

Mechanical Heart Valve Replacement in a Low-Middle Income Region in the Modern Era: Midterm Results from a Sub-Saharan Center

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Abstract

Background The management of patients with mechanical heart valves remains a major concern in populations with limited resources and medical facilities. This study reports the clinical outcomes of patients who underwent mechanical valve implantation in a sub-Saharan center over an 8-year period.

Methods A total of 291 mechanical valves were implanted in 233 patients in our institution between February 2008 and June 2016. A total of 117 patients underwent mitral valve replacement (MVR, 50.2%), 57 had aortic valve replacement (AVR, 24.4%), and 59 underwent both AVR and MVR (double valve replacement [DVR], 25.7%). The mean age at surgery was 27.6 ± 13.4 years (range, 7–62 years). Rheumatic etiology was found in 80.6% of the patients. Hospital mortality, late deaths, and valve-related events were reviewed at follow-up (839 patient-years, range: 1–9.4 years, complete in 93%).

Results The 30-day mortality was 4.7% (11/233). The overall survival at 1 and 6 years for the whole cohort was $88.8 \pm 2.1\%$ and $78.7 \pm 3.3\%$, respectively. The 6-year survival for AVR, MVR, and DVR was $89.3 \pm 4.8\%$, $73.2 \pm 5.4\%$, and $79.3 \pm 5.8\%$, respectively ($p = 0.15$). The freedom from neurologic events and anticoagulation-related bleeding at 6 years was $93.1 \pm 2.1\%$ and $78.9 \pm 3.7\%$, respectively. No patient had reoperation at follow-up. No case of prosthetic valve thrombosis was identified. Eight full-term pregnancies were reported.

Conclusion This preliminary experience reports acceptable midterm results after mechanical heart valve implantation in our region. Both accurate surgical evaluation and strategies, either financial or social, facilitating patient's education and medical assistance are crucial to ensure good results. Long-term follow-up and further studies comparing current nonthrombogenic options are warranted to draw reliable conclusions.

Keywords

- mechanical valve
- developing countries
- rheumatic disease

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Introduction

Rheumatic heart disease (RHD) is the most common cause of heart failure and cardiovascular mortality in young and socially disadvantaged populations living in the sub-Saharan region.¹ Recent echocardiography-based studies have reported a prevalence between 15 and 30 cases per thousand people living in this area, which is the highest rate in the world.^{2,3}

Although palliative, valve surgery represents the only option for many as the local preventive measures to limit the incidence of acute rheumatic fever (ARF) and RHD remains ineffective. However, the ideal valve procedure in rheumatic etiology is still subject to debate especially among the populations in developing countries. Indeed, since the early era of valve surgery, nonthrombogenic options are advocated in these patients to avoid complications associated with lifelong anticoagulation required after mechanical valve implantation. On the other hand, the high rate of reoperation resulting from the poor durability of tissue valves in young patients⁴ and the suboptimal results of technically demanding valve repair in rheumatic disease^{5–7} have potentially supported the use of mechanical valves even in disadvantaged communities.

In fact, the limited access to repeat surgery in low-middle income regions mainly due to financial constraints and the recent improvement in mechanical valves properties have further supported an increase in use of mechanical valves for their possible even though unproven freedom from reoperation.

With the exception of few studies,^{8,9} reports on the use of mechanical valves in the sub-Saharan populations are anecdotal mainly due to the great deficit of cardiosurgical institutions in this region.^{10,11}

This paper reviews the outcomes of patients who underwent mechanical valve replacement at a unique Central Africa cardiosurgical center,¹² serving one of the world's poorest regions with an estimated population of 40 million.

Patients and Methods

The clinical files of 233 patients who underwent 291 mechanical valve replacements in our institution between February 2008 and June 2016 were reviewed. Patients with thoracic aorta surgery, coronary disease and those with history of stroke were excluded. However, patients with associated valve repair, aortic root enlargement, pericardiectomy, and atrial septal defect closure were included in the study.

One hundred and seventeen patients underwent mitral valve replacement (MVR group; $n = 117$, 50.2%), 57 had aortic valve replacement (AVR group; $n = 57$, 24.4%) and 59 underwent both aortic and mitral replacement ($n = 59$, 25.3%, double valve replacement [DVR] group). Rheumatic disease was the most common etiology (80.6%). Associated procedures were performed in 150 patients ($n = 80/117$ in MVR, $n = 27/57$ in AVR, and $n = 43/59$ in DVR). The clinical characteristics of patients are listed in (► **Table 1**).

The institutional review board approved the study and the consent form was waived for this retrospective study.

Sponsorship and Planning of Surgeries

Due to the absence of a local healthcare coverage and the lower-middle income status of the country, few patients are able to afford their medical care (Cameroon Per-capita Gross National Income in 2014: 1,360 USD; minimum annual salary: 583 USD; mean cost of heart surgery: 5,348 USD). A social case office was created with the contribution of local and international nongovernmental organizations (NGO) to assist the underprivileged patients. Since 2011, this system has covered more than 88% of patients who had heart surgery in our institution although only one-third of the patients on our waiting surgical list have benefited from it.

The surgical activities started in 2005 during surgical missions by foreign teams. A total of 47 foreign surgical teams have visited the institution during the study period including 25 and 22 pediatric and adults' missions respectively. Following the recruitment of a Cameroonian born adult senior surgeon in 2013, the autonomy of the local team was empowered with consequent reduction of visiting teams for acquired heart disease (AHD). Thus, the local team has been fully autonomous since 2013 with regards to the surgical treatment of patients with AHD. However, the pediatric missions have continued as well as the periodical visits (1–6 months) of foreign anesthesiologists to support the young local anesthesiology staff. Between 2009 and 2011, the surgeries performed by the local team represented only 1% of the surgical activities, whereas this percentage increased to ~45% (98% AHD surgery) during the last 2 years of the study.

Surgical Technique

Intraoperative transesophageal echocardiography was routinely used in all the patients to assess the morphology and the function of the cardiac valves. A full median sternotomy was performed in all cases. Cardiopulmonary bypass was established through the cannulation of the ascending aorta and right atrium or both caval veins according to the specific procedure. The mode of administration and the type of cardioplegic solution either crystalloid (mainly Custodiol HTK solution) or warm blood were chosen according to the preference of the surgeon. The mitral valve was approached mainly through a standard left atriotomy whereas a supracoronary "Hockey Stick" aortotomy was done in the majority of aortic procedures. The decision to replace the valve was taken by the senior surgeon and the model of the mechanical prosthesis was chosen based mainly on availability at the time of the surgery (On-X valves in 82.1% of patients; ► **Fig. 1**). In patients who underwent mitral replacement, subvalvular apparatus was maintained whenever possible. The posterior mitral leaflet was preserved in cases with less fibrotic involvement especially and in presence of impaired preoperative left ventricular function. In alternative, artificial PTFE chords implantation was performed after complete resection of fibrotic or calcified sub-valvular apparatus. Aortic valves were implanted in the supraannular position in all cases.

Follow-up

All patients received oral anticoagulation from the first postoperative day when possible following a target International

Table 1 Patient's characteristics and operative data

Variables	AVR (n = 57)	MVR (n = 117)	DVR (n = 59)
Age (y), mean \pm SD	25.7 \pm 12.1	27.8 \pm 13.3	27.6 \pm 14.1
Male sex, n (%)	39 (68.4)	45 (38.4)	36 (61.0)
Body mass index, kg/m ² , mean \pm SD	23 \pm 4.7	21.6 \pm 5.1	22.6 \pm 3.8
Body surface area, m ² , mean \pm SD	1.61 \pm 0.3	1.49 \pm 0.3	1.42 \pm 0.6
New York Heart Association class \geq III, n (%)	52 (91.2)	99 (84.6)	56 (94.9)
Previous cardiac surgery, n (%)	2 (3.5)	2 (1.7)	0 (0.0)
Valve regurgitation, n (%)	43 (75.4)	64 (54.7)	–
Valve stenosis, n (%)	4 (7.0)	25 (21.3)	–
Mixed valve disease, n (%)	10 (17.5)	28 (23.9)	–
Rheumatic etiology, n (%)	38 (66.6)	99 (84.6)	51 (86.4)
Left ventricle ejection fraction, mean \pm SD	60.9 \pm 12.2	62.2 \pm 12.3	57.3 \pm 10.7
Left ventricle ejection fraction \geq 50%, n (%)	7 (12.2)	18 (15.4)	6 (10.1)
PAPs, mean \pm SD	–	76.7 \pm 23.7	75.5 \pm 23.0
Atrial fibrillation, n (%)	–	28 (23.9)	10 (16.9)
Main concomitant procedures	27 (47.3)	80 (68.3)	43 (72.8)
Tricuspid valve repair	8 (14.0)	76 (64.9)	27 (45.7)
Mitral repair	11 (19.2)	–	–
Aortic repair	–	4 (3.4)	–
Aortic annulus enlargement	8 (14.0)	–	16 (27.1)
Cardiopulmonary bypass time (min), mean \pm SD	101.3 \pm 54.5	118.2 \pm 64.2	173.7 \pm 79.6
Cross clamping time (min), mean \pm SD	66.7 \pm 33.3	75.6 \pm 47.6	125.8 \pm 68.7
Intensive care unit stay (h), mean \pm SD	58.3 \pm 30.6	75.3 \pm 34.8	86.9 \pm 49.3
Hospital stay (d), mean \pm SD	16.5 \pm 5.1	15.9 \pm 3.6	17.2 \pm 4.4
Hospital death (30-d mortality), n (%)	2 (3.5)	6 (5.1)	3(5.0)

Abbreviation: PAPs, systolic pulmonary artery pressure.

Normalized Ratio (INR) of 2.5 to 3.5 for MVR and DVR groups and 2.0 to 3.0 for AVR group. In cases with controlled bleeding, concomitant subcutaneous injections of low-molecular weight heparin (*Clexane*, SANOFI: 60–100 UI/kg twice daily) were administered from the first postoperative day as bridging anticoagulant therapy. All patients had postoperative transthoracic echocardiogram before discharge and during follow-up in our outpatient department or during external screening campaigns in remote areas. Other information was collected by interview to the patient's physicians or cardiologist. A monthly INR control was recommended in all the patients whenever possible. The mean global clinical follow-up was 839 patient-years (range: 1–9.4 years) and it was 93% complete (16 [7%] of the 222 patients who were discharged from the hospital were lost at follow-up).

Assessment of Patient's Compliance

To assess the compliance to oral anticoagulation therapy at follow-up, we classified the patients in three different groups according to both the regularity of oral anticoagulation intake and the INR control (**Table 2**).

Statistical Analysis

Statistical analysis was performed with StatView 4.5 (SAS Institute Inc, Abacus Concepts, Berkeley, California, United States). Overall survival, freedom from valve and anticoagulation related events (bleeding, thromboembolism, reoperation, endocarditis, and neurologic events) were expressed as mean values \pm 1 standard deviation, and computed by using the Kaplan–Meier method. Differences among curves were analyzed by means of the log-rank Mantel–Cox test. For all statistical analysis a *p*-value $<$ 0.05 was considered significant. Hospital deaths and lost at follow-up were included in the survival analysis. The patients lost at follow-up were included in the survival analysis up to their last period of control.

Results

In-Hospital Mortality

The overall 30-day mortality was 4.7% (11/233); by groups: AVR = 2 (3.5%), MVR = 6 (5.1%), DVR = 3 (5%). Six deaths were due to postoperative low cardiac output syndrome

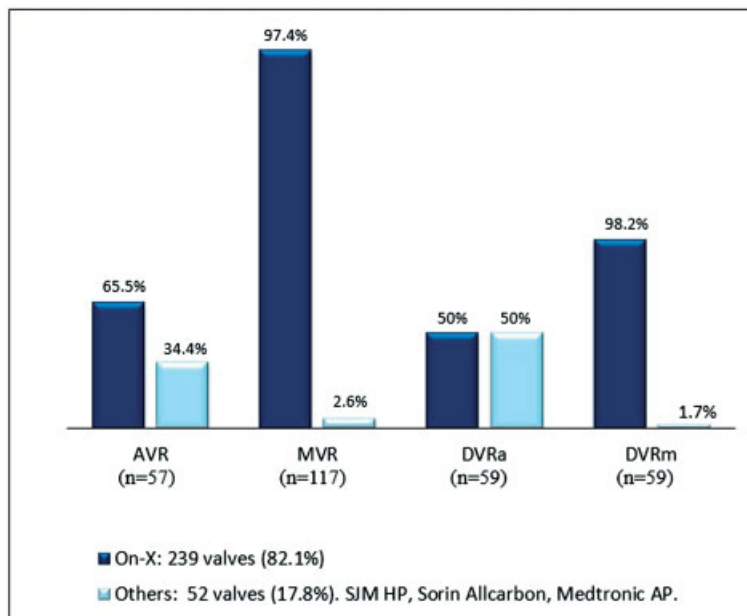


Fig. 1 Mechanical valves data—models and sizes. AP, advance performance; AVR, aortic valve replacement; DVRa, aortic prosthesis in double valve replacement; DVRm, mitral prosthesis in double valve replacement; MVR, mitral valve replacement; SJM HP, St Jude Medical Hemodynamic Plus.

whereas other causes were pneumonia ($n = 1$), acute renal failure ($n = 1$), sudden death ($n = 2$) and pulmonary embolism ($n = 1$).

Survival

Twenty nine late deaths were recorded (AVR = 3; MVR = 18; DVR = 8) reporting a 1 and 6-year survival for the whole cohort of $88.8 \pm 2.1\%$ and $78.7 \pm 3.3\%$, respectively (►Fig. 2A). The 6-year survival divided by groups was $89.3 \pm 4.8\%$, $73.2 \pm 5.4\%$ and $79.3 \pm 5.8\%$ for AVR, MVR, and DVR, respectively (►Fig. 2B). The Log-rank test did not detect any significant difference between the groups ($p = 0.15$). The causes of death at follow-up are listed in (►Table 3).

Valve-Related Events

The 1- and 6-year freedom from bleeding for the whole study was $98.6 \pm 0.8\%$ and $78.9 \pm 3.7\%$, respectively (6-year for the groups: AVR: $80.5 \pm 7.7\%$; MVR: $78.6 \pm 5.2\%$; DVR:

$71.5 \pm 9.0\%$, $p = 0.53$; ►Fig. 3A and B). Two patients with major bleeding (gastrointestinal) died at follow-up.

Prosthetic valve endocarditis was reported in two patients at follow-up. One patient who underwent AVR for aortic endocarditis presented 8 months after with persistent fever and vegetations on the mitral valve. A second patient with Human Immunodeficiency Virus infection who had DVR presented with prosthetic aortic valve endocarditis three months after surgery.

No case of prosthesis thrombosis was observed at follow-up.

Freedom from Neurologic Events

Twelve patients experienced neurologic events at follow-up and five of these events were fatal. The 1 and 6-year freedom from neurologic injury was $98.6 \pm 0.8\%$ and $93.1 \pm 2.1\%$ for the whole cohort (►Fig. 4A). The 6-year freedom for neurologic events according to valve procedure was 100%,

Table 2 Compliance to anticoagulation therapy at follow-up

Status	AVR ($n = 52$)	MVR ($n = 101$)	DVR ($n = 53$)	Total ($n = 206$)
-Regular intake of OAT -Monthly INR control	13	32	15	60 (29.1%)
-Regular intake of OAT -INR control ($>1 \leq 3$ mo)	32	54	29	115 (55.8%)
-Discontinued intake of OAT -INR control (> 3 mo)	7	15	9	31 (15.0%)

Abbreviations: INR, international normalized ratio; OAT, oral anticoagulation therapy.

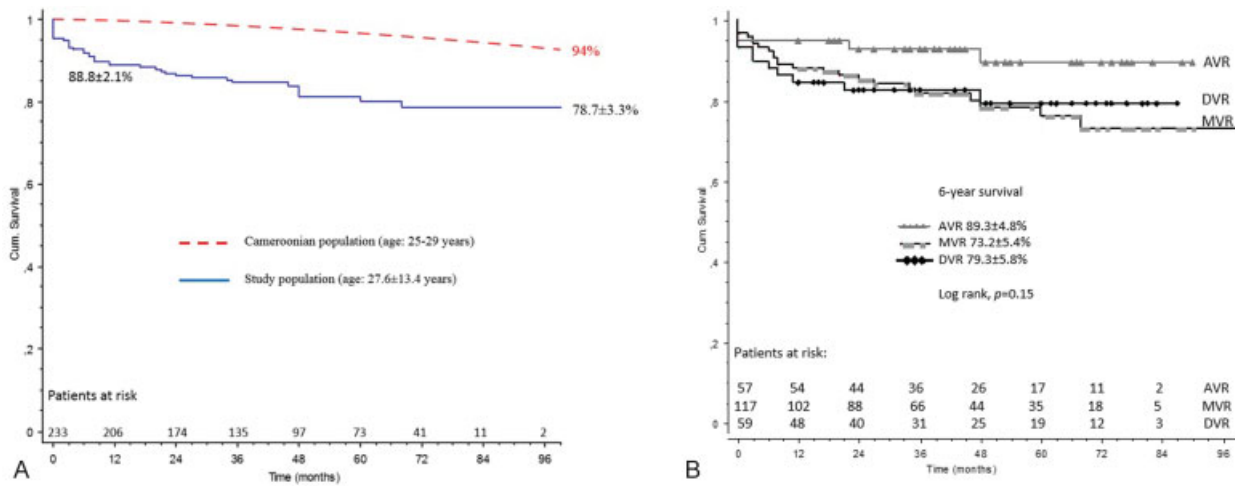


Fig. 2 Survival of the whole cohort and the expected survival of the Cameroonian population aged 25–29 years (A) Survival according to valve procedure (B).

$91.1 \pm 3.0\%$, $90.9 \pm 5.2\%$ for AVR, MVR, and DVR respectively (\rightarrow Fig. 4B).

Echocardiography Results

Three patients who received a 17 mm aortic prosthesis (St. Jude Medical, Hemodynamic Plus) reported moderate patient-prosthesis mismatch (Indexed Effective Orifice Area $0.65\text{--}0.85\text{ cm}^2/\text{m}^2$) at follow-up, whereas five patients who underwent MVR had moderate aortic regurgitation (AR) at follow-up as progression of mild AR at surgery. None of these patients reported significant symptoms requiring reoperation.

Pregnancies

Eight full-term pregnancies and five abortions were reported in 10 patients at follow-up. Five of the 8 patients who had full term pregnancy maintained oral anticoagulation therapy throughout their pregnancies and had subcutaneous heparin only a few days before Caesarean delivery. No cases of anticoagulation-related embryopathy were reported.

Patient's Compliance

Approximately 85% of the patients observed at follow-up ($n = 175/206$) were judged compliant with oral anticoagulation therapy (\rightarrow Table 2).

The 6-year freedom from cardiovascular events (cardiac death, endocarditis, bleeding, and neurologic events) suggested an increased complication rate among the noncompliant patients ($55.5 \pm 10.6\%$) as compared with the compliant group ($66.6 \pm 4.5\%$) although this difference was not found statistically significant ($p = 0.16$) (\rightarrow Fig. 5).

Discussion

In recent years, significant improvements have been made in mechanical heart valve properties, along with better hemodynamic performance and low thrombogenicity. However, their use in poorly compliant populations especially in low-income countries remains controversial for the lack of anticoagulation management facilities and the disadvantaged socio-economic environment that have been associated with major risk of prosthetic valve related complications.^{13,14}

Are mechanical valves safe enough to be used in the Sub-Saharan population? The reality is that little is known as few data have been presented in the medical literature. This scarcity of data reflects the lack of heart specialists and specialized centers in this region,^{10,11,15,16} one of the poorest in the world. The shortage of medical infrastructure, the extreme poverty and the cultural complexity expressed by patient's poor compliance, inexorably suggest a cautious selection of the surgical procedures to this particular environment.

In the Sub-Saharan region, valvular diseases are predominantly of rheumatic origin with a high prevalence among young patients from disadvantaged populations.^{1,3} In this subgroup, tissue valves and conservative techniques are limited by a poor durability due to early structural valve deterioration and repair failure over time.^{4-7,17} Thus, for many patients, mechanical valve replacement could represent an attractive compromise despite the risk of associated complications.

In our series, the choice of mechanical prosthesis was driven by several factors. First, the relatively young age of our cohort (mean age: 27.6 ± 13.4 years) and the predominance

Table 3 Causes of deaths at follow-up

Causes of death	AVR	MVR	DVR
Heart failure	1	8	3
Endocarditis	1	–	1
Bleeding	–	2	–
Stroke	–	4	1
Sudden death	1	1	1
Unknown		3	2
Total	3	18	8

Abbreviations: AVR, aortic valve replacement; DVR, double valve replacement; MVR, mitral valve replacement.

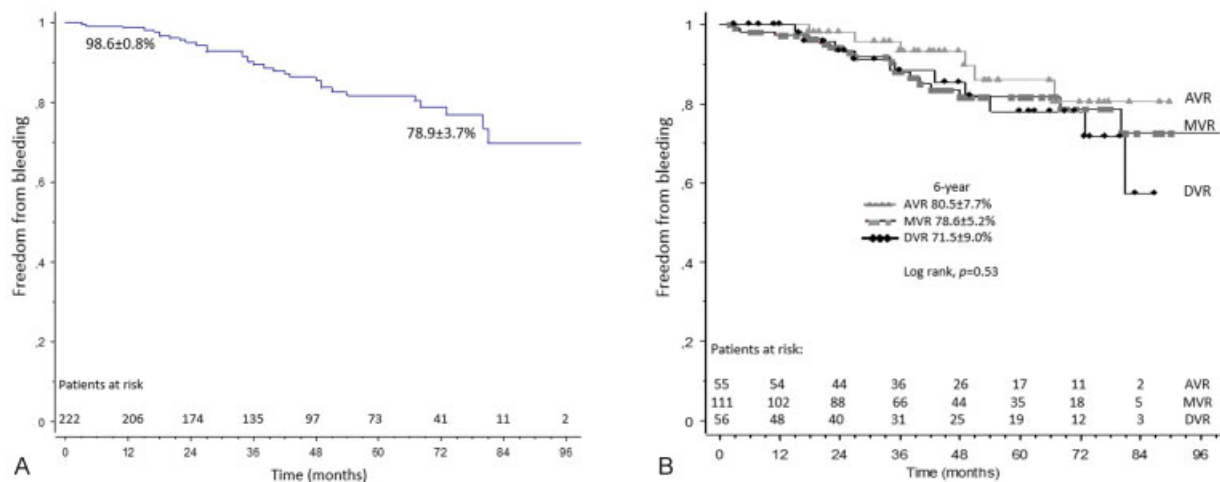


Fig. 3 Freedom from anticoagulation related bleeding: whole cohort (A) and procedure related (B).

of rheumatic etiology (80.6%). Second, the expected compliance and the facilities of patients and relatives to attend postoperative visits and medical therapy in our institution were judged acceptable. Third, the limited financial resources have potentially supported the choice of mechanical valves as costs arising from reoperation would have not been affordable in many cases. Indeed, in the absence of a local healthcare system, more than 88% of our patients were financially supported by private NGOs for their surgery. However, only 35% of the patients of our waiting list benefits from this sponsorship. Thus, it is difficult to guarantee multiple supports for a single case. Lastly but not the least, it is possible that the rate of valve replacement was also linked to surgeon factors.^{18,19} During the first 3 years of the study period, a great number of valve procedures were performed by foreign surgeons during surgical missions. With few exceptions, the surgeons' experience in rheumatic valve disease was limited.

The operative mortality was 4.7%. This ranges between 2.3 and 8.2% in series in similar populations.^{9,20} Furthermore,

our mortality rate was comparable with reports from the EACTS and STS databases²¹ ranging between 2.9 and 3.7% and 4.3 and 6% for AVR and MVR, respectively (3.5–5.1% in our study). Consistent with findings in a West African experience,⁸ the progression of heart failure was a common cause of death (41%) in our cohort at follow-up, especially in patients who had impaired ventricular function prior to surgery as a result of late referral due to both socio-cultural habits and the limited access to specialized institutions.

Approximately 85% of our patients at follow-up were judged compliant with oral anticoagulation therapy (►Table 2). This ranges between 40 and 56% in previous series in similar populations.^{9,22} We think the location of the institution in a rural area where the majority of our patients are living and our external screening campaigns in remote areas were supporting factors for patient's compliance.

The overall freedom from anticoagulation related bleeding was $78.9 \pm 3.7\%$ at 6-year. This was higher than previous reports from others third world populations^{9,20} and accounted for 6.8% (2/29) of the deaths at follow-up.

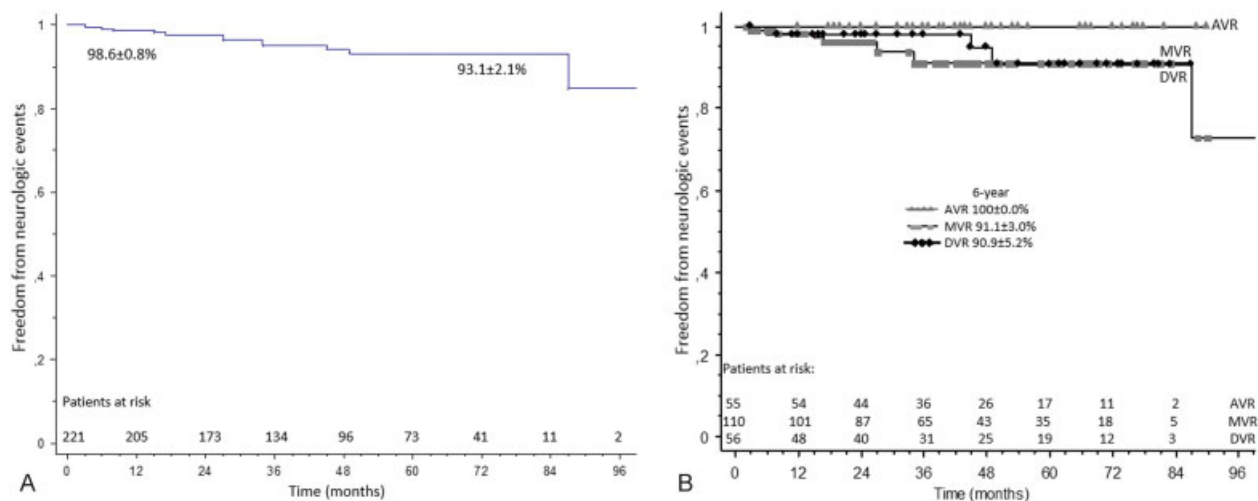


Fig. 4 Freedom from neurologic events at 1 and 6 years: whole cohort (A) and procedure related (B).

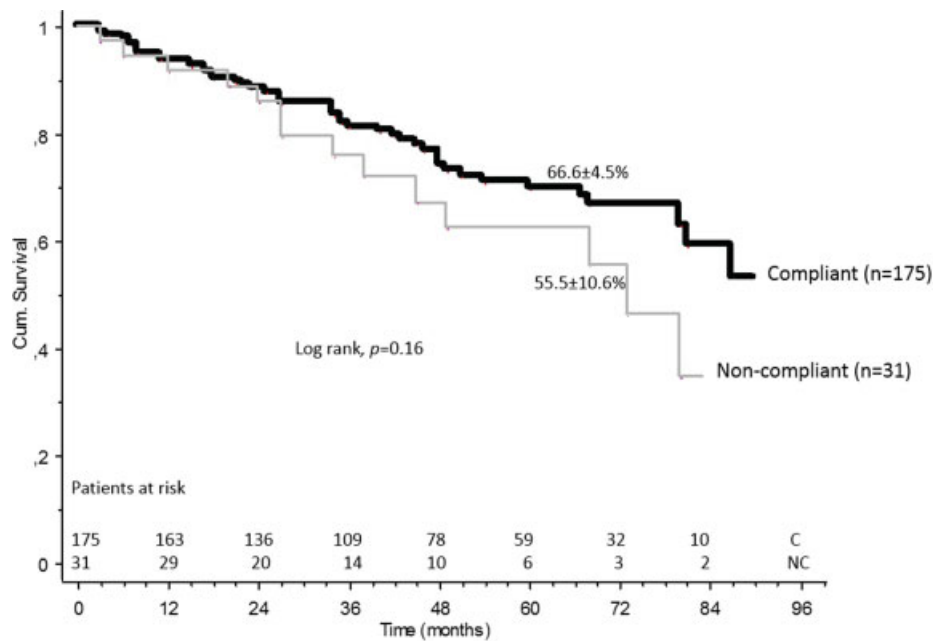


Fig. 5 Comparative event-free survival (cardiac death, stroke, bleeding, endocarditis) of compliant and noncompliant patients. C, compliant; NC, noncompliant.

We think the rate of bleeding was linked to the intensity of anticoagulation therapy in our cohort as reported by others.²³

Freedom from neurologic injury was similar to previous reports in western populations. However, the diagnosis of stroke was done clinically as the etiology (hemorrhagic or ischemic) of such events was not clearly defined in the majority of our patients for the lack of diagnostic facilities (CT scan, MRI).

Thus, no case of valve thrombosis was documented at follow-up, although we could not exclude this complication in patients who had sudden death or in those where the cause of death was unknown. This unexpected low incidence of prosthetic valve thrombosis could be linked to both the acceptable compliance in our cohort and the use of On-X mechanical valves (82.1% of patients). Although in poorly-anticoagulated patients, low rates of prosthetic valve thrombosis have been previously reported with the On-X valves when compared with other mechanical valves models.^{9,22,24} Williams et al⁹ reported a freedom from thromboembolism of 84% at 4 years using On-X valves even though only 56% of their patients were judged compliant with anticoagulation therapy. Furthermore, the Food and Drugs Administration has recently approved the use of On-X valves in the aortic position²⁵ with lower INR values (1.5–2.0 instead of 2.0–3.0). These reports emphasize on the key role of careful prosthesis selection in a setting where inadequate anticoagulation might be a factor.

No patient underwent reoperation, either on the implanted prosthesis or for other cardiac disease. This is consistent with the low rate of prosthetic valve events reported at follow-up. None of the patients with mitral prosthesis had significant patient-prosthesis mismatch (PPM) at follow-up. This was partly related to the implantation of adult size prosthesis in the majority of our young

patients (→Fig. 1) without requiring alternative techniques such as supra-annular implantation. The latter is a valuable alternative when conventional annular mitral replacement is not feasible in small native annulus despite it has been associated with increased morbidity including a significant risk of reoperation.²⁶ However, 3 of the 4 patients who received a 17 mm St. Jude HP valve in aortic position had moderate PPM (Indexed Effective Orifice Area 0.65–0.85 cm²/m²) and five patients with MVR presented with moderate AR at follow-up as progression of mild AR at surgery although no significant symptoms were reported in none of these patients.

Ten patients reported eight full-term pregnancies and five spontaneous abortions. No case of embryopathy was diagnosed among the eight pregnancies. Five of the eight women who delivered maintained oral anticoagulation until a few days prior to Caesarean delivery. One of these patients had severe postcaesarean bleeding requiring hysterectomy. Our current policy is to maintain oral anticoagulation throughout the whole pregnancy. The administration of unfractionated intravenous heparin is started only few days before a programmed caesarean delivery. First, because the home management of unfractionated intravenous heparin and low molecular weight heparin in our patients may be somewhat troublesome requiring careful monitoring. Second, their effectiveness to prevent thrombosis and thromboembolism in pregnant women with prosthetic heart valves remains questionable as fatal maternal and fetal events have been reported even at therapeutic doses compared with oral anticoagulation.^{27–29} Lastly, the rate of warfarin embryopathy was low in various series and seems to be dose dependent, with low risk with a daily dose of ≤ 5 mg.³⁰

Limitations of the study were those associated with retrospective studies. Moreover, the limited number of patients

and the shorter length of follow-up do not permit conclusions on long-term outcomes, which will be important for this young patient population.

Conclusion

Our preliminary experience suggests acceptable mid-term outcomes in patients with mechanical heart valves in our region. Both accurate surgical evaluation and strategies, either financial or social, facilitating patient education and assistance are crucial to ensure good results. Long-term follow-up and prospective studies comparing current non-thrombogenic surgical options are warranted to draw reliable conclusions.

Note

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