HUMANITARIAN ACTIVITIES IN PEDIATRIC CARDIOLOGY

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HUMANITARIAN ACTIVITIES IN PEDIATRIC CARDIOLOGY

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Table of Contents

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EDITORIAL
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Editorial: Humanitarian Activities in Pediatric Cardiology

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Keywords: humanitarian, cardiology, pediatrics, integrated healthcare, cardiac program

Editorial on the Research Topic

Humanitarian Activities in Pediatric Cardiology

Several studies have reported, in emerging economies, an incidence of congenital heart defects that is higher than average because of several factors, including genetics, high prevalence of consanguineous marriages, malnutrition, poor sanitation, and high fertility rates (1). Congenital malformations, of which heart defects represent nearly 50%, are the 4th leading cause of neonatal mortality. Since the care of patients with congenital heart defects requires significant resources, the main global issue remains that access to care is not equal for all (1). As a result, every year about 90% of over one million of children with congenital heart defects, predominantly born in low-income countries, do not have access to care or only receive sub-optimal care (1). This tragic situation has stimulated the creation of many non-profit humanitarian organizations, trying to reduce the imbalance existing for children across the globe. The purpose of this Research Topic was to share the experience of people involved in humanitarian activities in emerging economies in different locations of the world, combining different perspectives: anesthesists, surgeons, nurses, entire teams with long standing activity in one hospital, and also the recipients of one of these programs.

Jivanji et al. presented very clearly the situation in sub-Saharan East Africa: Kenya, Tanzania, and Uganda, with their commentaries on affordability, access, and awareness. They listed all challenges faced in developing a cardiac program in that region, with problems such as corruption at various levels described with a very clear narrative (Jivanji et al.).

Giamberti et al. presented their remarkable experience over a 17-year period of creating and developing a pediatric cardiac unit in Cameroon, central Africa, with accurate description of barriers and facilitators encountered for the set-up. This team not only organized the clinical activities but also a fruitful bilateral exchange of collaboration with the local caregivers, with continuous educational programs, and constant monitoring of the progress made. The most successful result is that this unit, the only one active in the entire country of Cameroon, is now attracting patients from surrounding countries (Giamberti et al.).

Cvetkovic reported her experience gained in various visits to India, Malaysia, Nigeria, Kenya, Tanzania, and Mauritius. Thanks to the opportunity of experiencing different environments, she presented her approach to improve the quality of anesthesia derived from the combination of the following: regular teaching and education sessions, careful patients selection, patients preparation for surgery with meticulous pre-operative care, individualized type of anesthesia, and structured daily team briefing (Cvetkovic). The results were very encouraging, particularly because every visit was followed by regular interaction between visiting and local teams (Cvetkovic).

Howes, a specialist nurse with years of experience in Pediatric Cardiac Intensive Care Unit who was involved in many visits with different teams, presented her interesting perspective regarding

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the protocol of early extubation after repair of complex congenital heart defects. Advantages and disadvantages of early extubation were analyzed, balancing the potential risks (lung collapse, respiratory insufficiency, re-intubation) vs. the needs dictated by limited resources in terms of personnel, equipment, infrastructures. Most of these aspects can be taken into consideration in different types of environments (Howes).

A relatively new perspective has been presented by Zain et al., who reported the experience of the local team in a rural area of North-East Malaysia, exposed to the beginning of pediatric cardiac surgery activities from scratch, initially with a surgeon in place for a couple of years, then with regular visits of alternating teams. Their experience is another confirmation that, if a program is well-organized and sustained, it can lead to stepwise growth of the local team until reaching autonomy for surgical management of the vast majority of children born with congenital heart defects in a region without any alternative available for treatment. The visiting teams now are mostly helping the local team for assistance in the surgical management of the most complex malformations, and to continue the educational and supporting program (Zain et al.).

The last two articles of this Research Topic reviewed the entire issue of humanitarian activities in low and middle-income countries.

Novick et al. reported their approach, accomplished after mastering the assistance in pediatric cardiac surgery, starting from visiting Colombia in 1991 and since then having visited 32 countries, having completed over 560 trips of between 1- and 4-weeks in duration, with nearly 10,000 patients operated on in total. Their comprehensive approach covers many steps, including the request for assistance, a site visit, the preparation for program implementation, different types of program models accordingly with the match between the local needs and the visiting team availability (intermittent visit model, resident senior surgeon model, team in residence model), the nursing education and empowerment, and the attention to the services of interventional cardiology, anesthesia, perfusion, biomedical engineering, operating room (Novick et al.). Because of their very extensive experience across many countries, Novick et al. also analyzed the difficulties of providing service in conflict zones, the need to provide benchmarks and indicators of improvement, as well as quality improvement and assessment, and ethical considerations on the entire matter.

Murala et al. provided a detailed overview of the current global situation, with report of the current units involved in these humanitarian activities with short and long-term programs. In particular, for the short-term programs the analysis included persistence and continuity, cooperation with Non-Governmental Organizations, focus on types of congenital heart defects, on site issues, view from the host programs, and financial aspects. Then they proposed elements to consider in a model for establishing long-term programs: shared vision, spark plug (organization or individual who is a dedicated leader, focused, invested, and physically present in a local program on a long-term basis), communication and coordination, training, material support, exit strategy, data collection, and analysis (Murala et al.).

In the final article, Nichani and Nichani explored in a clever and original way the potential benefits of this work performed by teams from the so called "high income countries" to the low-income regions of Africa and Asia to provide care for children born with congenital heart defects.

In fact, there are also advantages for those teams organizing these humanitarian activities, such as gained experience on unusual cases, team-building, and improvement. Furthermore, a deeper connection to the main meaning of the medical profession is an extremely important part of the experience.

This is, to the best of our knowledge, the first time that the many benefits for the traveling medical teams, in addition to the recipients, have been considered in all the literature published on this topic.

We hope that this Research Topic will help all readers and interested individuals so that in the future the diagnosis of congenital heart defects and rheumatic heart diseases will no longer be the death sentence, for the majority of children in the world, that it currently is.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

REFERENCES

1. Corno AF. Pediatric and congenital cardiac surgery in emerging economies: surgical "safari" versus educational program. *Inter Cardio-Vasc Thorac Surg.* (2016) 23:163–7. doi: 10.1093/icvts/ivw069

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PERSPECTIVE
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The Shisong Cardiac Center in Cameroon: An Example of a Long-Term Collaboration/Cooperation Toward Autonomy

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Congenital heart diseases (CHD) are present in nearly 1% of live births; according to WHO, there are 1. 5 million newborns affected by CHD per year and more than 4 million children waiting for cardiac surgery treatment worldwide. The majority of these children (∼90%) could be treated, saved and subsequently have a good quality of life but unfortunately, in developing countries with a suboptimal care or no access to care, they are destined to die. Cameroon, one of the 40 poorest countries in the world, is a typical example of this dramatic scenario and this is why we started a collaboration project with a local religious partner (Tertiary Sisters of Saint Francis) in 2001 with the aim of establishing the first cardiac surgery center in this country. There are various well-known organizational models to start a cooperation project in pediatric cardiac surgery in a developing country. In our case, the project included a long-term collaboration with a stable local partner, a big financial investment and a long period of development (10 years or more). It is probably the most difficult model but it is the only one with the greatest guarantee of success in terms of sustainability and autonomy. The aim of this study is to analyze the constructive and problematic aspects of the 17-year collaboration in this project, and to assess possible solutions regarding its critical issues. Although much has been done during this 17-year we are aware that there is still a lot that needs to be done.

Keywords: health, cooperation, cardiac surgery, congenital heart disease, collaboration project

INTRODUCTION TO THE PROBLEM

Cardiovascular diseases are the leading cause of death worldwide and, despite the progress of medicine in the last 25 years in this field, 17.5 million deaths annually occur due to these non-communicable diseases (1).

Congenital heart diseases (CHD) are present in nearly 1% of live births, according to WHO there are 1.5 million newborns per year affected by CHD and more than 4 million children waiting for cardiac surgery treatment in the world (2).

The majority of these children (∼90%) could be treated, saved and subsequently have a good quality of life. Unfortunately, children from developing countries are destined to die because they receive suboptimal care or have no access to healthcare (3). There is a dramatic disproportion between medical access and healthcare services within developed and developing countries, 89% of the world's healthcare resources are used only for 7% of the sick people (World-Health-Statistics, 2015). The unequal distribution and access to healthcare facilities are particularly evident when it comes to cardiac surgery. Data from literature demonstrate that there is a cardiac surgery center in the US every 120,000 people, in Australia and Europe each center can provide healthcare for 1,000,000 people. In Asia the number of people treated per center increases up to 16,000,000, the worst situation is seen in Africa with a rate of 1 center every 33,000,000 people (4, 5). If we analyze data regarding the CHD incidence (6), Novick and Cardarelli (7) estimate that 810,000 children born with moderate to severe forms of CHD should be surgically treated every year but <1.5% of them outside the industrialized countries receive the necessary surgical care (8).

Cameroon, one of the 40 poorest countries in the world, is a typical example of this dramatic scenario and this is the reason why we started a collaboration project with a local religious partner (Tertiary Sisters of Saint Francis, TSSF) in 2001, with the aim of establishing the first cardiac surgery center in the country.

CAMEROON

The Republic of Cameroon is situated in Central Africa at the juncture of the Gulf of Guinea with an estimated population of 23,920,887 in 2016. French and English are the official languages which are spoken by 70 and 30% of the population, respectively. There are two international airports served by the most important air companies in Yaoundè (administrative capital) and in Douala (economic capital).

In Cameroon, 45% of the population is under 15 years of age, as expressed in **Table 1** the birth rate of Cameroon is 36.2‰ with an infant mortality of 63‰, the life expectancy is 54.8 years for males and 57.1 years for females (9).

TABLE 1 | Comparative data between Italy and Cameroon.

	Italy	Cameroon
Surface in km²	301,341	475,442
Population	60,000,000	24,000,000
People younger man then 15 yr	15%	45%
Birth rate	7.8‰	36.2‰
Infant mortality	2.9 ‰	63‰
Life expectation male	80.6 yr	54.8 yr
Life expectation female	85.1 yr	57.1 yr

Calendario Atlante De Agostini 2018, Istituto Geografico De Agostini, (11/2017). p. 418–419; p.229–230.

The Cameroon healthcare system is officially organized in three levels: the Public Sector managed by the Ministry of Health, the Private Sector generally managed by NGOs and the Traditional Medicine sub-sector. The reality is that in Cameroon, missionaries are so far the great stakeholders in the health-domain especially in the peripheral area. The TSSF, local partner of our project, have been responding to the sick people's needs in Cameroon since 1935. They operate in four hospitals and 12 health-centers across the country. The most important hospital is the St. Elisabeth Catholic General Hospital (SECGH) in Shisong/Kumbo, in the anglophone North-West Province.

This is a general hospital with 350 beds including different departments (obstetrics/gynecology, urology, general-surgery, dentistry, ophthalmology, pediatrics, radiology, and infective-disease), laboratories, pharmacy and an internal Nurse School of Health Sciences. The hospital has been officially recognized by the Cameroonian Government since 1952.

In 2000, the Administration of the SECGH contacted our NGO (*Bambini Cardiopatici nel Mondo Association*) and our Hospital (*IRCSS Policlinico-San Donato*) in order to collaborate for the realization of the first Cardiac Center (CC) of Cameroon.

SHISONG CARDIAC CENTER PROJECT

After several visits, our NGO, together with another Italian NGO (Cuore Fratello), and the TSSF started the project in 2002, with the objective of establishing a center which could be completely autonomous.

We spent 8 years for the initial phase that included the building construction, staff training and instrumental equipment of the CC, it ended with the inauguration of the center on the 19th of November, 2009.

During this phase several training and diagnostic missions were carried out, 120 urgent cases of children with CHD were transferred to Italy for cardiac surgery. The total economic investment by the 3 partners consisted of about 6 million euros.

The CC is today a modern complex of 3,100 covered square meters (**Figure 1**) with 7 blocks including:

FIGURE 1 | Overview of the CC: the green roofs are the Cardiac Center [Internal archive, IRCCS Policlinico San Donato, San Donato M.se, (Mi), Italy].

Block-A: out patients department (reception, public-relations office, pharmacy, consultation-rooms, secretariat, administration, social-case office);
Block-B: pre/post-surgical unit;
Block-C: clinical unit;
Block-D: extended wards and X-Ray unit;
Block-E: critical area with cath lab, 2 operating theaters, and 2 intensive-care units with a total of 12 fully-equipped beds;
Block-F: left basement with technical department, procurement office and drugstore;
Block-G: right basement with a conference-hall, meeting-rooms, blood-bank, guest-house, changing rooms, laundry and research-committee office.

The infrastructures created are: a water-treatment plant, 2 uninterruptible power-supply, 2 standby power generators, autonomous oxygen production central, complete laundry service, blood-bank, and more recently an autonomous incinerator plant.

During the first 8 years, 3 doctors (2 cardiologists and 1 cardiac surgeon), 15 nurses, 4 technicians, 2 perfusionists, 1 pharmacist, 1 biomedical-engineer were trained in Italy in our Hospitals. All of them are Cameroonians, they trained in our Hospitals from a minimum of 6 months to a maximum of 2 years.

The cardiologists are now independent consultants in the CC and they can also operate with a Mobile Unit in the most important cities of Cameroon (Yaoundè, Douala, Bamenda, Bafoussam, and Garoua).

A scientific research committee has been created to stimulate and support the scientific activity with publications and congress presentations. The committee includes 2 local members and 2 foreign members with expertise in cardiac surgery and cardiological research, well-recognized at an international level.

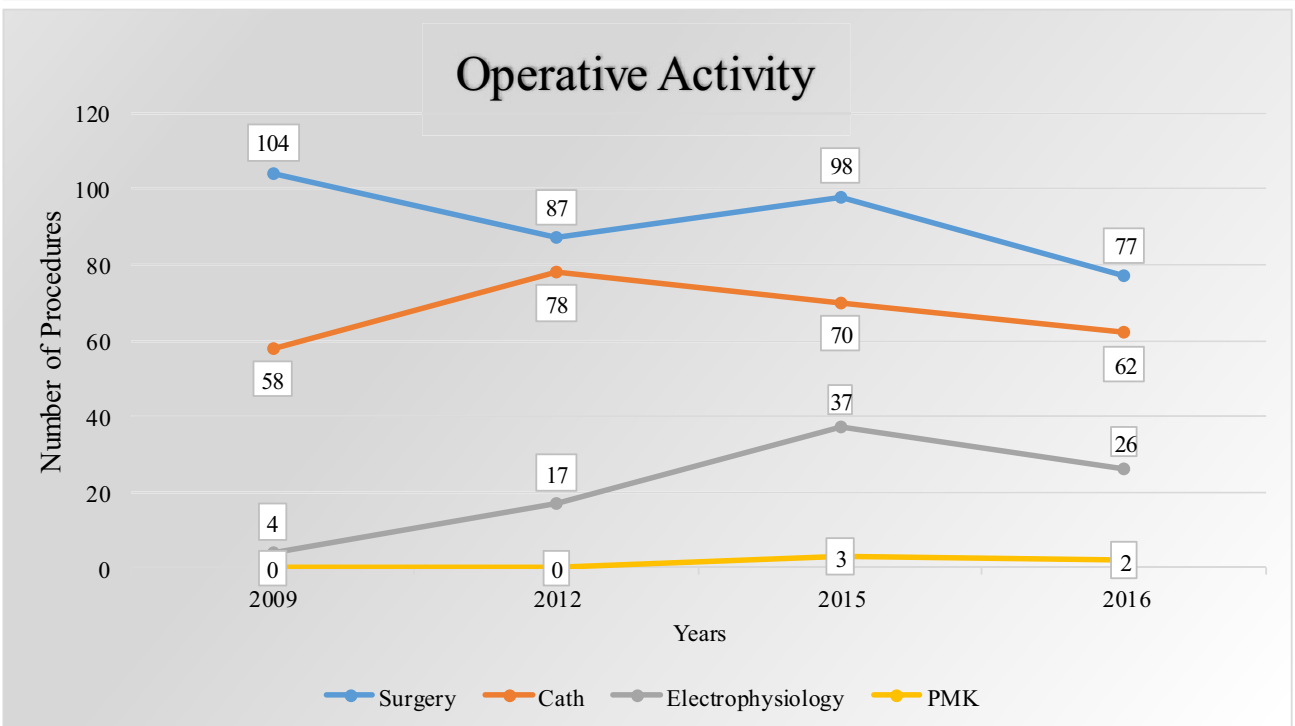
RESULTS

The CC is the only center performing cardiac surgery in Cameroon. In only a few years it has become a national reference center for cardiology and cardiac surgery activity for both pediatric and adult patients. The CC provides a total of 74 beds: 12 in ICU, 22 Post-Op, 20 for female hospitalization and 20 for male hospitalization. The healthcare team includes 56 nurses, 2 pharmacists and 4 physicians (2 cardiologists, 1 cardiac surgeon, and 1 anesthesiologists). In collaboration with the medical staff, there is also an administrative staff responsible for the non-medical management.

After an initial training phase, the cardiological activity at the CC is now improving every year, reporting ∼6,500 cardiological consultations each year with an average of 3,000 echo and EKG procedures per year.

The invasive activity includes cardiac surgery for CHD and acquired heart disease (AHD), diagnostic and interventional catheterization, and PMK implantation (**Table 2**); 719 patients underwent cardiac surgery between November 2009 and December 2017, including operations for 302 CHD (42%) and

TABLE 2 | Summary of clinical activities of the Cardiac Center of Shisong from November 2009 to December 2016 (Internal database, Shisong Cardiac Center, Cameroon).



The blue curve correspond to the number of surgeries. Similarly, the gray line indicates the electrophysiology activities.

417 AHD (58%) (**Table 3**), with a mean of 80 patients operated per year. The most frequent operations performed are shown in **Table 4**. The total activity of the CC is shown in **Table 5**. In the last 3 years, the surgical mortality at 30 days has been of 4.7% for CHD and 4.2% for AHD patients. The local team is completely autonomous for the AHD surgery, while for CHD patients the team still needs the support from surgical mission teams from foreign countries. In 2017, 43 patients with CHD have been operated during 5 surgical missions (3 from Italy, 1 from Belgium, and 1 from Mozambique), 30 of them (70%) have been operated by the local surgeon helped by more experienced surgeons and 13 by surgeons coming from abroad.

The number of cardiac surgery procedures depends on the funds that various charity associations, NGOs, and Foundations make available to cover the costs of the interventions.

TABLE 3 | Surgical activity of the CC (Internal database, Shisong Cardiac Center, Cameroon).

Years	Congenital heart disease	Acquired heart disease
2009–2015	221	332
2016	38	39
2017	43	46
Total	302	417

TABLE 4 | Most frequent cardiac operations performed (Internal database, Shisong Cardiac Center, Cameroon).

CHD (302)			AHD (417)		
Surgery	**Nr**	**%**	**Surgery**	**Nr**	**%**
TOF	86	28.4	Mitral replacement	151	36.2
VSD	82	27.1	Aortic replacement	64	15.37
ASD	29	9.6	Mitro-aortic replacement	67	16.0
PDA	30	9.9	Mitral repair	41	9.8
AVSD	21	6.9	Thoracic aortic aneurysm	26	6.2
Others	54	17.8	CABG	17	4
			OTHERS	51	12.2

TOF, Tetralogy of Fallot; VSD, Ventricular Septal Defect; ASD, Atrial Septal Defect; PDA, Patent Ductus Arteriosus; AVSD, Atrio-Ventricular Septal Defect; CABG, Coronary Artery Bypass Graft Surgery; PM, Pacemaker; ECG, Electrocardiogram.

TABLE 5 | Productivity enhancement since 2009.

Activity	2009–2014	2015	2016	2017	Total
Consulation	27.866	6.313	6.561	6.191	46.931
Echo diagnosis	12.475	2.956	3.063	2.632	21.126
ECG diagnosis	11.642	2.579	2.787	2.409	19.417
In-patients	5.621	1.342	1.099	1.082	9.144
Electrophysiology	87	40	28	24	179
Catheterization	309	70	62	58	499
Surgeries	455	98	77	87	717
Holter	255	70	47	81	453
Mobile consulation	6.338	3.625	3.335	3.385	16.683

Most of the patients assessed and operated at the CC come from Cameroon, especially from the near provinces of Littoral, Center and North-West. In the last 2 years, patients from other countries such as Democratic Republic of Congo and Equatorial Guinea have also been operated, demonstrating that the CC is a reference center not only for the local population but also for the neighboring population.

Out of the hospital environment, it is important to highlight that the consumable goods completely purchased abroad at the beginning of the CC, are now purchased on the local market when it comes to 40% of the goods.

From a scientific point of view, the CC medical staff in collaboration with the foreign staff has produced 20 publications on Index-Medicus since 2009.

DISCUSSION

There are different well-known organizational models to develop a cooperation project in pediatric cardiac surgery in a developing country. Hereunder, we have synthesized the most frequent and probably the best known collaboration models.

First

To send people in a foreign country for education and training in excellent centers for a period of variable duration. These people must come back to their country and start a local program in pediatric cardiac surgery. This model takes a long-time and frequently the training is not enough because in western countries the training stage can only be observational and not practical for legal reasons.

Second

To have visiting teams from abroad regularly visiting an institution doing surgery and training "on-site." Usually they spend short periods, several times a year, for a variable number of years. This is the most frequently used model and the easiest to use. It is expensive and the local training has been shown to be ineffective and suboptimal for skill transfer (9), and entirely dependent on donations.

Third

To have a senior physician, usually a retired cardiac surgeon or cardiologist who desires to help a developing country. This model needs a governmental support and often the senior leader is not enough to develop a local autonomous program.

Fourth

To establish a long-term collaboration between a local team/hospital and a well-known experienced international partner. This model requires stable partners, great financial investments, and a long period of development (10 years or more). It is the most difficult model to implement but the one with the greatest guarantee of success in terms of sustainability and autonomy.

The CC project can be included in this latter model of cooperation. Our NGO is involved only in collaborative projects with the goal of creating stable and autonomous cardiac surgery

centers in developing countries (3). The pioneer partners of our project have remained the same since the beginning (2001); this project required a lot of time for the developing phase. The work is not finished yet because a lot of time to complete the autonomy and sustainability of the CC will be needed.

Since the beginning, we conducted this project focusing not only on the surgical aspect but also trying to develop all the intrinsic aspects of an optimal medical-care organization. We have built a center with the most modern and complete medical equipment, providing also support infrastructures like the oxygen production central and, recently, an autonomous incinerator-plant but especially we have allocated a lot of resources for local staff training. As reported, since the beginning, the CC is a Cameroonian center totally managed by Cameroonian people, but above all it is a healthcare center for Cameroonian patients.

Not only the medical and nursing personnel have attended the training program, but also all the professional figures involved in all the CC activities such as technicians, perfusionists, pharmacists, biomedical-engineers, and administrators. At the same time, these people are continuously involved in the on-site training of the younger personnel.

Complete autonomy has not yet been reached by the healthcare staff: at least 2 cardiologists, a cardiac surgeon, an anesthetist and an intensivists are still missing.

The evaluation of the surgical procedures performed and the results achieved present both positive and critical aspects. It is relevant that mortality is <5% both for CHD and AHD patients. Unfortunately, the center is not yet autonomous for the medical care of CHD and much work is still necessary to increase the number of interventions performed per year and to avoid that the CC will be underutilized. The structures and infrastructures present at the CC potentially allow to perform more than 400 operations per year but only 80 take place.

There are various explanations for this discrepancy. Certainly, the lack of autonomy of the medical personnel plays an important role, but the greatest limit is the economic one.

The number of patients operated is related to the funds that various charity associations, NGOs, and Foundations make available to cover the costs of the intervention. Very few patients are able to pay for the cost of an intervention and the government's economic support is minimal or null. There are also cultural limits. The presence of a missionary religious order as local partner is, on the one hand, a guarantee of a stable, reliable, honest and continuous partner, which has been present on site for about 100 years. On the other hand, it is a partner without business-skills but rather bound to a celestial vision that Providence will help in any case. Moreover, the missionary religious order often does not have an incisive political weight in the government decisions and a supported economic strength.

Nine years after the inauguration, we can say that the government support has been minimal, and it is difficult to think that the situation will improve in the future. When it comes to this, during these years we hypothesized various explanations: a depressed economy, absence of a true health development plan, disorganization, corruption and absence of a national healthcare system. At the same time the existence of unhealthy competition and jealousy must also be considered. Over the past 20 years, many expensive and unsuccessful attempts were made in order to open other cardiac surgery centers in Yaoundè and Doaula, all without success. Moreover, every local hospital/university wants to grow and refuse to refer patients to the CC even if their service is not readily available; this lack of collaboration can only destabilize the progress and the development of both the CC and the other cardiac centers. **Table 6** summarizes the barriers and the facilitators that we identified during the set-up of the CC.

Most importantly, our data from CC should be evaluated in the African context of the Sub-Saharan area. A recent published study (5) showed that in 2012 twenty-two centers in the Sub-Saharian area performed 1,277 open heart operations with a mean of 58 operations per year. The majority of these centers offer open heart surgery only in complete collaboration with and dependency on foreign visiting teams. In this context, the quantitative and qualitative results produced at the CC assume a value that is certainly more positive than the raw analysis of numbers.

We have recently sent a simple questionnaire with three questions: (1)what has been working in this project? (2)what was wrong (not working) with this project? (3)what do you suggest to improve in the project in the future? to 100 people who have been involved in the project since 2001 (nurses, physicians, engineers, administrative staff, volunteers).

For the first question, the most frequent answers were: great enthusiasm, ability to work in partnership, ability to think "big" and professional training before the opening of the CC. For the second question, the answers were: western/global economic crisis, lack of new people involved, underestimation of difficulties, absence of complete autonomous local staff team, absence of economic support from the government. The solutions suggested have been: need of a complete local team; creation of new partnerships with NGOs, Charity Associations,

TABLE 6 | Barriers and facilitators to set up the CC.

Barriers	• Economic limit
	• Minimal or null government support
	• Absence of true development health plan
	• Disorganization
	• Corruption
	• Absence of a true national healthcare system
	• Culture limit
	• Low incisive political weight of the local partner
	• Absence of complete local medical staff team
Facilitators	• Stable, reliable, honest local partner
	• Long-term collaboration between same partner
	• Great enthusiasm
	• Professional training of local people before the opening of the CC
	• Modern complex with the best instrumental equipment
	• Cameroonians employers at every level

Foundations, Scientific Societies; need for a bigger "Fund-Raising" plan in the US and EU; need for new and younger people involved at every level in the project.

CONCLUSIONS

Despite the great scientific progress in the medical care of cardiovascular disease in the western countries, a significant proportion of children with CHD living in developing countries do not receive proper diagnosis and treatment.

The solution to this problem, especially in Sub-Saharian African area, will still require a long-time and it can only be done through better programming, collaboration and economic contribution of the public and private sectors.

International authorities (scientific societies and private medical companies) should identify and support the few active cardiac centers in order to finance them and concentrate both economic and human resources efforts. To do this, we need to open an international debate and create a productive cooperation between the associations already present in this sector sharing experiences and resources.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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REFERENCES

1. Dearani JA, Jacobs JP, Bolman RM III, Swain JD, Vricella LA, Weinstein S, et al. Humanitarian outreach in cardiothoracic surgery: from setup to sustainability. *Ann Thorac Surg.* (2016) 102:1004–11. doi: 10.1016/j.athoracsur.2016.03.062
2. Frigiola A, Moussaidi N, Giamberti A, Pomé G, Isgrò G, Youssef T, et al. International cooperation in healthcare: model of IRCCS Policlinico San Donato and Bambini Cardiopatici nel Mondo Association for congenital heart disease. *Eur Heart J Suppl.* (2016) 18(Suppl. E):E72–8. doi: 10.1093/eurheartj/suw023
3. Giamberti A, Mele M, Di Terlizzi M, Abella R, Carminati M, Cirri S, et al. Association of children with heart disease in the world: 10-year experience. *Pediatr Cardiol.* (2004) 25:492–4. doi: 10.1007/s00246-003-0627-8
4. Pezzella AT. Global aspects of cardiothoracic surgery with focus on developing countries. *Asian Cardiovasc Thorac Surg.* (2010) 18:299–310. doi: 10.1177/0218492310370060
5. Yankah C, Fynn-Thompson F, Antunes M, Edwin F, Yuko-Jowi C, Mendis S, et al. Cardiac surgery capacity in Sub-Saharian Africa: quo vadis? *Thorac Cardiovasc Surg.* (2014) 62:393–401. doi: 10.1055/s-0034-1383723
6. Hoffman Ji, Kaplan S. The incidence of CHD. *J Am Coll Cardiol.* (2009) 39:1890–900. doi: 10.1016/S0735-1097(02)01886-7
7. Novick W, Cardarelli M. Pediatric cardiac surgery in emerging countries. In: Dabbagh A. Conte A, Lubin L, editors. *CHD in Pediatric and Adult Patients.* Basel: Springer International publishing (2017). p. 981–94.
8. Leon-Wyss JR, Veshti A, Veras O, Gaitán GA, O'Connell M, Mack RA, et al. Pediatric cardiac surgery: a challenge and outcome analysis of the Guatemala effort. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu.* (2009) 12:8–11. doi: 10.1053/j.pcsu.2009.01.003
9. Tefera E, Nega B, Yadeta D, Chanie Y. Humanitarian cardiology and cardiac surgery in Sub-Saharian Africa: can we reshape the model? *World J Pediatr Congenit Heart Surg.* (2016) 7:727–31. doi: 10.1177/2150135116668834

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Levosimendan for Pediatric Anomalous Left Coronary Artery From the Pulmonary Artery Undergoing Repair: A Single-Center Experience

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Objectives: Our aim was to retrospectively evaluate the benefit of levosimendan in certain complicated congenital heart procedures such as the pediatric anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA) with moderate or severe cardiac dysfunction and its repair.

Study Design: We enrolled 40 pediatric patients with ALCAPA and moderate or severe left ventricular dysfunction. Patients who had a preoperative left ventricular ejection fraction (LVEF) of 50% or less and had undergone the surgical correction of their coronary artery through cardiopulmonary bypass met the criteria of our study. Twenty patients were given 0.1–0.2 μg/kg/min levosimendan at the induction of anesthesia, which lasted for 24 h. The remaining 20 patients were not given levosimendan.

Results: The mean preoperative LVEF in the levosimendan group was significantly lower than that in the non-levosimendan group (22.5 ± 10.7% vs. 31.8 ± 8.1%, $p = 0.004$). On postoperative day 7, the LVEF in the levosimendan group was still significantly lower (27.1 ± 8.9% vs. 37.5 ± 11.0%, $p = 0.002$). There was no significant difference in ΔLVEF detected on day 7 [median 30.8%, interquartile range (IQR) −4.4 to 63.5% vs. median 15.1%, IQR −3.5 to 40.0%, $p = 0.560$] or at follow-up of about 180 days (median 123.5%, IQR 56.1–222.6% vs. median 80.0%, IQR 36.4–131.3%, $p = 0.064$). There was no significant difference between the two groups in postoperative vasoactive-inotropic score (VIS) at any of the time points of 1, 6, 12, 24, and 48 h ($p = 0.093$). Three patients had to be supported by extracorporeal membrane oxygenation when difficulty appeared in weaning off cardiopulmonary bypass because of low cardiac output in the non-levosimendan group, but no patient needed extracorporeal membrane oxygenation after levosimendan infusion ($p = 0.231$). The length of intensive care unit stay (median 10.5 days, IQR 7.3–39.3 days vs. median 4.0 days, IQR 2.0–10.0 days, $p = 0.002$) and duration of mechanical ventilation (median 146.0 h, IQR 76.5–888.0 h vs. median 27.0 h, IQR 11.0–75.0 h, $p = 0.002$) were revealed to be longer in the levosimendan group.

Peritoneal dialysis occurred in eight patients (40%) in the levosimendan group and two patients (10%) in the non-levosimendan group ($p = 0.028$). No significant difference was revealed in all-cause mortality within 180 days, which occurred in two patients (10%) in the levosimendan group and one (5%) in the non-levosimendan group ($p = 1.00$).

Conclusion: Levosimendan's unique pharmacological properties have strong potential for cardiac function recovery among pediatric patients with ALCAPA with impaired left ventricular function who have undergone surgical repair.However, any improvement from levosimendan on postoperative outcomes or mortality was not substantiated by this study and must be investigated further.

Keywords: levosimendan, pediatric anomalous origin of the left coronary artery from the pulmonary artery, coronary artery reimplantation, left ventricular dysfunction, postoperative outcomes

INTRODUCTION

Anomalous origin of the left coronary artery from the pulmonary artery (ALCAPA), also known as Bland-White-Garland syndrome, is well-recognized as an uncommon congenital heart disease (1). It makes up a proportion of about 0.25–0.5% of all congenital heart diseases, and its incidence is about 1 per 300,000 newborns (1, 2). A high mortality rate (up to 90%) is reported if the defected is not repaired in the first postnatal year. ALCAPA is mainly characterized by chronic myocardial ischemia, even infarction, and various degrees of mitral regurgitation secondary to annual dilation or papillary muscle dysfunction. If the myocardium suffers steady long-term hypoperfusion, gradually, both subendocardial ischemia and fibrosis occurs, leading to arrhythmias and even sudden death (3, 4). In addition, either primarily compromised heart function or a cardiopulmonary bypass (CPB) procedure can result in postoperative low cardiac output syndrome (LCOS). This syndrome remains the most common complication of ALCAPA repair and occurs in as high as 25% of all cases (5). It has been suggested that preoperative systolic ventricular dysfunction could prolong CPB time or even lead to difficulty weaning from CPB. It can also become a risk factor for perioperative mortality (2). Thus, the appropriate selection of inotropes is a crucial strategy for procedures to repair ALCAPA, especially when the left ventricular ejection fraction (LVEF) is 50% or less.

The primarily perioperative objective is to maintain stable hemodynamics and avoid further cardiac function deterioration. However, there are limited perioperative management tactics for these objectives.

Levosimendan, a calcium-sensitizing inotropic agent, is a preferred inotrope that is able to enhance cardiac contractility without increasing cardiac oxygenation consumption. It has two principal mechanisms: (1) it enhances the sensitivity of cardiac troponin C to calcium and (2) it mediates the gateway of adenosine triphosphate-sensitive potassium, which is located at the vascular smooth muscle and mitochondrial inner membrane. Levosimendan performs these roles by improving contractility through positive inotropic function and dilating peripheral vessels and the coronary artery; it also has anti-ischemia effects (6–8). It has been widely used to treat heart failure in Europe (9), and studies have reported its increasing use among adult patients for surgery management (10, 11). In general, prophylactic levosimendan seems to be a promising intervention for improving cardiovascular function and it is an effective therapeutic approach for preventing perioperative LCOS in a surgical setting.

Despite a number of prospective or retrospective trials have been carried out on the practical applications of levosimendan in congenital cardiac surgery, proving that it can be well-tolerated, there is still no relevant report on ALCAPA repair. This retrospective analysis from our medical center is intended to explore the effect of levosimendan on the improvement of left ventricular function as well as in-hospital outcomes among pediatric patients with ALCAPA and LVEF of 50% or less undergoing coronary reimplantation.

MATERIALS AND METHODS

Patients and Data Collection

The study protocol was approved by our hospital institutional review board. **Figure 1** illustrates the enrollment process of the eligible pediatric ALCAPA population in our study scheme. Between 2010 and 2017, only 40 pediatric patients with ALCAPA in our medical center were admitted with moderate or severe left ventricular dysfunction, namely, with a LVEF of 50% or less. In addition, two patients treated with levosimendan as a remedial solution at the time of intensive care unit (ICU) admission were excluded from study. All patients received left coronary artery reimplantation, and 15 patients (37.5%) underwent concomitant mitral annuloplasty. Data were extracted retrospectively from our digital medical records, which covered the whole course from their initial hospitalization through the last follow-up visit.

Abbreviations: ALCAPA, anomalous origin of the left coronary artery from the pulmonary artery; LVEF, left ventricular ejection fraction; LCOS, low cardiac output syndrome; CPB, cardiopulmonary bypass; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; VIS, Vasoactive-Inotropic Score; AKI, acute kidney injury; pRIFLE, pediatric-modified risk, injury, failure and loss, and end-stage.

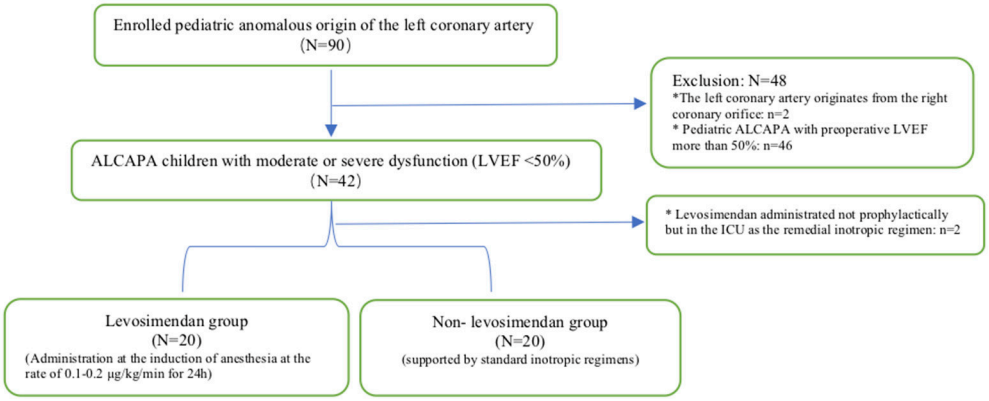

FIGURE 1 | Enrollment procedure. ALCAPA, anomalous origin of the left coronary artery from the pulmonary artery; LVEF, left ventricular ejection fraction; ICU, intensive care unit. *Represented the patient exclusion criteria.

Definition of ΔLVEF

All of the patient's cardiac systolic functions were assessed by transthoracic echocardiography at three time points (preoperative, day 7, and at follow-up ∼6 months later), and the baseline LVEF was collected on the day before surgery. The LVEF values on postoperative day 1 were not included because of incompleteness: there were missing data of more than 30%. We assumed the definition of ΔLVEF to evaluate cardiac function improvement, which was calculated as follows: (postoperative LVEF – preoperative LVEF)/preoperative LVEF × 100. After repair, baseline LVEF rose from 10 to 40%, which is different from a rise of 30–60%, and an ΔLVEF of 300 and 100%, respectively. The former would manifest a much more better recovery under the conditions of deteriorating cardiac function, which was the case before surgery, although both of the LVEF changes were 30%.

Vasoactive-Inotropic Score (VIS)

The VIS has been proposed as another indirect measurement to assess the hemodynamic conditions, whether improved or deteriorated. In the study, VIS was applied as: dopamine (μg/kg/min) + dobutamine (μg/kg/min) + [100 × epinephrine (μg/kg/min)] + [100 × norepinephrine (μg/kg/min)] + [10,000 × vasopressin (U/kg/min)] (12). The VIS at 1, 6, 12, 24, and 48 h after surgical repair was calculated separately for each group.

Criterion for Acute Kidney Injury (AKI)

The pediatric-modified Risk, Injury, Failure and Loss, and End-Stage (pRIFLE) system has been validated as the most sensitive criteria for identifying acute kidney injury (AKI) (13). Additionally, the estimated glomerular filtration rate required for pRIFLE assessment was derived from the most unbiased and sensitive Schwartz model formula, which was based on postoperative serum creatinine levels and patient height (14). The AKI in our study was qualified as early as within 12 postoperative hours.

Anesthesia Protocol

The general anesthesia technique was based on individual anesthesiologist preference. During induction, appropriate dosages of intravenous agents such as ketamine, midazolam, rocuronium, and sufentanil were combined with facemask oxygen and oral intubation was carried out. Both invasive blood pressure monitoring and blood gas analysis were achieved by radial artery catheterization, and the right internal jugular vein was cannulated for central venous pressure or left atrium pressure monitoring. Throughout the procedure, anesthesia maintenance was achieved by the continuous infusion of a combination of dexmedetomidine, propofol, sufentanil, and rocuronium at the appropriate dosage; additionally, all patients were mechanically ventilated with mixed air and oxygen; the oxygen level was 40–45%.

Surgical Technique

The surgical approach was achieved via median sternotomy, CPB, and coronary reimplantation, but the simultaneous mitral valvuloplasty was only considered whenever necessary. CPB consisted of aorta and bicaval cannulation, blood priming, antegrade cardioplegic arrest, and then mild hypothermia. First, the pulmonary and aortic trunks were transected and then the left coronary artery and it's attached pulmonary wall were resected. Then the left coronary artery was re-implanted into the aorta and, whenever necessary, the resected pulmonary wall was made into a coronary tunnel if there was a long distance between the aorta and coronary ostia. The defect in the pulmonary trunk was repaired with a pericardial patch, and the anastomosis of each main artery was completed separately. According to the identification of the grade and severity of mitral regurgitation, mitral valvuloplasty was performed if needed.

Administration of Levosimendan

All intra-operative inotropic management strategies were at the discretion of the attending anesthesiologists. We divided the pediatric patients with ALCAPA into the levosimendan group ($n = 20$) and the non-levosimendan group ($n = 20$).

TABLE 1 | Comparison of demographic parameters and surgical data.

	Levosimendan ($n = 20$)	Non-levosimendan ($n = 20$)	p-value
Male, *n* (%)	9 (45%)	12 (60%)	0.749
Age at operation, months, mean ± SD	7.5 (3.0–13.5)	8.5 (6.0–21.3)	0.532
Height, cm, median (IQR)	68.5 (60.0–74.8)	73.5 (66.3–89.3)	0.088
Weight, kg, median (IQR)	6.5 (5.4–8.9)	8.5 (6.6–10.8)	0.058
Left ventricular aneurysm, *n* (%)	1 (5%)	4 (20%)	0.342
Concomitant mitral annuloplasty, *n* (%)	8 (40%)	7 (35%)	0.744
LVEF			<0.01
<20%, *n* (%)	13 (75%)	2 (10%)	
20–30%, *n* (%)	3 (15%)	7 (35%)	
30–50%, *n* (%)	4 (20%)	11 (55%)	
CPB, min, median (IQR)	102.0 (88.3–126.8)	105.5 (94.5–116.5)	0.850
Aortic cross-clasp, min, median (IQR)	60.5 (48.0–71.0)	67.0 (53.5–89.3)	0.176

LVEF, left ventricular ejection fraction; CPB, cardiopulmonary bypass.

For the levosimendan group, no initial loading dosage was administered, but they were given a 24-h, 0.1–0.2 μg/kg/min continuous infusion after the procedure. Both groups received 3 μg/kg/min dopamine as a routine inotrope when being warmed during CPB, and if necessary, other medical regimens or mechanical supports could be applied at any time as a rescue to maintain both sufficient cardiac contractility and stable hemodynamics.

Endpoint

The primary outcome for our retrospective study was whether the prophylactic use of levosimendan could improve the cardiac function or not on day 7 and at follow-up to 180 days. Other outcomes included various in-hospital endpoints such as VIS, the length of ICU stay, duration of mechanical ventilation, peritoneal dialysis, and all-cause mortality though day 180. In addition, we analyzed the incidence of AKI, arrhythmia, the number of patients requiring perioperative circular support (as well as after being admitted to the ICU), and the rates of respiratory events such as re-intubation, tracheotomy, and postoperative pneumonia.

Statistical Analysis

We performed this retrospective analysis using SPSS, version 23 (IBM, Armonk, NY, USA).

Normally distributed continuous variables were presented as the mean ± standard distribution, whereas non-normally distributed data were presented as the medians with their interquartile ranges (IQR). Categorical variables were presented as frequencies and percentages. Group comparisons of the two types of variables above were used for the two-tailed *t*-test or the Mann–Whitney *U* test, chi-square test, or Fisher's exact test. Repeated measures analysis of variance was done when comparing the time course of the VIS between groups. We considered $p < 0.05$ as statistically significant.

RESULTS

Study Patient Characteristics

Forty pediatric patients (21 males and 19 females, 2 months−12 years old) undergoing ALCAPA repair in our medical center were reviewed. 20 patients were given levosimendan at anesthesia induction and the other 20 were not. The median age of the whole population at repair was 7.5 months (IQR, 4.5–18.0 months). The median weight was 8.1 kg (IQR, 5.9–9.5 kg). The mean LVEF was 27.2 ± 10.5%, and the patients in the levosimendan group suffered more severe left ventricular dysfunction. There were eight patients who underwent concomitant mitral annuloplasty in the levosimendan group compared with seven in the non-levosimendan group. There was no significant difference between groups in demographic parameters or surgical data, including CPB time or aortic cross-clasp time (**Table 1**).

Primary Outcome of Cardiac Function

Preoperative LVEF was revealed to be significantly lower in the levosimendan group than in the non-levosimendan group (22.5 ± 10.7 vs. 31.8 ± 8.1%, $p = 0.004$). Compared with the non-levosimendan group, on day 7 after coronary reimplantation, each median LVEF was still significantly lower in the levosimendan group (27.1 ± 8.9 vs. 37.5 ± 11.0%, $p = 0.002$; **Figure 2**). No significant difference in ΔLVEF was detected on day 7 or at follow-up ∼180 days later (median 30.8%, IQR −4.4 to 63.5% vs. median 15.1%, IQR −3.5 to 40.0%, $p = 0.560$; median 123.5%, IQR 56.1–226.0% vs. median 80.0% IQR 36.4–131.3%, $p = 0.064$; **Figure 3**). In addition, at follow-up, LVEF in nine patients (50.0%) in the levosimendan group and in 14 patients (73.7%) in the non-levosimendan group had increased more than 50% with the exception of three patients who died in the ICU.

VIS Variance

All 40 pediatric patients were simultaneously supported by dopamine at the time of repair and in the ICU. It was found that during surgery, 95% (19/20) of the levosimendan group required epinephrine to maintain cardiac contractility compared with 65.0% (13/20) of the non-levosimendan group ($p = 0.044$). After

admission to the ICU, four patients (20%) in the levosimendan group were maintained with vasopressin; however, no patient in the non-levosimendan group required vasopressin ($p = 0.106$; **Table 2**). Moreover, repeated measures analysis of variance for VIS implied no significant difference in the two groups ($p = 0.093$), nor was there any significant difference of interaction between group and time point ($p = 0.853$). There were significant changes in the postoperative VIS across different the time points of 1, 6, 12, 24, and 48 h ($p = 0.008$; **Figure 4**).

Other Postoperative Outcomes

There was a significant tendency toward longer ICU stays for those in the levosimendan group than for those in the non-levosimendan group (median 10.5 days, IQR 7.3–39.3 days vs. median 4.0 days, IQR 2.0–10.0 days, $p = 0.002$). All patients received continuous mechanical ventilation after being transferred to the ICU except for one patient who was extubated in the operating room for fast-track anesthesia, thus we did not include the duration of that patient's mechanical ventilation. The comparison of mechanical ventilation between groups did demonstrate statistical significance (median 146.0 h, IQR 76.5–888.0 h for the levosimedan group; median 27.0 h, IQR 11.0–75.0 h for the non-levosimendan group, $p = 0.002$). There were eight patients who underwent continuous or intermittent peritoneal dialysis in the levosimendan group whereas there were only two in the non-levosimendan group ($p = 0.028$). The incidence of AKI was 75% (15/20) in the levosimendan group and 95% (19/20) in the non-levosimendan group, which was not significant ($p = 0.184$).

In the non-levosimendan group, three patients had to be supported by extracorporeal membrane oxygenation (ECMO) because of difficulty in weaning off CPB due to LCOS (their preoperative LVEF was 29.2, 25, and 40%); ECMO support lasted for 4, 7, and 7 days, respectively. Eventually, all patients were successfully separated from CPB. Throughout the 180 postoperative days to follow-up, all-cause mortality was 10% (2 of 20) in the levosimendan group compared with 5% (1 of 20) in the non-levosimendan group, and three deaths occurred in the ICU. In the levosimendan group, two deaths were attributed to left ventricular failure on postoperative days 42 and day 40 (LVEF values at baseline were 10 and 34%, respectively), and the one death in the non-levosimendan group was attributed to extreme LCOS accompanied by acute respiratory distress syndrome on day 17 (LVEF value at baseline was 20%; **Table 3**).

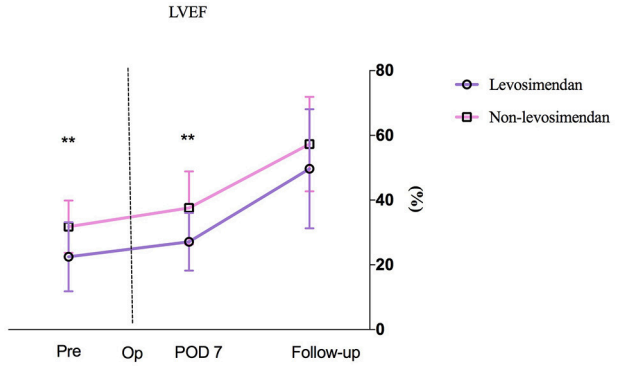

FIGURE 2 | A patient's LVEF at three time points: preoperation, on day 7 after surgery, and at follow-up. No mean LVEF on day 1 between the levosimendan and the non-levosimendan groups was compared because there were missing data of more than 30%. LVEF, left ventricular ejection fraction; Pre, preoperation; Op, operation; POD, postoperation. $^{**}p < 0.01$.

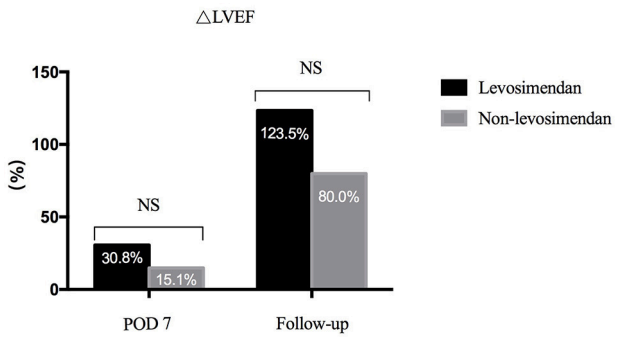

FIGURE 3 | Bar graph showing the ΔLVEF of the two groups. On day 7, there was no significance between the levosimendan and the non-levosimendan groups (median 30.8%, IQR −4.4 to 63.5% vs. median 15.1%, IQR −3.5 to 40.0%, respectively). In addition, no significant difference was revealed at their follow-up (median 123.5%, IQR 56.1–226.0% vs. median 80.0%, IQR 36.4–131.3%). LVEF, left ventricular ejection fraction; NS, no significance; POD, postoperation.

DISCUSSION

In our study cohort, levosimendan seemed to have a favorable association with post-surgical cardiac function recovery because the improvement of ΔLVEF was twice that of the non-levosimendan group on day 7, although no statistical significance was found and no trend of increasing VIS score was manifested in the levosimendan group. Furthermore, in the levosimendan group, no patient required ECMO support after infusion of levosimendan, whereas three patients in the non-levosimendan group did require ECMO because of poor cardiac conditions.

To the best of our knowledge, this is the first analysis that explores the effect of levosimendan solely within a pediatric population with ALCAPA with mildly or severely impaired left ventricular function undergoing left coronary artery reimplantation, although it is a retrospective study. In fact, there are very limited studies regarding levosimendan in the field of pediatric cardiac surgery compared with the adult population. Moreover, all of these studies were conducted in the field of pediatric congenital cardiac repair rather than zoning in on a unique complex lesion. The occurrence of ALCAPA itself carries a relatively higher risk, and the surgical reimplantation is defined as the risk-adjusted classification for congenital heart surgery category 3; and it is also characterized by critically poor cardiac function prior to repair.

In terms of the timing of levosimendan administration, there have been some different practice preferences revealed in clinical

TABLE 2 | Requirement for additional circular support regimens during perioperation.

	Levosimendan ($n = 20$)	Non-levosimendan ($n = 20$)	p-value
INTRAOPERATIVE MEDICAL CIRCULAR SUPPORT			
* Dopamine, *n* (%)	All	All	—
* Dobutamine, *n* (%)	18 (90)	15 (75)	0.407
* Epinephrine, *n* (%)	19 (95)	13 (65)	0.044
* Norepinephrine, *n* (%)	4 (20)	2 (10)	0.661
* Milrinone, *n* (%)	14 (70)	14 (70)	1.000
* Vasopressin, *n* (%)	Null	Null	—
POSTOPERATIVE MEDICAL CIRCULAR SUPPORT			
* Dopamine, *n* (%)	All	All	—
* Dobutamine, *n* (%)	20 (100)	17 (85)	0.231
* Epinephrine, *n* (%)	20 (100)	17 (85)	0.231
* Norepinephrine, *n* (%)	2 (10)	2 (10)	1.000
* Milrinone, *n* (%)	18 (90)	18 (90)	1.000
* Vasopressin, *n* (%)	4 (20)	0 (0)	0.106

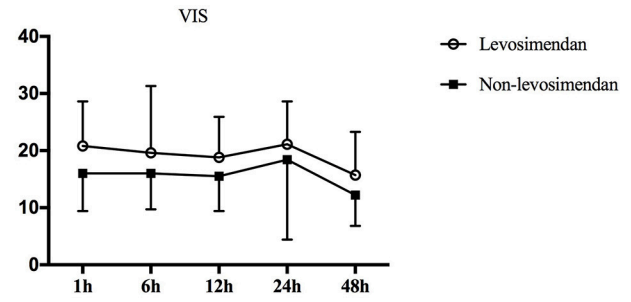

FIGURE 4 | Repeated measures of analysis of VIS variation over time in the two groups. $p_{group.} = 0.093$, $p_{time.} = 0.008$, $p_{time \times group.} = 0.853$. Therefore, levosimendan had no influence on VIS after surgery. VIS, vasoactive-inotropic score.

pediatric settings. Anesthesiologists in our center have adopted the mindset that levosimendan should be administered at the discretion of the clinician as early as possible, and generally be started at the induction of anesthesia to decrease the incidence of postoperative LCOS and to prevent any unwanted consequences. The retrospective but single-group analysis conducted by Amiet et al. (15) involving 62 pediatric patients in the ICU after cardiac surgery demonstrated that using levosimendan as a rescue treatment once LCOS occurred could increase central venous oxygen saturation and reduce lactate 24 h later. They reported that in their clinical routine, they even infused the drug 24 h before various complicated surgeries in newborns. On other occasions, levosimendan was only regarded as a Supplementary agent during CPB weaning (16–18) or even as a rescue when difficulty arose (15). The LEVO-CTS (10) trial even claimed that levosimendan administration started just before surgery was actually not effective enough to reduce or avoid cardiac damage.

Clinical work with levosimendan has supported the drug's efficacy in improving cardiac function, as shown by the majority of trials in the pediatric population, but the meta-analysis conducted by Hummel et al. (19) involving five randomized controlled trials where all 212 patients were younger than 5 years old and undergoing congenital heart surgery summarized that when compared with standard treatments, prophylactic levosimendan in fact had no clear beneficial effect on LCOS. Momeni et al. (20) adopted heart rate × systolic blood pressure as an indicator of cardiac oxygen demand among neonates and infants undergoing congenital cardiac surgery; compared with milrinone, levosimendan was demonstrated to decrease this rate-pressure index at 24 and 48 h postoperatively. Ricci et al. (16) demonstrated that after a 72-h infusion, levosimendan appeared to be an excellent inodilator and more potential to improve the postoperative hemodynamic state persistently than the standard inotropic regimens among neonates with risk-adjusted classification for congenital heart surgery categories three and four and with the use of CPB. Therefore, it is suggested that levosimendan is the best and most commonly used drug for occasions where other routine inotropic therapies are not adequate to maintain hemodynamic stability. This is particularly the case for seriously impaired left ventricular function (21, 22). Just as in our practice, levosimendan was appropriately administered to patients with ALCAPA who had initial lower LVEF. In theory, levosimendan improved cardiac output, and its vasodilation trait can effectively decrease systematic vascular resistance and avoid pressure or volume overload in the management of hemodynamics during ALCAPA surgical repair. In such cases, after the left coronary artery is re-implanted, levosimendan's coronary-dilating property could be a great asset to assure adequate oxygen supply for injured myocardial tissue. In addition, due to the pharmacodynamic properties of levosimendan, a 24-h infusion can prolong its hemodynamic effects for ∼7 days (23). Thus, this drug can support children through the most difficult postoperative phase in the ICU—that of postoperative cardiac deterioration. Moreover, ΔLVEF, reflecting the improvement of cardiac function to a more precise degree, was also greatly increased in the levosimendan group on day 7, Albeit cardiac functions were worse prior to surgical intervention. Our findings were consistent with the

TABLE 3 | The outcomes after left coronary artery reimplantation.

Postoperative outcomes	Levosimendan ($n = 20$)	Non-levosimendan ($n = 20$)	p-value
ICU duration, days, median (IQR)	10.5 (7.3–39.3)	4.0 (2.0–10.0)	0.002
Mechanical ventilation, hours, median (IQR)	146.0 (76.5–888.0)	27.0 (11.0–75.0)	0.002
AKI, *n* (%)	15 (75)	19 (95)	0.184
Risk	9 (45)	11 (55)	
Injury	5 (25)	8 (40)	
Failure	1 (5)	0 (0)	
Peritoneal dialysis, *n* (%)	8 (40)	2 (10)	0.028
All-cause mortality, *n* (%)	2 (10)	1 (5)	1.000
Arrhythmia, *n* (%)	3 (15)	2 (10)	1.000
ECMO, *n* (%)	0 (0)	3 (15)	0.231
Re-intubation, *n* (%)	6 (30)	2 (10)	0.235
Tracheotomy, *n* (%)	4 (20)	0 (0)	0.106
Postoperative pneumonia, *n* (%)	5 (25)	6 (30)	0.723

ICU intensive care unit, AKI acute kidney injury; ECMO, extracorporeal membrane oxygenation. In the item of mechanical ventilation, the sample size in levosimendan group was 19 for one patient was conducted for fast track and extubated in the operating room.

prospective clinical trial conducted by Lechner et al., who enrolled 39 neonates and infants undergoing open heart surgery and then compared the effect of prophylactic levosimendan against prophylactic milrinone administered after CPB. This trial indicated that changes in cardiac index were similar despite the fact that the levosimendan cohort presented with lower cardiac output prior to cardiac repair (17). Optimistically, there was no increase in VIS within 48 h and no ECMO requirement presented after levosimendan was used, which also indirectly affirmed its role in cardiac protection after a period of worse cardiac function prior to surgery. However, throughout the whole perioperation period, the number of patients requiring catecholamine administration in the levosimendan group was slightly higher than that of the non-levosimendan group; in particular, the use of epinephrine reached statistical significance. In the long-term follow-up to day 180, the ΔLVEF in the levosimendan cohort could be improved although it was not significant ($p = 0.064$ between the two groups); however, this is likely to be caused by multiple factors because it cannot be attributed to the performance of levosimendan independently.

Pediatric patients given levosimendan in our cohort had a longer ICU length of stay and mechanical ventilation support. These two unsatisfactory events may be associated with their persistent myocardial dysfunction. This may have also been a result of more patients requiring a second intubation for respiratory insufficiency and even necessitated a tracheotomy due to longer ventilation or deteriorating pneumonia. However, the requirement for peritoneal dialysis was just 4-fold that of the non-levosimendan group (8/2). In Ricci's cohort, renal function was replaced by urine output and peritoneal dialysis use, and a neutral outcome after levosimendan administration was demonstrated (16). However, a retrospective series conducted by Amiet et al. found that levosimendan could increase diuresis from 1.1 to 3.5 mL/kg/h by improving cardiac output (15). In our clinical practice, all 10 cases of peritoneal dialysis were applied to correct a series of consequences such as oliguria or anuria, which was secondary to the postoperative cardiac function of critically ill patients. Therefore, levosimendan is likely to have no potential in helping to avoid cardiac-renal syndrome among children with ALCAPA undergoing repair, but the incidence of AKI was 20% lower in the levosimendan group than in the non-levosimendan group. In our study, AKI was defined as early AKI that occurred within 12 h of the operation, and some late AKI cases were not identified because of the lack of late serum creatinine levels.

In fact, it is not certain that levosimendan, in our study, had any negative effect on postoperative 180-days all-cause mortality in our limited pediatric population despite the fact that two deaths occurred in the levosimendan group and only one in the control group. At present, only a few trials have discussed mortality in pediatric cohorts and negative conclusions have prevailed. In Ricci's study (16), there was also concern about mortality in the ICU among neonates undergoing cardiac surgery, with no reduced mortality observed in the levosimendan group. The meta-analysis mentioned previously (19) summarized that prophylactic levosimendan had no positive influence on mortality. Furthermore, the two multi-center and placebo-controlled trials published recently, the CHEETAH trial (11) and LEVO-CTS trial (10), have demonstrated that levosimendan could not reduce postoperative 30- and 90-days mortality, respectively, among adult patients with left ventricular dysfunction requiring cardiac surgery.

At present, levosimendan has been reported in most of the literature on regarding pediatric patients as having no adverse effects and as being well-tolerated. For instance, the randomized controlled trials of both Momeni (20) and Ricci (16) indicated that the postoperative heart rate in the levosimendan group was significantly lower than that of their own control groups. In a retrospective observational study, only one of 32 pediatric patients receiving levosimendan developed severe hypotension, with a diastolic blood pressure below 45 mm Hg, and the infusion had to be stopped 5 h later (24). However, we did record

that after infusing levosimendan, there was one ventricular tachycardia case, one case of ventricular premature beat, and one supraventricular tachycardia case; however, no case of atrial fibrillation was observed. In the non-levosimendan group, however, there was one patient with atrial fibrillation and another with ventricular fibrillation. All of these cases were immediately treated with lidocaine or amiodarone. After a 24-h infusion, four patients in the levosimendan group required vasopressin to correct extreme hypotension because two cases could not be corrected with a massive dosage of norepinephrine, and another two had to be directly supported with vasopressin due to the patient's critical condition. We speculated that this was most likely due to levosimendan because of its vasodilation effect, although no loading dosage was given and the infusion speed was within a safe range. No administration of levosimendan was stopped during the therapy process. Whether hypotension, tachycardia, or other arrhythmias were incurred because of levosimendan administration is not certain, because this series is a retrospective study and multiple uncertain variables coexist.

Our study cohort highlights the notion that the prophylactic infusion of levosimendan is an ideal inotrope for preventing the deterioration of cardiac function after surgical intervention for ALCAPA, although other postoperative outcomes and mortality must be further investigated by future prospective and large-sample trials among pediatric patients. Another notable future direction is that levosimendan is indicated for the critically ill population who suffer from marked cardiac dysfunction before surgery.

There are some limitations to our study that must be considered. First, it is a single-center retrospective, non-randomized study and some unknown heterogeneities that we were unable to control had some impact on our analysis. The phenomenon of ALCAPA itself is a malign cardiac anomaly, and our perioperative hemodynamic management tactic is one of the most pivotal steps to support these patients through this difficult treatment phase. However, patient prognosis is very dependent on early diagnosis and early surgery and is also associated with individual preoperative cardiac function and surgical technique. Therefore, it is not clear whether the lack of improvement in LVEF was totally attributable to levosimendan in our study. Second, the infusion rate differed among individuals although it was always within a safe range (0.1–0.2 μg/kg/min) because every anesthesiologist carried out his/her appropriate inotropic scheme based on the patient's preoperative condition. Third, no related continuous biomarker measurements were acquired in our study, thus we could not make an evaluation of metabolic and cardiac injury conditions as a result of levosimendan. Fourth, the lack of long-term outcomes such as mortality, readmission to hospital, and the occurrence of heart failure limit our study. Finally, only a small number of patients with ALCAPA were enrolled, as it is a rare congenital heart disease, and this could bias the result. Overall, the current available literature is not sufficient to point out the benefits and risks of levosimendan in the pediatric population, especially for extremely critical or complicated congenital cardiac surgery, and further academic work is required to address its clinical effectiveness.

CONCLUSIONS

The prophylactic infusion of levosimendan is confirmed to be a beneficial therapy in favor of recovering cardiac function among pediatric patients with ALCAPA and impaired left ventricular function who undergo surgical repair. However, this is a retrospective and observational analysis, and more rigid prospective studies are required to investigate its effect on a series of postoperative outcomes in the future.

ETHICS STATEMENT

This retrospective study was approved by the Institutional Review Boards of Fuwai Hospital, and informed consent was waived because of its retrospective nature.

AUTHOR CONTRIBUTIONS

All authors contributed extensively to the work presented in this paper. YW, JG, and CW proposed the idea of this investigation. SS, JW, YG, SW, and JS were responsible for the collection of data and material. CW helped with the statistical analysis and wrote the manuscript. YW and YP helped to revise the manuscript. All authors read and approved the final manuscript.

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REFERENCES

1. Keith JD. The anomalous origin of the left coronary artery from the pulmonary artery. *Br Heart J.* (1959) 21: 149–61.
2. Lange R, Vogt M, Horer J, Cleuziou J, Menzel A, Holper K, et al. Long-term results of repair of anomalous origin of the left coronary artery from the pulmonary artery. *Ann Thorac Surg.* (2007) 83:1463–71. doi: 10.1016/j.athoracsur.2006.11.005
3. Laks H, Ardehali A, Grant PW, Allada V. Aortic implantation of anomalous left coronary artery. An improved surgical approach. *J Thorac Cardiovasc Surg.* (1995) 109:519–23. doi: 10.1016/S0022-5223(95)70283-0
4. Wesselhoeft H, Fawcett JS, Johnson AL. Anomalous origin of the left coronary artery from the pulmonary trunk. Its clinical spectrum, pathology, and pathophysiology, based on a review of 140 cases with seven further cases. *Circulation* (1968) 38:403–25.
5. Chandler HK, Kirsch R. Management of the low cardiac output syndrome following surgery for congenital heart disease. *Curr Cardiol Rev.* (2016) 12:107–11. doi: 10.2174/1573403X12666151119164647

6. Yokoshiki H, Katsube Y, Sunagawa M, Sperelakis N. Levosimendan, a novel Ca^{2+} sensitizer, activates the glibenclamide-sensitive K+ channel in rat arterial myocytes. *Eur J Pharmacol.* (1997) 333:249–59. doi: 10.1016/S0014-2999(97)01108-4
7. Kersten JR, Montgomery MW, Pagel PS, Warltier DC. Levosimendan, a new positive inotropic drug, decreases myocardial infarct size via activation of K(ATP) channels. *Anesth Analg.* (2000) 90:5–11. doi: 10.1097/00000539-200001000-00003
8. Hasenfuß G, Pieske B, Castell M, Kretschmann B, Maier LS, Just H. Influence of the novel inotropic agent levosimendan on isometric tension and calcium cycling in failing human myocardium. *Circulation* (1998) 98:2141–7. doi: 10.1161/01.CIR.98.20.2141
9. Altenberger J, Parissis JT, Costard-Jaeckle A, Winter A, Ebner C, Karavidas A, et al. Efficacy and safety of the pulsed infusions of levosimendan in outpatients with advanced heart failure (LevoRep) study: a multicentre randomized trial. *Eur J Heart Fail.* (2014) 16:898–906. doi: 10.1002/ejhf.118
10. Mehta RH, Leimberger JD, van Diepen S, Meza J, Wang A, Jankowich R, et al. Levosimendan in patients with left ventricular dysfunction undergoing cardiac surgery. *N Engl J Med*. (2017) 376:2032–42. doi: 10.1056/NEJMoa1616218
11. Landoni G, Lomivorotov VV, Alvaro G, Lobreglio R, Pisano A, Guarracino F, et al. Levosimendan for hemodynamic support after cardiac surgery. *N Engl J Med.* (2017) 376:2021–31. doi: 10.1056/NEJMoa1616325
12. Gaies MG, Gurney JG, Yen AH, Napoli ML, Gajarski RJ, Ohye RG, et al. Vasoactive-inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass. *Pediatr Crit Care Med.* (2010) 11:234–8. doi: 10.1097/PCC.0b013e3181b806fc
13. Lex DJ, Toth R, Cserep Z, Alexander SI, Breuer T, Sapi E, et al. A comparison of the systems for the identification of postoperative acute kidney injury in pediatric cardiac patients. *Ann Thorac Surg.* (2014) 97:202–10. doi: 10.1016/j.athoracsur.2013.09.014
14. Zappitelli M, Joseph L, Gupta IR, Bell L, Paradis G. Validation of child serum creatinine-based prediction equations for glomerular filtration rate. *Pediatr Nephrol.* (2007) 22:272–81. doi: 10.1007/s00467-006-0322-0
15. Amiet V, Perez MH, Longchamp D, Boulos Ksontini T, Natterer J, Plaza Wuthrich S, et al. Use of levosimendan in postoperative setting after surgical repair of congenital heart disease in children. *Pediatr Cardiol.* (2018) 39:19–25. doi: 10.1007/s00246-017-1718-2
16. Ricci Z, Garisto C, Favia I, Vitale V, Di Chiara L, Cogo PE. Levosimendan infusion in newborns after corrective surgery for congenital heart disease: randomized controlled trial. *Intensive Care Med.* (2012) 38:1198–204. doi: 10.1007/s00134-012-2564-6
17. Lechner E, Hofer A, Leitner-Peneder G, Freynschlag R, Mair R, Weinzettel R, et al. Levosimendan versus milrinone in neonates and infants after corrective open-heart surgery: a pilot study. *Pediatr Crit Care Med.* (2012) 13:542–8. doi: 10.1097/PCC.0b013e3182455571
18. Ebade AA, Khalil MA, Mohamed AK. Levosimendan is superior to dobutamine as an inodilator in the treatment of pulmonary hypertension for children undergoing cardiac surgery. *J Anesth.* (2013) 27:334–9. doi: 10.1007/s00540-012-1537-9
19. Hummel J, Rucker G, Stiller B. Prophylactic levosimendan for the prevention of low cardiac output syndrome and mortality in paediatric patients undergoing surgery for congenital heart disease. *Cochrane Database Syst Rev.* (2017) 8:CD011312. doi: 10.1002/14651858.CD011312.pub3
20. Momeni M, Rubay J, Matta A, Rennotte MT, Veyckemans F, Poncelet AJ, et al. Levosimendan in congenital cardiac surgery: a randomized, double-blind clinical trial. *J Cardiothorac Vasc Anesth.* (2011) 25:419–24. doi: 10.1053/j.jvca.2010.07.004
21. Suominen PK. Single-center experience with levosimendan in children undergoing cardiac surgery and in children with decompensated heart failure. *BMC Anesthesiol.* (2011) 11:18. doi: 10.1186/1471-2253-11-18
22. Harrison RW, Hasselblad V, Mehta RH, Levin R, Harrington RA, Alexander JH. Effect of levosimendan on survival and adverse events after cardiac surgery: a meta-analysis. *J Cardiothorac Vasc Anesth.* (2013) 27:1224–32. doi: 10.1053/j.jvca.2013.03.027
23. Lilleberg J, Laine M, Palkama T, Kivikko M, Pohjanjousi P, Kupari M. Duration of the haemodynamic action of a 24-h infusion of levosimendan in patients with congestive heart failure. *Eur J Heart Fail.* (2007) 9:75–82. doi: 10.1016/j.ejheart.2006.04.012
24. Vilaboa Pedrosa C, Martinez Roca C, Yanez Gomez P, Martin Herranz MI. Experience with levosimendan in 32 paediatric patients. *Pediatr Cardiol.* (2015) 36:1038–41. doi: 10.1007/s00246-015-1117-5

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Challenges in Pediatric Cardiac Anesthesia in Developing Countries

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Introduction: Approximately 90% of a million children worldwide born with congenital heart defect do not have an access to adequate pediatric cardiac care. The World Society for Pediatric and Congenital Heart Surgery, established in 2006 shifted the focus from providing individual pediatric cardiac care to developing global standards for the practice of pediatric cardiac surgery and professional education of the local teams.

Materials and Methods: After recognizing the challenges of the local team regarding providing safe anesthesia and functioning as a broader team, we have focused our education on simplifying anesthetic procedures and advancing structured team approach. The appropriate selection of patients and simplifying anesthetic technique should be the standard of care. We introduced structured approach to daily education using just in time teaching, case based discussions and simple skill training simulation sessions. Furthermore, we enhanced team-training approach applying tools such as WHO surgical safety checklist and implementation manual, SAFE communication, introducing KDD with SMART aim, SCAMPs, advanced protocols of care and culture change tools.

Results: Following a significant number of short missions to developing centers we have, within NGO, succeeded to support building and maintaining several local pediatric cardiac centers with structured approach to anesthesia and team building.

Conclusion: The appropriate selection of patients is one of the most important contributing factors for decreasing morbidity and mortality rate in pediatric cardiac surgery patients. The anesthesia technique for pediatric cardiac procedures should be aimed at fast-track surgery, with early extubation as a goal. Regional blocks such as paravertebral and caudal should be considered for perioperative pain control. By introducing structured approach to daily education and by enhancing team-training approach we have contributed evolving sustainable pediatric cardiac centers in developing countries.

Keywords: pediatric, cardiac, humanitarian, anesthesia, developing, mortality, education

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INTRODUCTION

It is striking that ∼90% of a million children worldwide born with congenital heart defect (CHD) do not have an access to adequate pediatric cardiac care (1). Incidence of CHD ranges from 5 to 14 cases per 1,000 live births with higher absolute number in developing countries (2–4). Acquired heart diseases as rheumatic heart disease, endomyocardial fibrosis, Chagas, and Kawasaki disease

are common in children in developing countries and frequently lead to premature death as a result of suboptimal medical care (1).

According to World Health Organization (WHO) a populations of two million people, requires a pediatric cardiac center performing 300–500 operations annually. That is not always the case in developing countries where, in specific areas, populations between 15 and 70 million are without a single pediatric cardiac center (5). In Asia, there is approximately one pediatric cardiac center for population of 16 million. The distribution is even less in Africa where one pediatric cardiac center covers population of 33 million (6).

Various non-governmental humanitarian organizations (NGOs) have been providing pediatric cardiac surgeries in developing countries for many years. Majority of them were short-term missions called "surgical safaris" (7). The World Society for Pediatric and Congenital Heart Surgery established in 2006 shifted the focus from providing individual pediatric cardiac care to developing global standards for the practice of pediatric cardiac surgery and professional education of the local teams (5). Furthermore, the Lancet Commission on Global Surgery published in 2015 stated that all people should have access to safe, high-quality surgical and anesthesia care. The purpose of The Lancet Commission on Global Surgery is to make this vision a reality for provision of quality surgical and anesthesia care for all (8).

MATERIALS AND METHODS

Establishing Sustainable Pediatric Cardiac Centers

A Journey of a Thousand Miles Begins With a Single Step

Chinese philosopher Laozi (circa 604 BCE - circa 531 BCE)

Many anesthesiologists join NGOs in various missions to developing countries and function as a part of clinical, teaching, and research projects. Participating in NGO expeditions to Africa and Asia within pediatric cardiac team we have previously been exposed not only to the challenge of providing safe pediatric cardiac surgery but similarly to the challenge of providing safe general anesthesia to pediatric cardiac patients. Consequently, our NGO has identified existing local pediatric cardiac centers with potential for growing and developing into sustainable pediatric cardiac centers. Currently, the primary aim of our team is no longer to provide pediatric cardiac care. Our primary aim is focused on providing training for the local team and advancing their ability to independently diagnose and treat pediatric cardiac patients.

Pathway

Since 2007, our NGO visited India, Malaysia, Nigeria, Kenya, Tanzania, and Mauritius. The centers visited in developing countries were carefully identified. Our teams visited centers with existing pediatric cardiac program where the basic equipment required and basic infrastructure were already in place. One team contained pediatric cardiac surgeon, surgical fellow, cardiologist, anesthesiologist, perfusionist, two intensivists, and two intensive care nurses. Our teams were visiting the local center for 1 week at a time. Continuation was provided for several months and occasionally for more than a year if required. Furthermore, our team provided a function of long-term, off-site collaborator for sustainable local centers.

Pediatric Cardiac Anesthesia and Team Approach

Hence the visiting centers had basic equipment and infrastructure in place, the major challenge for the visiting anesthesiologist was not lack of equipment required. In our experience, the major challenge was lack of dedicated and sufficiently educated pediatric cardiac anesthetic team. The local anesthetic team was mainly adult trained and frequently required basic education about anatomy, physiology and appropriate anesthetic agents used for induction and maintenance of anesthesia for pediatric cardiac patients. Nevertheless, the support was required in selection of adequate endotracheal tube size (ETT), laryngoscope, intubation and ventilation techniques, ETT securing techniques, as well as selection of arterial and central line sizes, ultrasound guided insertion techniques and securing techniques. Lack of knowledge regarding cardiopulmonary bypass cannulas, circuit and oxygenator sizes (**Figure 1**) as well as insufficient supply of blood and blood products were often a supplementary challenge. In addition, the persistent safety treats were infection control due to reusing and recycling disposable equipment by local team (**Figure 2**).

Transthoracic and transoesophageal echocardiography machines were available in majority of the centers. None of the local anesthesiologists performed echocardiography. Echocardiography was performed by local cardiologists. Our team focused on improving basic pediatric cardiac anesthesiology techniques as a primary goal of our missions rather than introducing advanced echocardiography teaching for local anesthetic team.

Moreover, we have identified a second considerable challenge for local team: Functioning as a broad team of experts. Common aims, team briefs, safety checks, and structured protocol based approach to patient care were not existing.

The local centers did not have a structured method of data collection in place related to anesthetic or surgical procedures prior to our visits. Therefore, our observations were limited to descriptive rather than objective study in order to measure the impact of our implementations.

Ways to Make It Better

After recognizing the challenges of the local team regarding providing safe anesthesia and functioning as a team we have focused our education on simplifying anesthetic procedures and advancing structured team approach in patient care.

Providing Safe Anesthesia

Teaching and Education

One of the goals of our team was introducing "Just in time teaching" (9). Daily education in relation to intubation and ventilation techniques, ultrasound guided line insertion

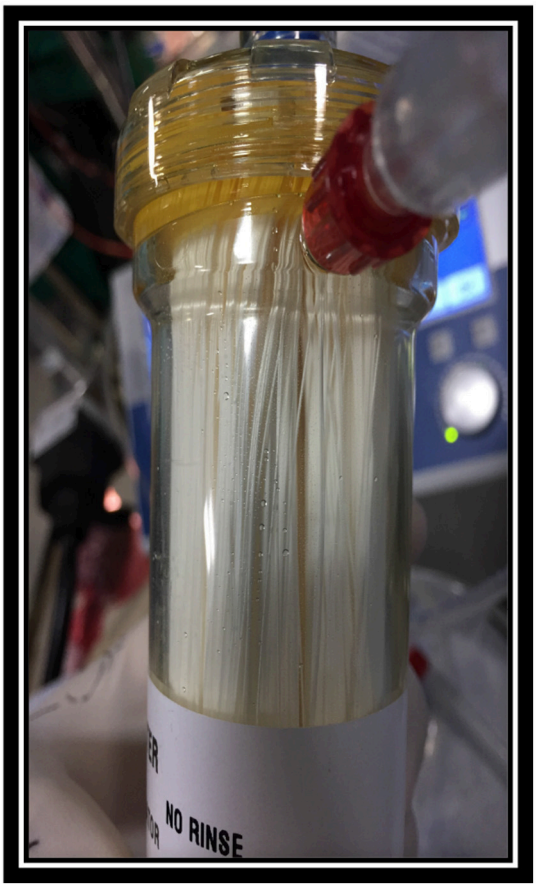

FIGURE 1 | Reusing large adult oxygenator. Private collection India 2016.

FIGURE 2 | Reusing syringes. Private collection India 2.

FIGURE 3 | Teaching session. Private collection India 2016.

(**Figure 3**), anesthetic agents and vasopressor support before and after cardiopulmonary bypass was provided. Weight and age related charts for ETT, laryngoscope, arterial and central line sizes as well as cardiopulmonary bypass cannulas, circuit and oxygenator sizes were introduced together with securing techniques for ETT and vascular lines.

Furthermore, we have implemented structured case based discussions and basic simulation skill training according to current anesthetic guidelines[1]. Chosen subjects of discussion reflected the majority of cases treated in the local center. Difficult airway training using difficult airway cards was conducted[2].

In order to minimize perioperative morbidity rate, infection prevention, and control were introduced according to current standards[3].

We provided structured and simplified approach to:

Case Selection

- Appropriate selection of cases including patients with simple cardiac defects (**Figure 4**)
- Patients with high morbidity and mortality risk or risk for complex surgical procedures should be transferred to highly specialized centers
- Procedures with a high risk of major blood loss or risk of prolonged postoperative intensive care should not be undertaken

Preoperative Care

- Preoperative intravenous fluid resuscitation should be considered as dehydration and malnutrition were recurrent patient related issues

[1]https://www.rcoa.ac.uk/system/files/GPAS-2018-10-PAEDIATRICS.pdf (Assessed May 17, 2018).
[2]https://www.das.uk.com/guidelines/paediatric-difficult-airway-guidelines (Assessed May 17, 2018).
[3]https://www.nice.org.uk/guidance/QS61 (Assessed May 17, 2018).

- Premedication should be considered
- The care providers should be using universal precautions for possible exposure to infectious diseases (HIV, hepatitis), and as infection prevention

Type of Anesthesia

- Available appropriate anesthetic agents should be used in weight related doses
- The anesthesia technique should be aimed at fast-track surgery with early extubation in operating room (OR)
- Regional blocks such as paravertebral and caudal should be considered for perioperative pain control

Cardiology, surgical, perfusion, and intensive care training was undertaken simultaneously by other team members.

Structured Daily Team Approach

In order to help the local team in maintaining the structure and competencies we have developed and introduced several standardized perioperative procedures tailored for the requirements of the local team:

- WHO surgical safety checklist and implementation manual[4]
- SAFE communication (situation awareness for everyone)[5]
- Key Driver Diagrams (KDD) with SMART (specific, measurable, achievable, relevant, time-bound) aim (10)
- SCAMPs (Standardized Clinical Assessment and Management Plan) (11)
- Culture change tools (flat organizational structure)[6].

RESULTS

Supporting a pediatric cardiac center in developing countries in order to become self-sufficient and well-functioning requires time, individual enthusiasm, financial and personal investment, hard work, and dedication of NGO members. After a significant number of short missions to selected centers we have, within NGO, succeeded to support building and maintaining several local pediatric cardiac centers using structured approach to cardiology, surgery, anesthesia perfusion, and intensive care education together with team building strategy. Sustained centers have developed designated cardiology, surgical, anesthetic, perfusion, and intensive care teams and advanced team building skills. Currently, the patient care is provided on significantly higher level than prior to our visits rated by local team. Sustained centers report to have lower morbidity and mortality rate, and high success in selected surgical procedures. One center successfully provides extracorporeal membrane oxygenation (ECMO) in selected cases after collaboration with our team. Our team still functions as long-term, off-site collaborator for sustainable local centers. We are planning to provide overseas fellowships to local staff in order to advance their education and stimulate them to use the skills on return to their home country. Beyond that, we have established friendship for life.

FIGURE 4 | Case selection. Private collection, India 2017.

After several years of experience our motto became the famous phrase: "The success should not be measured by the number of successful operations of any given mission, but by the successful operations that our colleagues perform after we leave" (12).

After establishing the basic care for pediatric cardiac patients we are currently aiming to establish data collection and objective measures for skill acquisition, success rate, team performance, morbidity, and mortality.

Correspondence Within Teams

Team interaction within visiting and local team is very important for successful collaboration. Friendly atmosphere with zero tolerance for judgmental or discriminating behavior is fundamental for team building. Well-educated, compliant members facing challenges with professionalism are the crucial element for successful correspondence within teams. Not long ago, somebody asked me what was absolutely essential to bring on the trip. I replied, firstly your smile, and then your ultrasound equipment.

DISCUSSION

WHO supports the fact that "Safe surgery saves lives" (13, 14). Anesthesia is a specialty with low status in many developing countries and anesthetic services are often underdeveloped (15). It is well known that the majority of pediatric-related mortality is due to airway-related complications (16, 17). Similarly, it is a recognized fact that the number of trained pediatric cardiac anesthesiologist in developing countries is very small (18). That leads to increasing population of nonmedical anesthetic providers trained without appropriate supervision (19). A part of the anesthetic residents undertake their speciality training outside the country and frequently stay in developed countries (20). All of that contributes to two to three times increase in anesthesia related morbidity and mortality in the

[4] http://www.who.int/patientsafety/safesurgery/ss_checklist/en/ (Assessed May 17, 2018).

[5] www.steris.com (Assessed May 17, 2018).

[6] https://bcpsqc.ca/resource/culture-change-toolbox/, Culture toolbox (Assessed May 17, 2018).

developing world compared with decreasing anesthesia related complications in developed countries (21–23).

Anesthesia is a technology-based specialty and relay on functioning monitoring equipment (2). Providing anesthesia in developing countries becomes highly challenging considering the fact that more than 19% of operation theaters worldwide have no pulse oxymeter (23, 24). According to millennium development program (Goal-4), oxygen supply and pulse oxymeter should be provided to every healthcare facilities especially involving pediatric patients (25). Ultrasound machine for line insertions and regional blocks is commonly not available, which increases the risk of complications furthermore. Even well-established centers have unreliable supply of basic utilities including electricity, water and oxygen (20, 26, 27), and more than 70% of developing countries lack a national blood transfusion service (1, 16). In addition, there is frequently shortage of resuscitative equipment, airway and suction devices and other intraoperative monitoring systems (24). Likewise, the increasing trend of corruption and neglect is related to the impaired healthcare systems in developing countries (25). Combination of mentioned contributing factors has a negative impact on morbidity and mortality in developing countries (24, 28). To address this concern, the main focus of visiting anesthetic team should be to reduce total perioperative and anesthetic-related mortality with evidence-based best practice. Establishing local sustainable pediatric cardiac centers in developing countries providing both initial and continued training has made the greatest impact on mortality rates in the last decade (18). It is worth remembering that adequate education of local team requires involvement of local and central government (28).

Our NGO visited existing local pediatric cardiac centers with potential for growing and developing into sustainable pediatric cardiac centers. In our experience, the major challenge of pediatric cardiac anesthesia was lack of dedicated and sufficiently educated team. The primary aim of our team was to provide training for the local team in order to advance their ability to independently diagnose and treat pediatric cardiac patients. Previous review highlights that visiting anesthesiologist frequently provides pediatric cardiac anesthesia aiming to educate local team (18). Several international Internet sites are found to be helpful tool to local team. The online tutorial of the week available on the World Federation of Societies of Anaesthesiologists (WFSA) website at http://www.anaesthesiologists.org and textbooks from the World Anesthesia Society, are useful resources of education for local team (29). Furthermore, WFSA pediatric committee offers overseas fellowships, and supports international Teach The Teachers courses (30). Overseas fellowships can provide the longer-term solution for education of the local team (31).

It is well-known that the role of simulation is highly important in skill and team training of the local team. The mannequin-based resuscitation training is found to be very effective (32, 33). Significant mortality reduction in developing countries was achieved with simulation training in newborn resuscitation (34). In general, most of the anesthesia-related cardiac events are preventable (35). Careful labeling of medications (**Figure 5**) and resuscitation equipment including difficult airway carts can improve patient safety. Our team has managed to introduce simple anesthetic protocols and charts for local team allowing easy interpretation and use. We have developed structured approach to daily education establishing just in time teaching, case based discussions and simple skill training simulation sessions. Furthermore, we have enhanced team-training approach applying tools such as WHO surgical safety checklist and implementation manual, SAFE communication, introducing KDD with SMART aim, SCAMPs, advanced protocols of care and culture change tools. By introducing structured approach to daily education and by enhancing team-training approach we have contributed evolving sustainable pediatric cardiac centers in developing countries.

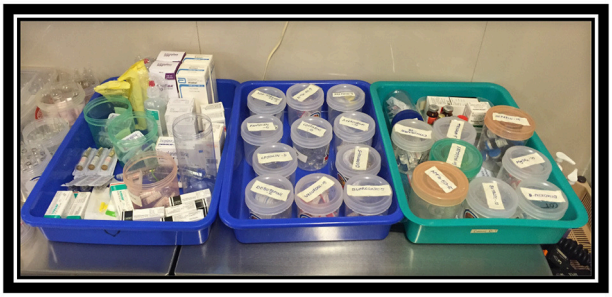

FIGURE 5 | Labeling of medication. Private collection India 2016.

Limitations of the Study

The local centers did not have a structured method of data collection in place related to anesthetic or surgical procedures prior to our visits. Therefore, this study is subjective and observational limited to description of methods and techniques. Currently, the impact of our implementations is rated by local team. Sustained centers report to have lower morbidity and mortality rate, and high success in selected surgical procedures.

CONCLUSION

Establishing local sustainable pediatric cardiac centers in developing countries providing both initial and continued training has made the greatest impact on mortality rates in the last decade (18). It requires careful determination of adequate center with potential for growing into sustainable pediatric cardiac center. The appropriate selection of cases including patients with simple cardiac defects is one of the most important contributing factors for decreasing morbidity and mortality rate in pediatric cardiac surgery patients. Anesthesia technique is a global challenge. The main focus of visiting anesthetic team should be to reduce total perioperative and anesthetic-related mortality with evidence-based best practice. Simplification of the care should be the primary anesthetic technique for pediatric cardiac procedures, and should be aimed at fast-track surgery, with early extubation as a goal. Regional blocks such as paravertebral and caudal should be considered for perioperative pain control.

Correspondingly, team performance is a considerable challenge for local team.

By introducing structured approach to daily education using just in time teaching, case based discussions and simple skill training simulation sessions, together with enhancing team-training approach by applying tools such as WHO surgical safety checklist and implementation manual, SAFE communication, KDD with SMART aim, SCAMPs, advanced protocols of care and culture change tools we have contributed evolving sustainable pediatric cardiac centers in developing countries.

AUTHOR CONTRIBUTIONS

The author confirms being the sole contributor of this work and has approved it for publication.

REFERENCES

1. Hodges SC, Walker IA, Bosenberg AT. Paediatric anaesthesia in developing countries. *Anaesthesia* (2007) 62(Suppl. 1):26–31. doi: 10.1111/j.1365-2044.2007.05294.x
2. Hoffman, JIE. The global burden of congenital heart disease. *Cardiovasc J Afr.* (2013) 24:141–5. doi: 10.5830/CVJA-2013-028
3. Liu J. Challenges and progress of pediatric cardiac surgery in Shanghai Children's Medical Center: a 25-year solid collaboration with project HOPE. *Semin Thac Cardiovasc Surg Pediatr Card Surg Ann.* (2009) 12:12–8. doi: 10.1053/j.pcsu.2009.01.020
4. Kumar R. Congenital Heart Disease management in developing countries. *Pediatr Cardiol.* (2003) 24:311. doi: 10.1007/s00246-002-0422-y
5. Yacoub MH. Establishing pediatric cardiovascular services in the developing world: a wake-up call. *Circulation* (2007) 116:1876–8. doi: 10.1161/CIRCULATIONAHA.107.726265
6. Neirotti R. Paediatric cardiac surgery in less privileged parts of the world. *Cardiol Young* (2004) 14:341–6. doi: 10.1017/S1047951104003191
7. Antonio FC. Paediatric and congenital cardiac surgery in emerging economies: surgical 'safari' versus educational programmes. *Interact Cardiovasc Thorac Surg.* (2016).23:163–7. doi: 10.1093/icvts/ivw069
8. Meara JG, Leather AJ, Hagander L, Alkire BC, Alonso N, Ameh EA, et al. Global Surgery 2030: evidence and solutions for achieving health, welfare, and economic development. *Lancet* (2015) 386:569–624. doi: 10.1016/S0140-6736(15)60160-X
9. Novak G, Patterson ET, Gavrin AD, Christian W. *Just-In-Time Teaching: Blending Active Learning with Web Technology*. Upper Saddle River, NJ: Prentice Hall (1999).
10. Britto MT, Fuller S, Kaplan HC, Kotagal, U, Lannon C, Margolis PA, et al. Using a network organisational architecture to support the development of Learning Healthcare Systems. *BMJ Qual Saf.* (2018). 1–10. doi: 10.1136/bmjqs-2017-007219
11. Rathod RH, Farias M, Friedman KG, Graham D, Fulton DR, Newburger JW, et al. A novel approach to gathering and acting on relevant clinical information: SCAMPs. *Congenit Heart Dis.* (2010) 5:343–53. doi: 10.1111/j.1747-0803.2010.00438.x
12. Backer CL. Humanitarian congenital heart surgery: template for success. *J Thorac Cardiovasc Surg.* (2014) 148:2489–90. doi: 10.1016/j.jtcvs.2014.09.013
13. Weiser TG, Regenbogen SE, Thompson KD, Haynes AB, Lipsitz SR, Berry WR, et al. An estimation of the global volume of surgery: a modelling strategy based on available data. *Lancet* (2008) 372:139–44. doi: 10.1016/S0140-6736(08)60878-8
14. Haynes AB, Weiser TG, Berry WR, Lipsitz SR, Breizat AH, Dellinger EP, et al. A surgical safety checklist to reduce morbidity and mortality in a global population. *N Engl J Med.* (2008) 369:491–9. doi: 10.1056/NEJMsa0810119
15. Walker I, Wilson I, Bogod D. Anaesthesia in developing countries. *Anaesthesia* (2007) 62:2–3. doi: 10.1111/j.1365-2044.2007.05288.x
16. Meaney PA, Topjian AA, Chandler HK, Botha M, Soar J, Berg RA, et al. Resuscitation training in developing countries: a systematic review. *Resuscitation* (2010) 81:1462–72. doi: 10.1016/j.resuscitation.2010.06.024
17. Zoumenou E, Gbenou S, Assouto P, Ouro Bang'na Maman AF, Lokossou T, Hounnou G, et al. Pediatric anaesthesia in developing countries: experience in the two main university hospitals of Benin in West Africa. *Paediatr Anaesth.* (2010) 20:741–7. doi: 10.1111/j.1460-9592.2010.03348.x
18. Doherty C, Holtby H. Pediatric cardiac anaesthesia in the developing world. *Paediatr Anaesth.* (2011) 21:609–14. doi: 10.1111/j.1460-9592.2010.03492.x
19. Walker IA, Morton NS. Pediatric healthcare– the role for anaesthesia and critical care services in the developing world. *Paediatr Anaesth.* (2009) 19:1–4. doi: 10.1111/j.1460-9592.2008.02866.x
20. Marchal B, Kegels G. Health workforce imbalances in times of globalization: Brain drain or professional mobility? *Int J Health Plann Manage.* (2003) 18:S89–101. doi: 10.1002/hpm.720
21. Bainbridge D, Martin J, Arango M, Cheng D. Evidence-based Perioperative Clinical Outcomes Research (EPiCOR) Group. Perioperative and anaesthetic-related mortality in developed and developing countries: a systematic review and meta-analysis. *Lancet* (2012) 380:1075–81. doi: 10.1016/S0140-6736(12)60990-8
22. Khan M, Khan FA. Anaesthetic deaths in a developing country. *Middle East J Anaesthesiol.* (2007) 19:159–72.
23. Hodges SC, Mijumbi C, Okello M, McCormick BA, Walker IA, Wilson IH. Anaesthesia services in developing countries: defining the problems. *Anaesthesia* (2007) 62:4–11. doi: 10.1111/j.1365-2044.2006.04907.x
24. Funk LM, Weiser TG, Berry WR, Lipsitz SR, Merry AF, Enright AC, et al. Global operating theatre distribution and pulse oximetry supply: an estimation from reported data. *Lancet* (2010) 376:1055–61. doi: 10.1016/S0140-6736(10)60392-3
25. Duke T, Subhi R, Peel D, Frey B. Pulse oximetry: technology to reduce child mortality in developing countries. *Ann Trop Paediatr.* (2009) 29:165–75. doi: 10.1179/027249309X12467994190011
26. Fisher QA, Politis GD, Tobias JD, Proctor LT, Samandari-Stevenson R, Roth A, et al. Pediatric anaesthesia for voluntary services abroad. *Anaesth Analg.* (2002) 95:336–50. doi: 10.1213/01.ANE.0000020920.14274.C4
27. Braz LG, Braz DG, Cruz DS, Fernandes LA, Modolo NS, Braz JR. Mortality in anaesthesia: a systematic review. *Clinics* (2009) 64:999–1006. doi: 10.1590/S1807-59322009001000011
28. Bharati SJ, Chowdhury T, Gupta N, Schaller B, Cappellani RB, Maguire D. Anaesthesia in underdeveloped world: present scenario and future challenges. *Niger Med J.* (2014) 55:1–8. doi: 10.4103/0300-1652.128146
29. Stevenson C. Educational resources: website and book review. *Anaesthesia* (2007) 62:103–7. doi: 10.1111/j.1365-2044.2007.05311.x
30. Enright A, Wilson IH, Moyers JR. The World Federation of Societies of Anaesthesiologists: supporting education in the developing world. *Anaesthesia* (2007) 62:67–71. doi: 10.1111/j.1365-2044.2007.05303.x
31. Walker IA. Con: pediatric anaesthesia training in developing countries is best achieved by out of country scholarships. *Paediatr Anaesth.* (2009) 19:45–9. doi: 10.1111/j.1460-9592.2008.02844.x

32. Murray DJ. Current trends in simulation training in anaesthesia: a review. *Minerva Anaestesiol.* (2011) 77:528–33.
33. Fehr JJ, Honkanen A, Murray DJ. Simulation in pediatric anaesthesiology. *Paediatr Anaesth.* (2012) 22:988–94. doi: 10.1111/pan.12001
34. Gonzalez LP, Pignaton W, Kusano PS, Módolo NS, Braz JR, Braz LG. Anaesthesia-related mortality in pediatric patients: a systematic review. *Clinics* (2012) 67:381–7. doi: 10.6061/clinics/2012(04)12
35. Ahmed A, Ali M, Khan M, Khan F. Perioperative cardiac arrests in children at a university teaching hospital of a developing country over 15 years. *Paediatr Anaesth.* (2009) 19:581–6. doi: 10.1111/j.1460-9592.2009.02992.x

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CASE REPORT
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A Case Report Examining Early Extubation Following Congenital Heart Surgery in a Low Resource Setting

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This case report aims to critically analyse the evidence surrounding early extubation in the post-operative phase following complex congenital cardiac surgery. Child A was an 8 year old female who had undergone complex congenital cardiac surgery during an international surgical charity mission. On admission to the paediatric intensive care unit Child A appeared to be in good condition and no major complications had occurred intra-operatively. This was considered alongside the situational pressures of resource limitations and the mission's aim to offer surgery to as many children as possible during the available time frame. The decision was made by the team that Child A was a suitable candidate for 'early extubation.' Some members of the team were uncomfortable with this approach and felt it could lead to poorer outcomes for patients. Current evidence surrounding early extubation both within international surgical mission trips to low-income and middle-income countries and established cardiac centres within high-income countries is examined and discussed alongside the context of resource limitation. Although the process and implications of early extubation following cardiac surgery needs further research, on the basis of the evidence currently available clinicians could potentially encourage the use of early extubation within clinical practice (for appropriately selected patients) through the utilisation of a multidisciplinary approach, both within the UK and during international surgical charity missions to low-income and middle-income countries.

Keywords: early, extubation, fast-track, surgical, mission, charity, paediatric, cardiac

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INTRODUCTION

This case report aims to critically analyse the evidence surrounding early extubation in the postoperative phase following complex congenital cardiac surgery. The child [identified only as 'Child A' in order to conform to NMC guidelines (1)] was an 8 year old female who had undergone complete tetralogy of Fallot repair during an international surgical charity mission. Child A had no previous intervention and her tetralogy was deemed severe, with surgery more complex than classically seen in the UK, requiring a prolonged period on cardiopulmonary bypass and placement of an extensive transannular patch. Tetralogy of Fallot is the most common cyanotic congenital cardiac defect (2). It is characterised by the presence of four cardiac abnormalities - a malaligned VSD, overriding aorta, pulmonary stenosis, and right ventricular hypertrophy (3). Children usually require surgical intervention within the first six months of life in order to minimise long term morbidity and promote growth and development (4).

Primary complete repair in infancy is the current preferred surgical approach for the treatment of tetralogy of Fallot (5). However, a late presentation of tetralogy of Fallot is not uncommon in low-income and middle-income countries (and therefore during 'surgical mission trips'), and a lack of surgical facilities may delay treatment further. As a result these 'older' children develop a number of significant risk factors including chronic hypoxaemia, polycythaemia, stunted growth, and significant left ventricular dysfunction. All of these risk factors were present in Child A - particularly stunted growth as a result of the underlying cardiac condition and malnutrition [often present in this group of patients as a result of living conditions and socioeconomic status (6)].

However, despite the presence of these risk factors there are a number of documented case series' where 'late' tetralogy of Fallot repair has been undertaken during later childhood in children from low-income and middle-income countries (with surgery completed in both the country of origin during surgical missions or pre-operative transfer of the child to an established cardiac centre in a high-income country). These show no difference in post-operative morbidity and mortality compared with children who undergo a standard infant repair, alongside fewer ventilation days and earlier discharge seen in the late repair group (6, 7).

Child A appeared to be in good condition on admission to the paediatric intensive care unit (PICU) post-operatively (run collaboratively between the local team and the international visiting team), maintaining appropriate vital signs, minimal bleeding and requiring minimal ventilation to achieve normal arterial blood gases. No major complications had occurred intra-operatively. This was considered alongside the situational pressures of resource limitations and the missions aim to offer surgery to as many children as possible during the available time frame. The decision was made by the team that Child A was a suitable candidate for 'early extubation' and extubation occurred within two hours of her admission to the PICU. Some members of the team were uncomfortable with this approach and felt it could lead to poorer outcomes for patients.

BACKGROUND

In recent years there have been significant advances in surgical, interventional cardiac catheterisation and hybrid procedures as treatments for congenital heart disease. Despite this, there are wide disparities in the treatment available for children around the world. It has been suggested that approximately 90% of children with congenital heart disease in low-income and middle-income countries do not have adequate access to essential treatment (8). This inequality in service provision is often due to the absence of a range of resources including lack of appropriately skilled paediatric cardiologists and cardiac surgeons, absence of suitable paediatric intensive care facilities, economic restraints and inadequate local infrastructure within low-income and middle-income countries.

In an attempt to bridge this gap, a number of international charities organise regular 'surgical mission trips' to low-income and middle-income countries across the world. These aim to provide services and education for areas of the world where access to treatment is limited by local health resources and/or cost, with the ultimate goal being to improve access and sustainability of local congenital heart disease programmes in low-income and middle-income countries (9). Whilst a number of different models of education and care exist within this context (10), all acknowledge that development of these programmes will take an extended period of time and frequent visits will be required. The ultimate aim is that the 'mission trips' will become redundant as local teams develop the skills and infrastructure required to run autonomous, self-sufficient programmes for children with congenital heart disease (11).

DISCUSSION

Within high-income countries (where paediatric cardiac surgery is generally accessible to all children) most surgical techniques developed to treat congenital heart disease involve the use of cardiopulmonary bypass. In order to facilitate this, intubation and mechanical ventilation are required and this is often continued during the post-operative period (12). The majority of children will be admitted to PICU intubated and ventilated for a period of time (often at least overnight) post cardiac surgery (13). The benefits of extubating children as soon as clinically possible is not new, having first been discussed in the literature in the 1970's (14). Early extubation following cardiac surgery in adults was introduced into standard clinical practice as early as the 1990's (15, 16). Since then, 'fast track' strategies have been developed in both populations, made up of four components: early extubation, early ambulation, cardiac rehabilitation, and early discharge (12).

Although 'early extubation' [extubation within the operating theatre or less than eight hours after a child's admission to PICU (17, 18)] has been described in the literature (19, 20), mechanical ventilation following cardiac surgery in children remains common practice (21). However, on reviewing the limited quantity of readily available literature, there is support for early extubation of appropriate patients. Large studies within adult cardiac surgery have clearly demonstrated that early extubation and 'fast-tracking' can be achieved safely and may be beneficial to the patient (22).

Harris et al. (23) performed a retrospective analysis on all neonatal and paediatric patients post cardiac surgery (within an established high-income centre) and concluded that early extubation led to a reduced length of stay in both PICU and hospital and correlated with low morbidity within the patient group. Other studies (24–26) also suggest that early extubation is safe and desirable and the benefits of early extubation are discussed including reduced risk of complications related to prolonged ventilation. It is clear that successful extubation of appropriately selected patients reduces the potential morbidity and mortality risks which are directly related to intubation and/or mechanical ventilation, including accumulation of respiratory secretions, atelectasis, nosocomial infections (including ventilator acquired pneumonia), airway trauma and unplanned extubation (27). Extubation may also remove or significantly reduce the need for continuous sedation

and the inevitable undesirable side effects which often include respiratory and hemodynamic depression, sedation tolerance (requiring escalating doses), delirium and withdrawal once sedation is discontinued (27).

Further studies and case reports have suggested that early extubation in children following cardiac surgery can be achieved without an increase in post-operative complications, or adverse effects on cardiac function (17, 28). Within PICU in established cardiac centres in high-income countries, early extubation is actively encouraged for some post-operative cardiac conditions where extubation is physiologically favourable (i.e. Fontan procedures) and has become 'standard' clinical practice. Studies show that within these subgroups the majority of children are extubated within a few hours of admission to PICU compared to the minority of children following tetralogy of Fallot repair (29). It is interesting to note that no literature was found which suggested early extubation (for appropriately selected patients) led to poor outcomes or increased morbidity and/or mortality.

It is important to appreciate that a significant proportion of the literature surrounding early extubation in this field of practice comes from high-income countries where children are treated in well-established cardiac centres which face different pressures when compared to a surgical mission. When the literature referring to low-income and middle-income countries is explored, it is evident that early extubation is seen as a safe and often preferable practice within these environments (30). Akhtar et al. (31) suggest that early extubation in their group of patients resulted in improved patient outcomes and improved utilisation of available resources as a result of increased patient turnover from the PICU. This allowed the team to treat more patients in the limited timeframe available. Early extubation has shown to be cost effective in low-income and middle-income countries with limited health care resources (18), which is a significant factor to take into consideration when planning surgical missions within countries with a seemingly endless patient population (27). It is clear that some high risk groups are not appropriate candidates for early extubation. It is also important to recognise the difficulties in directly comparing patient groups seen in high-income countries (which see the full range of children requiring cardiac surgery) and mid/low-income countries and mission trips which often focus on lower risk patients (who may present with additional risk factors not commonly seen in high-income countries).

In the case of Child A it may be that early extubation was in her best interests. A late complete tetralogy of Fallot repair in an older child may result in the occurrence of restrictive right ventricular physiology during the initial post-operative period more frequently than if the repair is completed electively during infancy due to ventricular hypertrophy and fibrosis (32). If clinically significant, left ventricular filling may also be indirectly affected (33). In this scenario it is fundamentally important to optimise right ventricular preload - this can be supported by decreasing intrathoracic pressures through extubating the child and discontinuing mechanical positive pressure ventilation at the earliest opportunity. The change from positive pressure ventilation to spontaneous ventilation enhances cardiovascular function by reducing right ventricular afterload and improves preload (6, 27). Studies have shown that for post-operative patients following a complete tetralogy of Fallot repair, cardiac output and cerebral oxygenation increased significantly once extubation took place and spontaneous ventilation was re-established (34). Early extubation in children following a complete tetralogy of Fallot repair in low-income and middle-income countries with limited health care resources has shown to be safe and effective, as in the case of Child A where early extubation was not associated with complications (35).

Contrary to the assumption that late repair of tetralogy of Fallot in an older child would potentially result in an increase in morbidity and or mortality when compared to elective repair as an infant, studies have shown this is not the case and that no significant difference is evident (6). Although surgical decision making and intraoperative events play a significant role in the feasibility of extubating patients soon after surgery, another area of clinical practice which has a significant impact is anaesthesia. The anaesthetic team play a fundamental role in the planning and delivery of early extubation in the form of premedication, induction technique, intraoperative anaesthetic agents, neuromuscular blockade reversal and post-operative analgesia (18, 36, 37).

The development of new and improved anaesthetic agents including inhalational anaesthetics, short-acting opioids, hypnotics and sedatives with favourable pharmacodynamics (particularly with respect to depression of cardiac function) make the concept of early extubation following cardiac surgery possible if the process of anaesthesia is both well planned and well managed in appropriately selected patients (17). As these drugs and anaesthetic techniques become more readily available in low-income and middle-income countries (or can be provided by the visiting team), early extubation of paediatric cardiac patients can be achieved safely during surgical missions (31). It has been suggested that alongside improved surgical and bypass techniques, the most important factor influencing the success of early extubation is adequate provision of effective analgesia (12). This includes the use of non-opioid drugs such as paracetamol and the use of local anaesthetic (38).

It is clear that teams travelling to low-income and middle-income countries in order to take part in surgical missions are likely to face resource limitations, particularly if working within a centre that does not ordinarily have the infrastructure for cardiac surgery or paediatric intensive care. It is well-documented within the literature that surgical missions often face the problem of limited resources not usually evident within clinical practice in established cardiac centres within high-income countries (39, 40). Cardiac surgery is known to be a technologically dependent area of clinical practice with a reliance on single use consumables (41). This was recognised as early as the 1980's with the development of the 'KISS (Keep It Simple and Safe)' approach which aimed to provide treatment to the maximum number of patients within the context of limitations of funding, equipment and manpower (42). Whilst some degree of technology is essential for even the most basic cardiac surgery, international teams will likely find resource limitations a constant challenge. Welling et al. (43) identify 'failing to match technology

to local needs and abilities' as one of their 'Seven Sins of Humanitarian Medicine.'

It is also important to recognise that within the PICU where child A was admitted, parents were not allowed to visit. Whilst this is different to 'standard' clinical practice within the UK, the local policies and customs were respected as far as possible during the surgical mission. Regular updates were given to the parents by the local team and this appeared to satisfy them. It is recognised that parents from deprived backgrounds whose child is admitted to PICU experience significantly higher stress levels and this must be considered (44). Within the UK, invasive procedures including extubation may further increase parents stress levels (45, 46) (particularly if parents are aware there is a deviation from 'usual' clinical practice and is referred to as 'early' by staff). If integrated into clinical practice, parents must be informed and involved in all aspects of their child's care. However, the opposite has also been suggested in that early extubation and fast track strategies reduce parent anxiety if a child is extubated rapidly as this allows verbal communication with their child and earlier mobilisation (12, 31).

It is clear that patient selection at the time of surgical listing must carefully consider a wide variety of factors including patient safety, anticipated time to discharge back to local services, educational objectives and resource availability within the time constraints of the surgical mission. Teamwork and communication (including both the local and visiting teams) is crucial to all aspects of a surgical mission, but vital if early extubation of children following cardiac surgery is to be implemented. It is also important for the team to understand that even if a child is identified as a candidate for early extubation following their pre-operative assessment or at the time of surgical listing, early extubation cannot be guaranteed and is dependent on many factors including intra-operative and post-operative events and clinical progress (18). Despite substantial evidence showing that early extubation in children following surgery for congenital heart disease can be achieved safely, significant individual and institutional concerns about integrating the approach within clinical practice remain (31, 47).

Inevitably, challenges will arise for both the local and visiting teams during their collaborative practice. These must be dealt with in a sensitive manner so that no member of the team feels their practice is in anyway substandard or could lead to poorer outcomes for patients. The international team must be aware that significant adjustments to what is perceived as 'standard' clinical practice may have to be made in order to function as an effective team within a resource limited environment (11).

CONCLUDING REMARKS

Upon reflection on this case, current knowledge suggests that early extubation following complex congenital heart surgery may not result in poorer outcomes for children if patients are selected and managed appropriately. Early extubation may in fact be beneficial for patients and lead to a faster recovery for children regardless of their underlying cardiac defect or the environment in which treatment is received. It has also been suggested that early extubation is a safe and effective method of reducing patient morbidity, improving patient turnover by accelerating a child's discharge from the PICU and has been shown to be a cost effective practice (12, 20). Studies have strongly supported the development of early extubation pathways for children undergoing congenital cardiac surgery in both low, middle, and high-income countries (17). As no large studies endorsing any potential benefits of early extubation have been undertaken, concerns about the practice remain an issue within daily clinical practice (47). It is clear that some high risk patient groups are not appropriate candidates for early extubation, particularly following highly complex surgery not commonly undertaken during mission trips. Although the process and implications of early extubation following cardiac surgery need further research, on the basis of the evidence currently available clinicians within the UK could potentially encourage the use of early extubation within clinical practice for appropriately selected patients through the utilisation of a multidisciplinary approach, both within the UK and during surgical missions.

CONSENT

Oral parental consent for the discussion of this case was obtained.

AUTHOR CONTRIBUTIONS

The author confirms being the sole contributor of this work and has approved it for publication.

REFERENCES

1. Nursing and Midwifery Council. *The Code*. London (2015).
2. Apitz C, Webb G, Redington A. Tetralogy of fallot. *Lancet*. (2009) 374:1462–71. doi: 10.1016/S0140-6736(09)60657-7
3. Burns J. *Illustrated Field Guide to Congenital Heart Disease and Repair*. Charlottesville, VA: Scientific Software Solutions (2010).
4. Bailliard F, Anderson R. Tetralogy of fallot repair. *Orphanet J Rare Dis.* (2009) 4:2. doi: 10.1186/1750-1172-4-2
5. Steiner M, Tang X, Gossett J, Malik S, Prodhan P. Timing of complete repair of non-ductal dependent tetralogy of fallot and short-term postoperative outcomes, a multicenter analysis. *J Thorac Cardiovasc Surg.* (2014) 147:1299–305. doi: 10.1016/j.jtcvs.2013.06.019
6. Benbrik N, Romefort B, Le Gloan L, Warin K, Hauet Q, Guerin P, et al. Late repair of tetralogy of fallot during childhood in patients from developing countries. *Eur J Cardio-Thorac Surg.* (2015) 47:3113–7. doi: 10.1093/ejcts/ezu469
7. Tchoumi J, Ambassa J, Giamberti A, Cirri S, Frigiola A, Butera G. Late surgical treatment of tetralogy of fallot. *Cardiovasc J Afr.* (2011) 22:179–81. doi: 10.5830/CVJA-2010-057
8. Nguyen N, Leon-Wyss J, Iyer K, Pezzella A. Paediatric cardiac surgery in low-income and middle-income countries: a continuing challenge. *Arch Dis Child.* (2015) 100:1156–9. doi: 10.1136/archdischild-2015-308173
9. Boston M, Horlbeck D. Humanitarian surgical missions planning for success. *Otolaryngol-Head Neck Surg.* (2015) 153:320–5. doi: 10.1177/0194599815587889
10. Butler M. Developing pediatric surgery in low- and middle-income countries: an evaluation of contemporary education and care delivery models. *Semi Pediatr Surg.* (2016) 25:43–50. doi: 10.1053/j.sempedsurg.2015.09.008

11. Molloy F, Nguyen N, Mize M, Wright G, St George-Hyslop C, O'Callaghan M, et al. Medical missions for the provision of paediatric surgey in low- and middle-income countries. *Cardiol Young*. (2017) 27:47–54. doi: 10.1017/S104795111700261X
12. Akhtar M, Hamid M, Anwar-Ul-Haq, Minai F, Rehman, N. Feasibility and safety of on table extubation after corrective surgical repair of tetralogy of fallot in a developing country: a case series. *Ann Card Anaesth.* (2015) 18:237–41. doi: 10.4103/0971-9784.154490
13. Egbe A, Mittnacht A, Nguyen K, Joashi U. Risk factors in morbidity in infants undergoing tetralogy of fallot repair. *Ann Pediatr Cardiol.* (2014) 7:13–8. doi: 10.4103/0974-2069.126539
14. Smith R. Pediatric anesthesia in perspective. Sixteenth *Ann Baxter-Travenol Lecture Anethes Analges*. (1978) 57:634–46.
15. Ott R, Gutfinger D, Miller M, Selvan A, Codini M, Alimadadian H, et al. Coronary artery bypass grafting "On Pump": role of three day discharge. *Ann Thorac Surg.* (1997) 64:478–81.
16. Cheng D, Karski J, Peniston C, Raveendran G, Asokumar B, Carroll J, et al. Early tracheal extubation after coronary bypass graft surgery reduces costs and improves resource use. A Prospective, Randomized, Controlled Trial. *Anesthesiology*. (1996) 85:1300–10. doi: 10.1097/00000542-199612000-00011
17. Iezzi F, Summa M, Sarto P, Munene J. Fast-Track extubation in pediatric cardiothoracic surgery in developing countries. *J Cardiac Crit Care*. (2017) 1:21–23. doi: 10.1055/s-0037-1604334
18. Akhtar M, Hamid M. Early extubation in adult and pediatric open heart surgery; an experience from a tertiary care hospital of a developing country. *Anaest Pain Inten Care*. (2016) 20:S81–5.
19. Alghamdi A, Singh S, Hamilton B, Yadava M, Holtby H, Arsdell G, et al. Early extubation after pediatric cardiac surgery: systematic review, meta-analysis, and evidence-based recommendations. *J Card Surg.* (2010) 25:586–95. doi: 10.1111/j.1540-8191.2010.01088.x
20. Mittnacht A, Hollinger I. Fast-tracking in pediatric cardiac surgery - the current standing. *Ann Card Anaesth.* (2010) 13:92–101. doi: 10.4103/0971-9784.62930
21. Mittnacht J, Thanjan M, Srivastava S, Joashi U, Bodian C, Hossain S, et al. Extubation in the operating room after congenital heart surgery in children. *J Thorac Cardiovasc Surg.* (2008) 136:88–93. doi: 10.1016/j.jtcvs.2007.11.042
22. Svircevic V, Nierich A, Moons K, Brandon Bravo Bruinsma G, Kalkman C, Van Dijk D. Fast-Track anesthesia and cardiac surgery: a retrospective cohort study of 7989 patients. *Aneth Analg.* (2009) 108:727–33. doi: 10.1213/ane.0b013e318193c423
23. Harris K, Holowachuk S, Pitfield S, Shubhayan S, Froese N, Potts J, et al. Should early extubation be the goal for children after congenital cardiac surgery? *J Thorac Cardiovasc Surg.* (2014) 148:2642–8. doi: 10.1016/j.jtcvs.2014.06.093
24. Gupta P, Rettigant M, Gossett J, Yeh J, Jeffries H, Rice T., et al. Risk factors for mechanical ventilation and reintubation after pediatric heart surgery. *J Thorac Cardiovasc Surg.* (2016) 151:451–58.e3. doi: 10.1016/j.jtcvs.2015.09.080
25. Gangopadhyay S, Acharjee A, Nayak S, Dawn S, Piplai G, Gupta K. Immediate extubation versus standard post-operative ventilation: our experience in on pump open heart surgery. *Ind J Anaesth.* (2010) 54:525–30. doi: 10.4103/0019-5049.72641
26. Shekerdemian L, Panny D, Novick W. Early extubation after surgical repair of tetralogy of fallot. *Cardiol Young*. (2000) 10:636–7. doi: 10.1017/S1047951100008933
27. Martin D, Crawford J, Uffman J, Michler R, Tobias J. Sugammadex and fast-track anesthesia for pediatric cardiac surgery in a developing country. *Anaesth Pain Inten Care*. (2016) 20:s17–22.
28. Meissner U, Scharf J, Dötsch J, Schroth M. Very early extubation after open heart surgery in children does not influence cardiac function. *Pediatr Cardiol.* (2008) 29:317–20. doi: 10.1007/s00246-007-9023-0
29. Mahle W, Jacobs J, Jacobs M, Kim S, Kirshbom P, Pasquali S, et al. Early extubation after repair of tetralogy of fallot and the fontan procedure: an analysis of the society of thoracic surgeons congenital heart surgery database. *Ann Thorac Surg.* (2016) 102:850–8. doi: 10.1016/j.athoracsur.2016.03.013
30. Hoda M, Haque A, Aijaz F, Akhtar M, Rehmat A, Amanullah M, et al. On-Table extubation after open heart surgery in children: an experience from a tertiary care hospital in a developing country. *Congenital Heart Dis.* (2016) 11:58–62. doi: 10.1111/chd.12277
31. Akhtar M, Hamid M, Minai F, Wali A, Anwar-ul-Haq, Aman-Ullah M, Ahsan, K. Safety profile of fast-track extubation in pediatric congenital heart disease surgery patients in a tertiary care hospital of a developing country: an observational prospective study. *J Anaesthesiol Clin Pharmacol.* (2014) 30:355–9. doi: 10.4103/0970-9185.137267
32. Xu Z, Zhang M, Zhu L, Gonq 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. *Congenital Heart Dis.* (2014) 9:521–8. doi: 10.1111/chd.12166
33. Ahmad N, Kantor P, Grosse-Wortmann L, Seller N, Jaeggi E, Friedberg M, et al. Influence of right ventricle restrictive physiology on left ventricular diastolic function in children after tetralogy of fallot repair. *J Am Soc Echocardiogr.* (2012) 25:866–73. doi: 10.1016/j.echo.2012.05.011
34. Bronicki R, Checchia P, Anas N, Adams G, Penny D, Bleiweis M, et al. cerebral and somatic oxygen saturations after repair of tetralogy of fallot: effects of extubation on regional blood flow. *Ann Thorac Surg.* (2013) 95:682–6. doi: 10.1016/j.athoracsur.2012.07.017
35. Karthekeyan R, Sundar A, Sulaiman S, Thangavelu P, Vakamudi M, Kasianandan T. Early extubation in tetralogy of fallot patients after complete repair. *Cardiol Young*. (2011) 21:378–82. doi: 10.1017/S1047951111000059
36. De Souza C, Romero F, Tardelli M. Assessment of neuromuscular blockade in children at the time of block reversal and the removal of the endotracheal tube. *Braz J Anesthesiol.* (2011) 61:145–9. doi: 10.1016/S0034-7094(11)70019-8
37. Meretoja O. neuromuscular block and current treatment strategies for its reversal in children. *Paediatr Anaesth.* (2010) 20:591–604. doi: 10.1111/j.1460-9592.2010.03335.x
38. Cattabriga I, Pacini D, Lamazza G, Talarico F, Di Bartolomeo R, Grillone G, et al. Intravenous paracetamol as adjunctive treatment for postoperative pain after cardiac surgery: a double blind randomized controlled trial. *Eur J Cardiothorac Surg.* (2007) 32:527–31. doi: 10.1016/j.ejcts.2007.05.017
39. Sykes K. Short-Term medical service trips: a systematic review of the evidence. *Am J Public Health*. (2014) 104:38–48. doi: 10.2105/AJPH.2014.301983
40. Wong E, Trelles M, Dominguez L, Gupta S, Burnham G, Kushner AL. Surgical skills needed for humanitarian missions in resource-limited settings: common operative procedures performed at médecins sans frontières facilities. *Surgery*. (2014) 156:642–9. doi: 10.1016/j.surg.2014.02.002
41. DeLeval M. Human factors in cardiac surgery: a multi-center study. *J Thorac Cardiovasc Surg.* (2000) 119:661–72. doi: 10.1016/S0022-5223(00)70006-7
42. Victor S, Kabeer M. Indian kiss approach to cardiac surgery. *Ind J Thorac Cardiovasc Surg.* (1989) 6:20–2. doi: 10.1007/BF02664018
43. Welling D, Ryan J, Burris D, Rich N. Seven sins of humanitarian medicine. *World J Surg.* (2010) 34:466–70. doi: 10.1007/s00268-009-0373-z
44. Franck L, McQuillian A, Wray J, Grocott GA. Parent stress levels during children's hospital recovery after congenital heart surgery. *Pediatr Cardiol.* (2010) 31:961–8. doi: 10.1007/s00246-010-9726-5
45. Dahav R, Annica S. Parents' experiences of their child being admitted to a paediatric intensive care unit: a qualitative study - like being in another world. *Scand J Caring Sci.* (2018) 32:363–70. doi: 10.1111/scs.12470
46. Lisanti A, Allen L, Kelly L, Medoff-Cooper B. Maternal stress and anxiety in the pediatric cardiac intensive care unit. *Am J Crit Care*. (2017) 26:118–25. doi: 10.4037/ajcc2017266
47. DiNardo J. Extubation in the operating room following pediatric cardiac surgery. *J Cardiothorac Vasc Anesth.* (2011) 25:877–9. doi: 10.1053/j.jvca.2011.06.027

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Humanitarian Mission in Pediatric Cardiothoracic Surgery: A Recipient's Perspective

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Introduction: Pediatric cardiac surgical mission programs are deemed as common practice, especially in developing nations funded by international non-governmental organizations (NGOs). This article presents and discusses the results and strategies implemented by this partnership, aiming at achieving the autonomy of the local center by this collaboration.

Materials and Methods: A retrospective review was conducted on patients with congenital heart disease who underwent surgical intervention from the beginning of the NGO collaboration (September 2015) until November 2018 in an existing cardiac center. In between those visits, any congenital heart disease patient with Risk Adjustment Congenital Heart Surgery (RACHS)-1 Category 1–3 would be discussed in a local multi-disciplinary meeting with regards to the feasibility of the surgery being performed by the local members.

Results: A total of 60 operations were performed during the trips. Throughout the visit, 46% (28) of the operations were performed by the local surgeon, with or without assistance from the visiting surgeon. Between September 2015 and November 2018, 27 cases were also performed by the local team independently. For the 27 cases performed by the local team independently, the median age of the patient was 42 days (ranging from 14 days to 20 years old), with median body weight of 3.2 kg (ranging from 2.8 to 64 kg).

Conclusion: Humanitarian pediatric cardiac surgical missions are safe to be done for the population in need. In order to achieve autonomy, continuous efforts by both teams are crucial, as the cooperation by the two parties ensures that the objectives are achieved.

Keywords: surgical mission, congenital heart defects, volunteerism, charity, surgical outcomes

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INTRODUCTION

Congenital Heart Disease (CHD) occurs in 1% of births per year (1). The detection rate and management to encounter CHD are increasing trends, especially in developed countries. In least developed countries, CHD is still a major burden for the population and most of children are left unattended. According to the WHO, a cardiac center with 300–500 operations performed annually

is required in order to accommodate a population of 2 million people (2). Nonetheless, there is not even a single pediatric cardiac center within areas of population of 15–70 million people in certain parts of developing countries (3). This also happens in Asia, where on average there is only one pediatric cardiac center for 16 million population (4). To tackle the issue, transferring, and accepting the expertise from developed countries by having a regular surgical visit to the areas that mostly in need are practiced. It might be asserted that the cost of sending a cardiac surgical team to operate on 10–20 children in the selected country is equal to sending one abroad (5, 6). Perhaps Pezzella (7) best elaborated this when he wrote "the era of bringing patients to the United States for free cardiac surgery is over."

As such, cardiac surgery services are limited in most developing countries, and many patients have no choice but to live in morbid conditions. In contrast, there are several cardiac programs available in other regions, but there are only a few caseloads noted. It is commonly practiced by health providers in developing nations to run collaborative mission programs sponsored by international or domestic non-governmental organizations (NGOs). The aim of this collaboration is to develop local cardiac surgery institutions to provide continuous treatment for patients in developing countries. Numerous approaches have been used: regionalization, "safari" missions, twinning programs, and "travels of hope" (8, 9). Since then, many non-governmental humanitarian organizations (NGOs) have been initiating pediatric cardiac surgery services in developing countries. This article presents and discusses the results and strategies implemented by this partnership, aiming at achieving autonomy at the local centers by collaborating with the NGO.

MATERIALS AND METHODS

A retrospective review was conducted on patients with congenital heart disease who underwent surgical intervention from the beginning of the NGO collaboration (September 2015) until November 2018 in an existing cardiac center. It is a part of the result in our internal clinical audit data regarding surgical humanitarian mission in the local center. This study has been revised by the local ethical committee [Human Research Ethics Committee USM (HREC)] and was exempted from ethical review. No informed consent was taken because it is a retrospective study.

The local unit's collaboration with the NGO for pediatric cardiac surgical mission was established in September 2015 with one of the co-authors (AFC). Since then, there have been 6 visits by the U.K. teams until November 2018. In general, the visiting team usually consists of 7–8 people, including a consultant pediatric cardiac surgeon, consultant intensivist, consultant pediatric cardiologist, Pediatric Cardiac Intensive Care Unit (PCICU) Registrar, and 1 or 2 PCICU nurses. In only one of the visits were there an operating room nurse and a consultant anesthetist.

The local cardiothoracic unit was established in 2001, and a majority of the cases performed were adult cardiothoracic cases. The pediatric cardiac surgical unit was established in 2013 but later in early 2015, it was closed due to the migration of the pediatric cardiac surgeon who contributed to organizing the unit from the beginning. The center received nearly 50 cases of pediatric congenital heart disease per year requiring surgery, and all of them were sent to the nearest pediatric cardiac center, which was 600 km away with very difficult transfer because of the geographic situation. The local team was composed of two fully trained adult cardiac surgeons (one of them had special interest in pediatric congenital heart cases), two cardiac anesthetists, one pediatric cardiologist, three neonatologists, and a few fully trained supporting staff (perfusionist, PCICU nurses, operating room nurses, respiratory physiotherapist, etc.) in the adult cardiothoracic program. There were only 3 cardiac Intensive Care Unit (ICU) beds available, which allowed for ∼90–120 cases per year.

After all the visits by the U.K. teams, all the patients were managed under a local multi-disciplinary approach, and there was also direct communication with the lead visiting team that had left. After the visit, any congenital heart disease patient with Risk Adjustment Congenital Heart Surgery (RACHS)-1 Category 1–3 would be discussed in a local multi-disciplinary meeting with regards to the feasibility of doing surgery by the local members. Expert opinions from the visiting team might be consulted for further evaluation. This involves frequent exchange of e-mail and the use of social media, e.g., WhatsApp. This autonomy led the local cardiac surgeon to choose the cases and proceed to perform the operations with the support of the local expertise available.

RESULTS

From September 2015 to May 2018 there were a total of six visits from U.K. teams to the local hospital, 60 patients were identified for surgical treatment, and a total of 60 operations were performed. For the 60 cases performed during missions, the median age of the patient was 2 years old (ranging from 15 days to 30 years), with a median body weight of 11 kg (ranging from 2.7 to 53 kg) and median height of 85 cm (ranging from 45 to 159 cm). Forty-seven (78%) of them were on-pump cases, while 13 (22%) were off-pump cases. During the visit, 46% (28) of the operations were performed by the local surgeon, with or without assistance from the visiting surgeon. The procedures done included 17 VSD closures, 3 ASD closures, 5 Pulmonary artery bandings, 2 AVSD repairs, and 1 TOF Repair.

From September 2015 to November 2018, there had already been 27 cases performed by the local team independently. The complexity of the case ranged from Modified Black-Taussig Shunt in neonates, VSD closure and PDA ligation (**Table 1**). For the 27 cases performed by the local team independently, the median age of patients was 42 days (ranging from 14 days to 20 years), with median body weight of 3.2 kg (ranging from 2.8 to 64 kg). Seven (26%) of them were on-pump cases while 20 (74%) were off-pump cases.

Post-operatively, all the patients were managed by a multi-disciplinary team, which included a pediatric cardiologist,

TABLE 1 | List of surgical procedures performed by local teams independently.

Number of procedures	Surgical procedures	Additional procedures
7	PDA closure	
6	VSD closure	3 RVOT reconstruction
4	Modified Blalock-Taussig Shunt in neonate	1 Carotid Artery-Main Pulmonary Artery Anastomosis
4	Permanent Pacemaker Implantation	1 Epicardial pacing wire insertion 1 Pacemaker-box change
3	Pulmonary Artery Banding	1 PDA closure
2	CCAM Excision	
1	Removal of dislodged PDA Device under CPB	1 RA wall tear repair

CCAM, Congenital Cystic Adenomatoid Malformation; CPB, cardiopulmonary bypass; PDA, Patent Ductus Arteriosus; RVOT, Right Ventricular Outflow Tract; VSD, Ventricular Septal Defect.

neonatologist, cardiac surgeon, and anesthetist. Out of 27 cases performed by the local team, 3 (11%) of the patients died post-operatively. Two-thirds of the patients were neonates with RACHS-1 Risk Category 3, with the body weight ranging from 2.90 to 3.50 kg, and the mortality occurred within 4–8 h post-operatively. The first patient died due to severe heart failure secondary to pulmonary overcirculation after neonatal Blalock-Taussig shunt for severe PS with underlying cCTGA. The second mortality was after pulmonary artery banding in a patient with Down syndrome and complete atrioventricular septal defect. The third mortality was in a patient with a dislodged Patent Ductus Arterious (PDA) occluder device during transcatheter procedure, complicated with cardiac tamponade requiring cardiopulmonary resuscitation x 3 preoperatively. Urgent operation was done under cardiopulmonary bypass for PDA device retrieval.

DISCUSSIONS

> *"The success should not be measured by the number of successful operations of any given mission, but by the successful operations that our colleagues perform after we leave".*
>
> –Dr. Gary Raff (10)

Dearani et al. (8) also mentioned the complexity of the cases that could be achieved in an NGO collaboration with the existing cardiothoracic services, which could be categorized from Level 1 to Level 4 in complexity. The role of the visiting team as a long-term, off-site collaborator was also important in accomplishing autonomy. To achieve this, we adopted the "twinning program" (8) approach, in which the local surgeon was attached to an established surgeon in a center of excellence. As for the local surgeons, performing those surgeries with the visiting team helped them to be familiar with the surgical procedures. In our case, the local surgeon performed at least 48% of the cases during the visit. This could only be achieved with careful selection of the cases and interactive communication between both the local and visiting surgeons. After the visit, all the patients had been managed by local multi-disciplinary approaches, with the assistance of direct communication with the lead visiting team. This constant way of working had developed the local team's confidence in handling pediatric cardiac patients, which in hand also led to autonomous development of the team.

We believe that the success of the program in achieving autonomy was based on both interdisciplinary communications as well as good insight of the local team regarding our strength and weaknesses. The selection of cases includes RACHS-1 Category 1–3, with a bodyweight of more than 5 kg for on-pump cases and avoidance of on-pump cases on neonates if permissible (8). Apart from that, minimizing ICU length of stay and early extubation were the main objectives postoperatively. This was due to the limitation of resources and trained personnel in the PCICU. Accidental extubation with frequent reintubation and errors in preparation of medications seem to be the most common errors found in prolonged mechanical ventilation or ICU stays. Whenever possible, one-to-one model pairing between the local team and visiting team members, as well as same-site recurring voluntary visits, should be done in order to properly assess the development of the local team achievement (11).

With regard to the 27 cases operated on our own (without the involvement of the visiting team), we had a relatively high mortality rate. In this notion, we must agree that most of the mortality occurred in very high-risk cases, with a high level of complexity and involving "rescue surgery." However, this had not stopped completely the activities and led us to better select cases and improve our care to boost surgical activities. In order to improve the clinical practice, the mortality and morbidity meetings were conducted by the local team together with the foreign team during the visits.

Sustainability

From a financial standpoint, the survival of an NGO collaboration with local cardiac centers depends on fulfilling the needs of the community by delivering quality care and publicizing its success. Sometimes, the visiting team's accommodation, hospitality, and transportation might be needed and the funds may come from the contribution of local communities rather than from the visiting NGO itself. Occasionally, the patients also need support in term of hospital bills and intervention involved (e.g., usage of tissue valve may not be subsidized by most hospitals). The program should be advertised in the local media, press, and online to increase public awareness, as well as to increase funding for the local team (5).

Data collection and analysis was a key for sustainability of this program. The data should involve patient demographics, diagnosis, surgical procedures, mortality, morbidity, complexity-adjusted outcome analysis, and resources involved, which could demonstrate the program's growth and its impact. Some surgical procedures could be modified more locally based with the resources available to perform the surgery. For example, doing five arterial switches in a 1-week NGO visit may overwhelm the resources of the local hospital, and it is less effective in training the local surgeon as well. These factors must be considered when determining whether a procedure could be supported and sustained in a resource-limited hospital or not (12). Additionally, developing pediatric specialty services might require longer

commitment, often exceeding 5 years before a surgical center reaches its independence (6).

Problems and Risks

Safety might be compromised during the visit since the local teams are not familiar with the large number of cases in a short trip, and this will also affect other specialties that use the same facilities (3). Another consideration that needs to be taken for a local team is the preparedness of the local setting in accepting the visiting NGO. The preparation might include hospitality, operating theater setting, equipment, and disruption of regular schedule. For example, other operation theaters might need to be closed during the visit to better accommodate the whole visiting surgical activities. The visiting team should also be prepared for any unsafe or substandard environments. For instance, when the ICU/OT are under renovation this might cause power supply disruption.

Interpersonal disagreement within the institution, political appointments without ability to expand the collaboration, and behavioral factors are some of the reasons that can lead to failure of this partnership. Occasionally, lack of hospital support from the administrators is an unavoidable problem (6). In our case, we were lucky because the administration was fully supportive of the program. This was achieved by continuous discussion and communication with all the parties involved. Sometimes, the lack of continuous communication between the local team and visiting team after the visit might cause significant distance in helping the local team to develop. As such, the majority of visiting surgeons do not maintain the communication with the local surgeon. This must be tackled, and the continuous communication should be extended to all levels of medical practitioner, not being limiting to surgeons only.

CONCLUSIONS

Humanitarian pediatric cardiac surgical missions are safe to be performed on the population in need. Achieving autonomy is possible with continuous effort provided by both teams. Cooperation between both teams will ensure all the objectives can be achieved.

AUTHOR CONTRIBUTIONS

AS, MM, and AZM contributed to the conception and design of this study. AMM and SA wrote sections of the manuscript. AC and YC revised the manuscript critically and contributed to the interpretation of data. All authors listed have made a considerable and direct contribution to the work, and approved it for publication.

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REFERENCES

1. Hoffman JI, Kaplan S. The incidence of congenital heart disease. *J Am Coll Cardiol.* (2002) 39:1890–900. doi: 10.1016/S0735-1097(02)01886-7
2. Reichert HA, Rath TE. Cardiac surgery in developing countries. *J Extra-Corporeal Technol.* (2017) 49:98–106.
3. Cvetkovic M. Challenges in pediatric cardiac anesthesia in developing countries. *Front Pediatr.* (2018) 6:254. doi: 10.3389/fped.2018.00254
4. Piros Kulandasamy Pillai C, Yoshida Y, Justin Lawrence P, Yamamoto E, Reyer JA, Hamajima N. Pediatric cardiothoracic program in Malaysia: a study based on the outcome of the program. *Nagoya J Med Sci.* (2016) 78:9–17.
5. Molloy FJ, Nguyen N, Mize M, Wright G, St George-Hyslop C, O'Callaghan M, et al. Medical missions for the provision of paediatric cardiac surgery in low- and middle-income countries. *Cardiol Young.* (2017) 27:S47–54. doi: 10.1017/s104795111700261x
6. Novick WM, Stidham GL, Karl TR, Arnold R, Anić D, Rao SO, et al. Paediatric cardiac assistance in developing and transitional countries: the impact of a fourteen year effort. *Cardiol Young.* (2008) 18:316–23. doi: 10.1017/S1047951108002175
7. Pezzella AT. Worldwide maldistribution of access to cardiac surgery. *J Thoracic Cardiovasc Surg.* (2002) 123:1016.
8. Dearani JA, Jacobs JP, Bolman RM III, Swain JD, Vricella LA, Weinstein S, et al. Humanitarian outreach in cardiothoracic surgery: from setup to sustainability. *Ann Thorac Surg.* (2016) 102:1004–11. doi: 10.1016/j.athoracsur.2016.03.062
9. Corno AF. Paediatric and congenital cardiac surgery in emerging economies: surgical 'safari' versus educational programmes. *Interact Cardiovasc Thoracic Surg.* (2016) 23:163–7. doi: 10.1093/icvts/ivw069
10. Backer CL. Humanitarian congenital heart surgery: template for success. *J Thoracic Cardiovasc Surg.* (2014) 148:2489–90. doi: 10.1016/j.jtcvs.2014.09.013
11. Iacona GM, Giamberti A, Abella RF, Pome G, Agredo J, Mendieta SG, et al. Paediatric cardiac surgery in a peripheral European region: is a joint programme a safe alternative to regionalisation? *Cardiol Young.* (2017) 27:273–83. doi: 10.1017/s1047951116000469
12. Boston M, Horlbeck D. Humanitarian surgical missions: planning for success. *Otolaryngol Head Neck Surg.* (2015) 153:320–5. doi: 10.1177/0194599815587889

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Pediatric Cardiac Surgery in Low-and Middle-Income Countries: Present Status and Need for a Paradigm Shift

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In low and mid-income countries, there has been a 50% global decrease in the incidence of preventable deaths of children since 1990. However, the mortality from non-communicable diseases (NCD) such as congenital heart disease (CHD) has not changed. Of the estimated 1.3 million children born with CHD annually, over 90% do not have access to cardiac care. With the increasing fertility rates in sub-Saharan Africa, the health burden of CHD will increase as well. Over the last 30 years much has been achieved with short term cardiac medical missions. However, much remains to be done to provide long term solutions needed to achieve the sustainable development goal of reducing deaths of children <5 years of age. This review discusses the present status and the need for a paradigm shift to achieve long term sustainability.

Keywords: humanitarian medicine, cardiac disease, developing countries, children, congenital, rheumatic heart disease

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INTRODUCTION

The global population is approaching 8 billion. Over the last few decades progress has been made in reducing maternal and child mortality as well as diseases such as malaria, tuberculosis, and HIV. The UN, WHO, and UNICEF data show that global mortality in the first 5 years of life declined from 93 deaths per 1,000 live births in 1990 to 39 in 2017 (58%) (1, 2). The decline was over 50% in 144 of 199 countries and 1/3 of those countries reduced their mortality rates by 67%. However, the estimated under-5 mortality for sub-Saharan Africa is 76/1,000 live births. Six countries from this region have mortality rates >100/1,000 live births, among the highest in the world. This translates to 6 million children per year (or 16,000 per day) dying before their 5th birthday (3). **Figure 1** shows the causes of death in this age group.

The United Nations Development Program (UNDP) sustainable development goal for 2030 is to reduce under-5 mortality to 25 per 1,000 live births. We know from the current UNDP data that roughly 70 million children may die before reaching their 5th birthday and most will be from sub-Saharan Africa (2). Nine out of 10 children living in extreme poverty ($1.90/day family income) will be from this region. Importantly, the countries with the lowest income and highest fertility rates are from sub-Saharan Africa. There are multiple reasons for poor healthcare access among children, including lack of political commitment, maldistribution of resources (especially financial support), human resources, and lack of collective will. The time to act is now if we are to reach our sustainable goal by 2030 (2).

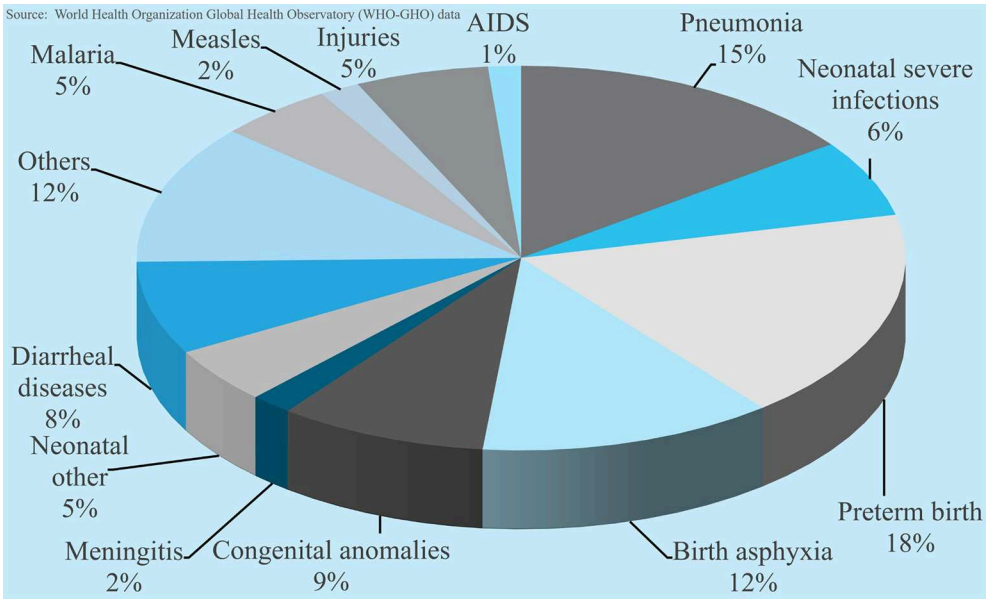

FIGURE 1 | Causes of global mortality for children <5 years' age.

The world has often focused on communicable diseases as they are public health issues. In the last three decades there has been a fall in number of new HIV infections by 30% and over 6.2 million lives saved from malaria (2). However, the non-communicable diseases (NCD) such as cardiovascular diseases (CVD) have been gradually reaching epidemic proportions, causing an increased health care burden. According to WHO data, out of the 17 million premature deaths (under the age of 70) due to NCD in 2015, 82% are in low and middle income countries (LMICs), and 37% are caused by CVDs. Recent estimates for the incidence of congenital heart disease (CHD) are in the vicinity of 8–12/1,000 live births (4). In addition to CHD, the prevalence of acquired heart disease among children e.g., rheumatic heart disease (RHD) is also high in Africa and Asia. The approximate incidence of RHD in the African population ranges from 2.7 to 20/1,000 population (5). In Africa alone, of the 50 million live births annually, at least 335,000 will have CHD (**Figure 2**) and many more will develop RHD. Less than 5% have access to cardiac care. Without availability or accessibility to cardiac care one in three children born with CHD die within the first month of birth (4). It is estimated that 1.3 million children are born each year in the world with CHD (**Figure 2**). However, <100,000 have access to heart care leaving over one million each year without care. The cumulative numbers create a sizable back log. There is very little data about the prevalence of CHD or RHD from LMICs. The reasons are multifactorial. In addition to mortality from heart disease many of these children also die from infectious causes prevalent in these countries and since prevalence is determined by both incidence and survival it becomes harder to predict (6).

To achieve the sustainable development goal of 2030, care of CHD needs to be an integral part of the big picture.

COMMON GOAL

The common goal should be a universal reach of cardiac care with a concurrent decrease in mortality and morbidity from CHD. Presently there is a wide disparity in cardiac facilities. Over 70% of the facilities reach <20% of the world's population, leaving over 90% of children born with CHD without any access to cardiac care. In a detailed review, Bode-Thomas and Olga et al. have outlined all the challenges in the management of CHD in developing countries, and possible solutions (6, 7). In our review our aim is to discuss the practical aspects of dealing with the neglected cohort of CHD patients, review current efforts, and discuss possible future plans. We believe in the need for a paradigm shift i.e., a change in our thinking and strategies if we are to achieve the goals for 2030.

CURRENT PROGRAMS

The current organizations involved in the care of children with CHD are shown in **Figure 3**. Congenital cardiac surgery programs exist as part of larger adult cardiac surgery programs or as separate divisions. They are parts of general hospitals, separate children's hospitals or stand-alone pediatric cardiac centers. The various cardiac programs can be categorized as follows:

1) Developed (established) programs
2) Developing programs
3) "*De novo*" programs
4) Restarting programs (failed or abandoned)

There are two types of volunteer cardiac surgery programs described by Dearani et al. (8, 9). They include:

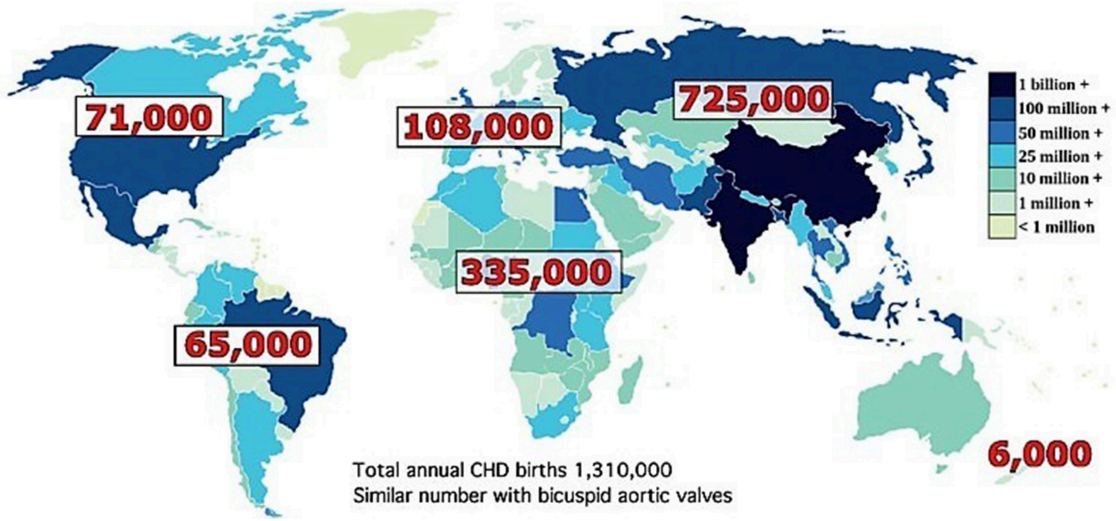

FIGURE 2 | Total annual birth of children with CHD by continent wise. Total number is roughly 1,310,000. Similar number with bicuspid aortic valves. Reproduced with permission from Hoffman (4).

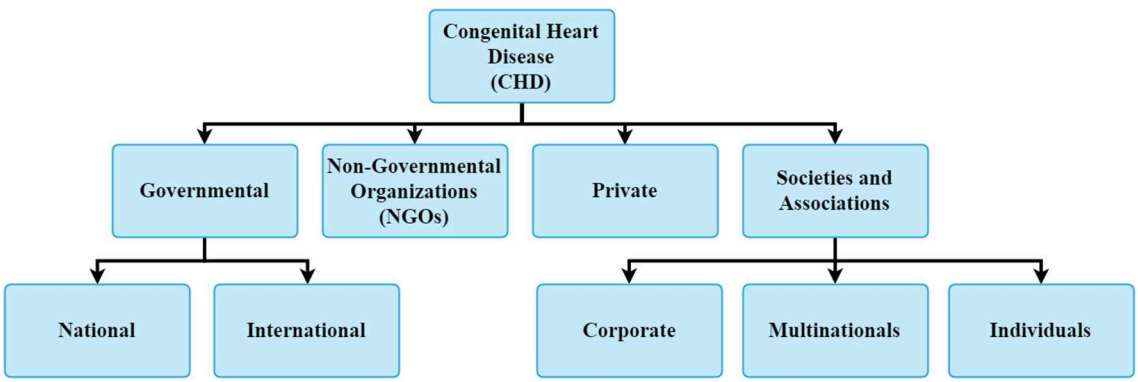

FIGURE 3 | The various organizations providing cardiac care in LMICs.

1) Short term (1–2 weeks or once or twice per year) medical missions. Some of the missions in the world are listed in **Table 1**. For a more comprehensive list please refer to Nguyen et al. (10).
2) Long term, pairing programs, or imbedding models are programs in the developed world partnering with programs in the developing world for long-term partnerships, commonly 5–10 years. The focus is on education, training, skill set development, improving outcomes, quality control, and long-term sustainability.

SHORT TERM MEDICAL MISSIONS

Short term cardiac medical missions have been offered for many years in Asia, Africa, Central and South America. In the earlier era these missions only performed closed heart procedures before gradually introducing open heart surgery. In later stages some of the native surgeons and cardiologists were sent to developed countries for training. These countries receiving short-term missions usually fell into three categories including:

1) Developing countries with *in-situ* cardiac programs.
2) Developing countries which will likely never have a program of their own (e.g., Caribbean and surrounding islands with a population of 40 million and the Pacific with similar populations).
3) Previous failed programs

Over the last two decades there has been a proliferation of short term missions, especially in Asia and Africa. Based on different strategies, some of these missions have been improperly labeled as "medical/surgical safaris" (11, 12). The authors believe that the criticism may be unfair as these "medical/surgical safaris," though not perfect, were able to help scores of patients who otherwise had no access to surgery. Good hearted and well-meaning surgeons, cardiologists, nurses,

TABLE 1 | Some groups doing cardiac surgical missions.

Number	Name of organization	Websites
1	American College of Surgeons	https://www.facs.org/ogb
2	Bambini/Cardiopatici Nel Mondo	www.bambinicardiopatici.it/
3	Be Like Brit	https://www.belikebrit.org/
4	Cardiostart	https://cardiostart.org/
5	Chain of hope	https://www.chainofhope.org/
6	Children's Heart link	https://childrensheartlink.org/
7	Crudem	http://crudem.org/
8	CTSNET	https://www.ctsnet.org/
9	European Association for Cardiothoracic Surgery	https://www.eacts.org/
10	Earth Med	https://www.earthmed.org/
11	European heart for Children	http://www.europeanheartforchildren.com/
12	For hearts and Souls	http://forheartsandsouls.org/
13	Foundation Mauritanienne duCoeur	www.mauritanie-coeur.org
14	Frontier Lifeline	http://www.frontierlifeline.com/
15	Gift of Life International, Inc.	http://www.giftoflifeinternational.org/
16	Global Healing	https://globalhealing.org/
17	Global Heart Network	https://globalheartnetwork.wordpress.com/
18	Global Impact	https://www.charity.org/index.html
19	Haitian Hearts	http://www.haitianhearts.org/
20	Healing the Children	http://healingthechildren.org/
21	Hearts Around the World	http://www.heartsaroundtheworld.org/
22	Heart to Heart	https://www.heart-2-heart.org/
23	Heartbeat International Foundation	https://www.heartbeatsaveslives.org/
24	Heart Care International	https://www.heartcareintl.org/
25	Hearts for All	https://www.coeurspourtous.ch/
26	International Aid	http://www.internationalaid.org/
27	International Children's Heart Foundation	https://www.babyheart.org/
28	International Children's Heart Fund	http://www.ichfund.org/
29	Heal A Child	https://www.heal-a-child.org/
30	Magdi Yacoub Foundation	https://myf-egypt.org
31	MAP International	https://www.map.org/
32	Mending Kids International	https://www.mendingkids.org/
33	Mercy Ships	https://www.mercyships.org/
34	Novick Cardiac Alliance	https://cardiac-alliance.org/
35	Open Heart International	https://ohi.org.au/
36	Palestine Children's Relief Fund	https://www.pcrf.net/
37	Pan-African Academy of Christian Surgeons	https://www.paacs.net/
38	Physicians for Peace	http://www.physiciansforpeace.org/
39	Project Kids	https://www.projectkidsworldwide.org
40	Project Haiti Heart	http://projecthaitiheart.org/
41	Project Hope	https://www.projecthope.org/
42	Project Open Hearts	http://www.poh.org/
43	Project Medishare	http://projectmedishare.org/
44	Russian Gift of Life	http://rgolusa.org/
45	Samaritan's Purse-International Relief	https://www.samaritanspurse.org/
46	Save A Childs Heart Foundation	https://www.saveachildsheart.org/
47	Surgeons of Hope Foundation	https://surgeonsofhope.org/
48	Team Heart- Rwanda	https://teamheart.org/
49	The Heart of a Child Foundation	http://www.heartofachild.org/
50	The Childrens Lifeline	http://childrens-lifeline.org/
51	Vina Capital Foundation	https://vinacapitalfoundation.org/en/
52	Walter Sisulu Pediatric Cardiac Foundation	https://wspcf.wordpress.com/
53	World Heart Federation	https://www.world-heart-federation.org/
54	World Pediatric Project	https://www.worldpediatricproject.org/

Source- International Children's Heart Fund website (http://www.ichfund.org/Content/Organizations.htm). For more comprehensive list please refer to Nguyen et al. (10).

and other professionals often take vacation time to travel to impoverished areas, putting their personal safety aside. However, it is difficult to discern how many of the host units have become self-reliant. This was highlighted in a study of 26 medical missions in sub-Saharan Africa (13). The authors concluded that the current model of collaboration via short term medical missions appears sub optimal for skill transfer and suggested deeper involvement of universities, governmental institutions, and visiting teams. The communication, networking, defined training, and long term goals need to be defined to achieve the complex goal of a sustainable program. We believe that there is a role for these short-term missions. In a detailed study of the financial implications of their many short term missions to LMICs, Cardarelli et al. have shown the cost effectiveness of intervention and the benefit to the society (14). In 2015, 446 patients received intervention in 10 LMICs at a total cost of $3,210,873. Each intervention was estimated at $171 per disability adjusted life-year averted. Each survivor potentially gained $159,533 in gross national income per capita during his or her extended lifetime (14). It is difficult to assess the number children who have come to developing countries over the years for free surgery. However, these children become productive members of society on a long term basis.

Here we discuss the present condition of the medical missions and possible future strategies. There are many pertinent questions. Do we continue with these short term teams? How do we better utilize human resources? How can we build programs in low resource countries? Can there be a better coordination between non-governmental organizations (NGOs)? What is the exit strategy? Can there be a unified approach? What are the long term strategies? What are the possible strategies to maximize

the benefit? The big questions are sustainability, accountability, transparency, and training. There is no "one size fits all" strategy.

WHAT WE KNOW THUS FAR

1) PERSISTENCE AND CONTINUITY: In one of the largest experiences in starting multiple pediatric cardiac centers in Russia, Young et al. acknowledged the importance of careful site selection based on demographic research as well as initial and secondary site assessments (15). Surgical education in the form of donor continuity and annual surgical education missions are important to achieve pairing of two cardiac centers, one of which is an established program. As the programs evolve and mature regular evaluations help with growth and sharing ("cross fertilization").

   This was further reiterated by Dearani et al. in their review of humanitarian efforts in developing countries and emerging economies (9). System factors influencing the delivery of healthcare include accessibility, availability, awareness, and affordability. They identified several key areas needing attention for a successful medical mission. They include: (1) Background study of the host country, (2) Identifying a dedicated host team with definable leader, (3) A Memorandum of Understanding (MOU) which stresses the exit plan, (4) Government help must be included, (5) Consider reliable NGOs for low cost items as well as locally available disposables and devices, (6) Successful programs depend on vision, appropriate skill sets, accessibility, availability, awareness, affordability, and action plan. They conclude that humanitarian, medical, and surgical outreach activities should focus on education and sustainability reserving "surgical tourism" for those countries that will likely never have the capability to have free standing cardiothoracic programs (9).
2) COOPERATION OF NGOs: Multiple organizations working in synergy to realize a common goal is crucial to success. Frigiola et al. highlight the success of the Bambini Cardiopatici Nel Mondo association and their cooperation with various NGOs, which has paved the way for various cardiac programs in Africa and beyond (16). Similarly, Dearani et al. have also described the importance of developing partnerships between governments and communities (8). The factors essential for successful partnerships include shared responsibility, pooling of resources, open communication, quality control, proper channeling of resources, and auditing (16).
3) FOCUS ON CHD: It is common knowledge that the priority in developing world is to combat communicable diseases. Very little attention is given to congenital or acquired heart disease in children. We must recognize the problem and the contributing factors, provide access to cardiac operations for common congenital diseases, and provide infrastructure through partnerships with governments and NGOs. When a program is initiated, starting with adult cardiothoracic surgery before pediatric cardiac surgery may be logical. Other important points include increasing human resources in health care via training programs and ongoing research with quality improvement (17).
4) ON SITE ISSUES: Once an "onsite" campus is identified, there are many factors which determine the success of the mission. The donor (NGO) and the host (on site) need to better coordinate the necessary needs and wants. Molloy et al. have identified the many on site issues and their possible solutions (18). The issues related to infrastructure, biomedical equipment, disposables (including devices and drugs), patient selection, human resources, training, quality control, security, credentialing, malpractice, finances, and host issues have all been well described. The key is to prepare oneself for all possibilities. Dr. Graham Nunn, a retired congenital heart surgeon from Australia, has spent the last 20 years of his career traveling to Papua New Guinea on annual short term missions. On request from the authors, he has sent the following communications about his experience and insight, which are summarized in **Tables 2**, **3**. Most importantly, he describes the need to have back up for failures of blood gas analyzers, autoclave, heart lung machines, and ventilators. In **Figures 4**, **5**, we detail the essentials needed for a cardiac operating room (OR) and intensive care unit (ICU), respectively.
5) VIEW FROM HOST PROGRAMS: Africa has many unique problems. They are over 1 billion in population with more than 50% under 25 years of age (5, 6, 19). Challenges include political instability, civil unrest, refugee populations, apathy, maldistribution, corruption, mounting debt, and frequent conflicts. The communicable diseases dominate the health programs. Only a small portion of gross domestic spending is for health care. The burden of CHD is only a part of the problem with RHD remaining the most common cardiac disease. Treatment often requires the availability of both adult and pediatric cardiac surgeons. However, surgeons who visit on medical missions from western countries are not necessarily trained to operate on and treat RHD. Furthermore, after valve replacement, long-term anticoagulation remains a problem in remote areas of Africa. Surgical training with hands-on approaches is another difficulty (5, 19).
6) FINANCES: This is the biggest predicament of the short-term mission trip. In a recent study published by Dr. William Novick and team, the humanitarian pediatric cardiac surgery programs to LMICs showed that they are very cost effective on a long-term basis (14). Cost cutting is achievable with local corporations and distributors.

A MODEL FOR ESTABLISHING A LONG-TERM PROGRAM

There is a collective experience of over 30 years dealing with short term missions. There are many lessons learned and few can be used to model a long term program. We have many years of catching up to do. The global challenge of CHD is ever increasing. In order to achieve the shared goal of accessible cardiac care for every child, the objective should be more global collaboration

TABLE 2 | The list of resources and the contingency plans for a short-term mission (Dr. Nunn).

Resources	Have contingency plans for
We should take adequate staff. Limit doctors and take more nurses, OR, ICU, anesthetic, and floor staff	Loss of water, Oxygen, and Electrical supply to OR and ICU. It will happen at some point
Biomedical staff are important ICU staff must back up local staff	Hand ventilating every patient in OR and ICU
Team manager role is critical	Emergency evacuation
We should select people who are "lateral thinkers" and who are willing to innovate in given circumstances- especially surgical and perfusion teams	Dealing with all possible post-operative complications in ICU
We should take enough materials and equipment	Local equipment failure e.g., we should have portable monitors in case of failure of standard monitors
We must take enough drugs for all contingencies	Emergency and resuscitation drugs
We must be prepared for inadequate blood banking support. We must take hemostatic agents e.g., Tranexamic acid and if possible, Factor VII A components	Provision for using fresh whole blood if components are not available. Will need to stock with blood drawing kits
We must take enough instruments/drapes/dressings	Local sterilization equipment failures

TABLE 3 | The Do's and Don'ts in a short-term mission (Dr. Nunn).

DOs	DON'Ts
The trip should only happen at the invitation of the host country	We should not force a team onto the host if they are not ready for us
We should engage with the local administrators and provide positive feedback each trip and ask them what they would like to achieve on the next trip and try to put that into practice	We should not impose our strategy on the host. Successful teams are those whose mission aligns with that of the host
Training must be hands on and very much "do as I do", rather than "do as I say"	We should not compromise on patient safety
We must work within the local politics, local trainees …. Competencies……	We just do not know all the background linkages between people in another society and can quickly offend
These things take time and certainly the worst thing is to try to tell the local administrators what to do	This also applies to local funding We have to say to ourselves, "this is the reality, how are we going to get done what we came here to do?" More importantly though, local funding needs to build and sustain the program that develops from these visits, so it is the essential ingredient for home grown success long term
Well one thing we will do is do it ethically and without compromise and try to live by example	We must be wary of using the voluntary work as a conduit for private practice
We should try to achieve outcomes that are the same as our parent institution	Deaths will be long remembered and will not lead to good will amongst the administrators and providers of funds when we are not there
We should select patients who can expect a good outcome and can reasonably be expected to be helped by the local team when they get up to speed	This means that heroic surgery should not be done. Just because the patient will die if we do not "have a go" is the worst way to select the patients for surgery
Attend socials but limit them so we can rest and concentrate on work ahead	Try not to spend every evening going to social functions. It is natural for a team to want to socialize but those working days are hard and no one can perform to their own standard with that dragging them back each day. We do not do it at home so how can we think we are super human on one of the trips
We should take a very long-term view about how quickly the local team will come up to speed	We must stop being critical of the hosts
Security is very important and must be provided by the local teams. Professional indemnity must be granted from the government of the country	In unsafe areas we should not venture on our own- no "Bravado" actions
Immunization must be a pre-requisite for all team members	

and shared strategies. This strategy depends on several questions. There is an established program which needs further help? Was there a program which is now closed and needs rebuilding? If there are no existing programs, does the country need or want one?

The task of providing cardiac care and surgery for all children in need appears daunting. There is a global shortage of skilled workers in congenital cardiac care. Leblanc proposes a "KISS" (keep it simple and safe) approach (20). Everything needs to be organized and simplified. This planning includes: site evaluation, training, on site infrastructure development, necessary OR and ICU equipment and training, laboratory training, blood banking, and administrative work. Despite hard work and tremendous effort, experience shows that it takes many years to achieve sustainable growth. Corno, in his review, writes that a successful long-term program must have the following requirements: high

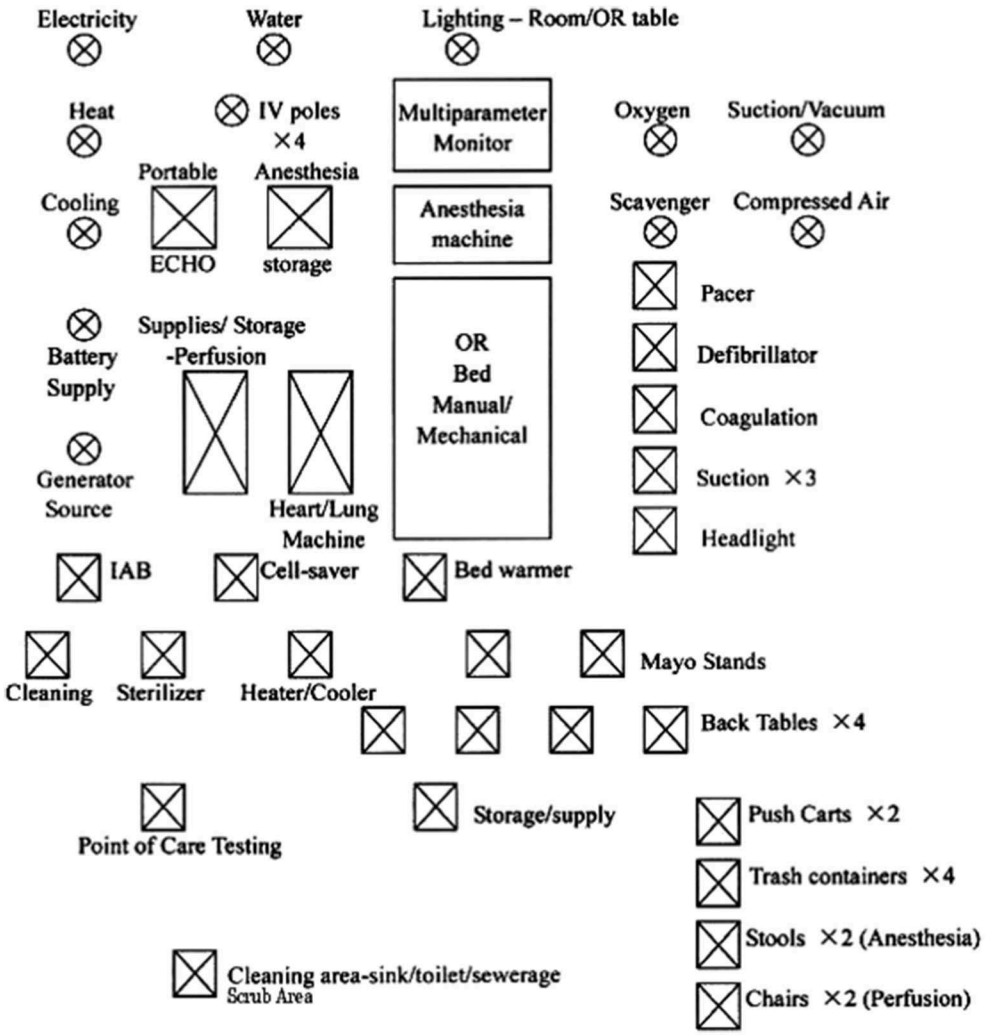

FIGURE 4 | Essentials for a cardiac OR (OR, Operation rom; IV, Intravenous pole; IAB, Intraaortic Balloon pump). Reproduced with permission from Dr.Pezzella http://www.ichfund.org/Content/OR-ICU_lists.htm.

quality measurable outcomes, sustainability, scalability, and efficacy (12).

Here we review some suggested ways to achieve a successful long-term program:

1) SHARED VISION: If our common goal is to provide cardiac care for all children in the world, the existing societies (Society of Thoracic surgery (STS), American association of Thoracic surgery (AATS), Asian Society of Cardiovascular and Thoracic Surgery (ASCVTS), European association of Cardiothoracic Surgery (EACTS), World Society of Pediatric and Congenital heart surgery (WSPCHS), World congress of Pediatric cardiology and cardiac surgery etc.) must, as well as the CTS Net play an important and expanded role in a top down approach. In addition to establishing volunteer platforms and conducting annual sessions of development of cardiac surgery in LMICs, there should to be a larger cooperation and collaboration between various societies. One such example is the Cape Town declaration on access to cardiac surgery (especially the scourge of RHD) in the developing world (21). This top down approach creates awareness and fosters collaboration between international cardiac surgery societies, industries, and government. Their aim is to establish international working groups from the above groups to evaluate and endorse development of cardiac care in LMICs and training of surgeons and other professionals in these countries (21). Similarly, the "global statement" sponsored by the Pediatric Cardiac Intensive Care Society is another step for collaboration and top down approach. The statement fosters partnerships, education, and training (22).
2) "SPARK PLUG": An essential component for a long term success is a "spark plug." The term was used by Dr. Terry Davis, a congenital surgeon, from Ohio, in a private conversation. He described it as an "organization or

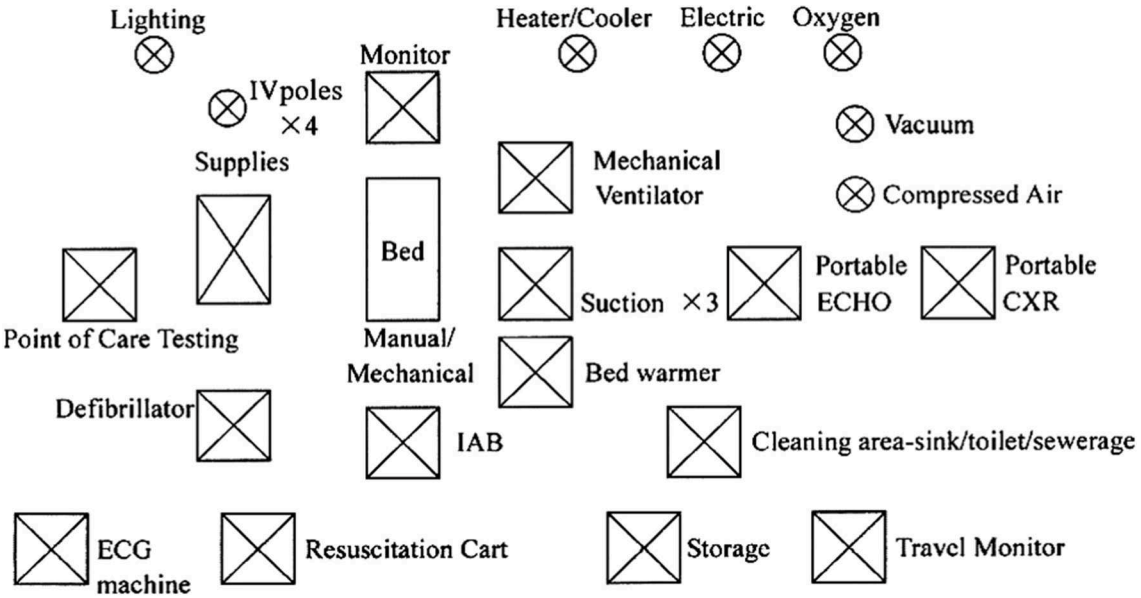

FIGURE 5 | Essentials for an ICU (IV, Intraveonus; IAB, Intraaortic Ballon pump). Reproduced with permission from Dr.Pezzella http://www.ichfund.org/Content/OR-ICU_lists.htm.

individual, often from the host country, who is a dedicated leader, focused, invested, and physically present in a local program on a long term basis." There are many examples of "spark plugs" in the world. We have previously described work of some organizations in Russia (15) and Africa (16). One such is Dr. Efrain Montesinos. He took an early retirement from the United States and went back to his native country of Peru. He worked to establish a cardiac surgery program among the indigent (23). He and his wife were physically present in Peru, navigated the bureaucracy and the deficiencies of the system, and started short-term medical missions in an old prison ward in the late 1990s with the support of philanthropic societies and hospitals in US. This initiative over the years has resulted in one of the major cardiac surgery departments in Peru. He did not live to see the entire success as he died in 2007, but his legacy remains (23). Another "spark plug" is Dr. Aldo Castaneda. His hard work, persistence, and dedication led to the establishment of a sustainable pediatric cardiac surgical program in Guatemala City, Guatemala (11). Similarly, other surgeons such as Alain Carpentier, Magdi Yacoub, Alain DeLoche and many others have all been "spark plugs."

3) COMMUNICATION AND COORDINATION: We believe there are enough resources for many LMICs if there is better coordination between the various donor and host organizations (NGOs, corporates, individuals, governments, and hospitals). The inadequate communication between these organizations leads to insufficiency and duplication of work. Centers of excellence in the developed countries need to be identified. Coordination between these centers, the NGOs, and the host countries can be very beneficial. Within the host country there is usually a vast maldistribution of medical care. The location of the hospital should be selected based on population distribution, urban/rural location, income divide among the people, availability of materials, and ease of access of the facility. A formal MOU between NGOs/charitable trusts, societies, governments, corporations, and individuals is encouraged. Developing regional "hubs" which serve smaller satellite centers for a geographical zone or region would be ideal. Examples of "hubs" could include: (1) Europe looking after certain African countries, (2) North America helping Central and South American as well as the Caribbean countries, (3) Australia helping with the Pacific Islands and some Asian countries, (4) Israel and Saudi Arabia helping with the surrounding countries, and (5) Emerging economies such as China India, and South Korea also helping with training and material support. This method is more logistical and feasible as these countries are often in the same time zones. The question would be who would oversee such an organization. What is really needed is a worldwide body to divert allocation- but we all know this is unlikely. Some of these initiatives were detailed by Dr. Cox in his presidential address in 2001 (24). The "hub" philosophy may be ideal, but this should not preclude people from going anywhere/everywhere to help. This goes with the philosophy "perfection may be an enemy to good."

One of the earliest successful partnerships which resulted in a long-term program is the Vien Tim institute in Vietnam. It was a result of partnerships with government, Carpentier foundation, and numerous other charities. Over the years the institution grew and currently performs over 1,500 open heart operations annually (25, 26). Another successful partnership is the cooperation between the model of IRCCS Policlinico San Donato and the Bambini Cardiopatici nel

Mondo association for CHDs. Many countries in Northern Africa, Middle East, Eastern Europe, and Latin America have benefitted from their collaboration. Cardiac surgery departments evolved in countries such as Cameroon, Syria, Northern Iraq (Kurdistan), Peru, and Romania (16). The Shisong Cardiac Center Project in Cameroon is another great example of cooperation between various organizations, Bambini Cardiopatici nel Mondo Association and Hospital (IRCSS Policlinico-San Donato) another Italian NGO (Cuore Fratello) and local faith-based hospital (Tertiary Sisters of Saint Francis). They started work to establish cardiac care in 2002 and in 2009 were successful in establishing an autonomous institution which is the largest cardiac care center in Cameroon (27). Another good example of "taking cardiac surgery to the people" is the model from Egypt which is mainly funded by donations from Egyptian people (28).

Some practical aspects of coordination include:

a) Choosing one country of interest and then coordinating with all agencies interested in that country. This is idealistic and may be difficult to follow. But an attempt can be made. Young et al. have described the establishment of 6 new congenital programs over 25 years of focused approach in Russia (15).
b) Teams going sequentially for a defined period creating an overlap of resources. This is hard to achieve with little coordination between the involved NGO's. This has been the request from many of the host countries from Africa (19).

4) TRAINING: The strategy for training is very important. Training which involves administrative, clinical, and research areas should be an effective component of a mission. However, the most difficult piece is the hands-on training in the OR. The training can be divided into several phases (1) observational training in a developed center (2) hands-on training by visiting teams on site, and finally (3) having an embedded on-site mentor, consultant, or proctor. The role of retired or semi-retired surgeons is invaluable for a fixed 1 month stay or longer (27). The role of senior surgeons is very valuable as shown by Dr. Aldo Castaneda in the Guatemala experience (11). There is a role for cross training (e.g., OR nurses can be trained for perioperative care of patients, the perfusionists can be trained to help in closure of wounds, etc.). This is a cost-effective strategy for a starting program. This is like some sort of "military special forces" who are trained as "multipurpose workers." This may be better in the initial stages for building a team philosophy. Previously, Australia, the United Kingdom (UK), and the US have trained many surgeons from developing countries helping them establish programs in their own countries. However, the current immigration and training regulations preclude easy access.

Recently, countries such as India have become the new hub for training as they have increased the number of cardiac programs. There are surgeons being sent there for hands on training (29). Bastero et al. have presented 4 models of partnership models in pediatric cardiac surgery and cardiac intensive care programs in LMICs (26). The sustainable model of pediatric cardiac surgery program in Mexico which is a private-public partnership, with help from NGO and the Texas Heart Institute in the US is one example. Similarly, sustainable programs have been developed in India and Vietnam with education and training of the nurses and medical staff via organizations in the UK, France, and Australia. Similarly, Chain of Hope helped in developing a program in Jamaica. These examples prove the importance of partnerships (26).

World societies such as WSPCHS, EACTS, and the hubs can help with periodic education programs. Simulation training is invaluable. Other modalities like use of 3-D technology, virtual reality, and augmented reality may also play a role in the future. Remote training can be achieved with telemedicine. It cannot be stressed enough how invaluable this technology is for remote discussions, training, and consultations. However, this can never replace hands-on training for the local teams.

5) MATERIAL SUPPORT: Developing infrastructure is a challenge. There should be development in all supporting departments such as the OR, ICU, anesthesia, perfusion, biomedical, cardiology, pharmacy, nursing, blood bank, and administrative support. Basic infrastructure needs to be provided. The equipment/disposables, devices, sutures, instruments and drugs are expensive. Here the donations of equipment (ideally <10 years old) in good condition from developed centers may be invaluable. There are aid agencies which refurbish used equipment including perfusion machines which can be useful. The disposables and materials may be cheaper to buy locally. Post-operative follow-up is also crucial to success of teams. A continual supply of drugs needs to be made available. A final and important question is where will the financial resources come from (e.g., government, private institution, charitable trust, or out of pocket)?
6) EXIT STRATEGY: Long term programs may be more successful if there are already "*in-situ*" cardiac programs. However, there needs to be an exit strategy to prevent the creation of an entitled program or dependent program with no growth for the local teams. One successful venture by project HOPE is the pediatric cardiac surgery program in Shanghai, China spearheaded by Richard Jonas. The *in-situ* program which was performing 200 cases annually in the past is now performing over 4,000 operations annually on its own (30). This is a successful cooperation among various players in the country of interest but there was a clear exit strategy and the host hospital became self-reliant.
7) DATA: For long term success a data base needs to be maintained for evaluation of progress. The epidemiological studies pertaining to incidence and prevalence in CHD and RHD need to be better understood. Then the center specific/surgeon specific data can be evaluated. This includes the cases performed and their follow

up. There could be a better role for the WSPCHS in the US and the European Congenital Heart Surgeons Association in Europe to spearhead the data acquisition of these programs.

WHAT IS THE FUTURE?

We have written about the past and what is being done presently by many organizations.

There is very little written about the reasons for failure of programs in developing and developed countries. It is human nature not to talk about failures. We have identified a few reasons for failure of projects. Often the reasons are due to (1) unsustainability and no exit strategy (e.g., Haiti and Nigeria), (2) "Bridge too far"-Caribbean and many Pacific islands are spread over hundreds of islands with small populations and it would be impractical to have individual cardiac centers in all islands (e.g., Cook Islands, Kiribati, Tonga, Fiji). Developing regional hubs for them is probably the right thing. The Dominican Republic acting as a hub for the Caribbean and either Australia, New Zealand, Hawaii or Papua New Guinea can be developed as a hub for the Pacific, (3) poor results-often the surgeon is blamed but it is multifactorial and a system failure, (4) financial issues are one of the most glaring problem. Many programs in Central and South America are finding it difficult to run their current cardiac programs (e.g., Guatemala), (5) personal egos of bureaucrats and medical professionals, (6) safety and war situation such as programs in Middle East, and finally (7) lack of government support.

We believe that much depends on developing regional hubs and using embedding as an effective tool. Dr. Aldo Castaneda once said "Development of a sustainable pediatric cardiac program in emerging countries presents many difficult challenges. Hard work, perseverance, adaptability, and tolerance are useful aptitudes to develop a viable program in an 'emerging' country. We are not in favor of medical surgical safari efforts, unless these efforts include training of a local team and eventual unit independence. It helps if an experienced (± senior/retired) surgeon leads this effort on a full-time, pro-bono basis. Local and international fund raising is essential to complement vastly insufficient government subsidies" (11).

"Embedding" involves a trained surgeon, retired or on sabbatical spending long periods of time helping a center. It could be 6 months or 1 year. One of the authors (Pezzella) has had the experience of spending long periods of time in China, Vietnam, and other countries (31, 32). The "embedding" program could be sponsored by associations like AATS (Graham traveling scholarship), STS, EACTS, and ASCVTS. These will be cost effective in the long term. As the hands-on training is becoming harder for new surgeons the "embedding" program may be an answer for onsite training.

SUMMARY

Much has been written by scores of individuals and organizations about their experience in providing cardiac care for LMICs. Much has been done and lessons learned. We believe that a comprehensive global cooperation is urgently needed if we are to provide heart care to every child born and fulfill our goal of sustainable care by 2030. There needs to be active participation from different cardiac societies, collaborations with NGOs and other organizations. This needs to be on the top of agenda for their organizations. Regional hubs need to be identified and supported. Training needs to be coordinated and we hope that there is a fire lit in all cardiac surgeons/cardiologists to help with this cause. We hope for many "spark plugs" who are willing to give their time for training and help with any unit on a long-term basis. The time to act is now.

DATA AVAILABILITY

All datasets for this study are included in the manuscript and/or the supplementary files.

AUTHOR CONTRIBUTIONS

JM has done over 50% of the draft. TK has introduced concepts and contributed to 20% of the draft. AP has initiated this review and helped with literature search and thus helped with 30% of the draft.

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REFERENCES

1. UNICEF data. Retrieved from https://www.unicef.org/sowc2016/, https://www.unicef.org/publications/files/UNICEF_SOWC_2016.pdf (accessed January 23, 2019).
2. UNDP data. Retrieved from http://www.undp.org/content/undp/en/home/sustainable-development-goals/goal-3-good-health-and-well-being/targets/ (accessed October 30, 2018).
3. WHO Global Health Observatory Data. *Causes of Child Mortality*. (2017). Retrieved from https://www.who.int/gho/child_health/mortality/causes/en/ (accessed January 23, 2019).
4. Hoffman JIE. The Global burden of congenital heart disease. *Cardiovasc J Afr*. (2013) 24:141–5. doi: 10.5830/CVJA-2013-028
5. Hewitson J, Zilla P. Children's heart disease in sub-Saharan Africa: challenging the burden of disease. *J South Afr Heart Ass*. (2010) 7:18–29. doi: 10.24170/7-1-1964
6. Bode-Thomas F. *Challenges in the Management of Congenital Heart Disease in Developing Countries*. Available online at: http://cdn.intechopen.com/pdfs/26663/InTech-Challenges_in_the_management_of_congenital_heart_disease_in_developing_countries.pdf (accessed May 1, 2019).
7. Olga MA, Lameira E, Yaksh A, Paul L, Ferreira MB, Sidi D. Challenges on the management of congenital heart disease in developing countries. *Int J Card*. (2011) 148:285–8. doi: 10.1016/j.ijcard.2009.11.006
8. Dearani JA, Neirotti R, Kohnke EJ, Sinha KK, Cabalka AK, Barnes RD, et al. Improving pediatric cardiac surgical care in developing countries: matching resources to needs. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Ann*. (2010) 13:35–43. doi: 10.1053/j.pcsu.2010.02.001

9. Dearani JA, Jacobs JP, Bolman RMIII, Swain JD, Vricells LA, Weinstein S, et al. Humanitarian outreach in cardiothoracic surgery: from setup to sustainability. *Ann Thorac Surg.* (2016) 102:1004–11. doi: 10.1016/j.athoracsur.2016.03.062
10. Nguyen N, Jacobs JP, Dearani JA, Weinstein S, Novick WM, Jacobs ML, et al. Survey of Nongovernmental organizations providing pediatric cardiovascular care in low- and middle-income countries. *World J Ped Cong Heart Surg.* (2014) 5:248–55. doi: 10.1177/2150135113514458
11. Leon-Wyss JR, Veshti A, Veras O, Gaitán GA, O'Connell M, Mack RA, et al. Pediatric cardiac surgery: a challenge and outcome analysis of the guatemala effort. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Ann.* (2009) 12:8–11. doi: 10.1053/j.pcsu.2009.01.003
12. Corno AF. Paediatric and congenital cardiac surgery in emerging economies: surgical 'safari' versus educational programmes. *Int Cardio Vasc Thorac Surg.* (2016) 23:163–7. doi: 10.1093/icvts/ivw069
13. Tefera E, Nega B, Yadeta D, Chanie Y. Humanitarian cardiology and cardiac surgery in Sub-Saharian Africa: can we reshape the model? *World J Pediatr Cong Heart Surg.* (2016) 7:727–31. doi: 10.1177/2150135116668834
14. Cardarelli M, Vaikunth, Molloy F, DiSessa TG, Sauter L, Bowtell K, et al. Cost effectiveness of humanitarian pediatric cardiac surgery programs in low-and middle-income countries. *JAMA Netw Open.* (2018) 1:e184707. doi: 10.1001/jamanetworkopen.2018.4707
15. Young JN, Everett J, Simsic JM, Taggart NW, Litwin SB, Lusin N, et al. A stepwise model for delivering medical humanitarian aid requiring complex interventions. *J Thorac Cardiovasc Surg.* (2014) 148:2480–9. doi: 10.1016/j.jtcvs.2014.07.067
16. Frigiola A, Moussaidi N, Giamberti A, Pomd G, Isgro G, Youssef T, et al. International cooperation in healthcare: model of IRCCS policlinico san donato and bambini cardiopatici nel mondo association for congenital heart diseases. *Eur Heart J Suppl.* (2016) 18:E72–E78. doi: 10.1093/eurheartj/suw023
17. Musa NL, Hjortdal V, Zheleva B, Murni IK, Sano S, Schwartz S, et al. The global burden of paediatric heart disease. *Cardiol Young.* (2017) 27(Suppl. 6):S3–S8. doi: 10.1017/S1047951117002530
18. Molloy FJ, Nguyen N, Mize M, Wright G, George-Hyslop C, O'Callaghan M, et al. Medical missions for the provision of paediatric cardiac surgery in low- and middle-income countries. *Cardiol Young.* (2017) 27 (Suppl. 6):S47–S54. doi: 10.1017/S104795111700261X
19. Tefera E. Treatment of children with Rheumatic heart disease in sub Saharan Africa by overseas medical missions: challenges left behind. *J Cardiol Clin Res.* (2014) 2:1016–21.
20. Leblanc JG. Creating a global climate for pediatric cardiac care. *World J Pediatr.* (2009) 5:89–92. doi: 10.1007/s12519-009-0019-0
21. Zilla P, Bolman RM, Yacoub MH, Beyersdorf F, Sliwa K, Zuhlke L, et al. The Cape town declaration on access to cardiac surgery in the developing world. *Ann Thorac Surg.* (2018) 106:930–3. doi: 10.1016/j.athoracsur.2018.05.020
22. Brown K, Beke D, Cooper D, MacLaren G. Pediatric cardiac intensive care society statement: caring for children with critical cardiac disease across the globe. *Cardiol Young.* (2017) 27:S1–S2. doi: 10.1017/S1047951117002517
23. Martinez JJ, Rafael AY, Rodriguez JP, Davis JT, Murala JS. A tribute to dr montesinos: 20 years from medical missions to a cardiothoracic surgery department. *World J Pediatr Cong Heart Surg.* (2019) 10:250–2. doi: 10.1177%2F2150135119831965
24. Cox JL. Presidential address: changing boundaries. *J Thorac Cardiovasc Surg.* (2001) 122:413–8. doi: 10.1067/mtc.2001.118489
25. Lajos PS, Carpentier AF. Viện tim institut du coeur: success of a congenital heart disease center in a developing country. *Ann Glob Health.* (2016) 82:621–4. doi: 10.1016/j.aogh.2016.08.002
26. Bastero P, Staveski S, Zheleva B, Scanlan E, Cabrera A, Araujo A, et al. Partnership models for the establishment of sustainable paediatric cardiac surgical and cardiac intensive care programmes in low- and middle-income countries. *Cardiol Young.* (2017) 27(S6):S55–S60. doi: 10.1017/S1047951117002621
27. Giamberti A, Butera G, Mve Mvondo C, Cirri S, Varrica A, Moussaidi N, et al. The Shisong cardiac center in cameroon: an example of a long-term collaboration/cooperation toward autonomy. *Front Pediatr.* (2018) 6:188. doi: 10.3389/fped.2018.00188
28. Yacoub M, ElGuindy A, Afifi A, Yacoub L, Wright G. Taking cardiac surgery to the people. *J Cardiovasc Transl Res.* (2014) 7:797–802. doi: 10.1007/s12265-014-9598-9
29. Davies P. Could a passage to India be the way to get more surgical experience? *Br Med J.* (2012) 345:e6637. doi: 10.1136/bmj.e6637
30. Liu J. Challenges and progress of the paediatric cardiac surgery in Shanghai Children's Medical Center: a 25-year solid collaboration with project HOPE. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Ann.* (2009) 12:12–8. doi: 10.1053/j.pcsu.2009.01.020
31. Pezzella AT. Initiation of a model six-year cardiothoracic surgery residency program in Shanghai, China. *Ann Afr Chir Thor Cardiovasc.* (2009) 4:81–99. Available online at: https://www.aactcv-aatcvs.org/2009/volume42/7-initiation-of-a-model-six-years.pdf (accessed March 1, 2019).
32. Pezzella AT. Model 5 year cardiothoracic surgery residency program in Ho Chi Minh city, Vietnam. *Ann Afr Chir Thor Cardiovasc.* (2014) 9:7–16. Available online at: https://www.aactcv-aatcvs.org/2014/Revue-Volume-9-n1-2014.pdf (accessed March 1, 2019).

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Congenital Heart Disease in East Africa

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Congenital Heart Disease (CHD) is an enormous problem in Low Middle Income Countries and particularly in sub-Saharan Africa. There is an estimated 500,000 children born in Africa with CHD each year with a major proportion of this in sub-Saharan Africa. The vast majority of these children receive sub-optimal or no care at all. In East Africa: Kenya, Tanzania, and Uganda have all attempted to create a CHD service for the last 20 years with minimal success due to various factors. Visiting cardiac missions have made considerable contributions in the development of CHD services in these countries, however there remains a significant number of children with lack of care. We explore the positive aspects of the current projects, the various factors that hinder growth in this area, and what can be done to promote CHD service growth in these countries.

Keywords: congenital heart disease, cardiac missions, charity, pediatric cardiology, cardiac surgery, charity, cardiac catheterization

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The incidence of congenital heart disease (CHD) ranges from 19 to 75 per 1,000 live births (1). It is also the leading cause of birth defects and the second leading cause of death in the first year of life after infectious diseases (2).

Factors contributing to birth defects include single gene and chromosomal disorders, environmental teratogens, multifactorial inheritance, and micro-nutrient deficiencies (1, 3). Whilst exposure to medicines and recreational drugs—including alcohol and tobacco—may not greatly contribute to the incidence in low-middle income countries (LMICS) and particularly in sub-Saharan Africa, maternal infectious diseases such as syphilis and rubella greatly increases it (3). Additionally due to the high fertility rate and high neonatal mortality rate, the incidence of CHD in sub-Saharan Africa is greatly underestimated (4).

The burden of CHD is immense. Advancing technology has improved the outcomes of children with these defects in developed countries. However, the financial impact of a child with CHD has exponentially increased over the last few decades. A recent study found that of the total pediatric hospitalizations in the United States, only 3.6% accounted for treating children with CHD. However, it represented more than 15% of the annual costs for pediatric hospitalizations (5). As such in sub-Saharan Africa, the cost burden is significant and carries important implications in treating children with CHD.

CONGENITAL HEART DISEASE IN SUB-SAHARAN AFRICA

The Global Burden of Disease Study estimated that 80% of deaths from non-communicable diseases, including CHD, now occur in LMICs (6, 7). Additionally the World Health Organization (WHO) estimates that 1% of live births have CHD accounting for ∼1.5 million per year. There have been estimates by WHO to suggest that 90% of these children have suboptimal or no access to

care at all with most of these children are concentrated in LMICs, particularly sub-Saharan Africa (8). These numbers however have been mitigated in recent years, by the rapid rise of the Chinese and the Indians' development of their congenital heart service, and their support to LMICs.

Health Care Considerations

Any established healthcare system goes beyond hospitals, doctors, nurses, and allied health care providers. A successful healthcare system requires a robust infrastructure, which includes government support, good relations with business and industry, and a university program. Importantly, it should include a continuing education program and good governance (9).

Factors that impact healthcare delivery include affordability, access, and awareness (8). All three of these elements must exist for successful healthcare delivery. In CHD, particularly in sub-Saharan Africa, each of these three factors contributes to numerous children being unable to obtain appropriate care.

Affordability

Without governmental (or humanitarian) support, the treatment of CHD is unaffordable for the vast majority of the population in sub-Saharan Africa. The costs are prohibitive even though the treatment can sometimes be curative or often have a strikingly positive impact on the individual's clinical status. The current setup, particularly in East Africa, is self-funding for the vast majority of patients with CHD. However, there are many discouraging factors in the pathway. For example, once seen by the cardiologists, numerous tests may be required to confirm the diagnosis and identify the type of intervention. This can include electrocardiogram, echocardiogram, or diagnostic cardiac catheterization, which often have a significant individual cost. As such the economic odds heavily favor the wealthy similar to other developing countries (10). Those who cannot afford the treatment will either accept their fate or attempt to raise some money, often with the help of their families or local village communities. However, the money raised frequently falls short or is too late. In the rare instance where they are able to pay for treatment, the financial impact to the family and their village is considerable, not only in their existing state of affairs, but also for their future planning.

Public hospitals (where the care is free or for a nominal cost) attempt to bridge the cost of the care, but are congested and overwhelmed. Political interference, self-preservation, enhanced private pay for skilled professionals, and lack of funding often impedes these centers, which have made recurrent unsuccessful attempts to start and establish a robust program since the early 1970s (9, 11).

Fortunately in the last decade, there has been progress with the three East African countries (Kenya, Tanzania, and Uganda) all taking steps to address the lack of cardiac services and in some cases making progress to ensure that their citizens have full health coverage. However, there still remains a lot to be done.

Access

Very few cardiac centers exist in each of these countries (12) and they are always located in the main cities. Some countries, such as Kenya, have adopted the use of helpful but infrequent satellite clinics to provide care for patients, who live outside major cities. However, any treatment, which requires admission into a hospital with cardiac expertise, would result in a long, and arduous journey (11).

Awareness

Late presentation of CHD in western countries is an exception rather than the rule. This is following numerous educational programs, a wide infrastructure of well-trained medical workforce, and several access points for patients to seek help (13). This infrastructure is an investment that has taken decades to develop. In sub-Saharan Africa, where the setup and educational awareness programmes are not as extensive, providing care for patients with CHD becomes a substantial challenge. Several patients, who have initial benign heart conditions, end up developing secondary irreversible damage, as they are not picked up in their early life. Those with more complex conditions, such as duct-dependent lesions, rarely survive.

EAST AFRICA

Kenya

Kenya's population is just under 50 million with more than 46% living below the poverty line (14). The under-5 mortality rate is 45 per 1,000, a factor of more than 10 compared with developed countries (**Table 1**). Encouragingly, the mortality rate has halved in the last 15 years with improvement in public health, with better basic hygiene, wider availability of clean water, and rising uptake of childhood vaccination. The first open-heart surgery, closure of an atrial septal defect, was performed in 1973 (11).

Based on the population and WHO report, ∼5,000 children require congenital heart surgery in Kenya each year. The number of children who do not receive these interventions is daunting. On an annual basis, Kenya performs between 120 and 150 congenital open-heart operations, with a similar number of congenital catheter interventions (personal communication—local pediatric cardiologists, current cardiology trainees; free-lance anesthetists, intensive care nurses, perfusionists; local consumable suppliers, administrative staff in various Kenyan hospitals, 2019). Approximately 50–100 additional patients receive treatment outside Kenya, most of whom are self-funded. This does not include those with rheumatic heart disease, which accounts for a significant workload in Kenya and sub-Saharan Africa. This aligns to WHO's estimate that the vast majority of CHD patients receive suboptimal or no care at all. The number of procedures performed by the local team has remained desperately low for several years despite no shortage of patients.

Most cardiac operations and catheter procedures take place in Nairobi with only recent commencement of another small programme in Mombasa. There are 6 hospitals capable of performing open-heart operations and cardiac catheterizations in Kenya, of which 4 are private. However, not all of them perform congenital heart interventions. The previously active congenital cardiac programme in Kenyatta National Hospital, a public hospital, has been defunct for over 2 years, with no indication of when it is likely to restart. The Mater Misericordiae Hospital has been running a cardiac programme for the

TABLE 1 | Comparison of country demographics and congenital heart services provided by each country.

	Population (millions)[a1]	Infant mortality rate[b2]	Under 5 mortality rate[b2]	CHD surgery	Surgical units	Catheter interventions	Intervention centers
Kenya	48.5	33.6	45.6	∼120	6*	∼120	6#
Uganda	41.5	35.4	49	70@	1	90@	1
Tanzania	55.5	38.3	54	∼40%	1		1
UK	65.6	3.7	4.3	>5,500[3]	16&	>3,500	20^
USA$	325.7	5.7	6.6	∼39,800[4]	>119[5]	>20,000[6]	166[4]
Sweden	9.9	2.3	2.8	∼600	2[7]	∼300	3[8]
Japan	127	1.9	2.6	>9,000 (15, 16)	121 (15)	>4,800 (17)	100 (16)

[a] *Data Gathered from the World Bank—last update 2016.*

[b] *Child Mortality rate—(Children under 5) expressed as deaths per 1,000 in 2017 (Median)—UNICEF. Infant Mortality Rate (Children under 1 year) expressed as deaths per 1,000 in 2017 (Median).*

**Centers, which can perform cardiac surgery in Nairobi with operating theaters, bypass machines (not all centers perform regular procedures). Staff are usually free lance, with local surgeons going from one hospital to another.*

 # All are based in Nairobi (as of 2017). CHD surgical and interventional numbers are annual average between 2015 and 2017.

@ CHD surgical and interventional numbers are annual average between 2015 and 2017. Note this number has reported to have increased significantly.

% CHD Surgical numbers are annual average between 2015 and 2017. Note this number represents half the total number (only CHD) of annual cardiac surgeries.

& as of 2017—UK has 11 pediatric cardiology heart units and 5 adult congenital surgical centers.

^ There are an additional 4 centers, which performs simple adult congenital interventions such as ASD closures.

$ For the year 2018.

last 20 years through various charitable fundraising activities. Charitable missions, ranging from 3 to 4 annual visits, perform a significant proportion of interventions, with various levels of local involvement. The other private hospitals perform *ad-hoc* congenital procedures. Recently MP Shah Hospital has hosted charitable missions with an ambitious view to establish itself as a fully functioning congenital heart service in Kenya. By using the visiting expertise, they are establishing an infrastructure, slowly aligning the staff training, and ensuring the right skills are recruited, to help establish their goal.

The enhanced implementation of the National Health Insurance Fund (NHIF) in Kenya has improved the affordability and subsidized the care of patients presenting to hospitals (18). Founded in the 1960s, the NHIF is a government state corporation, with a directive to provide health insurance to Kenyans over the age of 18 and their families. The mandate for NHIF is to provide accessible, affordable, sustainable, and quality health insurance for all Kenyan citizens. The fund, as of 2017, had more than 6.3 million members covering more than 25 million of the population, which include dependents of the principal member. There has been a recent impetus by the government to cover a larger population addressing all the three points listed above under "health care considerations." Since 2016 congenital cardiac procedures are covered under this programme. Although the entire cost is not covered, it provides a significant contribution. The challenge for NHIF coverage is that a considerable proportion of the population is informally employed. This means that mandatory contribution to the NHIF, as those by formally employed individuals, does not take place, leaving them vulnerable to the high cost of health care. However, all Kenyans are eligible for coverage with membership contributions aligned to their income, with the aim for universal health coverage by 2030 (18).

Tanzania

Tanzania has a population of over 55 million, with approximately half the population below the poverty line (19). The infant and under-5 mortality rate is comparable to the other two East African countries (see **Table 1**). Like its counterparts, it is going through a renaissance with strengthening economy, resulting in improved health service delivery.

Similar to Kenya the first cardiac surgery dates back to the 1970s. It is not until early 2000, that there was a legitimate investment in bringing about a cardiac service in Tanzania. A task force set up by the Ministry of Health visited countries with established cardiac units, with a view to setting up its first cardiac unit in Tanzania (20).

The first unit opened in 2008 as part of the Muhimbili National Hospital. Visiting missions, particularly from China and neighboring Zimbabwe, heavily supported the initial operations in Tanzania. In its inaugural year alone, more than 100 patients were operated, of which 35% consisted of CHD supported by Chinese medical staff.

[1] https://data.worldbank.org/indicator/SP.POP.TOTL?locations=VN-KE

[2] *Estimates Generated by the UN Inter-Agency Group for Child Mortality Estimation* (UN IGME) (2018). Available online at: http://data.unicef.org

[3] *National Institute for Cardiovascular Outcomes Research – NICOR.* Available online at: https://nicor4.nicor.org.uk/CHD/an_paeds.nsf/vwContent/NCHDA%20Report%20Analyses%202014-17?Opendocument

[4] *The Society of Thoracic Surgeons.* Available online at: https://publicreporting.sts.org/chsd

[5] *American College of Cardiology. ACC Congenital Heart Disease Clinic Directory.* Available online at: https://www.cardiosmart.org/Heart-Conditions/Congenital-Heart-Defects/CHD?w_nav=LN

[6] IMPACT Registry: https://cvquality.acc.org/NCDR-Home/registries/hospital-registries/impact-registry

[7] *SWEDEHEART Swedish Cardiac Surgery Registry.* Available online at: http://www.ucr.uu.se/swedcon/arsrapporter

[8] *National Quality Registry for Congenital Heart Disease (SWEDCON).* Available online at: http://kvalitetsregister.se/englishpages/findaregistry/registerarkivenglish/nationalqualityregistryforcongenitalheartdiseaseswedcon.2279.html

In 2013 a new cardiac center, The Jakaya Kikwete Cardiac Institute was opened with funding from the Chinese government designed to run independently of other services within the main hospital. The center has a fully functioning operating theater and a cardiac catheter laboratory. In the 3 years leading up to 2016, a total of 259 cardiac surgeries have taken place with a peak in 2015, when 164 cardiac operations were performed due to government drive inviting overseas cardiac missions to operate in Tanzania. The local team independently operated on a small number of patients a year but allowed them to establish themselves with the help of the visiting team. Half of the cardiac operations consisted of CHD patients, whilst the rest consisted of rheumatic heart disease and other cardiac conditions. Recently the number of independent (by the local team) and mission supported heart surgeries has increased with reports that they are undergoing a robust process in the establishment of an organized CHD service.

Uganda

Uganda is the smallest of the three East African nations with a population of just over 41 million people. With a similar public health profile compared with its neighboring countries, Uganda is also committed to setting up a CHD service. The first closed heart operation was in 1997 (21). However it has taken some time before the Uganda Heart Institute (UHI) in Kampala was set up in 2012. UHI is slowly building up its cardiac service with the help of visiting charity missions. It is the only center in Uganda, which has a combined open heart and cardiac catheterization service. There are two more institutes, which perform open-heart surgery in small numbers, however very few CHD procedures are performed outside Kampala.

Similar to Tanzania, the focus in Uganda has been to try and establish a CHD service by training and recruiting doctors and surgeons in one center. This process is slowly establishing a reliable service over the last 6 years. Notably, the local medical team perform majority of the procedures and the annual numbers are slowly increasing (see **Table 1**).

Importantly UHI, from an early stage, has accepted pediatric cardiology rotations and fellowships for training. This is an important investment in the development of this specialty with local graduates.

CHALLENGES OF DEVELOPING A CARDIAC PROGRAM IN EAST AFRICA

Development in East Africa is progressing rapidly. There has been significant progress in the economy, infrastructure, and primary health care with objective data supporting this in all the three East African countries. However, there remain challenges in developing healthcare particularly specialized cardiac healthcare, on a consistent basis. The following points addresses some of the challenges faced:

1. Inconsistent funding from the government.
2. Charitable missions provide a considerable proportion of CHD interventions. The care is often free and equipment is for nominal costs.
3. Huge variation in individual income results in inconsistent charges for procedures to each family.
4. Challenges in recruiting and retaining staff, due to inconsistent number of congenital heart interventions and poor pay.
5. Unreliable supply of consumables to perform cardiac surgery or interventional procedures.
6. Heavy custom charges and distributor's margin of profit for imported consumables and equipment required for surgery or catheter interventions. This often results in the procedures being more expensive than other well-established countries. As a result the possibility of obtaining items in bulk to offset costs has not developed.
7. Irregular number of cardiac interventions resulting in poor relationships being developed with local procurement agents.
8. Lack of investment by industry and individual donators in supporting the services in Kenya.
9. Corruption at various levels, which has hindered development of services.

It is worth emphasizing that almost all the current centers, which are being established in developing countries, have required the help of visiting missions (see **Table 2** for current cardiac missions visiting East Africa). This is essential to offset the heavy cost of implementing these techniques and perhaps more importantly, transferring the experience and training from the visiting teams—locally. It is often not possible for the local team of doctors and nurses to visit developed countries to work and gain experience due to difficulties in obtaining registration of medical/nurses. Additionally funding is often an additional

TABLE 2 | List of Cardiac Charity Missions to East Africa—not exhaustive.

Kenya	Tanzania	Uganda
Healing Little Hearts (UK)	Healing Little Hearts (UK)	Chain of Hope (UK)
World Medical Mission (USA)	Save a Child's Heart (Israel)	Rotary International
Medical & Education Aid to Kenya (UK)	Mending Kids (USA)	World Children's Initiative (USA)
Kothandam Sivakumar Cardiac Mission (India)	CardioStart (USA)	Mission Bambini (Italy)
Slovakia Republic Cardiac Mission (Slovakia)	Open Heart International (Australia)	Samaritan's Purse (USA)
		Hwan Sung (Korea)

The Chinese cardiac input in Tanzania was a governmental arrangement between the two countries and not strictly a charity organization.

insurmountable barrier. Those who have visited as observers have often found the lack of participation in procedures and decision-making overseas a difficult challenge to convert to their own practice.

With the exception of Egypt, Morocco, and South Africa, the rest of Africa is still in the process of trying to provide consistent congenital cardiac care than is currently available. Even these three countries have benefited from regular charity mission visits in the last few decades before establishing their services.

DISCUSSION

Establishing a CHD service is difficult and has numerous obstacles. The investment (both financially and as an infrastructure) required is significant and must be considered a long-term and progressive project. All three East African countries have been a part of this process for more than 20 years with limited but encouraging results.

For any healthcare project to succeed, it is vital that all three elements: awareness, access, and affordability, need to be addressed. Moreover, in addition to governmental support, a successful healthcare system requires good relations with business and industry (logistical and financial) and a university program to allow continuing educational development.

The development of a successful CHD service should be limited to a few centers. This would allow concentration of patients, resources, expertise, and international assistance. Once sustainability is achieved, these centers can become hubs for the development of even more centers.

All three countries have high quality university medical programmes. Pediatric cardiology needs to be formally recognized as a specialty with rotations in this field, similar to the achievements in Uganda. Hospitals, which do not have pediatric cardiology service, should work with others to allow rotations for their students or trainees to lay the foundation of future development of this specialty. Medical students and junior doctors educational programmes should allow participation in visiting charity missions. Education and training is critical in establishing the service and spreading awareness.

Rarely, some of the local medical teams have been fortunate to visit overseas and be part of an established training programme. This core team is particularly permeable to the incremental expertise brought by visiting international teams.

It is worth noting that all three countries rely heavily on charity missions to carry out relatively small number of CHD procedures. This is a consistent finding in numerous developing countries, where establishment of a CHD service is being attempted or has been established (21–23). In East Africa in the short term, this is necessary to promote development and sustainability of the cardiac services, however, to avoid stagnation of progress, this approach should be considered supportive and governmental in addition to societal buy-in is essential.

Countries such as Kenya are investing in the NHIF with the aim of universal health coverage in the next 15 years. The recent addition of coverage for CHD procedures is progressive, however but remains short of the actual cost. The shortfall remains a significant burden to the local population and needs further development.

In Tanzania, the national cardiac center is part of a large hospital with governmental support ensuring that the local team are paid well and motivated to improve their skills. However, the governmental subsidies specifically for cardiac procedures although helpful remain limited. Uganda in a short time has built up its service by focusing on one center. Development of local motivated medical staff by visiting missions, a key factor, has slowly led to independence in simple congenital open heart and cardiac catheterization procedures.

CHD has a significant burden on families and simple conditions if left untreated can lead to a debilitating condition. This not only creates a considerable burden but can also affect the future earning potential of families, which are already financially constrained.

Lastly, it could be argued that CHD forms a minor part of morbidity and mortality in public health compared with malaria, HIV, malnutrition, and other endemic conditions. It may be debated that to have a greater impact, the focus of sub-Saharan Africa and indeed LMICs should be to tackle these conditions. However, it has been shown in several studies that the development of CHD services has an impact on the wider hospital. By way of a "towing" effect, it raises the standard and performance and improves quality of the existing services, such as intensive care units and management of other specialties (8). It also brings about an increase in experience to manage other important cardiac conditions, such as rheumatic heart disease and Chagas disease. Additionally, those successfully treated form the basis of economic stability in their respective families and contribute to the society.

CONCLUSION

CHD is a huge problem. Various estimates suggest that there are close to 500,000 children born with CHD in Africa annually (24). India, over the last 2 decades, has shown that providing high quality cardiac care is achievable at a significantly reduced cost. After 4 decades of faltering starts, countries such as Kenya, Tanzania, and Uganda, are poised to make a spirited effort in addressing this huge issue. By creating "CHD hubs" in these countries, there is every chance that the East African nations can emulate countries like India and develop a robust cardiac service. These hubs can then be used to accept patients and trainees, which would not only further develop their own programme but also reduce the cost of sending patients to western countries.

AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, participated in drafting the article, and revising it critically for important intellectual content. All authors gave final approval of the version to be submitted.

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REFERENCES

1. Hoffman JI, Kaplan S. The incidence of congenital heart disease. *JACC.* (2002) 39:1890–900. doi: 10.1016/S0735-1097(02)01886-7
2. *Causes of Death*. Geneva: World Health Organization (2008). Available online at: http://www.who.int/healthinfo/global__burden__disease/cod__2008__sources__methods.pdf
3. Bruneau BG. The developmental genetics of congenital heart disease. *Nature.* (2008) 451:943–8. doi: 10.1038/nature06801
4. Hoffman, JI. The global burden of congenital heart disease. *Cardiov J Africa.* (2013) 24:141–45. doi: 10.5830/CVJA-2013-028
5. Simeone RM, Oster ME, Cassell CH, Armour BS, Gray DT, Honein MA. Pediatric inpatient hospital resource use for congenital heart defects: costs congenital heart defects. *Birth Defects Res Part A Clin Mol Teratol.* (2014) 100:934–43. doi: 10.1002/bdra.23262
6. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, Aboyans V, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet.* (2012) 380:2095–128. doi: 10.1016/S0140-6736(12)61728-0
7. Lim SS, Vos T, Flaxman AD, Danaei G, Shibua K, Adair-Rohani H, 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) 380:2224–60. doi: 10.1016/S0140-6736(12)61766-8
8. Dearani JA, Neirotti R, Kohnke EJ, Sinha KK, Cabalka AK, Barnes RD, et al. Improving pediatric cardiac surgical care in developing countries: matching resources to needs. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu.* (2010) 13:35–43. doi: 10.1053/j.pcsu.2010.02.001
9. Dearani JA, Jacobs JP, Bolman RMIII, Swain JD, Vricella LA, Weins tein S, et al. Humanitarian outreach in cardiothoracic surgery: from setup to sustainability. *Ann Thorac Surg.* (2016) 102:1004–11. doi: 10.1016/j.athoracsur.2016.03.062
10. Kumar RK, Tynan MJ. Catheter interventions for congenital heart disease in third world countries. *Pediatr Cardiol.* (2005) 26:241–9. doi: 10.1007/s00246-005-1005-5
11. Yuko-Jowi CA. African experiences of humanitarian cardiovascular medicine: a Kenyan perspective. *Cardiovasc Diagn Ther.* (2012) 2012:2231–9. doi: 10.3978/j.issn.2223-3652.2012.07.04
12. Yacoub MH. Establishing pediatric cardiovascular services in the developing world: a wake-up call. *Circulation.* (2007) 1161876–8. doi: 10.1161/CIRCULATIONAHA.107.726265
13. Sharland G. Fetal cardiac screening and variation in prenatal detection rates of congenital heart disease: why bother with screening at all? *Future Cardiol.* (2012) 8:189–202. doi: 10.2217/fca.12.15
14. *The United Nations International Children's Emergency Fund*. Available online at: https://www.unicef.org/kenya/
15. Takahashi A, Kumamaru H, Tomotaki A, Matsumura G, Fukuchi E, Hirata Y, et al. Verification of data accuracy in japan congenital cardiovascular surgery database including its postprocedural complication reports. *World J Pediatr Cong Heart Surg.* (2018) 9:150–6. doi: 10.1177/2150135117745871
16. Committee for Scientific Affairs, The Japanese Association for Thoracic Surgery, Masuda M, Endo S, Natsugoe S, Shimizu H, et al. thoracic and cardiovascular surgery in japan during 2015: annual report by the Japanese association for thoracic surgery. *Gen Thorac Cardiovasc Surg.* (2018) 66:581–615. doi: 10.1007/s11748-018-0968-0
17. Pediatric Interventional Cardiology. Establishment of the Japanese Society of Pediatric Interventional Cardiology (JPIC) database. *Pediatr Cardiol Card Surg.* (2015) 31:30–8. doi: 10.9794/jspccs.31.30
18. Okungu V, Chuma J, McIntyre D. The cost of free health care for all Kenyans: assessing the financial sustainability of contributory and non-contributory financing mechanisms. *Int J Equity Health*. (2017) 16:39. doi: 10.1186/s12939-017-0535-9
19. World Bank. *Tanzania Mainland Poverty Assessment: A New Picture of Growth for Tanzania Emerges*. World Bank (2015).
20. Nyawawa ETM, Ussiri EV, Chillo P, Waane T, Lugazia E, Mpoki U, et al. Cardiac surgery: one year experience of cardiac surgery at muhimbili national hospital, Dar es Salaam, Tanzania. *East Centr Afr J Surg.* (2010) 15:111–8.
21. Aliku TO, Lubega S, Lwabi P, Oketcho M, Omagino JO, Mwambu T. Outcome of patients undergoing open heart surgery at the uganda heart institute, mulago hospital complex. *Afr Health Sci.* (2015) 14:946. doi: 10.4314/ahs.v14i4.25
22. Noedir A, Stolf G. Congenital heart surgery in a developing country: a few men for a great challenge. *Circulation.* (2007) 116:1874–5. doi: 10.1161/CIRCULATIONAHA.107.738021
23. Giamberti A, Butera G, Mvondo CMVE, Cirri S, Varrica A, Moussaidi N, et al. The shisong cardiac center in cameroon: an example of a long-term collaboration / cooperation toward autonomy. *Front Paediatr.* (2018) 6:188. doi: 10.3389/fped.2018.00188
24. Hewitson J, Zilla PPT. Children's heart disease in sub-saharan africa: challenging the burden of disease. *SA Heart*. (2017) 7:18–29. doi: 10.24170/7-1-1964

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REVIEW
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Pediatric Cardiac Service Development Programs for Low- and Middle-Income Countries in Need of Improving or Initiating Local Services

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Pediatric cardiac services are deficient in most of the world. Various estimates are that between 80 and 90% of the world's children do not receive adequate cardiac care for their congenital or acquired heart disease. We began a modest effort in 1992 to assist in the development of pediatric cardiac services in low- and middle-Income countries (LMIC). Since then, we have provided services in 32 countries based on 3 distinctive development strategies, in order to meet the local needs for pediatric cardiac services. Our goal has always been to provide education, training and sufficient experience so that eventually we leave a site with a fully functional, independently operating pediatric cardiac service that is sustainable over time. The margin between success and failure is dependent upon a number of factors and we hope that this chapter will provide others with the tools for success.

Keywords: global surgery, humanitarian assistance, pediatric cardiac surgery, congenital heart, education

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INTRODUCTION

Pediatric cardiac services are widespread in North America, Europe and along the industrialized portion of the Pacific Rim. However, in the remaining parts of the world these services range from simply inadequate to meet the national, regional or local need to entirely absent (1). The result is that an estimated 80–90% of the children in the world with various forms of heart disease do not have adequate care (2). The most common congenital defect, congenital heart disease (CHD), and a preventable disease, rheumatic fever, account for a significant proportion of the burden of child mortality in LMIC. Out of the over 1 million children born annually with CHD (3) 250,000 died untreated in the first year of life in those countries. Likewise, nearly 275,000 die of the cardiac complications of rheumatic fever (4). While industrialized nations have a very low surgical mortality for CHD or fully prevent rheumatic fever, these heart diseases continue to exert a taxing toll in children born in LMIC.

Pediatric cardiac surgery is relatively a young specialty, with a simple yet significant first successful ligation of a ductus arteriosus by Gross at Boston Children's Hospital in 1938. Followed 6 years later by Crafoord's first coarctation repair and Blalock-Taussig systemic to pulmonary artery shunt historical operations (5–7). Cardiopulmonary bypass followed years later after Lillehei had

used cross-circulation to perform intra-cardiac surgery (8). By the late 50's only two centers in the United States (University of Minnesota and Mayo Clinic) and less than a handful in the world (9, 10) were performing open heart surgery and the spread of pediatric cardiac surgery did not began in earnest until the early 60's. We may struggle to understand why modern pediatric cardiac surgery, after being practiced and refined for 60 years has failed, unlike many other modern medical advances, to spread world-wide (11). Several issues come to mind including, but not limited to, excessive costs of imported capital equipment and disposables, resulting in a limited number of sites performing enough surgeries as to function as training sites. That combined with a much slower pace of communications so that new techniques and developments required months and sometimes years to spread within the scientific community. The result was that while centers developed and multiplied in the developed world, only but a few successful ones developed in LMIC. Assistance in pediatric cardiac surgery by teams from developed countries began in the 70's and has mushroomed since then (12–15). We began our assistance in Colombia in 1991 and since then have visited 32 countries, having completed over 560 trips of between 1- and 4-week duration, with nearly 10,000 patients operated to this date (16, 17). We have used a number of training-education models to develop sustainable programs, whether *de novo* or for improving existing sites. The success or failure of an assistance program hinges on multiple factors which we will explain in this chapter.

REQUEST FOR ASSISTANCE

The request for assistance (RFA) can come for practically any source. Over the years we have received RFA from; colleagues returning home after training, non-medical and medical ex pats living in the United States, pediatricians and pediatric cardiologists/surgeons in LMIC, civic groups/foundations in the United States or abroad, Hospital Directors and Ministers of Health (MOH) in LMIC and occasionally from the offices of executive power officials (Vice Presidents or Presidents) of LMIC. We have entertained every request with a response to determine the viability of the RFA. The process of validating a RFA varies depending upon the origin of the request. If the RFA comes from a Hospital Director, MOH or the Executive offices of the government, then they require less validation since the decision and the funding to implement have usually been approved (18). Meanwhile RFA coming from other sources may require substantial work. Once we have determined the validity of the source of the request, we send a detailed questionnaire regarding the hospital facilities and a separate one regarding the medications available locally (**Appendices 1** and **2**) for the local team to complete. Photos are requested with the returned questionnaire and from this we determine if a site visit is warranted. The major issues to be considered before a site visit is made are; adequate infrastructure and accessibility of the hospital, local staff in all specialties to train, equipment needs (will need to reconfirm on site visit), locally available supplies and medications, philosophical support for program development from the local team, hospital administration, regional and national health directorates/ministries and local need for such a service. Invariably the media will become involved which one must remember can be good or bad for the local program if not handled appropriately (19).

SITE VISIT

Occasionally a site visit is not necessary when adequate information, photographic documentation and the completeness and veracity of responses can be verified by a trusted local or expat, fluent in the local language and preferably with some medical background. We have been able to make a first surgical trip without a site vetting visit to approximately 20% of the more than 50 institutions we have assisted. Site visits, when needed before the first trip, should be conducted by a biomedical engineer, operating room individual (surgeon or nurse), ICU person (physician or nurse) and an executive administrator representing the visiting group. The basic requirements must be reviewed for completeness in all areas of infrastructure, equipment, power plant capabilities (and back up), personnel and support services (radiology, laboratory, blood bank) (20). The language of the visiting team can be problematic if the local language is not the same, so translators will need to be present if needed.

Discussions with all local stakeholders is critical as a thorough understanding of local enthusiasm, support for the program and motivation must be determined in all area's personnel. We have found that it is important to hold meetings with individual groups by area first before a final discussion with the decision makers. Local personnel are frequently anxious of sharing their honest feelings or opinions when faced with administrative or decision-making individuals present. Moreover, it is imperative that you understand from the local team if there is a real consensus on what type of program is desired. The visiting team should not impose its plan for the site on the local team, rather the visiting team must adhere to the local desires for their program's development. The plan must be consistent otherwise frustration can develop on both sides. Once a decision is made as to the type of program a site desires a plan can be drafted, a program can be implemented, and actions undertaken (21).

PREPARATION FOR PROGRAM IMPLEMENTATION

Once the site visit is completed a comprehensive overview of the deficiencies in infrastructure, equipment, supplies, medications and personnel should be constructed in a concise yet complete manner. Depending upon the visiting teams experience in providing pediatric cardiac services in LMIC this may be done before departure or upon returning home. The benefit to preparing the assessment before departure is that it can be discussed with the local stakeholders prior to the site visit team's departure and earlier decisions made regarding who will be responsible for correcting or alleviating the deficiencies, thus allowing both sides to develop a financial budget for the program

(22). Funding is a critical issue and the visiting team should have a thorough understanding of who will be responsible for each line item in the budget needed to correct deficiencies, transport the visiting team and house them on location. The total expenses for a program will depend upon the correction of the deficiencies as well as the number of trips to be made within the timeframe of the program.

PROGRAM MODELS

We are committed to the initial visiting team model as a means to assess the local team and to determine which of our teaching/training model will provide the local team with the result, they desire upon program completion. Essential in the assessment is a discussion with the local stakeholders regarding the length of time they want to achieve the final result of an independently functioning pediatric cardiac service or improved service. Requests vary for program endpoints, from a service able to provide routine pediatric cardiac surgery to those wishing to improve their neonatal results. There are models used by others which have been successful, but our focus is on the efforts we have employed over the last 27 years.

Intermittent Visit Model

The Intermittent Visit Model (IVM) is the most frequently used model by us as well as other charities to provide clinical and educational services (23–25). In this model a team of pediatric cardiac specialists visits the LMIC hospital for a variable period of between 1 and 4 weeks. Early in the program, our teams tend to be larger with enough individuals to provide safe and complete care to all children undergoing intervention (catheterization or surgery). Our usual team composition consists of senior pediatric cardiac surgeon, pediatric cardiac anesthesiologist, pediatric perfusionist, scrub nurse, pediatric cardiologist, pediatric intensivists, pediatric cardiac ICU nurses, pediatric respiratory therapist and biomedical engineer. Total team size is dictated by the number of ICU beds and operating rooms available. The team works as the primary caregiver until we determine the capabilities of the local staff who are working side by side with all our team members from the start. We are adherents to the concept of graduated responsibility based upon the local individuals' skills and capability. Moreover, we are advocates of high-volume caseloads since multiple publications have shown that large volume centers tend to have lower mortality rates (26, 27). Literature in surgical education suggests that the more the trainee operates in simulations the faster and thoroughly they learn surgical skills (28). Simulation is impractical for cardiac surgical trainees in most LMIC secondary to cultural issues and so volume of cases performed is important (29). Certainly, the same applies across all specialties involved in pediatric cardiac care. We must caution however on only operating for large volumes of cases, whether in the OR or Cath lab. An ICU filled to capacity with high acuity patients with a limited number of experienced staff can lead to unwanted events and mistakes (30–32).

Under optimal circumstances and with appropriate severity case scheduling, up to 16–20 children may receive surgery during a 2-week visit. We do not like to begin any program at an inexperienced site with neonatal operations (33). Ideally, we begin each trip with RACHS-1 category I and II cases and only once we are certain that all organizational, personnel and equipment issues are solved we will move to category III and IV cases (34). We have started all our programs in this manner when working at either inexperienced or *de novo* program. Sites with developed programs requesting assistance to help improve care with complex cases or neonatal surgery are started much differently as dictated by the requested need.

The frequency of annual visits and the duration of the program are dependent upon the end-point the institution desires to achieve the time they want to achieve the goal and of course the available funding for supporting the endeavor. Our experience is that with *de novo* programs 5–7 years may be required with 3–4 visits annually. Programs that are established require less time, but we believe the frequency of visits should not fall below 2 annually. Less visits allow a return to the old habits and standards that you have been asked to change.

Mentorship in every aspects of the specialty is the cornerstone of our educational approach. However, scheduled and impromptu lectures and learning opportunities constitute a significant part of the educational experience we provide (35). Superb educational opportunities exist in two very important multi-disciplinary meetings: The patient evaluation/management conference (held at the beginning of a trip) and the daily morning rounds in the ICU (36, 37). The cardiology/cardiac surgery management conference is based upon the pre-visit evaluations and diagnostic studies performed by the local caregivers. All specialties are invited to attend, and interactive participation is encouraged and expected and occasionally solicited from the local participants who are not cardiologists. Expected participants aside from the surgeons and cardiologists are anesthesiologists, perfusionists and the lead ICU nurses from the visiting and local teams. Each case presented is thoroughly reviewed and if additional studies are required an explanation is provided. A surgical approach is recommended by the lead visiting surgeon and options solicited from the local team. Once the cases are reviewed and plans agreed to, then a surgical schedule is constructed that will provide optimal movement and bed availability in the ICU. Emergencies can alter the schedule and we leave the decision of which case to cancel so the emergency can be cared for to the local team. Daily multi-disciplinary rounds are made in the ICU each morning. We provide 24-h ICU coverage with our team's ICU nurses and either an Intensivist or Nurse Practitioner. Morning rounds in the ICU are led by the bedside nurse who cared for the child during the night. Upon completion of the trip the afternoon of the last day is reserved for the debriefing session.

Resident Senior Surgeon Model

A senior retired surgeon or a surgeon fully dedicated to humanitarian efforts can assume residence in-country for several years or permanently (38). This model generally occurs at a site where an existing program wishes to expand surgical volume and/or complexity and often to improve morbidity and mortality. We have no experience in using this model to

establish *de novo* programs. We have used this model successfully in Nicaragua. Several years are required, and the surgeon-in-residence must be prepared to provide guidance in all aspects of pediatric cardiac services; clinical, administrative, financial, media relations and politics. The growth of the assisted program requires careful yet progressive nurturing and the support of the hospital administration. The development of a relationship with a local charity and with philanthropic individuals and corporate entities is critical to the success of the program.

The clinical management is similar to the Intermittent Visit Model but due to the number of inexperienced local healthcare professionals the volume of work is usually less initially. Education is at all levels and the establishment of locally driven continuing medical education is a must. A Quality Improvement program should be started, and monthly meetings held with all stakeholders involved in the clinical care. Research projects can be generated and should be pursued at both the nursing and medical staff levels. The initial design and implementation of a patient registry and database provide the site with the opportunity to review results regularly, identify problems early, provide data for clinical studies and stimulate patient follow-up. A relentless approach is necessary to achieve success with all development programs, but with this model it is essential that early in the process the surgeon-in-residence must enlist local leaders to cover all needs.

Team in Residence Model

A very ambitious model is the Team in Residence (TIR) model. The concept is to place a team of specialists in-country residence for periods of 1–2 years on a nearly continuous basis (39). We have essentially 3 different but interconnected teams with this model; surgical team (surgeon, anesthesiologist, perfusionist, ± scrub nurse), the ICU team [(one or two Intensivists, a ICU Nurse Practitioner and/or Nurse Educator and 2 ICU nurses) and the cardiology team (interventional cardiologist]. The surgical team is on-site for 1 month and the ICU team for that month and then a week stay over, whereupon the surgical team returns with a new ICU team and the cycle repeats for the entire 12 months. Breaks occur according to the local and visiting team holiday calendar. Usually the surgical team is on-site 36–38 weeks out of 52 and the ICU team 44–46 weeks during the same period. The interventional cardiology team provides coverage when devices are available, and this usually is not more than 1–2 weeks every 3–4 months.

The major advantage to this model is that the local team is exposed and trained on a variety of cases from simple to complex with moderate volumes of patients each month (**Table 1**). The progress of the local team is usually faster by gaining responsibility as primary caregivers over a shorter period (40–44). The major disadvantages to this program are the expense and the difficulties regarding recruitment for the visiting team. We have used this model in only two countries, Iraq and Libya, but at 4 different sites to date (Nasiriyah in Iraq and Benghazi, Tobruk and Tripoli in Libya) (45, 46). Placing pediatric cardiac specialists in-country for 4–5 weeks could potentially be solved by a volunteer team, but not 9 times in 12 months. We have full time staff working for the foundation in each aspect of the specialty and they provide a steady foundation as the basic team. We augment the team with volunteer nurses and occasionally respiratory therapist in addition to the interventional cardiologist. Expenses are provided by the government of the country requesting help, usually from the Ministry of Health, but in some cases from the regional health care directorate.

TABLE 1 | Variety and Complexity of Cases under Team in Residence Model.

	Nasiriyah, Iraq (01/05/14–01/29/14)	Tripoli, Libya (06/04/18–06/29/18)
Age *(N)*		
Newborns	2	2
Infant	11	4
Children	30	34
Adults	2	0
Total	45	40
Rachs Class		
RACHS I	7	8
RACHS II	26	20
RACHS III	8	11
RACHS IV	1	1
Non-RACHS	3	0
Total	45	40

Nursing Education/Empowerment

The process of collaboration to develop nurse education requires recognition of the already the established processes and practices at any given site. It is not conducive to building trust to come in and to "takeover." Our organization focus on inclusion of the local team, respect for their ways and developing a practice over time. Our goal is to build sustainable services and this process requires that our local counterparts are invested and feel valued in the program.

Our philosophy is to educate the local nurses so that they can competently care for all the children before or after cardiac surgery or intervention. Nursing education in LMIC varies greatly and a thorough assessment of the educational foundation and experience in caring for children is necessary before clinical services begin (47). The formal learning needs assessment is performed on site during the first visit. During this stage each local nurse is directly supervised and supported by a nurse mentor from NCA. The direct supervision and support in the early phase enables us to provide education and explore local policies and procedures without compromising patient safety or quality of care.

The aim of nurse education is to ultimately empower local nurses to make decisions about the care they provide using a systematic process. Initial teaching focuses on task and skill acquisition, for example drug calculations, basic life support, equipment use, blood port sampling and recording of vital signs. With each subsequent visit by the team we reinforce the already learned practice and build the complexity of the

educational development (48). In most of the countries we visit the nurse education system has focused on didactic teaching and memorization type learning which means the nursing team often "know" information, however, they have no experience of applying the principles of knowledge to different situations. Learning clinical decision making requires a different type of mental activity than merely remembering or knowing information and to facilitate this we introduce learning strategies that encourage productive models of thinking such as medium fidelity simulation and problem-based learning. These teaching modalities support the nurses as they learn to apply their new level of knowledge and reasoning to multiple clinical situations (49).

The ability to make decisions in practice is often aided by strong and supportive Multi-disciplinary team (MDT) working and we encourage each site to develop a flat hierarchy which empowers team members to contribute their ideas and opinions. In the ICU we undertake formal MDT ward rounds every day and nurse led handover is encouraged and facilitated. We actively perform this process from the first visit so that local nurses come to understand that they are active participants in the care of the children and that their contribution is essential in the child's recovery. The combination of education and empowerment of the nursing team aids in the development of nurses who can make informed and accurate clinical decisions, quickly detect patient deterioration and positively impact patient care (50).

Interventional Cardiology Services

The addition of an interventional cardiology program constitutes a necessary goal when aiming to organize a sustainable congenital heart program (23).

Although the development of a successful interventional cardiology program depends on the availability of a specialized catheterization laboratory, often times in our experience we choose to team up with available adult catheterization labs, which happen to be ubiquitous in low- and middle-income countries.

Thus, the key issue would be the choice of a person suitable, after proper training, for the role of pediatric interventional cardiologist. When a trained local interventional cardiologist is not available, then the search for an appropriate candidate is conducted among local non-invasive pediatric cardiologists or adult interventional cardiologists. The advantage of the former is a better understanding of the physiology of the heart defects and the familiarity with echo, while the latter have the best technical skills in working with catheterization equipment.

Although catheterization laboratory practice may differ in different countries, nevertheless we would like to point out some common features, typical for almost all catheterization laboratories we have worked with:

1. Significant limitations exist in supplies availability.

   A visiting interventional cardiologist should realize that the majority of diagnostic procedures will have to be performed using a minimal set of diagnostic catheters and guidewires. Berman catheters or wedge balloon catheters are quite rare, as well as delicate equipment used in small children (e.g., 4 French introducers and catheters).

   As most cardiac catheterization materials are disposable, a steady supply chain must be established to provide uninterrupted services. A cost-benefit analysis of certain catheterization procedures has to be weighed against the ready availability of re-sterilizable surgical supplies. For example, a simple surgical PDA ligation may be more cost-effective than device closure in the cardiac catheterization lab when taking into account the cost of sheaths, catheters, wires, and the actual PDA occluder device. However, a similar cost-benefit analysis for procedures requiring open heart surgery may indicate quite the opposite. For instance, surgical closure of an atrial septal defect would require the additional costs of an oxygenator and tubing set, sutures, temporary pacing wires, temporary pacemaker, chest tubes, additional ventilator supplies and ICU disposables, multiple lab tests and blood bank products. Whereas, an uncomplicated transcatheter device closure of an atrial septal defect can be done safely, with minimal ancillary support, transthoracic echocardiographic guidance, and conscious sedation. Another consideration to be addressed are the societal and cultural implications of surgical scars especially in the female patients. Where applicable and safe, transcatheter repair of some defects may be the procedure of choice (51–53).
2. The absence of an anesthesiologist member in the team with enough experience to work with children.

   It should be taken into account during trip planning phase, because most often you have to recruit staff from the ICU team to work in the catheterization lab, unless specific preparations have been made in advance.
3. The need to re-educate staff in adult catheterization labs to work with children.

   The key strategies are the introduction of more delicate vascular access (use of thinner needles and introducers, puncture under echo-guidance, avoidance of unnecessary arterial access); precise monitoring of hemodilution and blood loss (use of small syringes for flushing, accounting the flush volume); temperature management with obligatory patient warming; careful monitoring of hemodynamic changes (arrhythmias, hypotension) with aggressive management and strict infection control, In other words, implementing strategies that usually do not play a significant role in the coronary catheterization lab. As a rule, the introduction of such philosophy takes a significant amount of time, depending on trips frequency and volume of cases.
4. Challenges with hemodynamic evaluation.

   In many catheterization labs in LMIC the absence of a hemodynamic module or its malfunction is common. In these cases, any hemodynamic studies, such as pulmonary hypertension study, become quite problematic. In several cases, we managed to get out of a difficult situation by using an ICU patient's monitor with the possibility to freeze the invasive pressure curve and measure a pressure at a certain point of the curve (e.g., end-diastolic pressure of the systemic ventricle).
5. A bias against routine hemodynamics assessment.

   The tendency for most interventional cardiologists working at sites we have visited, tends to be biased toward

performing procedures (e.g., device placement) rather than doing methodological diagnostic catheterizations (54). It is not uncommon to receive Cath reports, performed by local pediatric interventional cardiologists in the LMIC we visit that have incomplete data. This bias although not limited to developing programs, it is widespread among local practitioners and a sensible education process must be implemented early on to change the culture of the site.

In conclusion, the development of the pediatric interventional cardiology program as part of the whole congenital program is depending on maintaining the focus on the three main training strategies to be developed simultaneously:

1) Basic diagnostic and hemodynamic studies, which, combined with perioperative interventions, could provide a basic support for the surgical program. It usually takes about 1 year to develop depending on trips frequency and number of procedures performed on each trip.
2) Neonatal catheterizations and interventions for critical heart defects (55). In our opinion, this is the key strategy for the development of a sustainable congenital program. Firstly, because the learning curve for neonatal interventions for critical defects is significantly shorter than that for emergent neonatal surgery. Secondly, such neonatal interventions as balloon atrial septostomy, aortic or pulmonary valvuloplasty, and in some special patients stenting of PDA or RVOT, which cover the majority of critical heart defects, allowing for the stabilization of the neonate, providing a bridge to correction. The successful development of neonatal interventions will open, in a relatively short period of time (usually 1–2 years depending on frequency and volume), the possibility to provide an emergency services for the most vulnerable category of patients in the covered region. In our experience, such approach significantly increases the credibility of the program by pediatricians and neonatologists in the region, facilitating the organization of a country wide referral network for critical defects, contributing to the development of the program as a whole.
3) Interventions that include balloon valvuloplasty, implantation of stents and devices may, in time, amount to a significant group of patients. Such "curative interventions" could provide an additional motivation for local interventional cardiologists, and eventually bring extra media, financial or political benefits for the congenital program. Unfortunately, devices remain underutilized in LMIC due to high cost. In many countries, device implantation is still a more expensive intervention when compared to open-heart surgery (56).

Anesthesia Services

At every site we visit, we aim to perform cardiac anesthesia with similar standards as we are used to practice in our countries of origin. In order to do so, there are a few hazards that must be accounted for as we set up.

Medication Error

Local drugs are often labeled in languages our anesthesiologists are not familiar with. The packaging dose may differ from the one we are familiar at our home institution. Brand names may or may not be similar. Standardization of effective drug concentration may differ from what it is printed on the label, such as it is the case with some generic drugs produced in laboratories with lower or absent quality control (57). These issues have been particularly noticeable when using Heparin/Protamine from different manufacturers.

Time has to be taken to understand these differences, to draw the drugs to be used in labeled syringes with enough anticipation and, when available, take advantage of the invaluable help a local anesthesiologist or anesthesia technician fluent in both languages may provide, as to avoid potentially lethal iatrogenic mistakes.

Blood Loss/Coagulopathy/Blood Products

Hospital blood banks, while always available (a litmus test during our vetting process), tend to be less sophisticated than those in developed countries. This is particularly evident when confronted with the limited offer of fractioned blood products (e.g., Cryoprecipitate and platelets). The theoretical advantage of working in resource limited countries is that whole fresh blood from a family member is almost always readily available, limiting potential cross-reactions while offering young red cells, platelets and factors with a lower Potassium concentration than old blood bank bags (a deadly issue when dealing with neonatal/small infant surgery), at a relatively low cost (58).

Early diagnosis and consequent management of post-operative coagulopathy is not simple unless the proper equipment is available. Unless a specific defect on the coagulation cascade is identified through the timely use of thromboelastography (TEG) or Rotational thromboelastometry (ROTEM), it will be unlikely that a true coagulopathy could be treated before depleting the blood bank reserves and spending hours in the operating room, with the known deleterious effects of hypothermia and multiple transfusions (59). In our experience, as well as others (a) we have found that, when available, the use of HepCon coagulation monitor does improve the monitoring of Heparin/Protamine dosage, to a better degree of accuracy than Activated Clotting Time (ACT Test) while significantly lowering the need for unnecessary transfusions and time in the operating theater (60).

As it is the case in more affluent societies, there is no substitute for good post-operative surgical hemostasis and regulated patient temperature control.

Temperature Control

A critical part of open-heart surgery is the ability to control patient body temperature throughout the surgical event and in the early post-operative period. This is especially important in neonates due to their own limitations to self-regulation.

A normal temperature may be easier to achieve on patients undergoing open heart surgery with cardiopulmonary bypass but in many sites less than ideal operating room temperature control may induce early hypothermia and in rare occasions hyperthermia. The lack of external means of temperature control (warm air flow, cooling/warming blankets, etc.) should be a significant concern in the anesthesiologist mind as surgical planning takes place.

Time-Out Before Procedures

As part of our daily practice, but most importantly, part of our education process, we have implemented a Time-Out routine in every country we operate regardless of local custom (61).

The process is carried out by our anesthesiologists after draping of the patient but before skin incision. It includes name, age, diagnosis, planned intervention, need for synthetic materials (shunt, patch), planned cannulation, aimed temperature, dose of cardioplegia, planned inotropic support, use of modified-ultrafiltration, and need for residual shunts measurement at the end of the case as well as blood availability and use of perioperative antibiotics.

We have achieved, over the last 4 years, a 95% compliance to the Time-Out routine, independently of primary surgeon (our staff member or a local one).

Modified Ultrafiltration (MUF)

We use MUF in all patients under 10 kg and some patients under 15 kg (surgeon's choice) as part of a larger fluid management strategy that is initiated in the operating room and continues in the intensive care unit. The aim of this strategy is to avoid unnecessary fluid overload and to promote early extubation since a fast-track pathway is essential when operating in environments with a limited number of ICU beds that do not allow for prolonged post-operative ventilator support. The extension of this tight fluid management strategy in the ICU includes the early use of a peritoneal dialysis catheter on post-operative day one when urine output is less than satisfactory.

Limitations to Post-operative Evaluation

Poor cardiac function after aortic cross-clamp, residual air in left sided cavities and residual shunts play a significant role in the postoperative morbidity and mortality of these populations. The inability to rule out these issues by performing trans-esophageal (TEE) ultrasound, either due to absence of trans-esophageal probe (a common occurrence in our experience) or lack of a second ultrasound machine for exclusive use in the operating theater undoubtedly play a significant role in the higher morbidity/mortality.

This issue may be palliated by epicardial echocardiogram (when a machine is available) using a sterile sleeve and the regular trans-thoracic probe. In the absence of TEE or Epicardial echo, as it is the case in most of our surgical sites, we have tried to implement an alternative substitute by performing a residual shunt calculation by direct measurement (SVC and PA) on 50% or less FIO2. While this procedure prolongs the anesthesia time by 15 min or so, it may avoid an unplanned trip to the operating theater for reoperation of residual intra-cardiac shunting and a protracted postoperative ICU stay. Likewise, while still in the operating room often we use direct measurements of hemodynamics (needle and sterile pressure tubing) to measure blood pressures in different cavities as well as residual gradients.

Perfusion Services

Currently the state of formal perfusion education in the LMICs we service is virtually non-existent. Since the ability to attend perfusion school is unfeasible, many LMIC perfusionists learn via an apprentice model as it was the case in the USA in the 1960s (61) Although some sites already have experience with perfusion (particularly adults) almost all sites require long term intensive perfusion assistance. This enables the techniques, unique to pediatric perfusion, to be fully and safely implemented. Utilizing experienced pediatric perfusionists certified in Western countries who may have clinical experience based on hundreds of perfused cases combined with a strong base knowledge to draw from, enables a rich educational experience for the local perfusionist.

Perfusion circuitry is single use medical equipment, so the availability of this equipment varies by country. Operating in many different locales, we can appreciate the need to perform perfusion techniques differently albeit safely. To maintain a united front in our varied practices' we adhere to The American Society of Extracorporeal Technology Standards and Guidelines for Perfusion Practice which have allowed us to enact meaningful change, including pre-bypass checklists and intra operatively charting of perfusion parameters at our sites (62).

Pediatric perfusion has become a niche practice and now even offers a fellowship credential (63). As the practice of pediatric perfusion grows every day, more literature becomes available inclusive of technique articles that we have published in peer reviewed, open access journals (64, 65). We continue to explore new means to conduct pediatric perfusion while maintaining optimal outcomes during our goal of producing expert perfusion clinicians which in turn can train the next local generation.

Biomedical Engineering

Working in LMIC is challenging and one area where it can be especially difficult is equipment. The site questionnaire will give you some indication of the equipment present but until the site visit you cannot be sure if the equipment listed is actually functional and has all components needed. We routinely solicit donations of equipment from hospitals and clinics when they upgrade. Donated used equipment from the United States or Canada to be used abroad must be check for capability of dual power input (110v/220v) otherwise a voltage converter or transformer should also be included in the donation. The need for a biomedical engineer on each trip is paramount to the success of a surgical trip, particularly when visiting sites with old, refurbished or poorly maintained equipment. The individual should have a broad range of experience as repair can be required on bypass units, heater/coolers, electro-cautery units, surgical overhead and fiber-optic headlights as well as a variety of anesthesia machines. The ventilators, monitors, infusion and syringe pumps in the ICU also can come from a variety of manufacturers. Also, we utilize our biomedical engineer to assess and familiarize himself with the hospitals back-up generator and oxygen sources, whether central or tank supply.

Operating Room Services

Work in the cardiac operating room department involves multidisciplinary teamwork including anesthesia, perfusion, OR nurses and scrub technicians. The operating room (OR) team of NCA works in close collaboration with the local OR team to provide safe and successful surgical outcome. Prior the first

inaugural trip NCA surgeon, perioperative nurse and biomedical engineer communicate with local staff to ensure that all essential medications, disposables, and equipment are available locally. In general, host hospitals are responsible to provide surgical instruments, medicines and supplies necessary to provide open heart surgery. Items not obtainable locally are provided by NCA with the help of donations from medical companies and private donations and shipped to the hospital. In many instances NCA team is responsible to provide instrument sets for surgeries because new centers are not equipped with delicate and specific pediatric tools. Many centers lack emergency opening set which is designated for emergency chest opening in the ICU. The centers that commit to a program building often receive request from NCA surgeon to secure at least two full surgical sets and one emergency set. Other essential equipment that are usually lacking at new sites are surgical headlight, reliable blood gas machine, oscillating saw and infant/pediatric defibrillator paddles. NCA team would bring all this equipment per trip needs and eventually as the program grows the host hospital secures those items locally.

Procurement of medical supplies for surgical trips is extensive and ongoing. Many countries require a full support from NCA to provide disposable materials for surgeries. Thanks to donations from medical companies, non -profit charities and hospitals from the United States we are able to meet the challenges and provide necessary supplies. Many donated items are close to expiration date or expired and some countries are willing to accept those items while other require a minimum of 1 year of a shelf life for the same items. Expired supplies are repackaged and re sterilized in host country according to the type of material in autoclave, ethylene oxide or formaldehyde sterilization process for the heat sensitive items.

One of the main reasons why NCA is traveling to low income countries is to provide education in pediatric cardiac surgery and to bring the latest standards and practices in pediatric cardiac care to local physicians and nurses.

In the countries where we travel, we have experienced the shortage of cardiac anesthesiologists, OR nurses and pediatric perfusionists. Due to the shortage of personnel, many hospitals would offer us the group of doctors and nurses to teach but only few of them would accept to continue with education. The problem that we face in low income countries is that these professionals are doing two jobs in order to meet living needs and they simple cannot afford to spend more time in the hospital. In order to be successful, we need to be aware of the culture and sensitive to the needs of the host. Therefore, our educational approach must meet the needs that would go side by side with their respective beliefs. The education is conducted in English language. Most physicians speak English language while the main challenges are with non-English-speaking nurses. In that case we would ask physician to translate, provide on site medical translator and translate educational materials in a local language. Most commonly we work side by side with a local nurse and doctor and monitor their work closely.

Each center is required to perform a time out before the procedure begins to ensure that the entire surgical team is familiar with the patient, procedure and that patient is ready for the surgery (66, 67).

The role of NCA operating room staff is not only to teach about particular surgery but also to provide education and additional information in all other aspects of the perioperative department from cleaning, disinfection and sterilization to keeping up with correct temperature, relative humidity and air currents to prevent airborne transmission of infectious particles (68).

Providing Service in Conflict Zones

For the most part, global conflicts have been limited to LMIC since the end of World War ll. However, terrorists' attacks have occurred in several European countries in addition to the United States as well as LMIC. The emergence of Al Qaeda and ISIS in the Middle East, North Africa and Central Asia over the last 18 years has created armed conflict zones in LMIC where previously there were none. The world has become a more dangerous place over the last two decades and nowhere is totally safe (69, 70). Since the most underserved regions of the world for children with heart disease are LMIC, the chances of being in or near a conflict zone are considerable (71). Children located in or near conflict zones deserve our assistance just as much as children anywhere else. Security and safety for the team is paramount and an objective assessment should be made by experts coupled with trusted individuals on-site if you are entertaining working in a conflict zone (72). Additionally, the Foreign Ministries or State Departments in the countries of origin of the visiting team can also provide you with security assessments/warnings. Those doing humanitarian work in a conflict zone should notify their Embassy at the place of deployment, with arrival and departure dates and a local telephone number to contact you should a change in events warrant early departure/evacuation. Our teams have been evacuated twice in our 27-year history, from Belgrade after the NATO bombing started in 1999 and in Benghazi in 2014 when the civil war erupted in that city. On both occasions we were evacuated by the Ministry of Interior and no team member suffered any physical or significant psychological injury. We have been in conflict zones when fighting started nearby but did not require evacuation; West Bank with the second Intifada, Pakistan when Al Qaeda attacked the Pakistan Army's General Headquarters, Iraq with invasion of ISIS and Tripoli when a militia attempted to overthrow the government. When working in such areas it is critical to have daily security updates in order to make decisions insuring the safety of the team.

Benchmarks and Indicators of Improvement

We are pleased and rewarded when we provide or assist in successful interventions that improve the life of a child providing them with the opportunity of a future. Such altruistic action benefits the child, removes psychological and financial burdens from the family and is seen by the local staff as a reward for their hard work. Each intervention must also serve as an educational event in order to advance the experience of the local healthcare providers. The goals set for the program prior to beginning must

be focused on with every trip. We establish benchmarks for achievement and will frequently focus on a particular type of defect during a trip, collecting a few cases so that we can allow the local team to assume primary responsibility for all phases of care. Careful mentorship and active assistance are needed so that success is achieved, and confidence is instilled in the local team. We are responsible for the safety of the child first but maintaining the moral of the local team is essential for their progress and development of confidence.

Earlier we mentioned the need for a local database and one of the benefits is that both the visiting team and local team can see the interval progress made when the visiting team is absent. We cannot overstate the need for interval advancement assessment by both participants in this collaborative effort to improve pediatric cardiac care. We also recommend that each site participate in the International Quality Improvement Collaborative in Pediatric Cardiac Disease (IQIC) (73). A review of interval work formally or informally should be done at the beginning of each trip. We have found that this provides us, the teachers, with the information needed to decide whether to take the next step or continue to work on the previous defect until satisfactory results are obtained. Our approach is to review interval data for volume of work done, complexity of defects receiving intervention, mortality, morbidity along with ICU and hospital length of stay. A comprehensive annual review with comparison to previous year(s) should be performed and statistically analyzed if possible. The IQIC provides reports to each site as well so that the site can compare themselves to similar programs (74).

The registry of patients evaluated allows the local team to assess the impact of their program by enabling them to determine if the volume of patients being evaluated is increasing. Additionally, the registry can provide the local team information regarding prevalence of defects within their referral area. Moreover, by maintaining and reviewing the registry the local team can assure that patients are seen and followed in a timely fashion thereby possibly preventing some of the complications of palliative and untreated CHD.

Quality Improvement/Assessment

A review of the work performed on the visit to highlight improved areas as well as discussing issues that remain organizationally is important and we combine this with a mortality and morbidity discussion. One must be attuned to the cultural issues when conducting this review/de-briefing and avoid personalizing failures. Catastrophic failures resulting in deaths should be addressed immediately so if systems failure is the issue it can be corrected to prevent future failures. If the catastrophe is the result of an individual's mis-adventure a direct discussion privately with the involved individual(s) should be conducted (75). Transparency and honesty are needed if personnel and program growth is to continue. The QI/A meeting should be a regular occurrence on a monthly basis conducted by the local team.

System failures may be organizational and more easily solved than infrastructural ones. We must be aware that expensive alterations in infrastructure may require significant time to correct and short-term alternative options may be needed. We have partnered with sponsors both abroad and locally in some cases to provide expensive infra-structure improvements. When then issue is exclusively limited to equipment failure, then donation of refurbished equipment is something that is much easier to solve, keeping in mind differences in electrical current types and furnishing the appropriate transformers along with the devices.

Ethical Considerations

Ethical issues are to some degree dependent upon the location and culture of the country you are assisting (76). Some cultural beliefs espouse a policy of no withdrawal of life support even in patients declared brain dead. Others forbid extended visitation in the ICU and still others do not want to "*waste resources*" on children with chromosomal abnormalities. Whereas, you may be the expert in congenital heart disease you may be ignorant of ethical differences depending on the country. It is always best to defer to the hosts in delicate issues unless they impact patient care. One example would be a site which does not want to utilize the resources for open repair cases in patients with Trisomy 21 but will reluctantly agree to a palliative procedure (77). You may want to avoid a controversial situation which could potentially result in an argument and disrupt the relationships you are trying to develop, while trying to explain the decreased burden on the health care system if such patient receives a complete repair (78). Navigating situations like these can be difficult, but we have successfully removed the stigmata of "Downs Syndrome operations" in every country that has initially resisted. Religious and ethnic differences are also excuses used to deny operations in some countries and one must work hard to overcome this discrimination against a child. The differences in gender approach can result in very uncomfortable to outright disastrous situations if one is not cognizant of cultural differences (79). When one is dealing with someone of a different gender it is always helpful to allow the hosts to lead the approach whether it is with a greeting, performance of a physical or diagnostic exam. All trips eventually come to an end and this can be the most stressful and ethically challenging time of the visit. Once parents realize that your visit is nearing an end, they may become frantic if their child is not on the operative list. Moreover, they will at times hide critical information from the team regarding recent infections. Also, it is not uncommon that some child with complex defect appears at the end of the trip and both the local team and parents are expecting an operation (80). We routinely provide an ICU stay over team in the initial stages of our programs, but even in this situation we prefer to decrease the complexity of the cases performed so that the ICU acuity is reduced, and we are confident that the stay over team can depart without anyone in the ICU. Performing a complex repair on the last days of a visit that will require ICU care beyond the time limits of the stay over team is an ethical challenge and has no simple answer.

SUMMARY

Pediatric cardiac care is deficient in most of the world and as a result hundreds of thousands of children with congenital and rheumatic heart disease die annually. The majority of population growth is in LMIC, the very regions where deficiencies in pediatric cardiac care exist. Bringing children out of their countries for surgery in more developed healthcare systems results at best in a few hundred receiving life-saving care at a prohibit cost for the family or the sponsoring government or institution. The only long-term solution is to build local capacity. We have described our models which have all led to the development of successful programs, but we have failures as well. The choice of the site for development is critical, but cannot always predict the imponderables of politics, conflict, financial collapse, or personnel failures.

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All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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REFERENCES

1. Neirotti R. Paediatric cardiac surgery in less privileged parts of the world. *Cardiol Young.* (2004) 14:341–6. doi: 10.1017/S1047951104003191
2. Tchervenkov CI, Jacobs JP, Bernier PL, Stellin G, Kurosawa H, Mavroudis C, et al. The improvement of care for pediatric and congenital cardiac disease across the World: a challenge for the World Society for Pediatric and Congenital Heart Surgery. *Cardiol Young.* (2008) 18 (Suppl. 2):63–9. doi: 10.1017/S1047951108002801
3. Bernier PL, Stefanescu A, Samoukovic G, Tchervenkov CI. Tchervenkov. The challenge of congenital heart disease worldwide: epidemiologic and demographic facts. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Ann.* (2010) 13:26–34. doi: 10.1053/j.pcsu.2010.02.005
4. World Heart Federation. *RHD Affects the World's Poorest, Most Vulnerable Populations*. (2018). Available online at: https://www.world-heart-federation.org/programmes/rheumatic-heart-disease (accessed July 15, 2018).
5. Gross RE, Hubbard JP. Surgical ligation of a patent ductus arteriosus: report of first successful case. *JAMA.* (1939) 112:729–31. doi: 10.1001/jama.1939.02800080049011
6. Crafoord C, Nylin G. Congenital coarctation of the aorta and its surgical treatment. *J Thorac Surg.* (1945) 14:347.
7. Blaylock A, Tassig HB. Surgical treatment of malformations of the heart: in which there is pulmonary stenosis or pulmonary atresia. *JAMA.* (1945) 128:189–202. doi: 10.1001/jama.1945.02860200029009
8. Warden HE, Cohen M, Read RC, Lillehei CW. Controlled cross circulation for open intracardiac surgery: physiologic studies and results of creation and closure of ventricular septal defects. *J Thorac Surg.* (1954) 28:331–41; discussion, 341–3.
9. Lillehei CW, Cohen M, Warden HE, Varco RL. The direct-vision intracardiac correction of congenital anomalies by controlled cross circulation; results in thirty-two patients with ventricular septal defects, tetralogy of Fallot, and atrioventricularis communis defects. *Surgery.* (1955) 38:11–29.
10. Kirklin JW, Dushane JW, Patrick RT, Donald DE, Hetzel PS, Harshbarger HG, et al. Intracardiac surgery with the aid of a mechanical pump-oxygenator system (gibbon type): report of eight cases. *Proc Staff Meet Mayo Clin.* (1955) 30:201–6.
11. Nguyen N, Leon-Wyss J, Iyer KS, Pezzella AT. Paediatric cardiac surgery in low-income and middle-income countries: a continuing challenge. *Arch Dis Child.* (2015) 100:1156–9. doi: 10.1136/archdischild-2015-308173
12. Replogle RL. International Community of Cardiac Surgeons. *Ann Thorac Surg.* (1996) 62:635. doi: 10.1016/S0003-4975(96)00560-7
13. McGrath LB. Establishing a pediatric cardiac surgical unit in the Commonwealth of Independent States (formerly the Soviet Union). *J Thorac Cardiovasc Surg.* (1992) 104:1758–9.
14. Lansing LM. Heart surgery in underdeveloped countries. Success in Panama and Romania. *Ann Thorac Surg.* (1993) 56:1439–40. doi: 10.1016/0003-4975(93)90718-W
15. Cohen AJ, Tamir A, Houri S, Abegaz B, Gilad E, Omohkdion S, et al. Save a child's heart: we can and we should. *Ann Thorac Surg.* (2001) 71:462–8. doi: 10.1016/S0003-4975(00)02243-8
16. Novick WM, Stidham GL, Karl TR, Guillory KL, Ivanćan V, Malcić I, et al. Are we improving after 10 years of humanitarian paediatric cardiac assistance? *Cardiol Young.* (2005) 15:379–84. doi: 10.1017/S1047951105000806
17. Novick WM, Stidham GL, Karl TR, Arnold R, Anić D, Rao SO, et al. Paediatric cardiac assistance in developing and transitional countries: the impact of a fourteen year effort. *Cardiol Young.* (2008) 18:316–23. doi: 10.1017/S1047951108002175
18. Pezzella AT. International aspects of cardiac surgery. *Ann Thorac Surg.* (1998) 65:903–4.
19. Neirotti RA. Cardiac surgery: the infinite quest. *Rev Bras Cir Cardiovasc.* (2012) 27:614–20. doi: 10.5935/1678-9741.20120104
20. Dearani JA, Neirotti R, Kohnke EJ, Sinha KK, Cabalka AK, Barnes RD, et al. Improving pediatric cardiac surgical care in developing countries: matching resources to needs. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu.* (2010) 13:35–43. doi: 10.1053/j.pcsu.2010.02.001
21. Dearani JA, Jacobs JP, Morton Bolman R, Swain JD, Vricella LA, Weinstein S, et al. Humanitarian outreach in cardiothoracic surgery: from setup to sustainability. *Ann Thorac Surg.* (2016) 102:1004–11. doi: 10.1016/j.athoracsur.2016.03.062
22. Neirotti RA. Barriers to development pushing the boundries. *Rev Bras Cir Cardiovasc.* (2015) 30:104–13. doi: 10.5935/1678-9741.20150007
23. Polivenok IV, Molloy FJ, Gilbert CL, Danton M, Dodge-Khatami A, Rao SO, et al. Results of international assistance for a paediatric heart surgery programme in a single Ukrainian centre. *Cardiol Young.* (2019) 29:363–8. doi: 10.1017/S1047951118002457
24. Swain JD, Sinnott C, Breakey S, Charles RH, Mody G, Nyirimanzi N, et al. Ten-year clinical experience of humanitarian cardiothoracic surgery in Rwanda: building a platform for ultimate sustainability in a resource-limited setting. *JTCVS.* 155:2541–50. doi: 10.1016/j.jtcvs.2017.11.106
25. Young JN, Everett J, Simsic JM, Taggart NW, Litwin SB, Lusin N, et al. A stepwise model for delivering medical humanitarian aid requiring complex interventions. *JYCVS.* (2014) 148:2480–9. doi: 10.1016/j.jtcvs.2014.07.067
26. Welke KF, O'Brien SM, Peterson ED, Ungerleider RM, Jacobs ML, Jacobs JP. The complex relationship between pediatric cardiac surgical case volumes and mortality rates in a national clinical database. *J Thorac Cardiovasc Surg.* (2009) 137:1133–40. doi: 10.1016/j.jtcvs.2008.12.012
27. Welke KF, Diggs BS, Karamlou T, Ungerleider RM. The relationship between hospital surgical case volumes and mortality rates in pediatric cardiac surgery: a national sample, 1988–2005. *Ann Thorac Surg.* (2008) 86:889–96. doi: 10.1016/j.athoracsur.2008.04.077

28. Shah AA, Aftab M, Tchantchaleishvili VT, LaPar DJ, Stephens EH, Walters DM, et al. Characterizing the operative experience of cardiac surgical trainees: what are residents really doing in the operating room? *Ann Thorac Surg.* (2016) 101:2341–9. doi: 10.1016/j.athoracsur.2015.12.069
29. Vaporciyan AA, Yang SA, Baker CJ, Fann JI, Verrier ED. Cardiothoracic surgery residency training: past, present, and future. *JTCVS.* (2013) 146:759–67. doi: 10.1016/j.jtcvs.2013.06.004
30. Gabler NB, Ratcliffe SJ, Wagner J, Asch DA, Rubenfeld GD, Angus DC, et al. Mortality among patients admitted to strained intensive care units. *Am J Respir Crit Care Med.* (2013) 108:800–6. doi: 10.1164/rccm.201304-0622OC
31. Montgomery VL. Effect of fatigue, workload, and environment on patient safety in the pediatric intensive care unit. *Pediatr Crit Care Med.* (2007) 8 (Suppl. 1):S11–6. doi: 10.1097/01.PCC.0000257735.49562.8F
32. Fortenberry JD. Making the pediatric intensive care unit a safe haven. *Pediatr Crit Care Med.* (2007) 8 (Suppl. 1):S1–2. doi: 10.1097/01.PCC.0000257734.84591.1F
33. Larrazabal LA, Jenkins KJ, Gauvreau K, Vida VL, Benavidez OJ, Gaitán GA, et al. Improvement in congenital heart surgery in a developing country the guatemalan experience. *Circulation.* (2007) 116:1882–7. doi: 10.1161/CIRCULATIONAHA.107.695403
34. Leon-Wyss JR, Veshti A, Veras O, Gaitán GA, O'Connell M, Mack RA, et al. Gaitán pediatric cardiac surgery: a challenge and outcome analysis of the guatemala effort. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Ann.* (2009) 12:8–11. doi: 10.1053/j.pcsu.2009.01.003
35. Maher KO, Chang AC, Shin A, Hunt J, Wong HR. Innovation in pediatric cardiac intensive care: an exponential convergence toward transformation of care. *World J Pediatr Congenit Heart Surg.* (2015) 6:588–96. doi: 10.1177/2150135115606087
36. Checchia PA, Laussen PC, Macrae D, Bohn D, Chang AC, Wessel DL. Pediatric cardiac intensive care: a transition to maturity. *Pediatr Crit Care Med.* (2016) 17 (8 Suppl. 1):S110–1. doi: 10.1097/PCC.0000000000000824
37. Stocker M, Pilgrim SB, Burmester M, Allen ML, Gijselaers WH. Interprofessional team management in pediatric critical care: some challenges and possible solutions. *J Multidiscip Healthc.* (2016) 9:47–58. doi: 10.2147/JMDH.S76773
38. Fenton KN, Castillo SH, Claro CD, Novick WM. Teamwork and program organization in developing countries. *World J Pediatr Cong Heart Surgery.* (2011) 2 219–24. doi: 10.1177/2150135110395334
39. Almandel A, Younis H, Gilbert C, Marr S, Bowtell K, Forsberg B, et al. Pediatric cardiac services in Iraq: current status and future plans. *J. Cardiothor Surg.* (2013) 8 (Suppl. 1):O303. doi: 10.1186/1749-8090-8-S1-O303
40. Lou X, Lee R, Feins RH, Enter D, Hicks GL Jr, Verrier ED, et al. Training less-experienced faculty improves reliability of skills assessment in cardiac surgery. *J Thorac Cardiovasc Surg.* (2014) 148:2491–6. doi: 10.1016/j.jtcvs.2014.09.017
41. Kogon B, Karamlou T, Baumgartner W, Merrill W, Backer C. Congenital cardiac surgery fellowship training: a status update. *J Thorac Cardiovasc Surg.* (2016) 151:1488–95. doi: 10.1016/j.jtcvs.2016.02.039
42. Babb DA, Salerno TA. Setting the standard: the necessity of internationalizing residency training programs. *J Thorac Cardiovasc Surg.* (2018) 157:2547–8. doi: 10.1016/j.jtcvs.2018.10.118
43. Starnes VA, Sullivan ME. The American board of thoracic surgery congenital fellowship: have we lost our international heritage? *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu.* (2017) 20:77–8. doi: 10.1053/j.pcsu.2016.09.006
44. Stawicki SP, Nwomeh BC, Peck GL, Sifri ZC, Garg M, Sakran JV, et al. Training and accrediting international surgeons. *BJS.* (2019) 106:e27–33. doi: 10.1002/bjs.11041
45. Novick W, Molloy F, Cardarelli M, Gilbert C. Pediatric Cardiac Development Assistance in Iraq: 2012–2016. *Cardiol Young.* (2017) 27 (Suppl. 4):S227.
46. Novick W, Amer W, Cardarelli M, Rodriguez H. Pediatric cardiac assistance and development in Eastern Libya. *Cardiol Young.* (2017) 27 (Suppl. 4):S228.
47. Busse H, Aboneh EA, Tefera G. Learning from developing countries in strengthening health systems: an evaluation of personal and professional impact among global health volunteers at Addis Ababa University's Tikur Anbessa Specialized Hospital (Ethiopia). *Global Health.* (2014) 10:64. doi: 10.1186/s12992-014-0064-x
48. McCrary NE, Mazur JM. Conceptualizing a narrative simulation to promote dialogic reflection: using a multiple outcome design to engage teacher mentors. *Edu Technol Res Dev.* (2010) 58:325–42. doi: 10.1007/s11423-008-9100-y
49. Satish U, Streufert S. Value of a cognitive simulation in medicine: towards optimizing decision making performance of healthcare personnel. *Qual Saf Health Care.* (2002) 11:163–7. doi: 10.1136/qhc.11.2.163
50. Lapkin S, Levett-Jones T, Bellchambers H, Fernandez R. Effectiveness of patient simulation manikins in teaching clinical reasoning skills to undergraduate nursing students: a systematic review. *Clin Simulat Nurs.* (2010) 6:207–22. doi: 10.1016/j.ecns.2010.05.005
51. Law MA, Grifka RG, Mullins CE, Nihil MR. Atrial septostomy improves survival in select patients with pulmonary hypertension. *Am Heart J.* (2007) 153:779–84. doi: 10.1016/j.ahj.2007.02.019
52. Almanla A, Charafeddine F, Abutaqa M, Mustafa H, Tabbakh A, Hussein HB, et al. Transcatheter closure of atrial septal defects: comparable experience and outcomes between developing and developed countries. *Pediatr Cardiol.* (2019) 40:610–5. doi: 10.1007/s00246-018-2034-1
53. Askari B, Soraya H, Ayremlu N, Golmohammadi M. Short-term outcomes after surgical versus trans catheter closure of atrial septal defects: a study from Iran. *Egypt Heart J.* (2018) 70:249–53. doi: 10.1016/j.ehj.2018.09.003
54. Alwi M. Stenting the ductus arteriosus: case selection, technique and possible complications. *Ann Pediatr Cardiol.* (2008) 1:38–45. doi: 10.4103/0974-2069.41054
55. Alwi M, Choo KK, Latiff HA, Kandavello G, Samion H, Mulyadi MD. Initial results and medium-term follow-up of stent implantation of patent ductus arteriosus in duct-dependent pulmonary circulation. *J Am Coll Cardiol.* (2004) 44:438–45. doi: 10.1016/j.jacc.2004.03.066
56. Glatz AC, Petit CJ, Goldstein BH, Kelleman MS, McCracken CE, McDonnell A, et al. Comparison between patent ductus arteriosus stent and modified blalock-taussig shunt as palliation for infants with ductal-dependent pulmonary blood flow. *Circulation.* (2017) 137:589–601. doi: 10.1161/CIRCULATIONAHA.117.029987
57. Frenkiel O, Overton I, O'Connor K. *Bad Medicine: The Counterfeit Drug Industry is Huge and the Profits are Vast. Some are Harmless but Others are Lethal*. Available online at: http://news.bbc.co.uk/2/hi/programmes/this_world/4656623.stm (accessed November 9, 2018).
58. Manno CS, Hedberg KW, Kim HC, Bunin GR, Nicolson S, Jobes D, et al. Norwood. *Blood.* (1991) 77:930–6.
59. Whiting D, DiNardo JA. teg and rotem: technology and clinical applications. *Am J Hematol.* (2014) 89:228–32. doi: 10.1002/ajh.23599
60. Despotis GJ, Joist JH, Hogue CW Jr, Alsoufiev A, Kater K, Goodnough LT, et al. The impact of heparin concentration and activated clotting time monitoring on blood conservation: a prospective, randomized evaluation in patients undergoing cardiac operation. *J Thorac Cardiovasc Surg.* (1995) 110:46–54. doi: 10.1016/S0022-5223(05)80008-X
61. White MC, Randall K, Capo-Chichi NFE, Sodogas F, Quenum S, Wright K, et al. Implementation and evaluation of nationwide scale-up of the Surgical Safety Checklist. *BJS.* (2019) 106:e91–102. doi: 10.1002/bjs.11034
62. Plunkett PF. Perfusion education in the USA. *Perfusion.* (1997) 12:233–41. doi: 10.1177/026765919701200405
63. AmSECT. *The American Society of ExtraCorporeal Technology Standards and Guidelines for Perfusion Practice.* (2019). Available at: http://www.amsect.org/p/cm/ld/fid=1617 (accessed October 25, 2018).
64. AmSECT. *AmSECT Fellow of Pediatric Perfusion.* (2019). Available online at http://www.amsect.org/page/pediatric-fellow-requirements
65. Forsberg BC, Novick WM. A simplified approach to pediatric modified ultrafiltration: a novel circuit design. *J Extra Corpor Technol.* (2013) 45:259–61.
66. Croti UA, Jenkins KJ, Braile DM. Checklist in pediatric cardiac surgery in Brazil: an useful and necessary adaptation of the Quality Improvement Collaborative International Congenital Heart Surgery in Developing Countries. *Rev Bras Cir Cardiovasc.* (2011) 26:511–5. doi: 10.5935/1678-9741.20110034
67. Congenital Checklist. *Congenital Heart Surgery Checklist.* (2018). Available online at: https://www.sts.org/sites/default/files/files/PDF/CongenitalChecklist2016.pdf (accessed January 4, 2019).
68. Hauk L. Periop breifing: did you know. *AORN J.* 2 108:14. doi: 10.1002/aorn.12318
69. Boyle D, Horton H, Yorke H, Sawer P. *Westminster 'Terror Attack': Driver Arrested after Car Mows Down Cyclists and Ploughs into Parliament Barrier.*

Available online at: www.telegraph.co.uk/news/2018/08/14/car-crashes-barrier-outside-parliament-armed-police-surround (accessed September 19, 2018).
70. Jenkins N. *A Timeline of Recent Terrorist Attacks in Europe.* (2018). Available online at: http://time.com/4607481/europe-terrorism-timeline-berlin-paris-nice-brussels/ (accessed September 18, 2018).
71. Hoffman JIE. The global burden of congenital heart disease. *Cardiovasc J Afr.* (2013) 24:141–5. doi: 10.5830/CVJA-2013-028
72. Zakaria T, Cornwell S, Al Shalchi H. *For Benghazi Diplomatic Security, U.S. Relied on Small British Firm*. Available online at: www.reuters.com/article/us-libya-usa-bluemountain/for-benghazi-diplomatic-security-u-s-relied-on-small-british-firm-idUSBRE89G1TI20121018 (accessed September 19, 2018).
73. Jenkins KJ, Castañeda AR, Cherian KM, Couser CA, Dale EK, Gauvreau K, et al. Reducing Mortality and Infections After Congenital Heart Surgery in the Developing World. *Pediatrics.* (2014) 134:e1422–e1430. doi: 10.1542/peds.2014-0356
74. Schidlow DN, Jenkins KJ, Gauvreau K, Croti UA, Giang DTC, Konda RK, et al. Transposition of the great arteries in the developing world surgery and outcomes. *J Am Coll Cardiol.* (2017) 69:43–51. doi: 10.1016/j.jacc.2016.10.051
75. Novick WM, Fenton KN. Chapter: The ethics, power and influence of leadership. In: Firstenberg M and Stawicki S, editors. *Fundamentals of Leadership for Healthcare Professionals*. Hauppauge, NY: Nova Publishing (2018).
76. Steyn E, Edge J. Ethical considerations in global surgery. *BJS.* (2019) 106:e17–9. doi: 10.1002/bjs.11028
77. Kathleen N. Fenton, Marcelo Cardarelli, Frank Molloy and William M. Novick. Ethics in humanitarian efforts: when should resources be allocated to paediatric heart surgery? *Cardiol Young.* (2019) 29:36–9. doi: 10.1017/S1047951118001713
78. Cardarelli M, Vaikunth S, Mills K, DiSessa T, Molloy F, Sauter E, et al. Cost-effectiveness of humanitarian pediatric cardiac surgery programs in low-and middle-income countries. *JAMA Netw Open.* (2018) 1:e184707. doi: 10.1001/jamanetworkopen.2018.4707
79. Shrime MG, Sleemi A, Ravilla TD. Charitable platforms in global surgery: a systematic review of their effectiveness, cost-effectiveness, sustainability, and role training. *World J Surg.* (2015) 39:10–20. doi: 10.1007/s00268-014-2516-0
80. Kinsley RH. The third Aldo Castaneda lecture: the neglect of neonatal/infant cardiac disease in Africa–continental genocide? *World J Pediatr Congenit Heart Surg.* (2012) 3:241–3. doi: 10.1177/2150135111425394

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OPINION
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The Unexplored Benefits of Paediatric Cardiac Humanitarian Work in the Developing World

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INTRODUCTION

Congenital heart disease is the most common type of birth defect with an average incidence of ∼9.0 per 1,000 live births (1). There are 1.4 million children born with congenital heart disease in the world every year with over a million of these children being born in low and middle income countries (LMIC). As the rate of infectious diseases has fallen by 50% since 1990, birth defects have become the 4th highest cause of childhood mortality in the world (1). In response to this, there has been a proliferation of teams from across the developed world that visit various LMIC to perform cardiac surgery on children and in certain instances to help build capacity for paediatric cardiac services. Whilst these lifesaving endeavours are laudable and well-documented, what has not been explored are the significant mutual benefits accrued to the visiting international teams and local teams during these missions. Typically, each international team is composed of the same personnel required to carry out paediatric cardiac surgery in their home countries which therefore means a paediatric cardiologist, paediatric cardiac anaesthetist, paediatric cardiac surgeon, a paediatric perfusionist, and a PICU team of two doctors and four nurses.

Each team member is responsible for and delivers their own aspect of paediatric cardiac surgery provision using the facilities and equipment available whilst working with their counterparts in the local hospital. Although hospitals that undertake adult cardiac surgery in lower and middle income countries are not usually able to provide the exact or optimum facilities required for paediatric cardiac surgery, it is possible to adapt an adult service safely enough to be able to operate on children as well. Deficiencies in equipment and other facilities as well as the near absence of congenital heart disease experience in the local team poses a huge challenge to the visiting team. This variance requires adaptability and flexibility from each team member who must call upon clinical skills acquired from working in developed health care systems where there is a strong emphasis on the basics of medicine and nursing. In addition, as the team is much smaller than the volunteers are used to working with back in their respective countries where there is a considerable pool of expertise to call upon in the case of clinically challenging patients, the smaller team must coalesce and support each other to help manage clinically fraught situations. Managing difficult clinical situations with a smaller pool of personnel and in resource constrained environments can potentially produce an uplifting of the clinical skills within the visiting team which may then translate into improved care for their local populations when they return.

The National Institute for Cardiac Outcomes Database (NICOR) in the UK, collects data and produces analysis to enable hospitals and healthcare improvement bodies to monitor and improve the quality of care and outcomes of cardiovascular patients (2). Examination of the database reveals that most paediatric cardiac centres in the UK, perform paediatric cardiac surgery on 6–8 children in a typical week.

We used the data derived from the NICOR database as a benchmark for the average number of cases performed per week in the UK and compared the activity of one international paediatric cardiac charity (Healing Little Hearts UK Registered Charity 1130194) with which the authors are associated, to describe our resource and time utilisation as the charity's operations are funded by public donations.

The number and type of cases performed between 1st April 2018 and 1st April 2019 were analysed using the charity database. Further analysis of the database explored the following: follow-up, costs of the trip, composition of the travelling teams, complications during the trips and mortality.

RESULTS

Between April 2018 and April 2019, Healing Little Hearts (HLH) undertook 23 international trips to countries including India, Malaysia, Nigeria, Romania, Tanzania, and several more.

In the 12 months, a total of 270 operations were performed which means that on average, 12 children were operated by HLH teams during each week the charity travelled which demonstrates a very efficient use of time, resources and donated funds.

As **Table 1** highlights, the complexity of cases operated upon ranged from VSD closures, ASD closures, TOF repair and modified Blalock-Taussig shunt in neonates. The figures highlight that each surgeon and their supporting medical and nursing team are operating on and caring for significantly more children during this week compared to a typical week back in majority of paediatric cardiac centres in the UK. Crucially, all of this happens in resource limited settings. This amount of operating, provides the team with an excellent platform to teach and train the local teams. The teams usually work in adult setups both in theatre and in the intensive care unit, using equipment that is more suited for adult cardiac surgery. Often, surgeons with this charity undertake 2 week-long trips per year, operating on ∼24 children during these trips. This is equivalent to 2 months operating per surgeon in many UK centres. Additionally, from the HLH database it is evident that the teams are comprised of doctors and nurses from across the developed world, i.e., all over the UK, parts of Europe, North America, and as far away as Australia. Many of these surgeons, nurses and physicians find these experiences so rewarding and beneficial that they travel numerous times in a year which in turn contributes to their own professional development. Again, with members of the team coming from across the globe, they bring a significant amount of varied experience, knowledge and expertise to the bedside which is shared with the local healthcare professionals and amongst the travelling team members who then become exposed to different ways of working clinically.

FOLLOW-UP

HLH only works with hospitals that have a cardiologist who in turn coordinates the patients referred and organises follow up on children post-surgery. In addition, because HLH works with hospitals wishing to build capacity, the practise is usually to visit each partner hospital between two and four times per year which enables follow up on the children operated upon on previous visits.

TEAM COMPOSITION

Teams are bespoke to the requirements of each hospital that HLH works with but in general the teams consist of 8–10 volunteers whose designations have already been described. A unique aspect of the service that HLH provides is to tailor each trip to the needs of each partner hospital. In other words, if a hospital has a surgeon and a cardiologist but no paediatric cardiac anaesthetist and PICU team then only those specific team members would constitute the HLH team.

TABLE 1 | List of surgical and interventional catheter procedures performed by the travelling team between 1st April 2018 and 1st April 2019.

Number of procedures	Surgical procedures	Additional procedures
81	VSD closure	
51	Tetralogy of Fallot repair	
46	ASD closure	
41	PDA closure	
7	TAPVR	
6	AVSD repair	
5	Glenn shunt	
4	Mitral valve replacement	
3	TAPVD	
1	Modified Blalock–Taussig shunt in neonate	
26		Non-surgical procedures (including PDA stents and ASD device closure)

COSTS ASSOCIATED WITH THE TRIP

HLH costs are primarily related to the cost of flights needed to get the teams to the various hospitals that HLH works with. Each trip costs ∼£6,000 and that money has been donated by the generous British public over the last 11 years. All HLH team members volunteer their time usually by taking annual leave and do not receive any remuneration for the clinical work that is done.

OPERATING PLAN DURING THE WEEK

All the patients are screened thoroughly at a multidisciplinary meeting between the visiting team and the local team usually on the weekend and an operation list is finalised.

At the beginning of each week, the team operates on the simplest cases, increasing the complexity of the cases from Tuesday through to Thursday and then reducing the complexity on Friday. Extubation in theatre or soon thereafter is our standard approach although inevitably there is the odd patient or two still on the ventilator when the team leaves.

In these instances, HLH either tries to ensure that a member of the PICU team stays behind for a while longer or if that is not possible then we provide clinical support to the local team with help of internet based technology.

COST OF SURGERY

The host hospital's costs of cardiac surgery are recuperated from a combination of government funding and donations. It is essential that hospitals do not profit from the charity work that HLH does. Details of all patients operated upon by HLH are maintained on the charity's database. Equally, each partner hospital keeps its own database of patients operated upon.

COMPLICATIONS

Out of the 270 cases performed by the team, 10 (4%) of the patients died post-operatively.

It is worth remembering that compared to the case load in higher income countries, the types of patients managed by travelling teams is entirely different from the patients back home as these patients usually present late with their clinical conditions, often as a result of adverse socioeconomic factors. Infective complications were more prevalent and postoperative sepsis is a significant factor causing mortality on these missions, something rarely seen in developed countries. Additional complications include unfortunate nursing errors such as potassium overdoses due to less stringent nursing checks as well as other drug errors and much slower reaction times to deteriorating patients due to the inexperience of local medical and nursing staff. In addition, due to the late diagnosis and presentation, a percentage of these children require longer stays in ICU and appear to have greater respiratory morbidity than observed in the UK such as ventilator associated pneumonias and pulmonary haemorrhage secondary to reperfusion injury. Pulmonary hypertension is also more prevalent in these settings due to the same confounding factors in these children.

DISCUSSION

CHD is a huge problem worldwide. Lack of access to care and insufficient expertise within the developing world to correct these defects results in vast numbers of children dying prematurely from eminently treatable cardiac conditions. The enormous global child health issue of untreated CHD has spawned the development of many charities from across the developed world that travel to low and middle-income countries to perform heart surgery on children (3–5). These projects are often looked at with great admiration, however, a key aspect which is often overlooked is the gradual empowerment of local medical and surgical teams. Firstly, let's explore the various challenges faced by the travelling healthcare teams during these endeavours.

The Challenges

The Patient

The patients are often much more unwell than the cohort of patients looked after in the developed world as a result of delayed diagnoses and other co-morbidities of poverty. The late diagnoses are usually associated with significant structural changes to the patient's cardiorespiratory system which means that their pre- and post-operative course is often stormy.

The Environment

Resource-constrained and relatively alien working environments requires an upgrading of the ability and skills of each team member. The team can no longer rely on high-end technology and immediately available near-patient testing but instead they must adapt to a management method based on clinical skills and the first principles of medicine and nursing. The team often works within an adult ICU, usually with limited bed capacity, which requires considerable adaptation when managing paediatric cases. Resources so readily available back in the UK such as blood products are either not available or associated with considerable delay. In certain hospitals, cryoprecipitate is not available and often the easiest blood product to administer for postoperative bleeding is whole blood which can be associated with significant pro- inflammatory effects and subsequent morbidity.

The Operating Room and the ICU

Travelling surgeons are usually having to use adult cardiac surgical instruments for very delicate operative procedures. Anaesthetists must successfully anaesthetise and ventilate the patients using machines not entirely suitable for children. Similarly, in the ICU, the team must adapt to adult ventilators. Whilst these challenges result in difficult and testing times for the travelling teams, they transform into unique learning experiences which the teams take back with them to their respective countries.

The Benefits

The Local Team

The local team of doctors and nurses have often had no prior training or experience in paediatric intensive care or paediatric cardiology. Consequently, they are often unfamiliar with normal physiological parameters for children, let alone the complexity and nuances of the various cardiac cases operated upon. To combat this problem, the travelling team provides constant education to the local teams to boost their knowledge and skills when managing complex paediatric cases. Examples of this include short but informative daily tutorials held by the travelling doctors and nurses on important topics such as drug administration and vital observations. Additionally, a mentorship scheme is established wherein the lead travelling surgeon will train a local surgeon for the entire week in theatre to boost his/her skills, competence and confidence. This example of pedagogy has ultimately led to two paediatric cardiac services within India, previously with minimal experience, being signed off as self-sufficient and able to perform life-saving cardiac surgery without assistance from travelling teams. It is a strategy that potentially bodes well for the future with the goal to make all collaborating cardiac centres self-sufficient through this global initiative. Greater cardiac surgical activity within the developing world leads to a reduction in the number of children tragically dying due to these correctable defects.

The Travelling Team

New experiences, challenging cases and suboptimal environments provide a positively unique opportunity for each member of the travelling team. These altruistic acts are undoubtedly extremely satisfying and rewarding. In addition, as the entire volunteer team has cared for a much larger number of cases in a typical week than they would do in their own units, it could translate into enhanced expertise within each member of the team. Based on the above comments, we propose that a surgeon who has operated on an average of 12 children in a week may return home with his or her operative skills finely honed and that would hopefully produce better outcomes for patients back at home. The same analogy is applicable to all members of the travelling teams. Beyond the clinical realm, it is worth stating that each visit by a volunteer to a foreign country represents a life experience that they would not necessarily have had otherwise nor indeed even contemplated.

THE FUTURE

It is all too easy to label such missions as charity endeavours which unfortunately misses the crucial point which is that the recipient healthcare teams and the children operated upon benefit immensely from such collaborations. The children are given a new lease of life through these operations. Through the continuous training and teaching that occurs during these missions, it gradually builds up confidence, knowledge and expertise within the local teams such that they can become self-sufficient. With this being the ultimate goal in mind, this rewarding project can have a domino-like effect and translate into increasing numbers of hospitals, previously ill-equipped to treat paediatric cardiac patients, becoming trained in doing so. The world is now a much smaller place which lends itself very nicely to such rewarding, life saving, and mutually beneficial partnerships.

Underpinned by robust data collection along with stringent risk assessment and strict governance arrangements of the work carried out by visiting international teams, there is no reason why such medical relationships should not be formalised. In a globalised world, trade links between countries could become the template for the sharing of good medical practise across the globe. Using either ongoing trade and commerce relationships or previous historical ties such as the Commonwealth as a template, health partnerships should be established whereby governments of higher income countries should seek to work with governments of lower and middle income counties to help build capacity, i.e., train and empower local doctors and nurses to carry out and perform the entire range of paediatric cardiac surgery through multiple visits over a medium term collaboration of 5–10 years. These partnerships will be a win-win situation whereby both the teams from higher income countries and the hospitals and children in lower income countries can benefit. Continuous training and education provision for local teams within the developing world can result in increasing numbers of cardiac centres becoming self-sufficient and able to provide cardiac care without additional support. Goal 3 of the United Nations Sustainable Development Goals 2015 is to reduce the staggering 6 million childhood deaths in children <5 years occurring annually of which CHD comprises a significant proportion (6, 7).

The only way that can be achieved is if managing the health of children in our ever-shrinking world is no longer constrained by geographical borders but instead is guided by need and delivered by such partnerships.

LIMITATIONS

Our study and the subsequent discussion attempts to explore the potential benefits of international charity work for both the travelling, but more importantly, the local healthcare teams by identifying the challenges and solutions to overcome them. Whilst the aforementioned points provide strong arguments outlining these positive mutual effects, we appreciate and recognise the lack of robust and conclusive data to support such conclusions. In order to address this, future qualitative analysis including distribution of surveys to both the travelling and local team members soliciting their opinions on how these missions positively impact their skills and expertise would be warranted.

CONCLUSION

A burgeoning amount of literature exists about the catastrophic lack of resources available in many parts of the developing world for paediatric cardiac surgery and the benefit that accrues to the children in the poorest countries because of the charitable visits. However, there has been virtually no evaluation of the considerable and mutual benefits to both the visiting and more importantly the local teams during these humanitarian endeavours. The authors hope that such observations provide a template for the formalising of such mutually beneficial and

life-saving collaborations between higher and lower and middle income countries. It is our duty to share our world-renowned expertise and skills with these less fortunate countries to save lives on an international scale.

AUTHOR CONTRIBUTIONS

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

REFERENCES

1. van der Linde D, Konings E, Slager M, Witsenburg M, Helbing W, Takkenberg J, et al. Birth prevalence of congenital heart disease worldwide. *J Am Coll Cardiol.* (2011) 58:2241–7. doi: 10.1016/j.jacc.2011.08.025
2. *NICOR*. Nicor.org.uk. Available online at: https://www.nicor.org.uk/ (cited January 1, 2021).
3. Tchervenkov C, Jacobs J, Bernier P, Stellin G, Kurosawa H, Mavroudis C, et al. The improvement of care for paediatric and congenital cardiac disease across the World: a challenge for the World Society for Pediatric and Congenital Heart Surgery. *Cardiol Young.* (2008) 18:63. doi: 10.1017/S1047951108002801
4. Hoffman J. The global burden of congenital heart disease: review article. *Cardiovasc J Afr.* (2013) 24:141–5. doi: 10.5830/CVJA-2013-028
5. Global, Regional and National Burden of Rheumatic Heart Disease, 1990-2015. *Pediatr Infect Dis J.* (2017) 36:1155. doi: 10.1097/INF.0000000000001805
6. *Health - United Nations Sustainable Development*. United Nations Sustainable Development (2015). Available online at: http://www.un.org/sustainabledevelopment/health/ (cited April 2, 2018).
7. Wang H, Bhutta Z, Coates M, Coggeshall M, Dandona L, Diallo K, et al. Global, regional, national, and selected subnational levels of stillbirths, neonatal, infant, and under-5 mortality, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet.* (2016) 388:1725–74. doi: 10.1016/S0140-6736(16)31575-6

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