriatric Depression Scale; GFI, Groningen Frailty Indicator; (i)ADL, (instrumental) Activities of Daily Living; MMSE, Mini-Mental State Examination; MNA, Mini Nutritional Assessment; MOCA, Montreal Cognitive Assessment; MUST, Malnutrition Universal Screening Tool.



**Table 2** The association between statin treatment and short-term outcomes after TAVI

Outcomes	Statin	No statin	OR (95% CI)	P value	Adj OR (95% CI)	P value
Primary outcomes	<b>n=324</b>	<b>n=260</b>				
90-day mortality	15 (4.6%)	10 (3.8%)	1.21 (0.54 to 2.75)	0.64	1.17 (0.51 to 2.70)*	0.71
90-day readmission	39 (12.0%)	34 (13.1%)	0.91 (0.56 to 1.49)	0.71	0.91 (0.54 to 1.52)†	0.70
Major postoperative complications‡	115 (35.5%)	98 (37.7%)	0.91 (0.65 to 1.28)	0.58	0.95 (0.67 to 1.37)§	0.79
Secondary outcomes						
Cardiovascular complications	59 (18.2%)	52 (20.0%)	0.93 (0.62 to 1.41)	0.74	1.05 (0.67 to 1.63)§	0.84
Respiratory complications	8 (2.5%)	8 (3.1%)	0.80 (0.30 to 2.15)	0.66	0.86 (0.32 to 2.36)¶	0.77
Neurological complications	23 (7.1%)	20 (7.7%)	0.92 (0.49 to 1.71)	0.78	1.05 (0.55 to 2.01)**	0.87
Renal complications	12 (3.7%)	6 (2.3%)	1.63 (0.60 to 4.40)	0.34	1.60 (0.59 to 4.36)¶	0.36
Other complications	49 (15.1%)	36 (13.8%)	1.11 (0.70 to 1.77)	0.66	1.01 (0.61 to 1.66)§	0.97
Acute kidney injury††	15 (4.6%)	14 (5.4%)	0.88 (0.41 to 1.85)	0.73	0.86 (0.40 to 1.85)*	0.70
Missing	19 (5.9%)	9 (3.5%)	–			

\*Adjusted for age and gender.

†Adjusted for age, gender, a CCI 3 or higher, BMI $\geq$ 30 kg/m<sup>2</sup>, smoking, eGFR $<$ 60 and alcohol use.

‡Clavien–Dindo Grade $\geq$ II.

§Adjusted for age, gender, a CCI 3 or higher, BMI $\geq$ 30 kg/m<sup>2</sup>, smoking, eGFR $<$ 60, alcohol use and falls in previous 6 months.

¶Adjusted for age.

\*\*Adjusted for age, gender, a CCI 3 or higher and BMI $\geq$ 30 kg/m<sup>2</sup>.

††Increase in serum creatinine of  $\geq$ 26.5  $\mu$ mol/L from baseline or an increase in serum creatinine to  $\geq$ 1.5 times the baseline value.

BMI, body mass index; CCI, Charlson Comorbidity Index; eGFR, estimated glomerular filtration rate; TAVI, transcatheter aortic valve implantation.

In addition, the finding that statin treatment was not significantly associated with short-term outcomes after TAVI is consistent with previous observational studies on short-term cardiovascular complications and short-term mortality. Merdler *et al* found no significant effect of statin treatment on 1-month mortality and postoperative cardiologic complications.<sup>11</sup> Moreover, Huded *et al* found no significant effect of statin treatment on post-TAVI myocardial infarction, AKI, in-hospital mortality and 30-day mortality.<sup>12</sup> Furthermore, Klinkhammer demonstrated no effect of statin treatment on postoperative cardiologic complications or mortality 1 and 6 months after TAVI.<sup>20</sup> In all studies, including our study, statin non-use in patients with an indication for statins treatment was highly prevalent. Therefore, matching on covariates indicative of high cardiovascular risk, including prior cardiovascular events, diabetes, hypercholesterolaemia and hypertension, poses a risk of overestimating statin treatment after TAVI by selecting high-risk patients already known to benefit from statin treatment. Our outcomes are in line with RCTs on statin treatment during coronary artery bypass grafting surgery, which revealed no association with short-term mortality and postoperative complications.<sup>21</sup>

### Strengths and limitations

This study has several strengths. First, the data were collected from a relatively large cohort that included patients over a long period of time. Together with the broad inclusion criteria, this has probably resulted in a high representation of the study population for the total

older population of TAVI patients and thus good external validity of the outcomes. Second, this study examined the effect of statin treatment on the overall risk of short-term negative outcomes using both short-term mortality and morbidity. Third, all postoperative complications occurring after TAVI were classified according to the Clavien–Dindo classification, therefore, in addition to the standard reported complications, such as myocardial infarction, stroke and AKI, all other postoperative complications were included as relevant clinical outcomes. However, due to the retrospective nature of the study, we were not able to report on all endpoints specified by the Valve Academic Research Consortium.<sup>22</sup>

This study also has several limitations. First, the number of events was relatively low, which could have led to residual confounding in the analyses, as only a limited number of possible confounding variables could be included. Second, due to the retrospective nature of the study, a possibility of residual confounding also exists, since reasons for non-use were not available. Third, we only had information on statin treatment before hospitalisation from a structured medication review and on statin exposure during the hospital stay for the TAVI procedure. Fourth, we did not have access to public pharmacy outpatient dispensing records; therefore, we did not have information on the duration of statin treatment before the procedure or its continuation after TAVI. Lastly, the HIS subgroup was small, which could have resulted in insufficient power to demonstrate significant associations between HIS and the outcomes.

**Table 3** The association between statin treatment and short-term outcomes after TAVI, stratified by age and intensity of statin therapy

	Statin	No statin	OR (95% CI)	P value	Adj OR (91% CI)	P value
Age <80 years (n=207)	<b>n=137</b>	<b>n=70</b>				
90-day mortality	4 (2.9%)	4 (5.7%)	0.50 (0.12 to 2.05)	0.33	na.*	
90-day readmission	19 (13.9%)	7 (10.0%)	1.45 (0.58 to 3.63)	0.43	1.45 (0.57 to 3.69)†	0.43
Major postoperative complications‡	48 (35.0%)	23 (32.9%)	1.10 (0.60 to 2.03)	0.76	0.88 (0.45 to 1.70)§	0.69
Age ≥80 years (n=377)	<b>n=187</b>	<b>n=190</b>				
90-day mortality	11 (5.9%)	6 (3.2%)	1.92 (0.69 to 5.29)	0.21	1.91 (0.89 to 5.29)¶	0.21
90-day readmission	20 (10.7%)	27 (14.2%)	0.72 (0.39 to 1.34)	0.30	0.72 (0.38 to 1.36)**	0.31
Major postoperative complications‡	67 (35.8%)	75 (39.5%)	0.86 (0.56 to 1.30)	0.47	0.91 (0.59 to 1.42)††	0.69
LMIS (n=519)	<b>n=259</b>	<b>n=260</b>				
90-day mortality	14 (5.4%)	10 (3.8%)	1.43 (0.62 to 3.28)	0.40	1.37 (0.59 to 3.19)†	0.46
90-day readmission	32 (12.4%)	34 (13.1%)	0.94 (0.56 to 1.57)	0.81	0.93 (0.54 to 1.58)‡‡	0.78
Major postoperative complications‡	95 (36.7%)	98 (37.7%)	0.96 (0.67 to 1.37)	0.81	1.02 (0.70 to 1.48)††	0.94
HIS (n=325)	<b>n=65</b>	<b>n=260</b>				
90-day mortality	1 (1.5%)	10 (3.8%)	0.39 (0.05 to 3.11)	0.37	0.35 (0.04 to 2.86)¶	0.33
90-day readmission	7 (10.8%)	34 (13.1%)	0.80 (0.34 to 1.90)	0.62	0.70 (0.28 to 1.74)**	0.45
Major postoperative complications‡	20 (30.8%)	98 (37.7%)	0.74 (0.41 to 1.32)	0.30	0.69 (0.37 to 1.29)††	0.24

\*Not applicable, less than 10 outcomes.

†Adjusted for age and gender.

‡Clavien-Dindo Grade≥II.

§Adjusted for age, gender, a CCI 3 or higher, BMI≥30 kg/m<sup>2</sup>, smoking, eGFR<60 and alcohol use.

¶Adjusted for age.

\*\*Adjusted for age, gender, a CCI 3 or higher, BMI≥30 kg/m<sup>2</sup>.

††Adjusted for age, gender, a CCI 3 or higher, BMI≥30 kg/m<sup>2</sup>, smoking, eGFR<60, alcohol use and falls in previous 6 months.

‡‡Adjusted for age, gender, a CCI 3 or higher, BMI≥30 kg/m<sup>2</sup>, smoking and eGFR<60.

BMI, body mass index; CCI, Charlson Comorbidity Index; eGFR, estimated glomerular filtration rate; HIS, high intensity statin; LMIS, Low-moderate intensity statin; TAVI, transcatheter aortic valve implantation.

### Clinical implications and recommendations for future research

Based on the lack of an association between statin treatment and short-term outcomes post-TAVI in this study as well as in previous studies, the initiation of statin treatment is not specifically advised for improving short-term outcomes after TAVI. Yet, statins are often indicated to improve long-term negative outcomes, as atherosclerotic comorbidity is common in these patients. A clinical trial could answer critical questions about the short-term effects of statin treatment after TAVI as well as whether initiating statin treatment before TAVI improves long-term outcomes. Furthermore, because our study included a relatively small number of patients treated with HIS, different statin dosages could be incorporated into a trial as well to determine whether HIS treatment has an effect on short-term outcomes in patients who can tolerate high statin dosages.

### CONCLUSION

This study demonstrated that preoperative statin treatment is common in TAVI patients, but is not associated with decreased risks of negative short-term outcomes after a TAVI, including 90-day mortality, 90-day readmissions

and major postoperative complications. Given the magnitude of statin non-use in all observational TAVI statin studies, an RCT with different statin doses could be warranted for investigating whether initiating statin treatment before TAVI improves both postoperative outcomes and long-term survival.

**Contributors** Study concept and design: GL, HLK, CH, MB, AdB and ME-V.

Acquisition of data: GL, LD, CH, MV and AOK. Analysis and interpretation of data: GL, LD, CH and HLK. Drafting of the manuscript: GL, LD, CH and HLK. Critical revision of the manuscript: all authors critically revised the manuscript. All authors critically reviewed and approved the final manuscript. GL had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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**Patient consent for publication** Not applicable.

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**Data availability statement** Data are available on reasonable request. The data that support the findings of this study are available from the corresponding author upon reasonable request.

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