MID-TERM OUTCOMES OF AORTIC VALVE REPLACEMENT USING THE FREEDOM SOLO® STENTLESS BIOPROSTHESIS AT BACH MAI HOSPITAL

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Summary

Objectives: To evaluate mid-term outcomes of aortic valve replacement using the Freedom Solo® stentless bioprosthesis (Sorin Biomedica Group) at Bach Mai hospital, Hanoi. ***Subjects and methods:*** This prospective and descriptive study was carried out in patients undergoing aortic valve replacement using Freedom Solo® stentless bioprosthesis (Sorin Biomedica Group) at Bach Mai Hospital from 01/2016 to 5/2022. ***Results:*** 53 patients aged 62.8 ± 6.1 years old were enrolled in the study. Male patients were 67.9%. The predicted mortality risk by EuroScore II was 1.42 ± 0.69%. The most common prosthetic sizes were 25 mm (56.6%) and 23mm (35.8%), respectively. The mortality and early re-operation rates were 5.7% and 3.8%. The mean follow-up time was 50 months. Survival rates at 3 and 5 years were 90.1% and 86.3%. Heart failure improved gradually after surgery, with NYHA class I at 3-year being 95.6%. Hemodynamic parameters (maximum, mean gradients, valve area) and left ventricular mass index were improved immediately after surgery and remained stable during follow-up. Mid-term follow-up showed no structural valve degeneration or prosthesis-related complication. ***Conclusion:*** Aortic valve replacement using a stentless bioprosthesis showed favorable mid-term outcomes, with improvement in clinical hemodynamic parameters and normalization of the left ventricular mass index. However, a longer study with a larger sample size would be required to validate the results of this study.

** Keywords: Aortic valve; Aortic valve replacement using a bioprosthesis; Freedom Solo® stentless bioprosthesis.*

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Date received: 02/6/2022

Date accepted: 26/6/2022

http://doi.org/10.56535/jmpm.E20220526

INTRODUCTION

Freedom Solo® stentless bioprosthesis (Sorin Biomedica Group), the 3rd bioprosthetic generation, produced from 2 layers of the bovine pericardium and carbonfilm-coated sutures, was first introduced to clinical practice in 2004. Besides its advantages as a bioprosthesis, i.e., avoidance of long-term anticoagulation, the design of this prosthesis tackles higher trans-valvular gradients of classic stented bioprostheses due to their smaller effective orifice area [1]. Previous mid- and long-term studies have shown immediate and sustainable improvement in hemodynamics, which contributes to the normalization of the left ventricular mass index. Freedom Solo® stentless bioprostheses have also presented their durability compared to currently available bioprostheses [2, 3]. The Freedom Solo® valve has been used for aortic valve replacement (AVR) in the Cardiovascular Institute, Bach Mai Hospital since 2013. However, the outcomes of this prosthesis in Vietnamese patients have not been fully investigated. Therefore, we carried out this study: *To evaluate the mid-term results of aortic valve replacement with the Freedom Solo® stentless bioprosthesis at Bach Mai Hospital.*

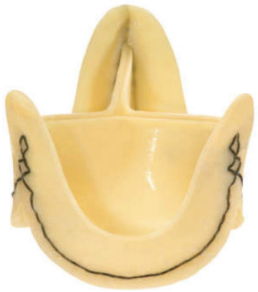

Figure 1: Freedom Solo® prosthesis. "Source*: Repossini A. (2019)"* [1]

SUBJECTS AND METHODS

1. Subjects

53 patients underwent aortic valve replacement with the Freedom Solo® stentless biological valve at Bach Mai Hospital, from 01/2016 to 5/2022.

** Selection criteria:*

Patients had a surgical indication of isolated aortic valve replacement due to aortic valve stenosis, aortic valve regurgitation, or mixed and underwent AVR using the Freedom Solo® stentless bioprosthesis. The patient medical records and consent to participate in the study were completed.

** Exclusion criteria:*

Patients underwent AVR combined with other cardiac surgery, e.g., mitral or tricuspid replacement or repair, coronary bypass surgery, or aortic root repair.

2. Methods

** Study design:* A prospective, non-controlled, descriptive study. Convenient sampling was used.

** Surgical protocol:*

As in conventional open-heart surgery, the patient was under general anesthesia. Following median sternotomy, cardiopulmonary bypass was established. The aorta was opened, and antegrade warm blood cardioplegia was administered directly to coronary ostia. The aortic valve, aortic root, and the location of the coronary ostia were evaluated. Subsequently, AVR with a stentless Freedom Solo® valve was performed for anatomically suitable candidates, following the surgical steps as previously described by Glauber M. et al. [4]. The aortic incision was closed in a two-layer suture fashion, the heart is de-aired, and the aortic clamp was removed. Cardiopulmonary bypass was gradually weaned off and discontinued when the heart resumed function favorably. The arterial and venous cannulas were removed. Heparin was reversed, temporary pacing wires were inserted and, chest drains were placed, and the chest was closed in layers, as usual in open-heart surgery.

** Postoperative care:*

The patient was put on aspirin from postoperative day 2, and discharged with aspirin 100 mg daily. Other anticoagulants were used if necessary, e.g. the patient had chronic atrial fibrillation or risks of thrombotic complications.

Early death was defined as death during the postoperative in-hospital stay or within 30 days of surgery. All patients were follow-up at Bach Mai hospital. Follow-up results were documented in medical records. Patients who were unable to turn up for follow-up were remotely interviewed via mail or telephone. The mid-term monitoring variables included: NYHA class, electrocardiography: Sinus rhythm of atrial fibrillation, transthoracic echocardiography: Trans-valvular gradients, (maximum gradient (P-peak), mean gradient (P-mean)), aortic valve area (AVA), effective orifice area index (i-EOA)); left ventricular ejection fraction (LVEF%), left ventricular mass and left ventricular mass index (LVM, LVM-i). The mid-term events included: Death, re-operation, valve degeneration, thrombosis, embolism, or postoperative endocarditis.

** Statistical analysis:*

Continuous data are shown as mean ± standard deviation (ranges). Categorical variables are expressed as numbers and percentages. Rates of overall survival were estimated according to the Kaplan-Meier method. The data were analysed by the SPSS software (IBM SPSS Statistics for Windows, version 20, IBM Corp., Armonk, NY, USA).

A p-value of less than 0.05 was considered statistically significant.

** Research ethics:*

The study was approved by the Ethics Committee of Vietnam Military Medical University. Research consents were obtained from all the patients. The patient information was kept confidential.

RESULTS

Table 1: Patient characteristics.

Characteristics (n = 53)	**Values**
Mean age (year) ($\bar{X}$ ± SD)	62.8 ± 6.1 (45 - 77)
Male (n, %)	36 (67.9)
Mean BSA (m^2) ($\bar{X}$ ± SD)	1.55 ± 0.15
Mean BMI (kg/m^2) ($\bar{X}$ ± SD)	21.70 ± 2.50
Comorbidity	
Diabetes (n, %)	3 (5.7)
Hypertension (n, %)	21 (39.6)
Dyslipidaemia (n, %)	1 (1.9)
Stroke (n, %)	2 (3.8)
NYHA classification	
I (n, %)	2 (3.8)
II (n, %)	39 (73.6)
III (n, %)	12 (22.6)
IV (n, %)	0 (0)
Clinical presentation	
Chest pain (n, %)	32 (60.4)
Syncope (n, %)	5 (9.4)
Atrial fibrillation (n, %)	3 (5.7)
Predicted mortality by EuroScore II (%)	1.42 ± 0.69 (0.75 - 4.74)
Echocardiographic findings of the aortic valve	
Severe AS (n, %)	17 (32.1)
Severe AR (n, %)	9 (17.0)
Combination of AS and AR (n, %)	27 (50.9)
Mean LVEF (%) ($\bar{X}$ ± SD)	60.1 ± 11.9
Reduced LVEF (< 50%) (n, %)	11 (20.8)
Valve size	
21 (n, %)	4 (7.5)
23 (n, %)	19 (35.8)
25 (n, %)	30 (56.6)
Mean CBP time (min) ($\bar{X}$ ± SD)	78.9 ± 17.2 [54 - 138]
Mean aortic clamp time (min) ($\bar{X}$ ± SD)	59.3 ± 14.1 [42 - 124]
Mean hospital stay (day) ($\bar{X}$ ± SD)	11.0 ± 6.4 [0 - 35]
Early reoperation (n, %)	2 (3.8)
Postoperative stroke (n, %)	3 (5.7)
Permanent pacemaker due to A-V block (n, %)	0 (0.0)
Early death (n, %)	3 (5.7)

** AS: aortic stenosis, AR: aortic regurgitation, BMI: body mass index, BSA: body surface area, NYHA: New*

York Heart Association, LVEF: left ventricular ejection fraction, CPB: cardiopulmonary bypass,

A total of 53 patients underwent aortic valve replacement surgery with stentless Freedom Solo®, 67.9% were male. The mean age was 62.8 ± 6.1 years. NYHA III-IV was 22.6%. Moderately reduced LVEF was seen in 20.8% of patients. Intra-operatively, the most common valve sizes were 25mm (56.6%), followed by 23mm (35.8%). The aortic cross-clamp time and bypass time were 59.3 ± 14.1 and 78.9 ± 17.2 minutes, respectively.

There were 3 early deaths after surgery (5.7%): 1 patient had low cardiac output syndrome due to postoperative myocardial infarction, 1 patient had fatal postoperative ventricular arrhythmia, and 1 patient had a respiratory failure due to fungal pneumonia. Re-operation was carried out in 2 patients: 1 patient was re-operated immediately after surgery due to fatal ventricular arrhythmia, and 1 patient was operated on 1 month after surgery due to para-valvular leakage. No patient required a postoperative permanent pacemaker.

Mid-term results

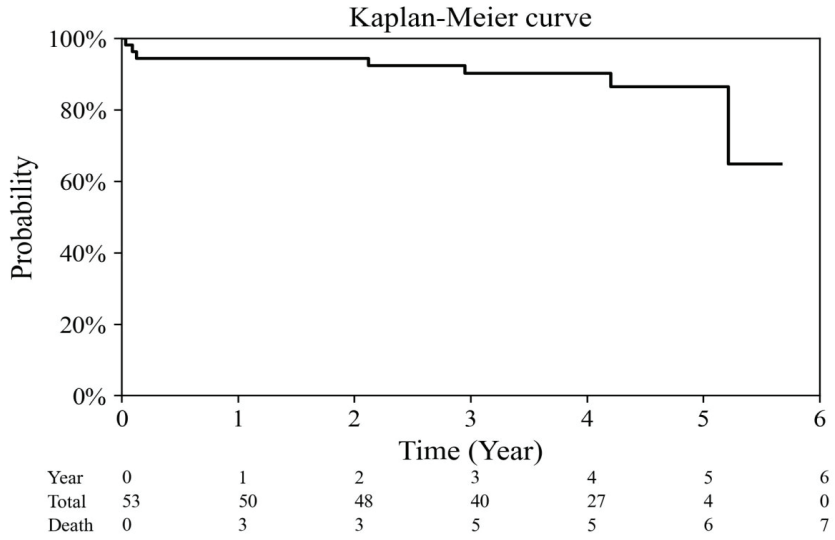

Figure 2: The Kaplan-Meier survival curves of the study.

The mean follow-up time was 50 months, ranging from 20 to 69 months. The overall survival rates at 3 years and 5 years were 90.1% and 86.3%, respectively (*Figure 2*). 4 patients died during follow-up: 2 patients died at home in the third year (1 patient died of unknown cause, another patient died of liver cancer). The other 2 patients died suddenly at home in the fifth and sixth year after surgery.

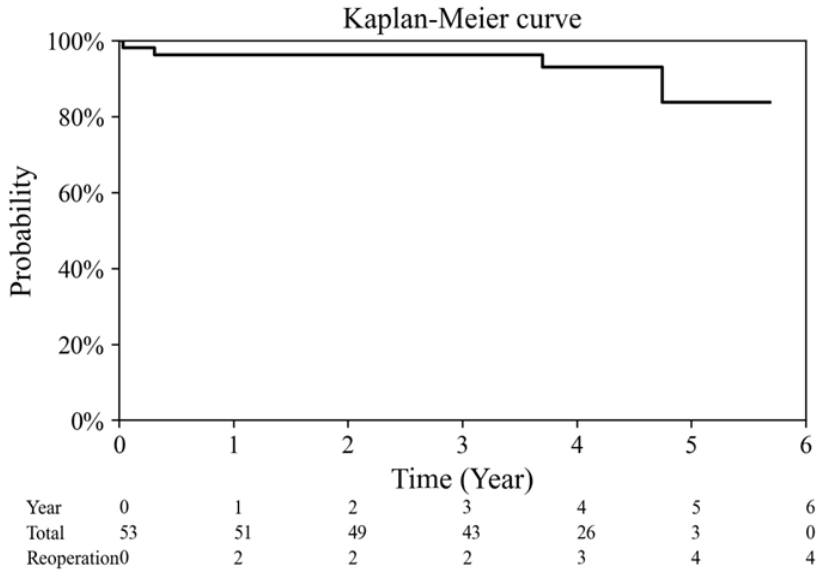

Figure 3: The Kaplan-Meier curves of re-operation.

96.2% and 83.7% of patients did not require re-operation in 3-year and 5-year after surgery, respectively (*Figure 3*). Re-operation was required in 2 patients due to endocarditis at year 4 and 5. Unfortunately, these 2 patients had sudden deaths at home due to unknown causes 6 months after re-operation. No patient underwent re-operation due to degenerative valve disease.

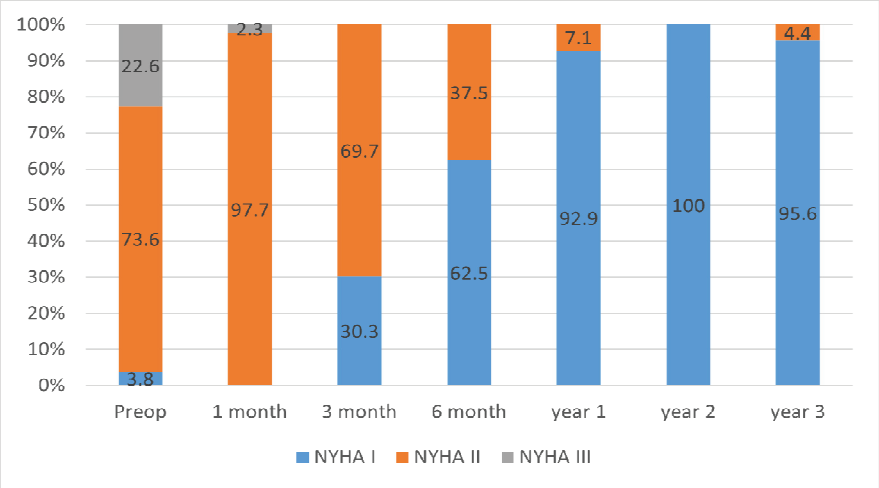

Figure 4: Perioperative heart failure.

All patients showed clinical improvement during follow-up. Most patients recovered to NYHA I within 1 year after surgery (*Figure 4*).

Table 2: Perioperative echocardiographic findings.

Parameter	Valve size	Preoperative (1)	1st month (2)	2nd year (3)	p_{1-2}	p_{2-3}
Ppeak (mmHg) ($\overline{X}$ ± SD)	21	100.2 ± 13.7	21.7 ± 8.1	29.0 ± 0.0	0.250	1.000
	23	82.1 ± 33.0	17.5 ± 6.2	21.8 ± 10.8	< 0.001	0.322
	25	76.4 ± 42.5	14.8 ± 4.6	16.9 ± 7.0	< 0.001	0.194
Pmean (mmHg) ($\overline{X}$ ± SD)	21	64.2 ± 8.7	11.3 ± 2.8	18.0 ± 0.0	0.250	1.000
	23	50.2 ± 20.9	9.7 ± 3.4	12.0 ± 5.6	< 0.001	0.343
	25	47.2 ± 29.0	8.4 ± 3.8	8.5 ± 3.9	< 0.001	0.903
AVA (cm^2) ($\overline{X}$ ± SD)	21	0.7 ± 0.3	1.3 ± 0.0	1.6 ± 0.0	0.250	1.000
	23	1.0 ± 0.6	1.8 ± 0.3	2.0 ± 0.4	< 0.001	0.770
	25	1.2 ± 0.9	2.1 ± 0.3	2.1 ± 0.3	< 0.001	0.119
iEOA (cm^2/m^2) ($\overline{X}$ ± SD)	21	0.5 ± 0.2	0.9 ± 0.0	1.0 ± 0.0	0.250	1.000
	23	0.7 ± 0.4	1.2 ± 0.2	1.3 ± 0.3	0.001	0.492
	25	0.8 ± 0.6	1.3 ± 0.2	1.3 ± 0.2	< 0.001	0.023
LVEF (%) ($\overline{X}$ ± SD)	< 50%	42.3 ± 3.8	48.6 ± 7.4	67.6 ± 8.2	0.027	0.062
	> 50%	64.8 ± 8.2	64.9 ± 7.8	65.4 ± 4.5	0.142	0.952

Table 2 shows significant improvement of the trans-valvular pressure gradients at 1 month after surgery. The changes were not significant during the later follow-up period (*Table 2*). The mean trans-valvular pressure gradients in patients receiving all 3 sizes of valve were less than 20 mmHg. The postoperative aortic valve area (AVA) increased immediately, and no moderate to severe patient-prosthesis mismatch (PPM) was noted.

Table 3: Perioperative left ventricular mass and mass index.

Parameter	Lesion	Preoperative (1)	1st month (2)	2nd year (3)	p_{1-2}	p_{2-3}
LVM (gram) ($\overline{X}$ ± SD)	Combined AS + AR	273.0 ± 102.6	189.7 ± 67.9	150.8 ± 36.6	< 0.001	0.011
	Severe AS	245.1 ± 108.5	191.1 ± 71.5	154.6 ± 56.4	0.005	0.074
	Severe AR	249.0 ± 73.3	185.6 ± 48.8	152.0 ± 17.0	0.078	1.000
LVMI (g/m^2) ($\overline{X}$ ± SD)	Combined AS+AR	176.1 ± 60.6	120.2 ± 41.1	92.4 ± 22.4	< 0.001	0.009
	Severe AS	160.1 ± 66.2	124.6 ± 46.0	97.8 ± 34.4	0.006	0.036
	Severe AR	157.1 ± 43.8	117.0 ± 27.7	91.5 ± 6.4	0.078	1.000

** LVM: Left ventricular mass; LVMI: left ventricular mass index; AS: aortic stenosis; AR: Aortic regurgitation*

Table 3 shows that reduction of left ventricular volume and regression of left ventricular mass index occurred immediately after surgery and during follow-up. After 2 years, the left ventricular mass index in patients with severe aortic stenosis, severe aortic regurgitation, and the combination of both was 97.8 ± 34.4 (g/m^2), 91.5 ± 6.4 (g/m^2), and 92.4 ± 22.4 (g/m^2), respectively.

DISCUSSION

In our study, the NYHA class of the patients improved gradually over time. The majority of patients (92.9%) recovered to NYHA I within 1 year and this remained stable during follow-up. The favorable change in the NYHA class contributes to the success of this surgery. These results are similar to those in previously published studies [2, 5].

A randomized study by Schaefer et al. comparing stent vs. stentless valves in 60 patients showed that patients receiving stentless aortic valves had larger valve size (25.7 mm vs. 22.9 mm)

despite similar body surface area (BSA) (1.83 vs 1.81 m^2) [6]. The tendency to use larger valves when using the stentless aortic valves was also observed in our study, with the most patients replaced with the 25 mm (56.6%) and 23 mm valves (35.8%), and only 7.5% of patients received 21 mm valves. One of the factors affecting the long-term outcomes of patients with prosthetic valves is the patient-prosthesis mismatch (PPM). PPM is defined as the incompatibility of the prosthetic open area and the physical demand of a patient and normally occurs when the effective orifice area index (iEOA) < 0.85 cm^2/m^2 [7]. Various degrees of PPM can occur in 8 - 80% of patients with aortic valve replacement [8]. Long-term PPM is associated with postoperative mortality, with reports showing that patients with severe PPM have significantly lower survival rates than patients without PPM. If a patient has PPM and LVEF < 40%, the mortality rate is 77 times higher than in those with normal LVEF [8]. In addition, the incompatibility between the patient and prosthetic valves worsens heart failure and accelerates the degeneration of bioprosthetic valves. Stentless aortic valves were developed to increase the valve size and effective orifice area, thereby reducing postoperative PPM in patients requiring valve replacement, especially in patients with small aortic roots and those with high body mass index. For stentless valves, the risk of PPM is minimized because the valves are pliable, and their structure facilitates trans-valvular hemodynamics. Wollersheim found that the rate of PPM after stentless aortic valve replacement in 350 patients was 9.6%, of which 1.3% had severe PPM (< 0.65 cm^2/m^2) and 8.3% had moderate PPM (0.65 - 0.85 cm^2/m^2) [9]. The results of our study showed significant improvement in transvalvular hemodynamics after Freedom Solo valve replacement. At 1 month postoperatively, the mean and maximum trans-valvular gradients decreased to low levels for all implanted valve sizes. The mean gradient in all valve sizes was below 20 mmHg after 2 years of follow-up (12.0 ± 5.6 mmHg for 23 mm valves and 8.5 ± 3.9 mmHg for 25 mm valves) (*Table 2*). The results also show that the valve area and valve orifice index increased after surgery and remained stable during the 3-year follow-up. The lowest area was seen in the 21 mm valve, with the valve area ranging from 1.3 to 1.6 cm^2 and the effective valve orifice area index ranging from 0.9 to 1.0 cm^2/m^2. Larger valve sizes, e.g., 23 and 25 mm, had larger valve orifice areas. There were

no patients with PPM, or iEOA < 0.85 cm^2/m^2. The marked improvement of transvalvular hemodynamics facilitated the reconstruction as well as the left ventricular function after surgery. In our study, preoperative echocardiography showed left ventricular hypertrophy with a mean left ventricular mass of 260 ± 99.4g and left ventricular mass index of 167.8 ± 59.6 g/m^2. Both of these indexes decreased after 1 month of surgery and were maintained throughout the follow-up period, regardless of severe aortic stenosis, severe regurgitation, or a combination of stenosis and regurgitation (*Table 3*). Similar improvements were seen in left ventricular function; 20% of patients had preoperative moderately reduced LVEF of 30 to 50%. The improvement of LVEF was noted in all patients after surgery and remained stable at a 3-year follow-up.

Valve durability is the primary determinant of biological valves, and it is even more crucial for stentless biological valves due to the complexity of suture technique as well as techniques in re-do valve replacement. The results of the 3-year follow-up of patients in our study show that none of the patients required re-operation due to reasons related to valvular degeneration. 3 years after surgery, echocardiography results show that the biological valve was working well, and there were no cases of valve degeneration as well as moderate or higher levels of valve regurgitation. A review by Wollersheim et al. summarizing 9 different studies involving 1296 patients showed a re-operation rate of 0.9% (0.5% per patient per year) over a mean follow-up period of 22 months (maximum of 83 months). The indications for re-operation were valve regurgitation in 5 patients, the oversized valve in 1 patient, and prosthetic endocarditis in 5 patients, but no patient had re-operation because of valvular structural failure [5]. Redo-aortic valve replacement of a stentless valve is still challenging and may even require aortic root replacement and is associated with increased mortality. Stanger et al. reported the re-do of the Freedom Solo® valves in their study, which shows a high percentage of calcification, not only on the valve but also spreading to the aortic root, making surgery difficult. However, with re-operations due to tearing of the leaflets, redo-valve replacement surgery is relatively manageable [10]. With advances in transcatheter aortic valve implantation (TAVI), some patients with Freedom Solo® valve degeneration had this procedure successfully performed [11]. The challenge of this procedure is that the coronary ostia are very close

to the suture line compared to other stented valves, thus, degenerated leaflets are more likely to block the coronary ostia during the procedure. However, the advantage of TAVI for valve-in-Freedom Solo® valve is the possibility to insert a larger valve compared to other stented biological valves [11].

Wollersheim et al. studied over 350 patients and found that overall survival rates after 1, 5, and 9 years were 92%, 74%, and 47%, respectively. During the follow-up, 71 patients died. The causes of death include pneumonia, infective endocarditis, heart failure, myocardial infarction, stroke, cancer, kidney failure, bleeding, abdominal aortic aneurysm, and unknown causes. According to multivariable regression analyses, the independent risk factors were myocardial infarction, pneumonia, postoperative cerebrovascular accident, PPM, male gender, diabetes mellitus, and age [9]. In our study, the survival rates at 3-year and 5-year were 90.1% and 86.3%, respectively. Of these, only 3 patients died suddenly of possible cardiovascular causes, and one patient died of liver cancer.

CONCLUSION

Aortic valve replacement with a Freedom Solo® stentless bioprosthetic valve is feasible with promising mid-term results. However, a study with a larger sample size and longer follow-up would be required to validate the results of our study.

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