

Experience with Prosthetic Valve Replacement in Indigents with Rheumatic Heart Disease in Nigeria: 10 Years Follow-Up

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Abstract

Purpose: Active heart surgery programs are few in sub Saharan Africa outside of South Africa, with majority being low volume centers performing small numbers annually. We reviewed our long term outcome to identify factors associated with increased morbidity and mortality, to guide future choice of prosthetic valves in our mostly indigent patients afflicted with rheumatic valvular disease. **Methods:** Retrospective analysis of patients who underwent heart valve replacement at Lagos State University and Ahmadu Bello University Teaching Hospitals from November 2004 to February 2009. **Results:** Twenty six patients, 19 (73.1%) females, age 12 - 47; mean 26.69 ± 9.87 years, underwent heart valve replacement. 19 (73.1%) patients had mitral and 7 (26.9%) aortic valve replacement. Mechanical valve was implanted in all except in 2 (7.7%) patients. Left ventricular ejection fraction was >50% in 14 (53.8%), 24 (92.3%) were in New York Heart Association class III/IV, 10 (38.5%) had severe pulmonary hypertension and logistic euroscore was 5.84 ± 3.81. Operative mortality was 11.5% (3/26) and morbidity 7.7% (2/26). Follow-up for survivors was 83.0 ± 27.9 months. 10-year freedom from bleeding and thromboembolism was 70.0% and survival 86.0%. Linearized rate for bleeding was 4.58 and thromboembolism 1.52. **Conclusion:** Late complications in survivors were primarily anticoagulant related occurring predominantly in child bearing age females especially during pregnancy. Bleeding complications were often associated with noncompliance due to poor socioeconomic status. With average life expectancy of 53 years for females, bioprosthetic valves despite higher structural failure rate, may be best suited especially in child bearing age females still desirous of childbirth to decrease valve related complications. Longer duration of follow-up and meta-analysis of future reported series from the sub

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region may help clarify the optimal prosthetic valve in sub Saharan Africa with its known poor health infrastructures and delivery system.

Keywords

Rheumatic Valve Disease, Prosthetic Valve, Anticoagulation Complications

1. Introduction

The first open heart surgery in the West African sub region was performed at the University of Nigeria Teaching Hospital (UNTH) in 1974 [1]. Subsequent heart surgeries were however inconsistent and sporadic with the program ultimately closing in 2000 due insurmountable manpower and financial challenges [2]. The program later reopened in 2013 with the assistance of foreign partners from the USA and Britain. Therefore many patients needing heart surgery in Nigeria often succumbed prematurely to their disease with the exception of the wealthy and a few indigents sponsored by government or private philanthropists to travel overseas for surgery. Consequently Nigeria the most populous country in Africa with 170 million citizens following closure of the UNTH program had no heart surgeries performed locally until 2004 when Global Eagle Foundation (GEF), a USA based nongovernmental organization in partnership with the Lagos State Government again commenced open heart surgery. Due to the small and inconsistent heart surgeries performed previously in Nigeria, there are no published series of heart valve replacement despite the large number of patients with valvular heart disease needing surgery. With ongoing debate on whether a mechanical or bioprosthetic is a better choice especially in younger patients 50 years or less, we decided to review our long term experience to see which replacement valve might be better suited for our mostly indigent patient population.

2. Material & Methods

We reviewed the medical records of all patients who underwent heart valve replacement between November 2004 and February 2009 at Lagos State University Teaching Hospital, Lagos (LASUTH) and Ahmadu Bello University Teaching Hospital, Zaria (ABUTH) by a single surgeon (the lead author). Patients selection were from the pool of cardiac patients been followed at the cardiology clinics. Diagnosis of valvular heart disease was usually suspected on clinical examination and confirmed through chest X-ray (CXR), electrocardiogram (ECG) and transthoracic echocardiogram (TTE). Transesophageal echocardiogram (TEE) and cardiac catheterization (CC) were not available at both institutions. Patients who tested positive for HIV or Hepatitis B and C were excluded from surgical consideration. All patients met the American College of Cardiology/American Heart Association (ACC/AHA) class 1 recommendation for surgery. Logistic euroscore was used for preoperative risk scoring. All surgeries were elective and performed via standard median sternotomy with cardiopulmonary bypass (CPB) under moderate systemic hypothermia. Myocardial protection during the period of aortic cross clamping was achieved with cold blood cardioplegia delivered either antegrade, retrograde or both. Blood conservation strategy used during surgery included antegrade and retrograde autologous pump priming, cell saver, removal of patient's blood for later reinfusion after heparin reversal and aprotinin. No attempt was made at valve repair due to unavailability of TEE to assess adequacy of repair intraoperatively and also considering the known higher failure rate with repair of rheumatic valves. All mitral valve replacements were performed with preservation of the subvalvular apparatus. Central venous pressure (CVP) and arterial lines were the main invasive monitoring used for most patients. Swan Ganz catheter was limited, and was utilized in some patients with severe left ventricular dysfunction to help guide hemodynamic management. Intraaortic balloon pump (IABP) became available in later years and was used for cardiogenic shock refractory to inotropic therapy. Postoperatively all patients were started on intravenous heparin and warfarin after 48 hours if no major bleeding. Heparin was stopped when the target international normalized ratio (INR) of 2.0 - 3.0 and 2.5 - 3.5 for aortic and mitral valves respectively was attained. Warfarin was continued for all patients with mechanical valves and for three months in patients with bioprosthetic valve and sinus rhythm. Follow up post discharge was through clinic visits and telephone calls. Collected data such as demographics, aortic cross clamp, cardiopulmonary bypass times, duration of follow up were entered into an excel spreadsheet and imported into SigmaPlot (Systat Software, Inc.,

San Jose, CA) for statistical analysis. Categorical variables were reported using number and percent of observations, while continuous variables were reported as mean \pm standard deviation. Operative mortality was death within 30 days of surgery. Survival and freedom from bleeding and thromboembolic complications were calculated using the actuarial Kaplan Meier method.

3. Results

Twenty nine patients with rheumatic heart disease (RHD) underwent median sternotomy for heart valve replacement. Planned procedure was abandoned in 3 females with mitral valve disease due to the unexpected intraoperative finding of severe suprasystemic pulmonary hypertension following direct pulmonary artery pressure measurement. These patients were therefore excluded from further analysis. Twenty six patients consisting of 19 (73.1%) females and 7 (26.9%) males, age range 12 - 47, mean 26.69 ± 9.89 years completed the planned operative procedures. All patients had rheumatic valvular disease with 92.3% (24/26) in New York Heart Association (NYHA) Class III/IV preoperatively. 38.5% (10/26) with mitral disease had chronic atrial fibrillation (CAF) (**Table 1**). Logistic euroscore mean was 5.84 ± 3.81 , range 1.51 - 19.58. 73.1% (19/26) had mitral valve replacement (MVR) and 26.9% (7/26) aortic valve replacement (AVR), predominantly with St. Jude mechanical valve. Only 1 patient with CAF had concomitant left and right atrial radiofrequency ablation. IABP was used in 11.5% (3/26) with chronic aortic insufficiency, left ventricular (LV) dysfunction and cardiogenic shock. Operative mortality was 11.5% (3/26) occurring in 2 aortic and 1 mitral patients (**Table 2**). The mitral patient operated

Table 1. Baseline patient demographics.

Factors	Number
Age, yrs. (mean, range)	26.6 (12 - 47)
Sex	
Female	19 (73.1%)
Male	7 (26.9%)
Valve pathology	
MS	3 (11.5%)
MR	5 (19.2%)
MS/MR	11 (42.3%)
AI	6 (23.1%)
AS/AI	1 (3.9%)
Chronic atrial fibrillation	10 (38.5%)
Pulmonary Hypertension	10 (38.5%)
LV Ejection Fraction	
50% or greater	14 (53.8%)
30% - 49%	12 (46.2%)
NYHA Class	
I	0
II	2 (7.7%)
III	7 (26.9%)
IV	17 (65.4%)
Poor socioeconomic status	25 (96.0%)

MS = mitral stenosis; MR = mitral regurgitation; AI = aortic insufficiency; AS = aortic stenosis; LV = left ventricle; NYHA = New York Heart Association.

Table 2. Operative Data.

Mitral valve replacement	19 (73.1%)
ACP (minutes)	98.0 ± 19.4
CPB (minutes)	150.1 ± 51.2
Aortic valve replacement	7 (26.9%)
ACP (minutes)	109.5 ± 17.2
CPB (minutes)	158.0 ± 33.9
Valve type & sizes	
St Jude	12 (46.2%) range 21 - 29
ATS	9 (34.6%) range 21 - 31
On-X	3 (11.5%) range 21 - 33
CE	2 (7.7%) 33
IABP Insertion	3 (11.5%)
Mortality	3 (11.5%)

ACP = aortic cross clamp; CPB = cardiopulmonary bypass; IABP = intraaortic balloon pump; CE = Carpentier Edwards.

during our first mission had suprasystemic pulmonary hypertension with end stage cardiomyopathy and died of cardiogenic shock despite maximal inotropes with no mechanical heart support available at the time. The second patient underwent AVR and following weaning from CPB had severe protamine reaction with cardiovascular collapse requiring reinstitution of CPB. IABP was inserted and after discontinuing bypass the second time, heparin was not reversed, and patient subsequently died from coagulopathy, as there were no component blood therapy available. The third patient after AVR developed sudden hypotension during transfer to the ICU and stabilized following insertion of IABP. She required prolonged intubation and later died of sepsis. Major morbidity was observed in only 7.7% (2/26) patients and consisted of one prolonged ventilation with pneumonia and one mediastinal reexploration for bleeding.

Amongst the 23 patients who survived surgery, follow up was complete in 91.3%, with 2 patients lost to follow up. Mean follow up duration was 83.0 ± 27.9, range 39 - 123 months. There were 3 (13.0%) late deaths, all occurring in females with mechanical MVR. Two patients were noncompliant with their anticoagulation regimen; one had recurrent first trimester abortions and subsequently died of severe vaginal bleeding during one of the pregnancies, while the other died after an embolic stroke. The third patient who was compliant with anticoagulation regimen had an unexplained sudden death at home, and autopsy was declined by family. Major valve related morbidity was bleeding and thromboembolism, and occurred only in females with MVR who were all noncompliant with their anticoagulation regimen. There was no structural valve deterioration, endocarditis or reoperation during the study period. One patient with a St. Jude valve had four spontaneous first trimester abortions with bleeding, but finally had a life birth through cesarean section 7 years after her heart surgery. Another patient with an ATS valve had two spontaneous first trimester abortions with bleeding. Two patients had major embolic stroke, one with an ATS valve and the other with Carpentier Edwards tissue valve with chronic atrial fibrillation. Linearized rate for bleeding was 4.58, thromboembolism 1.52 and composite 6.10. Overall 10 years' survival was 86.0% and freedom from bleeding and thromboembolism 70.0% ([Figure 1](#) and [Figure 2](#)).

4. Discussion

Cardiac surgery which is routinely performed in the developed and many developing countries, to date remain nonexistent in most of sub Saharan Africa (SSA). Although the need for heart surgery is enormous, the lack of adequate funding for required equipments acquisition and scarcity of trained surgical manpower, cardiac anesthesiologists, perfusionists, ICU nurses and other allied health personnel presently makes establishment of open heart surgery programs a near impossible task in many SSA countries. Meanwhile valvular heart disease from rheumatic fever is endemic in most of SSA especially Nigeria the most populous country in Africa with 170

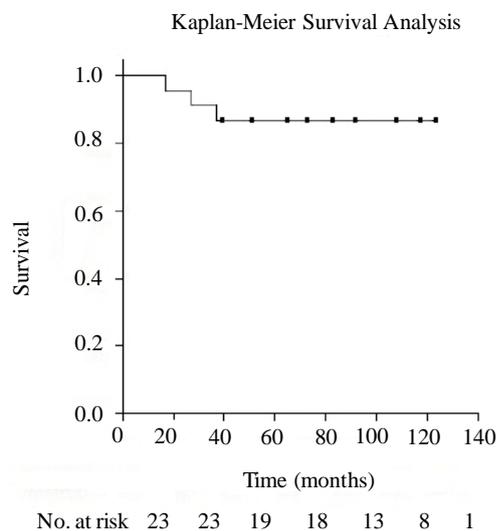


Figure 1. Kaplan Meier estimate of survival.

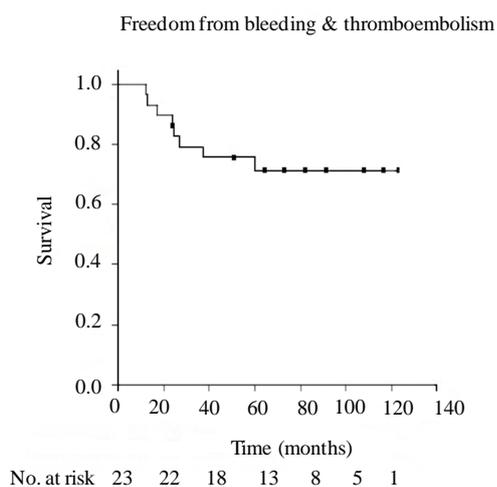


Figure 2. Kaplan Meier estimate of freedom from bleeding & thromboembolism.

million population, and over 70% of whom live in poverty on less than \$ 1.00 a day. Many of these patients with RHD are therefore condemned to untimely death as a result of absent or limited surgical treatment locally.

At the commencement of our open heart surgeries we were focused primarily on valve durability with preference therefore for mechanical valve as all the surgeries were done on charity basis. Little consideration was given to the demographics of the local population and the overall poor National healthcare delivery system. Furthermore it was felt that obtaining sponsorship for future reoperation from bioprosthetic structural valve failure was highly unlikely for most of these patients. Moreover there was also no previous heart valve replacement series from Nigeria to use as a guide. However during the subsequent follow up years after valve replacement, two major problems gradually became apparent. The first was lack of enforcement of government regulatory oversight resulting in quality control variations amongst different diagnostic laboratories and consequently sometimes reporting of inconsistent and unreliable INR results. Secondly many patients found it increasingly difficult to comply due to the financial burden of drugs and laboratory monitoring expenses associated with mechanical valve. Although the surgeries were done on a charity basis with government subsidy, no further financial support or medicaid assistance was made available after surgery. Many patients and their families had underestimated the financial burden and commitment associated with lifelong anticoagulation for mechanical valves. With limited financial resources and competing interests such as food, housing etc. most struggled with daily survival and be-

come noncompliant. Even in affluent industrialized nations, anticoagulation noncompliance remains a problem as evidenced by the US warfarin compliance trial [3] which showed INR was out of range 38% of the time in the adherent group and 50% in the nonadherent group at mean follow up of 38 weeks. This concern with compliance is also reflected in the review of the Society of Thoracic Surgeons (STS) database from North America by McCarthy *et al.* [4] and a recent USA National inpatient sample review [5], both showing a recent trend towards increasing use of bioprosthetic and decrease in mechanical valves as a result of complications from long term anticoagulation.

On the other hand two recent reviews from SSA based on their experience both recommended mechanical valves. Edwin *et al.* [6] from Ghana in a 9.1 years follow up of 114 patients undergoing mechanical heart valve replacement with St. Jude and Sorinmonoleaflet valves, observed valve thrombosis in 5 patients, 1 major bleeding, 1 prosthetic valve endocarditis, 2 reoperations and 4 pregnancies without complications. Similarly Williams *et al.* [7] report on 438 South African patients with On-X valve, poorly anticoagulated at follow up of 1.7 years, observed low incidence of hemorrhagic and thrombotic complications and seven full term pregnancies. Since RHD is more prevalent in females [8] and mostly in their child bearing years, anticoagulant related complications in our series were more frequently observed in this group especially during pregnancy. Some patients in desperation for babies undertook great personal risk against medical advice as observed in 2 patients with St. Jude valve. The first had recurrent first trimester abortions for 5 years, and finally decided to stop warfarin during the first trimester with subsequent delivery of a life birth after 7 years of marriage. The second patient also after multiple abortions stopped anticoagulation completely during subsequent 2 pregnancies and delivered 2 live births without any observed complications. With the benefit of hindsight and experience with our patient population, we now recommend bioprosthetic valve in child bearing age females desiring future pregnancies. Patient's life span may not be significantly reduced compared to age matched population even with the prospect of possible future reoperation, given the average life span of 53 and 52 years for females and males respectively in Nigeria, which is similar in most SSA countries.

Anticoagulation during pregnancy definitely increases the hazards to both mother and fetus in the largely indigent population seen in most of SSA. None of the current strategies for anticoagulation with mechanical valves during pregnancy is completely safe. Al-Lawati *et al.* [9] from Oman reviewed retrospectively 63 pregnancies in 21 women divided into group 1 who received oral anticoagulation throughout pregnancy and group 2 who received subcutaneous heparin during first trimester and oral anticoagulation for the rest of the pregnancy. Both groups received subcutaneous heparin 2 weeks prior to expected delivery date. They found a statistically non-significant higher incidence of abortion in Group 1, and no case of Coumadin embryopathy in both groups, and concluded by recommending oral anticoagulation throughout pregnancy in countries with poor socioeconomically disadvantaged patients. Similarly Geelani *et al.* [10] from India reviewed 250 pregnancies in 245 women with mechanical heart valves, divided into group 1 who took oral anticoagulation throughout pregnancy and group 2 who received subcutaneous heparin during first trimester and then oral warfarin, with both groups receiving heparin at time of delivery. They found similar rate of spontaneous abortion and Coumadin embryopathy in both groups. They concluded that in countries such as India with poor socioeconomic status that it was probably safer to use Coumadin throughout pregnancy as many patients from remote villages may not be able to report to hospital 2 - 3 times daily for needed subcutaneous heparin shots. With our patient population in Nigeria and most SSA countries, switching to heparin during the first trimester may be difficult to attain as patients often are unaware of their pregnancy at this stage and the logistics of reporting to hospital twice daily for subcutaneous heparin may be difficult for most patients living in rural areas. Although majority of our patients with mitral valve disease had CAF and may therefore still require anticoagulation even after bioprosthetic valve replacement, concomitant radiofrequency ablation during surgery may convert many of these patients to sinus rhythm thus eliminating need for any long term anticoagulation. The only patient in our series who had ablation has remained in sinus rhythm for 9 years. While the two reviews on mechanical valves [6] [7] from SSA reported good long and short term results respectively, the health care infrastructures in both Ghana and South Africa are better developed and organized than Nigeria and several other SSA countries, making their results more difficult to reproduce. Another factor likely to favor tissue valve in the horizon is a promising novel low cost stented pericardial valve designed for developing countries like in SSA reported by Legg *et al.* [11] It features a clip in mechanism that secures the valve assembly into the sewing ring stitched independently of the frame and leaflets. Reoperation is easily performed by clipping the new valve into the receptacle previously attached to the valve annulus.

5. Conclusion

In conclusion, determining the choice of prosthetic valve replacement is usually based on age at implant and informed consent discussion with patients and their families on which complications of either anticoagulation therapy with mechanical valve or structural valve deterioration with bioprosthetic valve they prefer [12]. Additional factors to consider in the equation in SSA, include life style, literacy level, socioeconomic status, local infrastructural limitations and restricted access to health services for those living in rural areas. With these considerations in our rheumatic valve patients, our preference now is to recommend bioprosthetic valve in child bearing age females and other patients unable to afford or deemed highly unlikely to comply with the requirements for lifetime anticoagulation, which represents the majority of our patients. Mechanical valves are reserved for patients who can both afford the associated postoperative maintenance costs and also understand the obligation for lifetime anticoagulation and the consequences of noncompliance. Our study limitations include being retrospective and the small sample size. However it represents the only review to date on long term follow-up for valve replacement surgery in Nigeria, and would serve as the basis for future study to validate whether bioprosthetic valves are indeed associated with lower long term complications and better suited than mechanical valves given the demographics of our patient population afflicted with rheumatic heart disease.

Disclosure Statement

Conflict of Interest: The authors have no financial or other interests in the manufacture or distribution of any of the implanted valves.

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