Outcomes of Transcatheter Aortic Valve Implantation in Patients Receiving Chronic Systemic Corticosteroid Treatment

Alexandre Gautier, MD[a,b], Marina Urena, MD, PhD[a,b,c], Caroline Chong-Nguyen, MD[a,b,c], Quentin Fischer, MD[a,b], Jérémie Abtan, MD[a], Jose Luis Carrasco, MD[d], Eric Brochet, MD[a], Bernard Iung, MD[a,b,c], and Dominique Himbert, MD[a,c,*]

The aim of this study was to describe the effects of chronic systemic corticosteroid treatment (SCT) on early and late outcomes after transcatheter aortic valve implantation (TAVI). From October 2006 to November 2018, 1,299 patients underwent TAVI in our institution. Among them, 48 (3.7%) received chronic SCT at the time of procedure (SCT group). They were more frequently women (p = 0.08) and needed more often dialysis (p = 0.002). All other baseline characteristics were similar between both groups. At 30 days, there was no difference on mortality. However, after adjustment, the SCT group had more major vascular complications: 16.7% versus 7.4%, hazard ratio (HR) 2.52 (95% confidence interval [CI] 1.14 to 5.9, p = 0.023), major or life-threatening bleedings: 22.9% versus 12.4%, HR 2.02 (95% CI 1.00 to 4.08, p = 0.05), and tamponades: 8.3% versus 2.4%, HR 4.05 (95% CI 1.35 to 12.15, p <0.001) than the non-SCT group. One-year all-cause mortality was significantly higher in the SCT than in the non-SCT group (37.5% vs 12.5%, p <0.0001). Multivariate analysis confirmed that SCT use was an independent predictor of 1-year mortality (HR 2.29, 95% CI 1.16 to 4.50, p = 0.017). In conclusion, chronic use of SCT significantly increases the rates of early vascular complications, major or life-threatening bleedings and tamponade and is an independent predictor of 1-year all-cause mortality after TAVI. **(Am J Cardiol 2020;130:108−114)**

Transcatheter aortic valve implantation (TAVI) has become a routine procedure to treat high-risk patients with symptomatic severe aortic stenosis[1−3] and its indications are extending to lower-risk populations.[4,5] Systemic corticosteroid treatment (SCT) is commonly used for several chronic diseases. Long-term use of SCT has many well-known side effects, such as tissue fragility, in particular cutaneous and vascular, and delayed wound healing.[6−9] Data from percutaneous coronary interventions have shown a significant increase in the rate of complications in these patients.[10] To date, only few studies have assessed the effects of the use of corticosteroids on outcomes after TAVI, with some discrepancies.[11−14] In the current context of expanding TAVI indications,[15] the identification of predictors of poor outcomes is necessary for a better patient selection to prevent complications and avoid futile procedures. The aim of this study was to describe the impact of chronic use of SCT on the early and late outcomes after TAVI.

Methods

All patients consecutively treated with TAVI in our center from October 2006 to November 2018 were prospectively included in a dedicated local database. Eligibility for TAVI was based on the judgement of a local Heart Team composed of clinical and interventional cardiologists, anesthesiologists and cardiac surgeons. Patients in the SCT group were defined by the use of oral corticosteroids for at least 30 days before the procedure. Prednisone equivalent was calculated for each of them. Patients treated with a short course of systemic corticosteroids or with inhaled corticosteroids and all other patients without previous SCT were included in the non-SCT group. Follow-up was achieved by means of outpatient visits or phone contacts at 30 days and 12 months.

TAVI procedures were performed in catheterization laboratory by experienced operators using either balloon-expandable heart valves (Edwards SAPIEN, SAPIEN XT or SAPIEN 3 − Edwards Lifesciences, Irvine, California) or self-expanding devices (CoreValve, Evolut R or Evolut PRO − Medtronic, Minneapolis, Minnesota). Before the procedures, a careful assessment of the diameter, tortuosity, and degree of calcification of the iliac and femoral arteries was performed for each patient to assess the suitability of the transfemoral access. Antiplatelet (Aspirin and/or clopidogrel) and anticoagulation therapy were administered according to current recommendations. All patients were monitored in the intensive care unit during at least 24 hours after the procedure.

[a]Department of Cardiology, Bichat Hospital, AP-HP, Paris, France; [b]University of Paris, Paris, France; [c]INSERM U1148, Laboratory for Vascular Translational Science (LVTS), Paris, France; and [d]Department of Anesthesiology, Bichat Hospital, AP-HP, Paris, France. Manuscript received April 8, 2020; revised manuscript received and accepted June 8, 2020.

See page 113 for disclosure information.

*Corresponding author: Tel: + 33 1 40 25 66 01; fax: + 33 1 40 25 88 65.
E-mail address: dominique.himbert@aphp.fr (D. Himbert).

0002-9149/
https://doi.org/10.1016/j.amjcard.2020.06.021

Table 1
Baseline characteristics of the patients

Variable	Overall (n = 1,299)	Corticosteroid use		p Value
		No (n = 1,251)	Yes (n = 48)	
Age (years)	81 ± 10	81 ± 10	80 ± 9	0.68
Women	618 (48%)	589 (47%)	29 (60%)	0.08
BMI (kg/m^2)	26 ± 5	26 ± 5	25 ± 5	0.16
Euroscore II (%)	4.7 (2.8-7.5)	4.7 (2.8-7.6)	4.6 (3.6-6.9)	0.68
NYHA class III or IV	1061 (82%)	1017 (81%)	44 (92%)	0.08
Diabetes mellitus	332 (26%)	322 (26%)	10 (21%)	0.50
Coronary artery disease	470 (36%)	455 (36%)	15 (31%)	0.54
Previous cardiac surgery	271 (21%)	263 (21%)	8 (17%)	0.59
Coronary bypass	188 (14%)	181 (14%)	7 (15%)	0.10
Previous TIA/Stroke	142 (11%)	138 (11%)	4 (8%)	0.81
Atrial fibrillation/Flutter	452 (35%)	437 (35%)	15 (32%)	0.76
Pacemaker	202 (17%)	198 (16%)	4 (8%)	0.22
Peripheral artery disease	269 (21%)	260 (21%)	9 (19%)	0.86
Chronic obstructive pulmonary disease	195 (15%)	185 (15%)	10 (21%)	0.30
eGFR (ml/min)	62.3 ± 25.2	62.3 ± 25.2	59.4 ± 23.9	0.68
Dialysis	39 (3%)	33 (3%)	6 (12%)	0.002
Echocardiographic findings				
LVEF (%)	53 ± 13	53 ± 13	55 ± 12	0.26
Mean transaortic gradient (mmHg)	48 ± 16	48 ± 17	47 ± 13	0.80
AVA index (cm^2/m^2)	0.7 (0.6-0.9)	0.7 (0.6-0.9)	0.8 (0.6-0.9)	0.91
PASP (mmHg)	46 ±13	46±13	46 ± 12	0.88
Antithrombotic therapy				
- Aspirin	632 (49%)	612 (49%)	20 (42%)	0.38
- Clopidogrel	206 (16%)	201 (16%)	5 (10%)	0.42
- Oral anticoagulant	302 (23%)	293 (23%)	9 (19%)	0.72

Data are presented as mean ± SD, median (IQR) or n (%).

AVA = aortic valve area; BMI = body mass index; eGFR = estimated glomerular filtration rate; IQR = interquartile range; LVEF = left ventricular ejection fraction; NYHA = New York heart association class; PASP = pulmonary artery systolic pressure; TIA = transient ischemic attack.

Study end points were 30-day vascular and bleeding complications, permanent pacemaker (PPM) implantation, acute kidney injury, stroke and cardiac tamponade, which were defined according to the Valve Academic Research Consortium-2 criteria and 1-year all-cause mortality.

Categorical variables are presented as numbers and percentages. Continuous variables are expressed as means ± standard deviation if normally distributed, as median and interquartile range if not normally distributed. Comparisons between the 2 groups (SCT and non-SCT) were performed using the two-sided chi-square or Fisher's exact tests for categorical data. For continuous data the Student's *t*-test or Wilcoxon test were performed according to data distribution. Statistical significance was considered for p values <0.05. Survival rates were estimated by Kaplan-Meier analysis, and groups were compared using the log-rank tests. Cox proportional hazard stepwise regression analysis was carried-out to identify independent predictors of 1-year all-cause mortality. All univariate predictors of 1-year mortality with p <0.05 were included in the final model. Statistical analyses were performed using the Statistical Package for Social Sciences version 22 (SPSS Inc., IBM, New York)

Results

From October 2006 to November 2018, a total of 1,299 patients underwent TAVI in our institution. Among them, 48 (3.7%) received chronic SCT treatment at the time of intervention. The median daily prednisone equivalent dose was 7.5 [5 to 10] mg. Table 1 shows the main demographic and echocardiographic characteristics at baseline, according to the use of chronic SCT. Indications for SCT use are listed in Table 2.

Overall, the mean age of the study population was of 81 ± 10 years with no difference between both groups. Patients with SCT tended to be more frequently women (60% vs 47%; p = 0.08) and were more often treated with dialysis (12% vs 3% p = 0.002). All other co-morbidities and baseline echocardiographic data were similar between both groups. As well, computed tomography, which was performed in 93% of the patients, did not show any difference between groups in femoral minimal luminal diameters of patients treated via a transfemoral access.

Procedural findings are shown in Table 3. Most procedures were performed under conscious sedation and loco-regional anesthesia (68%), using the transfemoral access, without differences between the SCT and non-SCT groups (85% vs 81% respectively, p = 0.57). Balloon-expandable and self-expanding prostheses were similarly used in both groups. There was no difference regarding procedural outcomes.

Thirty-day outcomes are displayed in Figure 1 and Table 4. The SCT group had more frequently major vascular complications, major or life-threatening bleedings and cardiac tamponades than the non-SCT group. These differences remained significant after adjustment by the need for

Table 2
Indications for chronic use of systemic corticosteroid therapy

Indications	n = 48
Giant cell arteritis and/or polymyalgia rheumatica	14
Renal or liver transplantation	10
Chronic arthritis	8
Other autoimmune diseases	7
Pulmonary fibrosis	4
Neoplasia	2
Unknown	2

dialysis before the procedure: major vascular complications: hazard ratio (HR) 2.52, (95% confidence interval [CI] 1.14 to 5.9), p = 0.023; major or life-threatening bleedings, HR 2.02 (95% CI 1.00 to 4.08), p = 0.050; cardiac tamponades, HR 4.05, (95% CI 1.35 to 12.15), p <0.001. The causes of tamponade in the SCT-group were left ventricle perforations due to the guide wire in 3 cases and annulus rupture in 1 case. Moreover, patients receiving corticosteroids were less frequently discharged to home than those without. No significant difference was observed between both groups regarding other complications, although there were trends towards higher rates of mortality, stroke and myocardial infarction, and lower rates of pacemaker implantation in the SCT than in the non-SCT group.

At 1-year follow-up, 18 (37%) patients had died in the SCT group versus 157 (12%) in the non-SCT group (log-rank p <0.0001; Figure 2 and Table 4). Of the 175 deaths observed at 1 year in overall population, 132 (75%) were cardiovascular. The leading cause of death in the SCT-group was cardiovascular (55%). However, compared with the non-SCT group, the noncardiovascular mortality rate was higher in the SCT-group (44% vs 22%, p = 0.047). Univariate and multivariate predictors of 1-year all-cause mortality are shown in Table 5. The use of chronic SCT was an independent predictor of all-cause mortality (HR 2.29 (95% CI 1.16 to 4.50; p = 0.017) at 1 year.

Table 3
Procedural findings

Variable	Overall (n = 1,299)	Corticosteroid use		p Value
		No (n = 1,251)	Yes (n = 48)	
Anesthesia				
Loco-regional/ conscious sedation	890 (68%)	859 (69%)	31 (65%)	0.53
General	409 (31%)	392 (31%)	17 (35%)	–
Primary access				
Transfemoral	1059 (81%)	1018 (81%)	41 (85%)	0.57
Non-transfemoral	240 (18%)	233 (19%)	7 (15%)	–
Predilation	733 (56%)	706 (56%)	27 (56%)	0.88
Transcatheter heart valve				
Balloon-expandable	780 (61%)	754 (61%)	26 (55%)	0.45
Self-expanding	506 (39%)	485 (39%)	21 (45%)	–
Post-dilation	91 (7%)	89 (7%)	2 (4%)	0.77
Outcomes				
Procedural success	1232 (95%)	1188 (95%)	44 (92%)	0.31
Death	17 (1%)	16 (1%)	1 (2%)	0.48
Conversion to open surgery	1 (0.1%)	1 (0.1%)	0	1.0
Aortic regurgitation>2	51 (4%)	49 (4%)	2 (4%)	0.70

Discussion

The present study is the largest among the few studies on TAVI patients using chronic systemic corticosteroid treatment reported to date. The main findings suggest an association between the use of chronic SCT and worse clinical outcomes. It increases the rates of procedural and early major complications of TAVI and represents an independent predictor of 1-year mortality, related to non-cardiovascular deaths in nearly 50% of the patients.

Our findings show that the chronic use of SCT is associated with an increased rate of major vascular complications, major or life-threatening bleedings and tamponades related

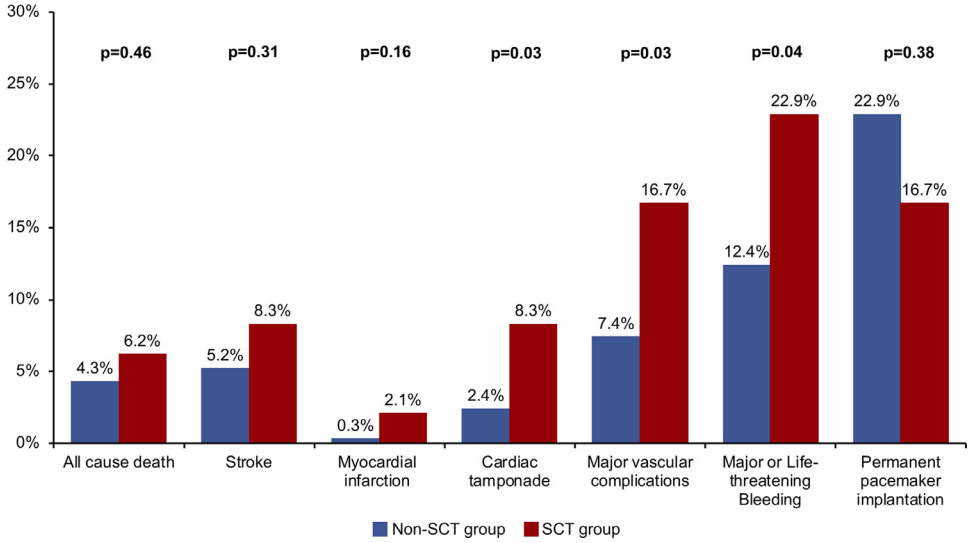

Figure 1. Thirty-day outcomes after TAVI according to the use of chronic systemic corticosteroid therapy.

Table 4
TAVI outcomes according to the use of chronic corticosteroids treatment

Variable	Overall (n = 1,299)	Corticosteroid use		p Value
		No (n = 1,251)	Yes (n = 48)	
30-day outcomes				
All cause death	57 (4%)	54 (4%)	3 (6%)	0.46
Stroke	69 (5%)	65 (5%)	4 (8%)	0.31
Myocardial infarction	5 (0.4%)	4 (0.3%)	1 (2%)	0.16
Cardiac tamponade	31/1169* (3%)	27/1122* (2%)	4 (8%)	0.03
Annulus rupture	6 (0.5%)	5 (0.42)	1 (2%)	–
Left ventricle perforation	18 (1.5%)	15 (1.25)	3 (6%)	–
Right ventricle perforation	7 (0.6%)	7 (0.58)	0	–
Major vascular complications	101 (8%)	93 (7%)	8 (17%)	0.02
Major or Life-threatening bleeding	166 (13%)	155(12%)	11 (23%)	0.04
Acute kidney injury	89 (7%)	86 (7%)	3 (6%)	0.99
Permanent pacemaker implantation	295 (23%)	287 (23%)	8 (17%)	0.38
New-onset atrial fibrillation	88 (7%)	84 (7%)	4 (8%)	0.56
Discharge at home	783 (60%)	760 (61%)	23 (48%)	0.07
1-year mortality				
All cause death	175 (13%)	157 (12%)	18 (37%)	<0.001
Cardiovascular death	132/175 (75%)	122/157 (78%)	10/18 (55%)	0.047
Non-cardiovascular death	43/175 (25%)	35/157 (22%)	8/18 (44%)	–

* excluding the transapical access

to perforation of the left ventricle by the wire in patients undergoing TAVI. The tissue fragility induced by the treatment can probably explain this excess risk. The longer hospital stay of this population further reflects its high-risk profile. Our results slightly differ from those of Fink et al[11] who found an excess of only minor vascular complications after TAVI in steroid-treated patients, but their work had several limitations. Only 25 patients received corticosteroid therapy and most of them (52%) were treated with inhaled corticosteroids for chronic obstructive pulmonary disease or asthma, which may have underestimated the complications related to the systemic effect of corticosteroids. Indeed, recent robust data from randomized controlled studies and meta-analyses show that inhaled corticosteroids have an excellent safety profile and no impact on cardiovascular outcomes.[16,17] The 30-day outcomes in the overall study population are consistent with those found in randomized trials[18,19] or real-world registries[20,21] regarding major vascular complications (4.1% to 7.9%), major or life-threatening bleeding (10.4% to 26.3%), cardiac tamponade (1.0%

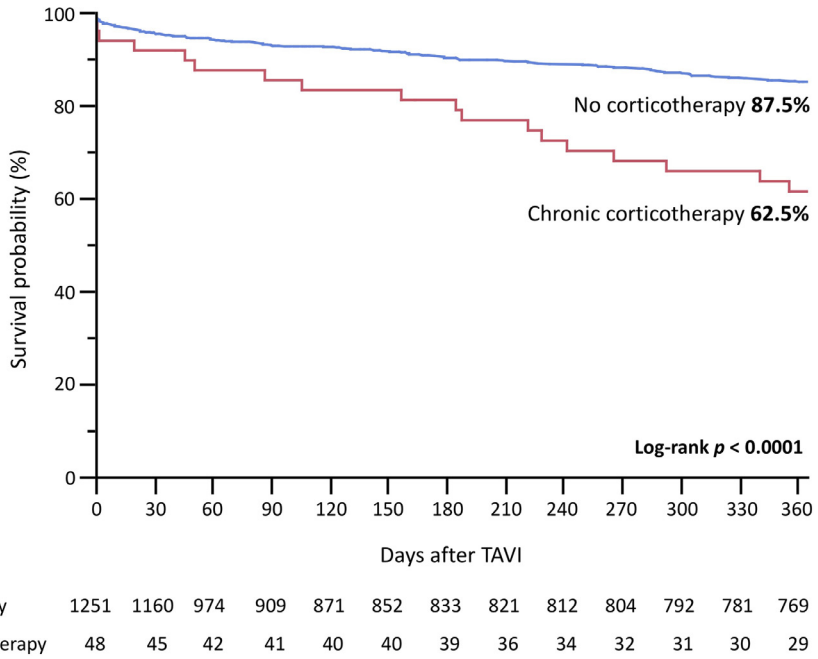

Figure 2. One-year survival estimated by Kaplan-Meier analysis according to the use of chronic systemic corticosteroid therapy.

Tableau 5
Cox hazard regression analysis for predictors of one-year all-cause mortality

Variable	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p Value	HR (95% CI)	p Value
Age, years	1.00 (0.99-1.02)	0.99		
Female	0.96 (0.71-1.29)	0.77		
BMI (kg/m^2)	0.96 (0.93-0.99)	0.011	0.96 (0.92-0.99)	0.046
Euroscore II (%)	1.05 (1.05-1.06)	<0.0001	1.07 (0.98-1.05)	0.26
NYHA class III or IV	1.74 (1.10-2.75)	0.017	1.09 (0.64-1.86)	0.75
Diabetes mellitus	1.16 (0.83-1.61)	0.38		
Coronary artery disease	1.56 (1.16-2.10)	0.004	1.17 (0.77-1.79)	0.46
Previous cardiac surgery	1.40 (1.01-1.93)	0.047	0.93 (0.55-1.56)	0.78
Coronary bypass	1.22 (0.63-2.33)	0.56		
Previous TIA/Stroke	0.82 (0.50-1.36)	0.45		
Atrial fibrillation/Flutter	1.77 (1.31-2.39)	<0.0001	1.31 (1.06-1.62)	0.014
Pacemaker	1.43 (0.99-2.05)	0.055		
Peripheral artery disease	1.88 (1.37-2.59)	<0.0001	1.76 (1.15-2.67)	0.009
Chronic obstructive pulmonary disease	1.27 (0.86-1.88)	0.22		
eGFR (ml/min)	0.99 (0.99-1.00)	0.11		
Dialysis	1.99 (1.05-3.78)	0.034	1.67 (0.70-3.95)	0.25
LVEF (%)	0.98 (0.97-0.99)	0.003	0.99 (0.98-1.01)	0.80
Mean transaortic gradient (mmHg)	0.99 (0.97-0.99)	0.001	1.00 (0.99-1.00)	0.078
PASP (mmHg)	1.02 (1.00-1.03)	0.016	1.00 (0.99-1.02)	0.98
Chronic systemic corticosteroid treatment	2.84 (1.74-4.62)	<0.0001	2.29 (1.16-4.50)	0.017

BMI = body mass index; CI = confidence interval; eGFR = estimated glomerular filtration rate; HR = hazard ratio; LVEF = left ventricular ejection fraction; NYHA = New York heart association class, PASP = pulmonary artery systolic pressure; TIA = transient ischemic attack

to 2.0%), PPM implantation (8.5% to 25.9%), and all-cause death (2.2% to 5.4%).

At 1-year follow-up, the chronic use of SCT appears to be an independent predictor of all-cause mortality. The excess mortality observed in the SCT group, which was non-significant at discharge, progressively increased with time, reflecting the impact of frailty and the severity of comorbidities present in this population. This statement is supported by the large proportion of noncardiovascular deaths in the latter (44%, vs only 22% in patients not receiving SCT), in the context of frequent severe underlying diseases. The estimated cumulative survival rate at 1-year in the whole population (86%) is close to that described in the literature.[18,19]

Conduction disturbances after TAVI have various causes including baseline conduction defects, annulus size, type of prosthesis, calcification of the left ventricular outflow tract and depth of implantation. However, this adverse event remains largely unpredictable. Due to mechanical compression, the implanted aortic bioprosthesis induces a local inflammatory reaction and edema with potential secondary conduction disorders. Based on this pathophysiology, the anti-inflammatory properties of corticosteroids have been studied in this setting. Havakuk et al studied a cohort of 39 patients who received a loading dose of prednisone the day before the TAVI procedure, followed by intravenous administration of hydrocortisone 1 hour before the procedure, mostly because of an allergy to iodine. No difference was found regarding the incidence of new conduction defects and the need for PPM implantation.[14] However, Oestreich et al recently found a lower rate of 30-day PPM implantation in 16 patients receiving corticosteroids before TAVI procedure, supporting the anti-edematous theory.[13] Our findings do not fully support this theory. However, although the difference was not statistically significant, there was a trend toward a lower 30-day PPM implantation rate in the SCT than in the non-SCT group (17% vs 23%). The implantation of PPM after TAVI remains a concern since many patients only require the pacemaker during the first weeks/months and do not use it anymore afterward. The reversibility of these conduction disorders supports the hypothesis of a transient inflammation of the septal myocardium. Further large-scale studies will be needed to assess the place of inflammation modulating drugs and try to decrease the number of patients requiring PPM implantation.

TAVI has generated enthusiasm for the treatment of patients with severe aortic stenosis in the last decade. Given its rapid development and the increased life-expectancy of the population, the risk stratification of the procedure will become even more crucial. Indeed, a substantial number of patients still do not really benefit from TAVI because of procedural complications or severity of their comorbidities.[22] Therefore, 1 challenge ahead is to better identify the predictors for poor outcomes after TAVI and establish an accurate risk stratification for each individual patient. Chronic use of SCT is present in almost 4% of TAVI patients in our experience. Our findings suggest that this is an important parameter to be considered when stratifying the risk of TAVI candidates, and that procedural complications should be particularly anticipated and prevented in this specific population.

Despite careful collection of prospective data, this is a nonrandomized, observational study based on a single-center experience. Moreover, the sample size of steroids-treated patients was relatively small and the number of events that occurred was quite low. These limitations did not allow us to perform other analyses according to the treatment doses or the nature of underlying diseases. They

precluded performing a propensity score matching analysis integrating potential confounding factors to provide some evidence of causality. Even more, we cannot exclude that these finding are a play of chance. The study results should be seen rather as hypothesis generating than a true finding.

In conclusion, although no evidence of causality can be provided, this study suggests that the chronic use of SCT is a marker of risk of early major complications and of 1-year all-cause mortality after TAVI. In the light of these results, particular attention should be paid when discussing TAVI to adequately anticipate and prevent procedural complications and assess the estimated life expectancy to avoid futile interventions in this high-risk population.

Disclosures

D. Himbert is a proctor for Edwards Lifesciences and Medtronic. B. Iung received consultant fees from Edwards Lifesciences. All other authors have no conflicts of interest to declare.

CRediT author statement

Alexandre Gautier and Marina Urena: Conceptualization, methodology, formal analysis, writing original draft

Caroline Chong-Nguyen, Quentin Fischer, Jérémie Abtan, Jose-Luis Carrasco, Eric Brochet: Investigation, resources

Bernard Iung: Conceptualization, validation, supervision

Dominique Himbert: Conceptualization, methodology, formal analysis, writing, review & editing, supervision

1. Figulla L, Neumann A, Figulla HR, Kahlert P, Erbel R, Neumann T. Transcatheter aortic valve implantation: evidence on safety and efficacy compared with medical therapy. A systematic review of current literature. *Clin Res Cardiol* 2011;100:265–276.
2. Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, Iung B, Lancellotti P, Lansac E, Rodriguez Muñoz D, Rosenhek R, Sjögren J, Tornos Mas P, Vahanian A, Walther T, Wendler O, Windecker S, Zamorano JL, ESC Scientific Document Group. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J* 2017;38:2739–2791.
3. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, Fleisher LA, Jneid H, Mack MJ, McLeod CJ, O'Gara PT, Rigolin VH, Sundt TM, Thompson A. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the american college of cardiology/american heart association task force on clinical practice guidelines. *J Am Coll Cardiol* 2017;70:252–289.
4. Mack MJ, Leon MB, Thourani VH, Makkar R, Kodali SK, Russo M, Kapadia SR, Malaisrie SC, Cohen DJ, Pibarot P, Leipsic J, Hahn RT, Blanke P, Williams MR, McCabe JM, Brown DL, Babaliaros V, Goldman S, Szeto WY, Genereux P, Pershad A, Pocock SJ, Alu MC, Webb JG, Smith CR. Transcatheter aortic-valve replacement with a balloon-expandable valve in low-risk patients. *N Engl J Med* 2019;380:1695–1705.
5. Popma JJ, Deeb GM, Yakubov SJ, Mumtaz M, Gada H, O'Hair D, Bajwa T, Heiser JC, Merhi W, Kleiman NS, Askew J, Sorajja P, Rovin J, Chetcuti SJ, Adams DH, Teirstein PS, Zorn GL, Forrest JK, Tchétché D, Resar J, Walton A, Piazza N, Ramlawi B, Robinson N, Petrossian G, Gleason TG, Oh JK, Boulware MJ, Qiao H, Mugglin AS, Reardon MJ. Transcatheter aortic-valve replacement with a self-expanding valve in low-risk patients. *N Engl J Med* 2019;380:1706–1715.
6. Sholter DE, Armstrong PW. Adverse effects of corticosteroids on the cardiovascular system. *Can J Cardiol* 2000;16:505–511.
7. Poetker DM, Reh DD. A comprehensive review of the adverse effects of systemic corticosteroids. *Otolaryngol Clin North Am* 2010;43:753–768.
8. Liu D, Ahmet A, Ward L, Krishnamoorthy P, Mandelcorn ED, Leigh R, Brown JP, Cohen A, Kim H. A practical guide to the monitoring and management of the complications of systemic corticosteroid therapy. *Allergy Asthma Clin Immunol Off J Can Soc Allergy Clin Immunol* 2013;9:30.
9. Wei L, MacDonald TM, Walker BR. Taking glucocorticoids by prescription is associated with subsequent cardiovascular disease. *Ann Intern Med* 2004;141:764–770.
10. Ellis SG, Semenec T, Lander K, Franco I, Raymond R, Whitlow PL. Effects of long-term prednisone (≥5 mg) use on outcomes and complications of percutaneous coronary intervention. *Am J Cardiol* 2004;93:1389–1390.
11. Fink N, Segev A, Barbash I, Bogdan A, Hamdan A, Mazin I, Maor E, Hay I, Guetta V, Fefer P. Vascular complications in steroid treated patients undergoing transfemoral aortic valve implantation. *Catheter Cardiovasc Interv* 2016;87:341–346.
12. Higuchi R, Tobaru T, Hagiya K, Saji M, Mahara K, Takamisawa I, Shimizu J, Takanashi S, Takayama M. Transcatheter aortic valve implantation in patients on corticosteroid therapy. *Heart Vessels* 2017;32:1236–1243.
13. Oestreich B, Gurevich S, Adabag S, Kelly R, Helmer G, Raveendran G, Yannopoulos D, Biring T, Garcia S. Exposure to glucocorticoids prior to transcatheter aortic valve replacement is associated with reduced incidence of high-degree AV block and pacemaker. *Cardiovasc Revasc Med* 2019;20:328–331.
14. Havakuk O, Konigstein M, Ben Assa E, Arbel Y, Abramowitz Y, Halkin A, Bazan S, Shmilovich H, Keren G, Finkelstein A, Banai S. Steroid therapy and conduction disturbances after transcatheter aortic valve implantation. *Cardiovasc Ther* 2016;34:325–329.
15. Rahhab Z, El Faquir N, Tchetche D, Delgado V, Kodali S, Mara Vollema E, Bax J, Leon MB, Van Mieghem NM. Expanding the indications for transcatheter aortic valve implantation. *Nat Rev Cardiol* 2019:1–10.
16. Brook RD, Anderson JA, Calverley PM, Celli BR, Crim C, Denvir MA, Magder S, Martinez FJ, Rajagopalan S, Vestbo J, Yates J, Newby DE, SUMMIT Investigators. Cardiovascular outcomes with an inhaled beta2-agonist/corticosteroid in patients with COPD at high cardiovascular risk. *Heart Br Card Soc* 2017;103:1536–1542.
17. Jing X, Li Y, Xu J. Risk of cardiovascular events associated with inhaled corticosteroid treatment in patients with chronic obstructive pulmonary disease: a meta-analysis. *Can Respir J* 2018;2018:7097540.
18. Leon MB, Smith CR, Mack MJ, Makkar RR, Svensson LG, Kodali SK, Thourani VH, Tuzcu EM, Miller DC, Herrmann HC, Doshi D, Cohen DJ, Pichard AD, Kapadia S, Dewey T, Babaliaros V, Szeto WY, Williams MR, Kereiakes D, Zajarias A, Greason KL, Whisenant BK, Hodson RW, Moses JW, Trento A, Brown DL, Fearon WF, Pibarot P, Hahn RT, Jaber WA, Anderson WN, Alu MC, Webb JG. Transcatheter or surgical aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2016;374:1609–1620.
19. Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Søndergaard L, Mumtaz M, Adams DH, Deeb GM, Maini B, Gada H, Chetcuti S, Gleason T, Heiser J, Lange R, Merhi W, Oh JK, Olsen PS, Piazza N, Williams M, Windecker S, Yakubov SJ, Grube E, Makkar R, Lee JS, Conte J, Vang E, Nguyen H, Chang Y, Mugglin AS, Serruys PWJC, Kappetein AP. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2017;376:1321–1331.
20. Walther T, Hamm CW, Schuler G, Berkowitsch A, Kötting J, Mangner N, Mudra H, Beckmann A, Cremer J, Welz A, Lange R, Kuck K-H, Mohr FW, Möllmann H, Board GE. Perioperative results and complications in 15,964 transcatheter aortic valve replacements: prospective data from the GARY registry. *J Am Coll Cardiol* 2015;65:2173–2180.
21. Auffret V, Lefevre T, Van Belle E, Eltchaninoff H, Iung B, Koning R, Motreff P, Leprince P, Verhoye JP, Manigold T, Souteyrand G, Boulmier D, Joly P, Pinaud F, Himbert D, Collet JP, Rioufol G, Ghostine S, Bar O, Dibie A, Champagnac D, Leroux L, Collet F, Teiger E, Darremont O, Folliguet T, Leclercq F, Lhermusier T, Olhmann P, Huret B, Lorgis L, Drogoul L, Bertrand B, Spaulding C, Quilliet L, Cuisset T, Delomez M, Beygui F, Claudel J-P, Hepp A, Jegou A, Gommeaux A, Mirode A, Christiaens L, Christophe C, Cassat C, Metz D, Mangin L, Isaaz K, Jacquemin L, Guyon P, Pouillot C, Makowski

S, Bataille V, Rodés-Cabau J, Gilard M, Le Breton H, Le Breton H, Eltchaninoff H, Gilard M, Iung B, Le Breton H, Lefevre T, Van Belle E, Laskar M, Leprince P, Iung B, Bataille V, Chevalier B, Garot P, Hovasse T, Lefevre T, Donzeau Gouge P, Farge A, Romano M, Cormier B, Bouvier E, Bauchart J-J, Bodart J-C, Delhaye C, Houpe D, Lallemant R, Leroy F, Sudre A, Van Belle E, Juthier F, Koussa M, Modine T, Rousse N, Auffray J-L, Richardson M, Berland J, Eltchaninoff H, Godin M, Koning R, Bessou J-P, Letocart V, Manigold T, et al. Temporal trends in transcatheter aortic valve replacement in France: FRANCE 2 to FRANCE TAVI. *J Am Coll Cardiol* 2017;70:42–55.

22. Puri R, Iung B, Cohen DJ, Rodés-Cabau J. TAVI or No TAVI: identifying patients unlikely to benefit from transcatheter aortic valve implantation. *Eur Heart J* 2016;37:2217–2225.