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MAJOR ARTICLE

Infective Endocarditis After Transcatheter versus Surgical Aortic Valve Replacement

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Background: Scarce data are available comparing infective endocarditis (IE) following surgical aortic valve replacement (SAVR) and transcatheter aortic valve replacement (TAVR). This study aimed to compare the clinical presentation, microbiological profile, management, and outcomes of IE after SAVR vs. TAVR.

Methods: Data were collected from the “Infectious Endocarditis after TAVR International” (enrollment from 2005 to 2020) and the “International Collaboration on Endocarditis” enrollment from 2000 to 2012) registries. Only patients with an IE affecting the aortic valve prosthesis were included. A 1:1 paired matching approach was used to compare patients with TAVR and SAVR.

Results: A total of 1688 patients were included. Of them, 602 (35.7%) had a surgical bioprosthesis (SB), 666 (39.5%) a mechanical prosthesis, 70 (4.2%) a homograft, and 350 (20.7%) a transcatheter heart valve. In the SAVR vs. TAVR matched population, the rate of new moderate or severe aortic regurgitation was higher in the SB group (43.4% vs. 13.4%, $p<0.001$), and fewer vegetations were diagnosed in the SB group (62.5% vs. 82%, $p<0.001$). Patients with a SB had a higher rate of perivalvular extension (47.9% vs.27%, $p<0.001$) and *Staphylococcus Aureus* was less common in this group (13.4% vs. 22%, $p=0.033$). Despite a higher rate of surgery in patients with SB (44.4% vs. 26.8%, $p<0.001$), 1-year mortality was similar (SB: 46.5%, TAVR: 44.8%, log-rank $p=0.697$).

Conclusions: Clinical presentation, type of causative microorganism and treatment differed between patients with an IE located on SB compared to TAVR. Despite these differences, both groups exhibited high and similar mortality at 1-year follow-up.

KEYWORDS: Infective endocarditis, TAVR, SAVR, heart surgery, prognosis.

ABBREVIATIONS LIST

IE: infective endocarditis

IQR: interquartile range

PVE: prosthetic valve endocarditis

SAVR: surgical aortic valve replacement

SB: surgical bioprosthesis

TAVR: transcatheter aortic valve replacement

THV: trans-catheter heart valve

INTRODUCTION

Transcatheter aortic valve replacement (TAVR) has revolutionized the treatment of severe aortic valve stenosis over the past decade [1,2]. In recent years, there has been a notable shift in the preference for TAVR over surgical aortic valve replacement (SAVR), with an increasing number of patients, including those at low surgical risk. One could expect that a less invasive procedure such as TAVR would be associated with a lower rate of infective complications compared to SAVR. However, randomized trials showed similar annual rates of infective endocarditis (IE) following SAVR and TAVR [3,4]. Also, patients treated with TAVR have a different profile, as they have more co-morbid and frail conditions than those undergoing SAVR. Furthermore, some post-procedural complications which are more frequently observed in patients with TAVR such as the need for permanent pacemaker implantation may predispose to bacterial infections over time. Lastly, the specific design of the transcatheter heart valve (THV) with a stent frame and a high amount of metal around the valve may also influence the presentation, management, and outcomes of these patients. Differences in IE presentations after surgical versus percutaneous procedures may help to better understand their pathophysiology and define the most appropriate preventive measures and management. The evolving landscape and changing trend reflect the need for comprehensive research comparing these populations. We therefore sought to compare the clinical presentation, microbiological profile, management, and outcomes of IE after SAVR versus TAVR.

METHODS

Study population

Data were collected from two registries: “The Infectious Endocarditis after TAVR International Registry” and the “International Collaboration on Endocarditis (ICE) registry”. Details of the design of these registries have been previously reported [5,6].

The “Infectious Endocarditis after TAVR International Registry” included data from 604 patients with definite IE determined by the modified Duke criteria after TAVR from 59 centers in 11 countries across Europe, North America, and South America between June 2005 and November 2020 (**Figure 1**). A dedicated uniform database was used at all sites. Informed consent was obtained before the procedure and the individual anonymized data sharing was performed according to the local ethics committee of each participating center.

The ICE Prospective Cohort Study (ICE-PCS) database contains prospective data on 5,591 patients with definite and possible IE collected between 1st January 2000 and 31st December 2006. The

ICE-Plus database contains prospective data on 2,124 patients with IE collected between 1st September 2008 and 31st December 2012. Overall, sites from 30 countries participated in both cohorts. Data for each patient were collected prospectively on a standardized case report form by site investigators. Both databases are maintained at the Duke University School of Medicine, which serves as the coordinating center for the ICE studies, and approvals were obtained from the institutional review boards of the Duke University School of Medicine. Only 1,338 patients with a prosthetic valve endocarditis located on the aortic valve were included in this study.

Study definitions

The definition of definite IE was based on the modified Duke criteria [7]. Outcomes were defined according to the Valve Academic Research Consortium-2 criteria [8]. Persistent bacteremia was defined as positive blood cultures despite appropriate antibiotic therapy for > 7 days. Early IE was defined as IE occurring within 1-year after surgery according to the European guidelines [7].

Statistical analysis

Categorical variables were expressed as absolute number and percentages. Continuous variables were expressed as mean (SD) or medians (interquartile range [IQR]) for normal and non-normal distributions, respectively. Differences between groups were assessed using the χ^2 test, Fisher exact test, Student t-test, or Mann-Whitney U test, as appropriate. A 1:1 paired matching approach was used (between patients treated with SAVR and TAVR) to create comparable populations based on different baseline variables. By using this approach, we aimed to balance the distribution of covariates between two groups reducing potential confounding factors and making the population more comparable. The following variables were included for matching: age, sex, diabetes, chronic renal failure, and previous IE episode. Patients were selected by 1:1 matching without replacement using the nearest neighbor method. A caliper width of 0.2 of the pooled standard deviation of logit propensity scores was used for matching. The balance of the distribution of the baseline characteristics between the 2 groups was assessed by evaluating the absolute standardized differences. The risk of all-cause 1-year mortality was evaluated with the use of logistic regressions. The multivariable analysis was performed using all significant variables in univariable analyses ($p < 0.05$). Kaplan-Meier survival curves were compared using log-rank test. Statistical significance was 2-sided for all comparisons, and a $p < 0.05$ was considered significant. Stata v.15.0 (College Station, TX) was used for all analyses.

RESULTS

Study population baseline characteristics

A total of 1688 patients were included (**Figure 1**). IE involved a SB, a mechanical prosthesis, a homograft, or a THV in 602 (35.7%), 666 (39.5%), 70 (4.2%), and 350 (20.7%) patients, respectively. The baseline characteristics of the population are presented in **Table 1**. Patients with IE located on a mechanical valve, or a homograft were younger (64.6 years IQR [53.2-72.9] and 50.2 years IQR [38-64.9] respectively) compared to those with a SB or a THV (73.8 years IQR [66.1-78.5] and 80 years IQR [74.6-84] respectively), $p < 0.001$. Patients with IE on the THV had more comorbidities (chronic obstructive pulmonary disease, cerebrovascular disease, and chronic kidney disease) compared with the remaining groups. A previous IE episode was more frequent in patients with SB (20.0%), mechanical valve (20.6%) and homograft (51.4%), compared to patients post-TAVR (1.4%). IE after TAVR affected respectively 159 (45.4%) and 191 (54.6%) self and auto-expandable THV. The mean STS score of patients before TAVR was 7.2 (SD: 6.5).

Infective endocarditis episode

Early IE (≤ 12 months) was more frequently found in patients after TAVR (65.3%) than in patients with SB (40.8%), mechanical prosthesis (41.5%) or homograft (50.0%) ($p < 0.001$). The rate of new moderate or severe aortic regurgitation was higher in SB (39.4%), mechanical valve (36.3%), and homograft (63.8%) compared to patients with a THV (15.7%). However, the presence of a vegetation was more common in patients with IE post-TAVR (83.4%) compared to patients with SB (62%), mechanical valve (60.2%) or homograft (68.6%) ($p < 0.001$). Perivalvular extension was also more prevalent in patients with IE following SAVR (bioprosthesis: 38.8%, mechanical valve: 35.4%, homograft: 39.4%) compared to patients with IE post TAVR (26.0%) ($p < 0.001$). The main causative micro-organism was coagulase negative staphylococci (19.4%) in the SB population, *Staphylococcus aureus* (21.2%) in the mechanical valve population, *Streptococcus viridans* (28.6%) in the homograft population, and enterococcus species in the THV group (24.7%). Clinical presentation was characterized by a lower incidence of stroke and systemic embolism but more heart failure episodes and persistent positive blood cultures in the TAVR group compared to the patients who had SAVR.

Outcomes

During the index endocarditis hospitalization, patients with an infected SB, mechanical valve or homograft had more frequent cardiac surgery (46.5%, 44.2%, 49.3%, respectively) than those with an infected THV (24%) ($p < 0.001$). Before propensity match adjustment, in-hospital mortality ($p = 0.006$) and 1-year all-cause mortality was higher in patients after TAVR compared to SAVR (log-rank $p = 0.0002$) (**Figure 2**).

Propensity matched cohorts

The main characteristics and outcomes of the propensity matched cohorts (SB and THV) are shown in **Table 2**. After matching, early IE was more frequent after TAVR than in patients with a SB (64.8% vs. 44.8%, $p=0.006$). IE episodes ≤ 3 months were similar between groups ($p=0.374$). Patients with a SB had higher rates of moderate or severe aortic regurgitation (43.4% vs. 13.5%, $p<0.001$). Perivalvular extension was also more frequent in patients with a SB (47.9%) compared to THV (27%), $p<0.001$. Causative microorganisms were similar except for a higher incidence of *Staphylococcus aureus* in the THV group (13.4% vs. 22%, $p=0.03$). Patients with IE on a SB had a higher rate of stroke (16.6% vs. 8.9%, $p=0.023$) compared to TAVR-IE patients. Despite a higher rate of patients managed surgically in the SB group (44.4% vs. 26.8%, $p<0.001$), patients with a SB had a similar in-hospital (38.0 vs. 31.8%, $p=0.196$) and 1-year estimated mortality (46.5% vs. 44.8%, log-rank $p=0.697$) compared to patients with a THV (**Figure 3**). After matching, the THV cohort consisted of 93 (46.5%) patients who received a self-expandable THV and 107 (53.5%) patients with an auto expandable THV. The rate of moderate to severe aortic regurgitation was similar between these prostheses: 15.1% patients with self-expandable THV vs. 12.3% with auto expandable THV ($p=0.549$). Mean STS score of the TAVR cohort was 6.1 (SD: 5.8). A description of early IE cohort in the propensity matched population ($n=156$) is available in **Supplemental Table 1** and show similar results except for comparable rate of perivalvular extension between the two populations. The description of a matched mechanical valve population ($n=130$) and THV population ($n=130$) is available in **Supplemental Table 2**. These matched cohorts exhibit comparable disparities in terms of aortic regurgitation, peri-annular damage, vegetation, rates of surgical intervention, and comparable mortality echoing the findings observed between the matched SB and THV cohorts.

Patients treated with surgery

A description of the surgically treated patients in the matched population is available in the **Supplemental Table 3**. Among patients undergoing surgical therapy for IE, intracardiac complications were more common in both SB and THV group, respectively: new moderate or severe aortic regurgitation (55.8% and 28.3%, $p=0.002$), intracardiac vegetation (69.8% and 90.6%, $p=0.004$), perivalvular extension (67.4% and 43.4%, $p=0.005$) and heart failure (51.7% and 62.3%, $p=0.636$). Among this subgroup of surgically treated patients, the most frequent causative organism was coagulase negative staphylococcus (40.8%) in patients with SB and enterococcus species in the THV group (24.8%). Death after surgery was high in both SAVR and TAVR groups (42.5% and 32.7% respectively, $p=0.250$).

Factors associated with death

In the propensity-matched cohort, factors associated with one year mortality in the TAVR population were: perivalvular extension (ORadj: 1.73 95% CI (1.04-2.87), $p=0.035$), heart failure during IE hospitalization (ORadj: 2.50 95% CI (1.50-4.14), $p<0.001$), stroke (ORadj: 2.61 95% CI (1.22-5.61), $p=0.014$) and persistent bacteremia (ORadj: 3.68 95% CI (2.04-6.64), $p<0.001$) (**Table 3**). Factors associated with 1-year mortality in the SB population were: heart failure during

IE hospitalization (ORadj: 2.26 95% CI (1.17-4.35), p=0.015) and stroke (ORadj: 3.32 95% CI (1.34-8.19), p=0.015) (**Table 4**).

DISCUSSION

The main findings of this study including 1688 patients with an IE after surgical or transcatheter aortic valve replacement are: (i) clinical presentation of the IE episode, causative microorganism and in-hospital complications differed between different aortic valve prostheses; (ii) after paired matching on baseline characteristics, a higher rate of perivalvular extension and new moderate or severe aortic regurgitation was found in the SB group compared to the THV group along with a higher rate of *Staphylococcus aureus* in the THV group; (iii) in-hospital complications and treatment strategies differed between the matched surgical and transcatheter groups; (iv) in-hospital and 1-year mortality were high and similar in both groups.

Clinical presentation

Numerous studies have investigated factors associated with the occurrence of IE in patients after TAVR [9], and compared the incidence of IE in SAVR vs TAVR [10–12]. However, this study is the first to provide a description of the differences that can be seen in clinical presentation among aortic valves implanted surgically or catheter-based. The number of patients with early IE was higher in patients after TAVR compared to patients with SAVR. This finding may be related to a higher risk of health-care associated IE. A previous work has shown a worrying prevalence of IE ≤ 30 days after TAVR [13]. The resistance of causative microorganisms to the antibiotic prophylaxis regimen has been described and could be a potential explanation [13,14]. Interestingly, in the early IE subgroup of the matched population, fewer perivalvular extension (26.9%) were found in patients with SB compared with the global matched cohort merging early and late IE (47.9%). This finding suggests a higher incidence of this complication in patients with SB with late IE. Nevertheless, in this same sub-population, the rate of aortic regurgitation was higher in the SB group and outcomes remained similar between groups. However, caution must be taken concerning these findings given the number of missing data surrounding the timing of the IE episode in patients after SAVR.

The rate of moderate or severe newly diagnosed aortic regurgitation and perivalvular extension differed substantially between subgroups. Indeed, these aortic valve and aorta root complications were higher in SAVR compared to TAVR. These findings may be related to a greater vulnerability of the periaortic structures in patients after SAVR. The surgical manipulation of the aortic tissues and the sutures may explain this susceptibility to the infection. Since differences in the timing of the IE episode have been noticed, this factor could also have influenced the occurrence of these complications. Given the severe impact on the prognosis of perivalvular extension in both surgical valves [15] and THV [16], a better understanding of these differences is of clinical interest.

Patients with an IE on the aortic THV presented with a higher rate of vegetations than patients with SB. The stent frame of the THV could be more favorable for vegetation development than bioprosthetic leaflets. THV endocarditis has been reported to be more obstructive than others [17]. This can be related to the more frequently observed vegetations in this subgroup. Paradoxically, the rate of stroke or systemic embolism was lower in TAVR recipients. A previous work investigating stroke episodes in patients with IE after TAVR suggested that the low rate of embolic events in the TAVR population may be related to the misleading clinical presentation of such events in an elderly and highly comorbid population [18]. Also, vegetations at the level of the stent valve frame may be less prone to systemic embolization than those on valve leaflets. Specific studies with routine cerebrovascular imaging techniques and a precise description of the vegetations are warranted to better investigate these findings.

Causative microorganisms

The causative bacteria implicated in the IE are usually related to the presumed source of entry. The various profile of patients receiving different aortic valves may explain the heterogeneity of causative microorganisms in our population. After adjustment for baseline characteristics, the microbiological profile was similar in the matched cohorts, except for a predominance of *Staphylococcus aureus* in the THV group compared to SB. Del Val et al. found that several factors were associated with *Staphylococcus aureus* IE after TAVR: major bleeding, sepsis complicating TAVR, neurological symptoms or systemic embolism at admission and IE with cardiac device involvement [19]. Therefore, the higher rate of *Staphylococcus aureus* may be related to the higher risk of diagnostic and therapeutic invasive procedures after TAVR-related complications. Interestingly, the rate of enterococcus was similar in both groups after propensity matching suggesting that the high observed rate of this bacteria in TAVR series [20] is probably related the patient's frailty rather than the TAVR procedure itself.

Choice of treatment and outcomes

Cardiac surgery was performed in nearly half of the patients after SAVR, and this was in accordance with the results previously described in the literature [21,22]. The role of surgery in native valve IE has been well investigated and clear recommendations have been established in this setting [23]. However, in the presence of a prosthetic valve, the role of cardiac surgery compared to medical therapy alone has been more controversial [22,24]. In our study, after adjusting for age, sex and comorbidities, patients with a SB were more prone to have surgery to remove the infected material than patients with a THV. These discrepancies may be related to the aforementioned differences in clinical presentation. Indeed, patients with SB had more aortic root complications and embolic episodes with an indication for surgery compared to patients with a THV. The only indication for surgery that was predominant in the THV group was persistent bacteremia in blood cultures. The persistence of bacteremia despite an effective antibiotic therapy can be related to antibiotic resistance or the greater capability of biofilm formation on THV prostheses. However, it is important to consider the impact of the matching process on our findings.

Given the predominance of elderly and potentially frail patients in the TAVR-IE group, similar characteristics were selected in the SB group. Consequently, it is unsurprising that the outcomes including those related to surgical intervention were similar between groups. While our study underlines the high mortality associated with endocarditis, these results do not reflect the overall mortality of SB recipients or patients treated with surgery in a broader sense. Therefore, the impact of our matching process does not allow us to draw definitive conclusions regarding the role of surgery in patients prognosis.

Limitations

This study has some limitations. Due to the retrospective design of the TAVR registry, some data were not available. It is important to acknowledge the temporal disparity between the two cohorts included in this study. The ICE cohort encompasses data collected from 2000 to 2012 while the other cohort included data from 2005 to 2020. This substantial time gap introduces the potential for variations in diagnosis and management patterns over time. Consequently, these differences could introduce time-related bias which may affect the generalizability and interpretation of our findings. Numerous patients had missing data concerning the timing of the IE episode and the hypotheses surrounding this point of interest remain therefore largely uncertain. Scarce data are available about imaging modalities used to define each diagnosis and the differences observed may result from difference in imaging methods. Another limitation could be the primary cause of aortic valve replacement that was not captured in our study and could have influenced our findings. Lastly, due to its multicenter design, diagnosis and treatment modalities of patients may have been different between participating centers.

CONCLUSION

This study underlines differences in clinical presentation, microbiology, complications, treatment, and outcomes of the infectious episode in various transcatheter and surgical aortic valves. After propensity matching, the main differences were the higher rate of valve dysfunction and perivalvular extension in the patients with SAVR and the predominance of *Staphylococcus aureus* in TAVR patients. Despite a higher rate of cardiac surgery in patients with SAVR, their 1-year prognosis was similar compared to their TAVR counterparts. These differences observed suggest that the IE episode characteristics are largely influenced by the type and the method of aortic valve replacement.

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DATA AVAILABILITY STATEMENT: The data that support the findings of this study are available from the corresponding author, upon reasonable request.

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Table 1: Baseline characteristics, infective endocarditis description and outcomes in the whole population.

Variable	Bioprosthesi s N= 602 (35.7%)	Mechanical prosthesis N= 666 (39.5%)	Homograft N= 70 (4.2%)	THV N= 350 (20.7%)	p-value
Demography					
Europe, n (%)	291 (49.7)	365 (56.7)	30 (42.9)	287 (82.5)	
North America, n (%)	65 (11.1)	54 (8.4)	10 (14.3)	50 (14.3)	
South America, n (%)	120 (20.5)	82 (12.7)	6 (8.6)	11 (3.1)	<0.001
Asia/Mid East, n (%)	11 (1.9)	32 (5.0)	4 (5.7)	0 (0)	
Australia / New Zealand / Africa, n (%)	98 (16.8)	111 (17.2)	20 (28.6)	0 (0)	
Baseline characteristics					
Year of the episode, median (IQR)	2006 (2003-2009)	2005 (2003-2009)	2005 (2002-2006)	2015 (2013-2017)	
Age, median (IQR)	73.8 (66.1-78.5)	64.6 (53.2-72.9)	50.2 (38-64.9)	80 (74.6-84)	<0.001
Sex (Male), n (%)	429 (71.6)	494 (74.3)	52 (74.3)	237 (67.7)	0.162
Chronic obstructive pulmonary disease, n (%)	70 (18.4)	48 (12.3)	0 (0)	95 (27.1)	<0.001
Cerebrovascular disease, n (%)	33 (8.6)	48 (12.3)	0 (0)	47 (13.4)	0.050
Diabetes mellitus, n (%)	124 (21.1)	141 (21.6)	16 (24.6)	123 (35.1)	<0.001
Mild to severe renal insufficiency	67 (18.0)	58 (15.9)	4 (16.0)	162 (46.7)	<0.001

Previous IE episode, n (%)	119 (20.0)	136 (20.6)	36 (51.4)	5 (1.4)	<0.001
Timing of the IE episode					
Month between prosthesis implantation and IE, mean (SD)	50.8 (59.5)	48.7 (63.1)	38.9 (55.6)	12.3 (14.5)	<0.001
Early IE (≤ 12 months), n (%)	80/196 (40.8)	76/183 (41.5)	13/26 (50)	228/349 (65.3)	<0.001
IE ≤ 3 months, n (%)	37/196 (18.9)	38/183 (20.8)	7/26 (26.9)	102/349 (29.2)	0.029
Echocardiographic findings					
Mitral valve involvement, n (%)	93 (16.1)	145 (22.4)	7 (10.6)	49 (14.0)	0.001
New moderate or severe aortic regurgitation, n (%)	232 (39.4)	238 (36.3)	44 (63.8)	55 (15.7)	<0.001
Intracardiac vegetation, n (%)	362 (62.0)	393 (60.2)	48 (68.6)	292 (83.4)	<0.001
Perivalvular extension	227 (38.8)	233 (35.4)	26 (39.4)	91 (26.0)	0.001
Abscess, n (%)	222 (38.9)	226 (35.6)	22 (33.9)	75 (21.4)	<0.001
Fistula, n (%)	30 (5.0)	30 (4.5)	3 (4.3)	6 (1.7)	0.087
Nosocomial, n (%)	171 (30.4)	148 (24.1)	7 (10.8)	145 (41.4)	<0.001
Causative micro-organism					
<i>Staphylococcus aureus</i> , n (%)	85 (15.2)	129 (21.2)	12 (19.1)	71 (20.3)	0.058
Coagulase-negative staphylococci, n (%)	108 (19.4)	85 (14.0)	7 (11.1)	67 (19.1)	0.032
<i>Streptococcus Viridans</i> , n (%)	83 (14.9)	66 (10.9)	18 (28.6)	47 (14.0)	0.001
<i>Streptococcus bovis</i> , n (%)	42 (7.5)	48 (7.9)	1 (1.6)	13 (3.9)	0.029
Other streptococci, n (%)	31 (5.6)	28 (4.6)	2 (3.2)	14 (4.2)	0.704
Enterococci, n (%)	105 (18.2)	92 (15.1)	8 (12.7)	83 (24.7)	0.002
In hospital complications					
Fever, n (%)	473 (86.0)	559 (89.0)	51 (83.6)	264 (77.0)	<0.001
Stroke, n (%)	83 (14.0)	119 (18.1)	8 (11.8)	31 (9.3)	0.001
Systemic embolism, n (%)	96 (16.2)	92 (14.1)	17 (24.6)	39 (11.8)	0.031
Heart failure, n (%)	210 (35.9)	186 (28.4)	26 (38.2)	152 (45.8)	<0.001

Persistent positive blood cultures, n (%)	52 (9.1)	51 (8.3)	7 (10.3)	103 (33.9)	<0.001
Treatment / outcomes					
In-hospital surgical therapy (%)	275 (46.5)	293 (44.2)	34 (49.3)	82 (24.0)	<0.001
In-hospital death (%)	154 (25.9)	153 (23.0)	13 (18.6)	110 (32.5)	0.006
One-year mortality (%)	206 (41.1)	194 (35.7)	23 (36.5)	155 (44.3)	0.062
Estimated one-year mortality (95% CI)	37.0 (33.1-41.2)	31.4 (27.8-35.2)	34.5 (24.4-47.3)	47.4 (42.1-53.1)	0.0002*

*by log-rank test

Table 2: Baseline characteristics, infective endocarditis description and outcomes after propensity matching of the SB and the THV cohorts.

Variable	SB N= 200	THV N=200	p-value
Baseline characteristics			
Age, mean (SD)	75.8 (7.6)	76.3 (8.1)	0.570
Sex (Male), n (%)	135 (67.5)	138 (69.0)	0.747
Chronic obstructive pulmonary disease, n (%)	37 (19.1)	54 (27.0)	0.062
Cerebrovascular disease, n (%)	20 (10.3)	24 (12.0)	0.594
Diabetes mellitus, n (%)	54 (27.0)	57 (28.5)	0.738
Mild to severe renal insufficiency	42 (21.0)	41 (20.5)	0.902
Previous IE episode, n (%)	6 (3.0)	5 (2.5)	0.760
Timing of the IE episode			
Month between prosthesis implantation and IE	50.8 (59.5)	12.3 (14.5)	<0.001
Early IE (≤ 12 months), n (%)	26/58 (44.8)	130/199 (64.8)	0.005
IE ≤ 3 months, n (%)	14/58 (24.1)	60/199 (29.7)	0.374
Echocardiographic findings			
Mitral valve involvement, n (%)	35 (18.4)	29 (14.5)	0.296
New moderate or severe aortic regurgitation, n (%)	86 (43.4)	27 (13.5)	<0.001
Intracardiac vegetation, n (%)	120 (62.5)	164 (82.0)	<0.001

Perivalvular extension	92 (47.9)	54 (27.0)	<0.001
Abscess, n (%)	91 (47.4)	44 (22.0)	<0.001
Fistula, n (%)	19 (9.5)	4 (2.0)	0.001
Nosocomial, n (%)	74 (39.2)	75 (37.5)	0.737
Causative micro-organism			
Staphylococcus aureus, n (%)	24 (13.4)	44 (22.0)	0.030
Coagulase-negative staphylococci, n (%)	39 (21.8)	35 (17.5)	0.293
<i>Streptococcus Viridans</i> , n (%)	27 (15.1)	24 (12.5)	0.470
<i>Streptococcus bovis</i> , n (%)	9 (5.0)	9 (4.7)	0.879
Other streptococci, n (%)	14 (7.8)	10 (5.2)	0.307
Enterococci, n (%)	38 (21.2)	44 (22.9)	0.695
In hospital complications			
Fever, n (%)	169 (84.5)	156 (80.4)	0.286
Stroke, n (%)	33 (16.6)	17 (8.9)	0.023
Systemic embolism, n (%)	30 (15.3)	23 (12.1)	0.361
Heart failure, n (%)	84 (42.6)	86 (45.0)	0.636
Persistent positive blood cultures, n (%)	21 (10.9)	57 (32.5)	<0.001
Treatment / outcomes			
In-hospital surgical therapy (%)	87 (44.4)	53 (27.3)	<0.001
In-hospital death (%)	76 (38.0)	62 (31.8)	0.196
One-year mortality (%)	93 (46.5)	82 (41.0)	0.268
Estimated one-year mortality (95% CI)	46.5 (39.9-53.7)	44.8 (37.9-52.4)	0.696*

* by log-rank test

Table 3: Univariate and multivariate analysis of factors associated with 1-year mortality in the THV matched-population (only variables with a p-value <0.2 are displayed).

	Unadjusted Odds ratios	Unadjusted <i>p</i>-value	Adjusted Odds Ratios	Adjusted <i>p</i>-value
Baseline characteristics				
Age	1.02 (0.99-1.05)	0.120		
Male sex	0.64 (0.42-0.98)	0.042	0.67 (0.40-1.14)	0.140
Chronic obstructive pulmonary disease	0.78 (0.49-1.26)	0.318		

Mild to severe renal insufficiency	1.51 (0.93-2.45)	0.098		
Echocardiographic findings				
Mitral valve involvement	2.01 (1.17-3.47)	0.012	1.20 (0.63-2.29)	0.584
New moderate or severe aortic regurgitation	1.46 (0.94-2.26)	0.089		
Intracardiac vegetation	1.70 (1.08-2.69)	0.022	1.34 (0.74-2.42)	0.340
Perivalvular extension	1.74 (1.15-2.64)	0.009	1.73 (1.04-2.87)	0.035
Causative microorganisms				
<i>Staphylococcus aureus</i>	2.12 (1.23-3.63)	0.007	1.25 (0.64-2.43)	0.340
<i>Streptococcus bovis</i>	0.34 (0.11-1.07)	0.065		
Complications during IE hospitalization				
Heart failure	2.63 (1.74-3.98)	<0.001	2.50 (1.50-4.14)	<0.001
Stroke	2.70 (1.46-4.99)	0.001	2.61 (1.22-5.61)	0.014
Systemic embolism	2.12 (1.18-3.81)	0.012	1.65 (0.79-3.47)	0.186
Persistent bacteremia	3.76 (2.21-6.40)	<0.001	3.68 (2.04-6.64)	<0.001

Table 4 – Univariate and multivariate analysis of factors associated with one year mortality in the SB matched-population (only variable with a p-value <0.2 are displayed).

	Unadjusted Odds ratios	Unadjusted p-value	Adjusted Odds Ratios	Adjusted p-value
Baseline characteristics				
Age	1.03 (0.99-1.07)	0.098		
Male sex	0.65 (0.36-1.17)	0.149		
Echocardiographic findings				
Mitral valve involvement	2.02 (0.96-4.27)	0.065		

Intracardiac vegetation	1.90 (1.05-3.46)	0.034	1.50 (0.76-2.95)	0.245
Perivalvular extension	1.57 (0.88-2.78)	0.128		
Causative microorganisms				
<i>Staphylococcus aureus</i>	2.56 (1.03-6.33)	0.042	2.06 (0.79-5.41)	0.140
Complications during IE hospitalization				
Heart failure	2.07 (1.16-3.67)	0.013	2.26 (1.17-4.35)	0.015
Stroke	3.23 (1.45-7.22)	0.004	3.32 (1.34-8.19)	0.009
Systemic embolism	2.01 (0.91-4.43)	0.085		
Persistent bacteremia	2.10 (0.83-5.33)	0.118		

Figure 1: Study flowchart

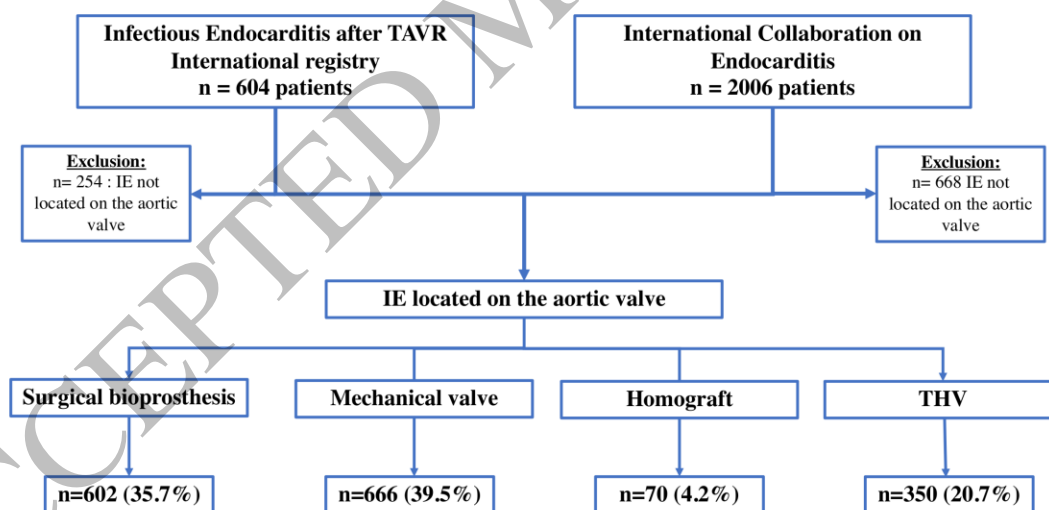


Figure 2: Kaplan-Meier curves comparing survival stratified into the type of valve in the whole population.

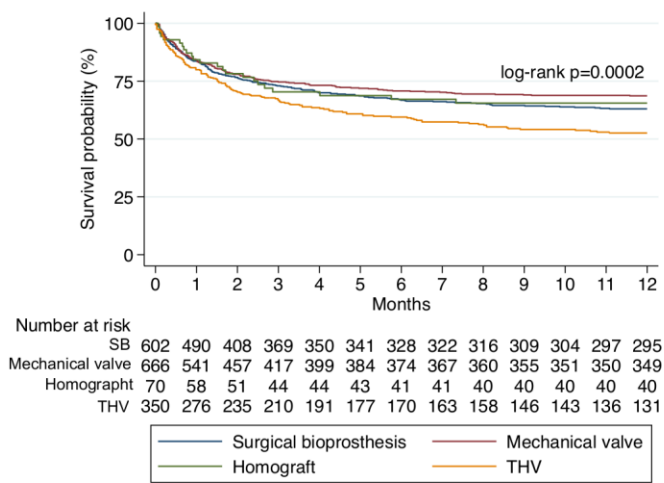


Figure 3: Kaplan-Meier curves comparing survival stratified into the type of valve in the propensity-matched population.

