ORIGINAL ARTICLE

Infective Endocarditis Following Transcatheter Aortic Valve Replacement

Comparison of Balloon- Versus Self-Expandable Valves

Ander Regueiro, MD; Axel Linke, MD; Azeem Latib, MD; Nikolaj Ihlemann, MD; Marina Urena, MD; Thomas Walther, MD; Oliver Husser, MD; Howard C. Herrmann, MD; Luis Nombela-Franco, MD; Asim Cheema, MD; Hervé Le Breton, MD; Stefan Stortecky, MD; Samir Kapadia, MD; Antonio L. Bartorelli, MD; Jan Malte Sinning, MD; Ignacio Amat-Santos, MD, PhD; Antonio J. Munoz-Garcia, MD; Stamatios Lerakis, MD; Enrique Gutiérrez-Ibanes, MD; Mohamed Abdel-Wahab, MD; Didier Tchetche, MD; Luca Testa, MD; Helene Eltchaninoff, MD; Ugolino Livi, MD; Juan Carlos Castillo, MD; Hasan Jilaihawi, MD; John G. Webb, MD; Marco Barbanti, MD; Susheel Kodali, MD; Fabio S. de Brito Jr, MD; Henrique B. Ribeiro, MD; Antonio Miceli, MD; Claudia Fiorina, MD; Guglielmo Mario Actis Dato, MD; Francesco Rosato, MD; Vicenç Serra, MD; Jean-Bernard Masson, MD; Harindra C. Wijeysundera, MD; Jose A. Mangione, MD; Maria-Cristina Ferreira, MD; Valter C. Lima, MD; Luis A. Carvalho, MD; Alexandre Abizaid, MD; Marcos A. Marino, MD; Vinicius Esteves, MD; Julio C.M. Andrea, MD; David Messika-Zeitoun, MD; Dominique Himbert, MD; Won-Keun Kim, MD; Costanza Pellegrini, MD; Vincent Auffret, MD; Fabian Nietlispach, MD; Thomas Pilgrim, MD; Eric Durand, MD; John Lisko, MD; Raj R. Makkar, MD; Pedro Lemos, MD; Martin B. Leon, MD; Rishi Puri, MBBS, PhD; Alberto San Roman, MD; Alec Vahanian, MD; Lars Søndergaard, MD; Norman Mangner, MD; Josep Rodés-Cabau, MD

BACKGROUND: No data exist about the characteristics of infective endocarditis (IE) post-transcatheter aortic valve replacement (TAVR) according to transcatheter valve type. We aimed to determine the incidence, clinical characteristics, and outcomes of patients with IE post-TAVR treated with balloon-expandable valve (BEV) versus self-expanding valve (SEV) systems.

METHODS: Data from the multicenter Infectious Endocarditis After TAVR International Registry was used to compare IE patients with BEV versus SEV.

RESULTS: A total of 245 patients with IE post-TAVR were included (SEV, 47%; BEV, 53%). The timing between TAVR and IE was similar between groups (SEV, 5.5 [1.2–15] months versus BEV, 5.3 [1.7–11.4] months; P=0.89). Enterococcal IE was more frequent in the SEV group (36.5% versus 15.4%; P<0.01), and vegetation location differed according to valve type (stent frame, SEV, 18.6%; BEV, 6.9%; P=0.01; valve leaflet, SEV, 23.9%; BEV, 38.5%; P=0.01). BEV recipients had a higher rate of stroke/systemic embolism (20.0% versus 8.7%, adjusted OR: 2.46, 95% CI: 1.04–5.82, P=0.04). Surgical explant of the transcatheter valve (SEV, 8.7%; BEV, 13.8%; P=0.21), and in-hospital death at the time of IE episode (SEV, 35.6%; BEV, 37.7%; P=0.74) were similar between groups. After a mean follow-up of 13±12 months, 59.1% and 54.6% of the SEV and BEV recipients, respectively, had died (P=0.66).

CONCLUSIONS: The characteristics of IE post-TAVR, including microorganism type, vegetation location, and embolic complications but not early or late mortality, differed according to valve type. These results may help to guide the diagnosis and management of IE and inform future research studies in the field.

VISUAL OVERVIEW: A visual overview is available for this article.

Key Words: endocarditis = incidence = registry = transcatheter aortic valve replacement

Correspondence to: Josep Rodés-Cabau, MD, Quebec Heart & Lung Institute, Laval University, 2725 Chemin Ste-Foy, G1V 4GS, Quebec City, Quebec, Canada. Email josep.rodes@criucpq.ulaval.ca

The Data Supplement is available at https://www.ahajournals.org/doi/suppl/10.1161/CIRCINTERVENTIONS.119.007938.

For Sources of Funding and Disclosures, see page 8.

^{© 2019} American Heart Association, Inc.

Circulation: Cardiovascular Interventions is available at www.ahajournals.org/journal/circinterventions

WHAT IS KNOWN

- The rate of infective endocarditis within the year following transcatheter aortic valve replacement has been reported to be about 1%, similar to infective endocarditis after surgical aortic valve replacement.
- Infective endocarditis following transcatheter aortic valve replacement is associated with very high rates of major complications and death

WHAT THE STUDY ADDS

- Incidence and timing of infective endocarditis is similar irrespective of valve prosthesis type.
- The characteristics of infective endocarditis posttranscatheter aortic valve replacement, including causative organism, vegetation location, and embolic complications differed according to valve type.
- These differences did not translate in different strategies about the management of infective endocarditis complications.

Nonstandard Abbreviations and Acronyms

BEV	balloon-expandable valve
IE	infective endocarditis
SAVR	surgical aortic valve replacement
SEV	self-expanding valve
TAVR	transcatheter aortic valve replacement

Prosthetic valve endocarditis following surgical valve replacement occurs in 1% to 6% of patients and is associated with a high mortality.^{1,2} The risk of infective endocarditis (IE) following valve surgery may be influenced by the type of prosthetic heart valve, and the implantation of bioprosthetic valves has been associated with a higher risk of IE compared with mechanical valves.³ Also, this increased risk seems to occur both early and late (>1 year) after surgical valve replacement.⁴

In recent years, transcatheter aortic valve replacement (TAVR) has become the treatment of choice for patients with severe aortic stenosis who are considered to be at intermediate to increased surgical risk² and is currently expanding towards the treatment of low risk patients.⁵ Similar to surgical aortic valve replacement (SAVR), patients undergoing TAVR are also at risk of IE. In fact, randomized trials have shown similar rates of IE in TAVR and SAVR recipients up to 5-year follow-up^{6,7} Also, IE post-TAVR has been associated with high rates of major complications and death.8 TAVR can be performed with a balloon-expandable valve (BEV) or self-expanding valve (SEV) system. Although both systems have been proven safe and effective for the treatment of aortic stenosis,⁹ differences in the design, preimplantation processing of valve tissues, delivery system and procedural steps

may play a role in the risk and outcomes of IE following TAVR.¹⁰ Therefore, we sought to evaluate the incidence, clinical characteristics, and outcomes of patients with IE post-TAVR treated with BEV versus SEV.

METHODS

The design and details of the Infectious Endocarditis After TAVR International Registry have been reported previously.⁸ Briefly, this was a multicenter study from a total of 47 sites that including patients with definite IE following TAVR. Baseline, periprocedural TAVR features, IE characteristics, and in-hospital and follow-up outcomes were collected in a dedicated database. In addition to the IE cohort, all centers were asked to provide information about the total number of patients who had undergone TAVR but did not had IE (with a minimum follow-up of 1 year). In addition, a total of 31 centers provided individual data on baseline, procedural, and follow-up outcomes for the entire TAVR population. For the purpose of this study, patients with aortic stenosis who were treated with BEV and SEV were compared.

Procedure and Devices

The transcatheter heart valve prosthesis used in the BEV group were Edwards Sapien, Sapien XT, and Sapien 3 valve systems (Edwards Lifescience Corporation, Irvine, CA). The transcatheter heart valve systems used in the SEV group were the Medtronic CoreValve and Evolut R systems (Medtronic, Minneapolis, MN). All patients gave written consent before the procedures, and all studies were performed in accordance to the local ethics committee of each center. Patients were selected for TAVR at the institutional level. TAVR indication and approach were determined after discussion within a multidisciplinary heart team in each center, which also determined the valve type. All TAVR procedures were conducted in accordance with local guidelines using standard techniques.

Definitions and Outcomes

The definition of definite IE was based on the modified Duke criteria.¹¹ Only patients with definite infective endocarditis were included in the registry. Early infective endocarditis, healthcare-associated endocarditis, and persistent bacteremia were defined as previously reported.⁸ Clinical outcomes were defined according to the Valve Academic Research Consortium-2 criteria.¹² Periannular complication was defined as the presence of an intracardiac abscess, pseudoaneurysm, or fistula by transthoracic or transesophageal echocardiography. Systemic embolization was defined as embolism to any major arterial vessel, excluding stroke. Perioperative mortality risk was defined according to the logistic EuroSCORE.¹³

Statistical Analysis

The analysis was performed according to the valve type (BEV versus SEV). Categorical variables were expressed as number (percentage), and continuous data as mean \pm SD or median (interquartile range) depending on their distribution, which was assessed using the Kolmorogov-Smirnov test. Comparison between groups was performed using the *t* test or Wilcoxon

rank-sum test for continuous variables and χ^2 or Fisher exact test for categorical variables. The factors associated with infective endocarditis after TAVR were assessed from a subsample of centers that provided individual data from all patients who had undergone TAVR irrespective of the occurrence of infective endocarditis. The association between (1) causative organisms of infective endocarditis and (2) IE characteristics and in-hospital outcomes after IE, and the type of transcatheter valve was assessed with logistic regression models. The purpose of the multivariable model was to evaluate the association between valve type and IE characteristics within a population of patients that had confirmed IE. The association between valve type and late outcomes (death, recurrent IE) was assessed with hazard proportional models. Selection of variables to control confounding was based on a combination of background knowledge of causal relationships along with statistical association (P<0.1 in the bivariable analysis). Covariates included in multivariable models are described in the Data Supplement. Data analyses were performed using version 14.0 of the STATA statistical software (StataCorp LP). The data that support the findings of this study are available from the corresponding author on reasonable request.

RESULTS

The risk of IE post-TAVR according to the type of valve was evaluated in a subset of 6363 patients (individual study cohort with data available from 31 centers, including 6255 patients [SEV 2719 and BEV 3536] without and 108 patients [SEV 42 and BEV 66] with IE). The cumulative incidence of IE at 1-year post-TAVR was 0.95% in the SEV group versus 1.25% in the BEV group (P=0.33). In the individual study cohort, patients who received a SEV were younger (81.4 versus 81.9 years; P < 0.01), had a higher prevalence of chronic renal failure (49.3% versus 36.3%; P<0.01), chronic pulmonary disease (26.3% versus 20.6%; P<0.01), and prior stroke (15.2% versus 12.6%; P<0.01). TAVR procedure was more frequently performed through a transfemoral approach (92.6% versus 66.3%; P<0.01) in patients receiving a SEV. Rates of stroke and permanent pacemaker implantation after TAVR were higher in patients receiving a SEV (3.5% versus 2.3%; P<0.01 and 21.4% versus 6.5%; P<0.01, respectively; Table I in the Data Supplement).

The study global cohort included 245 patients with definite IE following TAVR; 130 (53.1%) patients were included in the BEV group and 115 (46.9%) in the SEV group. Baseline and periprocedural characteristics according to the type of valve are shown in Table 1. Baseline characteristics were similar between SEV group and BEV groups except for the perioperative mortality risk (Logistic EuroSCORE, SEV: 22.7%, BEV: 18.2%, P=0.01). SEV recipients had received more frequently antibiotic prophylaxis before TAVR (99.1% versus 90.0%; P<0.01), with a more frequent use of beta-lactam antibiotics alone (SEV, 84.6% versus BEV,

Table 1. Baseline Clinical and Procedural Characteristics of Patients With Infective Endocarditis Following Transcatheter Aortic Valve Replacement According to Prosthesis Type

	SEV (n=115)	BEV (n=130)	
Baseline characteristics			
Age, y	77.4 (7.4)	78.5 (12.2)	
Male	76 (66.1)	80 (61.5)	
Diabetes mellitus	39 (33.9)	55 (42.3)	
Chronic renal failure	49 (42.6)	64 (49.2)	
COPD	39 (33.9)	38 (29.2)	
Atrial fibrillation	53 (46.1)	42 (32.3)	
Previous stroke	14 (12.2)	17 (13.1)	
Previous infective endocarditis	2 (1.7)	1 (0.8)	
Logistic EuroSCORE, %	22.7 (15.0)	18.2 (10.8)	
Mean transaortic gradient, mmHg	44.4 (16.1)	45.7 (16.6)	
Left ventricular ejection fraction, %	51.7 (13.8)	53.7 (14.2)	
Procedural characteristics			
Antibiotic prophylaxis	114 (99.1)	117 (90.0)	
β-lactam alone	98 (85.2)	94 (72.3)	
Vancomycin alone	10 (8.7)	5 (3.8)	
Valve implantation site			
Catheterization laboratory	53 (46.1)	54 (41.5)	
Operating or hybrid room	62 (53.9)	76 (58.5)	
Transfemoral approach	112 (97.4)	92 (70.8)	
In-hospital (TAVR) outcomes			
Mean residual transaortic gradient, mmHg	10.7 (7.2)	12.2 (7.8)	
Aortic regurgitation (≥moderate)	19 (16.5)	12 (9.2)	
Stroke	4 (3.5)	8 (6.1)	
Major or life-threatening bleeding	14 (12.2)	13 (10.0)	
Acute kidney injury	19 (16.5)	13 (10.0)	
Permanent pacemaker implantation	35 (30.4)	17 (13.1)	

Data are expressed as No. (%) of patients and mean (SD) unless otherwise indicated. BEV indicates balloon expandable valve; COPD, chronic obstructive pulmonary disease; SEV, self-expanding valve; and TAVR, transcatheter aortic valve replacement.

72.3%; P=0.03). A higher percentage of patients in the SEV group had TAVR through transfemoral approach (97.4% versus 70.8%; P<0.01). Regarding postprocedural complications, the rates of permanent pacemaker implantation was higher in the SEV group (SEV, 30.4%; BEV, 13.1%; P<0.01). There was a tendency toward a higher rate of moderate-severe paravalvular aortic regurgitation in the SEV group (16.2% versus 9.2%; P=0.097).

Clinical characteristics, management, and outcomes of IE after TAVR according to transcatheter valve type are shown in Table 2. The median time between TAVR and the first symptoms of IE, and the rate of early (versus late) IE post-TAVR were similar between groups. There were no differences about initial IE symptoms between groups except for neurological deficit as the initial symptom (SEV, 7.8%; BEV, 24.6%; *P*<0.01;

Unadiusted Adjusted OR*++ Adjusted SEV (n=115) BEV (n=130) P Value (95% CI) P Value Time from TAVR, median (IQR), mo 0.89 5.5 (1.2-15) 5.3 (1.7-11.4) Early post-TAVR endocarditis (<1 y) 78 (68.4) 96 (76.2) 0.18 Initial symptoms 96 (83.5) 100 (76.9) 0.20 Fever 47 (40.9) 51 (39.2) 0.79 Heart failure 9 (7.8) 32 (24.6) 3.01 (1.19-7.68) 0.02 Neurological < 0.01 3 (2.6) 5 (3.8) 0.59 Cutaneous 64 (55.6) 66 (50.8) Healthcare-associated infection 0.45 Exposure to sources of bacteremia before IE Unknown 77 (66.9) 93 (71.5) 0.58 Vascular access/soft tissue infection 11 (9.4) 15 (11.5) 0.68 Gastrointestinal 9 (7.7) 8 (6.1) 0.62 Urologic 8 (6.9) 7 (5.4) 0.62 Odontological 4 (3.4) 5 (3.8) 1.00 Pacemaker implantation 5 (4.3) 3 (2.3) 0.48 Causative organism 42 (36.5) 20 (15.4) 0.37 (0.18-0.79) 0.01 Enterococcus spp < 0.01 31 (27.4) 28 (24.6) 0.62 Staphylococcus aureus 17 (15.0) 29 (25.4) 0.05 2.21 (1.02-4.76) 0.04 Coagulase-negative Staphylococci 7 (6.2) 10 (8.8) 0.461 Viridans streptococci 4 (3.5) 7 (6.1) 0.36 Culture negative Echocardiographic findings Vegetations 79 (68.7) 84 (71.8) 0.54 Transcatheter aortic valve leaflets 27 (23.5) 50 (38.5) 0.01 2.72 (1.21-6.09) 0.02 Transcatheter aortic valve stent 21 (18.6) 9 (6.9) 0.34 (0.11-1.03) 0.06 0.01 Mitral 24 (20.9) 17 (13.1) 0.10 Pacemaker lead 6 (5.2) 1 (0.8) 0.04 0.18 (0.02-1.69) 0.13 3 (2.6) 3 (2.3) 0.94 Tricuspid Periannular complication 14 (12.1) 28 (23.5) 0.02 2.08(0.84 - 5.14)0.11 12 (10.4) 12 (10.3) New aortic regurgitation 0.98 New mitral regurgitation 13 (11.3) 20 (17.1) 0.20 Complications during IE hospitalization Any complication 71 (61.7) 87 (66.9) 0.39 Heart failure 43 (38.7) 42 (34.4) 0.49 Acute kidney injury 51 (45.9) 53 (43.4) 0.70 33 (29.7) 33 (26.8) Septic shock 0.62 Stroke/systemic embolism 10 (8.7) 26 (20.0) 0.01 2.46 (1.04-5.82) 0.04 6 (5.4) 18 (14.7) 0.06 0.02 2.95 (0.98-8.90) Stroke 5 (4.5) 17 (13.8) 0.01 2.77 (0.94-8.18) 0.06 Systemic embolism 22 (19.1) 29 (22.3) 0.74 Persistent bacteremia Management and in-hospital outcomes Surgery during IE hospitalization 14 (12.1) 22 (16.9) 0.29 Surgical transcatheter valve explantation 10 (8.7) 18 (13.8) 0.21 Transcatheter valve-in-valve procedure 3 (2.6) 0 0.06 Isolated pacemaker extraction 5 (4.3) 1 (0.8) 0.07

Table 2. Clinical Characteristics, Management, and Outcomes of Patients With Infective Endocarditis Posttranscatheter Aortic Valve Replacement According to Prosthesis Type

(Continued)

Table 2. Continued

	SEV (n=115)	BEV (n=130)	Unadjusted <i>P</i> Value	Adjusted OR*†‡ (95% Cl)	Adjusted <i>P</i> Value		
In-hospital death	41 (35.6)	49 (37.7)	0.74				
Follow-up outcomes							
Median follow-up post-IE, mean (SD), mo	10.6 (4.2–20.8)	8.0 (2.6–15.9)	0.20		-		
Recurrent IE	7 (7.7)	10 (8.4)	0.82				
Death at follow-up	27 (36.5)	22 (27.2)	0.21				
Cumulative death	68 (59.1)	71 (54.6)	0.66				

Data are expressed as No. (%) of patients and mean (SD) unless otherwise indicated. BEV indicates balloon-expandable valve; IE, infective endocarditis; IQR, interquartile range; OR, odds ratio; SEV, self-expanding valve; and TAVR, transcatheter valve aortic replacement.

*SEV as reference.

+For recurrent IE, death at follow-up, and cumulative death, the adjusted analyses are presented as hazard ratio with 95% CI.

*Multivariable models are described in the Data Supplement.

adjusted OR, 3.01; 95% CI, 1.19-7.68; P=0.02). Whereas there were no differences between groups in the exposure to sources of bacteremia (including the rate of healthcare-associated infection), significant differences were observed regarding the causative microorganism. The incidence of enterococcus spp. as the causative organism of IE was higher in patients with a SEV prosthesis (SEV, 36.5%; BEV, 15.4%; P<0.01), and coagulase-negative Staphylococci were more frequently encountered among BEV recipients (SEV, 15.0%; BEV, 25.4%; P=0.05). After adjusting for confounding factors, the association between BEV-IE and the causative organism remained significant for enterococcus spp. (OR, 0.37; 95% CI, 0.18-0.79; P=0.01) and coagulase-negative staphylococci (OR, 2.21; 95% Cl, 1.02-4.76; P=0.04). Echocardiography findings revealed that the presence of vegetations anchored to the stent frame was more frequent in SEV recipients (SEV, 18.6%; BEV, 6.9%; P=0.01), whereas vegetations at the valve-leaflet level were more frequent among BEV recipients (SEV, 23.5%; BEV, 38.5%; P=0.01; Figure 1). Differences in vegetation location remained significant after adjusting for baseline and procedural differences between groups for the presence of vegetations attached at valve leaflets (OR, 2.72; 95% Cl, 1.21-6.09; P=0.02) and borderline for vegetations attached at the stent frame (OR, 0.34; 95% CI, 0.11-1.03; *P*=0.06).

The incidence of IE complications was similarly high in both groups, but BEV patients exhibited a higher rate of stroke/systemic embolism complications (SEV, 8.7%; BEV, 20.0%; P=0.01). These differences remained significant after adjusting for after adjusting for baseline/procedural differences between groups (OR, 2.46%; 95% CI, 1.04-5.82; P=0.04). Patients in the BEV group had a higher rate of periannular complications (SEV, 12.1%; BEV, 23.5%; P=0.02), but these differences were no longer significant after adjusting for baseline/procedural confounders (OR, 2.08; 95% Cl, 0.84-5.15; P=0.11). The rate of surgery during IE hospitalization was similar between groups (SEV, 12.1%; BEV, 16.9%; P=0.29) and there were no differences between groups in the valve explant rate during the IE episode.

In-hospital death occurred in 90 (36.7%) cases. The multivariable analysis for determining the factors associated with in-hospital mortality is shown in the Table II in the Data Supplement). Patients who died in the hospital were more likely to have a higher logistic EuroSCORE (OR, 1.02%; 95% CI, 1.00–1.06), and higher rates of heart failure (OR, 2.79%; 95% CI, 1.42–5.49) and renal failure during index hospitalization (OR, 2.79%; 95% CI,



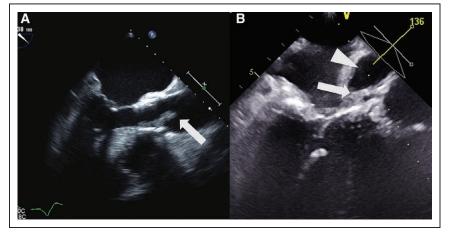


Figure 1. Transesophageal echocardiogram images of transcatheter aortic valve vegetations.

Transesophageal echocardiography images from 2 different patients (left ventricular outflow tract view) showing the presence of a large vegetation (white arrow) at the level of the valve leaflet of a balloon-expandable transcatheter valve (**A**) or stent frame of a self-expanding transcatheter valve (**B**) with a large periannular abscess (white arrowhead).

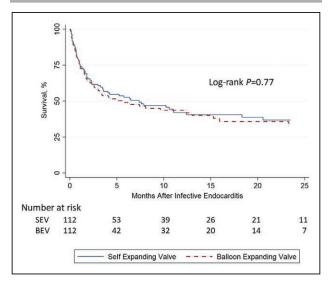


Figure 2. Survival curve for patients with infective endocarditis following transcatheter aortic valve replacement (TAVR) according to the type of valve.

Kaplan-Meier survival curve during the 24-month follow-up after infective endocarditis following TAVR according to the type of implanted valve. BEV indicates balloon-expandable valve; and SEV, self-expanding valve.

1.42–5.49). In-hospital death rates during IE index hospitalization were similar between both types of valves (SEV, 35.6%; BEV, 37.7%; P=0.74).

After a mean follow-up of 13 ± 12 months, 49 patients had died and 17 patients had recurrent IE, with no differences between groups. The Kaplan-Meier survival curves up to 24 months post-TAVR according to valve type are shown in Figure 2.

DISCUSSION

The results of the present study comparing IE post-TAVR in SEV versus BEV recipients can be summarized as follows: (1) the incidence and timing of IE was similar between groups, (ii) both groups exhibited a similar exposure to different sources of bacteremia but causative microorganisms differed, with enterococcus and coagulase-negative Staphylococcus being more frequent in SEV and BEV recipients, respectively, (3) vegetation location also differed between groups, with vegetations attached to the stent frame being more frequently seen in SEV patients, (4) overall complication and death rates were similarly high in both groups, but stroke/systemic embolism events occurred in up to one-fifth of BEV patients, a much higher rate compared with their SEV counterparts, (5) there were no differences between groups regarding IE management (surgical explant of the transcatheter valve was low, <15%, in both groups) and mortality rates at midterm follow-up.

Previous reports including a small number of patients suggested a higher risk of IE following TAVR in patients receiving a SEV (as compared with BEV).¹⁴ The results

of the present study showed that the risk of IE in patients undergoing TAVR was similar irrespective of the type of valve. These results are in accordance with prior studies that have evaluated the incidence of IE at 1-year follow-up after TAVR with BEV (0.6% at 1 year),⁶ and SEV (0.6% at 1 year).⁷

The rate of enterococcal IE among SEV recipients was as much as twice the one that was observed in BEV recipients. Differences in baseline characteristics or procedural outcomes could partially explain these differences, but the risk of enterococcal IE for SEV recipients remained higher even after adjusting for possible confounders that included baseline and TAVR procedural characteristics. Patients with enterococcal IE are usually older and have more comorbidities and a higher rate of healthcare-associated IE.15,16 Although the mean age was similar between SEV and BEV patients, SEV patients included in the present study had a higher logistic EuroSCORE, which indicates a higher comorbidity burden in this group. Also, the proportion of patients undergoing transfemoral TAVR with a SEV was higher than those receiving a BEV, and the use of femoral catheters has been recognized as a risk for enterococcal bacteremia.¹⁷ Finally, patients in the SEV group had a higher rate of permanent pacemaker implantation following TAVR and exhibited longer hospitalization times compared with BEV patients. On the contrary, the most frequently encountered pathogens in BEV patients were Staphylococcus aureus and coagulase-negative Staphylococci, similar to early IE following surgical prosthetic valve IE.¹⁸

Echocardiographic characteristics also differed according to transcatheter valve type. Although the proportion of patients with vegetations was similar between groups, SEV recipients had the vegetation more frequently attached to the stent frame of the valve system. On the contrary, the proportion of patients with vegetation attached to the valve leaflet was higher in the BEV group. Differences in transcatheter prosthesis valve design may explain these differences, in particular, the much larger stent frame of SEVs that could act as an anchor during bacteremia. Although the differences were not statistically significant, patients who received a SEV had a higher proportion of vegetations attached to the mitral valve, probably related to a higher prevalence of previous valve surgery in this group. Similarly, the percentage of vegetations attached to a pacemaker lead was higher in the SEV group, which could be partially explained by the higher rate of permanent pacemaker implantation after TAVR observed in this group. On the contrary, the proportion of periannular complications was higher (nonadjusted analysis) in patients with BEV when compared with the SEV group. The mechanism could be related to the different delivery technique as BEV implantation could cause greater tissue damage secondary to balloon dilatation during prosthetic

valve deployment. Another possible explanation may be related to the longer valve stent frame among SEV recipients, which could impede a proper visualization of the aortic annulus in some cases.

Neurological complications occur in ≈25% of patients with left-sided native IE.19 Patients with IE caused by S. aureus and the presence of large vegetations increase the risk of neurological events.²⁰ In the present study, patients who received a BEV presented more frequently with neurological symptoms as the initial manifestation of IE and had a higher rate of stroke and systemic embolism during the index hospitalization for IE post-TAVR. Differences in vegetation size and location may have contributed to this difference, and further studies including a larger number of patients are needed to confirm these findings regarding such an important complication of IE. In addition, possible confounders such as peripheral vascular disease may have had an influence in stroke rates. The confirmation of these findings may influence the management of IE post-TAVR, with a more aggressive approach (eg, valve explant) among patients with IE post-BEV implantation. Despite of these differences in neurological complications, the overall rate of complications and mortality were similarly high (>60% for overall complications; >35% for in-hospital death) in both groups.

Valve explant remains the treatment of choice in prosthetic valve endocarditis in the presence of IE complications.²¹ Early surgery has been reported in close to 50% of patients diagnosed with prosthetic valve endocarditis postsurgical aortic valve replacement.^{18,22} In our study, surgery rates and valve explantation were similarly low (<17%) in BEV and SEV recipients, despite a high rate of IE complications. This may be explained by the advanced age and high risk profile of TAVR candidates. Surgical explantation technique of a transcatheter aortic valve prosthesis may vary according to the time from the implant and the type of prosthesis. Late surgical extraction of a SEV can be challenging because of the degree of endothelial ingrowth within the valve stent cells,²³ and the number of valve explants tended to be lower (but not statistically significant) in SEV recipients (8.6% versus 13.8% in the BEV group). However, the relatively low number of patients who underwent valve explanation may explain the lack of differences between groups. Future studies should further evaluate the potential influence of transcatheter valve characteristics on the rates of valve explantation following IE.

Study Limitations

Several limitations of the present study warrant further consideration including its nonrandomized and retrospective analysis design. First, there was no external monitoring or event adjudication committee to verify the accuracy of the data reported by each center. Second, data from the entire population of patients without IE were not available and comparisons between groups were performed within a population of patients who had confirmed IE. Third, information on baseline characteristics such as peripheral vascular disease and on the amount and distribution of aortic valve calcification, preand post-dilatation during TAVR were not available, as these factors may have influenced the rates of stroke, location of vegetation,²⁴ and the occurrence of periannular complications.

Conclusions

This study provides novel and clinical relevant information about the differences between transcatheter valve prosthesis in patients suffering from IE post-TAVR. The characteristics of IE post-TAVR, including causative organism, vegetation location, and embolic complications but not early or late mortality, differed according to valve type. However, these differences did not translate into different strategies regarding the management (valve explantation) of IE complications. These results may help to guide the diagnosis and management of IE and inform future research studies in the field.

ARTICLE INFORMATION

Received February 20, 2019; accepted August 13, 2019.

Affiliations

Quebec Heart & Lung Institute, Laval University, Quebec City, Canada (A.R., R.P., J.R.-C.). Heart Center, Leipzig University, Germany (A.L., N.M.). Interventional Cardiology Unit, Ospedale San Raffaele, Milan, Italy (A.L.). Righospitalet, Copenhagen, Denmark (N.I., L.S.). Bichat Hôpital, Paris, France (M.U., D.M.-Z., D.H., A.V.). Kerckhoff Klinik, Nauheim, Germany (T.W., W.-K.K.). Deutsches Herzzentrum, München, Germany (O.H., C.P.). Hospital of the University of Pennsylvania, Philadelphia (H.C.H.). Cardiovascular Institute, Hospital Universitario Clinico San Carlos, Madrid, Spain (L.N.-F.). Division of Cardiology, St. Michaels Hospital, Toronto, Canada (A.C.). Centre Hospitalier Universitaire de Rennes, France (H.L.B., V.A.). Bern University Hospital (on behalf of Swiss Registry Centres), Switzerland (S.S., T.P.). Cleveland Clinic (S.K.). Centro Cardiologico Monzino, Milan, Italy (A.L.B.). Heart Center Bonn, Germany (J.M.S.). Hospital Clinico Universitario de Valladolid, Spain (I.A.-S., A.S.R.). Department of Cardiology, Hospital Universitario Virgen de la Victoria, Malaga, Spain (A.M.-G.). Emory University School of Medicine, Atlanta (S.L., J.L.). Department of Cardiology, Instituto de Investigación Sanitaria Gregorio Marañon, Hospital Gregorio Maranon, Madrid, Spain (E.G.-I.). Heart Center, Bad Segeberg, Germany (M.A.-W.). Clinique Pasteur, Toulouse, France (D.T.). IRCCS Pol. San Donato, Milan, Italy (L.T.). Hôpital Charles Nicolle, University of Rouen, France (H.E., E.D.). AOU Santa Maria della Misericordia, Udine, Italy (U.L.). Department of Cardiology, Hospital Universitario Reina Sofia, Cordoba, Spain (J.C.). Cedars-Sinai Heart Institute, Los Angeles (H.J., R.R.M.). Center for Heart Valve Innovation, St. Pauls Hospital, Vancouver, Canada (J.G.W.). Ferrarotto Hospital, Catania, Italy (M.B.). Columbia University Medical Center, New York (S.K., M.B.L.). Hospital Israelita Albert Einstein, Sao Paulo, Brazil (F.S.d.B.). Instituto Nacional Cardiovascular (INCOR), Sao Paulo, Brazil (H.B.R., P.L.). Fondazione Toscana G. Monasterio, Massa, Italy (A.M.). Ospedali Civili di Brescia, Italy (C.F.). Ospedali Mauriziano, Torino, Italy (G.M.A.D.). S. Cocre e Carle Cuneo, Italy (F.R.). Hospital Vall d'Hebron, Barcelona, Spain (V.S.). Centre Hospitalier de l'Universite de Montreal, Canada (J.-B.M.). Sunnybrook Health Science Center, Toronto, Canada (H.C.W.). Hospital Beneficencia Portuguesa, Sao Paulo, Brazil (J.A.M.). Hospital Naval Marcilio Dias, Rio de Janeiro, Brazil (M.-C.F.). Hospital Sao Francisco-Santa Clara, Porto Alegre, Brazil (V.C.L.). Hospital Pró-cardíaco, Rio de Janeiro, Brazil (L.A.C.). Instituto Dante Pazzanese de Cardiologia, Sao Paulo, Brazil (A.A.). Hospital Madre Teresa, Belo Horizonte, Brazil (M.A.M.). Hospital Sao Luiz, Sao Paulo, Brazil (V.E.). Clínica Sao Vicente, Rio de Janeiro, Brazil (J.C.M.A.). University Hospital Zurich, Switzerland (F.N.).

Sources of Funding

None.

Disclosures

Dr Josep Rodés-Cabau has received institutional research grants from Edwards Lifesciences and Medtronic. Dr Tchetche has reported to receive consulting fees from Abbott Vascular, Boston Scientific, Edwards Lifesciencies, and Medtronic. Dr Webb has reported that he has received consulting fees from Edwards Lifesciences and St. Jude Medical. Dr Makkar has reported that he has received research grants from Edwards Lifesciences, Medtronic, Abbott, Capricor, and St. Jude Medical; has served as a proctor for Edwards Lifesciences; and has received consulting fees from Medtronic. Dr Kodali has reported that he has received consulting fees from Edwards Lifesciences; has served on the steering committees of Edwards Lifesciences and St. Jude Medical; has served on the Speakers' Bureau of Thubrikar Aortic Valve, Inc; and has equity in Thubrikar Aortic Valve. Dr Tamburino has reported that he has received support from Edwards Lifesciences, Abbott, and CardioKinetics; Dr Jilaihawi has reported that he has received consulting fees from Edwards Lifesciences, St. Jude Medical, and Venus Medtech. Dr de Brito has reported that he has received honoraria from Medtronic and Edwards Lifesciences for symposium speeches and proctoring cases. Dr Lerakis has reported that he has received consulting fees from Edwards Lifesciences. Dr Nietlispach has reported that he has received speaker and proctor fees from Abbott Vascular, Edwards Lifesciences and Medtronic. Dr Leon has reported that he has received research grants for clinical trials from Edwards Lifesciences. The other authors report no conflicts.

REFERENCES

- Akowuah EF, Davies W, Oliver S, Stephens J, Riaz I, Zadik P, Cooper G. Prosthetic valve endocarditis: early and late outcome following medical or surgical treatment. *Heart.* 2003;89:269–272. doi: 10.1136/heart.89.3.269
- Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, lung B, Lancellotti P, Lansac E, Rodriguez Muñoz D, et al; ESC Scientific Document Group. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J.* 2017;38:2739–2791. doi: 10.1093/eurheartj/ehx391
- Brennan JM, Edwards FH, Zhao Y, O'Brien S, Booth ME, Dokholyan RS, Douglas PS, Peterson ED; DEcIDE AVR (Developing Evidence to Inform Decisions about Effectiveness-Aortic Valve Replacement) Research Team. Long-term safety and effectiveness of mechanical versus biologic aortic valve prostheses in older patients: results from the society of thoracic surgeons adult cardiac surgery national database. *Circulation*. 2013;127:1647– 1655. doi: 10.1161/CIRCULATIONAHA.113.002003
- Glaser N, Jackson V, Holzmann MJ, Franco-Cereceda A, Sartipy U. Prosthetic valve endocarditis after surgical aortic valve replacement. *Circulation*. 2017;136:329–331. doi: 10.1161/CIRCULATIONAHA.117.028783
- Kolte D, Vlahakes GJ, Palacios IF, Sakhuja R, Passeri JJ, Inglessis I, Elmariah S. Transcatheter versus surgical aortic valve replacement in low-risk patients. J Am Coll Cardiol. 2019;74:1532–1540. doi: 10.1016/j.jacc.2019.06.076
- Mack MJ, Leon MB, Smith CR, Miller DC, Moses JW, Tuzcu EM, Webb JG, Douglas PS, Anderson WN, Blackstone EH, et al; PARTNER 1 Trial Investigators. 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial. *Lancet.* 2015;385:2477–2484. doi: 10.1016/S0140-6736(15)60308-7
- Gleason TG, Reardon MJ, Popma JJ, Deeb GM, Yakubov SJ, Lee JS, Kleiman NS, Chetcuti S, Hermiller JB Jr, Heiser J, et al; CoreValve U.S. Pivotal High Risk Trial Clinical Investigators. 5-year outcomes of self-expanding transcatheter versus surgical aortic valve replacement in high-risk patients. J Am Coll Cardiol. 2018;72:2687–2696. doi: 10.1016/j.jacc.2018.08.2146
- Regueiro A, Linke A, Latib A, Ihlemann N, Urena M, Walther T, Husser O, Herrmann HC, Nombela-Franco L, Cheema AN, et al. Association between transcatheter aortic valve replacement and subsequent infective endocarditis and in-hospital death. *JAMA*. 2016;316:1083–1092. doi: 10.1001/jama.2016.12347
- Abdel-Wahab M, Mehilli J, Frerker C, Neumann FJ, Kurz T, Tölg R, Zachow D, Guerra E, Massberg S, Schäfer U, et al; CHOICE Investigators. Comparison of balloon-expandable vs self-expandable valves in patients undergoing transcatheter aortic valve replacement: the CHOICE randomized clinical trial. JAMA. 2014;311:1503–1514. doi: 10.1001/jama.2014.3316

- Chamandi C, Puri R, Rodriguez-Gabella T, Rodés-Cabau J. Latest-generation transcatheter aortic valve replacement devices and procedures. *Can J Cardiol.* 2017;33:1082–1090. doi: 10.1016/j.cjca.2017.03.012
- Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG Jr, Ryan T, Bashore T, Corey GR. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. *Clin Infect Dis.* 2000;30:633–638. doi: 10.1086/313753
- Kappetein AP, Head SJ, Généreux P, Piazza N, van Mieghem NM, Blackstone EH, Brott TG, Cohen DJ, Cutlip DE, van Es GA, et al. Updated standardized endpoint definitions for transcatheter aortic valve implantation: the Valve Academic Research Consortium-2 consensus document. J Am Coll Cardiol. 2012;60:1438–1454. doi: 10.1016/j.jacc.2012.09.001
- Roques F, Michel P, Goldstone AR, Nashef SA. The logistic EuroSCORE. Eur Heart J. 2003;24:881–882. doi: 10.1016/s0195-668x(02)00799-6
- Amat-Santos IJ, Messika-Zeitoun D, Eltchaninoff H, Kapadia S, Lerakis S, Cheema AN, Gutiérrez-Ibanes E, Munoz-Garcia AJ, Pan M, Webb JG, et al. Infective endocarditis after transcatheter aortic valve implantation: results from a large multicenter registry. *Circulation*. 2015;131:1566–1574. doi: 10.1161/CIRCULATIONAHA.114.014089
- Pericás JM, Zboromyrska Y, Cervera C, Castañeda X, Almela M, Garcia-de-la-Maria C, Mestres C, Falces C, Quintana E, Ninot S, et al. Enterococcal endocarditis revisited. *Future Microbiol.* 2015;10:1215–1240. doi: 10.2217/fmb.15.46
- 16. Chirouze C, Athan E, Alla F, Chu VH, Ralph Corey G, Selton-Suty C, Erpelding ML, Miro JM, Olaison L, Hoen B; International Collaboration on Endocarditis Study Group. Enterococcal endocarditis in the beginning of the 21st century: analysis from the International Collaboration on Endocarditis-Prospective Cohort Study. *Clin Microbiol Infect.* 2013;19:1140–1147. doi: 10.1111/1469-0691.12166
- Raad II, Hanna HA, Boktour M, Jabbour N, Hachem RY, Darouiche RO. Catheter-related vancomycin-resistant Enterococcus faecium bacteremia: clinical and molecular epidemiology. *Infect Control Hosp Epidemiol.* 2005;26:658– 661. doi: 10.1086/502598
- Wang A, Athan E, Pappas PA, Fowler VG Jr, Olaison L, Paré C, Almirante B, Muñoz P, Rizzi M, Naber C, et al; International Collaboration on Endocarditis-Prospective Cohort Study Investigators. Contemporary clinical profile and outcome of prosthetic valve endocarditis. *JAMA*. 2007;297:1354–1361. doi: 10.1001/jama.297.12.1354
- Heiro M, Nikoskelainen J, Engblom E, Kotilainen E, Marttila R, Kotilainen P. Neurologic manifestations of infective endocarditis: a 17-year experience in a teaching hospital in Finland. *Arch Intern Med.* 2000;160:2781–2787. doi: 10.1001/archinte.160.18.2781
- 20. García-Cabrera E, Fernández-Hidalgo N, Almirante B, Ivanova-Georgieva R, Noureddine M, Plata A, Lomas JM, Gálvez-Acebal J, Hidalgo-Tenorio C, Ruíz-Morales J, et al; Group for the Study of Cardiovascular Infections of the Andalusian Society of Infectious Diseases; Spanish Network for Research in Infectious Diseases. Neurological complications of infective endocarditis: risk factors, outcome, and impact of cardiac surgery: a multicenter observational study. *Circulation*. 2013;127:2272–2284. doi: 10.1161/CIRCULATIONAHA.112.000813
- 21. Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP III, Guyton RA, O'Gara PT, Ruiz CE, Skubas NJ, Sorajja P, et al; ACC/AHA Task Force Members. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129:2440–2492. doi: 10.1161/CIR.000000000000029
- Lalani T, Chu VH, Park LP, Cecchi E, Corey GR, Durante-Mangoni E, Fowler VG, Jr, Gordon D, Grossi P, Hannan M, et al; International Collaboration on Endocarditis-Prospective Cohort Study Investigators. Inhospital and 1-year mortality in patients undergoing early surgery for prosthetic valve endocarditis. *JAMA Intern Med.* 2013;173:1495–1504. doi: 10.1001/jamainternmed.2013.8203
- Mangi AA, Ramchandani M, Reardon M. Surgical removal and replacement of chronically implanted transcatheter aortic prostheses: how i teach it. *Ann Thorac Surg.* 2018;105:12–14. doi: 10.1016/j.athoracsur. 2017.08.015
- Pressman GS, Rodriguez-Ziccardi M, Gartman CH, Obasare E, Melendres E, Arguello V, Bhalla V. Mitral annular calcification as a possible nidus for endocarditis: a descriptive series with bacteriological differences noted. J Am Soc Echocardiogr. 2017;30:572–578. doi: 10.1016/j.echo. 2017.01.016