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Review

Tetralogy of Fallot in Low- and Middle-Income Countries

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ABSTRACT

Low- and middle-incomes countries (LMICs) have limited resources for the diagnosis and treatment of congenital heart diseases such as tetralogy of Fallot. This is in part due to lack of infrastructures, financial means, and expertise. As a result, patients undergo surgery much later than in high-income countries. This delay in treatment results in right ventricular dysfunction, cardiac arrhythmias, and poor psychomotor development—complications that are all related to chronic hypoxia. There are limited data and a few small studies of patients treated for tetralogy of Fallot in LMICs, and, therefore, the aim of this review is to analyse and summarize the surgical outcomes of this LMIC population.

RÉSUMÉ

Dans les pays à revenu faible ou intermédiaire (PRFI), les ressources sont limitées pour diagnostiquer et prendre en charge les cardiopathies congénitales comme la tétralogie de Fallot. Cette situation est attribuable en partie au manque d'infrastructures, de moyens financiers et d'expertise. Les patients subissent donc une correction chirurgicale beaucoup plus tard que dans les pays à revenu élevé. Les délais de traitement peuvent entraîner une dysfonction ventriculaire droite, une arythmie cardiaque et des problèmes de développement psychomoteur : des complications toutes liées à l'hypoxie chronique. Il existe des données limitées et quelques études de faible envergure sur des patients traités pour une tétralogie de Fallot dans les PRFI. L'objectif du présent article de synthèse est donc d'analyser et de résumer les issues des interventions chirurgicales dans les PRFI pour cette population.

Tetralogy of Fallot (ToF) is the most frequent cause of cyanotic heart disease, accounting for 3%-5% of all congenital heart diseases (CHDs), and has an incidence of 0.28-0.34 per 1000 live births.[1,2] The overall incidence of ToF has remained quite stable over the last 15-20 years. Nevertheless, there are significant differences across the globe in terms of incidence, with Asia reporting the highest incidence and Africa the lowest.[3] Several factors may explain these observations. Notably, health care access differs significantly from one region to another. Furthermore, genetic, environmental, and economic factors may also have a role in disease development and incidence.

Tremendous progress has been made in the surgical management of patients with ToF, enabling over 85% of these patients to reach adulthood.[4] Surgical correction of ToF is generally performed in patients in high-income countries (HICs) between 3 and 11 months of age with excellent perioperative results and a hospital mortality rate of approximately 1% in the current era.[5,6] The benefits of early management include better long-term cardiac function and enhanced development of pulmonary arteries due to restoration of blood flow.[7] Early correction also avoids exposing the right ventricle (RV) to systemic pressures for an extended period, reducing the risks of RV failure and cardiac arrythmias.[8] Ultimately, this approach also has positive impacts on kidney function, cognitive development, and psychosocial outcomes.[9,10] Unfortunately, in low- and middle-income countries (LMICs; defined by the World Bank as a gross national income per capita of <CAD$4465), many obstacles may come in the way of early ToF correction.[11] Delayed diagnosis due to the scarcity of congenital cardiology experts, lack of infrastructures, and lack of financial resources are

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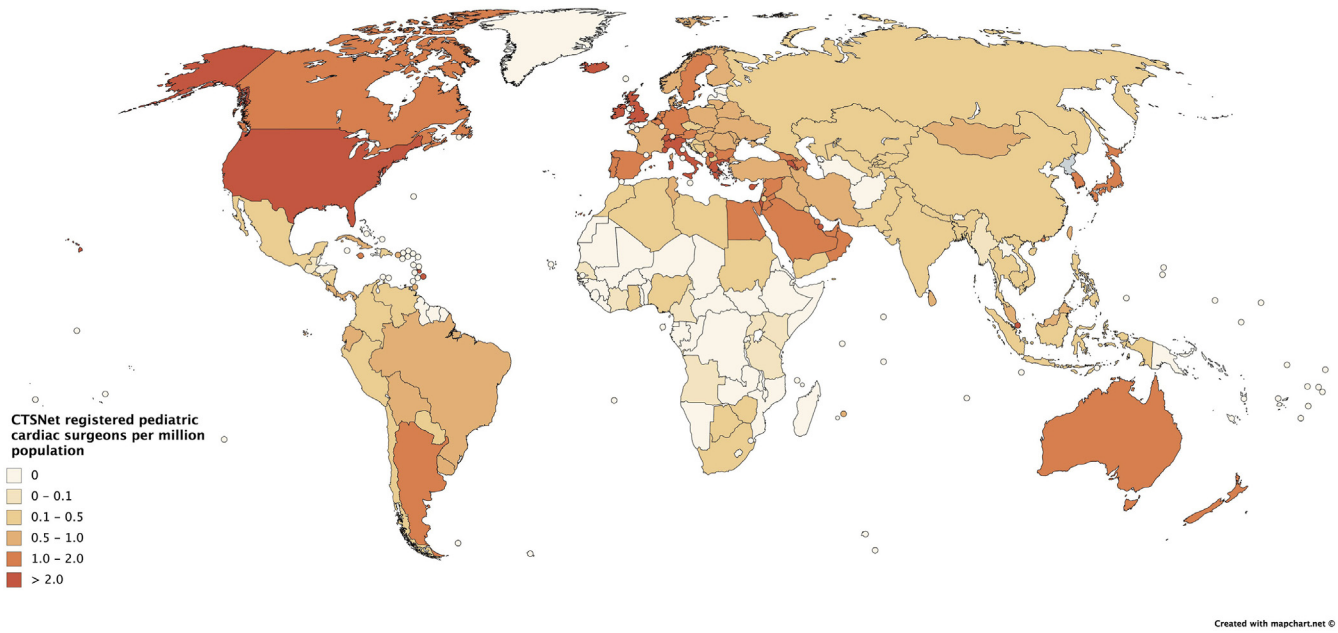

Figure 1. Paediatric cardiac surgeons per million population registered with the Cardiothoracic Surgery Network (CTSNet) in August 2017 (n = 3858). From Vervoort et al.[14]

among the hurdles found in most of these countries.[12,13] Globally, a recent study using the Cardiothoracic Surgery Network data estimated that many countries, particularly in Africa, do not have a paediatric cardiac surgery centre despite that their populations sometimes exceed 70 million.[14] There are also major disparities in the distribution of congenital heart surgeons, with a rate of 0.08 surgeons per million vs 2.08 surgeons per million inhabitants in sub-Saharan Africa and in North America, respectively (Fig. 1). As a result, there are approximately 2.5 million people in need of cardiac surgery in low-income countries.[14] Although the number of deaths due to CHD decreased worldwide by around 34% between 1990 and 2017, there were still >260,000 deaths caused by CHD in 2017.[15] Furthermore, there are great disparities depending on the country's income and sociodemographic category. The sociodemographic index (SDI) is a composite indicator of a country's development status. It includes the total fertility rate under the age of 25, the mean education of those aged 15 and older, and the distributed income per capita. This measure developed by the Global Burden of Disease Study group is strongly correlated with health outcomes.[16] In low-SDI countries, the age-standardized mortality per 100,000 individuals decreased by 10.6%, whereas high-SDI countries experienced a 61.7% decrease in CHD-related deaths over the same period.

In this article, we will discuss the differences in clinical presentation and surgical management focusing on patients with ToF between LMICs and HICs, highlight the experience of congenital surgeons working in Sub-Saharan Africa, review current surgical results, and discuss potential avenues for improvement.

Burden of Disease

The limited literature data available can be divided into: (1) reports from patients operated on in LMIC surgical centres, (2) reports from LMIC patients operated on in HIC centres, and (3) reports from LMIC multicentre collaborative databases. A summary of the current literature is presented in Table 1. Patients from LMICs exhibited a higher number of symptoms due to prolonged hypoxic exposure. Indeed, more than half of the patients experienced dyspnea, syncope, chest pain, and seizures.[12,13,17,21–23] In HICs, patients are typically operated pre-emptively between 3 and 11 months or as an emergency after the appearance of ToF spells. In contrast, the International Quality Improvement Collaborative for Congenital Heart Disease (IQIC), a study regrouping >2000 patients from 32 centres in 20 LMICs, found that 54% of patients operated on for ToF were over 1 year old. However, this study only included patients younger than 18 years, which may underestimate the true mean age of ToF operation in LMICs.[19] Indeed, the limited data from LMICs suggest that the mean age of repair is instead between 4.7 and 21 years. Based on our humanitarian experience (with Ste-Justine au Coeur du Monde for almost 20 years with missions in Morocco, Senegal, Ethiopia, South Africa, and Egypt), these metrics are more representative of the reality in LMICs.[13,17,21,22]

This delay in treatment has several impacts. Benbrik et al.[13] conducted a study in France where they compared patients operated on for ToF in France with patients from LMICs who were operated on in the same department (through the nonprofit organizations La Chaîne de l'Espoir or Mécénat Chirurgie Cardiaque). The patients from LMICs were operated on significantly later and had a significantly lower body mass index *Z*-score at the time of the intervention than the French patients.[13] Furthermore, patients from LMICs had a lower oxygenation rate and a higher haematocrit than French patients due to sustained hypoxia.

Chronic cyanosis also leads to the development of systemic collaterals in addition to pre-existing major aortopulmonary collateral arteries (MAPCAs). This complication affects over

Table 1. Summary of the current literature on ToF surgical treatment in LMICs

References	Patient population	Country of origin	Main outcomes
Bisoi et al.[17]	• 284 patients • Mean age at the time of surgery: mean 19.4 ± 2.5 years	India	• 10-year survival = 82.88% ± 3.80% • Risk of early mortality: preoperative NYHA class, high postoperative PRV/LV ratio (>0.5), and RVOT gradient >50 mm Hg
Tchoumi et al.[12]	• 22 patients • Mean age at the time of surgery: 9.18 ± 6.5 years	Cameroon	• Perioperative morbidity = 9% • No late death • RVOT gradient = 29 ± 1.5 mm Hg in the acute postsurgical period
Diop et al.[18]	• 40 patients • Mean age at the time of surgery: 7 years (range: 11 months to 18 years)	Patients operated during humanitarian missions in Senegal	• Perioperative mortality = 22.5% • There is an urgent need to operate these patients earlier and ensure better post-operative care
Benbrik et al.[13]	• 47 patients from LMICs and 90 French patients • Mean age at the time of surgery: 57.6 ± 38.4 months in patients from LMICs vs 8.3 ± 9.1 months in French patients ($P < 0.0001$)	Patients referred to the CHU of Nantes through La Chaîne de L'Espoir or Mécénat Chirurgie Cardiaque	• Patients from LMICs present with more comorbidities and are usually more symptomatic • No difference between patients from LMICs and French patients in terms of postoperative mortality and morbidity
Sandoval et al.[19]	• 2164 patients from 32 centres • Mean age at the time of surgery: 1 year (range: 0.7-2.2 years)	20 different LMICs • Pakistan • India • Columbia • Russia • China • Afghanistan • Dominican Republic • Brazil • Argentina • Costa Rica • Malaysia • Ukraine • Mexico • Peru • Serbia • Belarus • Vietnam • Uganda • Guatemala • Bangladesh	• Overall mortality: 3.6% • Age at the time of repair was not identified as a predictor of mortality • Low weight (<5th percentile) and low saturation were both associated with increased risk of mortality
Heinisch et al. (2019)[20]	• 25 patients • Mean age at the time of surgery: 70.8 ± 42 months	Patients from LMICs referred to the Inselspital Bern through a humanitarian programme	• Perioperative mortality = 0% • Late correction of ToF can be safely performed in older children with excellent early postoperative results and low mortality • A valve-sparing correction should be considered for those patients
Bamigboye-Taiwo et al.[21]	• 72 patients • Mean age at the time of surgery: 4.7 ± 4.0 years	Nigeria	• Less than half of the patients had corrective surgery • Average age at the time of corrective surgery was 5.13 years (range: 1.1-17 years) • The current health care infrastructure in Nigeria is unable to cope with the care and treatment of this large number of children with CHD
Bhushan et al.[22]	• 45 patients • Median age at the time of surgery: 21 years (range: 15-44 years)	India	• 42% of patients with long-standing hypoxia have significant MAPCAs • All these patients should have preoperative catheterization
Souaga et al.[23]	• 19 patients • Mean age at the time of surgery: 7.4 ± 4.52 years	Ivory Coast	• Perioperative mortality = 10.5% mortality • Perioperative morbidity = 17.6% of right heart failure, low cardiac output = 11.8%, and transient complete AV block = 5.9%

AV, atrioventricular; CHD, congenital heart disease; CHU, Centre Hospitalier Universitaire; LMIC, low- and middle-income country; MAPCA, major aortopulmonary collateral artery; NYHA, New York Heart Association; PRV/LV, right ventricular-left ventricular systolic pressure ratio; RVOT, right ventricular outflow tract; ToF, tetralogy of Fallot.

40% of patients in LMICs, which is 20 times higher than the rate reported in HICs.[22,24] MAPCAs increase blood flow in the pulmonary arteries and may lead to massive haemoptysis due to bronchial erosion.[25] Other complications seen in older patients with uncorrected ToF include cerebral abscesses or strokes, which can be caused by blood hyperviscosity due to prolonged hypoxia. Preoperative cerebral complications occur in as many as 20% of cases in patients with a delayed diagnosis, while being rare in HICs.[17,21,22]

Delayed ToF repair is also associated with electrophysiological complications. In fact, the rate of ventricular arrhythmia increases with the age of repair. In a multicentre study, the rate of ventricular arrhythmia was 20% in patients who had undergone surgery between the ages of 8 and 15 years, and it increased to 58% in patients operated on after the age of 16 years.[26] This complication is a result of the sustained elevated pressure within the RV, as well as the formation of ventricular fibrosis—a process that results in microreentry circuits.

Perspective From a Sub-Saharan Centre

Despite a growing economy, most sub-Saharan countries are faced with several important sanitary challenges. Neonatal mortality rates in this region remain among the highest in the world, with an average of 27 deaths per 1000 live births.[27] In a recent report, the World Health Organization highlighted several infrastructural and human resource challenges that may contribute to these figures. Notably, these countries have an average of 2 doctors, 11 trained nurses and midwives, and 9 hospital beds per 10,000 habitants.[28] The situation in congenital cardiac surgery is even more daunting. Up until recently, few countries had centres that were equipped to perform congenital cardiac surgery (eg, Senegal, Ghana, or Ivory Coast).[21]

The Fann National University Center in Senegal initiated its thoracic and cardiovascular surgery programme in 2004. At the beginning, the local team still relied on humanitarian missions for the care of certain patients, including a number of patients with ToF. Between 2004 and 2012, 40 patients with ToF or pulmonary atresia were operated on by collaborators (visiting teams).[18] The mean age at the time of surgery was 7 years, ranging from 11 months to 18 years. The average time on the surgical waiting list was 20 months. A complete repair was performed in 36 patients (90%), and 4 patients (10%) received a Blalock-Taussig-Thomas (BTT) shunt. There was no operative mortality. However, the 30-day mortality remained high at almost 23% in patients who underwent a complete repair. There was no 30-day mortality in patients who received a BTT shunt.

Between 2017 and 2021, a total of 316 patients with congenital cardiac malformations were operated at the Fann National University Center. The local team performed 224 of these surgeries (71%), and the remaining were performed by collaborators. The overall 30-day mortality over this period was 4.8% (unpublished data). Thanks to the support of collaborators, and also the implication of local leaders, the results of congenital cardiac surgery in Senegal have greatly improved over the last 2 decades.

Surgical Planning

There are a number to surgical treatment strategies for ToF. Like other congenital defects, the type of repair needs to be tailored to the patient's anatomy, in addition to taking into account local resources and expertise. A comprehensive review of the technical aspects of ToF repair is beyond the scope of this review. An overview of the surgical aspects of ToF repair in patients from LMICs is presented in Table 2. Still, several characteristics may present in patients operated in LMICs and need to be considered at the time of operation. These characteristics include (but not limited to):

- Previous palliative operations
- Presence of MAPCAs
- Higher incidence of endocarditis
- Presence of preoperative brain abscess or stroke
- High incidence of arrhythmias
- Coagulation anomalies (associated with polyglobulia and chronic hypoxia)

The preoperative assessment of older patients with ToF should include specific examinations aimed at identifying the potential complications of chronic hypoxia and RV hypertrophy. For example, blood hyperviscosity can result from prolonged hypoxia, leading to brain abscesses and strokes. To assess the risks associated with these complications, such as haemorrhagic remodelling due to extracorporeal circulation, further investigations are essential.[29] This includes computed tomography scan, cardiac catheterization, and biological blood tests for coagulation abnormalities and infectious foci. The presence of MAPCAs must be documented preoperatively using either a computed tomography scan or cardiac catheterization. Although more invasive, catheterization has the advantage of being both diagnostic and therapeutic as it allows concomitant occlusion of MAPCAs. The search for inducible ventricular arrhythmia seems essential with an in-depth electrophysiological study to establish the arrhythmia load. Targeted therapy can then be performed to limit or eradicate

Table 2. Overview of the surgical aspect of ToF repair in LMICs

Surgical approach	Special considerations
Staged procedure	• Often reserved for young patients with severe RVOT obstruction • Most often performed with a BTT shunt • Relatively high risk of thrombosis associated with a BTT shunt[24–26] • Transannular patch is another option • All palliative surgeries require close patient follow-up, which may be difficult in certain settings • Ductal and infundibular stenting may be considered in the absence of surgical expertise, but these procedures are associated with high rates of dysrhythmias and intimal hyperplasia[27]
Complete repair	• Most patients over the age of 3 months are candidate for complete repair[22] • In patients with MAPCAs, higher pump flow and lower target body temperature (28°C-30°C) will be required • A vent is often necessary to keep the field dry in older patients with significant collateral flow • Complete repair may be performed either with a transpulmonary-transatrial or a transventricular technique

BTT, Blalock-Taussig-Thomas; LMIC, low- and middle-income country; MAPCA, major aortopulmonary collateral artery; RVOT, right ventricular outflow tract; ToF, tetralogy of Fallot.

arrhythmias.[30] In our opinion, BTT shunts should be avoided, given their perilous management and high rate of perioperative complications and in-hospital mortality. Furthermore, the age of most patients operated in LMICs makes them eligible for a complete repair, an approach that has long been promoted in HICs.[31] As in HICs, preservation of the pulmonary valve should be a priority whenever possible. A pulmonary valve−sparing approach with wide commissurotomies may help in achieving this objective in patients with pulmonary valve hypoplasia. Finally, a perioperative and long-term complications should be monitored as closely as possible.

Surgical Outcomes

There are few reports looking at the perioperative and long-term outcome of patients with ToF operated in LMICs (Table 1). In these studies, in-hospital mortality ranges from 1.9% to 10.2%.[17,32] In contrast, an analysis from the Society of Thoracic Surgeons (STS) database showed a perioperative mortality of 1.3%.[5] This difference can be explained by the higher number of comorbidities due to chronic hypoxia and the presence of MAPCAs in older patients. Other studies have shown a similar trend and have identified older age at the time of surgery as a risk factor for postoperative mortality.[6] Nevertheless, the multicentre IQIC study, which included a majority of patient surgically addressed after the age of 1 year, did not find any association between the age at the time of repair and perioperative mortality. This study did however identify other "frailty" markers associated with an increased risk of mortality and infection, such as a weight below the 5th percentile at the time of the surgery.[19] The IQIC study also analysed the outcomes of the various surgical techniques. The BTT shunt appears to have the worst perioperative results with an in-hospital mortality of 8.0% (n = 16/200). In contrast, a recent STS analysis found a 3.4% (27 of 796) mortality in patients who underwent palliation (approximately 70% of these patients received a BTT shunt).[33] However, there are important caveats when comparing these outcomes. The patients included in the IQIC study were significantly older, with almost half of BTT shunts performed in children aged between 2 and 17 years. In contrast, more than 85% of the BTT shunts were performed before 3 months of age in the STS study. These significant differences preclude any comparison between these cohorts of patients. Furthermore, the benefits of a BTT shunt in a child older than 2 years are debatable.

As previously mentioned, patients from LMICs may present with specific complications of chronic hypoxia, such as the presence of multiple systemic collaterals, and MAPCAs. In this regard, several studies have demonstrated the benefit of preoperative MAPCA obliteration.[34] Historically, these collateral vessels were addressed surgically. However, these procedures were associated with longer aortic clamping and cardiopulmonary bypass times. Significant blood loss that could lead to low cardiac output and difficult ventilatory weaning due to pulmonary oedema were also among the possible complications.[35,36] Given these drawbacks, MAPCAs are now mostly addressed preoperatively by interventional cardiologists.[34] In a study from India, Bhushan et al.[22] reported that preoperative management of MAPCAs was necessary in >40% of patients. Nevertheless, this study reported an in-hospital mortality of 2%, which is comparable with most HICs.[22]

Finally, late ToF correction has been associated with high rates of postoperative pleural effusions. In fact, this complication affects up to 60% of patients.[21] This is due to several factors, including postoperative RV failure and impaired LV filling.[37,38] Reperfusion oedema may also lead to this complication. To prevent the formation of pleural effusion, early extubation (to reduce intrathoracic pressure), aggressive diuretic treatment, and careful postoperative vascular filling are recommended.

Discussion and Future Perspectives

Many LMICs still rely on humanitarian missions (such as Sainte-Justine au Coeur du monde, Surgeon of Hope, and Heart to Heart) to ensure the provision of congenital cardiac surgery. Although these missions help in treating patients who would otherwise not have access to surgical care, we strongly believe that there should be a broader objective. Ultimately, the aim is to develop centres in LMICs that can independently treat these patients and offer adequate follow-up. This is the premise on which "Sainte-Justine au Coeur du monde" was created. However, there are often several barriers that limit the implantation of such programmes. Table 3 summarizes some of the frequent challenges encountered in LMICs and offers ways that these can be addressed. Although this article focuses of the care of patients with ToF, the recommendations included in this section may be applied to programmes seeking to treat a variety of CHDs. This is why international databases such as the World Database for Pediatric and Congenital Heart Surgery are so useful in providing information and creating a support network between HIC and LMIC centres. This mutual support is essential, both technically (ie, surgical, anaesthesia-intensive care, nursing, and perfusion) and logistically, in terms of service management and postoperative follow-up.

With regards to the treatment of ToF, specific aspects require considerations. Early diagnosis is crucial to avoid the potential consequences of long-term hypoxia. In this regard, simple solutions, such as the distribution of pulse oximeters to primary care physicians and local medical teams, may improve the detection of ToF.[39] The preoperative assessment of patients with ToF may also be facilitated by the access to an interventional cardiology lab. Not only is this valuable during the preoperative workup, but transcatheter intervention, such as MAPCA occlusion, can ease future surgical treatment. Ensuring adequate access to surgical valve prostheses is also paramount for the treatment of older patients with ToF. This requires planning with local institutions, establishing local chain supply, and engaging industries in LMICs. Similarly, postoperative care may require the administration of medications such as anticoagulants, nitric oxide, and/or inotropes. In addition, regular postoperative follow-up is essential to detect long-term complications, including ventricular arrhythmias, and to assess the need for right ventricular outflow tract reoperation. Currently, there is a scarcity of resources to ensure long-term follow-up of patients and treat adult patients with congenital conditions. Ensuring that local centres have access to these resources will allow improvement in surgical outcomes. Finally, helping new programmes in gathering data and supporting research efforts in LMICs will allow policy changes, bring awareness to the specific local needs, and improve the treatment of patients with ToF in LMICs.

Table 3. Challenges in establishing congenital cardiac surgery centres in LMICs

Challenges	Potential solutions
Delay in diagnosis	• Providing education to referring physicians • Favouring the distribution of low-cost and high-yield screening equipment such as pulse oximetry • Engaging medical professionals (eg, physicians, nurses, and midwives) in assessing their patients for the presence of heart murmurs
Difficulties reaching treatment centres	• Leveraging the possibilities of telemedicine • Working with local communities to optimize transportation to surgical centres
Lengthy wait time	• Advocating for the prioritization of CHD care • Regionalization of surgical waitlist • Developing local electronic health records
Financial constraints	• Advocating for improvements in public health care coverage in LMICs • Facilitating contacts between philanthropic societies and congenital cardiac surgery centres • Providing local data showing the cost-effectiveness of congenital cardiac surgery in reducing disability-adjusted life years
Lack of medical professional	• Providing ongoing medical education during humanitarian missions • Offering financial support to gain additional expertise (eg, cardiac surgery fellowship). • Ensuring the training of dedicated cardiac surgery teams, rather than training specific groups of professionals • Help in establishing local leaders who will oversee the development and expansion of local programmes • Establishing simulation training in local centres
Lack of surgical resources	• Assist the local teams in making scale economies • Providing surgical equipment during humanitarian missions • Engaging industries in local supply chain • Donation of equipment from MEDC
Difficulties in ensuring adequate follow-up	• Help in establishing treatment and follow-up plans with referring physicians • Providing patients with comprehensive information regarding their condition • Leverage the possibilities of virtual follow-up.

CHD, congenital heart disease; HICs, high income countries; LMIC, low- and middle-income country.

Conclusions

There are still huge differences in the clinical presentation and treatment of patients with ToF between LMICs and HICs. Recent articles have looked into this issue.[14,40] Several recommendations are directly applicable to patients with ToF from LMICs. Indeed, there is an urgent need to train more surgeons with expertise in the care of paediatric patients from LMICs. Furthermore, training local staff to establish cardiac centres in LMICs also needs to be addressed. Ensuring safe patient transportation (either to local cardiac centre or in HIC centres) is also a priority. Ultimately, more economic resources need to be devoted to this challenge, keeping in mind that approximately 80% of treatable cardiac diseases exist in LMICs.[41] This metric is even more astonishing when we consider that cardiac surgery can add several decades of life in paediatric patients. Real awareness is needed to ensure optimal care for these patients.

Ethics Statement

The research reported in this review has adhered to ethical guidelines.

Patient Consent

The authors confirm that patient consent is not applicable to this article.

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References

1. Murphy JG, Gersh BJ, Mair DD, et al. Long-term outcome in patients undergoing surgical repair of tetralogy of Fallot. *N Engl J Med*. 1993;329:593–599.
2. Van der Linde D, Konings EEM, Slager MA, et al. Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. *J Am Coll Cardiol*. 2011;58:2241–2247.
3. Liu Y, Chen S, Zühlke L, et al. Global birth prevalence of congenital heart defects 1970-2017: updated systematic review and meta-analysis of 260 studies. *Int J Epidemiol*. 2019;48:455–463.
4. Blais S, Marelli A, Vanasse A, et al. The 30-year outcomes of tetralogy of Fallot according to native anatomy and genetic conditions. *Can J Cardiol*. 2021;37:877–886.
5. Al Habib HF, Jacobs JP, Mavroudis C, et al. Contemporary patterns of management of tetralogy of Fallot: data from the Society of Thoracic Surgeons database. *Ann Thorac Surg*. 2010;90:813–820.
6. Van Arsdell GS, Maharaj GS, Tom J, et al. What is the optimal age for repair of tetralogy of Fallot? *Circulation*. 2000;102(suppl 3):III123–I129.
7. Tamesberger MI, Lechner E, Mair R, et al. Early primary repair of tetralogy of Fallot in neonates and infants less than four months of age. *Ann Thorac Surg*. 2008;86:1928–1935.
8. Cohen MI, Khairy P, Zeppenfeld K, et al. Preventing arrhythmic death in patients with tetralogy of Fallot: JACC review topic of the week. *J Am Coll Cardiol*. 2021;77:761–771.
9. Derby CD, Pizarro C. Routine primary repair of tetralogy of Fallot in the neonate. *Expert Rev Cardiovasc Ther*. 2005;3:857–863.
10. Inatomi J, Matsuoka K, Fujimaru R, Nakagawa A, Iijima K. Mechanisms of development and progression of cyanotic nephropathy. *Pediatr Nephrol*. 2006;21:1440–1445.

11. Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet*. 2012;380:2224–2260.

12. Tchoumi JCT, Ambassa JC, Giamberti A, et al. Late surgical treatment of tetralogy of Fallot. *Cardiovasc J Afr*. 2011;22:179–181.

13. Benbrik N, Romefort B, Le L, et al. Late repair of tetralogy of Fallot during childhood in patients from developing countries. *Eur J Cardiothorac Surg*. 2015;47:e113–e117.

14. Vervoort D, Meuris B, Meyns B, Verbrugghe P. Global cardiac surgery: access to cardiac surgical care around the world. *J Thorac Cardiovasc Surg*. 2020;159:987–996.e6.

15. GBD 2017 Congenital Heart Disease Collaborators. Global, regional, and national burden of congenital heart disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Child Adolesc Health*. 2020;4:185–200.

16. GBD 2017 Mortality Collaborators. Global, regional, and national age-sex-specific mortality and life expectancy, 1950-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet*. 2018;392:1684–1735.

17. Bisoi AK, Santosh J, Murala K, et al. Tetralogy of Fallot in teenagers and adults: surgical experience and follow-up. *Gen Thorac Cardiovasc Surg*. 2007;55:105–112.

18. Diop MS, Ciss AG, Dieng PA, et al. La chirurgie de la tétralogie de Fallot et des agénésies pulmonaires: résultats de 40 cas opérés au Sénégal. *Le J Africain du Thorax des Vaiss*. 2014;5:395–399 [in French].

19. Sandoval N, Carreno M, Novick WM, et al. Tetralogy of Fallot repair in developing countries: International Quality Improvement Collaborative. *Ann Thorac Surg*. 2018;106:1446–1451.

20. Heinisch PP, Guarino L, Hutter DM, et al. Late correction of tetralogy of Fallot in children. *Swiss Med Wkly*. 2019;149:w20096.

21. Bamigboye-Taiwo OT, Adeyefa B, Onakpoya UU, et al. Tetralogy of Fallot in the nascent open-heart surgical era in a tertiary hospital in south-west Nigeria: lessons learnt. *Cardivasc J Afr*. 2022;33:122–126.

22. Bhushan R, Chugh V, Loona M, Bandey J. Intracardiac repair in late adolescent and adult tetralogy of Fallot—early and midterm results from a tertiary care Centre. *Braz J Cardiovasc Surg*. 2022;37:511–516.

23. Souaga KA, Bonny R, Katche EK, et al. Transatrial-transpulmonary correction of tetralogy of Fallot: experience of a developing country. *Kardiochir Torakochirurgia Pol*. 2022;19:130–134.

24. Sadiq N, Ullah M, Younis U, Akhtar K, Mehmood A. Perioperative major aortopulmonary collateral arteries (MAPCAs) coiling in tetralogy of Fallot patients. *J Cardiol Curr Res*. 2015;3:3–5.

25. Chang-Hsien Y, Chen M-R. Clinical investigation of systemic-pulmonary collateral arteries. *Pediatr Cardiol*. 2008;29:334–338.

26. Deanfield JE, Mckenna WJ, Presbitero P, et al. Ventricular arrhythmia in unrepaired and repaired tetralogy of Fallot: relation to age, timing of repair, and haemodynamic status. *Br Heart J*. 1984;52:77–81.

27. World Health Organization. *Newborn mortality*; 2022. Available at: https://www.who.int/news-room/fact-sheets/detail/levels-and-trends-in-child-mortality-report-2021#:~:text=Sub%2DSaharan%20Africa%20has%20the,36%25%20of%20global%20newborn%20deaths. Accessed January 14, 2024.

28. Ahmat A, Okoroafor SC, Kazanga I, et al. The health workforce status in the WHO African Region: findings of a sectional study. *BMJ Glob Health*. 2022;7(suppl 1):e008317.

29. Campbell M. Cerebral abscess in cyanotic congenital heart-disease. *Lancet*. 1957;272:111–115.

30. Waldmann V, Bessière F, Gardey K, et al. Systematic electrophysiological study prior to pulmonary valve replacement in tetralogy of Fallot: a prospective multicenter study. *Circ Arrhythmia Electrophysiol*. 2023;16:e011745.

31. Barratt-Boyes B, Neutze JM. Primary repair of tetralogy of Fallot in infancy using profound hypothermia with circulatory arrest and limited cardiopulmonary bypass: a comparison with conventional two stage management. *Ann Surg*. 1973;128:406–411.

32. Ghavidel AA, Javadpour H, Tabatabaei BM, et al. Complete surgical repair of tetralogy of Fallot in adults, is it ever too late? *J Card Surg*. 2008;23:23–26.

33. Clarke NS, Thibault D, Alejo D, et al. Contemporary patterns of care in tetralogy of Fallot: analysis of the Society of Thoracic Surgeons data. *Ann Thorac Surg*. 2023;116:768–775.

34. Yamamoto S, Nozawa T, Aizawa T, Honda MM M. Transcatheter embolization of bronchial collateral arteries prior to intracardiac operation for tetralogy of Fallot. *J Thorac Cardiovasc Surg*. 1979;78:739–745.

35. Liu Y, Shen X, Li S, et al. [An integral approach for cyanotic congenital heart disease with major aortopulmonary collateral arteries]. *Zhonghua Yi Xue Za Zhi*. 2006;86:228–231 [in Chinese].

36. Tang L, Zhou S. Transcatheter occlusion of multiple aortopulmonary collateral arteries for post-operative heart failure in a patient with tetralogy of Fallot using the Amplatzer vascular plug and a detachable coil. *Chin Med J (Engl)*. 2011;124:951–953.

37. Xu Z, Zhang M, Zhu L, Gong X, Li J. Elevated plasma B-type natriuretic peptide and C-reactive protein levels in children with restrictive right ventricular physiology following tetralogy of Fallot repair. *Congenit Heart Dis*. 2014;9:521–528.

38. Ahmad N, Kantor PF, Grosse-wortmann L, et al. Influence of RV restrictive physiology on LV diastolic function in children after tetralogy of Fallot repair. *J Am Soc Echocardiogr*. 2012;25:866–873.

39. Saxena A, Mehta A, Ramakrishnan S, et al. Pulse oximetry as a screening tool for detecting major congenital heart defects in Indian newborns. *Arch Dis Child Fetal Neonatal Ed*. 2015;100:F416–F421.

40. Ferraris VA, Pezzella AT. Commentary: Worldwide disparities in cardiac surgical care: thinking globally not locally to solve problems of limited resources and access to specialized care. *J Thorac Cardiovasc Surg*. 2020;159:997–999.

41. Oliveira GBF, Avezum A, Roever L. Cardiovascular disease burden: evolving knowledge of risk factors in myocardial infarction and stroke through population-based research. *Front Cardiovasc Med*. 2015;2:32.