Delirium After Transcatheter Aortic Valve Implantation Under General Anesthesia: Incidence, Predictors, and Relation to Long-Term Survival

Kees van der Wulp, MD, Marleen van Wely, MD,* Lars van Heijningen, MD,[†] Bram van Bakel, MD,[‡] Yvonne Schoon, MD, PhD,[†§] Michel Verkroost, MD,[¶] Helmut Gehlmann, MD,* Leen Van Garsse, MD, PhD,[¶] Priya Vart, DMD, PhD,*[‖] Peter Kievit, MD, PhD,* Marcel Olde Rikkert, MD, PhD,[†] Wim Morshuis, MD, PhD,[¶] and Niels van Royen, MD, PhD**

BACKGROUND/OBJECTIVES: Prospectively collected data on postoperative delirium (POD) after transcatheter aortic valve implantation (TAVI) are scarce. The aim of this study was to report the incidence and risk factors of delirium after TAVI under general anesthesia and to assess the association of POD with clinical outcome and short- and long-term survival.

DESIGN: Prospective cohort study.

SETTING: Academic medical center.

PARTICIPANTS: A total of 703 subsequent patients undergoing TAVI under general anesthesia between 2008 and 2017.

MEASUREMENTS: Delirium was assessed according to the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (*DSM-IV*), criteria. Outcomes were post-procedural clinical outcome and short- and long-term survival (30 days and 5 years, respectively).

RESULTS: POD was observed in 16.5% (116/703), was the strongest independent predictor of long-term mortality (hazard ratio = 1.91; 95% confidence interval [CI] = 1.36-2.70), and was associated with impaired 30-day and 5-year survival (92.2% vs 96.8% [*P* = .025] and 40.0% vs 50.0% [*P* = .007], respectively). Stroke and new onset of atrial fibrillation were more often observed in delirious patients (6.9% vs 1.9% and 12.1% vs 5.1%, respectively). Strongest independent predictors of POD were prior delirium (odds ratio [OR] = 2.56; 95% CI = 1.52-4.31) and aortic valve area less than 0.75 cm^2 (OR = 2.39; 95% CI = 1.53-3.74).

CONCLUSION: One in six patients experienced POD after TAVI under general anesthesia. POD was the strongest predictor of long-term mortality and was associated with impaired short- and long-term survival. Prior delirium and a more calcified aortic valve were the strongest independent predictors of POD. **J Am Geriatr Soc 67:2325-2330, 2019.**

Key words: general anesthesia; postoperative delirium; survival; transcatheter aortic valve implantation

From the *Department of Cardiology, Radboud University Medical Center, Nijmegen, The Netherlands; [†]Department of Geriatrics, Radboud University Medical Center, Nijmegen, The Netherlands; [‡]Department of Physiology, Radboud University Medical Center, Nijmegen, The Netherlands; [§]Radboud Institute for Health Sciences, Radboud University Medical Center, Nijmegen, The Netherlands; [¶]Department of Cardio-Thoracic Surgery, Radboud University Medical Center, Nijmegen, The Netherlands; and the [‖]Department of Health Evidence, Radboud University Medical Center, Nijmegen, The Netherlands.

Address correspondence to Niels van Royen, MD PhD, Department of Cardiology, Radbound University Medical Center, Geert Grooteplein Zuid 10, 6525 GA Nijmegen, The Netherlands. E-mail: niels.vanroyen@radboudumc.nl

DOI: 10.1111/jgs.16087

Postoperative delirium (POD), primarily an alteration in attention, represents a decompensation of cerebral function in response to one or more pathophysiological stressors, such as major surgery. It occurs frequently after cardiac surgery (incidence = 11%-46%),[1] and has been associated with long-lasting functional and cognitive impairment,[2] increased social and economic burden, and increased risk of mortality.[3]

Transcatheter aortic valve implantation or replacement (TAVI or TAVR, respectively) has emerged as the preferred management strategy for patients with severe, symptomatic aortic valve stenosis.[4-6] Annually, approximately 180 000 European and North American patients are considered potential TAVI candidates.[7] Given their advanced age and multiple comorbidities, these patients are at risk for developing POD.

Retrospective POD studies, based on a maximum of 300 patients, described in-hospital POD incidences of 12% to 53% after TAVI and focused on differences between treatment

JAGS 67:2325-2330, 2019

Journal of the American Geriatrics Society published by Wiley Periodicals, Inc. on behalf of The American Geriatrics Society. 0002-8614/19/$15.00

strategies (eg, surgical vs TAVR or different access routes for TAVI).[3,8-12] The reported use of general anesthesia varied in these studies between 19% and 100% of patients. Larger patient data, based on clinical modification codes, have been analyzed but question the true incidence of POD since they report much lower rates of POD.[13,14] Prospective data on the incidence and long-term consequences of delirium in large TAVI populations are not available.

The aim of the current study is to assess the incidence of POD after TAVI under general anesthesia, to assess the association of POD with short- and long-term survival, and to identify risk factors associated with the occurrence of POD.

METHODS

In this single-center study, we analyzed all consecutive patients treated with TAVI at the Radboud University Medical Center (Nijmegen, The Netherlands) between December 2008 and December 2017. Treatment allocation was performed by a dedicated heart team, according to the current guidelines.[15] General anesthesia was used in all patients, according to the local protocol. At the beginning of our TAVI program in 2008, the left axillary artery was selected as the primary access site in most patients. Over the years, this strategy changed toward a "femoral first" strategy. As for valve types implanted, Medtronic CoreValve and EvolutR were predominantly used. Additional procedural details and complications have been described previously.[16,17]

Study outcomes

The primary end point of the study was the occurrence of delirium during hospitalization after TAVI under general anesthesia. The definition of POD was based on the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (*DSM-IV*),[18] and was defined as an acute and fluctuating disturbance of consciousness with reduced ability to focus, maintain, or shift attention, accompanied by change in cognition and perceptual disturbances secondary to a general medical condition. The occurrence of delirium was assessed by a trained nurse, physician, or member of the geriatric in-hospital CareWell program by means of the Confusion Assessment Method,[19] which was performed three times a day. A delirium observational score (DOS) was used in case delirium was suspected or diagnosed. This way, further evolution (signs) of delirium could be monitored.[20] In case of DOS of 3 or greater, a geriatrician was consulted to either confirm or exclude the diagnosis of delirium.[18] State-of-the-art prevention and management of POD was guided by a geriatric team and consisted of both pharmacological and nonpharmacological treatments, such as improvement of orientation, early mobilization, promotion of sleep, and the provision of vision and hearing adaptations.[19]

Clinical outcome, including device success, was registered according to the updated Valve Academic Research Consortium-2 criteria.[21] Mortality tracking on all patients was performed on November 23, 2018, by consulting the Central Bureau for Statistics (The Hague, The Netherlands). Median follow-up at that time was 1290 (interquartile range [IQR] = 744-2039) days. All data were collected in an electronic data capturing system. Missing data or extreme values were excluded from analysis. Overall, the percentage of missing values (including mortality) did not exceed 1%. Given the observational design of the study, obtaining written informed consent was deemed unnecessary. Current analysis was approved by the institution's ethics committee and complies with the Declaration of Helsinki.

Statistical Analysis

Normality was tested using the Kolmogorov-Smirnov test. Categorical variables are expressed as frequencies and percentages and were compared using the χ^2 or Fisher's exact test. Continuous variables are expressed as mean and SD if normally distributed or as median and IQR if skewed and compared using the Student *t* or Mann-Whitney *U* test, respectively.

The effect of POD on 30-day and 5-year survival was visualized using Kaplan-Meier survival estimates, and difference in cumulative survival was tested using the log-rank test. Precipitating factors for POD were analyzed using univariate and multivariable binary logistic regression analyses. Univariate associated factors from Table 1 were offered for backward stepwise multivariable analysis with entry and exclusion limits at 0.05 and 0.10, respectively. Risk factors of 3-year mortality (selected based on the median follow-up duration of >3 years) were analyzed using Cox regression analysis based on variables from baseline and postoperative complications, including POD. Again, backward stepwise analysis with entry and exclusion limits of 0.05 and 0.10, respectively, were used. Independent risk factors for POD and 3-year mortality were reported as odds ratio (OR) and hazard ratio (HR) with 95% confidence intervals (CIs), respectively. Collinearity diagnostics were evaluated for all variables considered for multivariable analysis. In case of multicollinearity, the variable with the higher OR or HR was incorporated into the model. All tests were two tailed, and $P < .05$ was considered statistically significant. Analyses were performed using IBM SPSS Statistics software, version 25.0.0.1 (IBM Corp) and illustrated with GraphPad Prism, version 5.03 (GraphPad Software Inc).

RESULTS

In total, 703 consecutive TAVI patients were analyzed in the current study. Baseline characteristics are summarized in Table 1 and presented according to the occurrence of POD. POD was observed in 116 patients (16.5%). On average, POD occurred a median of 1 (IQR = 1-2) days after TAVI, and lasted for a median of 3 (IQR = 2-6) days (Supplementary Table S1).

POD and Clinical Outcome

Thirty-day survival after successful TAVI was significantly lower in patients with POD (92.2% vs 96.8%; $P = .034$). Consistently, long-term follow-up showed impaired 1-year (75.0% vs 86.5%; $P = .002$), 3-year (57.3% vs 69.4%; $P = .001$), and 5-year (40.0% vs 50.0%; $P < .001$) survival in patients with POD (Figure 1). In multivariable Cox regression analysis with correction for several baseline characteristics (including age, sex, body mass index (BMI), creatinine, chronic obstructive pulmonary disease (COPD), permanent atrial fibrillation, and

Table 1. Baseline Characteristics

Characteristics	Overall (n = 703)	Delirium Yes (n = 116)	Delirium No (n = 587)	*P* value
Age, y	80 (75-84)	82 (79-86)	80 (74-83)	<.001
Male sex	338 (48.1)	57 (49.1)	281 (47.9)	.803
BMI, kg/m^2	26.6 (24.0-30.2)	25.7 (23.1-28.2)	26.7 (24.1-30.8)	.002
Logistic EuroSCORE I	13.8 (8.9-21.6)	14.3 (10.7-23.1)	13.4 (8.4-21.5)	.060
NYHA functional class III-IV	528 (75.1)	90 (77.6)	438 (74.6)	.499
Diabetes mellitus	234 (33.3)	32 (27.6)	202 (34.4)	.154
Creatinine, mg/dL	1.0 (0.8-1.3)	1.0 (0.9-1.3)	1.0 (0.8-1.3)	.748
COPD	194 (27.6)	28 (24.1)	166 (28.3)	.362
Coronary artery disease	416 (59.2)	68 (58.6)	348 (59.3)	.894
Permanent atrial fibrillation	151 (21.5)	23 (19.8)	128 (21.8)	.635
Prior stroke or TIA	149 (21.2)	30 (25.9)	119 (20.3)	.178
Peripheral artery disease	252 (35.8)	38 (32.8)	214 (36.5)	.448
Carotid artery disease	133 (18.9)	23 (19.8)	110 (18.7)	.785
Psychoactive drug use[a]	174 (24.8)	28 (24.1)	146 (24.9)	.867
History of delirium[b]	103 (14.7)	30 (25.9)	73 (12.4)	<.001
Echocardiography findings				
LVEF 30%-49%	191 (27.2)	31 (26.7)	160 (27.3)	.906
LVEF <30%	21 (3.0)	6 (5.2)	15 (2.6)	.137
Aortic valve area, cm^2	0.75 (0.60-0.90)	0.70 (0.50-0.80)	0.79 (0.64-0.90)	<.001

Note. Data are presented as median (interquartile range) or number (percentage).

Abbreviations: BMI, body mass index; COPD, chronic obstructive pulmonary disease; EuroSCORE, European System for Cardiac Operative Risk Evaluation; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; TIA, transient ischemic attack.

[a]Psychoactive drug use indicates use of benzodiazepines, antidepressants, and antipsychotic medications.

[b]History of delirium was obtained by means of chart review and preoperative outpatient clinic patient and family reports.

peripheral artery disease), POD was the strongest independent predictor of 3-year mortality (HR = 1.91; 95% CI = 1.36-2.70; *P* < .001) (Figure 2, Supplementary Table S2).

Complications that were more frequently observed in patients with POD were stroke (6.9% vs 1.9%; *P* = .007), infection (20.7% vs 10.6%; *P* = .002), and new onset of atrial

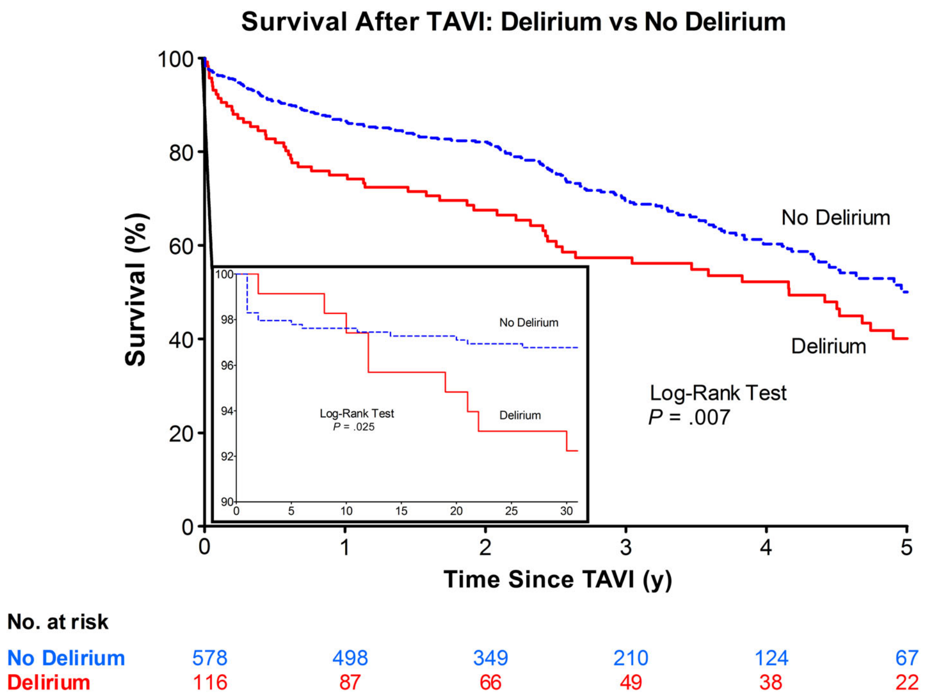

Figure 1. Kaplan-Meier survival curve of the association between postoperative delirium after transcatheter aortic valve implantation (TAVI) and short- and long-term survival.

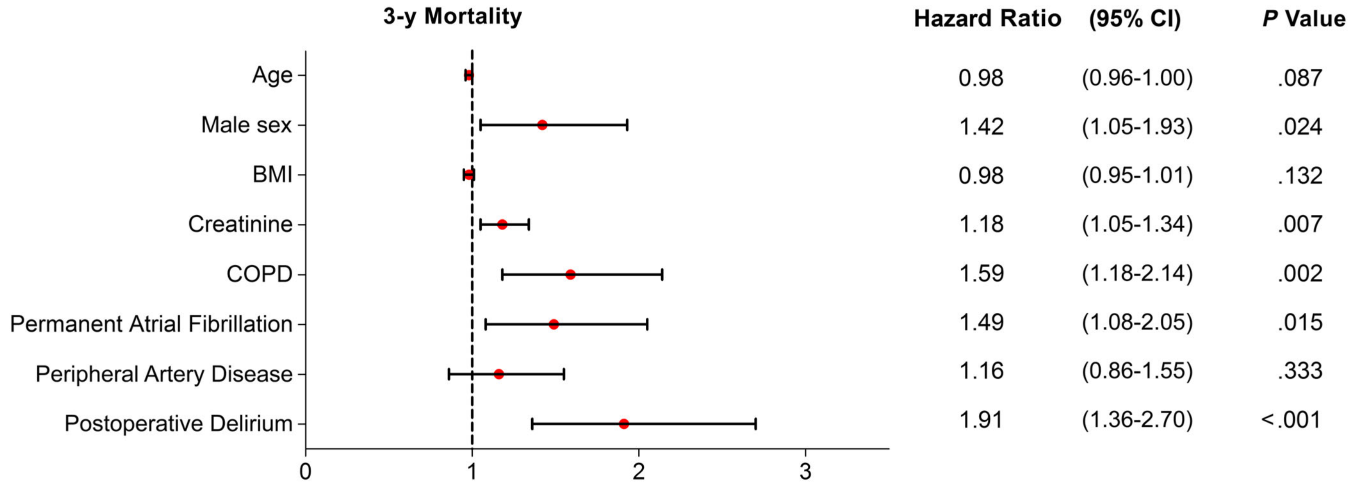

Figure 2. Risk factors of 3-year mortality. Multivariable analyses of covariates and their association with 3-year mortality. Details of analyses: supplementary Table S2. BMI indicates body mass index; CI, confidence interval; COPD, chronic obstructive pulmonary disease. [Color figure can be viewed at wileyonlinelibrary.com]

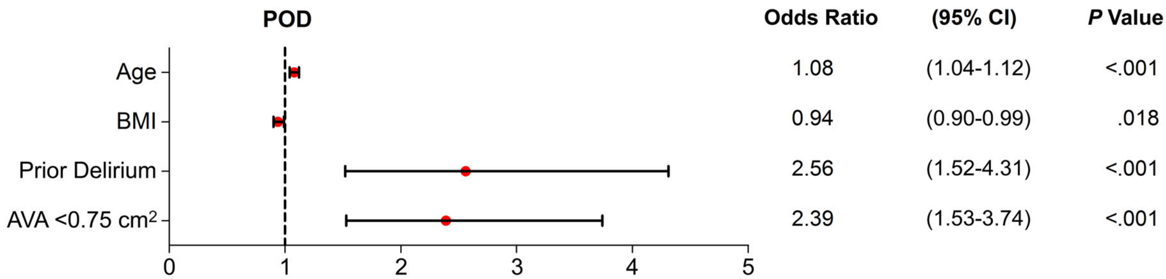

Figure 3. Precipitating factors of postoperative delirium (POD). Multivariable analyses of covariates and their association with POD. Details of analyses: supplementary Table S4. AVA indicates aortic valve area; BMI, body mass index; CI, confidence interval. [Color figure can be viewed at wileyonlinelibrary.com]

fibrillation (12.1% vs 5.1%; P = .005). The occurrence of POD was associated with a significant prolongation of hospital stay (median = 8 [IQR = 6-12] vs 5 [IQR = 3-7] days; P < .001) (Supplementary Table S3).

Baseline Characteristics Related to POD

Patients with POD were older (median = 82 [IQR = 79-86] vs 80 [IQR = 74-83] years; P < .001), had a lower BMI (median = 25.7 [IQR = 23.1-28.2] vs 26.7 [24.1-30.8] kg/m^2; P = .002), and had a smaller aortic valve area (AVA; median = 0.70 [IQR = 0.50-0.80] vs 0.79 [IQR = 0.64-0.90] cm^2; P < .001). Furthermore, patients with POD more often had a history of previous delirium (25.9% vs 12.4%; P < .001) (Table 1). Multivariable analyses identified the following precipitating factors of POD (Figure 3, Supplementary Table S4): prior delirium (OR = 2.56; 95% CI = 1.52-4.31; P < .001), AVA less than 0.75 cm^2 (OR = 2.39; 95% CI = 1.53-3.74; P < .001), age (OR = 1.08; 95% CI = 1.04-1.12; P < .001), and BMI (OR = 0.94; 95% CI = 0.90-0.99; P = .018).

Procedural Characteristics and POD

Device success was achieved in 93.6% of all patients and did not differ between patients with or without POD (92.2% vs 93.9%; P = .513). Axillary access was used in most patients (75.1%), and its use did not differ between patients with or without POD (80.2% vs 74.1%; P = .167). No significant differences in POD rates were observed between axillary access vs nonaxillary access (17.9% vs 12.6%; P = .096). No difference in procedural duration was observed between patients with or without POD (51 [42-70] vs 52 [41-65] minutes; P = .555). Conversion to surgical aortic valve replacement was required in six patients due to migration (n = 2), ectopic deployment (n = 2), or tamponade (n = 2). POD was observed in all these six patients (Supplementary Table S5).

DISCUSSION

After TAVI under general anesthesia, POD is observed in 16.5% of patients. Independent risk factors for POD are older age, lower BMI, smaller AVA, and prior delirium. POD resulted in significant prolongation of hospital stay and decreased short- and long-term survival. In multivariable analysis, POD was identified as the strongest predictor of 3-year mortality.

A recent meta-analysis illustrated the scarcity of data regarding POD after TAVI, with the largest included study describing retrospectively collected data of 294 patients.[3,22] They described an overall pooled incidence of POD of 23%. Small retrospective studies concerning POD after transarterial TAVI reported incidences varying between 8% and 18%,[3,8-12] and the higher incidences are mainly based on transapical TAVI procedures (incidence = 33%-60%). Larger studies, based on registered clinical modification codes, reported much lower incidences of 5% to 7%, which potentially led to underestimation of the true incidence of POD.[13,14] Our prospectively collected data in the largest reported cohort so far show that POD after TAVI under general anesthesia occurs in one of six patients.

Baseline characteristics of the present study represent a patient population that is comparable to other studies.[8,10,11] Older age, lower BMI, and a history of delirium were identified as precipitating factors for POD.[1] Lower BMI is a known frailty indicator that can be a result of malnutrition, chronic disease, or stressors of acute-on-chronic disease (eg, exacerbations of COPD or congestive heart failure). Potential inherent sarcopenia and hypoalbuminemia are known risk factors for delirium.[23] Smaller AVA (<0.75 cm^2), which is considered an expression of overall calcium/atherosclerotic burden and possibly lower cerebral perfusion,[24] was also found to be associated with POD. However, procedural time and contrast use did not significantly differ between both groups. Theoretically, a higher grade of calcification could result in more complex procedures with respect to accessibility, necessity of predilatation and/or postdilatation, and repositioning. As a result, embolization of atherosclerotic debris could cause (subclinical) cerebral microinfarctions that are known to be associated with neurological and cognitive impairment.[25]

Carotid artery disease, defined as prior or present carotid occlusion or stenosis of more than 50%, was not identified as a precipitating factor of POD in our population, which is in contrast to one of the main findings of the recent meta-analysis of Tilley et al.[22] Based on two different retrospective studies,[9,11] they described a four times higher risk of POD for patients with carotid artery disease. However, ORs were based on a mix of univariate and multivariate OR data and included transapical procedures, which had the highest OR in that same meta-analysis.

Preoperative use of psychoactive medication could not be identified as a precipitating factor of POD in our population. Conflicting evidence exists on the effect of psychoactive medication use prior to surgery on the incidence of POD. Whenever an association was found, preoperative use of psychoactive medication (not corrected for comorbidity) could lead to a two-fold to seven-fold higher risk of POD.[26] However, as in our study, psychoactive medication often included a range of medications, such as benzodiazepines, antidepressants, and antipsychotic medication; and indications for use were heterogeneous.

General anesthesia was used in all patients in the current study. Globally, a trend toward less invasive and more minimalistic approaches is being observed in which more and more general anesthesia is replaced by either conscious sedation or local anesthesia. Retrospective and matched studies suggest a less complicated postprocedural course with lower incidences of delirium in patients treated with local anesthesia or conscious sedation.[27] Moreover, it is conceivable that factors, such as infection due to intubation, narcotics, admission on different departments, and prolonged hospital stay, could provoke the development of POD in patients treated under general anesthesia.[27] Still, prospective randomized data are lacking, and true data on the incidence of POD in both treatment regimens remain unknown. New prospective data objectifying the incidence of POD with comparison between these anesthetic regimens are currently awaited (clinicaltrials.gov; NCT02786264).

Axillary access was predominantly used in our TAVI population (75.1%) and could not be related to POD. This is in contrast to previous studies that did identify nonfemoral access as an independent risk factor for POD.[8-11,28] However, the term "nonfemoral access" in these studies was mainly based on either transapical or direct aortic results and biased by patient selection. Transaxillary TAVI was used in less than 1% of all patients in these studies[3,8-14] and, therefore, no conclusion regarding this access and POD has been drawn so far. In our center, the axillary access has been used as default access for many years and in this setting did not lead to an increased risk for POD.

In-hospital stroke was observed in 2.7% of all patients and was, like new onset of atrial fibrillation, more frequently present in patients with POD. Prior or new cerebral lesions, caused by either previously unknown or newly diagnosed atrial fibrillation, combined with embolization during TAVI may have caused cerebral frailty, eventually leading to the observed cognitive alteration.[29] Cerebral embolic protection devices, which capture embolic debris and reduce the occurrence of new brain lesions, were recently introduced but are still under debate.[30,31] Stroke reduction is hard to investigate given its overall low incidence. Therefore, supported by cerebral imaging, POD might be useful as a surrogate outcome for stroke or as a primary outcome in future cerebral protection trials.

Short- and long-term survival were severely impaired in patients who had experienced POD, and POD remained an independent predictor of 3-year mortality when corrected for several baseline characteristics (Figures 1 and 2 and Supplementary Table S2). POD might be an expression of extreme vulnerability with diminished reserve capacity, but since delirium may be preventable in 30% to 40% of cases,[1,32] future research should focus on adequate identification and prevention of POD to circumvent the associated burden of downstream complications and costs. Improvement of patient-tailored treatment, implementation of more minimalistic approaches, and recognition of risk factors will hopefully lead to a decrease in incidence of POD after TAVI.

Limitations

Results are based on a single-center experience with predominantly axillary access. However, potentially contributory, frailty assessment was not included in the current analysis. Axillary access was not associated with POD when compared to femoral access. Also, we cannot provide data on POD after TAVI using local anesthesia or conscious sedation and, hence, cannot draw any conclusion on the risk of general anesthesia for the risk of POD. We are aware of the fact that routine assessment of POD is currently not part of standard clinical practice. However, we hope that this study will raise awareness of delirium so that it will become part of perioperative care.

CONCLUSION

In the current study, we show that POD occurs in one of six patients after TAVI under general anesthesia and is independently associated with decreased short- and long-term survival.

ACKNOWLEDGMENTS

The authors gratefully acknowledge the efforts of Geert Versteeg, Willem Aerts, and Gerwin van der Wal with regard to data management.

Financial Disclosure: The Departments of Cardiology and Cardiothoracic Surgery at Radboud University Medical Center, with which the authors are affiliated, have received an unrestricted grant from Medtronic. Dr van Wely has been a proctor and consultant for Abbott Vascular. Dr Verkroost has been a proctor for Medtronic. Dr Gehlmann has been a proctor for Abbott Vascular and Medtronic. Dr Van Garsse has been a proctor for Edwards Lifesciences. Dr Morshuis has been a consultant for Vascutek. Dr van Royen is a consultant for Abbott and Medtronic and has received grants from AstraZeneca, grants from Biotronik, grants from Philips, grants and personal fees from Abbott, and personal fees from Medtronic, outside the submitted work. All other authors have reported that they have no relationships relevant to the contents of this article to disclose.

Author Contributions: Study concept and design: K.v.d.W., L.v.H., N.v.R.

Acquisition of subjects and data: K.v.d.W., M.v.W., B.v.B., M.V., H.G., L.V.G., P.K.

Analysis and interpretation of data: All authors.

Preparation of manuscript: K.v.d.W., M.v.W., N.v.R.

Revision of manuscript for critical intellectual content: All authors.

Sponsor's Role: None.

REFERENCES

1. Inouye SK, Westendorp RG, Saczynski JS. Delirium in elderly people. Lancet 2014;383:911-922.
2. Koster S, Hensens AG, van der Palen J. The long-term cognitive and functional outcomes of postoperative delirium after cardiac surgery. Ann Thorac Surg 2009;87:1469-1474.
3. Huded CP, Huded JM, Sweis RN, et al. The impact of delirium on healthcare utilization and survival after transcatheter aortic valve replacement. Catheter Cardiovasc Interv. 2017;89:1286-1291.
4. Leon MB, Smith CR, Mack M, Miller DC, Moses JW, Svensson LG, Tuzcu EM, Webb JG, Fontana GP, Makkar RR, Brown DL, Block PC, Guyton RA, Pichard AD, Bavaria JE, Herrmann HC, Douglas PS, Petersen JL, Akin JJ, Anderson WN, Wang D, Pocock S Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med 2010;363:1597-1607.
5. Popma JJ, Deeb GM, Yakubov SJ, et al. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. N Engl J Med. 2019; 380:1706-1715.
6. Mack MJ, Leon MB, Thourani VH, et al. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. N Engl J Med. 2019;380: 1695-1705.
7. Durko AP, Osnabrugge RL, Van Mieghem NM, et al. Annual number of candidates for transcatheter aortic valve implantation per country: current estimates and future projections. Eur Heart J. 2018;39:2635-2642.
8. Bagienski M, Kleczynski P, Dziewierz A, et al. Incidence of postoperative delirium and its impact on outcomes after transcatheter aortic valve implantation. Am J Cardiol. 2017;120:1187-1192.
9. Sharma V, Katznelson R, Horlick E, Osten M, Styra R, Cusimano RJ, Carroll J, Djaiani G Delirium after transcatheter aortic valve implantation via the femoral or apical route. Anaesthesia 2016;71:901-907.
10. Maniar HS, Lindman BR, Escallier K, et al. Delirium after surgical and transcatheter aortic valve replacement is associated with increased mortality. J Thorac Cardiovasc Surg. 2016;151:815-823.e2.
11. Abawi M, Nijhoff F, Agostoni P, Emmelot-Vonk M.H., de Vries R., Doevendans P. A., Stella P.R. Incidence, predictive factors, and effect of delirium after transcatheter aortic valve replacement. JACC Cardiovasc Interv 2016;9:160-168.
12. Tse L, Bowering JB, Schwarz SK, Moore RL, Burns KD, Barr AM. Postoperative delirium following transcatheter aortic valve implantation: a historical cohort study. Can J Anaesth. 2015;62:22-30.
13. Stachon P, Kaier K, Zirlik A, et al. Risk factors and outcome of postoperative delirium after transcatheter aortic valve replacement. Clin Res Cardiol. 2018;107:756-762.
14. Soundhar A, Udesh R, Mehta A, et al. Delirium following transcatheter aortic valve replacement: national inpatient sample analysis. J Cardiothorac Vasc Anesth. 2017;31:1977-1984.
15. Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology, European Association for Cardio-Thoracic Surgery, Vahanian A et al. Guidelines on the management of valvular heart disease (version 2012). Eur Heart J 2012;33:2451-2496.
16. van der Wulp K, Verkroost MWA, van Wely MH, et al. Feasibility and outcomes of transcatheter aortic valve implantation using the left axillary artery as primary access site. Ann Thorac Surg. 2019;107:546-552.
17. van Wely MH, van der Wulp K, Verkroost MWA, et al. Procedural success and clinical outcome of the Portico transcatheter aortic valve using the left subclavian artery as primary access. JACC Cardiovasc Interv. 2018;11:1311-1312.
18. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, 4th Ed., Text Revision. Washington DC: American Psychiatric Association, 2000.
19. Bakker FC, Persoon A, Bredie SJH, et al. The CareWell in hospital program to improve the quality of care for frail elderly inpatients: results of a before-after study with focus on surgical patients. Am J Surg. 2014;208:735-746.
20. Gemert van LA, Schuurmans MJ. The Neecham Confusion Scale and the Delirium Observation Screening Scale: capacity to discriminate and ease of use in clinical practice. BMC Nurs. 2007;6:3.
21. Kappetein AP, Head SJ, Genereux P, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. J Thorac Cardiovasc Surg. 2013;145:6-23.
22. Tilley E, Psaltis PJ, Loetscher T, et al. Meta-analysis of prevalence and risk factors for delirium after transcatheter aortic valve implantation. Am J Cardiol. 2018;122:1917-1923.
23. Quinlan N, Marcantonio ER, Inouye SK, Gill TM, Kamholz B, Rudolph JL. Vulnerability: the crossroads of frailty and delirium. J Am Geriatr Soc 2011; 59(suppl 2):S262-S268.
24. Weisenberg D, Sahar Y, Sahar G, et al. Atherosclerosis of the aorta is common in patients with severe aortic stenosis: an intraoperative transesophageal echocardiographic study. J Thorac Cardiovasc Surg. 2005;130:29-32.
25. Vermeer SE, Longstreth WT Jr, Koudstaal PJ. Silent brain infarcts: a systematic review. Lancet Neurol 2007;6:611-619.
26. Kassie GM, Nguyen TA, Kalisch Ellett LM, Pratt NL, Roughead EE. Preoperative medication use and postoperative delirium: a systematic review. BMC Geriatr. 2017;17:298.
27. Husser O, Fujita B, Hengstenberg C, et al. Conscious sedation versus general anesthesia in transcatheter aortic valve replacement: the German Aortic Valve Registry. JACC Cardiovasc Interv. 2018;11:567-578.
28. Abawi M, Pagnesi M, Agostoni P, et al. Postoperative delirium in individuals undergoing transcatheter aortic valve replacement: a systematic review and meta-analysis. J Am Geriatr Soc. 2018;66:2417-2424.
29. Abawi M, Nijhoff F, Agostoni P, et al. Effect of new cerebral ischemic lesions on the delirium occurrence after transcatheter aortic valve replacement. J Am Coll Cardiol. 2016;68:1489-1490.
30. Kroon HG, Van Mieghem NM. Need for embolic protection during transcatheter aortic valve implantation: an interventionalist's perspective on histopathology findings. Interv Cardiol. 2017;12:36-39.
31. Van Gils L, Kroon H, Daemen J, et al. Complete filter-based cerebral embolic protection with transcatheter aortic valve replacement. Catheter Cardiovasc Interv. 2018;91:790-797.
32. 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.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article.

Supplementary Table S1. Details of delirium.

Supplementary Table S2. Baseline and in-hospital predictors for 3-year mortality in univariate and multivariable analysis.

Supplementary Table S3. In-hospital outcome.

Supplementary Table S4. Multivariable analysis association of preoperative factors in association with postoperative delirium.

Supplementary Table S5. Procedural outcome.