

Review Article

The Evolution and Future of Pediatric Cardiology

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From early descriptions of heart disease to its current interdisciplinary practice of antenatal diagnosis of heart defects, advanced imaging, interventional catheterization, cardiac surgery, electrophysiology, pediatric intensive care, pediatric heart transplantation, and lifelong follow-up of patients with congenital heart defects, pediatric cardiology has undergone significant changes and developments in the past centuries. This review aims to outline these developments in pediatric cardiology and attempts to predict the forces that will shape its future. Innovations to measure the hidden physiological processes of the circulation of blood, such as the stethoscope, the electrocardiogram, cardiac catheterization, and most importantly, the echocardiogram, have greatly contributed to the field of pediatric cardiology. The 20th century introduced the innovations of cardiopulmonary bypass and congenital heart surgery, followed by interventional catheterization, the use of prostaglandin E1 to support the circulation in neonates with duct-dependent heart defects, pediatric heart transplantation, and mechanical circulatory support. In the modern era of pediatric cardiology, high-quality images of cardiac structure and function are obtained by the use of cardiac magnetic resonance imaging and multidetector row computed tomography. There is also an increasing number of patients diagnosed with heart defects prenatally, which has led to the establishment of antenatal cardiology as a separate field of interest. Furthermore, pediatric cardiology has greatly benefited from the advances made in the genetic basis of inherited arrhythmias and cardiomyopathies. Also, quality improvement collaboratives have provided a structured environment for process improvement. An important area that pediatric cardiology is currently focusing on is the transition of care to adult congenital heart disease programs. The challenge of pediatric cardiology is not only to identify the cardiac anatomy of patients' heart defects but also to predict the clinical course of the defects, the causes of the defects, and the morbidity of the defects after surgical repair, and to provide durable care for children with heart disease throughout their childhood and into their adulthood. The future of pediatric cardiology will include the use of genomics for risk stratification of at-risk individuals and patients with heart

disease, pharmacologic therapy that is matched to specific pathways, regenerative medicine and cardiac tissue engineering, the development of smaller and more durable mechanical circulatory support devices, the development and use of computational models and digital clinical twins, and the use of artificial intelligence for imaging and monitoring of patients with heart disease. Pediatric cardiology must also evolve to become a system of care that includes neurodevelopmental, psychosocial, and transition of care outcomes in addition to the current measurement, interpretation, and intervention of heart disease in children and adults with congenital heart disease.

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1. Introduction and Background

For pediatric cardiology to continue to evolve and move forward, it has to measure what previously had only been the subject of educated surmise. Long ago, in ancient civilizations, it was recognized that the heart was at the center of life. Many diseases of the heart were characterized by severe pain and by symptoms of arrhythmia, weakness, and shortness of breath. Collapses could also be caused by heart disease. However, at that time it was not possible to formulate a conceptual model of the circulation, and it was not possible to be sure whether a cardiac lesion was a structural as opposed to a functional problem. The major breakthrough in the understanding of the circulation was the shift from the concept of a diffuse humoral process to that of a closed system. The latter thought provided the fundamental basis of modern cardiovascular medicine ^{[1][2][3][4][5][6][7][8]}.

For a long time, the correlation of clinical data and measurable physiological data was missing. The effect of Digitalis on heart failure, for the first time, was durable; heart sounds and murmurs changed from non-perceptible to stethoscope-measurable, the ECG allowed for the recording of electrical heart activity, and catheterization of the heart via the heart chambers correlated symptoms with pressures, flow, and shunts ^{[9][10][11][12][13][14][15][16][17][18][19][20][21][22][23][24]}.

The child with heart disease is now commonly stabilized as a neonate with prostaglandins and can be treated with staged single-ventricle palliation. A child with heart disease is now a candidate for heart transplantation as well as support with extracorporeal circulation and pediatric ventricular assist devices. Modern pediatric cardiology is therefore an integrated system of care for the heart in the fetus, child, and adult. This system of care consists of fetal diagnosis and treatment of heart disease, cross-

sectional imaging, cardiac catheterization and interventional procedures, cardiac surgery, and postoperative care in the Intensive Care Unit. This system also consists of postoperative care in outpatient clinics for children with heart disease. The child with heart disease also requires care and follow-up by an electrophysiology laboratory for children with heart disease. The child with heart disease also requires a program of heart failure management as well as heart transplant candidacy. This system of care for children with heart disease also requires quality improvement activities by collaboratives of pediatric cardiologists from around the world as well as monitoring of late survival and neurodevelopmental status of children with specific types of heart defects and strategies for optimized transition of adolescents and young adults with heart defects to adult programs of care for patients with heart defects [\[25\]\[26\]\[27\]\[28\]\[29\]\[30\]\[31\]\[32\]\[33\]\[34\]\[35\]\[36\]\[37\]\[38\]\[39\]\[40\]\[41\]](#).

As the subspecialty of pediatric cardiology evolved, the field became a unique system of care for all children with heart disease. The breadth of pediatric cardiology now includes the spectrum of diagnosis and management of congenital and acquired heart disease in infants, children, and adolescents as well as all adults with congenital heart disease. As a result, pediatric cardiology is a highly diverse field and has come to include fetal diagnosis and treatment of congenital anomalies as well as cross-sectional imaging and interventional catheterization and surgical techniques to treat children with heart disease. Many children with heart disease require evaluation and management of a wide variety of adult congenital cardiac diseases, including electrophysiological studies, management of heart failure and cardiomyopathy, and management of children with heart disease who require heart transplantation as well as postoperative care of children with heart disease in pediatric intensive care units. Thus, the field has come full circle and, as before, requires quality improvement collaboratives as well as assessment of the long-term outcomes of children with heart disease and development of strategies for transition of care to adult congenital heart disease programs. Advances in measurement and application of technology have been instrumental in the continued evolution of pediatric cardiology. Initially, Doppler and deformation imaging enhanced the assessment of children with heart disease. Subsequently, the use of MRI and CT, with three-dimensional measurements and models, has provided powerful tools to assess structure and function in children with heart disease. The advances in technology have also led to fetal intervention and the development of cardiac registries that will enable further evaluation of the mechanisms of and treatment of heart disease in children. Thus, powerful tools for inherited cardiac genetic disease have also been developed to assist in the prediction and potential cure of disease based on

mechanism in individual children [\[42\]\[43\]\[44\]\[45\]\[46\]\[47\]\[48\]\[49\]\[50\]\[51\]\[52\]\[53\]\[54\]\[55\]\[56\]\[57\]\[58\]\[59\]\[60\]\[61\]\[62\]\[63\]\[64\]\[65\]\[66\]\[67\]\[68\]\[69\]\[70\]](#).

In the next decade, pediatric cardiology is likely to transform from a disease-oriented, mainly anatomically focused, rescue-oriented field to a more mechanism-oriented, predictive, and reparative field. New challenges will be addressed by using genomics and targeted pathway therapies as well as by the development of regenerative and tissue-engineered substitutes for cardiac structures. In addition, new strategies for transcatheter-based structural interventions in children will be developed. Also, safe and effective pediatric-specific mechanical circulatory support strategies will have to be established. Digital models and AI-assisted imaging will become more and more important. In contrast to the current gold standard of in-person follow-up of outpatients with heart disease, a variety of forms of telemonitoring will supplement the evaluation and follow-up of children and adults with congenital heart disease. Pediatric cardiology will become a global health field with an increasing number of programs that provide cardiovascular care in low- and middle-income countries. This review provides an update on the current status of pediatric cardiology and gives a perspective on the future developments of this exciting field.

2. Methods and Scope of the Narrative Review

This article is a narrative educational review rather than a systematic review. The literature base was assembled from landmark historical reports, major society guidelines and statements, clinical trials, registry and quality-collaborative publications, review articles, and selected contemporary studies relevant to pediatric cardiology, congenital heart disease, imaging, interventional cardiology, cardiac surgery, inherited cardiovascular disease, mechanical circulatory support, artificial intelligence, regenerative medicine, and lifelong congenital care.

Because this is not a systematic review, formal risk-of-bias scoring, meta-analysis, and GRADE certainty assessment were not performed. Evidence strength is therefore interpreted descriptively: established clinical practice is emphasized when supported by guidelines, registries, multicenter studies, or long-standing clinical adoption; emerging clinical translation is described when supported by early-phase trials or device approvals; and speculative future directions are identified when evidence remains preclinical, early feasibility, or programmatic.

3. Review

3.1. Historical Development of Pediatric Cardiology

The history of pediatric cardiology can be portrayed by the increasing ability to explain, diagnose, and treat the circulation in children over time. The different eras increased the ability to make the heart and its problems in children more measurable, more interpretable, or more treatable.

Ancient Beginnings (Ebers Papyrus, 1550 BCE)

The heart as an organ has always been a subject of human interest. The Ebers Papyrus, one of the oldest medical documents from 1550 BCE, contains over 700 recipes for all kinds of diseases and afflictions ^[1]^[2]. Already in this papyrus, a special chapter is devoted to the heart and all its possible diseases and their cures. The author lists possible cardiac diseases and their various symptoms (e.g., heart pain, irregular heartbeats, heart inflammation, heart weakness, respiratory distress, etc.). He also describes treatment with garlic and onions, honey, in the form of decoctions, concoctions, infusions, pastes, poultices, etc., and some of the opiate preparations for chest pain. Some spiritual procedures for the treatment of heart diseases are also described ^[1]^[2].

Greek Medicine and Humoral Theory (400 BCE)

Data concerning a specific entity of cardiac disease in the pre-Greek era (some centuries before 400 BCE) are lacking ^[3]^[4]. No in-depth description of cardiac disease is found in the works of Hippocrates (400 BCE), which represent the first systematic documentation of such cases. As for the blood, Hippocrates assumed that it originated in the liver and was distributed throughout the body by the heart. He believed that heart disease was due to an imbalanced state of an individual's emotions, leading to a stagnation of the bodily fluids. According to Hippocrates, a treatment for these cases involved efforts to treat the heart by means of specific diets and increased levels of physical activity. It was his view that by modifying an individual's way of life, it was possible to prevent heart disease.

Anatomical Advances and the Galenic Era (3rd–2nd Century BCE to 2nd Century CE)

In the Hellenistic and Roman periods, there occurred a significant extension of the anatomical knowledge of the cardiovascular system. The physician Erasistratus (c. 304–250 BCE) stated that he had performed many dissections and that he knew the structure of the arteries and the veins very well. He

correctly described the heart as a pump but was not correct in his description of the circulation of the blood. In the 2nd century of the Christian era, the physician Galen (129-200/216 CE) read the works of all the earlier anatomists that had been written up to that time. He described the cardiac structures in great detail and presented a complete account of the heart's physiology, pathologies, and their cures. Galen was a careful clinician and, on the basis of a patient's symptoms and pulse assessment, was able to diagnose illnesses and assess bodily functions by bedside examination. In accordance with the humoral theory, he treated his patients with remedies, including herbs, and advised them to live a healthy life. In some cases, he performed bloodletting in order to cure an illness of his patients. His medical works were the major influence on Western medicine for nearly 1500 years ^{[5][6][7]}.

The Discovery of Circulation (1628)

In 1628, William Harvey published *De Motu Cordis*, in which he described the closed circulatory system consisting of the pulmonary and the systemic circulation. This work, in which he described the movement of blood propelled by the heart through the arteries and its return to the heart via the veins, was a milestone in the history of circulatory concepts. In contrast to traditional views, Harvey rejected the notion that the liver produced blood that was then consumed by the tissues. Harvey's analysis of the function of the heart from a mechanical viewpoint marked the beginning of modern cardiovascular physiology ^[8].

Limited Progress in the 17th and 18th Centuries

Although there were significant advances in the diagnosis and control of cardiac disease following the circulation of blood described by Harvey in 1628, the development of diagnosis and treatment of heart disease for centuries afterward was a slow process. The obvious physical signs and symptoms of cardiac disease, such as pitting edema, signs of cyanosis, shortness of breath, tachycardia, and collapse of a part or of the whole of the body, were for a long time recognized by the clinical observer. It was not until relatively recently that it has become possible to study in detail the beating heart of a living patient. In the meantime, the heart was treated for centuries with a variety of humoral or 'other' remedies such as bloodletting and purging with a wide variety of drugs and also with a variety of herbs, special diets, etc., which, in the light of present-day knowledge, were apparently for long times ineffective for structural lesions of the heart as opposed to their functional consequences, which also were for long times apparently intractable ^[9].

Digitalis and Early Pharmacotherapy (1785–Early 1900s)

The history of effective targeted pharmacotherapy for the cardiovascular system began with William Withering's 1785 account identifying *Digitalis purpurea* from foxglove as the effective component in a traditional folk remedy for 'dropsy' (now congestive heart failure) ^{[10][11]}. By the late 1800s, the cardiac drug digitalis from the foxglove plant had been combined with the edema folk remedy squill plant to act as a diuretic for 'dropsy' of heart failure. The first truly effective diuretics for 'dropsy,' however, were the mercurial diuretics introduced in the early part of this century ^{[12][13]}.

Rise of Clinical Cardiology (19th Century)

In 1816, Clinical Cardiology began with the invention of the stethoscope by René Laennec. Stethoscopes enabled physicians for the first time to hear the sounds of the heart and to diagnose, among other things, murmurs and additional heartbeats, stenosis and regurgitation of heart valves, congenital heart defects, and diseases of the pericardium ^{[14][15]}. Acquired heart disease was most commonly caused by rheumatic heart disease, a complication of recurrent streptococcal infections, leading to progressive deformation of the heart valves in severe cases of rheumatic fever ^{[16][17]}. Between 1901 and 1906, the Dutch physiologist Willem Einthoven laid the foundations for practical clinical electrocardiography (ECG), including the string galvanometer and organized clinical electrocardiographic recordings, enabling the diagnosis of arrhythmias, conduction disturbances, and damage to the heart muscle. Since then, the ECG has become one of the most important tools for diagnosis in Clinical Cardiology ^{[18][19]}.

Intracardiac Access and Early Hemodynamic Understanding (1929-1930s)

Werner Forssmann in 1929 was the first man to introduce a catheter into his own right atrium. This self-experiment demonstrated that access to the heart through a peripheral vein was possible; subsequent catheterization enabled intracardiac pressure measurements as well as determination of shunts in the heart. Thus, a systematic study of the heart with congenital anomalies was made possible ^{[20][21]}.

The Birth of Pediatric Cardiac Surgery (1930s–1940s)

The first successful correction of a heart defect was performed in 1938 by Robert E. Gross at the Boston Children's Hospital when he ligated a patent ductus arteriosus (PDA) in a 4-year-old boy; the report was published in 1939 ^[22]. In 1944, Alfred Blalock and Helen Taussig developed the first shunt to increase pulmonary circulation in children suffering from cyanotic congenital heart defects; the landmark report

was published in 1945 ^[23]. The first shunt was a connection between the subclavian artery and the pulmonary artery in children with tetralogy of Fallot ^[23]. Cardiac catheterization, developed into a useful clinical tool by Cournand and Richards, was used to measure intracardiac pressure, to determine oxygen saturation, to assess shunts, and to measure pulmonary vascular resistance ^{[21][24]}. Before the advent of penicillin, children and young adults developed an increasing number of valvular heart diseases due to rheumatic fever ^{[16][17]}.

Expansion of Diagnostics and Surgical Capability (1950s-1970s)

The post-war decades witnessed enormous advances in all fields of pediatric and adult congenital heart disease. Surgical, interventional, and diagnostic techniques improved dramatically. Cardiopulmonary bypass made possible definitive repairs 'on the inside' of the heart. Pediatric open-heart surgery evolved at an incredible pace. Echocardiography progressed from M-mode to 2D and to color flow Doppler, allowing for a very complete assessment of cardiac function and cardiac flow in children and adults with heart defects. Diagnostic catheterization also paralleled therapeutic catheterization. The balloon atrial septostomy became a potentially life-saving procedure in infants with transposition of the great arteries. There were landmark advances in the surgical repair of several congenital heart defects. These include the arterial switch operation for transposition of the great arteries, the staged repair for children with hypoplastic left heart syndrome, and the so-called Fontan-type repair for children with single-ventricle-type heart defects. These repairs dramatically improved the survival rate for children with complex heart defects. Advances in the pharmacologic management of children with congenital heart defects also had a major impact. The use of prostaglandin E1 to maintain a patent ductus arteriosus in a child with a ductal-dependent congenital heart defect and the use of nonsteroidal anti-inflammatory medications for the medical closure of a patent ductus arteriosus are two examples ^{[25][26][27][28][29][30][31][32][33][34][35][36]}.

Modern Era of Pediatric Cardiology (1984-2025)

Pediatric cardiology evolved from a subspecialty of general cardiology to a fully developed, independent medical discipline by the late 20th century. Today, pediatric cardiology is made up of several areas of expertise, including imaging and interventional therapy as well as cardiac surgery and electrophysiology. In addition to these areas, pediatric cardiology also includes treatment of heart failure, intensive care medicine, and long-term follow-up of individual patients.

Heart Transplantation and Mechanical Support (1984-1990s)

By the mid-1980s, pediatric heart transplantation for children with complex congenital heart problems and end-stage heart disease became an operation that continued to grow as the technical expertise of performing the surgery and the postoperative management of these patients using immunosuppression improved. With the advent of cyclosporine, the first effective calcineurin inhibitor immunosuppressive agent, used in the early 1980s, and the subsequent development of more effective immunosuppressive combinations, such as the use of tacrolimus and mycophenolate mofetil in the 1990s and 2000s, there has been a significant improvement in graft survival rates. This, together with improvements in mechanical support of the failing heart, such that ECMO is now a standard of care for refractory acute cardiopulmonary failure, and the growth of pediatric VADs to bridge children to transplantation, as with the Berlin Heart EXCOR pediatric ventricular assist device, has made pediatric heart transplantation a standard and successful form of therapy for children with end-stage heart disease ^{[37][38][39][40][41]}.

Advances in Echocardiography and Catheter-Based Therapy (1980s-2000s)

2D echocardiography and Doppler echocardiography have been the mainstay in the diagnosis of children with heart defects since their development. Tissue Doppler and strain/strain rate deformation imaging have further refined the assessment of ventricular function in children ^{[27][28][42]}. Furthermore, interventional catheterization, initially a diagnostic tool, has evolved into a therapeutic modality. Thus, in addition to the assessment of obstructive lesions, balloon valvuloplasty as well as device closure of septal defects (e.g., PDA and ASD) and stenting of obstructive lesions can be performed with low morbidity and without the need for repeat sternotomy ^{[43][44][45][46]}. Consequently, pediatric cardiovascular surgery has evolved into a “hybrid” field of imaging, interventional catheterization, and surgery ^{[43][44][45][46]}.

Evolution of Congenital Heart Surgery (1990s-2000s)

Recent advances in neonatal bypass strategies, myocardial protection, and postoperative care in the ICU have made primary complete correction of congenital heart disease possible in the neonate and have facilitated the implementation of neurodevelopmental strategies to protect these infants ^{[47][48]}. Cardiopulmonary interactions that were believed to be universally lethal in the neonate, such as transposition of the great arteries treated with an arterial switch operation and hypoplastic left heart

syndrome treated with a series of operations (Norwood, Glenn, Fontan), now have predictable outcomes with increasingly successful shunt strategies and arch repair [\[30\]\[31\]\[32\]\[33\]\[49\]](#).

Electrophysiology and the Genetics Revolution (1990s–2010s)

Catheter ablation technology also matured, enabling the precise treatment of abnormal heart rhythms utilizing three-dimensional electroanatomic mapping. The success of ablation could be increased while minimizing exposure to the patient and the operator from fluoroscopy, even in patients with complex congenital anatomy of the heart [\[50\]\[51\]](#). The field of inherited arrhythmia and cardiomyopathy genetics has also grown, and several pathogenic genetic variants have been identified in the long QT syndromes as well as other channelopathies and in the familial cardiomyopathies. A multidisciplinary approach now exists in programs for inherited cardiac disease, utilizing genetic testing in counseling for the risk of disease development in first-degree relatives and in risk stratification for individual patients [\[52\]\[53\]\[54\]\[55\]\[56\]](#).

Cross-Sectional Imaging and Structural Heart Innovation (2000s–2020s)

In addition to the assessment of ventricular volumes and flow, detection of fibrosis, and definition of complex anatomy, the cardiac, coronary, and extracardiac vascular anatomy can be accurately assessed using cardiac CT. These findings can be obtained using optimized pediatric dose protocols, reducing radiation exposure while preserving diagnostic quality [\[57\]\[58\]\[59\]\[60\]](#). 3D echocardiography has been increasingly used for advanced structural heart planning, virtual surgical planning, and 3D printing of heart models for surgery [\[61\]](#). In addition to the feasibility of the above applications, the clinical applications of MRI-guided and radiation-free catheterization are also expanding [\[62\]\[63\]](#). The high quality of advanced fetal cardiac evaluation has led to improved prenatal diagnosis, risk stratification, and even in-utero interventions, such as fetal aortic valvuloplasty in patients with evolving hypoplastic left heart syndrome [\[64\]\[65\]](#).

Quality Improvement, Outcomes Science, and Lifelong Care (2010s–2020s)

The creation of national registries and collaboratives such as STS-CHSD, IMPACT, and PC4 allows for the ability to benchmark, create outcomes-driven, standardized approaches to cardiac care, and embark upon multicenter quality improvement projects in the operating room, in the cath lab, and on the cardiac ICU floor [\[66\]\[67\]\[68\]](#). Neurodevelopmental surveillance of the infant with high-risk cardiac surgery has

become the standard of care with the recognition that neurodevelopmental issues are primary outcomes rather than late aftereffects of congenital heart disease ^{[47][48]}. The growth of the adult congenital heart disease (ACHD) population as survival has improved has led to the development of models of lifelong surveillance and of transition programs as described by major cardiac societies' guidelines ^{[69][70]}.

Technological Integration and Precision Cardiovascular Care (2020–2025)

Advances in genomics, particularly in whole-exome and whole-genome sequencing, have enabled accurate and timely genetic diagnosis for patients with inherited cardiomyopathies and arrhythmias as well as for those with syndromic congenital heart disease ^{[55][56][71]}. The ability to provide sequence-based diagnostic information has allowed for earlier diagnosis and the potential for more targeted medical therapy along specific disease pathways. Importantly, a growing amount of targeted therapeutics is being developed for specific genotypes of cardiomyopathy, and these are based on the disease biology. For instance, therapeutics targeting the RAS/MAPK pathway as well as emerging disease-modifying strategies for substrates of inherited cardiomyopathy are being developed for the RAS/MAPK-driven forms of cardiomyopathy and other forms of CHD along specific disease pathways ^{[72][73][74]}. In addition to advancing along pathway-based therapies for cardiomyopathy and other forms of CHD, there has also been significant progress in the area of regenerative medicine. Early-phase human clinical trials have been initiated that utilize strategies for single-ventricle heart (SVH) reconstruction that are aimed at enhancing the growth of the failing myocardium as well as the growth of other structures and organ systems that support the failing heart (myocardium-support strategies) ^{[75][76][77]}. Strategies for engineered growth-capable grafts and conduits for children with CHD are also being developed in the area of tissue engineering to better address the large number of children requiring surgical interventions for CHD ^[78]. Moreover, advances in the use of AI (artificial intelligence) have enabled improved accuracy in the assessment of cardiac function ^{[79][80][81][82]}.

4. Future Directions in Pediatric Cardiology

The future of pediatric cardiology is less about diagnosing lesions in children and more about how a child will decompensate, what intervention to give next, and how to build a repair that will last as the child grows.

Advancements in pediatric cardiology will go beyond incremental improvements in current diagnostic and therapeutic strategies and include novel applications of molecular corrections for biologic failures,

computational predictions, and the development of lifelong systems of care for children with heart disease [\[55\]\[56\]\[62\]\[69\]](#).

4.1. Evidence Maturity and Clinical Translation

The future-facing topics below are not equal in maturity. Fetal diagnosis, echocardiography, cardiac MRI/CT, interventional catheterization, registries, home monitoring for selected single-ventricle infants, and structured ACHD transition are already established or guideline-aligned parts of care. Gene therapy, regenerative cell therapy, tissue-engineered grafts, digital twins, and many AI-enabled tools remain earlier in translation and should be interpreted as promising but not yet broadly validated for routine pediatric cardiology practice.

4.2. Genomic and Molecular Medicine

Precision Genomics and Risk Stratification

Recent advances in whole-exome and whole-genome sequencing for individuals and their families have enabled improved genotype-phenotype correlation in CHD and the inherited cardiomyopathies, thus allowing the identification of at-risk children before the complete expression of the phenotype [\[55\]\[56\]\[71\]\[83\]](#). National-scale programs and pediatric genomic consortia have developed a variant catalog that is continually expanding and have improved the interpretation of the vast numbers of rare variants identified in families. The risk to affected family members can also be modeled using this data in combination with information regarding arrhythmia vulnerability and cardiomyopathy trajectory [\[71\]\[83\]\[84\]](#).

Gene Therapy and Gene Editing

For the gene therapy of monogenic cardiomyopathies, first preclinical and clinical studies are being developed for several inherited heart muscle diseases. For Danon disease, even a clinical trial with an AAV vector has already been started (see [\[74\]\[85\]](#)). Also for the cardiovascular system, several organ-specific genome editing tools such as base-editing and CRISPR/Cas, as well as first proof-of-concept experiments using patient-specific induced pluripotent stem cell-derived cardiomyocytes as well as cardiac organoids for modeling and correcting disease-causing mutations in these cells, have been established [\[86\]\[87\]\[88\]](#).

Targeted Pharmacotherapy

Therapy, particularly targeted therapy, is now increasingly administered in a fashion relevant to the underlying mechanisms of different pediatric cardiac diseases rather than by mere reference to organ-based diagnoses as was the case in the past. Thus, pathway-directed therapies are being used or studied in selected children with RASopathy-associated HCM. Additionally, there are also now emerging precision therapies for several of the pediatric inflammatory vasculitides as well as for various endotypes of acute myocarditis ^{[72][73][89][90]}.

4.3. Regenerative and Tissue-Engineering Solutions

Stem Cell-Based Myocardial Regeneration

Additional circulations where there are single ventricle failures and/or failures of the Fontan circulation, where there is a severe shortage of organ transplants to cover these failures, and in which the circulation fails over time are now in the early phase of studies with progenitor cells. Some of these studies include various types of cardiosphere-derived cell-based strategies as well as several products from the mesenchymal lineage that are already in early-phase clinical studies and need to be the subject of controlled phase II/III clinical trials ^{[75][76][77]}.

Engineered Valves, Vessels, and Patches

Using growth-capable blood vessels (conduits) or using tissue-engineered vascular graft platforms can help overcome the major restriction of pediatric surgery: somatic growth. The aim of such systems is to make the number of reoperations and necessary interventions as low as possible. So-called pediatric vascular grafts are already clinically applied. Scaffold design and host remodeling are, however, still being improved ^{[78][91]}.

Bioartificial Organ Development and Xenotransplantation

In addition to being potential long-term solutions to the organ donor shortage, bioengineering and xenotransplantation research could also have pediatric applications. Research into genetically modified pig-heart xenograft platforms as well as research into organ failure support and organ transplant immunology will help to further develop xenotransplanted organs for use in patients after more has been learned about the safety and rejection of such transplants ^{[92][93]}.

4.4. Advanced Interventional and Surgical Technologies

Transcatheter Structural Interventions

Transcatheter valve therapies and structural implants are expanding into anatomies previously requiring surgery, including transcatheter pulmonary valve strategies in native or augmented RVOTs, while ongoing device evolution targets durability, size constraints, and growth adaptability [\[94\]\[95\]\[96\]](#). Bioresorbable structural devices represent an emerging strategy to reduce the lifelong implant footprint in children, though pediatric validation remains early and trial-dependent [\[97\]](#).

Hybrid and Minimally Invasive Surgical Innovations

Hybrid surgical–catheter strategies in pediatric cardiac surgery have emerged as a less invasive alternative to manage high-risk neonates with complex heart defects within a stable environment. Recent improvements in pediatric cardiopulmonary perfusion have attempted to improve clinical results by optimizing perfusion strategies. The use of ultra-low priming volumes, for instance, has been aimed at decreasing the frequency of neurologic and inflammatory complications [\[49\]\[47\]\[48\]](#).

Mechanical Circulatory Support (MCS)

To support the failing pediatric heart, there is ongoing work in the Pediatric Mechanical Circulatory Support (MCS) field that includes the development of smaller-sized, highly hemocompatible devices for all ages, including the smallest infants. A key functional aspect of Pediatric MCS is evolving from being solely utilized as a ‘bridge-to-transplant’ for selected pediatric patients with end-stage heart failure to potentially functioning as a ‘bridge-to-recovery’ for select patient populations with heart failure. Several key developments will be required to assist in the progression to safe clinical use, including strategies to decrease the risk of stroke and device thrombosis [\[40\]\[41\]\[98\]](#).

4.5. Imaging, Computational Modeling, and Artificial Intelligence

Next-Generation Imaging

4D-flow MRI provides new parameters to quantify the complex pediatric circulation, like the energetics of the circulation in Fontan-type patients and the flow load in shunts. MRI-guided catheterization and totally radiation-free intervention concepts are new diagnostic tools for children, rich in information,

which—in contrast to current diagnostic tools—also focus on a stewardship of the lifetime risk and thus are of special interest ^{[62][63]}.

Computational Simulation and Digital Twin Technology

Computational simulation models can predict physiological changes that occur as a result of reconstruction, and there are several ‘digital twin’ systems currently under development. These systems use serial imaging and physiological data as input and function as a decision support system for the planning of the required intervention, in terms of timing and type ^{[99][100]}.

AI-Enhanced Diagnostics and Monitoring

Fetal echo assessment using AI and automatically generated quality scores may improve detection sensitivity and reduce dependence on the operator. Other applications of AI in pediatric cardiology, such as ECG analysis or imaging assessment for early signs of ventricular dysfunction or risk of arrhythmia, are currently under investigation ^{[79][80][81][82][101]}.

4.6. Systems of Care, Lifelong Management, and Population Impact

Fetal-Neonatal-Pediatric-Adult Continuity

With an increasing number of children born with heart defects that will need to be managed for the rest of their lives as adults, pediatric cardiology has become a specialty for the long-term management of a long-term condition. A well-structured transition program and access to services for Adult Congenital Heart Disease within the parameters of major guidelines ^{[69][70]} are therefore essential.

Remote Monitoring and Telecardiology

Home monitoring in single-ventricle infants has been shown to decrease interstage mortality and allow for earlier detection of decompensation. Emerging technologies such as tele-echocardiography and wearable monitoring are now being utilized to extend specialty monitoring in single-ventricle patients beyond the tertiary care setting ^{[80][81][82]}.

Global Equity and Access

The use of technology such as portable ultrasound and AI-assisted medical image interpretation and large-scale training platforms will help to overcome the disparities that currently exist in the ability to diagnose, manage, and triage children with CHD, while a number of global initiatives are currently underway to aid workforce development in regions of greatest need ^{[102][103]}.

Neurodevelopmental and Psychosocial Integration

As high-precision assessment is more and more combined with cardiology to continuously monitor and treat the neurodevelopmental problems of children with complex heart defects as well as children who have already undergone cardiopulmonary bypass surgery in early childhood, established neurodevelopmental risk profiles of these patient groups are being used as a basis for follow-up models ^{[47][48][104]}.

5. Conclusions

The history of pediatric cardiology has followed a sort of circular path. First, we gain more insight into the normal physiology of growing children, and then we do better things with that information. Then, after a number of years, that information leads to a reorganization of the healthcare that we deliver to children who are growing up with congenital heart disease as a result of the advances that we had previously developed.

Each of the technologies outlined above will likely find its way into the future of pediatric cardiology, but as separate threads that get woven together into a tapestry of molecularly stratified patients with growth-compatible repair; of improved, radiation-sparing imaging, coupled with sophisticated computational-based simulation; of detection by powerful, and hopefully wise, artificial intelligence that guides regenerative strategies. But, most importantly, as the field of pediatric cardiology progresses, better prediction will lead to better timing, and thus better repair, which in turn will result in less and less cumulative morbidity as the child grows. But, just as importantly, long-term survival of children with congenital heart disease will need to be paralleled by improvements in neurodevelopmental, psychosocial, and adult outcomes.

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Data Availability

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Author Contributions

Abenezer F. Kebede is the sole author of this manuscript and is responsible for the concept and design, acquisition, analysis, and interpretation of the literature, drafting of the manuscript, critical review for important intellectual content, final approval of the version to be posted, and accountability for all aspects of the work.

Use of Generative AI

No AI tool was used as a source of original scientific evidence, patient data, or clinical interpretation.

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