Long-term results of Freestyle stentless bioprosthesis in the aortic position: A single-center prospective cohort of 500 patients

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Objective: Stentless xenograft bioprostheses may be the future valve of choice for aortic valve replacement. The study aim was to investigate the long-term clinical outcome after aortic valve replacement with the Medtronic Freestyle bioprosthesis (Medtronic Inc, Minneapolis, Minn).

Methods: Between April 1997 and November 2004, a total of 500 patients (mean age, 74.5 ± 9.6 years; 52% were male) underwent aortic valve replacement with a Freestyle bioprosthesis, without population selection. The surgical procedure used a modified subcoronary technique in 479 patients and a complete root replacement in 21 patients, conducted with mini-extracorporeal circulation. Concomitant procedures included coronary artery bypass grafting in 122 patients (24%) and mitral valve repair/replacement in 11 patients.

Results: The mean cardiopulmonary bypass time was 98 ± 26 minutes, and total aortic crossclamp time was 77 ± 19 minutes. Operative mortality was 5.2%. The median follow-up time was 104.8 ± 5.7 months. During this period, there were 224 deaths ($n = 122$ cardiovascular and $n = 102$ noncardiovascular deaths). The actuarial survivals from cardiovascular and valve-related mortality were $67\% \pm 3\%$ and $70\% \pm 4\%$, respectively, at 10 years. Freedom from structural valve deterioration at 10 years was $94\% \pm 2\%$. The linearized structural valve deterioration incidence was 0.6% per patient/year. Multivariate Cox regression analysis revealed that older age, impaired renal function, and coronary artery disease were independent predictors of cardiovascular death. In the subgroup of patients aged less than 65 years at implantation ($n = 45$), the actuarial cardiovascular survival was $83\% \pm 8\%$ and freedom from structural valve deterioration was $89\% \pm 6\%$ at 10 years.

Conclusions: The use of the Freestyle bioprosthesis for aortic valve replacement resulted in good long-term cardiovascular survival and freedom from structural valve deterioration in this cohort regardless of age at implantation. (J Thorac Cardiovasc Surg 2014;148:1903-11)

See related commentary on pages 1911-2.

The use of bioprostheses for aortic valve replacement (AVR) is recommended by international guidelines in patients aged more than 65 years, because of the decreased risk of device structural deterioration and the absence of required anticoagulation in this population with high risk for bleeding.¹ Bioprostheses can be broadly divided into 2 categories according to the presence or absence of a metallic stent supporting the biological tissue leaflet. The choice of a stented or stentless device for AVR remains debated, because they are purported to confer advantages over their counterparts.¹

The Freestyle stentless (Medtronic Inc, Minneapolis, Minn) aortic bioprosthesis is a xenograft composed of a thin synthetic sewing cuff attached to a glutaraldehyde-preserved porcine aortic root using an alpha-amino oleic acid leaflet anti-calcification treatment. The absence of stent has been reported to provide better hemodynamic properties compared with stented biological valves, with less turbulent flow and larger efficient effective orifice area.² These characteristics could lead to lower transvalvular gradient and better valve duration.² Thus, the use of stentless bioprostheses (SLBs) might improve survival, reduce the structural deterioration risk, and minimize deleterious long-term impact on left ventricle function. Recent results from randomized trials and meta-analysis suggest a superiority of stentless over stented biological standard bioprostheses,^{3,4} especially in patients with left ventricle dysfunction and a small aortic annulus.²

Despite the introduction of SLBs in the early 1990s, long-term outcome data are still required to assess their durability and safety.¹ Our group previously reported excellent short- and mid-term survivals in patients of a wide age range.⁵ The purpose of the present study was to describe the clinical outcome in a large cohort of all-comer patients who received a Freestyle bioprosthesis implantation and were prospectively followed up for as long as 12 years.

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Abbreviations and Acronyms

AVR	= aortic valve replacement
CSB	= conventional stented bioprosthesis
LVEF	= left ventricular ejection fraction
SLB	= stentless bioprosthesis
SVD	= structural valve deterioration
TAVI	= transaortic valve implantation
VKA	= vitamin K antagonist

MATERIAL AND METHODS**Patient Population**

This prospective observational cohort study included patients who benefited from Freestyle bioprostheses implantation by 2 surgeons (O.M.B. and P.H.D.) working together in 2 institutions between April 1997 and November 2004.⁵ To provide realistic clinical results, the Freestyle bioprosthesis was used immediately after a choice of biological prosthetic valves had been made, with no selection on age, left ventricular function, or operative risk. There was no specific inclusion or exclusion criterion for Freestyle implantation in this all-comers cohort. Our local ethics committee approved the study, and informed signed consent was obtained.

Operative Technique

Cardiopulmonary bypass was conducted with a mini-extracorporeal circulation circuit (Jostra MECC System; Jostra AG, Hirrlingen, France), systemic normothermia, and warm antegrade discontinued blood cardioplegia. The Freestyle bioprosthesis was implanted using the modified subcoronary technique⁶ or the complete aortic root replacement with coronary artery reimplantation.⁷ Our first option was the subcoronary technique ("cylinder in a cylinder") to optimize the procedure of AVR by shortening the cardiopulmonary bypass and aortic crossclamp times. The full root replacement technique was performed in case of aortic root dilation.

In all techniques, a transverse aortotomy was used. In the subcoronary technique, the inflow of the porcine root was secured with simple interrupted sutures. The porcine valve was trimmed by excision of the remnants of the aortic tissue above the orifices for the coronary sinuses, leaving the non-coronary sinus wall intact. In case of a small aortic annulus and low right coronary ostium, the Freestyle device was rotated to avoid the potential obstruction created by the folded fabric cloth covering the muscle bar of the prosthesis.⁶ In the total root replacement, the aorta was transected above the sinotubular ridge. Both coronary ostia were mobilized with buttons of aortic wall. The remaining tissue of the sinus of Valsalva was excised. A quadrangular portion of the porcine aortic sinus was excised to remove the porcine coronary artery for both the left and right coronary arteries. The porcine valve was rotated to allow optimal right coronary artery implantation in the Freestyle noncoronary wall. The coronary buttons were sewn to the corresponding sinus of Valsalva with a continuous suture, and the outflow portion of the graft was sutured to the crest of the native aorta.

During the same period, the Freestyle bioprosthesis could not be implanted in a subcoronary fashion in 30 patients because of technical contraindications. These included heavy calcification of the native aortic wall itself and calcifications localized beneath the coronary ostia, both of which compromised the upper suture of the stentless valve. Problems were also encountered in redo aortic operations when the aortotomy could not always be performed at the appropriate location.

Clinical and Echocardiography Data

Preoperative clinical and surgical data were recorded prospectively for each patient. Preoperative and postoperative echocardiographic data were

obtained according to the international guidelines and included left ventricle ejection fraction, mean transvalvular gradient measurement, and effective orifice area calculation.⁸ The following variables were considered as potential outcome determinants: age, gender, body mass index, body surface area, diabetes, preoperative renal function (estimated by the Modification of Diet in Renal Disease calculation of the creatinine clearance), concomitant procedure, operative technique, re-replacement of the aortic valve, physiologic subgroup as aortic stenosis, aortic insufficiency or combined aortic valve disease, history of endocarditis, previous cardiac surgery, valve size, baseline pre-intervention transaortic gradient, left ventricular ejection fraction (LVEF), and preoperative pulmonary hypertension.

Anticoagulation Regimen

Our policy regarding anticoagulation followed the European Society of Cardiology guidelines.⁹ Oral anticoagulation with vitamin K antagonists (VKAs) was provided to patients with chronic and recurrent atrial fibrillation. Although the decision to give or not give VKAs to elderly patients was left to the discretion of the cardiologist, the general consensus in France at this time was to switch from VKA to aspirin in subjects aged more than 85 years. Other subjects with previous coronary artery disease or at high cardiovascular risk received aspirin therapy (75 mg/d) after surgery.

Follow-up Data Analysis

Outcomes were analyzed according to the guidelines of the American Association for Thoracic Surgery for reporting morbidity and mortality after cardiac valvular operations.¹⁰ Follow-up information was obtained by a single investigator between April 1997 and July 2010, using a standardized interview or telephone questionnaire. Data regarding all-cause, cardiac, and valve-related mortalities, structural valvular deterioration, operated valvular endocarditis, bleeding events, and thromboembolic events were collected and integrated into our database.

Statistical Analysis

Statistical analysis was performed with SPSS 21.0 (SPSS Inc, Chicago, Ill) and SAS 9.33 (SAS Institute Inc, Cary, NC). Data are expressed as mean and standard deviation.

Patient survivals from all-cause, cardiovascular, and valve-related mortalities, and structural valve deterioration (SVD) were analyzed, and Kaplan-Meier actuarial survival curves were constructed. In addition, we performed cumulative actual incidence analysis of SVD to provide a mortality-adjusted event-free percentage.¹¹ Differences between survival curves were evaluated using the log-rank test.

We used a multivariate Cox model with stepwise regression to assess the relation of covariates with the incidence of the different clinical end points during follow-up. Univariate Cox proportional hazards regression analyses were first performed among established predictors of long-term cardiovascular mortality. All covariates with a *P* value less than .1 were then included in the multivariate regression model to identify independent predictors of the primary end point. The validity of the proportionality assumption was verified for all covariates by the likelihood ratio test. A 2-sided alpha level of 0.05 was considered the threshold for statistical significance.

RESULTS**Baseline Characteristics**

Between April 1997 and November 2004, a total of 850 patients underwent AVR by the 2 selected surgeons. Among them, 500 patients (age range, 26-91 years) underwent AVR with implantation of a Freestyle bioprosthesis, 30 patients underwent AVR with implantation of another bioprosthesis because of Freestyle implantation impossibility, and 320

TABLE 1. Baseline clinical and echography characteristics of the study population

Parameter	N = 500
Age (y)	74.5 ± 9.6
Male gender, n (%)	259 (52)
Significant coronary artery disease, n (%)	178 (35)
Diabetes mellitus, n (%)	110 (22)
Peripheral artery disease, n (%)	60 (12)
Creatinine clearance ≤60 mL/min/m ² , n (%)	135 (27)
Body mass index (kg/m ²)	26.7 ± 13.6
Body surface area (m ²)	1.78 ± 0.23
Previous cardiac surgery, n (%)	10 (2)
Previous AVR, n (%)	4 (1)
Indications for AVR, n (%)	
Aortic stenosis with underlying tricuspid valve, n (%)	426 (85)
Aortic stenosis with underlying bicuspid valve, n (%)	13 (3)
Isolated aortic regurgitation, n (%)	37 (7)
Combined aortic valve disease, n (%)	14 (3)
Active endocarditis without aortic regurgitation, n (%)	3 (0.5)
Active endocarditis with aortic regurgitation, n (%)	7 (1.5)
Aortic dissection, n (%)	0
NYHA class, n (%)	
I/II	295 (59)
III/IV	205 (41)
Left ventricle ejection fraction (%)	58.6 ± 0.8
Preoperative pulmonary hypertension, n (%)	100 (20)
Mean preoperative transaortic gradient (mm Hg)	52.0 ± 15.6

AVR, Aortic valve replacement; NYHA, New York Heart Association.

patients underwent AVR with implantation of a mechanical prosthesis. Patients implanted after this period with a Freestyle device (n = 600) were not included in the study because it was focused on long-term outcome. The baseline characteristics of the population are shown in Table 1.

Operative Data

The modified subcoronary implantation technique was used in 479 patients (96%). The mean cardiopulmonary bypass time was 98 ± 26 minutes (88 ± 15 minutes for AVR alone), and the mean aortic crossclamp time was 77 ± 19 minutes (70 ± 13 minutes for AVR alone) (Table 2). Both mean cardiopulmonary bypass time and aortic cross-clamp times were significantly longer in the patients with complete root replacement versus modified subcoronary implantation (128 ± 34 minutes vs 97 ± 25 minutes, respectively, and 99 ± 25 minutes vs 76 ± 19 minutes, respectively, *P* < .001 for both). A concomitant procedure was performed in 31% of the cases. The remaining patients with coronary disease (10%) did not undergo coronary artery bypass grafting because the target lesions were distal or secondary. The mean Freestyle bioprosthesis diameter was 22.2 ± 2.2 mm. A total of 242 (48%) small-diameter bioprostheses (19 or 21 mm) were used, mostly in the older female group.

TABLE 2. Operative and postoperative characteristics

Parameter	N = 500
Cardiopulmonary bypass time (min)	98.5 ± 26.0
Total aortic crossclamp time (min)	77.3 ± 19.3
Prosthesis diameter (mm)	22.2 ± 2.2
Valve size, n (%)	
19 mm	82 (16)
21 mm	160 (32)
23 mm	159 (32)
25 mm	78 (15.5)
27 mm	19 (4)
29 mm	2 (0.5)
Freestyle implantation technique	
Modified subcoronary technique, n (%)	479 (96)
Complete root replacement, n (%)	21 (4)
Associated procedure, n (%)	157 (31)
Coronary artery bypass graft, n (%)	122 (24)
Mitral valve replacement, n (%)	3 (1)
Mitral valvuloplasty, n (%)	8 (2)
Ascending aortic tube-graft, n (%)	9 (2)
Other, n (%)	15 (3)
Anticoagulation regimen at discharge	
None, n (%)	215 (43)
VKA, n (%)	102 (20)
Aspirin, n (%)	285 (57)

VKA, Vitamin K antagonist.

Operative Mortality and Early Outcome

Twenty-six (5.2%) perioperative deaths occurred during the initial hospitalization or within 30 days after surgery. No death occurred in the younger age group (<65 years). Five of 120 patients aged more than 80 years died (4%).

Long-Term Outcome

Follow-up was achieved in 488 patients (median follow-up, 104.8 ± 5.7 months; range, 1-155 months; 2971 patient-years). During this period, there was a total of 224 all-cause deaths, including 122 cardiovascular and 109 valve-related deaths (n = 11 deaths caused by structural and nonstructural dysfunction, n = 8 fatal embolic events, n = 14 fatal hemorrhagic events, n = 4 fatal endocarditis, n = 19 sudden death, and n = 53 unexplained death). Figure 1, A shows the Kaplan–Meier curves for long-term survival among the whole cohort. The actuarial survivals for all-cause, cardiovascular, and valve-related mortality were 44% ± 3%, 67% ± 3%, and 70% ± 4% at 10 years, respectively, and 31% ± 5%, 50% ± 7%, and 58% ± 7% at 12 years, respectively.

Evidence of SVD was identified in 18 patients and led to reintervention in 10 subjects. The actuarial freedom from SVD was 94% ± 2% (Figure 1, B), and the actual cumulative incidence of SVD (Figure 1, C) was 3.7% at 10 years. The poorer actuarial rates reflected the burden of competing

FIGURE 1. Kaplan-Meier actuarial survival curves for all-cause, cardiovascular, valve-related mortality (A), and SVD (B) in the global cohort (n = 488). Cumulative incidence of SVD (C). SVD, Structural valve deterioration.

events (death from non-SVD-related causes) that censored the occurrence of SVD.

The pathologic assessment of the explanted bioprosthesis indicated that the mechanism responsible for valve failure was the association of leaflet calcification and tear in

60% of patients, leaflet tear in 20% of patients, and predominant calcification of leaflet and commissures in the remaining 20% of patients. The linearized annual incidence of SVD was 0.6% per patient/year. In addition, reoperation was required in 10 cases that were not related to SVD.

Fourteen patients had bioprosthesis valve endocarditis (linearized annual incidence: 0.5% per patient/year; actuarial freedom from endocarditis: $96\% \pm 1\%$, at 10 years), leading to death in 4 cases. There was no case of valve thrombosis observed during follow-up. A total of 25 patients presented peripheral thromboembolism (mean age, 77 ± 14.7 years; 53% male gender/linearized annual incidence: 0.8% per patient/year; actuarial freedom from peripheral embolic event $90\% \pm 3\%$ at 10 years), including stroke in 17, transient ischemic attack in 5, mesenteric ischemia in 1, and acute central retinal artery occlusion in 2. The embolic event was fatal in 32% of the cases and led to persistent neurologic disabilities in 28% of the patients. Patients were receiving oral anticoagulation before their embolic event in 36% of the cases, and 40% of the patients had evidence of atrial fibrillation or a history of recurrent AF before the embolic event. Finally, 19.6% of the patients were receiving anticoagulants during follow-up (mostly for atrial fibrillation treatment). Hemorrhages occurred in 28 patients (linearized annual incidence, 0.9% per patient/year; actuarial freedom from hemorrhagic event, $88\% \pm 3\%$, at 10 years), leading to death in 14.

Long-Term Outcome in Selected Subgroups

The Freestyle bioprosthesis showed excellent performance and durability in the younger patients of the cohort (age <65 years at implantation, $n = 45$). The 10-year actuarial survivals from all-cause, cardiovascular, and valve-related mortality were $69\% \pm 9\%$, $83\% \pm 7\%$, and $87\% \pm 6\%$, respectively (Figure 2, A). SVD was observed in 4 patients and led to reintervention in all of them (actuarial freedom from SVD $89\% \pm 6\%$ and actual cumulative incidence of SVD 9% at 10 years) (Figure 2, B and C).

Moreover, we analyzed outcome in patients aged 80 years or more at implantation ($n = 120$) and observed that the 10-year actuarial survival from cardiovascular and valve-related mortality were $41\% \pm 9\%$ and $50\% \pm 10\%$, respectively.

We observed no difference in outcome in patients who received a bioprosthesis with a diameter of 21 mm or less ($n = 234$) compared with the other patients (prosthesis diameter >21 mm), as demonstrated by the 10-year actuarial survival freedom from cardiovascular death ($66\% \pm 6\%$ vs $68\% \pm 4\%$, respectively, $P = .93$), valve-related mortality ($66\% \pm 6\%$ vs $72\% \pm 4\%$, respectively, $P = .62$), and SVD ($95\% \pm 2\%$ vs $94\% \pm 3\%$, respectively, $P = .95$). Finally, we did not observe any significant impact of impaired LVEF on outcome. Although there was a trend toward a higher cardiovascular mortality (10-year actuarial survival from cardiovascular death: $62\% \pm 7\%$ vs $71\% \pm 4\%$, respectively, $P = .13$), the patients with a baseline LVEF of 50% or less ($n = 111$) showed comparable 10-year survivals from valve-related mortality ($68\% \pm 8\%$ vs $72\% \pm 4\%$, respectively, $P = .52$) and SVD ($98\% \pm$

2% vs $94\% \pm 2\%$, respectively, $P = .46$) as the patients with baseline LVEF greater than 50%.

Predictors of Long-Term Outcome After Freestyle Implantation

Table 3 shows the predictors of cardiovascular death in univariable and multivariable analyses. Cox regression analysis revealed that age at implantation, presence of coronary artery disease, and preoperative creatinine clearance less than 60 mL/min/m² were independent predictors of cardiovascular mortality after adjustment for confounding factors.

Furthermore, we also analyzed predictors of valve-related mortality in these patients (Table 4). We observed that age at implantation and diabetes mellitus independently predicted valve-related mortality. There was no significant effect of other patients' clinical characteristics, operative technique, concomitant procedure, or device size on the outcome in the whole cohort.

DISCUSSION

The expanding use of valvular bioprostheses among a wide range of patients (including younger patients) highlights the need for durable, efficient, and safe devices. The Freestyle bioprosthesis is a xenograft composed of a thin synthetic sewing cuff attached to a preserved porcine aortic root. The stent-free design allows an excellent conformability of the valve with the native aortic root, leading to increased larger effective orifice area¹² and less turbulent flow¹³ compared with conventional stented bioprostheses (CSBs). SLBs have a better hemodynamic profile and demonstrate lower transvalvular gradient than CSBs.^{4,14} Moreover, the absence of struts could theoretically impede the degeneration process affecting all bioprostheses, because this phenomenon usually starts on the attachment zones between the leaflets and the struts in CSB, and thus leads to longer durability.^{15,16} Finally, the anticalcification treatment of the bioprosthesis might improve its potential longevity. Of note, recent results showed a $97.9\% \pm 0.6\%$ freedom of SVD at 10 years for patients who received the Medtronic Mosaic bioprosthesis (a third-generation alpha-amino oleic acid-treated porcine valve mounted on a stent).¹⁷ Because the Mosaic and Freestyle bioprostheses differ only by the presence of the stent and show comparable long-term durability, these data might suggest that the demineralization process applied to these devices could largely account for their excellent long-term durability.

Despite these potential benefits, the use of SLB is highly variable among institutions worldwide.¹⁸⁻²⁰ These paradoxical results might be explained by the concerns raised regarding SLB real advantages over their counterparts.^{1,21} Major criticisms relate to the increased complexity and higher surgical risk for SLB implantation,

FIGURE 2. Kaplan–Meier actuarial survival curves for all-cause, cardiovascular, valve-related mortality (A), and SVD (B) in patients aged less than 65 years ($n = 45$). Cumulative incidence of SVD (C). SVD, Structural valve deterioration.

as well as the limited and conflicting results regarding the durability of these bioprostheses and long-term outcome.^{1,2} Different authors have reported encouraging long-term

(>9 years) results with the use of the Freestyle bioprosthesis for AVR, regardless of the implantation technique (subcoronary or full aortic root replacement).^{19,22–24} In these different

TABLE 3. Predictors of long-term cardiovascular mortality

	Univariable analysis		Multivariable analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age (per y)	1.06 (1.03-1.09)	<.001	1.15 (1.08-1.23)	<.001
Female gender	0.91 (0.64-1.30)	.61		
Body surface area (per unit)	0.35 (0.13-0.94)	.04	—	>.1
Preoperative TA mean gradient (per mm Hg)	0.99 (0.97-1.00)	.06	—	>.1
Coronary artery disease	1.57 (1.10-2.24)	.014	1.72 (1.0-2.99)	.05
Associated surgical procedure	1.13 (0.78-1.65)	.52		
Complete root replacement technique	0.94 (0.35-2.55)	.9		
Previous cardiac surgery	1.03 (0.26-4.2)	.96		
Prosthesis diameter ≤21 mm	0.98 (0.69-1.40)	.92		
Preoperative endocarditis	2.93 (0.72-11.9)	.13		
Baseline LVEF (per %)	0.99 (0.70-1.0)	.11		
Preoperative creatinine clearance <60 mL/min/m ²	2.11 (1.41-3.15)	<.001	2.0 (1.15-3.47)	.01
Diabetes mellitus	1.83 (1.21-2.77)	.004		>.1
Preoperative PH	1.46 (0.94-2.25)	.09		>.1

Likelihood ratio test *P* < .001. *CI*, Confidence interval; *HR*, hazard ratio; *LVEF*, left ventricular ejection fraction; *TA*, transaortic; *PH*, pulmonary hypertension.

series, the 10-year overall survival ranged from 44% to 47% and the freedom from SVD ranged from 91% to 97%. Our present results are in line with these previous observations and confirm the excellent durability of the Freestyle bioprosthesis in the long term, as highlighted by the limited incidence of SVD. Although the overall survival in our cohort was relatively low, this point might be explained by the age of the patients at implantation (mean age, 74.5 ± 9.6 years), because the mortality rate in this series was similar to that observed in populations of similar age.¹⁹ We observed that the prominent deterioration mechanism for SVD involved leaflet tear in the majority of cases and only limited calcification. These data support the previous reports of the “wear and tear” phenomenon as the prominent mechanism for SVD in the Freestyle bioprosthesis¹⁶ and the beneficial role of the alpha-amino oleic acid valve pre-treatment to prevent calcification in vivo.

The comparison between SLB and CSB for survival currently relies on conflicting data, and the putative advantage of the SLB over stented ones remains debated. However, when analyzing the literature, one should bear in mind that these results are inhomogeneous, because they were obtained from studies investigating several SLB types, each with a specific design and specific anti-calcification treatment. These features might account for the differences observed in durability and structural deterioration.²⁵ Thus, the Toronto stentless porcine valve (St Jude Medical, Minneapolis, Minn) showed acceptable results on midterm clinical outcome, but late accelerated structural failure after 8 years.^{3,26} We did not observe this phenomenon in the present cohort, and the incidence of SVD and valve-related mortality appeared to be stable in time when compared with midterm results,⁵ supporting the previous reports regarding the excellent durability of the Freestyle

TABLE 4. Predictors of long-term valve-related mortality

	Univariable analysis		Multivariable analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age (per y)	1.07 (1.04-1.11)	<.001	1.08 (1.05-1.13)	<.001
Female gender	1.09 (0.73-1.60)	.71		
Body surface area (per unit)	0.40 (0.14-1.20)	.10	—	>.1
Preoperative transaortic mean gradient (per mm Hg)	0.99 (0.98-1.01)	.31		
Coronary artery disease	1.43 (0.96-2.11)	.08	—	>.1
Associated surgical procedure	1.28 (0.85-1.92)	.24		
Complete root replacement technique	1.15 (0.42-3.15)	.78		
Prosthesis diameter ≤21 mm	1.10 (0.75-1.63)	.63		
Previous cardiac surgery	1.90 (0.60-6.0)	.27		
Preoperative endocarditis	1.61 (0.22-11.6)	.64		
Baseline LVEF (per %)	0.99 (0.98-1.01)	.63		
Preoperative creatinine clearance <60 mL/min/m ²	1.32 (0.82-2.13)	.26		
Diabetes mellitus	1.57 (0.98-2.51)	.06	1.62 (1.01-2.59)	.046
Preoperative PH	1.35 (0.83-2.20)	.23		

Likelihood ratio test, *P* < .001. *CI*, Confidence interval; *HR*, hazard ratio; *LVEF*, left ventricle ejection fraction; *PH*, pulmonary hypertension.

bioprosthesis.^{19,22,23} Moreover, most of the data currently available on biological prostheses durability have been obtained in observational cohort studies. Thus, a direct comparison between the Freestyle bioprosthesis and the CSB is limited by the potential differences in baseline population characteristics,^{22,25} yet these methodological biases could be overcome by randomized clinical trials. Unfortunately, such data are rare for the Freestyle valve. However, El-Hamamsy and colleagues²⁷ observed a better durability and significantly less SVD of the Freestyle device when compared with the homograft for aortic root replacement.²⁷ Furthermore, Lehman and colleagues³ observed that survival might be improved by using the Freestyle bioprosthesis. Taken together, these different data strongly suggest that the Freestyle bioprosthesis performs similar to CSB and represents a valuable option for AVR in the general population. However, SLB might confer a disadvantage in case of future transaortic valve implantation (TAVI). Because “valve in valve” TAVI emerged as a therapeutic option in elderly patients for redo procedures in degenerated bioprosthesis,²⁸⁻³⁰ concerns have been raised regarding SLB, which may be more prone to coronary coverage during TAVI for prosthetic failure because of its leaflet height and lack of sinuses or a stent.¹ Dvir and colleagues²⁹ observed that valve-in-valve procedures for SLB degeneration created a higher rate of coronary ostial obstruction than the stented valves.

The evolution of the younger (<65 years) and older (>80 years) patients in this cohort also deserves special consideration. The use of conventional biological prostheses is usually avoided in younger patients because of the increased risk of device degradation leading to increased rates of SVD¹ (as high as 26%, 15 years after AVR³¹). In the present study, we observed an 89% of freedom from SVD at 10 years, confirming our previous midterm analysis⁵ and other long-term outcome results.³² Thus, the putative advantage of the Freestyle bioprosthesis over CSB and in terms of durability for this special group of patients seems justified. The Freestyle bioprosthesis may represent an alternative to a homograft in young patients²⁷ and could be considered when a bioprosthesis is required because the risk for eventual reoperation is known to be similar to that for primary isolated AVR.³³ In this young (and often very active) population, a full root replacement might be an attractive option when the annulus size is less than 23 mm, to ensure optimal hemodynamics in these physically demanding patients.³⁴ Finally, we also observed acceptable long-term survival in a large cohort of subjects aged more than 80 years (in consideration of the life expectancy of these patients in the general population). Although the implantation of SLB remains highly debated in this subpopulation considering the higher technical complexity and longer cardiopulmonary bypass time, these results are encouraging

and in line with data previously reported by Ennker and colleagues.³⁵ Thus, the Freestyle bioprosthesis may be a valuable option for AVR in octogenarians.⁵

Study Limitations

The present study is an observational assessment of outcomes. Patients were not randomly assigned to various therapies, and comparison between inherently dissimilar groups is problematic. Clinical follow-up was available through 12 years, but hemodynamic outcomes were not measured during this period in all patients, which does not allow us to draw any conclusion regarding this aspect, especially about long-term evolution and left ventricular remodeling.

CONCLUSIONS

The use of the Freestyle bioprosthesis for AVR resulted in good long-term cardiovascular survival at any age in this all-comers 500-patient cohort. These data suggest that this bioprosthesis could be considered as a valuable option for AVR, particularly for young patients aged more than 30 years who refuse the use of mechanical valves.

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EDITORIAL COMMENTARY

Do stentless valves make a difference?

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In the early 1960s, Ross and Barratt-Boyes separately introduced the aortic homograft into clinical practice. In 1965, Binet and colleagues¹ introduced a stentless porcine bioprosthesis, but this was not pursued because of difficulties with implantation at a time when myocardial protection was in its infancy. Stented bioprostheses were therefore developed because their placement required a much simpler technique and resulted in a reproducible performance. Nevertheless, the transvalvular gradients and limited durability became major concerns. The original free-sewn homograft circumvents most of these problems, but its limited availability prevents its widespread use. This