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ORIGINAL RESEARCH

Predictors of early mortality following cardiac surgery for rheumatic heart disease at a national referral hospital in Dar es Salaam, Tanzania: A retrospective study

Short title: Dar es Salaam, Tanzania: Early mortality after RHD surgery

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Abstract

Background: Rheumatic heart disease (RHD) is endemic in Tanzania. It is ranked third among the most common causes of heart failure after hypertensive heart diseases and cardiomyopathies. This study aimed to determine the predictors of early operative mortality for RHD at Muhimbili National Hospital, Tanzania.

Methods: This retrospective cross-sectional study of 212 patients operated due to RHD from May 2008 to December 2012. Patients' demographic and clinical data at admission and within 30 days of the index elective cardiac surgery were recorded in a predefined clinical record form. Data were entered and analysed using Statistical Package for Social Sciences version 24 and STATA version 13. The Chi-square and Fisher's exact tests were utilized to compare categorical variables. Variables with a p-value <0.2 at bivariable analysis were included in a multivariable modified Poisson regression model.

Results: Out of 212 patients, 140 (66%) were females. The median age was 21 years (interquartile range 15 – 32 years). One hundred and forty-five (68.4%) patients underwent valve replacement, out of which 113 (77.9%) were single (mitral), 17 (11.7%) aortic, and 15 (10.4%) double (aortic and mitral) valve replacement. Valve repair was done in 42 (19.8%) patients, of which 41 were mitral and one aortic. Surgical mitral commissurotomy was performed in 25 (11.8%) patients. Thirty (14.1%) patients died in-hospital. In multivariable analysis, mortality was more than five times higher among patients who underwent double than single valve replacement {adjusted prevalence ratio (95% CI) = 5.65 (2.46-12.99), p < 0.001}. The patient's age, disease duration, ejection fraction, surgical modality, pulmonary hypertension, intensive care unit stay were not predictors of mortality.

Conclusion: The in-hospital mortality observed in this study was higher than those reported in previous studies. In patients with RHD, double valve replacement is associated with increased early mortality, which may require greater technical expertise and careful postoperative management. Our findings need to be confirmed in prospective studies.

Keywords: predictors; early mortality; rheumatic heart disease; cardiac surgery; intensive care unit

Introduction

Rheumatic heart disease (RHD) is an important cause of cardiac morbidity and mortality among children and young adults, affecting an estimated 15.6 million people yearly and responsible for up to 300,000 deaths each year worldwide.[1] The disease is prevalent in developing countries, including sub-Saharan Africa, where the prevalence

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is as high as 1 – 3 for every 100 school children.[2,3] The most common clinical presentations are heart failure, pulmonary hypertension (PHT), atrial fibrillation, stroke, and infective endocarditis, all of which are factors signifying late presentation of patients to health facilities and/or delayed appropriate management.[4,5] Some of them are too late to be candidates of valvular interventions.[6–8] In studies done in Uganda, about 50% of newly diagnosed RHD patients presented with complications.[9,10]

Guidelines on the management of valvular heart diseases recommend valve surgery for clinically significant valve lesions.[11,12] However, most of these patients are likely to be managed conservatively in developing countries. Okello et al[13] found that out of 551 patients evaluated from the Uganda RHD Registry, 398 (72.3%) required invasive intervention, with 332 (60.3%) patients requiring surgery. Only 153 (27.7%) required medical management. Instead, 498 (90.4%) of the patients were on medical treatment. Of the 60.3% requiring surgery, only 44 (8.0%) patients underwent valvular surgery. Since the treatment of advanced forms of RHD is cardiac surgery, policymakers should improve access to cardiac surgery with simultaneous availability, affordability, and accessibility of medications for treating RHD complications such as heart failure.[14–18]

Several factors are known to affect the outcome of cardiac surgery for RHD.[8,19–24] Preoperative cardiac status of the patient such as advanced age, New York Heart Association (NYHA) class III-IV, PHT, left ventricular ejection fraction (LVEF) < 50%, and a large left atrium were found to be predictors of mortality.[22,25,26] Intraoperative predictors of early mortality include the duration of aortic cross-clamp, total surgical time, and cardiopulmonary bypass.[19,22–24,26] Double valve replacement (DVR), although technically difficult, offers excellent symptomatic relief and better late survival similar to that of single valve replacement (SVR).[22,23] It is important to recognize this because, in regions with a high prevalence of RHD, about 50% of patients have multivalvular involvement.[27,28] Post-operatively, low cardiac output syndrome, bleeding, thromboembolism, sepsis, and prosthesis-related complications are among the predictors of mortality.[19,21,24,29] Although the decision to repair or replace rheumatic mitral valve disease is controversial,[30] recent[31,32] and previous[8,33,34] publications have demonstrated that repair is superior to replacement for mortality and valve-associated complications. A recent review has reported that mitral valve repair may only outperform replacement in carefully selected patients as progressive valve deterioration and calcification may result in valves that cannot be optimally repaired.[35]

This study aimed at reporting the predictors of early mortality in a relatively large sample of 212 RHD patients who underwent cardiac surgery at Muhimbili National Hospital (MNH) over a period of four years.

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Methods

Study design, subjects, and setting

This was a retrospective cross-sectional study of 212 patients who were admitted at MNH for cardiac surgery due to RHD, from May 2008 to June 2012. MNH is a tertiary referral and teaching hospital located in Dar es Salaam city. Dar es Salaam, the largest commercial city in Tanzania, had a population of nearly 5 million in 2012.[36] MNH cardiac unit used to receive referred cardiac patients from all regions of Tanzania. Open-heart surgery started at MNH in May 2008. Referred patients for assessment and listing for open-heart surgery were initially admitted in medical wards and perioperatively were cared for in the hospital intensive care unit (ICU) and cardiac wards. From the year 2018, cardiac surgeries have been performed at Jakaya Kikwete Cardiac Institute.

Data collection procedures

Data were collected from medical ward admission books, operation books, and patients' files from hospital medical records. Information obtained was filled on a predefined clinical record form comprising of social demographics (age, sex, level of education, marital status, residential area, and employment); history and physical findings (symptoms and signs, duration of symptoms, co-morbidities, and a diagnosis made); investigations [chest X-ray, echocardiogram, electrocardiogram, and laboratory tests].

In all of the recruited patients, certified cardiologists performed echocardiograms. Before surgery, the valve team holds a clinical meeting to discuss each patient to reach a consensus for the operation. The hospital operates on RHD patients as per guidelines for the management of valvular heart disease.[11,12] Patients who had RHD but who underwent cardiac surgery for other cardiac conditions were omitted. We also excluded patients who were missing pulmonary arterial pressure records.

Operative technique

Local cardiac surgeons performed all surgeries on an elective basis. The general approach for surgery was median sternotomy with aortocaval (mitral/double valve surgeries) or aortic and two-stage cavoatrial cannulation (isolated aortic valve surgery) for cardiopulmonary bypass; cooling to 30-32^{0}C; antegrade (mitral valve surgeries); and coronary ostial (multiple/aortic valve surgeries) St. Thomas' Hospital solution cardioplegia administration every 20-25 minutes. Sondergaard groove was used for approaching the mitral valve and J incision into the non-

coronary cusp for the aortic valve surgeries. For securing the prosthetic valves, an interrupted suture technique was used. For patients who underwent valve replacement, mechanical heart valves were used.

Bilateral commissurotomy with chord-papillary preservation was a manoeuvre for open mitral valvotomy. Mitral valve repair was accomplished by the application of an annuloplasty ring, posterior mitral leaflet augmentation, and chordal splitting. For closed mitral valvotomy, the left atrial appendage was approached through the left anterolateral thoracotomy and the 4th intercostal space. The appendage was opened and the index finger was introduced through the opening and onto the stenotic mitral valve for dilatation.

Follow-up

We recorded the type and number of valve surgeries performed, the duration of stay in ICU, post-operative echocardiography, post-operative complications (surgical site infection, thromboembolism, endocarditis, anticoagulant-related bleeding), duration of in-hospital stay, and mortality at 30 days.

Definition of terms

This study defined PHT from echocardiography measurements as Right Ventricular Systolic Pressure > 35mmHg as determined by the peak systolic gradient across the tricuspid valve regurgitation.[37] PHT was classified as mild (35 – 50mmHg), moderate (50 – 70 mmHg), and severe (>70 mmHg). Early (operative) mortality was defined as death (in-hospital) within 30 days after index elective cardiac surgery, as recommended from the guidelines for reporting morbidity and mortality after cardiac valvular operations of the American Heart Association for thoracic and cardiovascular surgery.[38] SVR was defined as the replacement of the mitral valve alone, while DVR was a combined replacement of the mitral and aortic valve.

Data management and analysis

The collected data were checked for quality and coding was done before entry. Two different people entered the data twice and checking was done to ensure no double entry or wrong entry. The analysis was done using Statistical Package for Social Sciences version 24.0 and STATA version 13. The factors analysed as predictors of mortality include duration of disease, age, sex, employment, LVEF, type of valvular lesion, PHT, the modality of surgery, number of the replaced valve(s), and the duration of ICU stay. Continuous data were presented as mean with standard deviation when distributed normally and as median with range when skewed. Discrete data were given

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as counts and percentages. Chi-square and Fisher's exact tests were utilized to compare categorical variables. Variables with a p-value <0.2 at univariable modified Poisson regression were included in the multivariable modified Poisson regression model. The factors which were analysed in the multivariable regression model were duration of disease, age of the patient, LVEF, PHT, the modality of surgery, number of the replaced valve(s), and the duration of ICU stay. With each of the analyses, a p-value <0.05 was considered statistically significant.

Ethical consideration

Ethical clearance to conduct the study was obtained from the research and publications committee of MUHAS (Ref. No. MU/PGS/SAEC/Vol.VI). MNH provided permission to conduct this study.

Results

During the period of 4 years from May 2008 to June 2012, a total of 285 RHD patients were admitted and assessed for eligibility for cardiac surgery at MNH. Out of these, 240 (84.2%) had their pulmonary pressures recorded, with 212 (74.4%) of them being operated on. Twenty-eight patients were not operated on because they were not fulfilling the criteria for surgery which are adhered to by the hospital.[11] Data on pulmonary arterial pressure was missing in 45 (15.8%) patients, as shown in Fig 1.

The median age of the patients at the time of operation was 21 years (interquartile range: 15-32). About half of the patients were under the age of 20 years. There were 140 females and 72 males, giving a female/male ratio of 2:1. A majority, 176 (83%) of patients were not employed and 157 (74.1%) attained primary education. About two-thirds of the patients were residing outside of Dar es Salaam. The socio-demographic characteristics of the study population are presented in Table 1.

As per valvular lesions, 79 (37.3%) and 45 (21.2%) patients had pure mitral regurgitation and mitral stenosis (MS), respectively. Twenty-five (11.8%) had combined mitral regurgitation and MS, while 27 (12.7%) patients had combined mitral and aortic valve regurgitation as expressed in Fig 2.

The median (interquartile range) duration of symptoms was 36 (12 - 72) months. More than 95% of the patients had normal white blood cell counts and haemoglobin levels. PHT was detected in 178 (84%) patients. A majority, 182 (85.8%) of the patients, had normal LVEF. Valve replacement was done in 145 (68.4%) patients, out of which 113 (77.9%) were mitral, 17 (11.7%) aortic, and 15 (10.4%) double (aortic and mitral) valve replacement. Valve

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repair was done in 42 (19.8%) patients, of which 41 were mitral and one aortic. Surgical mitral commissurotomy was performed in 25 (11.8%) patients, out of which 5 and 20 were open and closed commissurotomies, respectively. De Vega tricuspid valve annuloplasty was done in 56 (26.4%) patients and tricuspid ring annuloplasty in 26 (12.3%) patients. Nearly a third, 62 (29.2%), of the patients stayed in ICU for more than five days. Clinical characteristics of the patients are depicted in Table 2.

The in-hospital mortality occurred in 30 (14.1%) patients, out of which 22 (73.3%) deaths occurred in ICU. Of the demographic characteristics (Table 3), there was comparable mortality among males and females, {prevalence ratio (PR)=1.30, 95% CI (0.66–2.54)}; individuals with longer duration (≥24 months) of symptoms 19 (16.4%) and those with a shorter duration 11 (11.5%), p=0.241; younger patients of <20 years of age 10 (9.3%) compared to those with ≥20 years 20 (19.0%), p=0.65; and among unemployed compared to employed patients {PR= 1.33 (0.49–3.59)}.

Patients with mitral regurgitation had comparable mortality to patients without mitral regurgitation, {PR= 1.13 (0.46–2.76)} and patients with mitral stenosis compared to those without mitral stenosis, {PR= 0.84 (0.43–1.64)}. The mortality was comparable among patients with PHT and without PHT {PR= 2.67 (0.67–10.74)}. In terms of the severity of PHT, the mortalities were 14 (22.6%) in the mild, 8 (11%) in the moderate, and 6 (14%) in the severe group, p=0.122. Mortality was comparable among individuals with LVEF ≥ 50% and with LVEF < 50% {PR= 0.21 (0.03 – 1.49)}. Patients who underwent valve repair had high mortality 10 (23.8%) when compared to patients who underwent valve replacement 19 (13.1%) or valvotomy 1 (4%), p=0.080. Mortality was higher among patients who underwent DVR than SVR {PR= 4.39 (2.00 – 9.64)} and among patients who had a longer ICU stay than a shorter ICU stay {PR= 2.42 (1.26 – 4.65), p=0.007}. There was no significant difference in mortality among patients with 7 (15.6%) and without 10 (16.9%) atrial fibrillation as well those with dilated 23 (14.0%) and without 2 (10.5%) dilated left atrium. The only independent predictor of early mortality was to be undergoing double (compared to single) valve replacement, adjusted prevalence ratio (APR) [95% CI] = 5.65 (2.46-12.99), p < 0.001}. The clinical characteristics predicting early mortality are shown in Table 3.

Discussion

This study reports an in-hospital mortality rate of 14.1% (30/212). Our findings are slightly similar to that reported by Prashant et al[24] and lower to that reported by Nyawawa et al[19] in which mortality rates were 11.3% and 24% respectively. However, other studies reported lower mortalities of 2.5% by Pillai et al,[39] 3.8% by Akhtar et al,[23] 4% by Panda et al,[22] and Sharma et al,[40] 4.4% by Debel et al,[21] 8% by Gupta,[26] and 9.2% by John et al.[29] The

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observed differences in mortality from these studies could be explained by the difference in the type of the study population: DVR alone;[22,24–26,29,39] DVR, aortic valve replacement and SVR;[19,21,23,40] and valve repair.[8,19,21] The experience of the operating surgeon[19,21,26] and technical issues can also explain the differences in mortality.[21,26,29] The mortality rate of 24% reported in a 1-year experience of RHD surgeries after the inauguration of cardiac surgery at MNH had dropped over a period of four years.[19]

Our study showed that in RHD patients, DVR imposes a significantly higher early mortality than SVR. Similarly, Akhtar et al[23] observed higher in-hospital mortality in the DVR group (4.2%) than the SVR group (3.5%), while Panda et al[22] reported a mortality rate of 4%. On contrary, Sharma et al[40] did not report any 30 days mortality from the DVR group while Pillai reported it at a lower rate of 2.5%. The hospital mortality rate of DVR ranges from 5 – 15%.[22,23] The strikingly higher mortality of 42% observed in our DVR group could be explained by several reasons. Firstly, our patients had a longer duration of symptoms, it could be possible that these patients had a more advanced disease as it was previously reported in a study done at the same institution in which at presentation 80% of the patients were in NYHA class III and IV.[19] Secondly, cardiac surgeries were newly established at the hospital and skills and expertise among the operating team was likely inadequate. Thirdly, our sample size was smaller compared to those of the cited studies. Lastly, there were differences among studies population such that while some studies included DVR alone;[22,24–26,29,39] others involved DVR, aortic valve replacement and SVR;[19,21,23,40] and valve repair.[8,19,21] DVR, although technically challenging, has been advocated as a standard surgical option in patients requiring surgery for combined rheumatic mitral and aortic valve disease.[22,23] It is essential to recognize this because, in regions with a high prevalence of RHD, about 50% of patients have multivalvular involvement.[27,28] Moreover, these patients are young and present with severe disease at the time of presentation; hence a DVR is a preferred surgical modality.

This study revealed a higher mortality rate among patients with < 20years than those with more than 20 years of age. On the contrary, advanced age has been reported in several studies to predict mortality following cardiac surgery.[22,25,26] The high mortality observed in young individuals in our study could be explained by the fact that RHD in developing countries presents at an early age with already advanced disease.[4,5]

Our patients had a longer duration of symptoms with a median of 36 (12 - 72) months. The mortality was higher among patients with a longer duration of symptoms. It could be possible that these patients had a more advanced disease as it was previously reported in a study done at MNH in which at presentation 80% of the patients were in

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NYHA class III and IV.[19] It can be postulated that the longer the disease duration the higher the chance of myocardial tissue remodelling.

Our study has shown a comparable mortality rate between patients with PHT and those without PHT (15.7% vs 5.9%, p=0.176). Debel et al[21] reported that three out of five deaths that occurred in their cohort had severe PHT. Also, in the current study, mortality was comparable between patients with mild PHT to those with moderate and severe PHT. Other studies have reported a significant association between PHT and mortality post-cardiac surgery for RHD.[22,25,26] However, most of these studies analysed the association of PHT with long-term mortality.

In our study, LVEF was not a predictor of early mortality. This finding is similar to what was observed by Nyawawa et al,[19] who concluded that the mere presence of suboptimal ventricular dysfunction should not contraindicate cardiac surgery. However, our findings should be cautiously interpreted because of a few patients with a low LVEF. In contrast to other studies,[22,25,26] LVEF <50% has been found to predict mortality post-cardiac surgery for RHD.

This study showed a mortality of 23.8% among patients who underwent valve repair compared to valve replacement (13.1%) and valvotomy (4%). Similarly, Nyawawa et al reported that mitral valve repair accounted for 64.3% of all deaths and concluded that it requires special consideration.[19] In a situation like this, where cardiac surgeries had just begun, skills and expertise must be acquired to reach acceptable outcomes post mitral valve repair. In contrast, Debel et al[21] found no death among patients who underwent mitral valve repair. The authors argued that they were too sceptical about mitral valve repair because the valves were calcified, and the durability of repaired valves in a setting with resource constraints is an issue.[21] The benefits of mitral valve repair have been established,[33,41] it offers better early and late survival and it is important to patients who do not require oral anticoagulants. In sub-Saharan Africa, managing a patient with a mechanical valve is challenging in terms of anticoagulants and monitoring of the International Normalized Ratio.[8,42] However, owing to the less durability of valve repair, advocating it in resource-constrained countries in which redo surgery is challenging remains debatable. The recommendations from a recent review is that in low- and middle-income countries mitral valve repair for RHD patients should be considered.[35] The authors suggested several approaches aiming at increased exposure and training in rheumatic valve surgery by initiating international bilateral collaboration in endemic areas, visiting cardiovascular surgeons from endemic areas, simulation methods of teaching, and courses by professional organizations.[35]

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In this study, mortality was higher among patients with a longer duration of ICU stay. This is similar to what was observed in the previous study in which mortality was higher among patients who stayed longer in ICU.[19] The authors argued that longer ICU stay was influenced by the total surgical time and the aortic cross-clamp duration. Similarly, other studies have reported a significant association between mortality with surgical time, aortic cross-clamp duration, and cardiopulmonary bypass.[22–24,26] There was no difference among patients who stayed shorter or longer in ICU in terms of the mean age, mean duration of symptoms, female sex, lower LVEF, pulmonary hypertension, and the modality of surgery. Therefore, it could be possible that the duration of ICU stay was driven by the intraoperative factors as previously elucidated.[19]

Despite the fact that cardiovascular disease remains the leading cause of morbidity and mortality globally, six million people have no access to timely, safe, and affordable cardiac surgery services when required.[43] As reported in several recent publications, there is a need of improving access to cardiac care services for RHD in sub-Saharan Africa.[16–18] With the increase in the coverage of interventions targeting RHD/acute rheumatic fever spectrum i.e primary, secondary, and tertiary prevention could prevent about 74,000 deaths from RHD and acute rheumatic fever from 2021 to 2030 in the African Union (AU).[16] From an economic perspective, if secondary and tertiary care interventions for RHD were scaled up, there would be a net benefit of US $ 2.8 billion for the AU through 2030.[16] Emmy Okello et al[17] stated in their comment on Coates et al study[16] that "scaling up tertiary intervention measures in the AU is achievable, but will need multisectoral involvement". By strengthening local health systems through investing in domestic services for heart surgery rather than referring patients abroad for treatment, governments of low and middle income countries can save millions of dollars every year.[44] However, that will only happen if there is a good political will and commitment, better understanding and availability of funds.[18]

In developing countries, patients' selection and the choice of valvular surgery are among the important issues to take into consideration because patients come late with a severe presentation of the disease. There are no local guidelines in our setting that could probably fit our patients' presentation with treatment outcomes. In Tanzania, from the year 2018 cardiac surgeries are solely performed at Jakaya Kikwete Cardiac Institute. Anecdotal data shows that the annual mortality following cardiac surgery for RHD at Jakaya Kikwete Cardiac Institute is < 4%. Our study findings show a milestone from the establishment of a cardiac centre towards success in offering a state-of-the-art cardiac service.

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Study limitations and strengths

This study has all the inherent limitations of a retrospective study. Firstly, missing/incomplete information like co-morbidity variables. For heart failure and NYHA functional class, LVEF was taken as a surrogate measure. Patients with missing/incomplete data could have predictive factors for early mortality. Other comorbidities were reported in small numbers and could not allow for detailed analysis. Secondly, we could not analyse intraoperative variables (such as total operation time, cardiopulmonary bypass time, and aortic cross-clamp time) and postoperative complications (congestive cardiac failure, arrhythmias, wound infection, and acute respiratory distress syndrome). However, the influence of those variables on patients' outcomes was previously analysed at the same institution,[19] albeit a small sample size of that study. Thirdly, our multivariable model is over-adjusted because we included ICU stay (an outcome) as a predictor. The strengths of our study are the relatively bigger sample size and the ability to contribute to the findings of the study which was previously done at the same institution. Although most of the variables that are known to influence early mortality post-cardiac surgery were not statistically significant, we believe that they are clinically significant to be considered upon the selection of candidates for valvular interventions.

Conclusion and recommendation

The in-hospital mortality observed in this study is higher compared to those reported in previous studies. In patients with RHD, double valve replacement is associated with increased early mortality, which may require greater technical expertise and careful postoperative management. Prospective studies with larger samples are needed to confirm these findings and explore the determinants of early and late mortality among such patients. There is a need for local guidelines for the management of these patients.

References

1. Carapetis JR, Steer AC, Mulholland EK, Weber M. The global burden of group A streptococcal diseases. Lancet Infect Dis. 2005;5: 685–694.

2. Beaton A, Okello E, Lwabi P, Mondo C, McCarter R, Sable C. Echocardiography screening for rheumatic heart disease in ugandan schoolchildren. Circulation. 2012;125: 3127–3132.

3. Marijon E, Ou P, Celermajer DS, Ferreira B, Mocumbi AO, Jani D, et al. Prevalence of rheumatic heart disease detected by echocardiographic screening. N Engl J Med. 2007;357: 470–476.

4. Zühlke L, Engel ME, Karthikeyan G, Rangarajan S, Mackie P, Cupido B, et al. Characteristics , complications , and gaps in evidence-based interventions in rheumatic heart disease : the Global Rheumatic Heart Disease Registry (the REMEDY study). Eur Heart J. 2015;36: 1115–1122.

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5. Kingué S, Abdou S, Balde D, Bocary M, Anzouan-kacou J, Anisubia B, et al. The VALVAFRIC study : A registry of rheumatic heart disease in Western Tropical Cardiology of the Société franc cardiologie. Arch Cardiovasc Dis. 2016;109: 321–329.

6. Ussiri E V, Jiang W, Nyangassa BJ, Mpoki U, Lugazia ER, Waane T, et al. Closed Mitral Valvotomy-a Life Saving Procedure in Facility Deprived Countries: Experience at Muhimbili National Hospital, TANZANIA. East Cent Afr J surg. 2011;16: 83–88.

7. Zühlke L, Karthikeyan G, Engel ME, Rangarajan S, Mackie P, Cupido-Katya Mauff B, et al. Clinical Outcomes in 3343 Children and Adults with Rheumatic Heart Disease from 14 Low-and Middle-Income Countries: Two-Year Follow-Up of the Global Rheumatic Heart Disease Registry (the REMEDY Study). Circulation. 2016;134: 1456–1466.

8. Mvondo CM, Pugliese M, Giamberti A, Chelo D, Kuate LM, Boombhi J, et al. Surgery for rheumatic mitral valve disease in sub-saharan African countries: Why valve repair is still the best surgical option. Pan Afr Med J. 2016;24: 1–8.

9. Okello E, Wanzhu Z, Musoke C, Twalib A, Kakande B, Lwabi P, et al. Cardiovascular Complications in newly diagnosed rheumatic heart disease patients at Mulago Hospital, Uganda. Cardiovasc J Afr. 2013;24: 80–85.

10. Zhang W, Mondo C, Okello E, Musoke C, Kakande B, Nyakoojo W, et al. Presenting features of newly diagnosed rheumatic heart disease patients in Mulago Hospital: a pilot study. Cardiovasc J Afr. 2013;24: 28–33.

11. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 2021; 1–72.

12. Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP, Gentile F, et al. 2020 ACC/AHA Guideline for the Management of Patients with Valvular Heart Disease: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2021.

13. Zhang W, Okello E, Nyakoojo W, Lwabi P, Mondo CK. Proportion of patients in the Uganda rheumatic heart disease registry with advanced disease requiring urgent surgical interventions. Afr Health Sci. 2015;15: 1182–1188.

14. Watkins DA, Beaton AZ, Carapetis JR, Karthikeyan G, Mayosi BM, Wyber R, et al. Rheumatic Heart Disease Worldwide. J Am Coll Cardiol. 2018;72: 1397–1416.

15. Ndagire E, Id YK, Id HN, Id JA, Sarnacki R, Pulle J, et al. Examining the Ugandan health system ' s readiness to deliver rheumatic heart disease- related services. PLoS Negl Trop Dis. 2021; 1–16.

16. Coates MM, Sliwa K, Watkins DA, Zühlke L, Perel P, Berteletti F, et al. An investment case for the prevention and management of rheumatic heart disease in the African Union 2021 – 30 : a modelling study. Lancet Glob Heal. 2021; 957–966.

17. Okello E, Beaton A. Targeted investment needed to end rheumatic heart disease in Africa. Lancet Glob Heal. 2021;9: e887–e888.

18. Vervoort D, Genetu A, Kpodonu J. Policy prioritisation to address the global burden of rheumatic heart disease. Lancet Glob Heal. 2021;9: e1212.

19. Nyawawa E, Ussiri E, Chillo P, Waane T, Lugazia E, Mpoki U, et al. Cardiac Surgery: One year experience of cardiac surgery at Muhimbili National Hospital, Dar es Salaam- TANZANIA. East Cent African J Surg. 2010;15: 111–118.

20. Nkomo V. Global burden of cardiovascular disease : Epidemiology and prevention of valvular heart diseases and infective endocarditis in Africa. Heart. 2007;93: 1510–1519.

21. Debel FA, Zekarias B, Centella T, Tekleab AM. Immediate outcome following valve surgery for rheumatic heart disease : the first local experience from Ethiopia. Cardiol Young. 2020;30: 1281–1287.

22. Panda BR, Shankar R, Kuruvilla KT, Philip MA, Shukla V, Korula RJ. Combined Mitral and Aortic Valve Replacement for Rheumatic Heart Disease : Fifteen-Year Follow Up and Long-Term Results. J Heart Valve Dis. 2009;18: 170–179.

23. Akhtar RP, Abid AR, Naqshband MS, Mohydin BS. Outcome of double vs . single valve replacement for rheumatic heart disease. J Coll Physiciansn Surg Pak. 2011;287: 77–78.

24. Prashant Mishra, Harsh Sateesh Seth, Jayant. V. Khandekar, Chandan Kumar Ray Mohapatra, Ganesh Kumar K. Ammannaya, Chaitanya Raut1, Jaskaran Singh Saini VS. Double Valve Replacement (Mitral and Aortic) for Rheumatic Heart Disease: A 20-Year Experience with 300 Patients. J Cardiothorac Med. 2016;4: 484–489.

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25. Litmathe J, Boeken U, Kurt M, Feindt P, Gams E. Predictive risk factors in double-valve replacement (AVR and MVR) compared to isolated aortic valve replacement. Thorac Cardiovasc Surg. 2006;54: 459–463.

26. Gupta M, Shoeb M, Mishra PK, Dhar S, Prasad J. Factors influencing the outcome of double valve replacement surgery. Int Surg J. 2017;4: 1913.

27. Mutagaywa RK, Kamuhabwa A, Wind A, Cramer MJ, Chillo P, Chamuleau S. Rheumatic heart disease anno 2020 : Impacts of gender and migration on epidemiology and management. Eur J Clin Invest. 2020; 1–9.

28. Koju R, Gurung R, Pant P, Pokharel B, Bedi T. Pattern of Heart Valve Involvement in Rheumatic Heart Disease. Nepal Hear J. 2009;6: 13–16.

29. John S, Ravikumar E, John CN, Bashi V V. 25-Year experience with 456 combined mitral and aortic valve replacement for rheumatic heart disease. Ann Thorac Surg. 2000;69: 1167–1172.

30. Antunes MJ. Repair for rheumatic mitral valve disease. the controversy goes on! Heart. 2018;104: 796–797.

31. Fu J, Li Y, Zhang H, Han J, Jiao Y. Outcomes of mitral valve repair compared with replacement for patients with rheumatic heart disease. J Thorac Cardiovasc Surg. 2020; 1–11.

32. Jiao Y, Luo T, Zhang H, Han J, Li Y, Jia Y, et al. Repair versus replacement of mitral valves in cases of severe rheumatic mitral stenosis: Mid-term clinical outcomes. J Thorac Dis. 2019;11: 3951–3961.

33. Yau TM, El-Ghoneimi YAF, Armstrong S, Ivanov J, Tirone E. David. Mitral valve repair and replacement for rheumatic disease. J Thorac Cardiovasc Surg. 2000;119: 53–61.

34. Kim JB, Kim HJ, Duk HM, Ho S, Jung S, Hyun C, et al. Long-term outcomes after surgery for rheumatic mitral valve disease : valve repair versus mechanical valve replacement. Eur J Cardio-Thoracic Surg. 2010;37: 1039–1046.

35. Vervoort D, Ouzounian M, Yanagawa B. Mitral valve surgery for rheumatic heart disease: replace, repair, retrain? Curr Opin Cardiol. 2021;36: 179–185.

36. United Republic of Tanzania. National Bureau of Statistics. Population and Housing Report. 2012.

37. Makubi A, Hage C, Lwakatare J, Kisenge P, Makani J, Rydén L, et al. Contemporary aetiology, clinical characteristics and prognosis of adults with heart failure observed in a tertiary hospital in Tanzania: The prospective Tanzania Heart Failure (TaHeF) study. Heart. 2014;100: 1235–1241.

38. Akins CW, Miller DC, Turina MI, Kouchoukos NT, Blackstone EH, Grunkemeier GL, et al. Guidelines for reporting mortality and morbidity after cardiac valve interventions. Eur J Cardio-thoracic Surg. 2008;33: 523–528.

39. Pillai VV. Survival and long-term outcomes after concomitant mitral and aortic valve replacement in patients with rheumatic heart disease. 2021;37: 5–15.

40. Sharma A, Panthee N, Bajracharya SM, Rajbanshi BG, Raj R, Sharma J, et al. Predictors of in-hospital mortality following mitral or double valve replacement for rheumatic heart disease. 2016;13: 19–24.

41. Brown JW, Fiore AC, Ruzmetov M, Eltayeb O, Rodefeld MD, Turrentine MW. Evolution of Mitral Valve Replacement in Children : A 40-Year Experience. Ann Thorac surg. 2012;93: 626–633.

42. Turina MI. European Association for Cardio-Thoracic Surgery : carrying the torch. Eur J Cardio-thoracic Surg. 2002;22: 857–863.

43. Vervoort D, Swain JBD, Pezzella AT, Kpodonu J. Cardiac Surgery in Low- and Middle-Income Countries: A State-of-the-Art Review. Ann Thorac Surg. 2021;111: 1394–1400.

44. Vervoort D, Edwin F. Treating pediatric and congenital heart disease abroad? Imperatives for local health system development. Int J Cardiol Congenit Hear Dis. 2021;2: 100082.

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Table 1. Socio-demographic characteristics of patients operated for RHD at MNH cardiac unit from May 2008 to June 2012 (n=212).

Variable	Median (IQR)/Frequency (%)
Age (years)	21 (15 – 32)
Age groups (years)	
< 20	105 (49.5)
21 – 40	83 (39.2)
41+	24 (11.3)
Sex	
Female	140 (66.0)
Male	72 (34.0)
Education level	
None/informal	23 (10.8)
Primary	157 (74.1)
Secondary	32 (15.1)
Employment status	
Employed	36 (17.0)
Not employed	176 (83.0)
Residence	
Dar es Salaam	76 (35.8)
Outside Dar es Salaam	136 (64.2)

IQR: Interquartile range

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Table 2. Clinical characteristics of patients operated for RHD at MNH cardiac unit from May 2008 to June 2012 (n=212).

Variable	Mean (±SD)/Frequency (%)
Median (IQR) duration of symptoms (months)	36 (12 - 72)
Duration of symptoms categories (months)	
< 24	96 (45.3)
24 – 60	46 (21.7)
60+	70 (33.0)
Mean White blood cell count ($x10^9$/L)	7.02 (±2.60)
Proportion with Abnormal WBC count	11 (5.2)
Mean Hemoglobin level (g/dl)	12.67 (±2.16)
Proportion with anemia	10 (4.7)
Mean Pulmonary Pressure (mmHg)	50.04 (±16.59)
Proportion with Pulmonary hypertension	178 (84)
Grades of Pulmonary arterial pressure	
Normal	34 (16)
Mild	62 (29.2)
Moderate	73 (34.4)
Severe	43 (20.3)
Mean Left Ventricular EF (%)	54.93 (±6.84)
Proportion with reduced EF	30 (14.2)
Valve surgery modality	
Mitral valvotomy	25 (11.8)
Mitral/aortic valve replacement	145 (68.4)
Mitral/aortic valve repair	42 (19.8)
Number of replaced valve (s)*	
Single	128 (88.3)
Double	17 (11.7)
Mean duration of ICU stay (days)	5.2 (±3.1)
Proportion with ICU stay of ≥5 days	62 (29.2)

IQR: Interquartile range; WBC = White Blood Cell Count; EF = Ejection Fraction;
ICU = Intensive Care Unit
*Valve replacement were single (mitral) or double (mitral and aortic) among 145 patients

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Table 3. Predictors of early operative mortality for rheumatic heart disease at MNH

Variable	Total, N = 212	Mortality, n (%)	Bivariate analysis		Multivariable analysis	
			PR (95% CI)	p-value	Adjusted PR (95% CI)	p-value
Sex						
Female	140	18 (12.9)	1			
Male	72	12 (16.7)	1.30 (0.66–2.54)	0.451		
Symptoms (months)						
<24	96	11 (11.5)	1		1	
24 - 60	46	10 (21.7)	1.89 (0.87–4.15)	0.109	1.03 (0.33-3.27)	0.956
61+	70	9 (12.9)	1.12 (0.49–2.57)	0.785	2.04 (0.65-6.39)	0.220
Age (years)						
<20	105	20 (19.0)	1		1	
21 - 40	83	6 (7.2)	0.38 (0.16–0.90)	0.029	0.44 (0.15-1.29)	0.135
41+	24	4 (16.7)	0.88 (0.33–2.33)	0.789	0.94 (0.28-3.15)	0.926
Employment						
Employed	36	4 (11.1)	1			
Not employed	176	26 (14.8)	1.33 (0.49–3.59)	0.574		
Mitral regurgitation						
No	72	7 (9.7)	1			
Yes	140	23 (16.4)	1.13 (0.46–2.76)	0.794		
Mitral stenosis						
No	122	20 (16.4)	1			
Yes	90	10 (11.1)	0.84 (0.43–1.64)	0.614		
Presence of PHT						
No	34	2 (5.9)	1			
Yes	178	28 (15.7)	2.67 (0.67–10.74)	0.165		
LVEF (<50%)						
No	182	29 (15.9)	1		1	
Yes	30	1 (3.3)	0.21 (0.03–1.49)	0.118	0.20 (0.03-1.17)	0.075
Valve surgery modality						
Mitral valvotomy	25	1 (4.0)	1			
MV/AV replacement	145	19 (13.1)	3.28(0.46-23.49)	0.238		
MV/AV repair	42	10 (23.8)	5.95(0.81-43.98)	0.080		
Replaced valve (s)*						
SVR	128	12 (9.4)	1		1	
DVR	17	7 (41.2)	4.39(2.00– 9.64)	<0.001	5.65 (2.46 12.99)	<0.001
Prolonged ICU stay (5 days)						
No	150	15	1		1	
Yes	62	15	2.42 (1.26–4.65)	0.007	1.36(0.55 – 3.38)	0.510

PR: prevalence ratio; APR: adjusted prevalence ratio; CI: confidence interval; PHT: pulmonary hypertension; LVEF: left ventricular ejection fraction; MV: mitral valve; AV: aortic valve; SVR: single valve replacement; DVR: double valve replacement; ICU: intensive care unit

*Valve replacement were single (mitral) or double (mitral and aortic) among 145 patients

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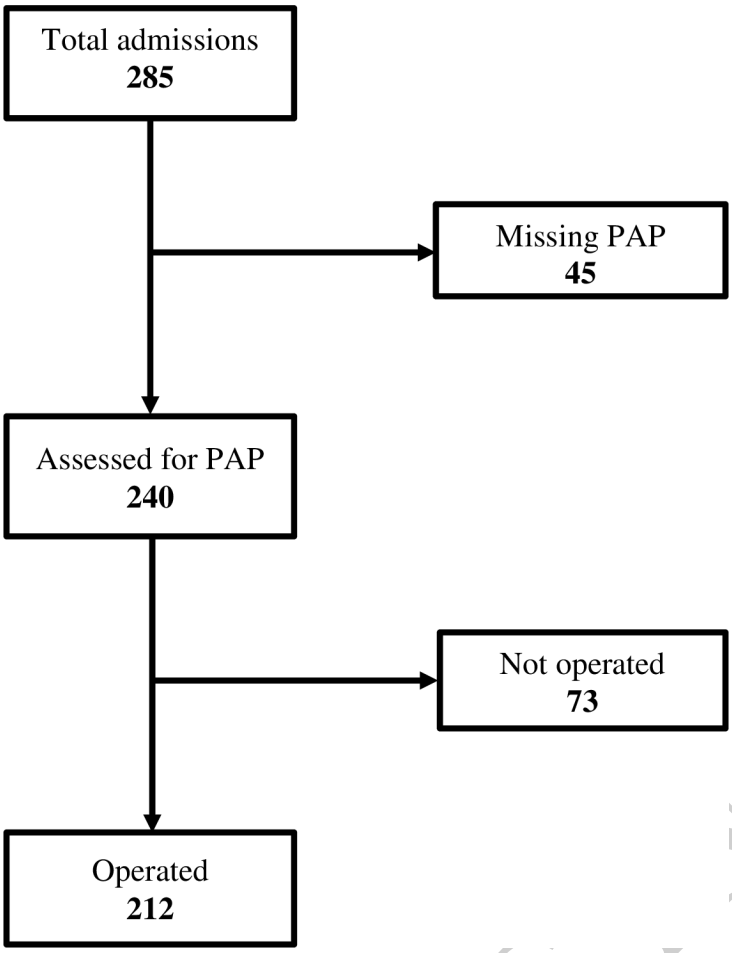


Figure 1. Consort diagram of RHD patients admitted at MNH cardiac unit from 2008 to 2012.
PAP = pulmonary arterial pressure

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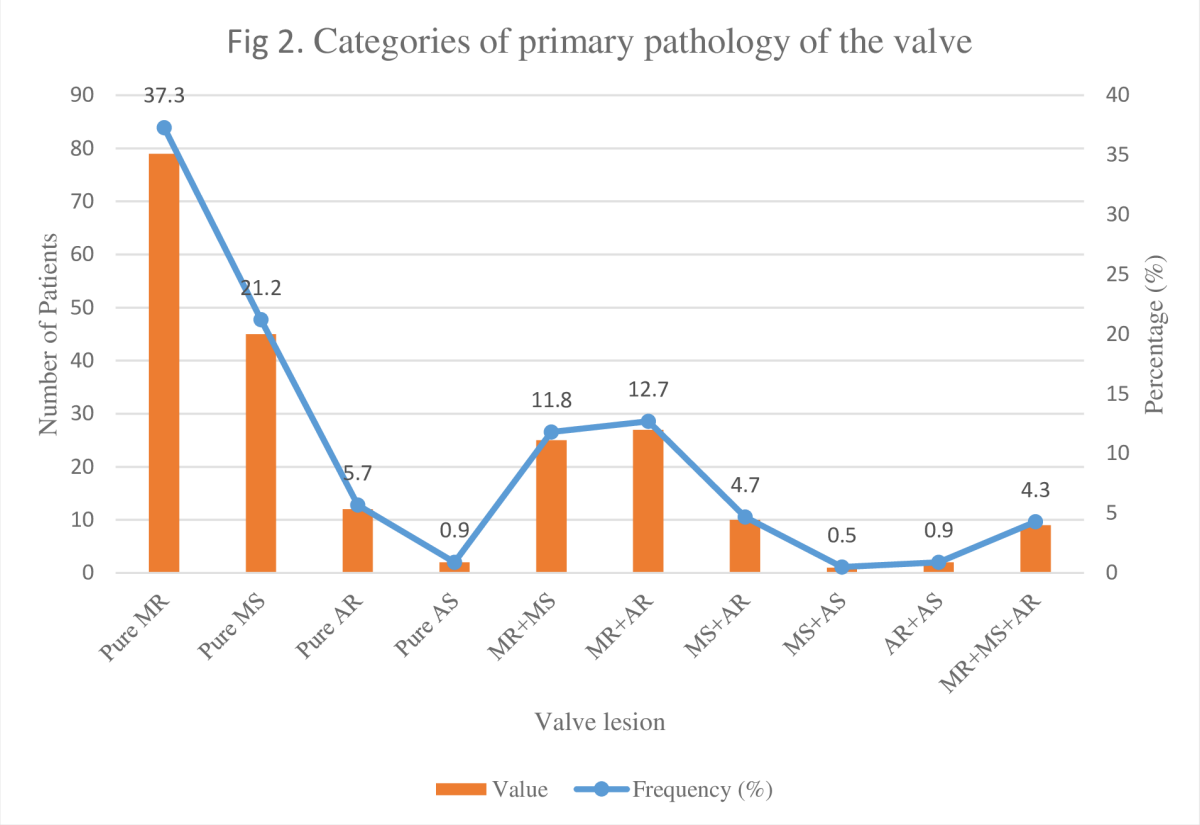


Figure 2. Categories of primary pathologies of the valve.
MR = mitral regurgitation, MS = mitral stenosis, AR = aortic regurgitation, AS = aortic stenosis

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