World Journal of Pediatrics (2023) 19:1–6
https://doi.org/10.1007/s12519-022-00654-x

EDITORIAL

# Innovative treatments for congenital heart defects

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Received: 18 July 2022 / Accepted: 30 October 2022 / Published online: 8 December 2022


The past few decades have witnessed substantial advances in the treatment of complex congenital heart defects, with most significant advances in surgical treatment strategies and improved outcomes dependent upon well-educated and calculated risk-taking innovations. In the present surgical era, doing nothing for complex congenital heart defects is unacceptable, and pioneering surgeons are willing to undertake and accept the substantial risks of innovative pediatric cardiac surgery [1]. New strategies, a team approach to decision-making, improved and refined operative skills, as well as new techniques to optimize cardiovascular physiology in all stages of care, have resulted in early treatment with decreased hospital mortality and improved long-term clinical outcomes [2]. The most important difference between previous versus modern surgical management strategies is the pursuit of bi-ventricular versus uni-ventricular physiology. This approach sometimes employs initial-staged palliation and ventricular recruitment instead of initial complete repair, with reductions in long-term morbidity, mortality, and resource utilization [2]. Despite these advances, risk-averse behavior, combined with an increasing rate of premature births and associated elevated surgical risk, have created an environment that is not always favorable for children born with truly complex congenital heart defects. Based on the experience of our department, the most challenging clinical situations in congenital heart defects require innovative approaches. The purpose of this editorial is to highlight the critical advances made in recent years that make this approach possible.

During the past several decades, management of complex congenital heart defects has seen substantial progress and improved treatment outcomes, with significant reduction in hospital mortality and increased attention by medical providers to patient and family quality of life. Advances have been achieved due to expanding knowledge gained by multidisciplinary collaborations among all people involved in the clinical care, including but not limited to cardiologists, anesthesiologists, surgeons, perfusionists, intensivists, nurses, and technicians, together with basic/translational science researchers, such as biologists, mathematicians, bioengineers, imaging experts, and neurodevelopmental specialists. Thus, for the present review, we examined the expanding horizons of this rapidly evolving field with regard to the surgical treatment of complex congenital heart defects.

The materials that we used originated from a MedLine search, together with a specific search in the major journals covering the field of congenital heart disease, including *Pediatric Cardiology*, *Cardiology in the Young*, *World Journal of Pediatrics* and *Congenital Heart Surgery*, *Journal of Thoracic and Cardiovascular Surgery*, *Annals of Thoracic Surgery*, *European Journal of Cardio-Thoracic Surgery*, and *Seminars in Thoracic Cardiovascular Surgery*.

Major scientific contributions have emerged from translation of basic science research to bedside applications, as well as through clinical pathways from prenatal diagnosis to long-term clinical follow-up.

Collaboration between mathematicians and bioengineers has produced computational and simulation studies that yielded better understanding of heart morphology and function [3–5]. Basic science research projects have compared the circulation of congenital heart defects with anatomically similar animals [6], while advanced techniques have investigated the possibility of enhancing myocardial performance [7–9]. Important experimental and clinical studies also have reduced the neurological and cardio-circulatory damages occurring during fetal life in the presence of congenital heart defects [10–13]. Improvements in prenatal diagnosis have resulted in coordinated delivery of babies with congenital heart defects in close connection to tertiary referral centers equipped with appropriate neonatal interventional critical care [14, 15].

During the past decade, our field has also seen significant advances in the quality of post-natal diagnosis. The

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introduction of technological innovations, such as three-dimensional echocardiography [16, 17] and low radiation dose computed tomography, provide accurate anatomic definition of congenital heart defects [18, 19]. Functional assessment of myocardial function with magnetic resonance imaging [20, 21] and particularly the introduction of the new technique of fusion of different diagnostic imaging modalities [22] facilitate appropriate operative decision-making. More precise clinical decision-making and planning of surgical repairs have been facilitated by modeling and 3-D printing of the heart structures in complex congenital heart defects [23, 24].

Progress in general anesthesia and cardiopulmonary bypass [25–27], as well as improved cardioplegia techniques for myocardial protection [28–30], have introduced substantial changes in perioperative management. Individualized general anesthesia with proper mechanical ventilation, anticoagulation, and blood product management, as well as more physiological strategies of cardiopulmonary bypass, have allowed physicians and surgeons to perform complicated operations more safely and with more confidence. Strategies that have been optimized for cardiopulmonary bypass include circuit priming, flow, pressure, and temperature; the avoidance of myocardial distension; and accurate weaning. As a result, the surgeon is now free to focus on all morphological and technical details without the pressure of time constraints; therefore, the surgeon can provide early repair even in the most complex congenital heart defects. Intra-operative surface and/or trans-esophageal echocardiography performed before, during, and after surgery, provides immediate assessment of surgical procedures [31, 32]. Furthermore, readily available and improved techniques of extracorporeal membrane oxygenation allow significant progress in the perioperative support for critical infants and children with complex congenital heart defects. Clinicians provide improved cardio-circulatory support by expanded knowledge of extracorporeal membrane oxygenation indications and timing, cannulations strategies, anticoagulation management, extracorporeal membrane oxygenation circuit management and optimal flow rates [33–35]. Collectively, these advancements have allowed for mitigation of patient complications.

In recent years, the dynamics of the early post-operative period have been given increased emphasis and attention, especially the critical process of transition from the operative room to the intensive care unit. Continuous monitoring and stabilization of all vital and laboratory parameters, appropriate oxygen delivery, homeostasis of cardiac function, fluid balance, and adequate respiratory and pharmacological support are all essential components of post-operative patient care [36, 37]. Children during the entire post-operative period are typically maintained with a minimum hematocrit above 40%. This maximizes oxygen delivery, as dictated by the following formula:

$$\text{oxygen delivery} = \text{cardiac output} \times \text{oxygen saturation} \times \text{hemoglobin}$$

Maximization of hemoglobin concentration is especially relevant for neonates and infants following cardiac surgery because cardiac output is recovering and the oxygen saturation is low due to mixing of systemic and pulmonary circulations. In this situation, the only way to improve the oxygen delivery is to increase the hemoglobin level. Finally, washing blood products to achieve physiologic fluid parameters are essential prior to transfusing an infant in the operating room and in the immediate post-operative period.

All the advances in prenatal assessment, imaging technology, and perioperative support, have allowed for more aggressive approaches to the surgical treatment of complex congenital heart defects with improved safety and confidence. More specifically, surgeons have changed their perspective regarding timing of surgery and surgical approach for complex reconstructions. Primary surgical reconstruction during the neonatal period or early infancy has become widely accepted within the congenital cardiology community. Early complete repair provides the major advantage of reducing the duration of exposure of all organs to the damaging effects of hypoxemia, poor perfusion, pulmonary hypertension, heart failure, and the associated long-term complications [38].

Another impetus for change has been the knowledge of the deleterious and irreversible complications occurring in adolescents and young adults from the long-term effects of the Fontan circulation [39, 40]. This understanding has promoted the investigation of all possible alternative options to Fontan circulation, with an increasing emphasis in our department to pursue a bi-ventricular circulation whenever possible. We believe that significant gains in patient quality of life can be achieved by avoiding a uni-ventricular circulation, or when already established, converting to a bi-ventricular circulation with operations to recruit hypoplastic ventricles and structures, as we have recently reported [41, 42].

Bi-ventricular circulation remains the goal, whenever feasible, for every patient treated in our department. Dedicated pre-operative imaging has facilitated pre-operative decision-making between a uni-ventricular or bi-ventricular surgical approach tremendously. The preferred tools in the surgical planning of complex repairs are advanced echocardiographic imaging, cardiac tomography, magnetic resonance imaging, and three-dimensional reconstructions. These tools provide detailed definition of intra-cardiac anatomy, including size and morphology of inflow and outflow tracts of both ventricles, as well as indexed ventricular volumes [43].

The concept of staged surgical approach for bi-ventricular circulation is not new. In 1984, Paul Ebert proposed "staged partitioning" for the single ventricle [44]. In 1986, Roxane McKay reported "staged septation" of a double inlet left ventricle [45]. In 2022 Jan Quaegebeur and colleagues revised their approach to surgical septation to avoid the Fontan pathway [46].

At our center, the pathway toward a bi-ventricular circulation is considered for all patients referred in the newborn period with borderline left heart structures and utilizes appropriate staging of surgical procedures [41, 42]. For patients evaluated after any steps toward a uni-ventricular pathway, either a Norwood, bidirectional Glenn, or Fontan completion, the possibility for a bi-ventricular conversion is ruled out only after all imaging and functional investigations have excluded this surgical possibility [41, 42, 47–55] (Fig. 1). For this decision-making process, the key elements to consider, in addition to the previous interventional and surgical history, are size of inflow and outflow of the left ventricle, morphology and shunt direction through any communication at the level of interatrial and/or ventricular septum, right and left ventricular function and volumes, and morphology and flow of ascending aorta and aortic arch [41, 42].

Recently, for neonates with borderline left heart structures in critical condition as a result of pulmonary over-circulation and poor systemic perfusion with subsequent multi-organ failure, we adopted the policy of bilateral pulmonary artery banding, augmented by either stenting of the patent ductus arteriosus or maintenance of Prostaglandins infusion [56–61]. This approach defers the Norwood procedure and the required long period of cardiopulmonary bypass in

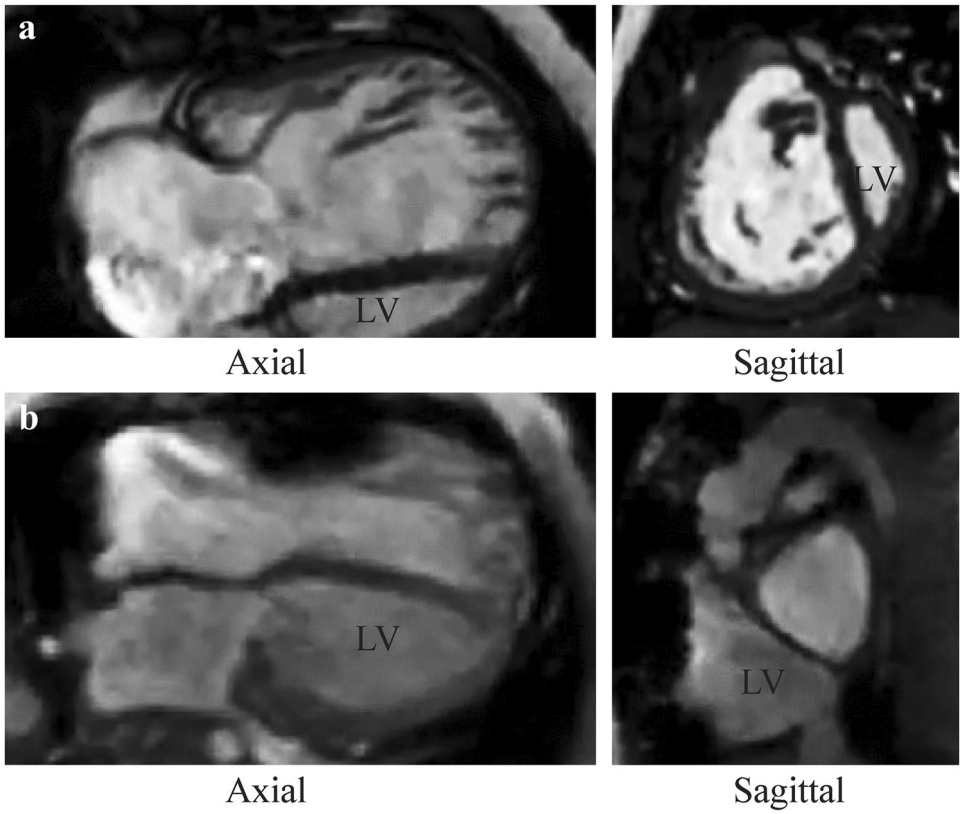


**Fig. 1** **a** Pre-operative and **b** post-operative cardiac MRI, showing a significant increase in the size of the left ventricle (LV), from 30.5 mL/m$^2$ to 59.7 mL/m$^2$. This girl, born with hypoplastic left-sided structures with mitral stenosis and a small ventricular septal defect (VSD), underwent a Norwood/Sano procedure in the neonatal period at another institution, followed by a bidirectional Glenn with enlargement of the left pulmonary artery at the age of 5 months. When referred to our department at the age of 3 years, 13 kg, the cardiac MRI (**a**) showed a small LV. A program of LV recruitment was then started, with resection of the right ventricular outflow tract, placement of a 6 mm Sano conduit, fenestrated (4 mm) closure of the atrial septal defect, bilateral enlargement of pulmonary arteries. The next day, the patient underwent resection of the left and right ventricular outflow tracts, VSD enlargement, and implantation of an epicardial pacemaker. After 9 months, she underwent bi-ventricular repair, with takedown of the Damus-Kaye-Stansel anastomosis, the Sano conduit and the bidirectional Glenn with a 14 mm PTFE interposition graft to reconnect the superior vena cava with the right atrium. A 16 mm conduit was interposed between the two pulmonary arteries, and the atrial septal defect and VSD were closed. The cardiac MRI (**b**) before discharge showed a normal sized LV, with an ejection fraction of 52%

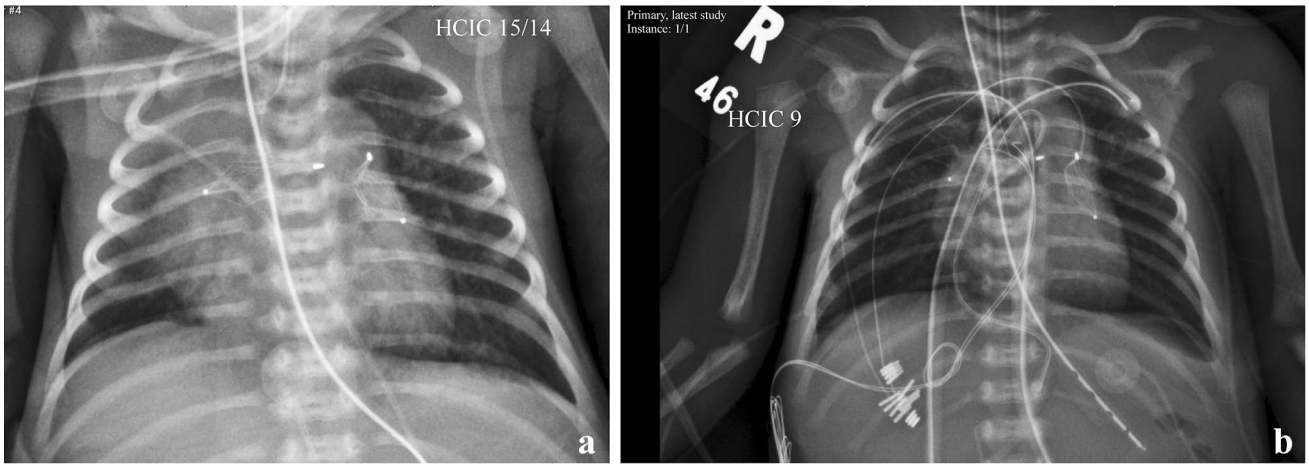


**Fig. 2** **a** Chest X-ray of a neonate, 11 days old, 2.0 kg, with hypoplastic left heart syndrome, pre-operative cardiomegaly (cardio-thoracic ration = 62.5, left), very elevated oxygen saturation (> 90%) due to elevated pulmonary-to-system flow ratio, who underwent bilateral pulmonary artery banding to reduce pulmonary blood flow and improve systemic perfusion, deferring the Norwood procedure; **b** The immediate post-operative chest X-ray confirms the significant reduction of cardiomegaly (cardio-thoracic ration = 37.5, right)

neonates with depleted metabolic and functional reserves. All organs, including the myocardium, kidneys, liver, lungs are able to recover, and the incidence of brain injuries from a period of diminished oxygen delivery is reduced (Fig. 2) [59–62].

In conclusion, the last two decades have witnessed substantial progress in the care of children with complex congenital heart defects owing to the pioneering efforts of innovative surgeons, cardiologists, nurses, basic scientists, and indeed the entire team charged with caring for these children. Undoubtedly, such progress has been facilitated by supportive hospital and surgical environments, which allow the treatment of children with very complex congenital heart defects. The most advanced techniques, including an emphasis on bi-ventricular recruitment and conversion, to avoid the pathway of uni-ventricular repair whenever possible, have helped to improve long-term survival and quality of life for these most critical lesions.

**Author contributions** The authors contributed to the concept and design of the review article, to the drafting the manuscript or revising it critically for important intellectual content, and to the final approval of the version to be published.

**Funding** No financial or non-financial benefits have been received or will be received by the authors from any party related directly or indirectly to the subject of this article.

**Data Availability Statement** All data used for the preparation of this manuscript have been derived from the available literature, and the sources of information are all included in the list of References.

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