Rheumatic heart disease: The role of global cardiac surgery

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Abstract
Rheumatic heart disease (RHD) remains a neglected disease of poverty. While nearly eradicated in high-income countries due to timely detection and treatment of acute rheumatic fever, RHD remains highly prevalent in low- and middle-income countries (LMICs) and among indigenous and disenfranchised populations in high-income countries. As a result, over 30 million people in the world have RHD, of which approximately 300,000 die each year despite this being a preventable and treatable disease. In LMICs, such as in Latin America, sub-Saharan Africa, and Southeast Asia, access to cardiac surgical care for RHD remains limited, impacting countries’ population health and resulting economic growth. Humanitarian missions play a role in this context but can only make a difference in the long term if they succeed in training and establishing autonomous local surgical teams. This is particularly difficult because these populations are typically young and largely non-compliant to therapy, especially anticoagulation required by mechanical valve prostheses, while bioprostheses have unacceptably high degeneration rates, and valve repair requires considerable experience. Devoted and sustained leadership and local government and public health cooperation and support with the clinical medical and surgical sectors are absolutely essential. In this review, we describe historical developments in the global response to RHD with a focus on regional, international, and political commitments to address the global burden of RHD. We discuss the surgical and clinical considerations to properly manage surgical RHD patients and describe the logistical needs to strengthen cardiac centers caring for RHD patients worldwide.

KEYWORDS
Global cardiac surgery, global health, rheumatic heart disease

“It is difficult to say what is impossible, for the dream of yesterday is the hope of today, and the reality of tomorrow.”

Robert H Goddard
1 | BACKGROUND

The etiology, incidence, and prevalence of acute rheumatic fever (ARF) and rheumatic heart disease (RHD) have been well-researched, along with widespread recognition and support by the World Health Organization (WHO). Yet, there remain global challenges in eliminating both. ARF results from pharyngeal infection secondary to Group A β-hemolytic Streptococcus. The global incidence of RHD in 2015 was >300,000 with a prevalence of >30 million, an annual death rate of >300,000, and 11.5 million disability-adjusted life years.2

The evolution of ARF and RHD can be divided into three phases. Phase one is the communicable disease, followed by immunemediated disease, and finally noncommunicable disease, that is, RHD with the resultant inflammatory heart valve changes, as well as possible sequelae that include heart failure, atrial fibrillation, endocarditis, stroke, systemic thromboembolism, and pulmonary hypertension. While RHD is largely eradicated in high-income countries due to timely detection and treatment of ARF, it remains highly prevalent in low- and middle-income countries (LMICs).

The WHO has recognized the neglect of RHD in national health policies and budgets in LMICs, the paucity of available data regarding RHD efforts, poor access to care, and insufficient clinical understanding by primary and community health workers.3 Following the WHO Resolution on Rheumatic Fever and Rheumatic Heart Disease in May 2018, the World Heart Federation established a Rheumatic Heart Disease Taskforce. The current approaches to ARF and RHD include early identification and treatment of Group A β-hemolytic Streptococcus, screening and surveillance of RHD, and aggressive medical, interventional, and surgical treatment strategies.3

Here, we discuss the progress made in addressing the global burden of RHD, present clinical considerations, and stress opportunities moving forward.

1.1 | Timeline of ARF and RHD developments

In Brazil, almost 40,000 patients develop chronic RHD each year, a burden that is growing each year and considered to be vastly underestimated.4,5 Similar trends are observed in the Caribbean, where the annual RHD burden grows and affects a young population, yet surgical and interventional care availability cannot meet the needs of local populations.6 In Pacific Island States, up to eight percent of the adult population is estimated to have RHD.6 In sub-Saharan Africa, the epidemiology and demographics of ARF and RHD remain major challenges with a prevalence of 5.7 per 1,000 children aged 5-14 years, whereas endemic regions have adolescent rates up to 210 per 1000 people at 16 years.7,9 Although ARF and RHD are driven by a combination of immune, environmental, and genetic factors, high heritability has been shown.7 Moreover, the most virulent and rapidly progressive forms of ARF and RHD have been found in Africa.7,8 Thus, most high-level RHD initiatives have stemmed from or with respect to sub-Saharan Africa.

In 1981, the Pan-African Society of Cardiology (PASCAR) was initiated, and in 1985, during the 3rd PASCAR congress, the use of echocardiography to diagnose RHD was highlighted. However, nothing further occurred until 2005, when the Drakensberg Declaration, formulated at the PASCAR meeting in South Africa along with the WHF and the WHO Regional Office for Africa (WHO-AFRO), focused on ARF and RHD in Africa.10,11 This seminal meeting hosted the 1st All-Africa Workshop on Rheumatic Fever and Rheumatic Heart Disease that stressed both ARF and RHD as major public health problems in Africa. The declaration supported four areas of needed activity: (1) raising awareness, (2) increasing RHD information availability, (3) collaborative partnerships to change public policy, and (4) establishing national primary and secondary prevention programs for ARF. In 2014, at the 2nd All-Africa workshop on ARF and RHD in Livingstone, Zambia, the Mosi-o-Tunya Action plan of PASCAR was endorsed by the WHO-AFRO and called for the elimination of ARF and control of RHD in Africa.10

In 2015 and 2016, experts from across Africa and across the globe met in Addis Ababa, Ethiopia, to develop a roadmap on the eradication of RHD in Africa.12 The roadmap included the establishment of prospective RHD registries at sentinel sites to reduce RHD mortality by 25% by 2025. In 2017, the Cairo Accord summarized ten key recommendations that expanded on the need for comprehensive data collection, screening programs, preventive measures, and centers of excellence, as well as a specific focus on valve repair and the development of tissue-engineered valve substitutes.13,14 These developments culminated with the adoption of the WHO Resolution WHA71.14 on ARF and RHD in 2018.1

1.2 | Moving forward: Building capacity

In 2013, Zuhlke et al.15 pointed out that established cardiac programs in Africa perform an average of 100 RHD operations per year in public and private centers. In 2014, Yankah et al.16 reviewed the status of cardiac surgery in 16 African countries and estimated that the capacity of cardiac surgery in 2012 was estimated at 11.8 open-heart operations per million people in Africa. Yankah et al.16 have been a major force in developing the Pan-African Society for Cardiothoracic Surgery (PASCATS) in 2016.

In 2018, Zilla et al.17 pointed out the global paucity of qualified cardiothoracic surgeons, cardiothoracic surgery teams, and the maldistribution of cardiac care centers, especially in LMICs. Subsequently, they signed the Cape Town Declaration that focuses on two major aims: (1) the establishment of a coalition of representatives from cardiac surgery societies, industry, cardiology, and governments to support the development of cardiac care in LMICs, and (2) advocating for capacity-building of cardiac surgeons and other healthcare professionals involved in treating cardiac surgical patients at endorsed centers in LMICs. In 2019, this declaration led to the establishment of the Cardiothoracic Surgery Intersociety Alliance, focused on supporting pilot surgical centers in LMICs, especially for RHD surgery.18 In 2020, Vervoort et al.19 further summarized the
need for cardiac surgery in LMICs, highlighting the maldistribution of cardiac surgery worldwide and the need for ready access, affordability, increased capacity, quality care, long-term outcomes, and sustainability. Recently, the Latin American Association of Cardiac and Endovascular Surgery was established to foster a stronger regional network of cardiac surgeons in Latin America to share experiences, create capacity-building opportunities, and advance clinical care in the region. Given the high RHD burden that persists in much of Latin America, RHD prevention and treatment will likely make up an important priority.

2 | AREAS OF CONCERN

2.1 | Administrative, political, governmental, logistical issues

Success in establishing cardiac centers or hubs depends on what transpires locally. Local leadership and devoted shareholder participation are crucial for this success. It is imperative that donor stakeholders achieve local cooperation with host country governments, public health, and individual healthcare networks. A memorandum of understanding is crucial and necessary, which should focus on those elements that will increase the quality, quantity, transparency, sustainability, and success strategy. Local government and hospital administration support, along with medical staff leadership, and a committed and motivated faculty with requisite skills are required. Specific metrics or elements related to affordability, ready access, awareness, accountability, transparency, and success strategy must be established. In addition, it is essential that the development also address financial support, local laws and regulations, malpractice, trade/customs/tariffs, passports, visas, and medical license requirements.

2.2 | Human resources

Workforce disparities are vast around the world. For cardiac surgery, workforce density ranges from 0.12 adult cardiac surgeons and 0.08 pediatric cardiac surgeons per million population in sub-Saharan Africa to 11.12 adult cardiac surgeons and 2.08 pediatric cardiac surgeons in North America. PASCATS has recommended using a low threshold of 40 open-heart surgeries per 1 million population per year as a realistic and achievable target goal for most African programs. Education and training of the local cardiac surgeons and cardiac surgery teams are a major part of cardiac surgery program development and should be linked with the local host site and the donor site programs abroad. Accordingly, PASCATS identified three mentorship models: local resident and senior consultant, mission teams, and senior expatriate consultant—with centralization through regional referral centers as viable pathways to develop cardiac surgery centers in sub-Saharan Africa.

Regionalization optimizes the scarce workforce and resources and can fast-track the skillsets of trainee surgeons by increasing institutional volume. Some programs in Africa (e.g., South Africa, Kenya, and Ghana) already have active training programs, whereas some African surgeons seek training in programs abroad (e.g., Pakistan, India, and China). In South America, training programs availability is highly variable but generally available locally; nevertheless, many programs remain with vacancies providing opportunities to train aspiring cardiac surgeons from other countries. It remains clear, however, that more programs are needed to adequately supply LMICs, especially in sub-Saharan Africa, with the needed number of cardiac surgeons and other healthcare professionals.

2.3 | Financial needs

Financial support is crucial and must be secured from multiple sources that include public government, private insurance, combined public/private, charity, and self-pay. The Salam Centre for Cardiac Surgery in Khartoum, Sudan is a model of a bilateral partnership that offers free care to needing patients, treating patients from across the African continent, whereas similar models have been observed elsewhere in the world, such as the UNICAR Cardiac Surgery Hospital in Guatemala. Falase et al. estimated that mitral valve replacement with a bioprosthetic valve costs $11,200 in Nigeria. However, such detailed descriptions of the costs of open-heart surgery in LMICs remain scarce. Nevertheless, it is clear that the thousands of dollars required for surgery are not affordable for LMIC populations without insurance.

Conversely, financial risk protection is equally critical to ensure that patients can access surgical care and postoperative (e.g., anticoagulation) management. While South American countries have achieved considerable health coverage of their population, most LMICs lack such coverage, requiring substantial out-of-pocket payments by patients and their families. However, despite such health coverage, RHD remains a common problem in South America, especially in slums and among poorer populations, giving rise to a healthcare paradox.

2.4 | Infrastructure, equipment, disposables, devices, drugs, and logistics

For newly developing programs, various health system and infrastructure requirements are critical to ensure sustainability and safe and quality care. New centers in LMICs are often financially constrained given the high upfront costs associated with establishing new infrastructure and may consider the use of used equipment or lower-cost items from upper-middle-income countries with growing cardiac surgical industry, such as Brazil, India, and China. However, caution should be exerted when using nonreusable or expired disposables, especially as these are often sterilized and reused or donated, as they may pose safety and durability risks for patients.
Moreover, when purchasing equipment and devices, warranty costs should include maintenance and biomedical support; local distributors play a major role in these areas.

2.5 | Screening, registries, and databases

Supporting the public health and primary care sectors with the prevention, education, recognition, screening, diagnosis, treatment, and follow-up care is crucial. Widespread screening of children at risk for RHD is warranted using two-dimensional, continuous-wave, and color-Doppler echocardiography. This is necessary to develop a waiting list for those individuals with RHD who are present or future candidates for intervention or surgery. Additionally, creating a database and/or registry is essential to trace and document both outcomes and transparency.

The backlog of RHD patients requiring surgery remains a major challenge in terms of triaging suitable surgical candidates. The target risk groups for RHD include older children, adolescents, young women, and adults. Delayed presentation, recognition and referral, along with incorrect diagnosis, poor access, and availability of medical, interventional and surgical procedures remain a major challenge. However, ultimately, it must be emphasized that prevention and eradication of RHD remains the primary goal. The cost of RHD valve surgery ranges between US$10,000–25,000 in LMICs, which is the same amount of money needed to fund one full year of an RHD screening program. This is further illustrated by the favorable cost-effectiveness of RHD screening among socioeconomically disadvantaged children.

2.6 | Nongovernmental organizations

Dearani et al. outlined a global approach to the development and sustainability of cardiac surgery partnerships of donor NGOs and host centers and, although the focus is pediatric cardiac surgery, it can also be applied to adult cardiac surgery. There are about 80 such NGOs worldwide, although only 18% have programs and partnerships in Africa, whereas most are active in Latin America and Southeast Asia. Nevertheless, the role of foreign NGOs in LMICs has been significant and well-reported. Rwanda is one example where NGOs have made a successful effort to develop the foundations for a cardiac surgery program over a 16-year period that stresses prevention of RHD and sustainability of local services. Mocumbi, from Maputo, Mozambique, described a model partnership with NGOs from the UK, France, Portugal, and Switzerland, and a local NGO that addresses increasing clinical capacity, education/training, as well as partnering with the government that provides some financial support. From this effort, a local team was trained that is now performing all types of open-heart surgery autonomously, with excellent results. Long-term bilateral alliances or partnerships are now emerging with other visiting and local partners, thus increasing the continuity of care. Embedding of visiting individual surgeons or teams for 6 months to 1 year is another practical and cost-effective concept to consider. The success of NGOs would be enhanced if they cooperated with each other and established regional hubs, included prevention of RHD in their game plan, stressed capacity, transparency, and sustainability, and set a timetable for success.

3 | SURGERY FOR RHD

3.1 | Preoperative phase

Especially in these circumstances, the cardiac surgeon and team must have a thorough understanding of the pathology, pathophysiology, and comorbidities of RHD in children, adolescents, and adults. Weekly cardiac surgery team conferences should discuss the phases of care, that is, preoperative, operative, and postoperative. This should include the clinical history and physical examination, electrocardiogram, echocardiogram, chest x-ray, clinical lab testing, current drugs, risk factors, patient conference, blood availability, operative permission, and discussion of complications including possible death. Surgical treatment selection should include the absolute and relative indications, and contraindications, as well as the timing of surgery (i.e., emergency, urgent, or scheduled), and the selected surgical techniques available that include interventional, surgical repair, and mechanical or bioprosthetic valve replacement. In developing programs, operations on less complicated patients and associated risk factors are recommended. Achieving good results promotes confidence and goodwill for both the patient, family, the hospital, the cardiac surgery team, the local community, and the financial donors.

3.2 | Operative phase

The local junior cardiac surgeons must have proctor-supervised education and training, as well as the opportunity to perform an increasing number of cases to improve clinical skillsets and gain more confidence, judgment, responsibility, and both operative and intensive care experience. A major advance in surgery, including cardiac surgery, has been the operative headlamp camera. This has made it easier to view the performed operation on sight or from afar for trainees and the rest of the cardiac team.

The list of available operative RHD procedures includes interventional percutaneous balloon valvuloplasty for isolated rheumatic mitral stenosis, closed mitral commissurotomy, open mitral valve repair, and open mechanical or bioprosthetic valve replacement. Advanced procedures, like the Ross procedure, aortic valve repair, and minimally invasive approaches, are not as common in LMICs due to technical complexity and/or costs. The procedure choices remain a debated issue.
3.3 | Valve surgery

In LMICs, patients requiring surgery for RHD are, on average, 20–25 years old, whereas half require surgery before the age of 20 years. More than 60% of operated RHD cases in Africa currently receive a mechanical prosthetic valve and require long-term anticoagulation management and follow-up. In Latin America, similar trends are observed, although with variable outcomes. Notable local experiences are described as follows: Yangni-Angate et al. reported the cardiac surgery experience in Cote d’Ivoire between 1978 and 2013. The majority of the cases were CHD and RHD. The RHD average age was 26 years (4–69 years) with 60% having a functional NYHA class III or IV. Mechanical prosthetic valve replacement was the most common operation, and overall late mortality after surgery was 8%. In their experience, late presentation in the younger patients with advanced RHD precludes valve repair. In addition, bioprosthetic valve replacement developed early deterioration. However, mechanical valve replacement was compromised by anticoagulation management, and especially with the management of young pregnant women. Nwiloh et al. also favored mechanical valves in Nigeria, reporting a 10-year freedom rate from bleeding and thromboembolism of 70%. Child-bearing age women were at higher risk, as were poor patients with anticoagulation non-compliance. Edwin et al. from Ghana advocated mechanical valves for children (6–18 years). Over a 15-year period, there were 114 operations with eight deaths. Anticoagulation was well-tolerated.

The major complications related to the mechanical prosthetic device include valve thrombosis, thromboembolism, and bleeding which are primarily anticoagulation-related problems. In younger patients, prosthesis-patient mismatch may also become an issue. On the other hand, bioprosthetic mitral prosthetic valves undergo early degeneration and may require early reoperation, especially in younger patients and fertile women. They are also more expensive than a mechanical valve. Finally, prosthetic valve endocarditis, be it mechanical or bioprosthetic, occurs in 3–4% within 5 years after index surgery.

For the above reasons, mitral valve repair is desirable. But repair is more complex, as the RHD valves get worse with time, and requires more experience, confidence, and advanced skills to achieve a favorable operative result. For younger patients, there are a number of surgical repair techniques available.

Antunes et al. with a long experience in RHD surgery in South Africa, Mozambique, and Portugal, emphasize that rheumatic mitral valve disease remains a challenge with regard to surgical repair versus valve replacement. Part of this is related to younger patients (20–30 years) with a persistent rheumatic inflammatory process that continues beyond surgery, and requires antibiotic prophylaxis following surgery and continued lifelong. Several pathological and clinical RHD areas need to be understood, notably that rheumatic mitral regurgitation is caused by elongated anterior leaflet chordae that causes prolapse of the leaflet, which is usually small and retracted, as is the posterior leaflet, and that the annulus is dilated in most cases, along with commissural fusion.

Yacoub et al. also point out that mechanical and bioprosthetic aortic valves are not ideal for younger RHD patients. Aortic valve repair and the Ross procedure are not readily performed or available in Africa and require increased surgical expertise and experience. Mocumbi cautions that the operations described are palliative at best. This is especially true for the younger group and fertile females. Finally, Antunes et al. highlight that tricuspid valve regurgitation is frequently found in association with rheumatic mitral valve disease. It is most commonly secondary to pulmonary hypertension and is treated with tricuspid repair. Rheumatic tricuspid stenosis is rare and treated with a bioprosthesis if indicated. It must be noted that prosthetic valve endocarditis, be it mechanical or bioprosthetic, occurs in up to 5% of patients in the first years after surgery.

Studies comparing long-term results between mechanical valves, bioprosthetic valves, and valve repair remain limited. Moorthy et al. have reported significantly higher survival in children with RHD who underwent repair versus replacement at follow-up for up to 22 years in Malaysia. Similar experiences have been reported by Fu et al. in China at a median follow-up of four and 5 years. However, these results are not always corroborated in different settings, where comparable results are occasionally observed, emphasizing the need for further investigation and careful patient selection.

Overall, the choice of operative technique and devices must consider age, sex, cost of the device, and postoperative drugs, especially anticoagulants, long-term access to medical follow-up, and cardiac surgeons’ confidence and experience.

3.4 | Postoperative phase and outcomes

Early and late postoperative complications include death, bleeding, stroke, endocarditis, valve thrombosis, and structural valve deterioration. Long-term outcomes and follow-up require an organized system. The patient and family should have an operative report and discharge summary. However, RHD in younger individuals remains a notable challenge. They will still require lifetime secondary monthly penicillin therapy following surgery and may require future reoperation. In patients with mechanical prostheses, lifelong anticoagulation requires routine and regular monitoring of international normalized ratio (INR) levels. Due to limited long-term durability, valve repairs and bioprosthetic valves require close follow-up and echocardiographic surveillance.

4 | PREGNANCY AND RHD

Pregnant women in LMICs with RHD, and especially with isolated mitral valve stenosis, are a high-risk group due to the potential for increased maternal and fetal mortality. Pregnant or nonpregnant fertile women with isolated mitral stenosis requiring intervention, have the option of percutaneous balloon valvuloplasty, if available, or closed mitral commissurotomy. If open surgery is required, the
options include open repair and mechanical or bioprosthetic valve replacement. Management of anticoagulation in women with RHD and mechanical heart valves can be compromised by the risk of valve thrombosis, stroke, and adverse fetal outcomes, whereas bioprosthetic valves do not require the use of anticoagulation, but are compromised by a higher incidence of structural bioprosthetic deterioration and failure rates that occur in 50% of childbearing women at 10 years.\textsuperscript{56}

5 | RESEARCH AND RHD

There has been a steady increase in cardiovascular disease research in Africa, of which RHD has been a major focus.\textsuperscript{57} The PASCaR and other African institutions have promoted research of cardiovascular epidemiological data, along with establishing a number of RHD registries.\textsuperscript{58} These registries were developed to improve clinical care and epidemiological surveillance, as reported by Longenecker et al.\textsuperscript{59} in Uganda (Table 1). More broadly, cardiac surgery research and publications in Africa have increased over the past 20 years.\textsuperscript{57} Sir Magdi Yacoub has especially been a major supporter of cardiac research in Africa at the "bench, bush, and bedside levels."\textsuperscript{60}

Nevertheless, compared to when RHD was still prevalent in high-income countries, research interests in RHD have declined across the globe, including in Latin America.\textsuperscript{61} For example, while death rates per year due to malaria are only three times greater than in RHD, research funding for malaria is over 500 times as much as for RHD.\textsuperscript{62}

6 | CONCLUSION

Moving forward, the focus should be to continue to decrease the incidence, prevalence, backlog, and surgical waiting lists of RHD patients. This will require local government and public health cooperation and support with the local clinical medical and surgical sectors. Building increasing capacity and quality of cardiac surgery in LMICs requires devoted and sustained leadership, public (government), and private (corporate) participation, and a well-trained and confident experienced cardiac team that is supported and trusted by the patients they serve.

TABLE 1  Rheumatic heart disease (RHD) categories

| Category                                      | Description                                                                 |
|-----------------------------------------------|-----------------------------------------------------------------------------|
| Acute rheumatic fever                         | Defined according to applicable Jones Criteria at the time of diagnosis but without evidence of chronic valvular heart disease |
| Clinical RHD                                  | Defined as patients presenting to clinical attention with symptoms or signs (i.e., murmur) and echocardiographic findings compatible with RHD |
| Definite latent RHD                           | Identified through echocardiographic screening studies                       |
| Borderline latent RHD                         | Identified through echocardiographic screening studies                       |

CONFLICT OF INTERESTS

The are no conflict of interests to declare.

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How to cite this article: Vervoort D, Antunes MJ, Pezzella AT. Rheumatic heart disease: The role of global cardiac surgery. J Card Surg. 2021;36:2857-2864. https://doi.org/10.1111/jocs.15597