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Clinical Research

Infective Endocarditis Caused by *Staphylococcus aureus* After Transcatheter Aortic Valve Replacement

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ABSTRACT

Background: *Staphylococcus aureus* (SA) has been extensively studied as causative microorganism of surgical prosthetic-valve infective endocarditis (IE). However, scarce evidence exists on SA IE after transcatheter aortic valve replacement (TAVR).

Methods: Data were obtained from the Infectious Endocarditis After TAVR International Registry, including patients with definite IE after TAVR from 59 centres in 11 countries. Patients were divided into 2 groups according to microbiologic etiology: non-SA IE vs SA IE.

Results: SA IE was identified in 141 patients out of 573 (24.6%), methicillin-sensitive SA in most cases (115/141, 81.6%). Self-expanding valves were more common than balloon-expandable valves in patients presenting with early SA IE. Major bleeding and sepsis complicating TAVR, neurologic symptoms or systemic embolism at admission, and IE with cardiac device involvement (other than the TAVR prosthesis) were associated with SA IE ($P < 0.05$ for all). Among patients with IE after TAVR, the likelihood of SA IE increased from 19% in the absence of those risk factors to 84.6% if $\geq$ 3 risk factors were present. In-hospital (47.8% vs 26.9%; $P < 0.001$) and 2-year (71.5% vs 49.6%; $P < 0.001$) mortality rates were higher among patients with SA IE vs non-SA IE. Surgery at the time of index SA IE episode was associated with lower mortality at follow-up compared with medical therapy alone (adjusted hazard ratio 0.46, 95% CI 0.22-0.96; $P = 0.038$).

Conclusions: SA IE represented approximately 25% of IE cases after TAVR and was associated with very high in-hospital and late mortality. The presence of some features determined a higher likelihood of SA IE and could help to orientate early antibiotic regimen selection. Surgery at index SA IE was associated with improved outcomes, and its role should be evaluated in future studies.

RÉSUMÉ

Contexte : *Staphylococcus aureus* (SA) a fait l'objet de nombreuses études en tant qu'agent causal de l'endocardite infectieuse (EI) sur prothèse valvulaire. Cependant, il existe peu de données probantes sur l'EI causée par SA survenant après un remplacement valvulaire aortique par cathéter (RVAC).

Méthodologie : Les données provenaient de l'*Infectious Endocarditis After TAVR International Registry* et concernaient notamment des patients chez qui une EI caractérisée s'était déclarée après un RVAC dans 59 centres répartis dans 11 pays. Les patients ont été divisés en deux groupes selon l'étiologie microbiologique, à savoir : EI non causée par SA *vs* EI causée par SA.

Résultats : Une EI causée par SA a été recensée chez 141 patients sur 573 (24,6 %); dans la plupart des cas (115/141, 81,6 %), SA était sensible à la méthicilline. Chez les patients atteints d'EI précoce causée par SA, les dispositifs implantés étaient plus souvent des prothèses autodéployées que des prothèses déployées par ballonnet. Des saignements majeurs et un sepsis compliquant le RVAC, des symptômes neurologiques ou une embolie systémique à l'admission et des EI mettant en cause des dispositifs cardiaques (autres que des RVAC) étaient associés à l'EI causée par SA ($p < 0,05$ dans tous les cas). Chez les patients atteints d'EI après un RVAC, la probabilité d'EI causée par SA passait de 19 % en l'absence de ces facteurs de risque à 84,6 % si $\geq$ 3 facteurs de risque étaient présents. Les taux de mortalité hospitalière (47,8 % *vs* 26,9 %; $p < 0,001$) et de mortalité à 2 ans (71,5 % *vs* 49,6 %; $p < 0,001$) étaient plus élevés chez les patients atteints d'EI causée par SA que chez ceux atteints d'EI non causée par SA. La chirurgie lors de la survenue du cas index d'un épisode d'EI causée par SA était associée à une mortalité plus faible durant la période de suivi par rapport au traitement médical seul (rapport des risques instantanés corrigé : 0,46, IC à 95 % : 0,22-0,96; $p = 0,038$).

Conclusions : L'EI causée par SA représentait environ 25 % des cas d'EI qui se sont déclarés après un RVAC et était associée à des taux très élevés de mortalité hospitalière et de mortalité tardive. La présence de certaines caractéristiques déterminerait une probabilité plus élevée d'EI causée par SA et pourrait aider à orienter le choix de l'antibiothérapie. La chirurgie lors de la survenue du cas index d'EI causée par SA se trouvait associée à de meilleurs résultats, et son rôle devrait être évalué dans le cadre des études à venir.

Transcatheter aortic valve replacement (TAVR) has revolutionised the management of severe symptomatic aortic stenosis. Infective endocarditis (IE) after TAVR is a rare but life-threatening complication associated with high in-hospital and long-term mortality rates.[1-3] Despite the evolution of the TAVR procedure (simplified and less invasive) along with device iterations, the overall incidence of IE after TAVR has remained stable over time.[4] In the near future, the number of TAVR procedures is expected to rise owing to its expansion to the treatment of younger and lower surgical risk patients. Therefore, the total number of patients at risk of developing this life-threatening complication may increase substantially.

Staphylococcus aureus (SA) remains the most frequent microorganism in both community-acquired and hospital-acquired bacteremia, with mortality rates ranging from 10% to 30%.[5-7] The increasing exposure to medical procedures along with the increasing number of patients with implantable medical devices (prosthetic heart valves, implantable cardiac devices, grafts) has translated into SA becoming the predominant causative microorganism of native or surgical prosthetic valve endocarditis in developed countries.[7-9] TAVR patients represent an elderly population with a high comorbidity burden and exposure to health care—associated procedures. Thus, these patients have a significant potential risk of bloodstream infections and IE due to SA. In the surgical field, several studies have suggested that prosthetic-valve IE (PVE) caused by SA is associated with worse clinical outcomes and high early mortality rates compared with other forms of IE.[10] Nevertheless, scarce data exist on SA IE in TAVR recipients, and fundamental features and prognosis of this particular group of patients remain unknown. The purpose of the present study was to evaluate the clinical characteristics, management, and in-hospital and late outcomes of patients with SA IE after TAVR.

Methods

The Infectious Endocarditis After TAVR International Registry

Data from the Infectious Endocarditis After TAVR International Registry were used for this study. Briefly, the registry included data from 604 patients from 59 centers in 11 countries across Europe, North America, and South America from June 2005 to December 2020 with definite IE, as determined by the modified Duke criteria, after TAVR (regardless of the structure involved). Informed consent was obtained from all patients before the procedure, and the individual anonymised data sharing was performed according to the ethics committee of each center, in compliance with the Declaration of Helsinki.

Patient selection and data collection

Each center retrospectively identified patients according to the modified Duke criteria. Only TAVR patients, regardless of the structure affected (native/prosthetic valve or implantable cardiac device), developing definite IE were included. Only the first episode of IE recorded for an individual patient was included in the analysis. A dedicated case report form was used at all sites for data collection that included baseline and periprocedural TAVR features, as well as IE characteristics, microbiological profile, management, and in-hospital and follow-up outcomes (191 variables). Based on the microbiological profile, the global cohort was divided into 2 groups of patients: patients with IE after TAVR caused by SA (SA IE), and patients with IE after TAVR caused by another microorganism (non-SA IE). Non-SA IE included enterococci (33.6%), coagulase-negative staphylococci (24.1%), oral streptococci (18.3%), *Streptococcus gallolyticus* (6.9%), other streptococci (5.3%), culture-negative IE (8.3%), and other pathogens (4.5%). A total of 573 patients with well documented data on IE etiology (94.9% of the entire cohort) were included in the analysis. After the index IE, the median follow-up was 15 (interquartile range [IQR] 5-33) months, and follow-up was complete in 96.7% of the patients (19 patients were lost to follow-up).

Definitions

Definite IE was based on the modified Duke criteria.[11] Perioperative mortality risk was defined according to the logistic EuroSCORE. Transcatheter aortic valve type was divided into 2 groups: balloon-expandable valves (BEVs) and self-expanding valves (SEVs) or mechanically expandable valves (Supplemental Appendix S1). Clinical end points were defined according to the Valve Academic Research Consortium 2 criteria.[12] Periannular complications and other systemic embolisation were defined as previously reported.[1] Persistent bacteremia was defined as positive blood cultures despite appropriate antibiotic therapy for > 7 days. Health care—associated IE was defined with the Friedman criteria.[13] Early prosthetic valve endocarditis was defined as occurring within 12 months from TAVR. The presumed source of entry was determined by each site investigator based on medical records.

Statistical analysis

Depending on the variable distribution, which was assessed by means of the Shapiro-Wilk test, continuous variables were expressed as mean $\pm$ SD or median (IQR). Categoric variables were expressed as n (%). Group comparisons between groups were analysed with the use of the Student t test or Wilcoxon rank-sum test for continuous variables and χ^2 or Fisher exact test for categoric variables. For bivariable analysis, patients with missing data were excluded. A multivariable Cox proportional hazard model was performed to determine the factors independently associated with 2-year mortality among patients with SA IE. This model included all variables considered *a priori* to contribute to in-hospital mortality. A multivariable logistic model was also performed to determine the associated factors of SA IE. Likewise, all variables considered *a priori* to contribute to SA IE were included in the multivariable model. The variables with a P value < 0.10 in the bivariate analysis were included in the multivariable models. Both models were built by backward stepwise (likelihood ratio) selection, and IE with TAVR involvement and surgery during IE hospitalisation were forced to remain in the Cox model. We used the Kaplan-Meier method to provide survival estimates, assessed with the use of a log-rank test. Event times were measured from initial IE symptoms to the date of death or last follow-up. Differences in the incidence of

mortality were determined by means of the log-rank test. A 2-sided P value < 0.05 was considered to be statistically significant. Data analyses were performed with the use of Stata (version 15.1; Stata Corp, College Station, TX) and Prism (GraphPad Software, San Diego, CA) software.

Results

Baseline and TAVR procedural characteristics

Definite IE was diagnosed in 604 patients after TAVR, and 31 were excluded for the analysis due to missing data of post-TAVR IE microbiologic etiology. The flowchart of the study population is depicted in Figure 1. SA IE was detected in 141 patients out of the 573 (24.6%), and most of them were associated with methicillin-sensitive SA (115 patients, 81.6%). Baseline and procedural features of the study population grouped according to the microbiological profile (SA IE vs non-SA IE) are presented in Table 1. Underlying comorbidities and surgical risk determined by the logistic EuroSCORE were well balanced in both groups, except for a higher median body mass index in non-SA IE patients (27.2 kg/m^2 [IQR 24.4-30.9] vs 25.6 kg/m^2 [IQR 23.4-28.9]; $P = 0.001$). Although there were no differences regarding the type of valve and IE etiology in the overall cohort, patients presenting early SA IE were more likely to have SEVs (59.4% vs 47.1% in patients with BEVs; $P = 0.041$). TAVR-related complications were more frequent in patients with SA IE compared with non-SA IE, including acute renal failure (19.2% vs 10.4%; $P = 0.005$), stroke (8.5% vs 3.2%; $P = 0.008$), and sepsis (16.3% vs 7.9%; $P = 0.001$). Although the median length of hospital stay was similar in both groups, patients with SA IE presented longer hospitalisations in an acute care facility after TAVR (2 days [IQR 1-5] vs 1.5 days [IQR 1-3]; $P = 0.011$).

Characteristics and outcomes of the index IE episode after TAVR

The features, management, and outcomes of the index IE episode after TAVR, comparing SA IE and non-SA IE are detailed in Table 2. The median time between TAVR and IE diagnosis was lower in SA IE patients (4.7 months [IQR 1.2-13.9] vs 6.3 months [IQR 2.1-14.9]; $P = 0.032$). Although fever was the most common presenting symptom in both groups, patients with SA IE showed higher rates of neurologic manifestations (27.0% vs 15.7%; $P = 0.003$) and systemic embolism (18.4% vs 10.7%; $P = 0.014$) at admission. Health care–associated IE was more frequent in the SA IE group (53.2% vs 40.7%; $P = 0.010$). IE episodes with TAVR prosthesis involvement were more likely in the non-SA IE group (63.4% vs 51.1%; $P = 0.013$), whereas the SA IE group presented a higher proportion of implantable cardiac device (other than TAVR prosthesis) infection (9.2% vs 2.6%; $P = 0.001$). The presence of vegetations as assessed by either transthoracic or transesophageal echocardiography was lower in the SA IE group (53.0% vs 66.3%; $P = 0.006$). Despite the high proportion of patients with unknown infection foci (SA IE 37.6% and non-SA IE 43.5%), SA IE episodes were more likely to be related to TAVR procedures (7.1% vs 3.2%; $P = 0.047$), skin/soft tissue infection (8.5% vs 1.9%; $P < 0.001$), and vascular access (9.2% vs 1.4%; $P < 0.001$), whereas gastrointestinal (SA IE 1.4% vs non-SA IE 8.3%; $P = 0.004$) and odontologic (SA IE 0.7% vs non-SA IE 5.3%; $P = 0.015$) foci were more frequent in the non-SA IE group.

The rate of patients presenting at least 1 IE-related complication during index hospitalisation was higher in the SA IE group (80.7% vs 66.1%; $P = 0.001$). SA IE patients were complicated more frequently with new-onset heart failure (53.3% vs 38.2%; $P = 0.002$), acute renal failure (58.7% vs 35.7%; $P < 0.001$), persistent bacteremia (41.8% vs 26.9%; $P = 0.003$), and septic shock (43.3% vs 22.2%; $P < 0.001$). There was an important variability of antibiotic regimens in both groups, with more than 40 different drug combinations. β-Lactam antibiotics alone were less likely used in SA IE (11.5% vs 25.3%; $P = 0.001$), whereas the use of vancomycin alone or in combination with other antibiotics was similar (SA IE 35.1% vs non-SA IE 27.5%; $P = 0.116$)

There were no differences between groups in surgical management rates (SA IE 21.0% vs non-SA IE 19.5%; $P = 0.694$). In-hospital mortality was substantially higher in the SA IE group (47.8% vs 26.9%; $P < 0.001$).

Factors associated with SA IE

The univariate and multivariate-adjusted logistic models determining the factors associated with SA as a causative microorganism in patients with post-TAVR IE are presented in Supplemental Table S1. The factors independently associated with SA IE were TAVR-related complications such as major bleeding (adjusted odds ratio [OR$_{adj}$] 2.82, 95% confidence interval [CI] 1.24-6.43; $P = 0.013$) and sepsis (OR$_{adj}$: 2.31, 95% CI 1.13-4.72; $P = 0.021$), neurologic symptoms (OR$_{adj}$: 2.16, 95% CI 1.19-3.92; $P = 0.011$), and systemic embolism (OR$_{adj}$: 2.06, 95% CI 1.04-4.08; $P = 0.038$) at IE admission, as well as IE with implantable cardiac devices involvement (other than TAVR) (OR$_{adj}$: 4.50, 95% CI 1.93-10.54; $P = 0.001$). The likelihood of IE due to SA in patients with none of the above-mentioned factors was 19.0% (95% CI 15.2%-23.5%), and it increased to 26.5% (95% CI 20.3%-33.8%), 37.7% (95% CI 26.6%-50.3%), and 84.6% (95% C, 57.8%-95.7%), in the presence of 1, 2 and ≥ 3 factors, respectively (Fig. 2).

Follow-up outcomes

The Kaplan-Meier estimate survival curves at 2-year follow-up comparing patients with SA IE and non-SA IE are shown in Figure 3. The mortality rate was higher in the SA IE group (71.5% vs 49.6%; $P < 0.001$ by log-rank test). The multivariate-adjusted Cox model determining the independent factors associated with follow-up mortality according to microbiologic etiology (non-SA IE vs SA IE) is presented in Figure 4 and Supplemental Table S2. A higher risk profile as determined by the logistic EuroSCORE, the lack of surgical management during the index IE hospitalisation, and IE-related complications such as septic shock and persistent bacteremia determined an increased risk of mortality in patients with SA IE.

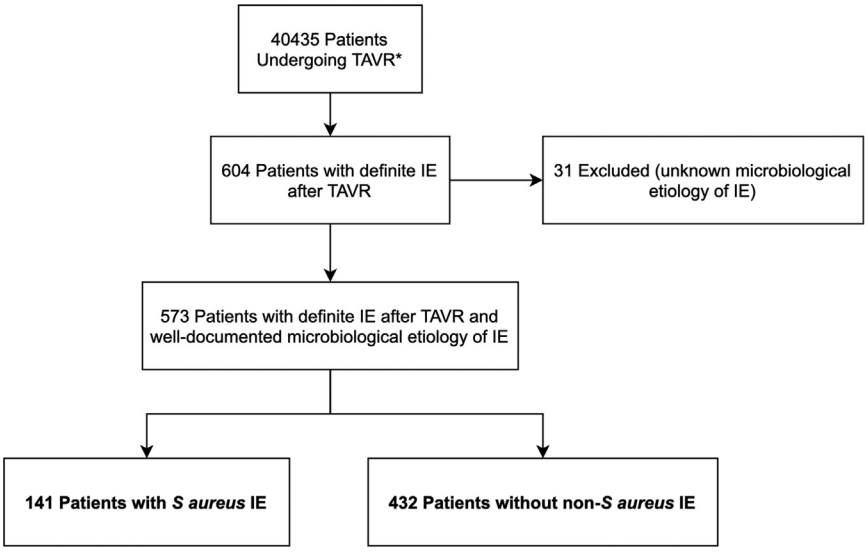

Figure 1. Flow-chart of study population of patients with infective endocarditis (IE) after transcatheter atrial valve replacement (TAVR). * Forty-four centers reported data on the total number of TAVR procedures.

Discussion

The main findings of this study can be summarised as follows: 1) About 25% of cases of IE after TAVR had SA as a causative microorganism; 2) patients with SA IE presented TAVR-related complications (acute renal failure, stroke, major bleeding and sepsis) more frequently and had longer intensive unit care hospitalisations after TAVR; 3) periprocedural TAVR major bleeding or sepsis, neurologic symptoms or systemic embolisms at admission and IE with signs of cardiac device involvement (other than the TAVR prosthesis) were associated with SA IE, and the presence of such factors (particularly in combination) at the index IE hospitalisation determined a high likelihood of SA IE ($>$ 80% in patients with $\geq$ 3 factors); 4) SA IE was associated with a higher incidence of IE-related complications (compared with non-SA IE) and a very high in-hospital (close to 50%) and follow-up ($>$ 70% at 2 years) mortality rates; 5) the lack of surgical management at index IE hospitalisation among SA IE patients determined an increased mortality risk.

PVE is the most severe subtype of IE, representing 10%-30% of all IE cases.[14] The incidence of post-TAVR IE has been previously reported as ranging from 0.6% to 3.4% per year.[1,2,15] Despite the evolution of TAVR over the years with simplified procedures and improved devices, the overall IE incidence remains stable.[4] There are scarce data comparing IE after surgical aortic valve replacement (SAVR) and TAVR. Although most studies reported similar incidence rates,[16,17] a recent study analysing a pooled cohort of 3 randomised clinical trials showed a lower incidence of IE after TAVR compared with SAVR.[18] Of note, the microbiological profile differs between SAVR-IE and TAVR-IE. While enterococci represent only ~10% of SAVR-IE, previous analyses using the same cohort of patients of the present study revealed this microorganism as the leading cause of TAVR-IE.[1,4] Our data showed that TAVR-IE was associated with SA in 1 out of 4 patients. These results are similar to those reported in SAVR-IE registries. However, the proportion of patients presenting with late SA IE after TAVR was slightly higher than those with late SA IE after SAVR.[8] This finding may be related to the particular TAVR patients' profile, leading to more frequent diagnostic and therapeutic invasive procedures during the follow-up period.

The diagnosis of PVE is challenging, and early diagnosis is essential because delayed treatment is associated with worse clinical outcomes.[19-21] This issue is even more relevant in patients with suspected IE after TAVR. First, TAVR recipients represent a particular population with a high comorbidity burden, with patients commonly presenting with atypical symptoms. Previous studies suggest that the modified Duke criteria show a lower diagnostic accuracy for TAVR-IE than native-valve IE, mainly related to a higher incidence of negative blood cultures and inconclusive echocardiographic findings.[1,2] Second, IE after TAVR has been associated with a high incidence of severe IE-related complications and poor outcomes, with a mortality rate at 1-year follow-up close to 50%. To date, no factors associated with SA as a causative microorganism of post-TAVR IE has been identified. Our data show that TAVR complicated by major bleeding or sepsis, the presence of neurologic symptoms or systemic embolism at IE index admission, and signs of infection involving implantable cardiac devices other than the TAVR prosthesis were independently associated with SA IE in TAVR patients. These findings may have important clinical implications as the presence of such factors, particularly in combination, determined a very high likelihood of SA IE ($>$ 80% in patients with $\geq$ 3 risk factors). Thus, in patients presenting with suspected IE after TAVR and exhibiting 2 or more risk factors for SA IE, treatment should be promptly initiated and oriented toward appropriate antibiotic regimens to cover SA while waiting for blood culture results. Further studies are warranted to determine if this strategy translates into a lower rate of IE-related complications and improved clinical outcomes. Importantly, there was no association between the prosthesis type and the overall risk of IE. However, patients presenting early SA IE were more likely to have SEVs than BEVs. This finding may be partially explained by the higher

Table 1. Baseline characteristics, procedural details, and in-hospital TAVR outcomes, according to the causative microorganism (*S. aureus* vs non–*S. aureus*) of IE

	Non–*S. aureus* IE (n = 432)	*S. aureus* IE (n = 141)	Unadjusted *P* value
Baseline characteristics			
Age, years	81 (75-84)	80 (75-84)	0.579
Female	154 (35.7)	58 (41.1)	0.241
Body mass index, kg/m^2	27.2 (24.4-30.9)	25.6 (23.4-28.9)	0.001
Diabetes mellitus	160 (37.0)	54 (38.3)	0.788
COPD	112 (25.9)	44 (31.2)	0.221
Atrial fibrillation	186 (43.1)	56 (39.7)	0.473
Chronic renal failure	173 (40.1)	67 (47.5)	0.162
Previous stroke	61 (14.1)	15 (10.6)	0.290
Previous valve surgery	48 (11.1)	14 (9.9)	0.683
Previous infectious endocarditis	6 (1.4)	3 (2.1)	0.545
Logistic EuroSCORE	14.0 (8-23.4)	13.5 (8.7-21.4)	0.581
Left ventricular ejection fraction, %	54.3 ± 13.1	51.5 ± 14.5	0.067
Mean transaortic gradient, mm Hg	46.0 ± 15.5	41.7 ± 16.0	0.005
Aortic valve area, cm^2	0.73 ± 0.22	0.72 ± 0.25	0.532
Periprocedural characteristics			
Implantation site			0.659
Catheterisation laboratory	181 (41.9)	55 (39.0)	
Operating or hybrid room	251 (58.1)	86 (61.0)	
Approach			0.360
Transfemoral	380 (88.0)	128 (90.9)	
Other	52 (12.0)	13 (9.2)	
Conscious sedation	213 (49.3)	76 (53.9)	0.272
Prosthesis type			0.233
Balloon-expandable	225 (52.1)	73 (51.8)	
Self-expandable	200 (46.3)	65 (46.1)	
Antibiotic prophylaxis			0.613
β-Lactam alone	313 (79.0)	109 (87.2)	
Vancomycin (alone or in combination)	17 (4.3)	4 (3.2)	
In-hospital outcomes (TAVR)			
Acute renal failure	45 (10.4)	27 (19.2)	0.005
Stroke	14 (3.2)	12 (8.5)	0.008
Major vascular complication	25 (5.8)	14 (9.9)	0.082
Major bleeding	34 (7.9)	20 (14.2)	0.023
Sepsis	34 (7.9)	23 (16.3)	0.001
New pacemaker implantation	74 (17.1)	30 (21.3)	0.257
Residual aortic regurgitation > 2 at discharge	63 (14.6)	19 (13.5)	0.839
Length of ICU stay, days	1.5 (1-3)	2 (1-5)	0.011
Length of hospital stay, days	8.5 (6-14)	9 (7-15)	0.060

Values are median (interquartile range), n (%), or mean ± SD.

COPD, chronic obstructive pulmonary disease; ICU, intensive care unit; IE, infective endocarditis; *S. aureus*, *Staphylococcus aureus*; TAVR, transcatheter atrial valve replacement.

proportion of patients receiving a permanent pacemaker after the TAVR procedure in the SEV group than in the BEV group (25.4% vs 10.4%), which might increase the risk of bacteremia and consequently the risk of SA IE.

IE after TAVR has been associated with a poor prognosis and high mortality rate. The present study results also highlight the virulence of SA IE. Patients developing SA IE presented a worse prognosis and higher in-hospital and late mortality rates than those in whom the IE was caused by other microorganisms (47.8% vs 26.9% in-hospital and 71.5% vs 49.6% late mortality). These mortality rates were also substantially higher than those reported in patients presenting surgical prosthetic-valve SA IE, with an in-hospital mortality rate around 35%.[22,23] This difference could be explained in part by the higher baseline risk of TAVR patients because of age and comorbidities, such that any complication would place them at greater risk of mortality than their surgical counterparts. The rate of acute renal failure, acute heart failure, and septic shock during the index hospitalisation in the SA IE group was twice that observed in the non-SA IE group. PVE management involves complex antibiotic regimens along with surgery (valve explantation) in selected patients. Previous studies reported that approximately half of the patients with native- or surgical prosthetic-valve IE secondary to SA undergo surgery during the IE index hospitalisation.[7,24,25] Current guidelines recommend combined and prolonged antibiotic regimens,[9,26] and the results of our study showed a wide variability of antibiotic regimens in patients with SA IE after TAVR. A possible explanation for this finding could be the noteworthy proportion of antimicrobial resistance, renal/hepatic toxicity, and drug interactions in the TAVR population, which could hamper the application of these recommendations in real-world situations. In addition, the rate of surgical intervention in patients with SA IE was particularly low. Although surgical treatment of PVE caused by SA should be

Table 2. Main clinical characteristics, management, and outcomes of IE after TAVR, according to the causative microorganism (*S. aureus* vs non–*S. aureus*)

	Non–*S. aureus* IE (n = 432)	*S. aureus* IE (n = 141)	Unadjusted *P* value
Time from TAVR, months	6.3 (2.1-14.9)	4.7 (1.2-13.9)	0.032
Early IE	291 (67.4)	101 (71.6)	0.379
Late IE	139 (32.2)	40 (28.4)	
Initial symptoms			
Fever	326 (75.5)	116 (82.3)	0.058
New-onset heart failure	171 (39.6)	58 (41.1)	0.602
Neurologic	68 (15.7)	38 (27.0)	0.003
Systemic embolism	46 (10.7)	26 (18.4)	0.014
Cutaneous	17 (3.9)	9 (6.4)	0.213
Health care–associated infection	176 (40.7)	75 (53.2)	0.010
Echocardiographic findings			
Vegetation	279 (66.3)	71 (53.0)	0.006
Vegetation size, mm	10 (6-15)	10 (7-17)	0.298
No TAVR platform affection	158 (36.6)	69 (48.9)	0.013
Periannular complication	83 (24.4)	22 (23.4)	0.840
New aortic regurgitation	54 (14.8)	6 (6.2)	0.025
New mitral regurgitation	63 (17.7)	12 (12.9)	0.274
Structure involved			
Isolated TAVR prosthesis	221 (51.2)	57 (40.4)	0.027
Mitral (native or prosthetic valve)	65 (15.1)	21 (14.9)	0.965
Implantable cardiac device	11 (2.6)	13 (9.2)	0.001
Right-side IE	8 (1.9)	0 (0.0)	0.210
Multiple (≥ 2 localisations)	127 (29.4)	50 (35.5)	0.176
Presumed source of entry			
Unknown	188 (43.5)	53 (37.6)	0.216
TAVR procedure–related	14 (3.2)	10 (7.1)	0.047
Urologic	43 (10.0)	10 (7.1)	0.309
Odontologic	23 (5.3)	1 (0.7)	0.018
Gastrointestinal	36 (8.3)	2 (1.4)	0.004
Pacemaker implantation	8 (1.9)	4 (2.8)	0.478
Skin/soft tissue infection	8 (1.9)	12 (8.5)	< 0.001
Intravascular source	6 (1.4)	13 (9.2)	< 0.001
Other	106 (24.5)	36 (25.5)	0.812
Complications during infective endocarditis hospitalisation			
Any complication	275 (66.1)	109 (80.7)	0.001
Heart failure	159 (38.2)	72 (53.3)	0.002
Acute renal failure	139 (35.7)	74 (58.7)	< 0.001
Septic shock	92 (22.2)	58 (43.3)	< 0.001
Stroke	41 (9.9)	16 (11.9)	0.508
Other systemic embolisation	40 (9.6)	19 (14.2)	0.138
Persistent bacteremia	101 (26.9)	46 (41.8)	0.003
Surgery during IE hospitalisation	82 (19.5)	29 (21.0)	0.694
Time to surgery, days	17 (7-37)	11.5 (5-22)	0.094
Isolated aortic valve replacement	44/77 (57.1)	11/29 (37.9)	0.078
Isolated mitral valve replacement	1/77 (1.3)	2/29 (6.9)	0.121
Isolated cardiac device extraction	7/77 (9.1)	11/29 (37.9)	< 0.001
Combined surgery	25/77 (32.5)	5/29 (17.2)	0.121
Follow-up outcomes			
Follow-up, months*	15.4 (4.8-35.6)	13.1 (3.7-24.3)	0.077
In-hospital mortality	113 (26.9)	66 (47.8)	< 0.001
1-year mortality rate, % (95% CI)	43.7 (38.8-48.9)	62.1 (53.8-70.5)	< 0.001†
2-year mortality rate, % (95% CI)	49.6 (44.5-55.1)	71.5 (62.9-79.7)	< 0.001†
Recurrence of IE, No./total (%)	41/307 (13.4)	7/72 (9.7)	0.312

Values are median (interquartile range) or n (%) unless otherwise specified.

CI, confidence interval; IE, infective endocarditis; *S. aureus*, *Staphylococcus aureus*; TAVR, transcatheter atrial valve replacement.

*Patients who survived the in-hospital period.

†Log-rank test.

considered (if there is a low likelihood of control with the use of antimicrobial therapy), the rate of surgery was similar to that of patients with non-SA IE. Previous studies have failed to demonstrate improved outcomes in patients with TAVR-IE undergoing surgery compared with those treated with antibiotics alone.[27] Importantly, our findings suggest that in patients with SA IE after TAVR, surgery may have a protective effect when adjusting for perioperative mortality risk (logistic EuroSCORE) and severe IE-related complications (acute renal failure, septic shock, persistent bacteremia). Nevertheless, the role of surgical treatment in TAVR patients is still debated and these results should be interpreted with caution. Until recently, a significant proportion of TAVR recipients exhibited absolute contraindications for

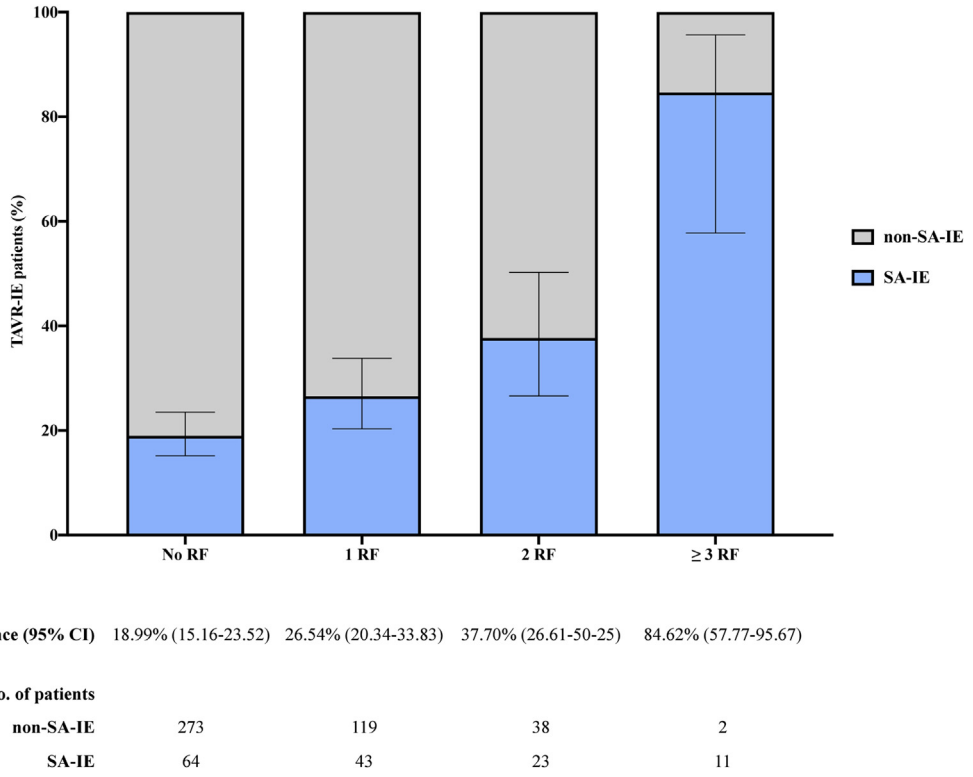

Figure 2. Likelihood of *Staphylococcus aureus* (SA) infective endocarditis (IE) in patients with IE after transcatheter aortic valve replacement (TAVR) according to the presence of associated risk factors (RFs).

surgery. Therefore, universal recommendations of surgery in native- or prosthetic-valve IE could not be extrapolated to TAVR recipients. Nevertheless, the contemporary TAVR patient profile is rapidly changing, with an increasing proportion of low-surgical-risk patients, which could lead to an increased number of TAVR-IE patients undergoing surgery in the coming years. Dedicated studies are crucial to further substantiate our findings and establish surgery indications in TAVR-IE patients.

The population at risk of IE after TAVR is projected to rise exponentially owing to the expansion of this treatment to younger patients with a higher life expectancy. Consequently,

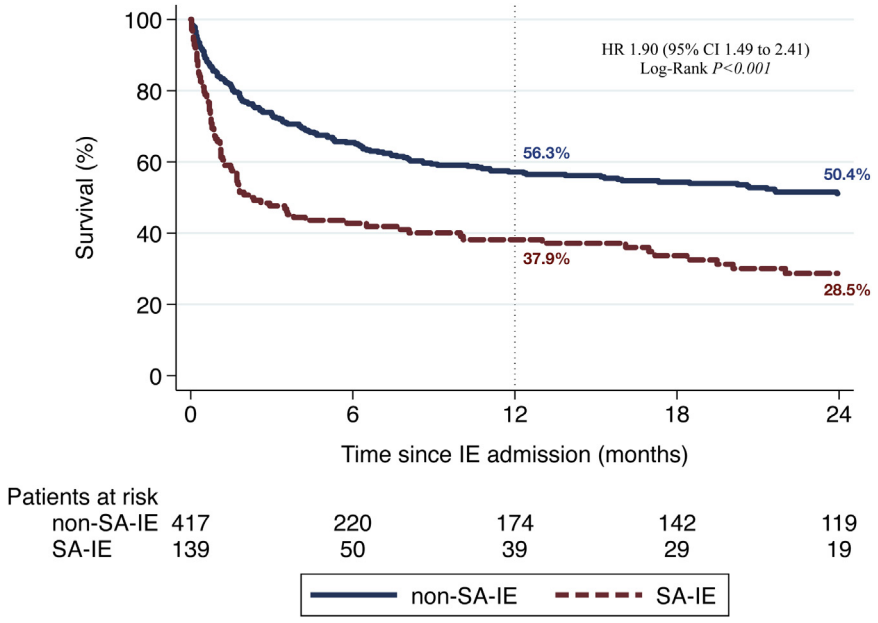

Figure 3. Kaplan-Meier estimated survival curve at 2-year follow-up comparing patients with and without *Staphylococcus aureus* infective endocarditis (SA IE). CI, confidence interval; HR, hazard ratio.

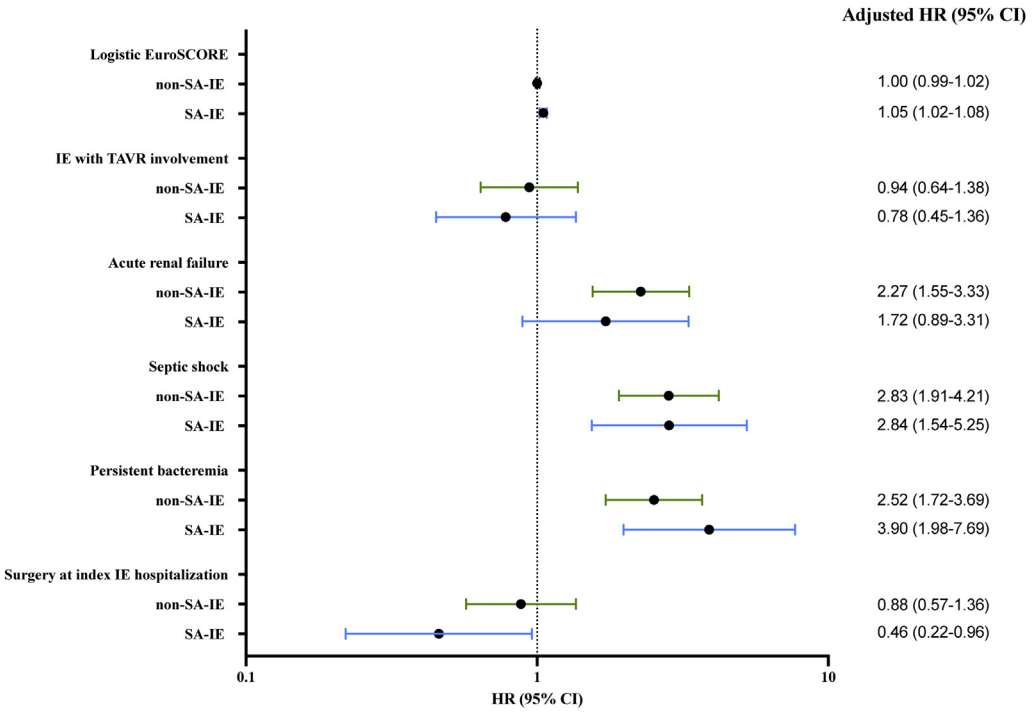

Figure 4. Factors associated with cumulative follow-up mortality in patients with infective endocarditis (IE) comparing *Staphylococcus aureus* (SA) IE and non-SA IE. CI, confidence interval; HR, hazard ratio; TAVR, transcatheter atrial valve replacement.

strategies aimed at limiting the occurrence of IE and improving the clinical outcomes of this population become even more relevant, and prevention should be the cornerstone of this life-threatening disease. First, TAVR should keep moving forward to more simplified (and less invasive) procedures leading to an earlier patient's ambulation and shorter hospital stays. Second, evidence and specific recommendations regarding the most appropriate antimicrobial prophylaxis (in addition to aseptic measures) before some invasive procedures are urgently required. Also, the importance of limiting health care–associated procedures that could potentially trigger a bloodstream infection in this population should be highlighted. Third, novel strategies for SA bacteremia prevention and prosthetic infection would address an important unmet medical need. Device iterations with innovative antibacterial biomaterials that prevent bacteria adhesion to the prosthetic surfaces could become be important to reduce IE in case of bloodstream infection.

Study limitations

The present study has certain limitations. First, it is an observational, retrospective study, with the limitations and potential bias inherent to that design. Centres participated voluntarily and there was no external monitoring committee to assess the accuracy of data reported by each center. Second, this study included patients with definite IE after the TAVR procedure regardless of the structure involved. Our cohort included approximately 60% of patients in whom the TAVR prosthesis involvement was clearly identified. The rest were subjects who had isolated cardiac devices IE (other than TAVR), mitral valve IE, or right-side IE or patients in whom TAVR involvement was not confirmed with the use of conventional imaging techniques. Unfortunately, we were unable to determine if some of these latter patients showed any undetected TAVR involvement. Third, detailed information concerning imaging assessment during the follow-up was not available in most patients.

Conclusion

SA IE after TAVR is a particular life-threatening complication among patients with post-TAVR IE, with a very high in-hospital (~50%, 2 times higher than non-SA IE) and long-term (> 70% at 2 years) mortality. The presence of some features (periprocedural TAVR complications such as major bleeding/sepsis, neurologic symptoms/embolism at index IE, and involvement of cardiac devices other than the TAVR valve) determined a higher likelihood of SA IE. In patients presenting with suspected IE after TAVR, the presence of 2 or more risk factors may prompt an early treatment oriented toward antibiotic regimens to cover SA while waiting for blood culture results. Although the role of surgery has not yet been established in TAVR-IE patients, the results of this study suggest that surgical treatment may have a protective effect in post-TAVR SA IE patients. Further studies are warranted.

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References

1. Regueiro A, Linke A, Latib A, et al. Association between transcatheter aortic valve replacement and subsequent infective endocarditis and in-hospital death. JAMA 2016;316:1083-92.
2. Harding D, Cahill TJ, Redwood SR, Prendergast BD. Infective endocarditis complicating transcatheter aortic valve implantation. Heart 2020;106:493-8.
3. del Val D, Linke A, Abdel-Wahab M, et al. Long-term outcomes after infective endocarditis after transcatheter aortic valve replacement. Circulation 2020;142:1497-9.
4. del Val D, Abdel-Wahab M, Linke A, et al. Temporal trends, characteristics, and outcomes of infective endocarditis after transcatheter aortic valve replacement. Clin Infect Dis 2021;73:e3750-8.
5. Laupland KB, Lyytikäinen O, Søgaard M, et al. The changing epidemiology of *Staphylococcus aureus* bloodstream infection: a multinational population-based surveillance study. Clin Microbiol Infect 2013;19:465-71.
6. Bai AD, Showler A, Burry L, et al. Impact of infectious disease consultation on quality of care, mortality, and length of stay in *Staphylococcus aureus* bacteremia: results from a large multicenter cohort study. Clin Infect Dis 2015;60:1451-61.
7. Murdoch DR, Corey GR, Hoen B, et al. Clinical presentation, etiology and outcome of infective endocarditis in the 21st century: the International Collaboration on Endocarditis—Prospective Cohort Study. Arch Intern Med 2009;169:463-73.
8. Wang A, Athan E, Pappas PA, et al. Contemporary clinical profile and outcome of prosthetic valve endocarditis. JAMA 2007;297:1354-61.
9. Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications: a scientific statement for healthcare professionals from the American Heart Association. Circulation 2015;132:1435-86.
10. Hill EE, Herregods M-C, Vanderschueren S, et al. Management of prosthetic valve infective endocarditis. Am J Cardiol 2008;101:1174-8.
11. Li JS, Sexton DJ, Mick N, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis 2000;30:633-8.
12. Kappetein AP, Head SJ, Généreux P, et al. Updated standardized end point definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. J Am Coll Cardiol 2012;60:1438-54.
13. Friedman ND, Kaye KS, Stout JE, et al. Health care—associated bloodstream infections in adults: a reason to change the accepted definition of community-acquired infections. Ann Intern Med 2002;137:791-7.
14. Habib G, Thuny F, Avierinos J-F. Prosthetic valve endocarditis: current approach and therapeutic options. Prog Cardiovasc Dis 2008;50:274-81.
15. Mentias A, Girotra S, Desai MY, et al. Incidence, predictors, and outcomes of endocarditis after transcatheter aortic valve replacement in the United States. JACC Cardiovasc Interv 2020;13:1973-82.
16. Butt JH, Ihlemann N, de Backer O, et al. Long-term risk of infective endocarditis after transcatheter aortic valve replacement. J Am Coll Cardiol 2019;73:1646-55.
17. Alexis SL, Malik AH, George I, et al. Infective endocarditis after surgical and transcatheter aortic valve replacement: a state of the art review. J Am Heart Assoc 2020;9:e017347.
18. Lanz J, Reardon MJ, Pilgrim T, et al. Incidence and outcomes of infective endocarditis after transcatheter or surgical aortic valve replacement. J Am Heart Assoc 2021;10:e020368.
19. Dickerman SA, Abrutyn E, Barsic B, et al. The relationship between the initiation of antimicrobial therapy and the incidence of stroke in infective endocarditis: an analysis from the ICE Prospective Cohort Study (ICE-PCS). Am Heart J 2007;154:1086-94.
20. Lodise TP, McKinnon PS, Swiderski L, Rybak MJ. Outcomes analysis of delayed antibiotic treatment for hospital-acquired *Staphylococcus aureus bacteremia*. Clin Infect Dis 2003;36:1418-23.
21. Saby L, Laas O, Habib G, et al. Positron emission tomography/computed tomography for diagnosis of prosthetic valve endocarditis. J Am Coll Cardiol 2013;61:2374-82.
22. Fernández Guerrero ML, González López JJ, Goyenechea A, Fraile J, de Górgolas M. Endocarditis caused by *Staphylococcus aureus*: a reappraisal of the epidemiologic, clinical, and pathologic manifestations with analysis of factors determining outcome. Medicine (Baltimore) 2009;88:1-22.

23. Nadji G, Rémadi JP, Coviaux F, et al. Comparison of clinical and morphological characteristics of *Staphylococcus aureus* endocarditis with endocarditis caused by other pathogens. Heart 2005;91:932-7.

24. Tornos P, Iung B, Permanyer-Miralda G, et al. Infective endocarditis in Europe: lessons from the Euro Heart Survey. Heart 2005;91:571-5.

25. Kiefer T, Park L, Tribouilloy C, et al. Association between valvular surgery and mortality among patients with infective endocarditis complicated by heart failure. JAMA 2011;306:2239-47.

26. Habib G, Lancellotti P, Antunes MJ, et al. 2015 ESC guidelines for the management of infective endocarditis: the Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). Eur Heart J 2015;36:3075-128.

27. Mangner N, Leontyev S, Woitek FJ, et al. Cardiac surgery compared with antibiotics only in patients developing infective endocarditis after transcatheter aortic valve replacement. J Am Heart Assoc 2018;7:e010027.

Supplementary Material

To access the supplementary material accompanying this article, visit the online version of the *Canadian Journal of Cardiology* at www.onlinecjc.ca and at https://doi.org/10.1016/j.cjca.2021.10.004.