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European Journal of Cardio-thoracic Surgery 37 (2010) 1025—1032

EUROPEAN JOURNAL OF CARDIO-THORACIC SURGERY

www.elsevier.com/locate/ejcts

Aortic valve replacement for active infective endocarditis: 5-year survival comparison of bioprostheses, homografts and mechanical prostheses☆

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Received 20 August 2009; received in revised form 15 November 2009; accepted 17 November 2009; Available online 29 December 2009

Abstract

Objective: In the surgical treatment of acute aortic valve infective endocarditis (IE), the long-term outcome depending on the choice of valve replacement remains uncertain. We aimed to compare the impact on 5-year mortality of use of three types of implanted valves: bioprosthesis (heterograft), mechanical prosthesis and homograft. **Methods:** A total of 167 patients with a definite aortic valve IE who underwent aortic replacement were selected from a prospective observational population-based study. Association between the type of implanted valve and 5-year mortality was examined by the use of an adjusted Cox model. **Results:** Bioprostheses were implanted in 31 patients (18.6%), homograft in 27 (16.2%) and mechanical valves in 109 (65.2%). Patients with bioprothesis had a higher 5-year mortality risk than patients with mechanical prosthesis (adjusted hazard ratio (HR) 2.39, 95% confidence interval (95% CI), 1.09—5.21; $p = 0.029$), particularly in patients $\leq$65 years old (adjusted HR 4.14 (1.27—13.45), $p = 0.018$) but not in patients $>$65 years old (adjusted HR: 1.45 (0.35—5.97), $p = 0.60$). Five-year mortality risk did not differ between patients with homografts and those with mechanical prostheses (HR 0.46, 95% CI (0.15—1.42), $p = 0.18$). **Conclusions:** A bioprosthetic valve used for aortic valve IE replacement may be associated with lower overall 5-year survival than the use of a mechanical valve in patients up to 65 years old. Further studies are needed to explain these results.

Keywords: Aortic valve replacement; Infective endocarditis; Surgery

1. Introduction

The aortic valve is the most-common infected site in infective endocarditis (IE), accounting for approximately 40—67% of the total infected IE sites [1—5]. From 60% to 72% patients with aortic valve IE undergo surgical intervention during the acute phase [1,6]. Aortic valve replacement (AVR: mechanical valve, bioprosthesis or homograft) is recommended as a standard surgical procedure for most patients with symptomatic aortic valve disease [7]. Current guidelines recommend the use of a mechanical valve for patients <65 years, but this recommendation is based on class II evidence (conflicting evidence or opinion) [8]. However, the age criteria for the choice of the valve type may differ for

☆ *Funding and support*: This work was funded by the Programme Hospitalier de Recherche Clinique (grant PHRC 1997-RC30) and supported by the following professional organisations: Société de Pathologie Infectieuse de Langue Française, Société Française de Microbiologie, Société Nationale Française de Médecine Interne, Société de Réanimation de Langue Française, Société Française de Gérontologie, Société Française de Cardiologie, Société Française de Chirurgie Thoracique et Cardiovasculaire, Société Française d'Anesthésie-Réanimation and the Fédération Française de Cardiologie.

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[1] See Appendix A.

1010-7940/$ — see front matter
doi:10.1016/j.ejcts.2009.11.035

patients with IE who receive valve implantation in an environment modified by infection and whose life expectancy may be substantially lower [9]. For patients with IE, the choice between these three types of valve replacement remains controversial [9—12].

To our knowledge, no randomised study has focussed on the impact of valve type for patients with IE. Some observational studies comparing different replacement valve devices for patients with IE [9—12] showed conflicting results: the 4-year mortality was higher for patients receiving bioprostheses versus mechanical valves in one study [11], but other authors found no difference in long-term mortality in comparing homografts, mechanical valves and bioprostheses [9], homografts and conventional prostheses (bioprosthetic and mechanical valves) [12] or homografts and mechanical prostheses. Moreover, all these studies were monocentric and had a long accrual period (6—31 years).

To compare the impact on 5-year mortality of the three types of implanted valves — endocarditis bioprosthesis (heterograft), mechanical prosthesis and homograft — in the surgical treatment of aortic valve, we conducted a 5-year prospective follow-up study of a contemporary large representative population-based cohort of patients with definite IE.

2. Methods

2.1. Definitions

Early mortality was any death that occurred within 30 days after operation. All deaths which occurred more than 30 days after operation were classified as late deaths.

2.2. Patient population

Between 1 December 1 1998, and 31 March 2000, 559 adult patients with definite IE (according to the Duke criteria [13]) were enrolled during a cross-sectional prospective population-based survey conducted in seven French regions (16 million inhabitants). The design of this study has been described in detail previously [1]. Among these patients, 283 had aortic IE (including 77 with both aortic and mitral IE), and 177 underwent surgical intervention during the active phase (i.e., during antibiotic treatment). Bioprostheses were implanted in 31 patients (18.6%), homografts in 27 patients (16.2%) and mechanical valves in 109 patients (65.2%). Several types of prostheses were used (Carpentier, Mosaïc, Stentless prima, Stentless O'brien, Saint-Jude, Björk-Shiley, Carbomedic, ATS and so on). We excluded from the analysis 10 cases: nine patients underwent vegetectomy, valvuloplasty or Ross' intervention, and one had insufficient data for analysis.

2.3. Ethics and legal considerations

This study was approved by the Comité consultatif sur le traitement de l'information en matière de recherche dans le domaine de la santé (CCTIRS), the Commission nationale de l'informatique et des libertés (CNIL) and the institutional review board of the Centre Hospitalier Universitaire de Besançon. Patients were informed and gave their verbal consent for participation in the study according to the European regulations.

2.4. Collected data

The following parameters were collected during the initial hospital stay: demographic data, co-morbidities, predisposing heart conditions (native valve disease, prosthetic valve and previous IE), complications of IE (vascular events, secondary septic location, septic shock, aseptic meningitis and heart failure), echocardiographic findings (presence and size of vegetation, presence of intracardiac abscess, degree or presence of a new valvular regurgitation, prosthesis dehiscence and left-ventricular ejection fraction), IE location (determined by echocardiographic and/or surgical findings), causative micro-organisms, biological data (C-reactive protein and serum creatinine levels), indication for surgery and implanted valve type.

Pre-existing severe co-morbidity was defined by at least one of the following diseases: ischaemic cardiomyopathy, congestive heart failure, peripheral vascular disease, previous stroke, chronic pulmonary disease, renal insufficiency, connective tissue disease, immunodeficiency, liver disease and neoplasic disease.

The presence of heart failure during the IE episode was defined as class III or IV according to the New York Heart Association (NYHA) classification.

2.5. Follow-up

The beginning of the follow-up was defined as the day patients underwent surgery. Patients were followed up until death or cut-off date (1 January 2005). Follow-up was 92.2% complete.

2.6. Outcomes

The primary outcome was 5-year mortality rate, including death from all causes. Ascertainment and confirmation of death was obtained for patients (1) born in France (data obtained from registries) and (2) born abroad (data obtained from practitioners).

2.7. Statistical analysis

2.7.1. Descriptive analysis

Descriptive statistics for quantitative variables are expressed as mean $\pm$ standard deviation (SD) and for qualitative variables as percentages. Probabilities of survival were estimated by use of the Kaplan—Meier method. The log-rank test was used to assess differences in the 5-year survival among the three treatment groups.

2.7.2. Predictors of the choice of valve type

Characteristics between groups were compared using the chi-square test or Fisher's exact test for categorical variables. For continuous variables, the Kruskal—Wallis test was used for the comparison of three groups and the Mann—Whitney test for the comparison of two groups. The

independent predictors of type of implanted valve were examined by use of a polychotomic regression model with ascending stepwise selection.

2.7.3. Prognostic factors

Bivariate and multivariate regression analyses (Cox proportional hazard models) were used to determine 5-year survival predictors. The following variables were candidates in the model: age, diabetes, renal disease, lung disease, liver disease, number of serious co-morbid diseases (e.g., ischaemic cardiomyopathy, heart failure, peripheral vascular disease, previous stroke, chronic pulmonary disease, renal insufficiency, connective tissue disease, immunodeficiency, liver disease and neoplastic disease), NYHA functional class, ejection fraction, septic shock, nature of infected valve (native or prosthetic valve endocarditis), number of infected valves, causative micro-organism, echocardiographic findings (presence of vegetation, vegetation size, presence of valvular or paravalvular abscess, presence of paraprosthetic leak and prosthetic dehiscence), time between hospitalisation and surgery and time between antibiotic therapy and surgery. All variables were analysed by bivariate regression analyses. Of those that were statistically significant were integrated, then, into the multivariate regression model.

2.7.4. Modelling of association between valve type and mortality

The hazard risk ratio of 5-year mortality rate according to the type of implanted valve was studied by the use of a Cox model adjusted on predictors related to the type of implanted valve and prognostic factors. All variables that were statistically significant in both above models (polychotomic regression model and multivariate regression model) were candidates in the final model. Age was forced into both statistical models. The mechanical valve group was chosen as the reference group.

2.7.5. Subgroup analyses

We performed an *a priori* planned subgroup analysis using an adjusted Cox regression analysis. The association between type of implanted valve and 5-year mortality was examined according to age subgroups ($\leq$65 and $>$65 years old).

Analysis involved use of SAS v9.1 (SAS Inst., Cary, NC, USA). A $p < 0.05$ was considered statistically significant.

3. Results

3.1. Patient characteristics and univariate comparisons between groups

Among the 167 patients with aortic valve endocarditis who enrolled, 14.4% and 85.6% had prosthetic and native valve infection, respectively (Table 1). Isolated aortic valve infection occurred in 67.7% of patients, both mitral and aortic valves in 31.1% and more than two valves in 1.8%.

Mean age was 58 $\pm$ 13 years, with a significant difference between the groups (63.2 $\pm$ 13.6, 53.9 $\pm$ 15.8, 57.3 $\pm$ 11.6 years in the bioprosthesis, homograft and mechanical prosthesis groups, respectively, $p = 0.016$). There was a predominance of males (82%).

The bioprosthesis group had a higher proportion of liver diseases than the other groups ($p = 0.003$; Table 1). The proportion of patients with low left-ventricular ejection fraction (LVEF) was higher in the bioprosthesis group than in the other groups ($p = 0.0006$). Other baseline characteristics were not significantly different among the three groups. Groups did not differ in causative micro-organisms.

3.2. Factors associated with choice of replacement valve device (Table 2)

Factors independently associated with the choice of bioprosthesis compared with mechanical valves were increased age, LVEF $< 30\%$ and history of liver disease.

Factors independently associated with the choice of homograft as compared with mechanical valve were LVEF $< 50\%$ and a low number of serious co-morbid diseases.

3.3. Mortality

In general, the 5-year mortality was 58.1% (18 deaths), 14.8% (four deaths) and 24.4% (28 deaths) in the bioprosthesis, homograft and mechanical prosthesis groups, respectively. The bioprosthesis group showed the lowest crude 5-year survival (Fig. 1, $p = 0.0004$).

The early mortality was 19.4% (six deaths), 7.4% (two deaths) and 10.1% (11 deaths) in the bioprosthesis, homograft and mechanical prosthesis groups, respectively ($p = 0.27$).

3.4. Factors associated with 5-year mortality

Factors independently associated with 5-year mortality were advanced age (adjusted hazard ratio (HR) = 1.03, 95% CI (1.002–1.051), $p = 0.037$), septic shock (adjusted HR = 10.8, 95%CI (5.10–22.87), $p < 0.0001$) and a number of serious co-morbid diseases (adjusted HR = 1.33, 95% CI (1.10–1.60).

3.5. Effect of implanted valve type on 5-year mortality (Table 3)

On multivariate analysis, with adjustment on the predictors of 5-year mortality and on the predictors of the choice of replacement valve devices, patients undergoing bioprosthetic aortic valve replacement (AVR) showed an increased risk of 5-year mortality than the patients undergoing mechanical AVR (adjusted HR = 2.39, 95% confidence interval (CI) (1.09–5.21), $p = 0.029$). Results remained unchanged on the analysis of patients without liver disease (adjusted HR = 2.55, 95% CI (1.25–5.22), $p = 0.01$). Patients with homografts and those with mechanical valves did not differ in 5-year mortality.

3.6. Age subgroup analysis (Table 3)

Among patients $\leq$65 years ($n = 14$ for those receiving bioprosthesis, $n = 21$ for homograft and $n = 79$ for mechanical prosthesis), those receiving a bioprosthetic valve showed a significant independent increased risk of 5-year mortality than those receiving a mechanical valve (adjusted HR 4.14, 95% CI (1.27–13.45), $p = 0.018$). This relationship was not

Table 1
Comparison of patient characteristics between the three treatment groups for acute aortic valve infective endocarditis.

	Total (n = 167)	Bioprosthesis (n = 31)	Homograft (n = 27)	Mechanical prosthesis (n = 109)	p
Age, mean ± standard deviation (SD) (years)	57.9 ± 13.0	63.2 ± 13.6	53.9 ± 15.8	57.3 ± 11.6	0.016*
Men, n (%)	137 (82)	25 (80.7)	24 (88.9)	88 (80.7)	NS
History of valvular disease	98 (58.7)	15 (48.4)	16 (59.3)	67 (61.5)	NS
Native valve endocarditis, n (%)	143 (85.6)	27 (87.1)	23 (85.2)	93 (85.3)	NS
Prosthetic valve endocarditis, n (%)	24 (14.4)	4 (12.9)	4 (14.8)	16 (9.6)	NS
Co-morbidities					
Ischaemic cardiomyopathy, n (%)	15 (9.0)	2 (6.5)	3 (11.1)	10 (9.2)	NS
Heart failure, n (%)	22 (13.2)	1 (2.2)	3 (11.1.)	18 (16.5)	NS
NYHA[a] ≥3 (n = 145), n (%)	73	11 (35.5)	10 (37.0)	51 (46.8)	NS
Peripheral vascular disease, n (%)	6 (3.6)	2 (6.5)	0	4 (3.7)	NS
Intravenous drug use, n (%)	4 (2.4)	1 (3.2)	2 (7.4)	1 (0.9)	NS
Diabetes mellitus, n (%)	19 (11.4)	3 (9.7)	2 (7.4)	14 (12.8)	NS
Stroke antecedent, n (%)	9 (5.4)	1 (3.2)	1 (3.7)	7 (6.4)	NS
Chronic pulmonary disease, n (%)	9 (5.4)	3 (9.7)	0	6 (5.5)	NS
Renal insufficiency, n (%)	16 (9.6)	4 (12.9)	1 (3.7)	11 (10.1)	NS
Liver disease, n (%)	19 (11.4)	9 (29.0)	3 (11.1)	7 (6.4)	0.003**
Neoplastic disease, n (%)	11 (6.6)	3 (9.7)	1 (3.7)	7 (6.4)	NS
Immunodeficiency, n (%)	10 (6.0)	1 (3.2)	0	9 (8.3)	NS
Number of serious co-morbid diseases[b] (±SD)	1.6 ± 1.3	1.6 ± 1.2	1.2 ± 1.1	1.7 ± 1.4	NS
Biologic perturbation					
CRP[c] (n = 154), mean ± SD (mg/l)	114.0 ± 81.7	117.4 ± 67.0	101.5 ± 68.9	116.1 ± 88.3	NS
Serum creatinine (n = 163), mean ± SD (μmol/l)	191.1 ± 257.2	150.8 ± 122.1	271.7 ± 498.5	182.8 ± 190.4	NS
Causative micro-organism					
Staphylococcus species, n (%)	28 (16.8)				
S. aureus (n = 14) (%)		3 (9.7)	3 (11.1)	8 (7.3)	NS
Coagulase negative (n = 14) (%)		2 (6.5)	1 (3.7)	11 (10.1)	NS
Streptococcus species, n (%)	100 (59.9)	18 (58.1)	16 (59.3)	66 (60.6)	NS
Enterococcus, n (%)	15 (9.0)	5 (16.1)	2 (7.4)	8 (7.3)	NS
Other, n (%)	15 (9.0)	3 (9.7)	3 (11.1)	9 (8.3)	NS
No micro-organism identified, n (%)	9 (5.4)	0	2 (7.4)	7 (6.4)	NS
Echocardiographic findings					
Left-ventricular ejection fraction (/n = 117)					
> 50%	92 (55.1)	16 (51.6)	6 (22.2)	70 (64.2)	0.0006**
30–50%	19 (11.38)	4 (12.9)	4 (14.8)	11 (10.1)	
<30%	6 (3.6)	3 (9.7)	2 (7.4)	1 (0.9)	
Presence of aortic vegetation	142 (85.0)	25 (80.7)	26 (96.3)	83 (76.2)	NS
Size of the largest vegetation, mean ± SD (mm)	10.2 ± 6.8	11.5 ± 6.5	10.9 ± 6.4	9.6 ± 6.9	NS
>10 mm (/n = 120), n (%)	63 (52.5)	7 (31.8)	6 (37.5)	44 (53.7)	NS
Aortic abscess, n (%)	53 (31.7)	10 (32.3)	8 (29.6)	31 (28.4)	NS
Valvular regurgitation, n (%)	155 (92.8)	28 (90.3)	27 (100)	96 (88.0)	NS
Prosthetic dehiscence, n (%)	9 (5.4)	1 (3.2)	1 (3.7)	7 (6.4)	NS
Number of damaged valves, n (%)					
1	113 (67.7)	19 (61.3)	20 (74.1)	74 (67.9)	NS
≥2	54 (32.3)	12 (38.68)	7 (25.9)	35 (32.1)	
Aortic and mitral ± right-sided, n (%)	52 (31.1)	11 (35.5)	6 (22.2)	35 (32.1)	NS
Complications					
Septic shock (/n = 165), n (%)	15 (9.0)	4 (12.9)	2 (7.1)	9 (8.3)	NS
Stroke, n (%)	23 (13.8)	1 (3.2)	3 (11.1)	19 (17.4)	NS
Emboli, n (%)	56 (33.5)	7 (22.6)	10 (37.0)	39 (35.8)	NS
Secondary location, n (%)	6 (3.6)	3 (9.7)	0	3 (2.8)	NS
Inpatient management (days)					
Time between hospitalisation and surgery, mean ± SD	25.8 ± 24.2	21.6 ± 16.6	24.6 ± 22.3	27.3 ± 26.4	NS
Time between antibiotic therapy and surgery, mean ± SD	21.5 ± 20.4	17.6 ± 14.7	20.4 ± 21.6	22.9 ± 21.5	NS
Duration of hospital stay, mean ± SD	51.0 ± 34.9	41.7 ± 27.5	47.0 ± 32.3	54.7 ± 37.1	NS
30-day death, n (%)	19 (11.4)	6 (19.3)	2 (7.4)	11 (10.1)	0.27***
Indication for surgery (n = 125)[d]					
Persistent infection[e]	21 (16.8)	3 (13.0)	2 (10.0)	16 (19.5)	NS
Important damage[f]	66 (52.8)	11 (47.8)	12 (60.0)	43 (52.4)	NS
Congestive heart failure	46 (36.8)	7 (30.4)	8 (40.0)	31 (37.8)	NS

Table 1 (*Continued*)

	Total (n = 167)	Bioprosthesis (n = 31)	Homograft (n = 27)	Mechanical prosthesis (n = 109)	p
Vegetation size >10 mm	15 (12.0)	2 (8.7)	1 (5.0)	12 (14.6)	NS
Embolic events	13 (10.4)	3 (13.0)	0	10 (12.2)	NS
Others[g]	12 (9.6)	1 (4.4)	3 (15.0)	8 (12.0)	NS

[a] Classification of New York Heart Association.
[b] Serious co-morbid diseases: ischaemic cardiomyopathy, heart failure, peripheral vascular disease previous stroke, chronic pulmonary disease, renal insufficiency, connective tissue disease, immunodeficiency, liver disease, neoplastic disease.
[c] C-reactive protein.
[d] One indication or more for each patient.
[e] Persistent infection with positive blood cultures after 1 week of antibiotic therapy.
[f] Perforation or rupture or fistula or large perivalvular abscess.
[g] Prosthetic dehiscence or infective endocarditis caused by *S. marcescens* or *Pseudomonas species*, etc.
[*] Kruskal–Wallis test.
[**] Fisher exact test.
[***] Log-rank test.

observed among patients >65 years (adjusted HR 1.45 (0.35–5.97), p = 0.60). Patients receiving homograft and mechanical prosthesis did not differ in risk of 5-year mortality, whatever the age class.

4. Discussion

In this study, patients with aortic valve IE receiving bioprosthetic AVR had a significantly independent lower overall 5-year survival rate than patients receiving mechanical AVR, especially patients ≤65 years. We found no 5-year survival difference between patients receiving homografts and mechanical valves.

4.1. Bioprosthesis versus mechanical prosthesis

Our multivariate analysis suggested that the overall 5-year mortality risk in patients with aortic valve endocarditis was 2.4 times higher in patients receiving bioprosthesis than in those receiving mechanical AVR. More precisely, in comparing the bioprosthesis group and the mechanical valve group, the 5-year mortality risk was 4 times higher for patients with aortic valve endocarditis who were ≤65 years old and was no different for patients >65 years. The mean interval between surgery and death did not significantly differ between the two groups (21.4 months for bioprosthesis and 21.6 months for mechanical valve, p = 0.5).

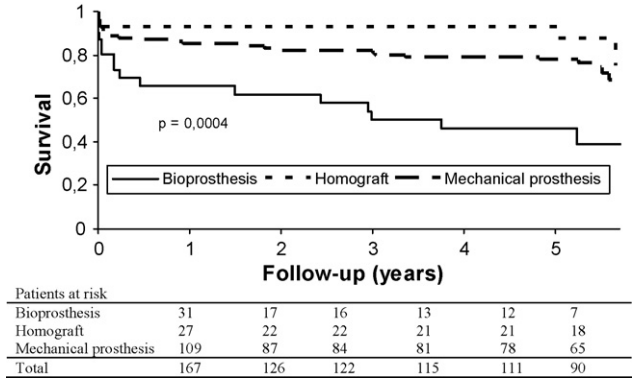
Sweeney et al. [11], in a study of 185 patients with valve replacement for IE (65% aortic valve), found a survival advantage at 4 years (excluding operative deaths) for mechanical versus bioprosthetic valves (87.4% vs 78.7%, $p < 0.05$). However, in another study of 306 patients with left-sided IE (62% patients with aortic valve endocarditis), Moon et al. [9] found long-term survival independent of valve type (p = 0.27). However, this was a study with a long-term accrual period (from 1964 to 1995), with a probable therapeutic-process confounding effect.

In a meta-analysis of 32 articles describing 15 mechanical and 23 biologic valve series totalling 17 439 patients, Lund et al. found no significant difference in death rate between patients with mechanical and those with bioprosthetic valves with correction for age and well-known risk factors [14]. This study focussed on non-infectious AVR (only 6.8% and 2.2% patients with active IE in the mechanical valve series and biologic valve series, respectively). Generalising these results to patients with IE would be inappropriate because of the different baseline and evolution of disease for patients with and without IE. Furthermore, in patients with IE, the anatomic valvular and paravalvular structure is modified by infection and could be the source of prosthesis-related events and high

Table 2
Factors associated with the choice of replacement valve device for acute aortic valve infective endocarditis.

Characteristics	Predictors of homograph replacement (vs mechanical prosthesis)		Predictors of bioprosthesis replacement (vs mechanical prosthesis)	
	OR	95% CI	OR	95% CI
Age	0.98	0.94–1.01	1.08	1.03–1.13
Number of serious co-morbidities[a]	0.65	0.43–0.99	–	
Liver disease	–		21.86	4.84–98.71
LVEF[b]				
> 50%	1.00		1.00	
30–50%	4.80	1.11–20.80	1.45	0.37–5.73
<30%	38.73	2.49–602.88	14.11	1.11–179.28

[a] Serious co-morbid diseases: ischaemic cardiomyopathy, heart failure, peripheral vascular disease, previous stroke, chronic pulmonary disease, renal insufficiency, connective tissue disease, immunodeficiency, liver disease, neoplastic disease.
[b] LVEF: left-ventricular ejection fraction.



Patients at risk						
Bioprosthesis	31	17	16	13	12	7
Homograft	27	22	22	21	21	18
Mechanical prosthesis	109	87	84	81	78	65
Total	167	126	122	115	111	90

Fig. 1. 5-year survival rates by types of implanted valve.

Table 3
5-year death rate hazard ratio (95% confidence interval) for patients with acute aortic infective endocarditis undergoing surgery (Cox model adjusted on independent prognostic factors of 5-year death rate and predictors of type of implanted valve).

Age at valve implantation	Type of aortic valve replacement	Bivariate analysis		Multivariate analysis[a]	
		HR (95% CI)	*p*	HR (95% CI)	*p*
Overall	Mechanical prosthesis (*n* = 109)	1.00		1.00	
	Bioprosthesis (*n* = 31)	3.58 (1.99–6.44)	<0.0001	2.39 (1.09–5.21)	0.029
	Homograft (*n* = 27)	0.38 (0.14–1.07)	0.08	0.46 (0.15–1.42)	0.18
≤65	Mechanical prosthesis (*n* = 79)	1.00		1.00	
	Bioprosthesis (*n* = 14)	3.43 (1.51–7.76)	0.003	4.14 (1.27–13.45)	0.018
	Homograft (*n* = 21)	0.62 (0.22–1.80)	0.38	0.83 (0.23–2.96)	0.77
>65	Mechanical prosthesis (*n* = 30)	1.00		1.00	
	Bioprosthesis (*n* = 17)	2.81 (1.16–6.82)	0.02	1.45 (0.35–5.97)	0.60
	Homograft (*n* = 6)	[b]		[b]	

[a] Adjusted on: valve type, age, liver disease, number of serious co-morbid diseases (ischaemic cardiomyopathy, heart failure, peripheral vascular disease, previous stroke, chronic pulmonary disease, renal insufficiency, connective tissue disease, immunodeficiency, liver disease, neoplastic disease), New York Heart Association function class, left-ventricular ejection fraction, septic shock, prosthetic or native valve endocarditis, number of infected valves.
[b] Subsample size was too small to carry out a Cox modelling.

mortality. For example, annular ring abscesses demand adequate debridement and add to the risk of reinfection by creating a more contaminated field than usual [11].

This difference in survival rates according to the treatment group could be explained by differences in patient characteristics between groups or by an effect of prosthesis *per se* as follows.

First, differences in patient characteristics (confounding by indication or prescription bias) could be an explanation because the age of patients at the moment of valve implantation plays an important role as a major confounding factor. Indeed, bioprostheses are usually used for elderly patients or for young patients with co-morbidities [8], such as liver disease history, which could have an unfavourable impact on life expectancy. For this reason, we compared baseline characteristics of patients among groups and adjusted on identified factors independently associated with the choice of valve type and risk factors of mortality. Moreover, some well-known risk factors of mortality with surgical treatment, in aortic valve endocarditis (e.g., age, prosthetic valve endocarditis and abscess formation) were forced in the multivariate analysis model if they were not significant on bivariate analysis. However, as with any observational study, some factors that could be related to the surgeon's therapeutic strategy could not be totally taken into account in our analysis.

Second, Hammermeister et al. have suggested that the high mortality in patients with bioprosthetic replacement is probably due to more deaths from primary valve failure [15]. The authors showed, in a randomised controlled trial of patients without IE, that primary valve failure after AVR with a porcine bioprosthesis began at about 7–8 years and accelerated after 9–10 years [15]. Until now, this estimate has not been established for IE in which prosthetic deterioration could be accelerated early because of prosthetic implantation in an infected bed. Moreover, Sweeney et al. suggested that the difference in mortality between treatment groups may be due to a higher resistance to clinically evident reinfection and reoperation of the mechanical valve, whereas the more fragile bioprosthestic valves are more likely to fail in an actively infected bed [11]. Moon et al. found a relatively higher reoperation rate in patients with mechanical valves for IE than those with bioprosthesis (74% vs 56% at 10 years and 74% vs 22% at 15 years) [9]. Unfortunately, we did not collect data on prosthesis-related events (e.g., reinfection or reoperation rate, anticoagulation-related events) or cause of death; so we are not able to confirm this hypothesis. Indeed, we could not determine causes of death reliably for all patients without autopsy reports [16]. In Moon et al.'s study [9], long-term freedom from reoperation after left-sided valve replacement was lower with bioprothesis than with mechanical valves only in patients <60 years old. This study also showed a lower survival, although not significant, for patients <60 years receiving bioprotheses than those receiving mechanical valves ($p = 0.08$, with an underlined lack of power). Furthermore, the risks of tissue valve failure increase over time and are accelerated in young patients [14,15,17]. In a clinical trial of patients without IE [15], Hammermeister et al. found a greater primary valve failure with bioprosthesis than with mechanical valve for AVR in patients <65 years. In patients ≥65 years, primary valve failure was not significantly different between those receiving a bioprosthesis and those receiving a mechanical valve for AVR. To avoid long-term reoperation due to structural valve degeneration of a bioprosthesis, the current guidelines recommend mechanical prostheses for AVR in patients <65 years [8]. This recommendation was drawn from studies that did not focus on patients with IE. Indeed, baseline and evolution of disease characteristics of patients with IE are different from those without IE. Particularly, their life expectancy may be substantially lower than those without IE [9]. Therefore, published data do not allow for determining an age cut-off for the choice of valve type in the surgical treatment of active aortic valve endocarditis.

4.2. Homograft versus mechanical prosthesis

We found no difference in 5-year mortality between patients receiving aortic homografts and those receiving mechanical valves. No study has compared the mortality at mid- or long-term of the homografts and mechanical prosthesis in patients with aortic endocarditis. In a retrospective study, Gross et al. compared the outcome of 45 young

patients (<50 years old) receiving an homograft for aortic IE and that of 40 young patients (<50 years old) without IE and receiving a mechanical prosthesis [10]. The authors found a comparable late death at 4 years between the two groups (five patients in each group). Another study of patients of AVR for IE [12] also found no difference of survival between the aortic homograft and prosthetic valve groups (bioprosthesis and mechanical prosthesis) at 5 and 15 years. Use of a homograft allows the surgeon to more effectively reconstruct the aortic root, particularly in the presence of deep abscesses, aortoventricular dehiscence and aortic root distortion [18,19]. The current American Heart Association guidelines recommend re-AVR with a homograft for patients with active prosthetic valve endocarditis (level of evidence: C) [15].

4.3. Strength and limitations

The major strength of our study is that it is the first prospective study with a comprehensive population-based recruitment and a short accrual period. Patients were recruited from all types of hospital settings (private and public facilities, primary-, secondary- and tertiary-care hospitals) in a 16-million-inhabitant area, during a 16-month period. So, our database is the most extensive representative sample used to study this issue. Moreover, IE surgery is complex, and the results depend on the experience of the surgeon. So, the multicentre recruitment, and consequently, the participation of various surgeons, may limit this effect. The short accrual period allows for avoiding confounding effects related to diagnostic measures, patient care and management, including surgical techniques, which may have changed substantially, when the recruitment period is longer.

According to several authors, an over-risk of re-operation and high risk of mortality exists for patients with prosthetic valve endocarditis [9]. However, the small size of our prosthesis subgroup did not allow us to perform a specific analysis.

This analysis should be interpreted with caution in terms of its observational design and imbalance of patients in the three treatment groups. This imbalance is a reflection of daily practice, because the high rates of early models implanted in younger patients during the 1970s and 1980s resulted in a high proportion of re-AVR, which caused the preference to swing back to mechanical valves in recent years [14]. As in any observational non-randomised study, despite our use of rigorous methods to adjust for confounding factors, our findings may still be hampered by biases related to unmeasured or hidden factors and incomplete and/or inexact adjustment [20–22]; thus, the survival difference may be partially or totally explained by the indication bias. Randomised studies provide the gold standard in evidence-based medicine but in heart valve research, especially in IE, they are difficult to carry out because of the extended time required to obtain meaningful results [14].

5. Conclusion

A bioprosthetic valve used for aortic valve IE replacement may be associated with lower overall 5-year survival than the use of a mechanical valve in patients up to 65 years old. For patients older than 65 years, the statistically significant difference could not be established probably due to the insufficient number of events. Further studies are needed to confirm and explain these results, and then, to help practitioners and patients in the decision of valve type choice when AVR is necessary in the acute phase of aortic valve IE.

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