Priorities in Cardiac Surgery for Rheumatic Heart Disease

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ABSTRACT

This review outlines a philosophy of surgical cardiac care for rheumatic heart disease, which has evolved over the past 2 decades, in the young in the Oceania region. Topics covered include the optimal timing of surgery, recommended strategies for mitral and aortic valve disease, and the importance of the team approach to these patients. There is a global priority for more cardiac surgeons to become skilled in repair of the rheumatic mitral valve. Surgeons operating on patients from remote regions with RHD are encouraged to audit outcomes and help these communities develop their health services to optimize continued RHD care.

As has been highlighted in other reports in this issue of *Global Heart,* 80% of the world's countries still have rheumatic fever and its important long-term sequel, rheumatic heart disease (RHD). Those with severe RHD that do not have access to cardiac surgery will die. The mean age of death in some regions of Africa is as young as 25 years [1] and for the indigenous Aborigine population of Australia, 22 years [2].

The particular challenge for a cardiac surgeon dealing with severe RHD is to repair as many valves as possible rather than replace them. The populations that suffer from rheumatic fever, and the affected families within those ethnic populations, have the least resources, lowest levels of education, and worst access to health care. There is good evidence to demonstrate how poorly people in these circumstances do with mechanical valve insertion and anticoagulation [3]. Unfortunately, rheumatic disease damages the valve leaflets and subchordal apparatus, making repair difficult in comparison to other mitral and aortic lesions. The surgeon and the cardiology unit need a team approach to achieve good outcomes. It is not just about what happens in the operating theater, but it also involves good triage, timely intervention, echocardiographic detailed assessment, outreach clinics, nursing input for family education, post-operative case audit, and more.

This review outlines some of the approaches we have used in Starship Hospital Auckland for the New Zealand and Pacific Island pediatric rheumatic population over the past 2 decades to improve the outcomes of these children and teenagers.

EVIDENCE FOR THE SURVIVAL VALUE OF MITRAL VALVE REPAIR

Antunes [4] in 1990 in South Africa was among the first to publish the dangers of using mechanical or bioprosthetic valves in the mitral position in the rheumatic population, both adult and pediatric. This included both mortality rate per patient-year and the mortality rate of reoperation (Table 1) [4].

In 1999, a similar message was reported from New Zealand in a study of women of child-bearing age requiring valve surgery, the commonest indication being rheumatic. The outcome for those who had mechanical valve replacements was significantly worse than those with repairs or bioprostheses, many of which were aortic homografts (Fig. 1) [5]. Pacific Islanders and the indigenous Māori women with mechanical valves had over 6 to 8 times higher mortality than other ethnic groups did (Table 2).

Our unit has recently reported a survival advantage following mitral valve (MV) repair compared with mitral valve replacement (MVR) for the young with RHD [6]. This retrospective study of 81 patients showed that from the time of patient discharge, the long-term durability of mitral repair was equal to that of MVR. Despite the need for early reoperation in 11% who underwent repair, freedom from reoperation was equal in the 2 groups for the duration of the follow-up. Analysis of those with MVR reveals that 50% of the patients with MVR had a significant hemorrhagic, thrombotic, or embolic event within 11 years, and rates of endocarditis were also high. There was 100% freedom from embolic, thrombotic, or hemorrhagic events in those with MV repairs in this and other studies in the young [7–10].

For adults, despite the absence of a randomized comparison between the results of valve replacement and repair, it is widely accepted that valve repair is the optimal surgical treatment in patients with severe mitral regurgitation (MR) [11–13]. Compared with valve replacement, MV repair has a lower perioperative mortality, better preservation of post-operative left ventricular function, improved survival, and lower long-term morbidity [13]. In adults who are in sinus rhythm, repair avoids the need for anticoagulation and risks of thromboembolism with prosthetic valves, makes pregnancy safe, allows for continued participation in contact sports such as rugby, and avoids the sudden deterioration that can occur with bioprosthetic valves in the mitral position.

These data challenge the assumption that if there is funding for 1 operation only, it is best to replace a valve rather than repair it. This needs to be confirmed with more studies specifically in these populations that are vulnerable to medication shortages, lack of monitoring, endocarditis,

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TABLE 1. Incidence of late mortality

	Total %/ Patient-Year	Valve-Related %/ Patient-Year	Ratio* %
Bioprosthetic MVR	7.4	4.2	56.8
Mechanical MVR	5.7	2.5	43.1
Mitral valve repair	2.6	1.0	38.5

MVR, mitral valve replacement.
*Valve-related/total.
Adapted, with permission, Antunes [4].

TABLE 2. Relative risk of death in women with bioprosthetic or mechanical valves

	RR (95% CI)
Mechanical valve	2.17 (0.78–5.88)
Age at valve replacement, yrs	1.00 (1.00–1.01)
Number of concurrent valves	0.86 (0.39–1.92)
Years of operation	1.04 (0.93–1.16)
Maori	8.45 (1.82–39.3)
Pacific Islander	6.54 (1.16–36.7)
Pregnancy	0.38 (0.17–0.84)
Valve site*	0.50 (0.11–2.39)

*Aortic or tricuspid versus mitral.
Adapted, with permission, from North et al. [5].

and medically unsupervised pregnancies, usually in early adulthood. Following cardiac surgery, the challenge is to achieve good follow-up by optimizing outreach clinics, rheumatic fever registries, and nursing networks and linking with the local staff who deliver secondary prophylaxis.

MITRAL VALVE REGURGITATION

Indications for cardiac surgery

There are many published guidelines addressing indications for cardiac surgery for adult patients [11,13,14] that are largely based on symptoms and echocardiographic assessment of left ventricular size and function (Table 3). Cardiologists, physicians, and pediatricians should use these guidelines to refer RHD cases in a timely fashion for surgery whether or not the patient is in a high-income or low-income country setting. Patients with chronic RHD who develop cardiac failure and impaired ventricular function may be too late for effective cardiac surgery due to failure of the myocardium to recover normal function. Physicians working in remote settings historically refer the sickest patients, but it may be appropriate for the cardiac unit to decline such patients when ventricular function is irrevocably impaired. A decision to not offer surgery may be more humane after assessment in the local setting rather than after the patient has traveled to an overseas cardiac unit.

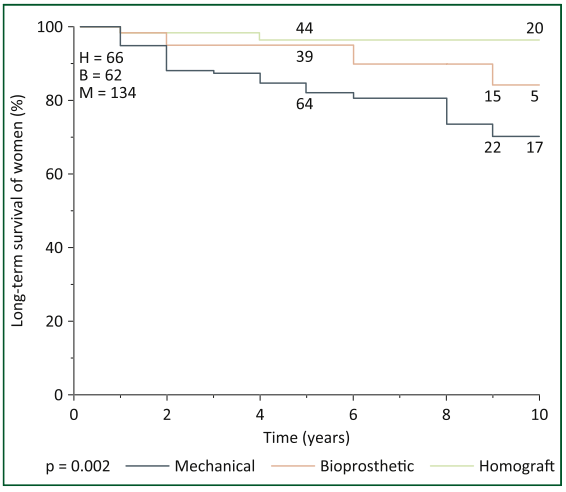

FIGURE 1. Long-term survival of women according to type of valve replacement. Among 232 women, 35 had >1 valve state included. Test of difference in survival between 3 valve types: p = 0.002. Test of difference between mechanical and bioprosthetic valve types: p = 0.04. B, bioprosthetic; H, homograft; and M, mechanical. Adapted, with permission, from North et al. [5].

MITRAL VALVE REPAIR

This complex topic is beyond the scope of this review, but we have included several tables and figures outlining the

TABLE 3. Class I indications for mitral valve surgery in adults

1	MV surgery is recommended for the symptomatic patient with acute severe MR. (Level of Evidence: B)
2	MV surgery is beneficial for patients with chronic severe MR and NYHA functional class II, III, or IV symptoms in the absence of severe LV dysfunction (severe LV dysfunction is defined as ejection fraction <0.30) and/or end-systolic dimension >55 mm. (Level of Evidence: B)
3	MV surgery is beneficial for asymptomatic patients with chronic severe MR and mild to moderate LV dysfunction, ejection fraction 0.30 to 0.60, and/or end-systolic dimension ≥40 mm. (Level of Evidence: B)
4	MV repair is recommended over MV replacement in the majority of patients with severe chronic MR who require surgery, and patients should be referred to surgical centers experienced in MV repair. (Level of Evidence: C)

LV, left ventricular; MR, mitral regurgitation; MV, mitral valve; NYHA, New York Heart Association.

important pathologic features and the repair techniques in current use (Tables 4 and 5, Fig. 2). Cardiac surgeons in different countries describe variable patterns of rheumatic involvement in their patients, and each surgeon needs to adapt techniques for these regional variations of RHD. The more cases seen, the more obvious these patterns become and the more practiced the surgeon can become. It is sensible, at least at first, for a surgeon at each unit to achieve expertise before training another, given the technical difficulty of achieving good durable repairs.

A successful repair strategy starts with an understanding of the patient's status: acute or chronic; degree of dilation of the left ventricle; body-mass index; and involvement of valves other than mitral. Following that, the echocardiograph needs to be reviewed with the cardiologist and it would be even better if this were repeated by a transesophageal study as the operation starts. The hallmark of the competent heart surgeon is the aim to repair rheumatic MV and to create repairs with good durability.

The echocardiographic detail of the site and severity of excessive leaflet motion (prolapse), valve deficiency, chordal thickening, and retraction is better than the information gained by direct inspection. Detailed echocardiography demonstrated by the cardiologist enables the strategy of repair to be planned in detail before the operation starts and saves cross-clamp time.

Each segment of anterior and posterior leaflet should be analyzed for prolapse and retraction, with an estimate of the misalignment of the leaflets (slight, moderate, severe). This allows the surgeon to plan how much to shorten cords by allowing for the fact that the annuloplasty will tend to aggravate the prolapse of the anterior leaflet particularly, so mild prolapse cannot be ignored. The pre-operative echo gives a better assessment of the valve mechanics than direct inspection does, so little time needs to be wasted on examining the valve once the cross clamp is on.

Replacement is a faster, easier job than repair, and there can be pressure placed on the surgeon to give up if the rest of the operative team has not been prepared for the longer cross-clamp time that repair entails. Surgeons should make sure these cases are scheduled with time available, including the potential for a second bypass run if the first echo off bypass shows that the valve needs more work. In our series, a long cross-clamp time is not a risk factor for mortality or prolonged intensive care stay.

Transesophageal echocardiography at the end of the procedure is used to decide whether the repair is adequate,

TABLE 4. Rheumatic mitral valve pathology

Softening of chordae, elongation, rupture
Prolapse of part or all of 1 or both leaflets (often opposite)
Dilation of annulus, loses oval shape
Leaflet thickening and fibrosis causing restriction of motion
Long-term evolution toward stenosis in adulthood, independent of penicillin

TABLE 5. Mitral repair: surgical tactics

Shorten primary chordae of anterior leaflet (different degrees according to echocardiogram)
Peel thickened layers off posterior leaflet
Resect small triangle from posterior leaflet (tends to be redundant when annuloplasty is done)
Divide or extend posterior chordae that are retracting leaflet—usually intermediate, not primary
Insert complete annuloplasty ring to restore oval shape
Close scallops in anterior or posterior leaflets to correct localized areas of prolapse
Add Gore-Tex chords, translocate chords, use partial rings in young children (not so durable)

and decisions are based on many factors beyond the degree of residual regurgitation and stenosis: the age of the patient; the expected lifestyle of the patient, including plan for pregnancy; the realistic chance of good anticoagulation control; and the surgeon's knowledge as to whether there is any further improvement that can be made. Mild-moderate valve regurgitation is often moderate by the time the patient is discharged. We use the left atrial pressure, measure the valve gradient and detail the anatomy of the residual valve regurgitation by transesophageal echocardiography. Technical considerations include: Are the chords overcorrected? Does the annuloplasty ring need downsizing? Is there still localized leaflet prolapse? The final decision whether to revise the repair, accept it, or replace the valve is made jointly by the surgeons and cardiologists.

Analysis of our own data has demonstrated some patient features that are risk factors for failure of mitral repair. Valves with mixed mitral stenosis and regurgitation (Fig. 3) or calcified valves in the older adult may also be difficult to

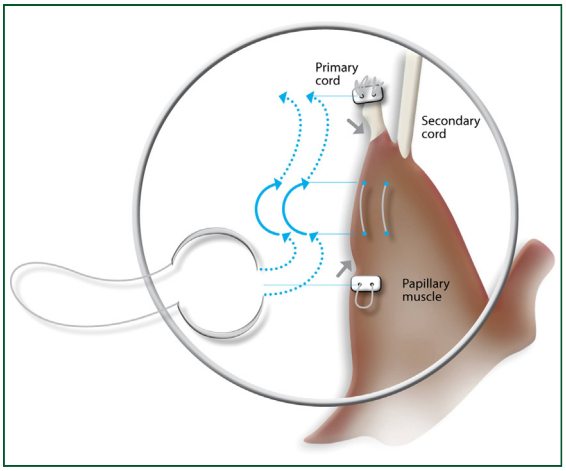

FIGURE 2. Chordal shortening technique using pledgeted 4-0 ti-cron mattress suture. The degree of shortening is honed by adjusting the distance from start of suture to the base of the chord.

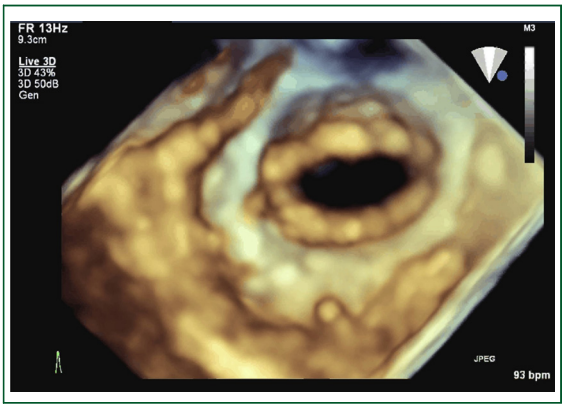

FIGURE 3. Three-dimensional transesophageal echocardiographic appearance of a severely thickened, immobile rheumatic mitral valve ("fish-mouth" appearance) with mixed stenosis and regurgitation.

repair. Repair can look acceptable on the operating table, but patients may return early with severe mitral stenosis. Kaplan-Meier survival curves and reoperation curves are shown for a personal series of 135 mitral rheumatic operations from 1996 to 2010, and they show that repair can be achieved in 90% of first-comers (Figs. 4 and 5).

Multivariate analysis from our unit's published retrospective series showed that a left ventricular end-systolic dimension of Z-score greater than 5 was the most important determinant for mortality [6]. The hazard for the myocardium not to recover appears especially high for those with combined mitral and aortic disease [15]. The clinical implication of this data is that referring physicians in remote regions need to refer early, rather than when the children are severely symptomatic, often with very dilated left ventricles. We have experience of children referred with massively enlarged left ventricles, and surgery will not improve their life expectancy.

The probability of a durable valve repair is of crucial importance. Until recently, durability of adult rheumatic mitral repairs were not as good as nonrheumatic mitral repairs [16], but there are several contemporary series from experienced repair centers with high mitral repair rates and low operative mortality [8,17–22].

ALTERNATIVES TO MITRAL REPAIR— MITRAL VALVE REPLACEMENT

As a junior surgeon, I once replaced a mitral bioprosthesis in a 12-year-old in whom it had been inserted only 2 years before. Figure 6 demonstrates how quickly it had calcified in this Polynesian boy. This case illustrates how mitral bioprostheses in the young are hazardous with frequent life-threatening early failures [4,6]. Their only place is in carefully supervised women intending to have pregnancies within the next few years to avoid a mechanical valve with warfarin.

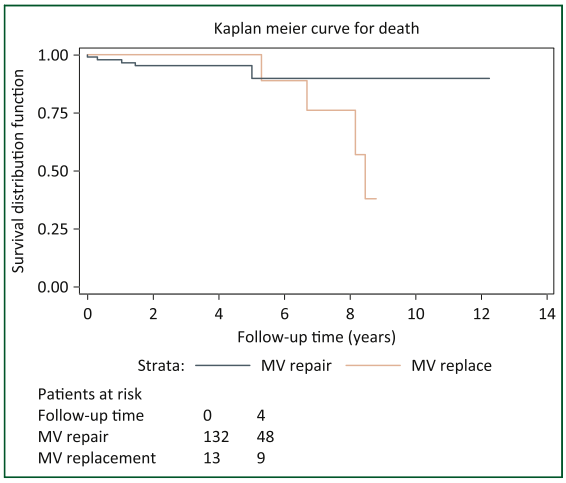

FIGURE 4. MV repair versus MV replacement survival.

For MV repair:

By 4 years, survival is 95%.

By 8 years, survival is 90%.

By 12 years, survival is 90%.

For MV replacement:

By 4 years, survival is 100%.

By 8 years, survival is 76%.

By 12 years, survival is 38%.

MV, mitral valve.

A better alternative for the unrepairable mitral is the On-X mechanical valve (On-X Life Technologies, Austin,

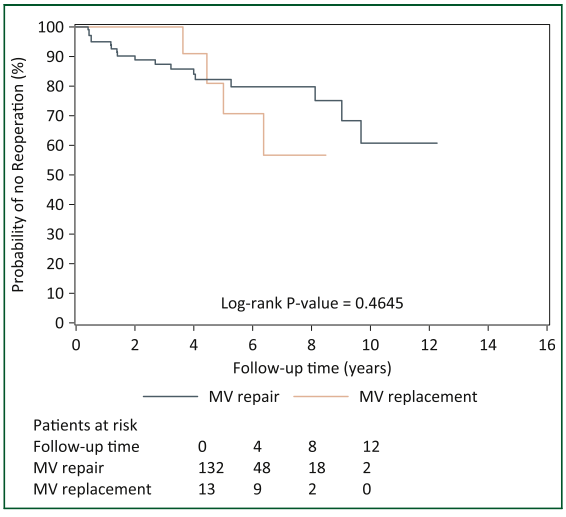

FIGURE 5. MV repair versus MV replacement freedom from reoperation.

For MV repair:

By 4 years, probability is 84%.

By 8 years, probability is 80%.

By 12 years, probability is 61%.

For MV replacement:

By 4 years, probability is 91%.

By 8 years, probability is 57%.

FIGURE 6. Calcified mitral bioprosthesis (porcine stented valve) inserted 24 months prior to removal.

Texas), a new-generation bileaflet prosthetic valve with design features that, compared with other mechanical valves, help reduce the risk of thrombosis. After an initial promising study from South Africa in patients who failed to take adequate warfarin [3], there is now increasing evidence of freedom from embolic or thrombotic events, including a U.S. Food and Drug Administration—approved study of large numbers of patients in the United States (PROACT [Prospective Randomized On-X Anticoagulation Clinical Trial]; U.S. registration NCT00291525) [23]. Although these are mostly nonrheumatic patients, the study confirms that in carefully audited populations, bleeding is closely linked to warfarin target levels of international normalized ratio. We need to study dose warfarin regimens in mitral patients to reduce the bleeding complication rates without increasing thrombotic valve complications.

We have a dedicated international normalized ratio program in our unit using nurse practitioners to manage warfarin in the community [24]. Surgeons inserting these valves have a responsibility to advocate for optimized systems for management of anticoagulation that will ensure patient safety. Otherwise, it is conceivable that a mechanical valve operation will shorten, not lengthen the life of some of these children and teenagers.

MITRAL STENOSIS

The treatment of choice of pure mitral stenosis is balloon mitral valvuloplasty [11,13,14], which usually is as effective as surgery and the hospital stay is short. However, in some regions of the world, closed surgical mitral valvotomy may be less expensive than transferring to a country with a cardiac catheterization laboratory. Open surgical mitral valvuloplasty allows surgical debridement of the valve and is more efficacious than balloon mitral valvuloplasty when there is significant calcification of the valve or there is mixed mitral stenosis and regurgitation.

AORTIC VALVE SURGERY

Pathologic features and repair tactics for aortic rheumatic disease are shown in Tables 6 and 7.

Rheumatic aortic regurgitation is common in our mitral cohort, but it is often only mild and therefore left alone. When there is moderate aortic regurgitation in conjunction with severe MR, echocardiographic analyses may show single leaflet prolapse, which is amenable to repair. Single leaflet prolapse produces an eccentrically directed jet on echo and can be corrected by shortening the free edge of the affected leaflet and slightly reducing the annulus using subcommisural annuloplasty sutures. However, if the aortic jet is directly back through the left ventricular outflow tract and all leaflets are at equal level, then the mechanism is pure leaflet retraction and repair is more difficult unless leaflet tissue is added. Our unit has not had a policy of adding tissue, as we have excellent results from homograft aortic valve insertion [25] and prefer to use that if the valve regurgitation is significant enough to warrant it (moderate to severe or severe aortic regurgitation). The homografts provide 8 to 12 years of anticoagulant-free childhood and seem to allow some annular growth so that a reasonable-sized mechanical valve can then be inserted in adulthood.

Alternatively, the On-X aortic valve is proving a durable alternative, with the promise of potentially avoiding warfarin in patients with good left ventricular function and normal rhythm. A current On-X trial. PROACT, aims to show that aspirin and clopidogrel are as safe as warfarin. We have been wary of using the Ross procedure in rheumatic patients given the degree of aortic annular dilation present and the difficulty of detecting whether the pulmonary has been damaged by the disease process [26].

OPTIMIZING PRE-OPERATIVE CARDIAC CARE

In our unit, we spend a lot of time discussing individual cases to optimize the timing of their operations. Acute patients are admitted and settled with diuretics and urgent operations are rare: only indicated if the patient is in

TABLE 6. Pathology—aortic

Dilation of annulus
Softening of leaflets, lose elasticity
Cup shape becomes like a saucer
Free edge becomes longer than attached edge, so prolapse occurs
Free edge retracts/rolls back leaving a triangle-shaped deficit centrally
Leaflets thicken, develop parallel ridges or folds
Dilation of annulus

TABLE 7. Aortic repair tactics

Subcommisural annuloplasty sutures
Shortening of free edge of prolapsing leaflet—resect or plicate
Reduce size of noncoronary sinus
Peel fibrous layers or ridges off very thick areas of leaflet—allows leaflet to extend
Extend 1 or more leaflets with autologous or animal tissue
Check opening is adequate with calibrator
Subcommisural annuloplasty sutures

pulmonary edema; does not settle with intravenous diuretics; and requires mechanical ventilation. Occasionally they present as acute pneumonia and on a ventilator, when the flail leaflet and severe MR is diagnosed on echo [27]. If this is the child's first episode of acute rheumatic fever, the noncompliant left atrium cannot dilate and pulmonary venous hypertension causes pulmonary edema, which sometimes has a remarkably unilateral appearance on the chest radiograph and is often misdiagnosed as pneumonia. Mitral repair is achievable in most of these acute cases.

Left ventricular dimensions are followed closely as well as the erythrocyte sedimentation rate, because some patients have such torrential MR, or mitral and aortic regurgitation, that the dimensions steadily increase to a level that requires early intervention. Data following up some of our combined valve disease patients suggest that the left ventricular dimensions do not return to the normal range at 6 to 12 months after surgery in those with severe pre-operative dilation [15].

Early surgery raises concerns: 1) that overall complication rates will be higher due to the presence of systemic inflammation; and 2) that the durability of repair will be affected due to the softness of the tissues that are being sutured. The technique of repair needs to be adjusted to allow for this softening and to allow for the remodeling process as the disease settles, which may shrink leaflets and shorten chordae. There is a balance between the need to protect the ventricle and the need for stronger tissues on which to operate. We often compromise and operate at 2 or 3 months into the course of the illness when the C-reactive protein has normalized and the ESR is settling.

DELIVERY OF CARE

There is a single pediatric cardiothoracic unit in New Zealand, with its population of 4.5 million, delivering pediatric and congenital cardiac care throughout the country. We perform around 350 bypasses per year with a mortality rate of 1.5% to 2.5% for the last decade. The service is publicly funded and free to New Zealand citizens. We accept children from Pacific Island countries of our region for assessment and operation who are able to get funding from a variety of charitable sources, but we are careful to triage these children so that costs of care do not exhaust the funds. Up to 50% of our rheumatic patients operated on each year are from overseas.

All members of our cardiology team are involved in outreach clinics, both around New Zealand and in many of the Pacific nations. The number of clinics has increased steadily, and these visits have also allowed links to develop between local doctors and our service. In the 2 decades since these links began, the triage of patients and their management in the community has improved markedly. In recent years, a 3-year follow-up project in New Zealand and the Pacific Island countries has allowed us to track patients after surgery and collect data on their survival and outcomes [6]. This valuable feedback then assists us in future decision making so that operations can be tailored to the population we are serving.

One of our concerns is the increasing number of teams visiting third-world countries to perform operations for a short period and then leaving. In many countries, these visits provide the only chance of surgery for children. They also provide valuable experience for those performing the operations and are a great team-building exercise. Some simpler congenital repairs are suitable for that situation, and we know the patients are likely to do well even if there is no further medical follow-up. However, the difficulty of achieving a rheumatic valve repair in the type of theater set up for such a visit leads many surgeons to perform mechanical valve replacements. Unless there is an adequate health structure developed and supported for those patients, they may not do well. It is the responsibility of the operating surgeon and team to audit the outcomes of this type of surgery rather than assuming the outcomes will be similar to those in a first-world situation. In our opinion, most rheumatic valve repair surgery is complex and requires machinery and skills not easily set up for a week in a third-world country.

The most worthwhile effort, particularly in the poorest countries, is probably not in replacing valves in sick children but in the less glamorous development of rheumatic disease registries, penicillin delivery, and cardiac care clinics with links to more-developed services. This is harder to sell to charities raising money, but surgeons involved in overseas visits or operating on these patients also advocate for continued development of medical cardiac programs for RHD and prevention in those countries they support. Some small countries may never have their own surgical pediatric cardiac service, but the local doctors and nurses can be educated and supported over a number of years to a level that will vastly improve the long-term outcomes for those with RHD.

SUMMARY

The main global priority for rheumatic heart surgery is to increase the number of surgeons able to perform durable repairs on mitral and aortic valves and to resort less often to the easier option of replacement. This can only be achieved by a multifactorial approach that includes careful workup of

TABLE 8. Gems or golden rules: Rheumatic heart surgery

1.	Rheumatic patients are at high risk for complications of anticoagulation. Mitral repair, even with some residual MS or MR, has a significant survival advantage over replacement.
2.	Mitral bioprostheses may calcify very rapidly (and silently) in children and young adults.
3.	Mitral repair is difficult and demands time and dedication, so concentrate the experience into the hands of 1 surgeon if possible.
4.	Exact echocardiogram details of each segment of a valve allows accurate planning for the operation and saves surgical time.
5.	Using a complete mitral annuloplasty ring restores the oval shape and makes the most of the leaflet area available.
6.	Achieving a durable repair in a valve during an acute episode of rheumatic fever is difficult. If possible, an operation is best avoided until the ESR settles.
7.	Encourage local pediatricians and hospital cardiologists to communicate closely to optimize timing of operation. Survival and repair durability are best if surgery is not left until the left ventricle is grossly dilated.
8.	Get involved in obtaining follow-up data, especially on patients from other countries, to learn what works and what is needed for the setting to which the patient will return.

ESR, erythrocyte sedimentation rate; MR, mitral regurgitation; MS, mitral stenosis.

patients, high-quality echocardiography, referral to a unit with a dedicated surgeon experienced in rheumatic repair, time allowed by the operative team, and development of the service in the local community to continue optimal medical care. Above all, RHD is an area that requires very good communication between the surgeon and the cardiologist, sometimes under stressful circumstances (leaky repair!), but with a great sense of achievement for the patient when a damaged valve is salvaged.

Our Unit's golden rules for rheumatic heart surgery are listed in Tables 8.

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