Aortic valve replacement with the Sorin Pericarbon Freedom stentless prosthesis: 7 years' experience in 130 patients

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Objectives: Aortic stentless pericardial valves were introduced into clinical practice to combine properties of both stentless and pericardial prostheses. The aim of this single-center retrospective study was to assess midterm clinical and hemodynamic results of aortic valve replacement with the Sorin Pericarbon Freedom stentless bioprosthesis.

Methods: From July 1999 through November 2005, 130 consecutive patients (73 [56.1%] male patients) underwent aortic valve replacement with the Sorin Pericarbon Freedom bioprosthesis at our institution. Mean age was 76 ± 5 years (range, 42–86 years), and associated procedures were performed in 50 (38.4%) patients; of these, 41 were coronary artery bypass grafts. Surgical intervention under urgent/emergency conditions and reoperations were performed in 18 (13.8%) and 7 (5.3%) patients, respectively. Mean crossclamp and cardiopulmonary bypass times were 82 ± 24 and 125 ± 40 minutes, respectively. All patients underwent clinical and echocardiographic follow-up (100% complete), and the total cumulative follow-up was 324 patient/years (mean, 2.5 ± 1.8 ; range, 6 months–7 years).

Results: Overall hospital mortality was 8.4%. Overall patient survival was $63\% \pm 6\%$ and $50\% \pm 10\%$ at 5 and 7 years, respectively. Late deaths occurred in 23 patients, and 6 of them were valve related (1.8% patient/years). Freedom from valve-related death and reoperation was $91\% \pm 4\%$ and $94\% \pm 4\%$, respectively, at 7 years. No structural valve deterioration was observed. Endocarditis, thromboembolism, and hemorrhagic complications occurred in 2 (0.6% patient/years), 1 (0.3% patient/years), and 1 (0.3% patient/years) patients, respectively. Mean transprosthetic gradients for valve sizes 23, 25, and 27 were 12.1 ± 3.8 , 10.8 ± 3.8 , and 9 ± 3.1 mm Hg, respectively.

Conclusions: The Sorin Pericarbon Freedom stentless bioprosthesis provides good early and midterm results in terms of hemodynamic performance, survival, and freedom from valve-related complications.

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Stentless aortic bioprostheses appear to provide improved transvalvular gradients and increased orifice areas and survival rates compared with stented valves.¹ Furthermore, pericardial aortic stented valves have demonstrated excellent durability, freedom from primary tissue failure, and freedom from prosthetic endocarditis.^{2,3}

The Sorin Pericarbon Freedom (SPF; Sorin Biomedica, Saluggia, Italy) is a stentless pericardial valve prosthesis made of two sheets of pericardium sutured together without any fabric reinforcement and prepared with a postfixation treatment with homocysteic acid, which neutralizes residues of unbound aldehyde groups left after the fixation process. This peculiar design, the anticalcification treatment, and the absence of any synthetic material except for sutures should provide good results

Abbreviations and Acronyms

AVR = aortic valve replacement
SPF = Sorin Pericarbon Freedom

in terms of hemodynamics, freedom from structural valve deterioration, and freedom from prosthetic valve endocarditis. The aim of this retrospective and single-center study was to assess early and midterm results of aortic valve replacement (AVR) with the SPF bioprosthesis.

Materials and Methods**Study Population**

From July 1999 through December 2005, 130 consecutive patients underwent AVR with the SPF bioprosthesis at our institution. Demographic and clinical preoperative data of the study population are listed in Table 1.

Selection criteria for the implantation of the SPF bioprosthesis were as follows: age older than 65 years, contraindication to oral anticoagulant therapy, request for a biologic valve by the patient, small aortic annulus, and surgeon's preferences. Furthermore, SPF bioprostheses were intentionally implanted in patients with abscesses of the aortoventricular junction. The contraindications for the implantation of the SPF were severe calcification of the aortic annulus and aortic root aneurysm.

Surgical Intervention

Surgical intervention was performed during moderate hypothermia in all patients. Myocardial protection was obtained by using ret-

rograde and selective antegrade cardioplegia. The SPF bioprosthesis was implanted with 3 continuous 4-0 polypropylene sutures both for the inflow and the outflow rim.

Valve sizes 21, 23, 25, and 27 were implanted in 1 (0.8%), 57 (43.8%), 54 (41.6%), and 18 (13.8%) patients, respectively.

Fifty-one associated procedures were performed in 50 (38.4%) patients: 41 coronary artery bypass graftings, 4 mitral valve repairs, 2 mitral valve replacements, 3 replacements of the ascending aorta, and 1 patent foramen ovale closure. Mean aortic crossclamp times were 82 ± 24 and 79 ± 18 minutes for the whole population and for isolated AVR, respectively. Mean cardiopulmonary bypass times were 125 ± 40 and 122 ± 36 minutes for the whole population and for isolated AVR, respectively. Indications for AVR were as follows: calcific aortic stenosis in 99 (76.2%), aortic regurgitation in 10 (7.7%), endocarditis in 8 (6.2%), rheumatic disease in 5 (3.8%), prosthesis malfunction in 6 (4.6%), and congenital bicuspid valve in 2 (1.5%) patients.

After implantation, oral anticoagulant therapy was prescribed in all patients and discontinued 3 months later; this is the routine anticoagulation protocol for all bioprostheses at our institution. Acetylsalicylic acid, 100 mg daily, or ticlopidine, 250 mg daily, were then used as antiplatelet agents. Permanent anticoagulant therapy in a dose adjusted to achieve a target international normalized ratio of 2.0 to 3.0 was prescribed in 6 (5%) patients with chronic atrial arrhythmias.

Follow-up

All patients underwent scheduled visits at our outpatient clinic 1, 6, and 12 months after the operation and on a yearly basis thereafter. Clinical follow-up was 100% complete. Mean clinical follow-up time was 2.5 ± 1.8 years (range, 6 months-7 years), and total cumulative follow-up was 324 patient/years.

From January through September 2006, all of the 96 survivors (74% of the initial study population) were purposely asked to undergo an echocardiographic evaluation. Echocardiography was performed at our institution by the same physician in 70 (72.9%) patients. Twenty-six (27.1%) patients underwent evaluation at different outside laboratories. Echocardiograms from outside laboratories were sent to us by patients or by the patients' referring cardiologists.

Mean echocardiographic follow-up time was 37.1 ± 20 months (range, 9.4-82.2 months). Echocardiography was performed with an iE 33 cardiac ultrasound scanner (Royal Philips Electronics, Amsterdam, The Netherlands) according to the American Society of Echocardiography guidelines. Peak and mean transvalvular pressure gradients were derived by using the modified Bernoulli equation, and the effective orifice area was calculated with the continuity equation.

Morbidity and fatal valve-related events were categorized as resulting from structural valve deterioration, nonstructural valve dysfunction, thromboembolism, prosthetic valve endocarditis, hemorrhagic complication, reoperation, valve-related mortality, or cardiac-related mortality according to the Society of Thoracic Surgeons and American Association for Thoracic Surgery guidelines for reporting morbidity and mortality after cardiac valvular operations.⁴

TABLE 1. Preoperative patient characteristics

	n	%
Age (y)	76 ± 5 (range, 42-86)	
Sex	Male: 73	56
	Female: 57	44
History of smoking	44	34
Hypertension	101	78
Hypercholesterolemia	61	47
Diabetes	30	23
History of CVA	12	9
Chronic renal failure	8	6
Bacterial endocarditis	8	6
Severe COPD	15	12
Previous surgical intervention	7	5
Atrial fibrillation	21	16
EF (%)	58 ± 14	
Urgent/emergency	18	14
NYHA class	I: 6	5
	II: 23	18
	III: 81	62
	IV: 20	15
Additive EUROscore	9.2 ± 2.2	

CVA, Cerebrovascular accident; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; NYHA, New York Heart Association.

Statistical Analysis

Continuous data are expressed as means $\pm$ 1 standard deviation. Categorical data are expressed as percentages. Survival analyses with the Kaplan–Meier method were used to estimate survival and freedom from valve-related adverse events. Statistical analysis was performed with the SPSS statistical package (SPSS, Inc, Chicago, Ill). The incidence of late adverse events is shown by using linearized rates (events per 100 patient/years).

Results

Operative mortality was 8.4% (11 patients). Among these, combined coronary artery bypass grafts and mitral valve replacement were performed in 8 patients and 1 patient, respectively. Causes of early deaths were acute myocardial infarction in 4 patients, multiorgan failure in 3 patients, sepsis in 2 patients, and stroke and acute respiratory distress syndrome in 1 patient each.

Four patients had a complete atrioventricular block and needed permanent pacemaker implantation before hospital discharge.

The overall patient survival rate was $63\% \pm 6\%$ and $50\% \pm 10\%$ at 5 and 7 years, respectively (Figure 1). There were 23 late deaths (7.1% patient/years). Causes and linearized rates of late deaths are listed in Table 2.

Reoperations were performed in 3 patients (0.9% patient/years) during the follow-up period. Causes of reoperation were as follows: endocarditis with annular abscess and consequent valve distortion, nonstructural valve deterioration (paravalvular leak with severe regurgitation), and coronary artery disease with mild paravalvular leak. In the latter case, the valve was not replaced but once again fixed in place.

Figure 1. Kaplan–Meier survival after aortic valve replacement with the Sorin Pericarbon Freedom stentless bioprosthesis (SPF). Filled circles represent estimated survival for the 76-year-old cohort (56% male subjects) in Italy in 2003 (data from the Italian Institute of Statistics, www.istat.it). Vertical lines represent 95% confidence intervals of survival for the SPF cohort.

TABLE 2. Causes and linearized rates of late deaths

Cause of late deaths	No. (% patient/y)
Valve related	
Sudden/unexplained/unexpected	4 (1.2)
Endocarditis	1 (0.3)
Hemorrhage	1 (0.3)
Cardiac related	
CHF	5 (1.5)
AMI	2 (0.6)
Noncardiac	8 (2.4)
Unknown	2 (0.6)

CHF, Congestive heart failure; AMI, acute myocardial infarction.

Freedom from valve-related death (Figure 2) and reoperation (Figure 3) was $91\% \pm 4\%$ and $94\% \pm 4\%$, respectively, at 7 years.

Endocarditis, thromboembolism, and hemorrhagic complications occurred in 2 patients (0.6% patient/years), 1 patient (0.3% patient/years), and 1 patient (0.3% patient/years), respectively. One patient had the SPF bioprosthesis explanted because of a prosthetic valve endocarditis (*Streptococcus bovis*) 1 month after the operation. Another patient with preoperative endocarditis died of acute septic shock 2 months after the operation, and at autopsy, the aortic annulus and the bioprosthesis appeared totally destroyed. A third patient underwent a major cerebrovascular accident. This patient had a clinical preoperative history of nonsignificant carotid artery disease and of diffuse peripheral arterial atherosclerosis. Lastly, another patient, during anticoagulant therapy, had gastric bleeding requiring homologous blood transfusions.

Figure 2. Kaplan–Meier freedom from valve-related death after aortic valve replacement with the Sorin Pericarbon Freedom stentless bioprosthesis.

Figure 3. Kaplan–Meier freedom from reoperation after aortic valve replacement with the Sorin Pericarbon Freedom stentless bioprosthesis.

Mild aortic regurgitation was found in 4 patients (1.2% patient/years); they are asymptomatic and scheduled to undergo an echocardiogram control every year.

Peak and mean transvalvular gradients, effective orifice area, and effective orifice area index are shown in Table 3 for valve sizes 23, 25, and 27 because only 1 patient received a size 21 prosthesis.

Discussion

Nowadays, several different models of aortic valve prostheses are available on the market. Choice depends on several issues: patient age, nature of the aortic valve disease, presence of annulus calcification, contraindication to oral anti-coagulant therapy, and patient and surgeon preferences.

Tissue valves are commonly indicated in patients older than 65 years because no data support implantation in younger patients.⁵ Among tissue aortic valve prostheses, 2 significant distinctions need to be made: between porcine and pericardial valves and between stented and stentless valves.

The first porcine valves were implanted almost 40 years ago,⁶ whereas the first pericardial prostheses were introduced at the end of the 1970s. The latter initially showed a significantly higher incidence of primary failure than porcine xenografts and were temporarily abandoned.⁷ They were reintroduced in 1981 and approved by the US Food and Drug Administration in 1991, and since then, thousands of stented pericardial valves have been implanted in the aortic position with excellent results. Gao and colleagues³ reviewed their long-term experience with 518 stented porcine and 1021 stented pericardial valves. They found that the pericardial valve had a significantly higher rate of 10-

TABLE 3. Hemodynamic data

	Valve size		
	23	25	27
EOA (cm ²)	1.7 ± 0.6	2.1 ± 0.7	2.3 ± 0.5
EOAI (cm ² /m ²)	0.98 ± 0.08	1.15 ± 0.11	1.21 ± 0.09
Peak gradient (mm Hg)	21 ± 7.4	19.5 ± 5.8	14 ± 2.9
Mean gradient (mm Hg)	12.1 ± 3.8	10.8 ± 3.8	9 ± 3.1

EOA, Effective orifice area; EOAI, effective orifice area index.

year actuarial freedom from explantation when compared with the porcine prosthesis (97% vs 90%, $P = .04$).

The difference between stented and stentless valves is primarily based on hemodynamic performance. Theoretically, the absence of a stent and of a sewing ring in a stentless valve should provide more space available for blood flow and result in lower transvalvular gradients and larger effective orifice areas. Many studies have demonstrated stentless valves' superiority in terms of hemodynamics,^{1,8,9} survival from valve-related mortality,¹⁰ and coronary blood flow¹¹ when compared with stented xenografts. However, recent studies have shown no significant differences in hemodynamic performance between stentless and last-generation porcine aortic valve prostheses.^{12,13}

The SPF bioprosthesis is a stentless pericardial valve introduced into clinical practice at the end of the 1990s. Its stentless design and pericardium could play a synergic role, mixing together the advantages of both pericardial and stentless valves to extend valve durability and to improve hemodynamic performance.

We reviewed our 7-year experience with the SPF bioprosthesis, and to the best of our knowledge, this is the first medium-term report of this prosthesis.

There are 3 different implantation techniques: continuous polypropylene sutures, interrupted simple sutures, and interrupted mattress sutures. There are no hemodynamic differences among these 3 techniques.¹⁴

Our preferred implantation technique is with 3 continuous sutures for both the inflow and the outflow rim, which provides reduced crossclamp times, as previously described by Beholz and associates.¹⁵

In our experience we did not find any structural valve deterioration, and in the 3 explanted valves, the leaflets were undamaged and without any sign of calcification.

Freedom from valve-related mortality was 91% ± 4% at 7 years (6 patients). Although this might appear to be rather low, one must take into consideration that 4 of 6 deaths were sudden/unexpected/unexplained, and 1 was due to a massive hemorrhage during reoperation. Furthermore, there are only few patients at risk after 5 years, and this fact inevitably causes a quick decrease of the Kaplan–Meier curve.

Nevertheless, the slope of the survival curve is similar to that of the estimated survival of the cohort from the Italian

population matched for age and sex. The difference between the 2 curves is due only to the early mortality of the SPF cohort; this could mean that if a patient survives the operation and is successfully discharged, his life expectancy decreases over time in the same way as that of the general population.

The hemodynamics of the SPF bioprosthesis, in terms of transvalvular gradients and effective orifice areas, have been shown to be similar to those of other routinely used stentless valves. Borger and coworkers¹ from Toronto, in a series of 310 stentless valves (Toronto SPV and Freestyle), reported the following midterm hemodynamic data: effective orifice area, $1.67 \pm 0.67 \text{ cm}^2$; peak gradient, $17 \pm 10 \text{ mm Hg}$; and mean gradient, $9 \pm 5 \text{ mm Hg}$.

Limitations of the study

Limitations owing to the retrospective design of the study are present. Because of the poor life expectancy of patients in their seventh or eighth decade of life with important comorbidities, patients at risk decrease with time independently from valve-related events.

Survival and event-free curves have few patients beyond 4 years. Continued follow-up will be necessary to assess results at time points during which prosthesis failure is more likely.

Echocardiography was not performed by the same physician and with the same machine.

Preoperative and discharge echocardiographic data are not available for all patients, and thus the evaluation of hemodynamic performance development over time was not possible.

The recently published American College of Cardiology (ACC)/American Heart Association (AHA) Guidelines for the management of patients with valvular heart disease¹⁶ state that routine annual echocardiograms are not indicated in the absence of a change in the clinical status in patients with a bioprosthetic valve (class III, level of evidence C) because the expectation of structural valve deterioration in this time period is low.

Conclusions

The SPF stentless bioprosthesis appears to be a good option for AVR in elderly patients and in those with contraindications to oral anticoagulant drugs. It provided good results in terms of valve durability and freedom from valve-related complications. Echocardiographic data showed that the he-

modynamic performance of the SPF bioprosthesis is excellent and overlaps that of other commercially available stentless bioprostheses.

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