Profile of adult patients presenting for rheumatic mitral valve surgery at an academic hospital

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, in the fulfilment of the requirement for the degree

of Master of Medicine in the branch of Anaesthesiology

Johannesburg, 2017

Declaration

I, Nolwazi Fiona Mokitimi, declare that this research is my own work. It is being submitted for the degree of Master of Medicine in the branch of Anaesthesiology in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or exam at this or any other university.

Signed

On this day of 2018

Abstract

Background

Perioperative morbidity and mortality are increased in patients with rheumatic heart disease. Preoperative risk stratification is imperative for optimisation and better outcome.

Methods

This was a descriptive, retrospective, contextual study. A consecutive convenience sampling method was used. Eighty-nine patients who underwent mitral valve surgery at Charlotte Maxheke Johannesburg Academic Hospital between January 2014 and December 2015 were enrolled.

Results

Forty-seven patients presented with mitral regurgitation (MR), 35 had mitral stenosis (MS). Data included two mixed mitral valve disease patients with predominant regurgitation that were classified under the regurgitation group. Forty-five percent (39) had arrhythmias and 49% (42) congestive cardiac failure at presentation for surgery. The overall mean (SD) pulmonary pressure was 57 (20) mmHg and the mean left atrial size was 53 (11) mm. Those with mitral stenosis presented with mean (SD) mitral valve area of 0.9 (0.2) cm^2. Of the analysed MR patients, 51% presented with left ventricular ejection fraction (LVEF)<60%, and 55% with left ventricular end systolic diameter (LVESD)>40mm. Amongst the analysed MS patients, 59% had mitral valve area <1cm^2. A substantial number (49% MR and 54% MS) of collected records were not eligible for analysis and stratification using the American Heart Association/American College of Cardiology Guidelines (ACC/AHA) for Valvular Heart Disease. Of the 24 MR patients analysed utilising the 2014/2017 AHA/ACC guidelines, 13 had a-symptomatic severe mitral regurgitation (Stage C) and 11 symptomatic severe mitral regurgitation (Stage D). One patient had progressive mitral stenosis (Stage B), 8 a-symptomatic severe mitral stenosis (Stage C) and 7 symptomatic severe mitral stenosis (Stage D).

Conclusion

The majority of the patients presented in Stage C and Stage D of disease progression; however they also presented with concomitant clinical and echocardiographic features that placed them at high risk of perioperative morbidity.

Acknowledgements

I would like to thank Dr PalesaMotshabi for her idea on a research topic and for her knowledgeable and tireless input as a supervisor. I would also like to thank Dr Katharina-Maria Vanderdonck for availing data used for this research and Dr Hlamatsi Jacob Moutlana for his tireless input in editing the document.

I would also like to extend my gratitude to the Department of Anaesthesia research co-ordinators for their assessment and feedback.

To my husband (Khotso Seth Mokitimi) for his support and encouragement (MokoenawaMonahengwa o jaseretsesamantidima).

Table of Contents

List of Tables

List of Figures

List of Abbreviations

AHA/ACC	American Heart Association/American College of Cardiology
CCF	Congestive cardiac failure
EROA	Effective Regurgitant Orifice Area
EF	Ejection fraction
IE	Infective endocarditis
PAP	Pulmonary artery pressure
LA	Left atrium
LVEF	Left ventricular ejection fraction
LVESD	Left ventricular end systolic diameter
PHT	Pulmonary hypertension
MR	Mitral regurgitation
MS	Mitral stenosis
NYHA	New York Heart Association

Section 1: Literature Review

1.1 Introduction

Rheumatic heart disease remains the most commonly acquired heart disease (1) and is ranked third amongst the common causes of heart failure in African adults (2). The World Health Organisation Report of 2001 noted that rheumatic heart disease accounts for significant premature death and disability in Africa (3). Robertson and Mayosi (4) reported the estimated worldwide prevalence of rheumatic heart disease in 2008 as 15.6 million, with 282 000 new cases arising each year, and 233 000 deaths per year in developing countries. In 2010, the incidence report of cardiac failure, due to rheumatic heart disease, in a South African township was between 30 per 100 000 per year in individuals aged 14 to19 years and 53 per 100 000 per year in individuals 60 years and older (5, 6).

The most common infectious cause of valvular heart disease in developing countries is recurrent pharyngeal infections with group A β haemolytic streptococci (7). This predisposes to development of acute rheumatic carditis, which can progress to rheumatic heart disease, particularly rheumatic valvular heart disease (7). The mainstay of treatment for valvular heart in developing countries remains open heart surgery due to late presentation of patients (8). In contrast, valvular heart disease in developed countries is largely due to non-infective causes and management of patients has evolved to become less invasive, involving procedures such as the performance of percutaneous balloon valvulotomies (8).

The rheumatic heart disease population poses anaesthetic challenges perioperatively as they are prone to life-threatening complications such as arrhythmias, congestive cardiac failure, infective endocarditis and pulmonary hypertension (9-14). It is therefore, important for anaesthetists to be able to stratify these patients preoperatively in order to develop management plans tailored for each patient.

To address the issue of risk stratification in patients presenting for valvular heart surgery due to rheumatic heart disease, the American Heart Association and American College Of Cardiology (AHA/ACC) developed Guidelines used for staging of severity of rheumatic valvular disease (based on symptoms at presentation and preoperative echocardiography findings), and recommends appropriate evidence based management strategies (15, 16). This literature review will describe the incidence and prevalence, aetiology, demographic profile, clinical presentation (with a focus on rheumatic heart disease complications), and echocardiographic findings of rheumatic heart disease.

It will also describe the AHA/ACC Guidelines for Valvular Heart Disease (with a focus on the mitral valve), as well as the clinical stage at which patients present for surgery. A brief summary of the surgical management of mitral valve disease due to rheumatic heart disease will also be given.

1.2 Rheumatic heart disease

1.2.1 Incidence and prevalence

There is a discrepancy in the reported incidence and prevalence of rheumatic heart disease between developed and developing countries, and within poorer and more affluent communities within each country (17-19). In his 2007 review, Nkomo(1) documented the prevalence of rheumatic heart disease as 5.7 per 1000 in sub-Saharan Africa compared with 1.8 per 1000 in north Africa and 0.3 per 1000 in economically developed countries. In 2008, Robertson and Mayosi (4) reported the estimated worldwide prevalence of rheumatic heart disease as 15.6 million, with 282 000 new cases arising each year, and 233 000 deaths per year in developing countries. A 2010 prospective cohort study by Sliwa et al (6) described the incidence in a population older than 14 years, in areas surrounding Chris Hani Baragwanath Academic Hospital in South Africa, as 23.5 cases per 100 000 per annum.

The incidence of disease in South Africa is higher in poor, overcrowded areas (6, 20). This is in similar to findings in developed countries such as Australia, where the incidence in non-indigenous Australians is very low at 0.25 per 1000 than that of the poorer indigenous people which is 26 times higher at 6.45 per 1000 (17). Cilliers(20) attributes the discrepancy between developed and developing countries to developed countries being able to eradicate rheumatic heart disease through implementation of successful health promotion initiatives and superior access to health care; which can also be extrapolated to the differences between upper and low socioeconomic status communities within countries.

1.2.2 Aetiology

The predominant aetiology of valvular heart disease in developed countries is valve degeneration which commonly occurs in the elderly population, whereas infective causes such as rheumatic fever rank high in developing countries and tend to affect the younger population (7, 21, 22). Rheumatic heart disease is the most significant consequence of rheumatic fever (23). Cardiac valves, especially the mitral valve, are affected owing to the postulated mechanism that the valve surface endothelium is a prominent site for lymphocytic infiltrates, coupled with the valvular endothelium's ability to express CD4 and CD8 receptors which aggravate the lymphocytic infiltrative process (24). The overall outcome is progressive scarring and damage resulting in isolated mitral stenosis, isolated mitral regurgitation, or mixed mitral valve disease (25).

1.2.3 Demographic profile of study patients with rheumatic heart disease

A description of the demographic profile of rheumatic heart disease patients allows for improved clinical management approaches. The profile includes age, gender and race, and socioeconomic status.

Age

Different studies report varied ages for the development of rheumatic heart disease. Faheem et al (26) reported a mean age of 22 (6) years in their study conducted in Pakistan. Joseph et al (23) found the mean age to be 33 (18) years in his study conducted in an urban area of South India. Sliwa et al (6) reported a median age of 42 (12) years in their study conducted in Soweto Johannesburg, Kim et al (27), on the other hand found a mean age of 49 (12) years in their study conducted in South Korea. There seems therefore, to be a wide range of age in years for disease presentation.

Gender and race

Studies have reported predominance of rheumatic heart disease amongst females (6, 10, 26, 27). Sixty-eight percent of Sliwa et al's(6) prospective cohort were female. Kim et al's(27) study had 66% females. Faheem et al (26) and Yau et al (10) also reported a female predominance of 58% and 81% respectively. The reasons for female predominance in rheumatic mitral valve disease have not been adequately described (6, 21, 26).
A direct link between race and high rates of rheumatic heart disease has not been established. Black South Africans still form the majority population in impoverished areas and therefore remain the race most commonly affected by the disease (5, 6, 20, 28).

Socioeconomic status

Low socioeconomic status has been associated with increased risk of developing rheumatic disease (20) . Hofer et al (19) noted the highest rate of rheumatic heart disease in Aboriginal Australians and attributed it in part to poor socioeconomic status. Gosh et al (18) also reported a link between high disease prevalence and poor socioeconomic status in Eastern India in their 2011 review.

1.2.4 Clinical complications of rheumatic heart disease

Arrhythmias, congestive cardiac failure, infective endocarditis, renal and hepatic dysfunction, and pulmonary hypertension are common complications of rheumatic heart disease (9-14). Okello et al (13) reported that 64% of their study patients presented with atrial fibrillation and 35% with decompensated cardiac failure, however the study population was that of patients with rheumatic heart disease who had poor access to cardiac surgery services. Koegelenberg et al (14) in their three year prospective study in 2003 at Tygerberg Academic Hospital, Cape Town, South Africa, found that even though 47 out of 92 patients had infective endocarditis, 36 out of 92 had rheumatic heart disease. A retrospective echocardiographic study done in Nigerian patients who presented with a diagnosis of rheumatic heart disease showed that 103 of 129 (72%) patients presented with secondary pulmonary hypertension(29).

1.2.5 Mortality and morbidity associated with rheumatic heart disease

Mortality and morbidity associated with complications of rheumatic heart disease is high. Literature on the perioperative outcomes is limited and therefore non-operative literature is reviewed. Prasad et al (30) reported out of a total of 972 medical records of patients admitted at Indira Gandhi Institute of Cardiology with rheumatic heart disease in the year 2013, 120 deaths were due to rheumatic heart disease. An observational study assessing the value of pulmonary artery pressure to predict in-hospital and one year mortality after valve replacement surgery in patients with rheumatic mitral valve disease reported that 3.8% of middle aged and aged patients died during or shortly after surgery (31). An Ethiopian study found that out of 457 patients with cardiovascular disease, 121 (26.5%) were from rheumatic heart disease and 70% of these died from congestive cardiac failure secondary to rheumatic heart disease (32).

Rheumatic heart disease valvulopathies can result in cardiac failure if left uncorrected. This associated decreased cardiac function has far reaching deleterious systemic effects including renal and liver dysfunction. There is paucity of literature on the impact of the perioperative course of renal and liver dysfunction as a consequence of rheumatic heart disease. However, renal and liver dysfunction from any cause can be associated with poor postoperative function. Rosner and Okusa(33) found a 50% increase in mortality in this patient population. Sabzi(34) reported an overall hospital mortality of 54% in a prospective study carried out on patients who developed liver failure secondary to cardiac failure.

1.3 Significant echocardiographic parameters in rheumatic valvular heart disease

The AHA/ACC guidelines for Valvular Heart Disease include echocardiographic parameters in staging of severity of rheumatic valve heart disease, and are more sensitive at detecting asymptomatic patients (15, 16). Important echocardiographic parameters to document in order to diagnose and stage rheumatic valvular disease include the dominant lesion, left atrial size pulmonary artery pressure, left ventricular end systolic diameter and left ventricular ejection fraction.

Mitral regurgitation, as detected on echocardiography, has been reported to be the predominant lesion in African studies. A study conducted in Nigeria reported mitral regurgitation dominance (37%), mixed aortic and mitral valvular heart disease of 19.5%and mitral stenosis prevalence of 8% (35). Sliwa et al (6), in their study conducted in South Africa, identified mitral regurgitation in 59% of their patients, 30% had mitral stenosis and 13% mixed mitral valve disease. Okello et al (13), in their Ugandan study, reported that 68% of patients had mitral regurgitation and only 29% had mitral stenosis. Manjunath et al (36) reported 73% of their patients from India had predominantly mitral stenosis and Faheem et al (26) reported that 70% of their patients from Pakistan had mitral stenosis.

Left atrial enlargement due to dysfunction of the valves from rheumatic heart disease is associated with atrial fibrillation, stroke and cardiac failure (37-39). Benjamin et al (40) found that every 5mm increase in left atrial size increased the risk of development of atrial fibrillation by 39%. Data from the Cardiovascular Health Study conducted in 2006 showed an independent association of left atrial volume with incidence and prevalence of congestive heart failure (41).

Pulmonary hypertension increases the perioperative risk in patients who are undergoing mitral valve surgery with a reported mortality as high as 31% (42) and Kumar et al (43) found that patients with valvular heart disease and preoperative severe pulmonary hypertension experienced early death.

1.4 2014 ACC/AHA Guidelines for Valvular Heart Disease

The AHA/ACC committee have translated scientific evidence into clinical practice guidelines with recommendations to improve cardiovascular health (15). The focus of the 2014 and the recently revised 2017 guidelines for the management of patients with valvular heart disease are on diagnosis and management. Parameters that are included in staging for mitral stenosis are shown in Table 1. According to these guidelines, patients with asymptomatic severe valvular heart disease are classified as Stage C and those with symptomatic severe valvular heart disease are classified as Stage D (15).

The guidelines recommend that open heart surgery be reserved for patients who present late in the course of their disease as evidenced by severe symptoms and corresponding echocardiography changes. It is suggested that patients with severe mitral stenosis are eligible for minimally invasive percutaneous mitral balloon valvulotomy provided valve tissue is amenable. The guidelines also recommend valve repair surgery in asymptomatic patients with severe disease on echocardiography (15).

1.4.1 2017 ACC/AHA Guidelines for Valvular Heart Disease Update

With regards to mitral valvular heart disease, the 2017 ACC/AHA Guidelines for Valvular Heart Disease Updates are with respect to specifically chronic primary regurgitation. According to the modified guidelines, patients with severe mitral regurgitation require early surgical intervention preferably before ejection fraction is less than 60% and left ventricular end systolic diameter is greater than 40 mm (15).

Table 1Staging for mitral stenosis as per 2014 AHA/ACC guidelines for Valvular Heart Disease(15)

Stage	Valve and Hemodynamic consequences
A	Asymptomatic with mild valve doming during diastole and no hemodynamic consequences.
B	Asymptomatic with rheumatic valve changes with commissural fusion and moderate diastolic doming of the mitral valve. Mitral valve area ≥1.5 cm^2 and normal pulmonary pressure at rest.
C	Asymptomatic with a mitral valve area of ≤1.5 cm^2, elevated pulmonary artery systolic pressure 30 mmHg
D	Symptomatic with a mitral valve area of ≤1.5 cm^2, elevated pulmonary artery systolic pressure 30 mmHg.

Table 2 Staging for primary mitral regurgitation as per 2014 AHA/ACC guidelines for Valvular Heart Disease(15)

Stage	Valve and Haemodynamic consequences
A	Asymptomatic with mild prolapse, thickening or leaflet restriction. No hemodynamic consequences
B	Asymptomatic with severe prolapse, rheumatic changes with loss of central coaptation, or prior infective endocarditis. Mild left atrial enlargement, no left ventricular enlargement, EROA ≤0.4 cm^2 and normal pulmonary pressures.
C1	Asymptomatic with preserved left ventricular end systolic dimension (LVESD< 40 mm) and adequate left ventricular ejection fraction (LVEF ≥60%). Moderate to severe left atrial enlargement, left ventricular enlargement and pulmonary hypertension at rest or on exercise.
C2	Asymptomatic with left ventricular end systolic dimension (LVESD≥40 mm) and impaired left ventricular ejection fraction (LVEF≤60%). Moderate to severe left atrial enlargement, left ventricular enlargement, pulmonary hypertension at rest or on exercise and effective regurgitant orifice area (EROA ≥0.4 cm^2).
D	Symptomatic with left ventricular end systolic dimension (LVESD ≥40 mm), pulmonary hypertension, effective regurgitant orifice area (EROA ≥0.4 cm^2).

Staging for mitral regurgitation is classified into primary and secondary according to the cause of the valve lesion (15). For the purpose of this literature review, emphasis will be on staging for primary causes of mitral regurgitation as rheumatic heart disease falls into this category. This is shown in Table 2. Recommendation for mixed valve disease is that evaluation and surgical intervention be done in accordance with recommendations for the dominant lesion (15).

1.5 Stage of presentation of patients as per the 2014 AHA/ACC guidelines for Valvular Heart Disease

Okello et al (13) found timing of initial presentation of rheumatic heart disease in their cohort study to have occurred late. They found a three-month mortality rate of 18% and 59 cardiac related deaths in one year. Sliwa and Mayosi (6) in their Insights from the Heart Of Soweto Study, also found that the majority of their patients presented late within the course of the disease as 66% of their newly diagnosed rheumatic heart disease patients presented with symptoms of congestive cardiac failure.

In India, a trend of late presentation (with regards to clinical stage of presentation in patients with rheumatic heart disease) similar to that in the above African patients was found however, this trend was observed in patients presenting for surgery. A cohort study conducted reported that of 898 patients with rheumatic heart disease, 565 (63%) presented with preoperative atrial fibrillation and 466 and 144 patients presented in New York Heart Association (NYHA) stages III and IV respectively (43).

1.6 Surgical management of mitral valvular rheumatic heart disease

The decision for early or late surgical intervention in patients with asymptomatic mitral regurgitation remains controversial. A study examining mitral valve repairs in patients with mainly mitral regurgitation secondary to degeneration and not necessarily rheumatic valvular heart disease noted that left ventricular ejection fraction and left ventricular end systolic diameter are good predictors of postoperative left ventricular function and can be used as objective markers to decide on timing of surgery (44).

Tribouilloy et al (45) noted that: “early surgical intervention is a reasonable consideration in asymptomatic patients booked for mitral regurgitation correction however, clinicians are hesitant to recommend surgery in patients with no or minimal symptoms for fear of exposure to operative mortality and morbidity.’’ De Bonis and Bolling(46) commented that “a randomised trial comparing the two approaches has never been performed and currently available literature is derived from observational prospective or retrospective studies which carry the inherent risk of selection bias”.

Historically, surgical intervention has improved from its first attempt in the 1920s. This is largely due to wider availability of mechanical valves and homografts (47, 48) . Mitral valve replacement for mitral regurgitation was previously the surgical procedure of choice, however, its association with complications such as life-long anticoagulation requirement, thromboembolic complications and degradation of bio-prostheses led to its limited use (49). Mitral valve repair for mitral regurgitation is now the preferred option as it leads to preservation of valve structure and is associated with decreased risk of endocarditis, thromboembolism, bleeding complications and breakdown of prosthetic material (27, 50).

Minimally invasive surgical techniques for mitral stenosis include balloon valvuloplasty and the surgical indications for this technique are asymptomatic patients with favourable valve anatomy (15, 16) There also exists controversy regarding the choice of mitral valve balloon valvuloplasty or valve replacement in patients with mitral stenosis. Percutaneous mitral balloon valvulotomy has been used for mitral stenosis (51). It is not however devoid of complications as restenosis rates of up to 7%-23% have been reported (52, 53). Thus, mitral valve replacement is still the preferred method (54).

Vassileva et al (55) reported operative mortality rates of 9% for mitral valve replacement compared to 4% for mitral valve repair. Several international studies advocate for the choice of mitral valve repair over replacement because of complications associated with valve replacement (43, 46, 48), however, literature on perioperative studies in developing countries is minimal and available studies are epidemiological. Thus, there is limited knowledge concerning the surgical practise in developing countries.

1.7 Summary

Rheumatic heart disease is a preventable medical condition which is being eradicated in high socioeconomic countries. The complications of rheumatic valvular surgery carry a burden of high morbidity and mortality.

Early diagnosis and treatment before development of severe complications could reduce the risk of morbidity and mortality. Stratification of patients preoperatively is essential for optimisation and proper planning to circumvent perioperative complications.

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Section 2: Authors' guidelines

This section outlines the guidelines that the author has followed in writing the draft article. The guidelines used were those of the Cardiovascular Journal of Africa, which is the intended journal of publication.

Cardiovascular Journal of Africa: Guidelines to authors

Article submission

All categories of manuscripts for the Cardiovascular Journal of Africa must be submitted on-line to Editorial Manager. You will be assigned your own password and user name. This will allow complete interaction between the editor and authors. Internally, reviewers will be approached to review material in their field of expertise and assigned with similar interaction. All information will be entirely protected and confidential. All submissions should be written in a clear and succinct manner, following the style of the Journal. Title page should include a descriptive title; authors' surname and forename, address of each author and full address, telephone, fax and e-mail contacts for the corresponding author. In text: tables and figures are either inserted as part of sentence, for example Table 1, or in parentheses, for example (Fig. 1). Each table should carry a descriptive heading.

Editorial Manager will clearly indicate which aspects of the submission must be supplied off-line (download off-line document). This must be provided to the Journal by mail (PO Box 1013, Durbanville, South Africa, 7551) or e-mail to info@clinicscardive.com. All images MUST be at or above intended display size, with the following image resolutions: Line Art 800 dpi, Combination (Line Art + Halftone) 600 dpi, Halftone 300 dpi Image files also must be cropped as close to the actual image as possible.

Preferred Image Format		Alternative Image Format	
Image Format	.tif	**Image Format**	.jpg
Image Width	Greater than or equal to intended display size	**Image Width**	Greater than or equal to intended display size
Colorspace	RGB	**Colorspace**	RGB
DPI	500+	**DPI**	500+
Alpha Channels	None	**Compression Quality**	Maximum
Layers	Flattened		

References numbered in the order of appearance in the text, according to Vancouver style. For articles: Author AB, Author C, Author M. The title of the article.Abbreviated journal title 1999; 14: 172–183. For book chapters: Author AB, Author CD. The title of the chapter. In: Editor A, Editor BC, ed. Title of the book, 2nd edn. Location: Publisher, 1999: 133 –139. DOI Numbers / PMID (Pubmed ID / PMC ID) must be added to all references to facilitate tagging for PubMed Central.

Original articles: Title page as above. Abstract (150 words) a short inclusive statement suitable for direct electronic abstracting, identifying the purpose of the study, key methods, the main results and the main conclusion. Keywords: maximum of six keywords for indexing. Introduction: concise description of background, sufficient for the non-specialist to appreciate the context of the work. Clear statement of the purpose of the study. Methods: a brief description of study design, procedures, analytical techniques and statistical evaluation.

Results: a clear account of the study findings using quantitative language where possible and cross-referenced to tables and figures. Discussion: an interpretation of the study placed within the context of current knowledge, leading to specific conclusions where possible. Acknowledgements.References, figures and tables as above.

Reviews

Title page as above. Abstract (150 words) setting out the scope, key messages and conclusions of the review. Body of text liberally partitioned with headings and subheadings leading to a synopsis with conclusions at the end. Key messages in a separate box itemising two to five short principal statements. Acknowledgements, references, tables and figures as above. Other articles should adopt a concise style consistent with similar articles previously published in the journal. Manuscripts should include a title page, and appropriate subheadings for text. Style of tables, figures and references as above.

Figures be sent to us in a high resolution JPEG format, but they MUST be sent separately from the Word document. If not in high resolution JPEG, then PowerPoint will do. Editorial Manager will clearly indicate which aspects of the submission must be supplied off-line (**download off-line document**). This must be provided to the Journal by mail (PO Box 1013, Durbanville, South Africa, 7551) or e-mail to **info@clinicscardive.com**

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Section 3: Draft article

This section outlines the draft article in the format according to the authors' guidelines. The format of this draft article is presented according to the Cardiovascular Journal of Africa.

Profile of adult patients presenting for rheumatic mitral valve surgery at an academic hospital

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Abstract

Background

Perioperative morbidity and mortality are increased in patients with rheumatic heart disease. Preoperative risk stratification is imperative for optimisation and better outcome.

Methods

This was a descriptive, retrospective, contextual study. A consecutive convenience sampling method was used. Eighty-nine patients who underwent mitral valve surgery at Charlotte Maxheke Johannesburg Academic Hospital between January 2014 and December 2015 were enrolled.

Results

Forty-seven patients presented with mitral regurgitation (MR), 35 had mitral stenosis (MS). Data included two mixed mitral valve disease patients with predominant regurgitation that were classified under the regurgitation group. In total forty-five percent (39) had arrhythmias and 49% (42) congestive cardiac failure at presentation for surgery. The overall mean (SD) pulmonary artery systolic pressure was 57 (20) mmHg and mean (SD) left atrial size was 53 (11) mm. Those with mitral stenosis presented with mean (SD) mitral valve area of 0.9 (0.2) cm^2. Of the analysed MR patients, 51% presented with left ventricular ejection fraction (LVEF)<60%, and 55% with left ventricular end systolic diameter (LVESD)>40mm. Amongst the analysed MS patients, 59% had mitral valve area <1cm^2. A substantial number (49% MR and 54% MS) of collected records were not eligible for analysis and stratification using the American Heart Association/American College of Cardiology Guidelines (ACC/AHA) for Valvular Heart Disease due to missing vital information. Of the 24 MR patients analysed utilising the 2014/2017 AHA/ACC guidelines, 13 had asymptomatic severe mitral regurgitation (Stage C) and 11 symptomatic severe MR (Stage D). One patient had progressive mitral stenosis (Stage B), 8 asymptomatic severe MS (Stage C) and 7 symptomatic severe mitral stenosis (Stage D).

Conclusion

The majority of the patients presented in Stage C and Stage D of disease progression; however, they also presented with concomitant clinical and echocardiographic features that placed them at high risk of perioperative morbidity and mortality.

Keywords: clinical profile, mitral valve, rheumatic heart disease, stratification

Introduction

The estimated worldwide prevalence of rheumatic heart disease was 15.6 million in 2008, with 282 000 new cases arising each year, and 233 000 deaths per year in developing countries [1]. In 2010, the incidence of cardiac failure, due to rheumatic heart disease, in a South African township was reported to be between 30 per 100 000 per year in individuals aged 14 to19 years and 53 per 100 000 per year in individuals 60 years and older [2, 3].

The commonest infectious cause of valvular heart disease in developing countries is Group A β haemolytic streptococci infection. The mainstay oftreatment for valvular heart disease in these countries remains open heart surgery due to late presentation of patients. [4]

The presence of complications such as arrhythmias, congestive cardiac failure, infective endocarditis and pulmonary hypertension increases mortality [5-7]. In 2004 Oli [7] found that out of 457 patients with cardiovascular disease, 121 (26.5%) were from rheumatic heart disease and 70% of these died from congestive cardiac failure secondary to rheumatic heart disease.

Patients presenting for open heart surgery, pose anaesthetic challenges perioperatively due in part to complications emanating from preoperative low ejection fraction (EF) and prolonged cross-clamp time [8]. An observational study assessing the value of pulmonary artery pressure (PAP) in predicting in-hospital and one-year mortality after valve replacement surgery in patients with rheumatic mitral valve disease reported gradual but significant increases in in-hospital mortality rate as the PAP level increased [6]. Timing of referral for surgery might therefore be important and may impact the perioperative course of patients.

Stratification of these patients preoperatively is imperative to develop management plans tailored to each patient. Towards this, The American Heart Association and American College of Cardiology (AHA/ACC) developed guidelines in 2014 which stage severity of rheumatic valvular heart disease (based on symptoms at presentation and preoperative echocardiography findings) [9]. These guidelines were updated in 2017 to recommend appropriate evidence-based management strategies [10].

It is unclear whether the AHA/ACC Guidelines for Valvular Heart Disease were utilised for stratification of patients presenting for surgery at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) as records had insufficient data to make conclusions. Post data collection, anecdotal information from Dr Tsabedze, the new Head of Department of Cardiology suggests that the department follows European guidelines. These are not significantly different from the American guidelines and use similar parameters. However, this information was not available on the charts at the time of data collection as indicated by the incomplete echocardiographic data. Thus, this study undertook to describe the profile of adult patients presenting for rheumatic mitral valve surgery at CMJAH.

Methodology

The study was conducted in the Cardiothoracic Unit and the Department of Anaesthesiology, affiliated to the Faculty of Health Sciences of the University of the Witwatersrand. Approval was obtained from the Human Research Ethics Committee (Medical) of the University of the Witwatersrand and other relevant authorities. A retrospective review was conducted of preoperative anaesthetic and cardiothoracic surgery records belonging to patients who presented for mitral valve surgery from January 2014 to December 2015. Charlotte Maxeke Johannesburg Academic Hospital is a quaternary hospital located in Parktown, Gauteng. It has a capacity of 1 200 beds and 23 theatres, which includes two cardiac (adult and paediatric) theatres and one thoracic theatre. It also has a dedicated cardiothoracic intensive care unit which admits both adult and paediatric patients. On average 23 000 surgical cases are performed annually of which approximately 250 are adult cardiac cases.

Reviewed variables were age, race, gender, preoperative vital signs, cardiovascular examination data focusing on the presence or absence of arrhythmias, congestive cardiac failure and infective endocarditis, liver and renal function tests, and preoperative echocardiographic parameters.

Relevant variables were then used to stratify patients according to the AHA/ACC guidelines for valvular heart disease. Demographic data, including ethnicity, were collected from hospital records as these were self-reported on them. These were utilised to classify patients into ethnic groups. All data were collected by one author (NM). A data collection flow chart is shown below (Figure 1). Descriptive stats were used: numbers and percentages were reported as means and standard deviations or medians and interquartile ranges, depending on the distribution of data

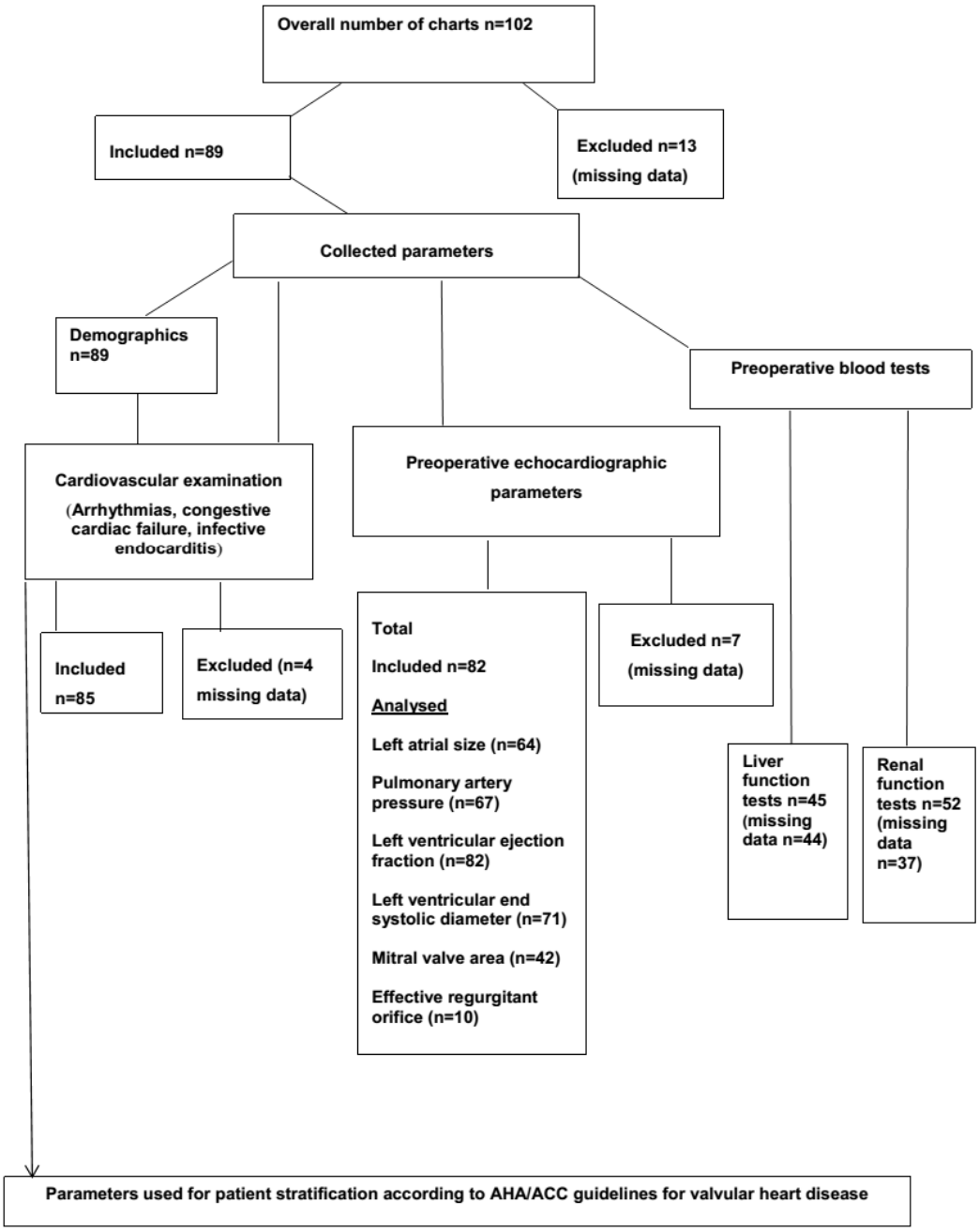

Figure 1 Flowchart indicating variables collected for the study

Results

One hundred and two records were eligible for review and 89 were enrolled. Thirteen were excluded due to missing vital data. The mean (SD) age of presentation was 42 (12) years ranging from 18-72 years. Of the 89 patients, each had different data sets available for review. The patient demographics and cardiovascular examination findings are illustrated in Table 1.

Table 3Demographic and cardiovascular examination findings of study patients

Variable	Frequency n (%)	
Gender n=89		
Female	52 (58)	
Male	37 (42)	
Ethnicity n=89		
Black	67 (75)	
White	16 (18)	
Other	6 (7)	
Preoperative cardiovascular examination findings n= 85		
	Yes	No
Arrhythmias	39 (46)	46 (54)
CCF	42 (49)	43 (51)
IE	10 (12)	75 (88)

*CCF (Congestive Cardiac Failure), IE (Infective Endocarditis).

Records for results of preoperative liver and renal function parameters were available in 51% and 58% of patients respectively. They were all normal (Table 2).

Table 4Preoperative liver and renal parameters

Liver function test n=45		
(mmol/L)	Median	IQ Range
Alkaline phosphatase	66	32-95
Gamma glutamine transferase	48	27-82
Alanine transaminase	52	28-111
Aspartate transaminase	45	29-83
Renal function test n=52		
(mmol/L)	Median	IQ Range
Urea	5.8	5.1-8.4
Creatinine	83	68-105

The predominant mitral valve lesion as diagnosed on echocardiography showed that 57% (47) of study patients had mitral regurgitation and 42% (35) had mitral stenosis. Two study patients presented with mixed mitral valve disease with predominant regurgitation and were thus classified under regurgitation as per the AHA/ACC Guidelines for Valvular Heart Disease. Combined echocardiographic results for mitral regurgitation and mitral stenosis are shown in Table 3.

Table 5 Echocardiographic data of interest for both mitral regurgitation and mitral stenosis

		Mean (SD)	Min-Max Range
LA size (mm) n=64		53 (11)	30-91
	Female n=40	54 (13)	30-91
	Male n=24	51 (6)	41-60
PAP (mmHg) n=67		57 (20)	21-101

*PAP: pulmonary artery pressure; LVEF: left ventricular ejection fraction; LVESD: left ventricular end systolic diameter; LA: left atrial,

The mitral regurgitation patients had mean (SD) left atrial size of 55 (13) mm for females and 49 (6) mm for males. The mean (SD) for pulmonary artery pressure was 55 (21) mmHg, mean (SD) left ventricular ejection fraction was 59 (11) % and the mean (SD) left ventricular end systolic diameter was 39 (14) mm.

Of the female patients, 28% had enlarged left atrial size while 43% had high pulmonary artery pressures. Normal left ventricular ejection fraction of more than 60% was found in 51% of mitral regurgitation patients and 55% had left ventricular end systolic diameters of less than 40mm. Echocardiographic data for mitral regurgitation are shown in Table 4. Seventy-nine percent (79%) of the effective regurgitant orifice area data were incomplete from the charts. These data are necessary for patient stratification.

Table 6Echocardiographic data for mitral regurgitation

Left atrial size n=35		n (%)
Female	≤ 43 mm	3 (9)
Male	≤ 47 mm	6 (17)
Female	43-47 mm	4 (11)
Male	47-52 mm	4 (11)
Female	>47 mm	13 (37)
Male	>52 mm	5 (15)
Pulmonary artery pressure n=32		
Mild	≤ 30 mmHg	5 (16)
Moderate	30-50 mmHg	7 (22)
Severe	>50 mmHg	20 (62)
Left ventricular ejection fraction n=47		
>60%		23 (49)
≤ 60%		24 (51)
Left ventricular end systolic diameter n=38		
≤ 40 mm		21 (55)
>40 mm		17 (45)
Effective regurgitant orifice area n=10		
≤ 0.4 cm²		4 (40)
≥0.4 cm² (+hemodynamic changes)		6 (60)

Echocardiographic parameters for mitral stenosis patients showed the mean (SD) mitral valve area of 0.9 (0.2) cm², and the mean (SD) left atrial size of 54 (13) mm for female patients and 52 (7) mm for male patients. The mean (SD) pulmonary artery pressure was 60 (19) mmHg.

Critically stenosed mitral valve disease with a mitral valve area of less than 1cm² was found in 59% of patients and 69% of mitral stenosis patients had severely elevated pulmonary artery pressures. Echocardiographic data for mitral stenosis are shown in Table 5; (however, similar to mitral regurgitation, some charts had missing parameters).

Table 7Echocardiographic data for mitral stenosis

Mitral valve area n=32		n (%)
1.5cm² -1.0cm²		13 (41)
≤ 1.0cm²		19 (59)
Left atrial size n=27		
Female	≤ 43 mm	2 (7)
Male	≤ 47 mm	2 (7)
Female	43-47 mm	5 (19)
Male	47-52 mm	2 (7)
Female	>47 mm	12 (45)
Male	>52 mm	4 (15)
Pulmonary artery pressure n=32		
Mild	≤ 30 mmHg	1 (3)
Moderate	30-50 mmHg	9 (28)
Severe	>50 mmHg	22 (69)

Patient stratification as per the AHA/ACC Guidelines for Valvular Heart Disease combines symptoms at presentation, haemodynamic consequences and valve anatomy for disease severity staging. In the current study the preoperative cardiovascular examination findings representing symptoms and signs were collected together with the preoperative echocardiography findings which demonstrated valvular structure and haemodynamic consequences.

Review of the data for mitral regurgitation patients (47) for the purposes of stratification revealed incomplete parameters in 23 (49%) of the patients. Of the remaining 24 (51%), 13 (54%) were stratified as a-symptomatic severe mitral regurgitation or Stage C and 11 (46%) as symptomatic severe mitral regurgitation or Stage D. Stratification for mitral stenosis patients (35) showed that 19 (54%) study patients had incomplete data. Only 16 (46%) could therefore be analysed with one patient (6%) having progressive mitral stenosis or Stage B, 8 (50%) as a-symptomatic severe mitral stenosis or Stage C and 7 (43%) as symptomatic severe mitral stenosis or Stage D.

Table 8Stratification (stage of presentation) as per AHA/ACC Guidelines for Valvular Heart Disease

Symptoms, Haemodynamic consequences and Valve haemodynamics	Mitral Regurgitation n (%)	Mitral Stenosis n (%)
Stage B (Progressive disease)	Nil	1 (3)
Stage C (severe asymptomatic disease)	13 (28)	8 (23)
Stage D (severe symptomatic disease)	11 (23)	7 (20)
Incomplete vital information	*23 (49)*	*19 (54)*

Discussion

Data on perioperative studies in patients with rheumatic heart disease are limited; therefore, our study relied on epidemiological studies. Rheumatic heart disease is a preventable medical condition which is being eradicated in high socioeconomic countries.

Different studies report varied ages at presentation of rheumatic heart disease. The mean (SD) age at presentation to surgery in the current study was found to be 42(12) years. An epidemiological study by Sliwa [3], which was conducted in Soweto, Johannesburg, looked at new onset of presentation of rheumatic heart disease and reported a median (IQR) age of 42 (31-55).

Similarity in age between this study and that by Sliwa et al [3] may be attributed to the fact that both studies are in the same geographical area of Johannesburg. Kim [11] reviewed patients post mitral valve surgery in South Korea and reported the mean age as 49 (12) years. Faheem [12] reported the mean age of new onset of presentation in a Pakistan population as 22 (6) years, while Joseph [13] found the mean age of new onset of presentation to be 33 (18) years. Their study was conducted in an urban area of South India. Data from the current study could be used to indicate only age at presentation to surgery in relation to clinical picture as these patients may have been followed up for periods of time before presentation to surgery. It is however, postulated that rheumatic valve disease progression in the developing world is characterised by considerably shorter latent phase periods, likely due to recurrent carditis [9].

Several studies reported predominance of rheumatic heart disease amongst females. [3,11, 12, 14, 15] with 68% being female in Sliwa [6], 66% in Kim [11], 58% in Faheem [12] and 81% in Yau [14]. Findings from the current study, although only reporting on mitral valvular disease, also showed female predominance with 58% of the patients being female. The reason for female predominance has not been explored in previous studies [6,14,15], and may have been coincidental.

Outcomes of the current study showed that 75% of study patients were of the black population. Although the finding of dominance of the black population in rheumatic heart disease has been shown before, a direct link between race and high incidence of rheumatic heart disease has not been established [2,3,16-19].

A link to low socioeconomic status has however been made previously [19]. The majority of black South Africans live in impoverished areas, which may have a relationship with the high prevalence of rheumatic heart disease in this population [2, 3, 16-19].The link between high rheumatic heart disease rates and poor socioeconomic status is supported by Hofer [19] who noted that the highest rates of disease were in Aboriginal Australians from poor indigenous areas. In addition, Gosh [18] in their review article in 2011 also reported high rheumatic heart disease prevalence in a poor rural region of Eastern India.

Arrhythmias, congestive cardiac failure, infective endocarditis and pulmonary hypertension are common complications of rheumatic heart disease [14, 19-25]. In the current study, 45% of study patients presented with arrhythmias. This was, however, less than that seen in an epidemiological non-operative Ugandan study in which 64% of patients had arrhythmias at initial presentation [24]. Okello et al [24] also reported that 35% of their Ugandan study patients presented with decompensated cardiac failure. In the current study, a higher rate (49%) of patients presented for surgery in congestive heart failure. Only 12% of study patients within this study presented with infective endocarditis. This was much lower than those in the study by Koegelenberg et al, [25] which found 51% of their patients presenting with infective endocarditis at Tygerberg Academic Hospital, Cape Town, South Africa in 2003.

The mean (SD) PAP in the current study was 57 (20) mmHg overall and the majority of the study patients presented with moderate to severe PHT (84% in mitral regurgitation and 97% in mitral stenosis). This has critical clinical implications as perioperative PHT is linked to increased complications and high rates of mortality perioperatively [6, 21].

Jiang [6] found a gradual but significant increase in in-hospital mortality rates as PAP levels increased in middle-aged and aged patients (mean (SD) age 57 (6) years) diagnosed with rheumatic mitral disease, undergoing valve replacement surgery. They found that PAP>52.5 mm Hg had a sensitivity of 60.3% and specificity of 67.7% in predicting in-hospital death (AUC=0.672, 95% CI 0.602 to 0.743, p<0.001). They also showed that patients with PAP>52.5 mm Hg had higher one-year mortality after operation than those without (p<0.001). [6]

Preoperative renal and liver function assessment is important as preoperative creatinine levels greater than 2 - 4mg/dl (176-352mmol/L) in patients scheduled for valve procedures have been identified as risk factors for the development of acute renal failure post open cardiac surgery [26]. Sabzi[27] reported an overall hospital mortality of 54% in a prospective study carried out on patients who developed liver failure secondary to cardiac failure. The current study found that preoperative urea, creatinine and liver function tests were normal for all study patients who had data.

The 2014 (updated in 2017) AHA/ACC guidelines for Valvular Heart Disease include the description of the dominant lesion, left atrial size, pulmonary artery pressures, left ventricular end systolic diameter and left ventricular ejection fraction as echocardiography parameters for staging of severity in rheumatic valvular heart disease [9, 10].

Rheumatic mitral regurgitation appears to be predominant in African countries as evidenced by studies conducted in the Savannah in Nigeria, Soweto in South Africa and a tertiary institution in Uganda which reported mitral regurgitation dominance of 37% (study reported mixed mitral valve as a separate group), 59% and 68% respectively [3, 24, 28]. The current study also found mitral regurgitation to be predominant as 53% of study patients were shown to have this lesion on echocardiography.

The decision for early or late surgical intervention in patients with asymptomatic mitral regurgitation remains controversial [32, 33, 34]. Tribouilloy et al [33] noted that "early surgical intervention is a reasonable consideration in a-symptomatic patients booked for mitral regurgitation correction. However, clinicians are hesitant to recommend surgery in patients with no or minimal symptoms for fear of exposure to operative mortality and morbidity." The AHA/ACC guidelines suggest that primary mitral regurgitation, being a mechanical leaflet problem, requires a mechanical surgical solution. "The goal of therapy in MR is to correct it before the onset of left ventricular systolic dysfunction and the subsequent adverse effect on patient outcomes" [9].

The overall mean (SD) LA size of patients in the current study was severely enlarged at 53(11) mm, placing them at risk of developing complications. Enlarged LA size on echocardiography results in significant complications such as atrial fibrillation, stroke and heart failure [29-31]. Reed [35], in their study of preoperative predictors of postoperative cardiac-related mortality concluded that "1) measures of both left ventricular systolic function and left atrial size are equally important in predicting postoperative cardiac-related mortality in patients with symptomatic chronic mitral regurgitation undergoing mitral valve replacement; 2) left atrial size may be important because it reflects the "history" (severity and duration) of mitral regurgitation" [35].

LVEF and LVESD are good predictors of postoperative left ventricular function and can be used as objective markers to decide on timing of surgery in patients with mitral regurgitation [32]. In the current study, 49% of MR patients presented with LVEF>60% and 45% presented with LVESD 40mm. Class 1 evidence for primary MR from the AHA/ACC guidelines suggests that "the goal of therapy in MR is to correct it before the onset of LV systolic dysfunction and the subsequent adverse effect on patient outcomes" [9]. It is deemed ideal to operate prior to indications of systolic dysfunction (LVEF≤60% or LVESD≥40 mm). The guidelines recommend a higher cut-off for "normal" LVEF in MR than in other types of heart disease.

Risk stratification of patients as per the AHA/ACC guidelines for the current study proved difficult as 49% of study patients within the mitral regurgitation group and 54% of study patients from the mitral stenosis group had missing important information necessary for stratification. Of the 51% of the study patients with available important information within the mitral regurgitation group, risk stratification as per the AHA/ACC guidelines showed that 13 (54%) had asymptomatic severe mitral regurgitation or Stage C and 11 (46%) symptomatic severe mitral regurgitation or Stage D. Stratification for mitral stenosis patients showed that one patient (6%) had progressive mitral stenosis or Stage B; 8 (50%) a-symptomatic severe mitral stenosis or Stage C and 7 (43%) symptomatic severe mitral stenosis or Stage D.

All patients in the current study underwent mitral valve replacement irrespective of the stage of disease at which they presented. As this data are retrospective, the reasons behind the decision regarding the choice of surgery/intervention and controversies thereof cannot be discussed. The decision however, is often informed by other factors such as valve morphology, presence or absence of left atrial clot, mixed valve disease and availability of expertise. The current study was undertaken to understand the profile of adult patients presenting for rheumatic mitral valve surgery and to open discussions and plan to further assess outcome in later studies. It is important to note that with the AHA/ACC guidelines "the focus is on medical practice in the United States, but guidelines developed in collaboration with other organizations may have a global impact" [10], as patient populations may differ.

Presentation with signs and symptoms associated with adverse outcome in this current study was similar in pattern to findings from Sliwa et al [3],in Insights from the Heart of Soweto Study, as it found that 66% of newly diagnosed rheumatic heart disease patients presented as Stage D on the AHA/ACC guidelines. Perhaps also indicating delay in surgical intervention as the population in Sliwa et al [3] is a feeder population into our institution.

Severe symptoms at initial diagnosis of rheumatic heart disease are a major predictor of mortality, thus, early presentation (before development of complications) could lead to better outcomes as pulmonary hypertension, arrhythmias and heart failure are associated with high mortality and morbidity. A further investigation looking at outcome measures and awaiting time from presentation to surgery is desirable.

Limitations

A great limitation of the study was that data on perioperative studies in patients with rheumatic heart disease was limited. Therefore, our study relied on epidemiological studies that were reviewing patients not scheduled for surgery. The extent of missing information on the echocardiographic reports reviewed made it difficult to risk stratify patients appropriately according to the AHA/ACC guidelines as clinical symptoms and signs alone are insufficient for this purpose. Furthermore, despite anecdotal information that the European guidelines were followed, such was not found on most echocardiographic reports reviewed. The study was a snapshot of a period in the preoperative stage and therefore gives no information on disease progression, postoperative outcomes or time to surgery parameters. Ethnicity in the current study was self- reported.

Summary

Most study patients were black adult females. Almost half presented in heart failure Echocardiographic data showed female study patients presented with moderate to severe disease as evidenced by left atrial size, pulmonary artery pressure, and valve area parameters in stenotic and regurgitant groups. Poor echocardiographic data record entry made it difficult to stratify a significant number of patients according to the AHA/ACC guideline recommendations. Much improvement is needed in this regard. Although the study did not look at outcomes, the echocardiographic and clinical parameters assessed, such as LVEF, LA size, PAP, arrhythmias and heart failure which are known to be associated with increased morbidity and mortality, indicate a possibility of poor outcome.

Acknowledgement

We acknowledge Dr HlamatsiMoutlana for his assistance with final editing. This research was done as partial fulfilment of a Master of Medicine degree.

Conflict of interest

We declare that we have no financial or personal relationship that may have inappropriately influenced us in writing this paper.

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Section 4: Appendices

Appendix 1: Human Research Ethics Committee (Medical) approval

R14/49 Dr Nolwazi Mokitimi

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M160106

NAME: (Principal Investigator)	Dr Nolwazi Mokitimi
DEPARTMENT:	Anaesthesiology Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	Profile of Adult Patients Presenting for Rheumatic Mitral Valve Surgery at an Academic Hospital
DATE CONSIDERED:	29/01/2015
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	Dr Juan Scribante and Dr Palesa Motshabi
APPROVED BY:	Professor P Cleaton-Jones,Chairperson, HREC (Medical)
DATE OF APPROVAL:	07/03/2016

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 10004, 10th floor, Senate House/2nd Floor, Phillip Tobias Building, Parktown, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**.

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix 2: Postgraduate approval

UNIVERSITY OF THE
WITWATERSRAND,
JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Ms Thokozile Nhlapo
E-mail: thokozile.nhlapo@wits.ac.za

03 March 2016
Person No: 0305708Y
PAG

Dr NF Mokitimi
123 Richmond Paris
Oakdene
2190
South Africa

Dear Dr Mokitimi

Master of Medicine: Approval of Title

We have pleasure in advising that your proposal entitled *Profile of adult patients presenting for rheumatic mitral valve surgery at an academic hospital* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

Appendix 3: Data collection sheet

ix F: Data collection sheet

		Preop vitals at echo			Preop clinical status at echo			Echo 1 & 2 parameters								
	Gender	HR	SBP	DBP	Asmth	CCF	IE	date	DML	LAS	MA	MPG	PAP	LVEF	LVES	ERO
					Y/N	Y/N	Y/N									

Section 5: Proposal

Profile of adult patients presenting for rheumatic mitral valve surgery at an academic hospital

NolwaziMokitimi

Student number: 0305708Y

Supervisor: PalesaMotshabi

5.1 Introduction

The emphasis of this descriptive study is on the profile of patients presenting for mitral valve surgery and their timeous referral for surgical intervention. A brief overview of the aetiology of rheumatic fever will be discussed as it is rather challenging to isolate rheumatic heart disease from rheumatic fever since the former is a complication of the latter. As stated by Joseph et al (1), "an in depth understanding of rheumatic fever leads to early diagnosis, treatment and prevention of progression to rheumatic heart disease''.

"Rheumatic fever is a multisystem disease which occurs as part of an autoimmune reaction from Group A Streptococcal (GAS) infection in genetically susceptible individuals" (1, 2). A

study done in urban south India found that of the 51 patients with rheumatic fever, 41.2% developed carditis (1). The concern around rheumatic carditis is that it can progress to rheumatic valvular heart disease which according to Nkomo et al (3) is the most predominant form of valvular heart disease on the African continent with prevalence of 5.7 per 1000 in sub-Saharan Africa compared to 0.3 per 1000 in economically developed countries. This discrepancy in burden of disease is largely attributed to developing countries being able to eradicate rheumatic fever and thus rheumatic heart disease via the implementation of successful health promotion initiatives coupled with superior access to health care (4).

Within the South African context, Mayosi (5) reported that the estimated incidence of heart failure due to rheumatic fever in Soweto ranges from 30 per 100 000 per year in individuals aged 14 to19 years to 53 per 100 000 per year in people 60 years or older. Rheumatic heart disease predominantly affects the mitral valve resulting in either isolated mitral stenosis or mitral regurgitation or mixed mitral valvular disease (6). However, the reason behind this mitral valve predominance has not yet been understood (1).

Complications related to valvular pathology carry significant morbidity and mortality (7-9). An Ethiopian study with 121 patients with rheumatic heart disease out 457 patients with cardiovascular disease showed that 70% (84) of patients enrolled in the study died from congestive cardiac failure as a consequence of rheumatic heart disease (7). Hence, a thorough understanding of this disease, its anticipated complications and relevant management is fundamental as it assists with optimisation of patients prior to surgery.

Valvular surgery is one of the common interventional therapeutic modalities for rheumatic valvular disease and until recently, mitral valve replacement was the only surgical option for patients with severe disease (10-12). Valve replacement, although warranted, is not devoid of complications and most patients who undergo the procedure require lifelong anticoagulation and constant monitoring of international normalised ratio (INR) levels (11, 13). This, coupled with poor access to adequate health care facilities in affected communities, leads to a high

rate of default in medical therapy post valve replacement and increased mortality secondary to systemic thrombo-embolic events (11).

Controversy exists on the efficacy of valve repair surgery in rheumatic mitral regurgitation disease as this procedure is associated with increased re-operation rates with one study reporting its re-operation rate as 27% (14). Current surgical trends now target valve repair where feasible as it offers several advantages over valve replacement including preservation of underlying valvular structure, preservation of left ventricular function and avoidance of long term anticoagulation (6, 11, 13).

To date the most preferred guidelines are those drafted in 2014 and revised in 2017 by the American Heart Association and American College of Cardiology (AHA-ACC) (15, 16). According to these guidelines specific indications for valvular surgery are: the presence or absence of symptoms, severity of disease, response of left and right ventricle to volume and pressure overload, effect on pulmonary or systemic circulation and changes in cardiac rhythm. The use of international guidelines within a South African context presents a challenge because vast socioeconomic differences exist between developed and developing countries. For instance, a study done in Nigeria reported that even with the existence of only two tertiary institutions established for open heart surgery, this procedure was still an intermittent undertaking due to scarcity of qualified personnel (resulting in reliance on periodic visits by a surgical team from the USA) and lack of funding (17).

A necessity for South African based guidelines clearly stating the stage of disease at which patients should be referred has been identified. Furthermore, guidelines would allow clinicians to stratify patients into those who require immediate surgical intervention versus those who can be closely monitored.

5.2 Problem statement

It has been noted that when patients for mitral valve replacement surgery are referred early in the course of the disease there is an improved clinical outcome postoperatively due to preservation of ventricular function (11). Late referral could be due to a myriad of socioeconomic factors. However, an additional compounding factor could be the lack of consensus regarding optimal timing of surgery amongst clinicians. Tribouilloy et al (18) noted that early surgical intervention is a reasonable consideration in asymptomatic patients booked for mitral regurgitation correction, however, clinicians are hesitant to recommend surgery in patients with no or minimal symptoms for fear of exposure to operative mortality and morbidity.

It is unclear whether the AHA/ACC Guidelines for Valvular Heart Disease are utilised for stratification of patients presenting for surgery at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH). Thus, this study undertakes to describe the profile of adult patients presenting for rheumatic mitral valve surgery at CMJAH.

5.3 Aim

The aim of this study is to describe the profile of adult patients presenting for rheumatic mitral valve surgery at the Cardiothoracic Unit at CMJAH.

5.4 Objectives

The objectives of this study are to:

- describe the demographic profile of the patients
- describe the preoperative cardio-vascular examination
- describe the preoperative liver and renal function
- describe relevant preoperative echo parameters
- stratify echo parameters and patients into early or late clinical presentation according to AHA/ACC guidelines

5.5 Research assumptions

The following definitions will be used in the study**:**

Adult: is a person 18 years and older

Mitral valve surgery: This will include mitral valve repair and mitral valve replacement.

Relevant echo parameters: echo 1 is the echo upon which decision to operate is made and echo 2 is the echo done immediately preoperation.

Records: cardiac clinic records from CMJAH. Other data accessed from the cardiothoracic database.

5.6 Demarcation of study field

This study will be conducted in the Cardiothoracic Unit of CMJAH within the Department of Anaesthesiology, affiliated to the Faculty of Health Sciences of the University of the Witwatersrand. Charlotte Maxeke Johannesburg Academic Hospital is a central hospital located in Parktown, Gauteng. It has a capacity of 1200 beds and 23 theatres which includes two cardiac (adult and paediatric) theatres and one thoracic theatre. It also has a dedicated cardiothoracic intensive care unit which admits both adult and paediatric patients. On average 23 000 cardiothoracic cases are done annually of which approximately 250 are adult cardiac cases.

5.7 Ethical considerations

Approval to conduct this study will be obtained from the Postgraduate Committee, the Human Research Ethics Committee (Medical) of the University of the Witwatersrand, the CEO of CMJAH, and the Medical Advisory Committee at CHBAH. (Appendix A and Appendix B). Approval to access stored perioperative records including cardiac clinic records and anaesthetic records will be requested from the gatekeepers of the databases from the Department of Cardiology and Cardiothoracic (Appendix C, Appendix D and Appendix E).

This will be a retrospective study and the name of the patients and doctors will not be recorded. A list with patient names and an allocated study number will be generated but filed separately. Only the supervisor and researcher will have access to the raw data. These measures will ensure anonymity and confidentiality. All collected data will be securely stored for six years following completion of the study. This study does not involve any drug or therapeutic management. It will be conducted by adhering to good clinical research practise as per the South African Good Clinical Practise Guidelines and The Declaration of Helsinki (19).

5.8 Research Methodology

5.8.1 Research design

According to De Vos(20): ‘’the research design is the blueprint or detailed plan of how a research study is to be conducted’’. The research design that will be used in this study is retrospective, contextual and descriptive. As stated by Brink et al (21): ‘’In a retrospective study, the data is collected on an outcome occurring in the present then linked retrospectively to determinants that occurred in the past. The researcher commences with an effect and works backwards to determine what was associated with this effect in the past’’. This approach is relevant to this study as data will be collected from relevant records.

This study will be contextual as it will only examine records originating from CMJAH. De Vos(20) describes contextual as: ‘’small-scale worlds’’ which include hospital wards, clinics etc. Descriptive designs may be used to identify problems with current practise, justify current practise, make judgements, develop a theory or determine what other professionals in similar situations are doing. Furthermore, these studies define the characteristics of the sample under investigation and the researcher does not manipulate any of the variables (21). This study will describe parameters as recorded on the cardiac clinic preoperative records and the anaesthetic record.

5.8.2 Study population

The study population will be the records of patients who presented for mitral valve surgery.

5.8.3 Study sample

Sample size

The sample size will be determined by the number of patients who have had mitral valve surgery from 1 January 2014 to 31 December 2015 at CMJAH. It is anticipated that this will be approximately 100 patients.

Sampling method

According to Burns and Grove (22) "In convenience sampling, subjects are included in the study because they happened to be at the right place at the right time.'' Endacott et al (23) explains consecutive sampling as a non- random method which uses the most readily accessible units in a study population. In this study the charts of every patient fulfilling the inclusion criteria who receive mitral valve surgery between 1 January 2014 and 31 December 2015 will be included in the study.

Inclusion and exclusion criteria

The inclusion criterion in this study is records of patients presenting for mitral valve surgery.

The exclusion criteria in this study are:

- records that are illegible
- records that are missing.

5.9 Data collection

A list of patient names that have undergone mitral valve surgery during the study period will be obtained from the Cardiothoracic Unit gatekeeper. Each patient will be allocated a study number, and this list will be filed separately.

The researcher will create a data collection sheet on Microsoft Excel® (Appendix C). The following parameters will be captured.

Section 1: demographics:

- age
- race
- gender
- mitral valve repair or replacement.

Section 2: cardio-vascular examination parameters at the time of the preoperative echo:

- heart rate
- blood pressure
- presence of arrhythmia
- presence of congestive cardiac failure
- presence of infective endocarditis.

Section 3: echo 1 and echo 2

- date
- dominant mitral lesion
- left atrial size
- mitral area
- mitral pressure gradient
- pulmonary arterial pressure
- left ventricular ejection fraction
- left ventricular end systolic dimension
- effective regurgitant orifice area.

Section 4: liver function and renal function:

- liver function
- urea and creatinine.

Records detailing demographic and clinical profile of patients in the preoperative phase are stored in the cardiac clinic at CMJAH and CHBAH. These are filed in alphabetical order according to the surnames of the patient. Records from these respective clinics will be obtained and reviewed from 1January 2014 to 31 December 2015. This will indicate the number of mitral valve repair operations that are performed on a monthly basis during this period i.e. the sample size.

Each entered record will be assigned a study number. The study number for each patient will be recorded on a Microsoft Excel spread sheet. Furthermore, the study number will be accompanied by the hospital number of the patient to allow easy identification of specific record but this will be recorded on a separate Microsoft Excel spread sheet. Only the assigned study numbers will be used for the purpose of data analysis.

A data collection sheet will be used to collect data from the records and enter it into a Microsoft Excel spread sheet. The data collection sheet will be divided into six sections: demographic profile, predisposing factors, preoperative clinical parameters, echo parameters from first presentation of patient at cardiac clinic and echo parameters of the patient pre-operation, preoperative liver function and urea and creatinine (See Appendix F). Data will be captured from the cardiac clinics at CMJAH and CHBAH respectively once permission has been received from the hospitals and the gatekeepers. The records will not be removed from these afore mentioned premises.

5.10 Data analysis

All recorded data will be captured and analysed on a Microsoft Excel® spread sheet. Descriptive statistics will be used to analyse the data. Categorical data will be summarised using frequencies and percentages. Means and standard deviations will be used for continuous variables that are normally distributed. For variables which are not normally distributed, medians and interquartile ranges will be used.

5.11 Significance of the study

Complications related to rheumatic valvular pathology carry significant morbidity and mortality. It has been noted that when patients for valvular surgery are referred in a timely manner, there is an improved clinical outcome post operatively due to preservation of ventricular function (11, 13, 18). Thus; a thorough understanding of this disease, its anticipated complications and relevant management is fundamental as it assists with optimisation of patients prior to surgery.

The results from this study will inform the Department of Anaesthesiology at which stage these patients present for surgery. These findings may also have an implication on the quality of life of the patients as they are less likely to suffer from incurred costs and complications associated with mitral valve replacement i.e. anti-coagulation therapy and anti-arrhythmia medication.

5.12 Validity and reliability of the study

Validity and reliability is part of the design of the study. As described by Botma et al (24), validity refers to: "The degree to which a measurement represents a true value. Reliability is represents the consistency of the measure achieved i.e. if a valid measuring instrument is used across the board, it should produce the same results''. Validity and reliability of this study will be ensured by the following:

- using an appropriate study design
- using appropriate data collection methods
- using a standardised data collection spread sheet
- a single researcher will collect data.

5.13 Potential limitations of the study

This will be a contextual study and therefore the results may not be generalisable to patients receiving mitral valve surgery in other settings. As this is a retrospective study, records with incomplete or illegible data will not be used and some records may be missing.

5.14 Project outline

5.14.1 Time frame

	2015		2016						
	Oct	Nov	Jan	Feb	March	April	May	Jun	July
Chapter 1-3									
Proposal									
Ethics approval									
Postgraduate approval									
Data collection									
Data analysis									
Chapter 4-5									
Submission									

5.14.2 Financial plan

The Department of Anaesthesiology will bear the cost of printing and paper for the proposal, ethics and postgraduate approvals for this study.

Description	**Price per item**	**Amount of items**	**Total**
Printing proposal	R1/page	±20 pages x 10	R200
Printing research report	R1/page	±50 pages x 4	R200
Binding final research report	R200	3	R600
Total			R1000

5.14 References

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