IntechOpen

IntechOpen Series
Cardiology and Cardiovascular Medicine,
Volume 13

Selected Topics in Pediatric Cardiology

Edited by Gabriel Cismaru

Selected Topics in Pediatric Cardiology

Edited by Gabriel Cismaru

Published in London, United Kingdom

Selected Topics in Pediatric Cardiology
http://dx.doi.org/10.5772/intechopen.1005692
Edited by Gabriel Cismaru

Contributors
Anca Reuț, Aniqa Batool, Aso F. Salih, Cristian Barsu, Danladi Musa, Gabriel Cismaru, Gabriel Voicu Răzvan, Ioana Georgiana Popescu, Juliah Githang'a, Maria Puriș Cătălina, Mirza Mohammad Kamran, Muhammad Mohsin, Nataša Marčun Varda, Oana Rus, Olivia Țăpîrdea Andrada, Oluwatoyin Toriola, Tavershima Kparev, Teja Senekovič Kojc, Ștefan Șonea

First published in London, United Kingdom, 2025 by IntechOpen
IntechOpen is the global imprint of INTECHOPEN LIMITED, registered in England and Wales, registration number: 11086078, 167-169 Great Portland Street, London, W1W 5PF, United Kingdom

For EU product safety concerns: IN TECH d.o.o., Prolaz Marije Krucifikse Kozulić 3, 51000 Rijeka, Croatia, info@intechopen.com or visit our website at intechopen.com.

British Library Cataloguing-in-Publication Data
A catalogue record for this book is available from the British Library

Selected Topics in Pediatric Cardiology
Edited by Gabriel Cismaru
p. cm.

This title is part of the Cardiology and Cardiovascular Medicine Book Series, Volume 13
Topic: Cardiovascular Diseases and Health
Series Editor: Kaan Kırali
Topic Editor: Mahi L. Ashwath

Print ISBN 978-1-83634-458-2
Online ISBN 978-1-83634-457-5
eBook (PDF) ISBN 978-1-83634-459-9
ISSN 3033-361X

IntechOpen Book Series

Cardiology and Cardiovascular Medicine

Volume 13

Aims and Scope of the Series

Today, since molecular science on structural causes of oncological pathologies and their molecular treatments are developing at an unbelievable rate, the primary medical cause of death in the twenty-first century will be cardiovascular disease. Neither pandemics that threaten all humanity nor deterioration in the ecosystem will be able to change this fact. Especially, this century seems poised to witness an incredible struggle against atherosclerotic disease, which develops in the arterial walls and results in narrowing and occlusion of the arterial lumen. In addition to this disease, there has been an increasing prevalence of heart rhythm problems, deterioration of heart valves due to aging, and heart failure. Serious vascular pathologies such as stenosis and occlusion, dissection and rupture, and aneurysmal enlargement are also major concerns. Medical and invasive treatment methods may work to save human lives, but they will never provide a real solution. All kinds of medical, technological, and genetic engineering developments obtained in these processes have not yet been sufficient to alleviate or eliminate cardiovascular disease. This book series, Cardiology and Cardiovascular Medicine, includes three topics. The first, Cardiovascular Diseases and Health, reviews important cardiovascular diseases and the developments in their prognosis. The second topic, Cardiovascular Electrophysiology, illuminates the abnormal functioning of the cardiac conduction system, which is caused by all heart pathologies and negatively affects prognosis. The third topic in this series, Cardiovascular Surgery, details treatment for cardiovascular pathologies and how to regulate normal physiological functions with percutaneous or extracorporeal interventions.

Meet the Series Editor

After completing his studies at the Medicine Faculty of Istanbul University in 1990, Prof. Kaan Kırali fulfilled his mandatory medical service and commenced his residency training at Koşuyolu Heart and Research Hospital in 1992. Following five years of assistant education, he pursued further training in England and the USA in 1998. Specializing in laparoscopic and minimally invasive cardiac surgery, he earned the titles of consultant cardiovascular surgeon in 1998, Assistant Professor in 1999, Associate Professor in 2002, and Chief in 2005 at the same hospital. Prof. Kırali also developed an interest in preventive medicine, obtaining an MSc in Public Health from Istanbul University in 2000. Over the past two decades, he has concentrated his scientific pursuits on cardiovascular repairs requiring specialized experience. With his expertise in coronary artery surgery, minimally invasive cardiac surgery, valve repair, and aortic root surgery, he has established new methods for awake coronary bypass revascularization, a new surgical approach for AVR during first and re-operations, aortic valve-sparing procedure, and radiofrequency ablation. Notably, he pioneered awake complete coronary artery bypass grafting (CABG) with bilateral internal mammary arteries (BIMA) and played a crucial role in advancing aortic root surgery with a new aortotomy incision, simplifying aortic valve interventions. Since the year 2000, Prof. Kırali has expanded his interests to heart transplantation, and in recent years, to left ventricular assist devices. He has served as the head of the transplantation department since 2015 and currently continues his work as the director of Koşuyolu High Specialization Education and Research Hospital in Istanbul, Turkey. In his prolific career, he has authored numerous papers in SCI journals, contributed to various book chapters, and served as an editor and reviewer for multiple academic journals. Additionally, he has edited several international books in the field of cardiovascular medicine.

Meet the Volume Editor

Dr. Cismaru obtained his medical degree in 2005 from the Medical University of Cluj-Napoca, Romania, and presently practices in the Electrophysiology Laboratory at the Rehabilitation Hospital in Cluj. Upon completing his cardiology specialization, he pursued a fellowship in cardiac electrophysiology at the Institut Lorrain du Cœur et des Vaisseaux Louis Mathieu, CHU de Nancy, France. During his time in France, he acquired proficiency in catheter ablation techniques for atrial fibrillation and ventricular tachycardia. Following the acquisition of the European certification in cardiac electrophysiology from the European Heart Rhythm Association (EHRA) in 2015, he expanded his practice to include the implantation of cardiac devices, including pacemakers, implantable defibrillators, loop recorders, and resynchronization devices. He attained his EHRA certification in cardiac pacing in 2016. His primary interest is in cardiac arrhythmias in both adults and children.

Contents

Preface

In the past few decades, pediatric cardiology has emerged as a subspecialty of pediatrics and cardiology. It covers cardiac disorders in developing children, from the fetal stage through adolescence. Lifelong follow-up is occasionally essential for children with congenital cardiac defects, whether operated on or not. Contemporary management of congenital heart disease has resulted in a normal or near-normal life.

Diagnostic modalities and therapeutic approaches have demonstrated revolutionary advancements in pediatric cardiology, leading to novel procedures with increased success rates and improved quality of life thereafter. Innovative imaging methods for pediatric patients include echocardiography, cardiac MRI, computed tomography, angiography, and electrophysiological studies with three-dimensional mapping.

Catheter interventions have progressed from atrial balloon septostomy to the development of new occluders for atrial and ventricular septal defects. Advancements in stent quality have improved long-term outcomes and reduced complications. Over the past two decades, pediatric invasive and semi-invasive electrophysiology has become a standard component of therapeutic interventions. Transesophageal procedures may be conducted in neonates and young children without the risks associated with invasive techniques.

The pharmacist now exerts a greater influence on the daily practice of pediatric cardiology. Pediatric patients use the same drugs as adult cardiac patients; yet, pharmaceutical products have rarely undergone extensive testing in children through large-scale studies. The pharmacist's assistance promotes a more tailored, pediatric-focused therapy.

The book comprises six chapters, each addressing a distinct topic: echocardiography, pharmaceutical treatment, interventional therapy, electrophysiological study, and physical activity. They share a common viewpoint regarding children with cardiac conditions.

In the chapter "The Role of Clinical Pharmacists in Pediatric Cardiology in Low- and Middle-Income Countries", Aniqa Batool and Muhammad Mohsin from Karachi, Pakistan, investigated the potential of personalized medicine and pharmacogenomics to improve pediatric cardiac treatment strategies. Pharmacists can improve the efficacy and safety of medical treatments by tailoring medication regimens to each patient's genetic profile. The pharmacist should have greater involvement in the application of pharmacogenomics, patient counseling, medication safety, and adherence to recommended drugs. In the end, the chapter addresses the obstacles that pharmacists face and offers suggestions to promote their integration into multidisciplinary healthcare teams, thereby improving pediatric cardiac care.

In the chapter "Utility of Right Ventricular Outflow Tract Stenting in Grown-Up with Congenital Heart Disease (CHD)", Mirza Mohammad Kamran from Calicut, Kerala, India discusses the utility of right ventricular outflow tract stenting in grown-ups with CHD. Right Ventricular Outflow Tract (RVOT) stenting has been implemented as the primary treatment for unrepaired tetralogy of Fallot or pulmonary stenosis with a ventricular septal defect. In adults, RVOT stenting can be a palliative option, as it enhances cardiac output, increases oxygen saturation, and promotes the development of branch pulmonary arteries.

In the chapter "Interventional Closure of Ventricular Septal Defects: A Focus on Pediatric Population", Aso F. Salih from Al-Sulaymaneyah, Iraq, presents the advantages and disadvantages of interventional closure of ventricular septal defects in children. Transcatheter closure is a less invasive alternative to surgery. Transcatheter closure of ventricular septal defects is associated with favorable short- and long-term outcomes and higher success rates. Compared with surgery, there are advantages in reduced invasiveness and shorter recovery time. Device embolism, valve dysfunction, and residual shunts are all potential complications. The procedure should be performed by a skilled interventionist with support from a multidisciplinary team.

In the chapter "Echocardiographic Strain Imaging in Pediatrics", Teja Senekovič Kojc and Nataša Marčun Varda from Maribor, Slovenia, present the advantages of strain imaging in pediatric echocardiography. They describe the use of strain for different pediatric pathologies from congenital heart disease to cardiomyopathies, heart failure, myocarditis, chemotherapy-induced cardiotoxicity, Pulmonary hypertension, cardiac ischemia, and infarction. A special chapter is dedicated to strain use in children with cardiac resynchronization therapy, which is used more and more in children with heart failure, left bundle branch block, and low ejection fraction.

However, the most valuable chapter of this book is an observational study, "Aerobic Fitness and Leg Muscle Power in Relation to Arterial Blood Pressure in Adolescents", performed by Danladi Musa, Tavershima Kparev, Oluwatoyin Toriola, and Juliah Githang'a, a team from Nigeria, Saudi Arabia, and Kenya who conducted research on 2047 adolescents aged 12–16 years from Nigeria. They found that the prevalence of systolic hypertension was 9.8% among Nigerian adolescents, with similar percentages between sexes. Furthermore, the leg muscle power was inversely associated with systolic blood pressure in both sexes. The authors conclude that social strategies should be advocated to enhance physical activity and avoid hypertension in teenagers.

In the chapter "Transesophageal Electrophysiological Study for Pediatric Arrhythmias", Gabriel Cismaru and coauthors from Cluj-Napoca, Romania, describe the use of transesophageal electrophysiological study in children with arrhythmias. They begin with a historical background, then describe the technique used to stimulate the esophagus. Next, they discuss the application of this technique for children with palpitations of unknown origin, atrial tachyarrhythmias, ventricular pre-excitation, and the follow-up of children after catheter ablation.

Advancements in the treatment of congenital cardiac diseases represent an exceptional achievement in medical history. Continuous progress and partnership with the medical industry will improve the life expectancy and quality of life of children affected by cardiac diseases.

Gabriel Cismaru
Cardiology Rehabilitation Department,
"Iuliu Hatieganu" University of Medicine and Pharmacy,
Cluj-Napoca, Romania

Chapter 1

The Role of Clinical Pharmacists in Pediatric Cardiology in Low- and Middle-Income Countries

Aniqa Batool and Muhammad Mohsin

Abstract

Clinical pharmacists play a crucial role in pediatric cardiac care by optimizing medication therapy, ensuring patient safety, and improving treatment outcomes. The challenges in managing pediatric cardiac conditions are amplified in low- and middle-income countries (LMICs), where healthcare resources are often constrained. Limited access to specialized care, inadequate infrastructure, and a lack of trained professionals contribute to a high incidence of medication errors, which can significantly impact patient outcomes. The integration of clinical pharmacists into pediatric cardiology teams is essential to address these challenges by providing expertise in medication management, reducing adverse drug events, and enhancing the overall quality of care. This chapter also explores the potential of pharmacogenomics and personalized medicine in optimizing pediatric cardiac treatment strategies, an emerging focus in LMICs. By tailoring medication regimens to individual genetic profiles, pharmacists can further enhance therapeutic efficacy and safety. The chapter highlights the vital role of pharmacists in pediatric cardiac care, focusing on medication safety, adherence, patient counseling, and their growing role in the application of pharmacogenomics. Additionally, it discusses the barriers to pharmacist involvement and provides recommendations to strengthen their integration into multidisciplinary healthcare teams to improve pediatric cardiac outcomes.

Keywords: pediatric cardiology, pharmacist role, congenital heart disease, medication management, pharmacogenomics

1. Introduction

1.1 Overview of pediatric cardiology in LMICs

Pediatric cardiology in low- and middle-income countries (LMICs) faces numerous challenges, including a high burden of congenital heart diseases (CHDs), limited healthcare infrastructure, and inadequate access to specialized care [1, 2]. In many LMICs, there is a significant shortage of trained pediatric cardiologists and cardiac surgeons, leading to delays in diagnosis and suboptimal treatment outcomes. The lack of specialized pediatric cardiac care centers means that many children with heart conditions do not receive timely interventions, further compounding the health burden [3].

Cardiac care for the pediatric population in LMICs is often constrained compared to high-income countries due to financial limitations, the absence of comprehensive newborn screening programs, and a lack of pediatric cardiologists and cardiac surgery services [4, 5]. These factors contribute to delayed diagnoses and poorer patient outcomes. The shortage of skilled pediatric cardiologists often leaves general practitioners and pediatricians to manage complex pediatric cardiac conditions, resulting in increased risks of misdiagnoses, inappropriate treatment, and medication errors [6, 7].

In such settings, the integration of clinical pharmacists into pediatric cardiology teams becomes even more critical. Pharmacists are well-positioned to address medication-related challenges and work collaboratively with limited healthcare teams to optimize treatment plans. However, the lack of formal recognition and integration of pharmacists in public-sector pediatric cardiac care teams limits their potential to improve patient outcomes. Local policy changes are necessary to formalize the role of pharmacists in multidisciplinary cardiac teams, particularly in public-sector hospitals, where resources are often more constrained. By promoting the inclusion of clinical pharmacists in cardiac care teams and providing them with specialized training, LMICs can enhance medication management, reduce medication errors, and improve overall care for pediatric heart patients [8–10].

1.2 Objectives of the chapter

The objectives of this chapter are to:

1. Explore the current landscape of pediatric cardiology in LMICs, with a focus on key challenges and barriers.

2. Highlight the role of pharmacists in managing pediatric cardiovascular diseases through multidisciplinary collaboration.

3. Address challenges faced by pharmacists in LMICs, such as limited training, resource constraints, and socioeconomic barriers. Examine the potential role of pharmacogenomics and personalized medicine in pediatric cardiology and how pharmacists can bridge the existing gaps. Provide recommendations and future directions to enhance the involvement of pharmacists in pediatric cardiology care in LMICs. Raise awareness about the role of clinical pharmacists in pediatric cardiology and the need for education and advocacy to promote their integration into healthcare teams in LMICs

2. Epidemiology of pediatric cardiovascular diseases in LMICs

2.1 Prevalence and burden

Globally, congenital heart disease (CHD) is the most common birth defect, with an incidence ranging from approximately 4 to 50 per 1000 live births. In Pakistan, studies have reported a CHD prevalence of 3.4 per 1000 live births, while specific prevalence data on inherited cardiac diseases in Pakistani children remain limited [10, 11]. Additionally, children can develop acquired heart conditions after birth due to infections, inflammatory diseases, or other factors, such as rheumatic heart disease and myocarditis. The prevalence of acquired heart conditions varies based

on regional health factors and the burden of contributing diseases. The incidence of rheumatic heart disease (RHD) remains high due to inadequate antibiotic prophylaxis and poor healthcare access [9].

Sudden cardiac death (SCD) is a major global concern, predicted to affect up to 5 million people annually. Incidence rates in Western countries range between 50 and 100 per 100,000, with comparatively lower rates in Asia. SCD accounts for 40–50% of potential years of life lost due to heart disease, with estimated rates ranging from 1.40 per 100,000 person-years in women to 6.68 per 100,000 person-years in men [12, 13]. There is an initial peak between 0 and 5 years of age, followed by a marked second peak in the elderly, between 75 and 85 years of age. Notably, 2–54% of sudden unexpected deaths in individuals under 35 years of age show no evidence of structural cardiac abnormalities upon autopsy, suggesting that ion channelopathies (inherited arrhythmias) and cardiomyopathies are likely causes in such cases [14].

The prevalence and management of pediatric cardiovascular diseases vary significantly across regions within LMICs due to differences in healthcare infrastructure, socioeconomic status, and access to specialized care. For instance, South Asia and sub-Saharan Africa report higher mortality rates due to CHDs compared to Latin America and Southeast Asia, where relatively better healthcare facilities are available. Urban areas often have better access to cardiac care compared to rural regions, leading to significant disparities in diagnosis and treatment. Bridging these gaps requires targeted policy interventions, strategic resource allocation, and enhanced training for healthcare professionals, including pharmacists, to ensure early detection and effective management of pediatric cardiovascular diseases [15, 16].

2.2 Regional statistics and disparities

The prevalence and management of pediatric cardiovascular diseases in LMICs vary significantly due to disparities in healthcare infrastructure, socioeconomic status, and access to specialized care. For instance, South Asia and sub-Saharan Africa report higher mortality rates from CHDs compared to Latin America and Southeast Asia, where healthcare facilities are relatively more developed. Additionally, urban centers generally offer better access to cardiac care than rural areas, exacerbating disparities in diagnosis and treatment. Bridging these gaps requires targeted policy interventions, strategic resource allocation, and enhanced training for healthcare professionals, including pharmacists, to facilitate early detection and effective management of pediatric cardiovascular diseases [17, 18].

3. Pediatric cardiology

Pediatric cardiac disorders encompass a range of conditions, including congenital heart disease, acquired heart diseases, arrhythmias, cardiomyopathies, valve diseases, aneurysms, and cardiac inflammatory diseases (e.g., pericarditis and myocarditis). Inherited arrhythmias and cardiomyopathies are the leading causes of sudden cardiac death (SCD) in children. Cardiomyopathies, which are often underdiagnosed, contribute significantly to heart failure and mortality, while inherited arrhythmias present a major diagnostic challenge due to the limited availability of genetic testing and specialized cardiac services in low- and middle-income countries (LMICs). The limited healthcare infrastructure and lack of awareness further complicate disease management and long-term outcomes [19].

Cardiomyopathies include dilated cardiomyopathy (DCM), arrhythmogenic cardiomyopathy (ACM), hypertrophic cardiomyopathy (HCM), and left ventricular noncompaction cardiomyopathy (LVNC), with the latter being an overlap disorder. These conditions are distinguished by structural heart defects that predispose patients to arrhythmias and sudden cardiac death, often triggered by specific genetic mutations. The primary underlying arrhythmias responsible for SCD are ventricular arrhythmias (VAs), particularly ventricular fibrillation (VF) [20, 21].

In contrast, channelopathies such as catecholaminergic polymorphic ventricular tachycardia (CPVT), short QT syndrome (SQTS), Brugada syndrome (BrS), long QT syndrome (LQTS), idiopathic ventricular fibrillation (IVF), and progressive cardiac conduction system disease (PCCD) are categorized by malignant arrhythmias occurring in a structurally healthy heart. These channelopathies are often caused by gene abnormalities that encode cardiac regulatory proteins, membrane ion channels (sodium, potassium, or calcium channels), or receptors. These genetic alterations can disrupt the cardiac action potential or intracellular calcium handling, leading to electrical instability and an increased susceptibility to life-threatening Vas [22, 23].

Congenital heart diseases (CHDs), cardiomyopathies, and inherited arrhythmias together represent a significant portion of the pediatric disease burden in LMICs. While cardiomyopathies contribute to heart failure and mortality among children, inherited arrhythmias remain a significant diagnostic challenge due to the lack of genetic testing and specialized cardiac care. The limited healthcare infrastructure and insufficient awareness only serve to complicate the management of these conditions, ultimately affecting long-term outcomes [24].

4. Pharmacist's role in pediatric cardiology

4.1 Medication management and optimization

Cardiac diseases are chronic, progressive conditions characterized by frequent hospital admissions and high mortality rates. The primary goal in managing these conditions is optimizing pharmacological therapy, improving medication adherence, and promoting lifestyle modifications, unless total correction, palliative surgeries, cardiac catheterization, or device implantation are planned [25].

Despite pharmacotherapy, outcomes for pediatric cardiac patients remain suboptimal, with high rates of hospitalizations and emergency department visits. This is largely due to medication discrepancies and poor adherence to treatment regimens. These discrepancies often occur at the time of hospital discharge, where insufficient patient education or lack of communication between healthcare providers—such as the general practitioner, community pharmacist, or the patient—about intentional medication changes significantly contribute to these issues. Medication errors are among the most common types of errors in hospitalized patients, with studies indicating that medication errors are three times more common in the pediatric population compared to adults. This is primarily due to complex medication dosing regimens and administration in children [26].

Congenital heart disease (CHD), the most prevalent congenital anomaly causing child mortality, is characterized by a range of structural defects present at birth. The complexity of treatment is heightened by the risk of medication errors, underlining the need for stringent evaluation and management strategies. Clinical pharmacists

play a vital role in optimizing pharmacotherapy in pediatric cardiac care, particularly in developing countries, through collaboration with other healthcare professionals. However, the role of clinical pharmacists in pediatric cardiac care is not fully established in Pakistan. Their involvement is mainly limited to private-sector hospitals, and their presence in public-sector hospitals remains negligible [27].

Clinical pharmacists contribute to healthcare teams by managing and optimizing medication use, thus enhancing safety and efficacy in pediatric cardiac care. In LMICs, where resources are limited, these challenges are even more pronounced, with high rates of medication errors significantly impacting patient outcomes. This chapter underscores the importance of clinical pharmacist intervention in ensuring the appropriate use of medications in pediatric cardiac care [28].

Pharmacists are involved in critical tasks such as dose calculation and frequency adjustments based on body weight and body surface area, as pediatric growth and development affect pharmacokinetics and pharmacodynamics. Their role extends to optimizing drug use, avoiding adverse drug events, monitoring drug therapy, managing drug-drug and drug-food interactions, adjusting dosages based on laboratory reports, and providing patient education and counseling. Pharmacists also play a key role in improving medication adherence through direct consultations or other medication education-related activities. By educating children and their caregivers, pharmacists significantly contribute to pediatric patient care.

In collaboration with other healthcare providers, clinical pharmacists actively participate in clinical services such as clarifying and documenting pharmacotherapy histories, engaging in bedside patient care rounds, performing medication reconciliation, communicating therapeutic recommendations, and identifying and resolving drug-related problems. This proactive involvement helps optimize medication therapy for these vulnerable populations [29].

4.2 Pharmacist-led anticoagulation management

A pediatric patient with congenital heart disease requiring warfarin therapy faced challenges with fluctuating INR levels. A clinical pharmacist implemented a structured anticoagulation monitoring program, resulting in improved INR stability and reduced bleeding episodes. This intervention highlights the essential role of pharmacists in managing anticoagulation therapy and improving patient outcomes [30].

4.2.1 Challenges of using direct oral anticoagulants (DOACs) in pediatric populations

While DOACs offer advantages over warfarin, their use in pediatric patients presents several challenges. Drug interactions remain a concern, particularly with anticonvulsants (e.g., carbamazepine, phenytoin) and certain antibiotics (e.g., rifampin, macrolides), which can either increase the risk of bleeding or reduce anticoagulant efficacy. Additionally, DOACs are primarily excreted by renal, necessitating careful dose adjustments in children with renal impairment to prevent accumulation and excessive anticoagulation. Special caution is also required for pediatric patients with epilepsy or a history of fainting, as falls can increase the risk of traumatic bleeding or intracranial hemorrhage. Furthermore, the lack of standardized pediatric dosing guidelines for DOACs poses a significant challenge, requiring clinical pharmacists to collaborate with physicians to ensure safe and effective dosing based on age, weight, renal function, and available pharmacokinetic data [25, 26].

4.3 Therapeutic drug monitoring (TDM)

Pharmacists play a vital role in optimizing the levels of drugs with narrow therapeutic indices, such as digoxin, antiarrhythmic, and anticoagulants. Through therapeutic drug monitoring, pharmacists ensure that drug concentrations remain within therapeutic ranges, minimizing the risk of toxicity or suboptimal drug effects [31].

4.3.1 Pharmacist's role in therapeutic drug monitoring (TDM) in pediatric cardiology

Therapeutic drug monitoring (TDM) plays a crucial role in optimizing medication therapy in pediatric cardiology, where individualized dosing is essential due to variations in metabolism and organ function. Pharmacists actively monitor drug levels by analyzing blood samples, interpreting laboratory results, and assessing clinical response to ensure medications remain within therapeutic ranges while minimizing toxicity. Dose adjustments are made based on patient-specific factors such as age, weight, renal and hepatic function, and potential drug interactions. Key medications requiring TDM in pediatric cardiology include digoxin, where subtherapeutic levels reduce efficacy and elevated levels increase toxicity risk, and aminoglycosides (e.g., gentamicin, amikacin), which require careful monitoring to avoid nephrotoxicity and ototoxicity. Through close collaboration with physicians and laboratory teams, pharmacists help optimize dosing regimens, prevent adverse effects, and improve clinical outcomes in pediatric cardiac patients [30, 31].

4.4 Medication reconciliation in postoperative pediatric cardiology patients

A pharmacist-driven medication reconciliation initiative in a pediatric cardiac surgery unit successfully identified and prevented multiple medication errors, thereby improving patient safety and adherence to post-discharge treatment plans. This initiative underscores the critical role of pharmacists in the postoperative care of pediatric cardiology patients, ensuring continuity of care and preventing potential adverse drug events [32].

4.5 Pharmacogenomics and personalized medicine in pediatric cardiology

Pharmacists are integral in incorporating pharmacogenomics into clinical practice, which is essential for optimizing personalized treatment strategies. By collaborating with physicians, genetic counselors, and other healthcare professionals, pharmacists ensure that drug regimens are tailored to the patient's genetic profile, thereby maximizing treatment efficacy and safety. This approach leads to better patient outcomes by improving the precision of pharmacological interventions in pediatric cardiology [33].

Genetic variations influence drug metabolism and response, which can impact treatment efficacy and safety. Notable examples include:

- *Warfarin sensitivity*: Genetic polymorphisms in CYP2C9 and VKORC1 enzymes can influence warfarin dosing, helping to avoid complications such as bleeding or clotting [34].

- *Beta-blocker response*: Variants in ADRB1 and ADRB2 genes can impact the efficacy of beta-blockers, particularly in managing heart failure [35].

4.5.1 Pharmacogenomics in beta-blocker dosing

Pharmacogenomics plays a vital role in optimizing beta-blocker therapy, particularly in pediatric cardiology, where genetic variations can significantly impact drug metabolism. The CYP2D6 enzyme, responsible for metabolizing beta-blockers such as metoprolol, carvedilol, and propranolol, exhibits genetic polymorphisms that categorize patients as ultrarapid, extensive, intermediate, or poor metabolizers. Pharmacists utilize genetic testing results to personalize dosing strategies—ultrarapid metabolizers may require higher doses to achieve therapeutic effects, whereas poor metabolizers need lower doses to avoid drug accumulation and adverse effects. For example, in metoprolol therapy, poor metabolizers experience prolonged drug exposure, increasing the risk of bradycardia and hypotension, necessitating careful dose titration. By integrating pharmacogenomic insights into clinical practice, pharmacists enhance the safety and efficacy of beta-blocker therapy in pediatric patients with cardiovascular conditions [34, 35].

- *Statin therapy*: SLCO1B1 polymorphisms can affect statin metabolism, influencing both the drug's effectiveness and the risk of adverse effects [36].

Despite these advances, the implementation of pharmacogenomics in low- and middle-income countries (LMICs) is limited by challenges such as high costs, inadequate infrastructure, and lack of awareness among healthcare providers. However, as the field progresses, pharmacists' role in implementing pharmacogenomics could become increasingly crucial in improving pediatric cardiology outcomes, particularly in resource-limited settings [37].

5. Challenges faced by pharmacists in LMICs

Despite their potential contributions, clinical pharmacists in LMICs encounter several challenges, including:

- Limited recognition and integration into multidisciplinary care teams.
- Shortage of trained personnel.
- Resource constraints and inadequate infrastructure.
- Regulatory and policy barriers.
- Financial constraints and high medication costs [1, 38].

5.1 Raising awareness and advocacy for pharmacist integration

In many LMICs, the role of clinical pharmacists in pediatric cardiology remains under-recognized, largely due to insufficient awareness among healthcare professionals and policymakers. Increasing recognition of pharmacists' contributions through education, advocacy, and policy reforms is essential to improving their integration into pediatric cardiology teams. Training programs for healthcare workers, public health campaigns, and official policy recognition are all key strategies that can help elevate pharmacists' roles in the management of pediatric cardiovascular diseases. By fostering a deeper understanding of pharmacists' expertise, we can ensure better medication management and improve patient outcomes [39].

6. Future directions and recommendations

To enhance the role of clinical pharmacists in pediatric cardiology in LMICs, the following steps are recommended:

- *Incorporation into multidisciplinary teams:* Establishing pharmacist-led cardiology services within hospitals.
- *Specialized training programs:* Developing postgraduate programs focused on pediatric cardiovascular pharmacotherapy.
- *Strengthening regulatory frameworks:* Defining clear roles and responsibilities for pharmacists in pediatric cardiac care.
- *Expanding pharmacogenomics research:* Encouraging studies on genetic variations affecting cardiovascular drug responses in LMIC populations.
- *Enhancing access to essential medicines:* Implementing policies to reduce medication costs and improve availability [40].

7. Conclusion

Clinical pharmacists play a crucial role in pediatric cardiology by optimizing pharmacotherapy, improving medication safety, and contributing to multidisciplinary care teams. However, several barriers limit their full potential in LMICs. Addressing these challenges through policy reforms, specialized training, and increased research in pharmacogenomics can enhance pharmacist involvement and improve outcomes for children with cardiovascular diseases in resource-limited settings.

Acknowledgements

We would like to express our gratitude to the National Institute of Cardiovascular Diseases (NICVD), Karachi, Pakistan, for their continuous support and resources. The institute has provided an invaluable foundation for our work in pediatric cardiology and pharmacy practice. Our heartfelt thanks go to our colleagues at NICVD for their ongoing collaboration and dedication to improving pediatric cardiac care.

Additionally, we acknowledge the contribution of healthcare professionals, researchers, and educators in the field of pediatric cardiology in LMICs, whose work has informed and inspired this chapter. Special thanks to our families for their patience and support throughout this endeavor.

Conflict of interest

The authors declare no conflict of interest related to the content of this chapter.

Nomenclature

CHD	congenital heart disease
RHD	rheumatic heart disease
SCD	sudden cardiac death
LMICs	low and middle-income countries
TDM	therapeutic drug monitoring
INR	international normalized ratio
CYP2C9	cytochrome P450 2C9 (enzyme)
VKORC1	vitamin K epoxide reductase complex subunit 1

Author details

Aniqa Batool* and Muhammad Mohsin
National Institute of Cardiovascular Diseases (NICVD), Karachi, Pakistan

*Address all correspondence to: aniqabatool46@gmail.com

References

[1] Babar Z-U-D. Ten recommendations to improve pharmacy practice in low and middle-income countries (LMICs). Journal of Pharmaceutical Policy and Practice. 2021;**14**(1):6

[2] Batool A, Shamim S, Mohsin M. Leveraging clinical pharmacy expertise for pediatric cardiology in low and middle-income country. Pakistan Heart Journal. 2024;**57**(1):71-74

[3] Dunn SP, Birtcher KK, Beavers CJ, Baker WL, Brouse SD, Page RL, et al. The role of the clinical pharmacist in the care of patients with cardiovascular disease. Journal of the American College of Cardiology. 2015;**66**(19):2129-2139

[4] Elhabil MK, Yousif MA, Ahmed KO, Abunada MI, Almghari KI, Eldalo AS. Impact of clinical pharmacist-led interventions on drug-related problems among pediatric cardiology patients: First Palestinian experience. Integrated Pharmacy Research and Practice. 2022:127-137

[5] Hailu BY, Berhe DF, Gudina EK, Gidey K, Getachew M. Drug related problems in admitted geriatric patients: The impact of clinical pharmacist interventions. BMC Geriatrics. 2020;**20**:1-8

[6] Malik S, Majeed R, Channer MS, Saleem MI. Frequency of cardiac defects among children at echocardiography Centre in a teaching hospital. Pakistan Journal of Medical Sciences. 2009;**25**(5):712-717

[7] Rychik J, Atz AM, Celermajer DS, Deal BJ, Gatzoulis MA, Gewillig MH, et al. Evaluation and management of the child and adult with Fontan circulation: A scientific statement from the American Heart Association. Circulation. 2019;**140**(6):e234-ee84

[8] Milfred-LaForest SK, Chow SL, DiDomenico RJ, Dracup K, Ensor CR, Gattis-Stough W, et al. Clinical pharmacy services in heart failure: An opinion paper from the Heart Failure Society of America and American College of Clinical Pharmacy Cardiology Practice and Research Network. Journal of Cardiac Failure. 2013;**19**(5):354-369

[9] Novick WM, Molloy F, Bowtell K, Forsberg B, Pavanić M, Polivenok I, et al. Pediatric cardiac service development programs for low-and middle-income countries in need of improving or initiating local services. Frontiers in Pediatrics. 2019;**7**:359

[10] Arshad MS, Anwar-ul-Haq HM, Adnan M, Zulqarnain A. Frequency and pattern of Paediatric Heart Diseases: Five years experience at The Children's Hospital, Multan. Pakistan Journal of Medical Sciences. 2020;**36**(6):1308

[11] Wamala I, Gongwer R, Doherty-Schmeck K, Jorina M, Betzner A, Zheleva B, et al. Infrastructure availability for the care of congenital heart disease patients and its influence on case volume, complexity and access among healthcare institutions in 17 middle-income countries. Global Heart. 2021;**16**(1)

[12] Kumar A, Avishay DM, Jones CR, Shaikh JD, Kaur R, Aljadah M, et al. Sudden cardiac death: Epidemiology, pathogenesis and management. Reviews in Cardiovascular Medicine. 2021;**22**(1):147-158

[13] Empana J-P, Lerner I, Valentin E, Folke F, Böttiger B, Gislason G, et al. Incidence of sudden cardiac death

in the European Union. Journal of the American College of Cardiology. 2022;**79**(18):1818-1827

[14] Markwerth P, Bajanowski T, Tzimas I, Dettmeyer R. Sudden cardiac death—Update. International Journal of Legal Medicine. 2021;**135**:483-495

[15] Khurshid R, Awais M, Malik J. Electrophysiology practice in low-and middle-income countries: An updated review on access to care and health delivery. Heart Rhythm O2. 2023;**4**(1):69-77

[16] Hasan BS, Bhatti A, Mohsin S, Barach P, Ahmed E, Ali S, et al. Recommendations for developing effective and safe paediatric and congenital heart disease services in low-income and middle-income countries: A public health framework. BMJ Global Health. 2023;**8**(5):e012049

[17] Setty SP, Reynolds LC, Chou VC, Yu MT, Kang S, Allen PM, et al. Racial health disparity associated with poor pediatric cardiac surgery outcomes: A multicentered, cross-sectional study. JACC: Advances. 2024;**3**(7_Part_2):100987

[18] Sliwa K, Viljoen CA, Hasan B, Ntusi NA. Nutritional heart disease and cardiomyopathies: JACC focus seminar 4/4. Journal of the American College of Cardiology. 2023;**81**(2):187-202

[19] Nasir A, Farooqi AT, Sattar S, Saeed Y. Prevalence and frequency of arrhythmias and electrocardiographic abnormalities in Pakistan: An outpatient ECG based study. Heart Rhythm O2. 2025;**6**(2025). (In press)

[20] Mohsin SS, Abbas Q, Chowdhary D, Khalid F, Sheikh AS, Ali Khan ZG, et al. Multisystem inflammatory syndrome (MIS-C) in Pakistani children: A description of the phenotypes and comparison with historical cohorts of children with Kawasaki disease and myocarditis. PLoS ONE. 2021;**16**(6):e0253625

[21] Ditaranto R, Caponetti AG, Ferrara V, Parisi V, Minnucci M, Chiti C, et al. Pediatric restrictive cardiomyopathies. Frontiers in Pediatrics. 2022;**9**:745365

[22] Schwartz PJ, Ackerman MJ, Antzelevitch C, Bezzina CR, Borggrefe M, Cuneo BF, et al. Inherited cardiac arrhythmias. Nature Reviews Disease Primers. 2020;**6**(1):58

[23] Priori SG, Wilde AA, Horie M, Cho Y, Behr ER, Berul C, et al. HRS/EHRA/APHRS expert consensus statement on the diagnosis and management of patients with inherited primary arrhythmia syndromes. Journal of Arrhythmia. 2014;**30**(1):1-28

[24] Spears DA, Gollob MH. Genetics of inherited primary arrhythmia disorders. The Application of Clinical Genetics. 2015;**8**:215-233

[25] McFarland MS, Buck ML, Crannage E, Armistead LT, Ourth H, Finks SW, et al. Assessing the impact of comprehensive medication management on achievement of the quadruple aim. The American Journal of Medicine. 2021;**134**(4):456-461

[26] Yin HS, Neuspiel DR, Paul IM, Franklin W, Tieder JS, Adirim T, et al. Preventing home medication administration errors. Pediatrics. 2021;**148**(6):e2021054666

[27] Brajković A, Bosnar L, Nascimento MMG, Prkačin I, Balenović A, Ramalho de Oliveira D, et al. Healthcare utilisation and clinical outcomes in older cardiovascular patients

receiving comprehensive medication management services: A nonrandomised clinical study. International Journal of Environmental Research and Public Health. 2022;**19**(5):2781

[28] Jonat B, Gorelik M, Boneparth A, Geneslaw AS, Zachariah P, Shah A, et al. Multisystem inflammatory syndrome in children associated with coronavirus disease 2019 in a children's hospital in New York City: Patient characteristics and an institutional protocol for evaluation, management, and follow-up. Pediatric Critical Care Medicine. 2021;**22**(3):e178-ee91

[29] Gurwitz JH, Kapoor A, Garber L, Mazor KM, Wagner J, Cutrona SL, et al. Effect of a multifaceted clinical pharmacist intervention on medication safety after hospitalization in persons prescribed high-risk medications: A randomized clinical trial. JAMA Internal Medicine. 2021;**181**(5):610-618

[30] Merks P, Cameron JD, Balcerzak M, Religioni U, Świeczkowski D, Konstanty M, et al. Evaluation of a pharmacist-led intervention to improve medication adherence in patients initiating dabigatran treatment: A comparison with standard pharmacy practice in Poland. BMC Primary Care. 2022;**23**(1):210

[31] Kapoor A, Crowley E. Advances in therapeutic drug monitoring in biologic therapies for pediatric inflammatory bowel disease. Frontiers in Pediatrics. 2021;**9**:661536

[32] DeCourcey DD, Silverman M, Chang E, Ozonoff A, Stickney C, Pichoff D, et al. Medication reconciliation failures in children and young adults with chronic disease during intensive and intermediate care. Pediatric Critical Care Medicine. 2017;**18**(4):370-377

[33] Cecchin E, Stocco G. Pharmacogenomics and personalized medicine. Genes. 2020;**11**(6):679

[34] Flockhart DA, O'Kane D, Williams MS, Watson MS, Gage B, Gandolfi R, et al. Pharmacogenetic testing of CYP2C9 and VKORC1 alleles for warfarin. Genetics in Medicine. 2008;**10**(2):139-150

[35] MyburghR,HochfeldWE,DodgenTM, Ker J, Pepper MS. Cardiovascular pharmacogenetics. Pharmacology & Therapeutics. 2012;**133**(3):280-290

[36] Generaux GT, Bonomo FM, Johnson M, Mahar Doan KM. Impact of SLCO1B1 (OATP1B1) and ABCG2 (BCRP) genetic polymorphisms and inhibition on LDL-C lowering and myopathy of statins. Xenobiotica. 2011;**41**(8):639-651

[37] Wells QS, Delaney JT, Roden DM. Genetic determinants of response to cardiovascular drugs. Current Opinion in Cardiology. 2012;**27**(3):253-261

[38] Miller R, Wafula F, Onoka CA, Saligram P, Musiega A, Ogira D, et al. When technology precedes regulation: The challenges and opportunities of e-pharmacy in low-income and middle-income countries. BMJ Global Health. 2021;**6**(5):e005405

[39] Crowe SJ, Karwa R, Schellhase EM, Miller ML, Abrons JP, Alsharif NZ, et al. American College of Clinical Pharmacy Global Health Practice and Research Network's opinion paper: Pillars for global health engagement and key engagement strategies for pharmacists. Journal of the American College of Clinical Pharmacy. 2020;**3**(6):1097-1112

[40] Yemeke TT, McMillan S, Marciniak MW, Ozawa S. A systematic review of the role of pharmacists in vaccination services in low-and middle-income countries. Research in Social and Administrative Pharmacy. 2021;**17**(2):300-306

Chapter 2

Utility of Right Ventricular Outflow Tract Stenting in Grown-Up with Congenital Heart Disease (CHD)

Mirza Mohammad Kamran

Abstract

RVOT stenting has traditionally been employed as a primary treatment for unrepaired tetralogy of Fallot (TOF) or other congenital heart defects characterized by VSD + Pulmonary stenosis physiology, particularly in neonates and young children experiencing significant cyanosis or symptoms of reduced Qp, serving as a temporary solution until complete surgical repair can be performed. Cyanotic congenital heart defects remain significant causes of morbidity and mortality, especially among infants and neonates. RVOT stenting additionally enhances the overall clinical condition of patients, thereby reinforcing its role as a viable and safe alternative to established palliative treatments aimed at addressing diminished Qp, such as Blalock–Taussig–Thomas shunts (BTT shunts) or central shunts. Nevertheless, in older patients (adolescents and adults), RVOT stenting presents a potential benefit as a definitive palliative solution. Its traditional function as a temporary procedure for newborns and infants with tetralogy of Fallot (TOF) who have anatomical challenges for complete repair. RVOT stenting improves the clinical condition of patients by increasing oxygen saturation and enhancing cardiac output, making it a potentially effective and safe option. RVOT stenting is believed to be more effective than traditional surgical palliation methods for older children and adult patients with unrepaired cyanotic congenital heart defects characterized by VSD + PS physiology, thereby effectively meeting the treatment objectives including improvement in oxygen saturation and promoting branch pulmonary artery growth.

Keywords: unrepaired tetralogy of Fallot, grown-ups, adolescents, adults, right ventricular outflow tract stent, pulmonary artery, oxygen saturation, palliation

1. Introduction

Traditionally, RVOT stenting has been utilized for the palliative management of unrepaired tetralogy of Fallot (TOF) patients, primarily in neonates and young children who are awaiting complete surgical correction. Cyanotic congenital heart defects remain a significant source of morbidity and mortality, particularly among infants and neonates. In pediatric cardiac surgery centers with advanced and well-established programs, most cases of VSD combined with pulmonary stenosis physiology are

addressed early during infancy. However, achieving surgical repair, whether corrective or palliative, can be challenging at times, especially for neonates with complex or unfavorable branch pulmonary artery anatomy or those who present with considerable risk factors. Particularly in neonates with intricate anatomical structures (such as hypoplastic main or branch pulmonary arteries, other concurrent cardiac conditions like double outlet right ventricle, atrioventricular septal defect, staged repair, or those with various non-cardiac risk factors including sepsis, premature birth, low birth weight, tracheoesophageal fistula, and gastrointestinal issues) that make surgery difficult. Right ventricular outflow tract stenting (RVOT) has become one of the primary bridging interventions for infants and neonates requiring urgent procedures, especially in cases with duct-dependent lesions or VSD + PS physiology that present significant cyanosis, frequent debilitating Tet spells, and unsuitable branch pulmonary artery anatomy. The majority of studies on RVOT stenting have been conducted in the western world, with patient profiles mostly involving neonates or infants [1]. On the opposite end of the spectrum, there exist adult patients, including adolescents and adults, who have not undergone repair for tetralogy of Fallot (TOF). Such cases are rarely observed in certain regions of the world due to various evident factors that will be elaborated upon later. Nevertheless, the occurrence of patients with unrepaired congenital cyanotic heart disease (CCHD) characterized by ventricular septal defect (VSD) and pulmonary artery (PA) physiology is relatively common in low- and middle-income countries. This situation necessitates a tailored approach to procedural interventions for this demographic. Currently, this population is managed conservatively through supportive treatments, including β-blockers, iron and vitamin B12 supplements, and phlebotomy, aimed at enhancing their quality of life [2–4]. This chapter examines the viability of this procedure for patients who have matured with congenital critical heart disease (CCHD) characterized by ventricular septal defect (VSD) and pulmonary stenosis (PS) physiology. It addresses the challenges faced by these individuals, who may present later due to a lack of awareness, restricted access to healthcare services that provide surgical and intensive care unit (ICU) facilities, and financial limitations,

RVOT stenting serves as a beneficial palliative intervention for patients with CCHD characterized by VSD + PS physiology, primarily due to its capacity to significantly alleviate symptoms related to hypoxemia, all while being executed in a minimally invasive manner. In rare instances, RVOT stenting may also be employed as a definitive palliative measure, especially in adults experiencing deteriorating ventricular function. By enhancing oxygen saturation levels—except in cases of transposition physiology, where no improvement in saturation is anticipated following the procedure—RVOT stenting improves the clinical condition of patients, particularly in terms of their exercise tolerance. This makes it a viable and safe alternative to traditional surgical palliative options, such as the BTT shunt or central shunts, which are associated with a wide range of complications in this demographic.

1.1 Historical aspects and some past studies

The first successful RVOT stenting was reported in 1997 by Gibbs et al. [5] performed in four patients with right ventricular outflow tract obstruction and different anatomical substrates, aged between 2 and 15 years. In the year 2009, Dohlen et al. [6] reviewed the effectiveness of RVOT stenting in nine symptomatic infants with TOF with or without pulmonary atresia and confluent pulmonary arteries. In their study,

stenting of the RVOT provided a safe and effective management strategy, thereby improving arterial oxygen saturation. In 2017, Quandt et al. [7] compared the outcome of RVOT stenting versus modified BT shunt in a 10-year single-centre retrospective study. They found that the RVOT stent group had significantly lower rates of admission to the pediatric intensive care unit ($p < 0.001$) with a shorter length of stay in comparison with BT shunt group. In TOF patients with associated atrioventricular septal defects, RVOT stenting is a safe and effective palliative option [8], promoting pulmonary arterial growth and improving oxygen saturations before surgical repair involving additional common AV valve repair. Finally, RVOT stenting has also been described in cases with very complex anatomy associated with infundibular/pulmonary valve atresia [9].

2. Indications

In neonates, the primary indications for right ventricular outflow tract (RVOT) stenting include severe desaturation, infants at elevated risk for undergoing a modified Blalock–Taussig–Thomas (BTT) shunt procedure, or those at high risk for total surgical repair despite having optimal pulmonary artery dimensions. Additional indications may encompass neonates with ventricular septal defect (VSD) and pulmonary stenosis (PS) physiology, particularly in the presence of risk factors such as prematurity, low birth weight, infections (such as sepsis), necrotizing enterocolitis, cerebrovascular incidents, pulmonary disorders, and other medical conditions necessitating non-cardiac surgical interventions, including tracheoesophageal fistula and gastrointestinal anomalies, serving as a temporary measure prior to definitive corrective surgery. Numerous studies have indicated that the presence of co-morbidities significantly elevates the risk associated with primary intra-cardiac repair, often leading to delays in surgical intervention [10–15]. Likewise, BTT shunts placed in infants with considerable co-morbidities are linked to a higher incidence of complications, which may include unpredictable postoperative outcomes, resulting in pulmonary over-circulation and alterations in the anatomy of the branch pulmonary arteries. Transcatheter RVOT stenting is increasingly favored due to its ability to facilitate a more physiological flow to the pulmonary arteries, promoting relatively uniform growth of smaller pulmonary arteries and thereby providing a more favorable surgical environment for future repairs [16–18].

The indications for RVOT stenting in older patients or adults can be summarized as follows:

Symptomatic Patients with Profound Desaturation and Unfavorable Anatomy

1. Hypoplastic branch PA which can be defined as z-score less than 3.5

2. Complex network of major aortopulmonary collaterals (MAPCAs) which are difficult to deal surgically for one stage complete repair (e.g., unrepaired TOF with hemoptysis, dual blood supply)

3. Those patients who were offered interim surgical options like central shunt or BT shunt.

4. Other associated cardiac anomalies requiring staged repair.

Symptomatic Patients with Profound Desaturation and Favorable Anatomy

1. Difficult to do one stage complete repair, in view of severe right or/and left ventricular dysfunction (**Figure 1**).

2. Major extracardiac issues for instance, thoracic deformities, cerebrovascular accidents, cerebral abscess or hematological disorders such as coagulopathies, or any other condition which can complicate post cardiopulmonary bypass period. [Author had experience of performing RVOT stenting in such a patient with severe kyphoscoliosis which was having otherwise cardiac anatomy favorable for complete repair]—**Figures 2** and **3**.

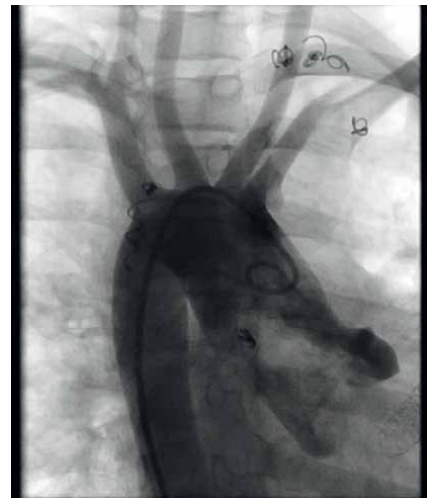

Figure 1.
Adult patient with unrepaired TOF with severe biventricular dysfunction and also multiple significant MAPCA. Patient presented with massive hemoptysis and profound desaturation. Though anatomy was favorable for complete repair but surgery deferred due to high risk involved. Patient undergone multiple MAPCA coil embolization along with RVOT stenting (stent is marked with star). Significant improvement noted in symptoms and ventricular function also improved. Eventually, after 1 year patient underwent complete with fantastic result.

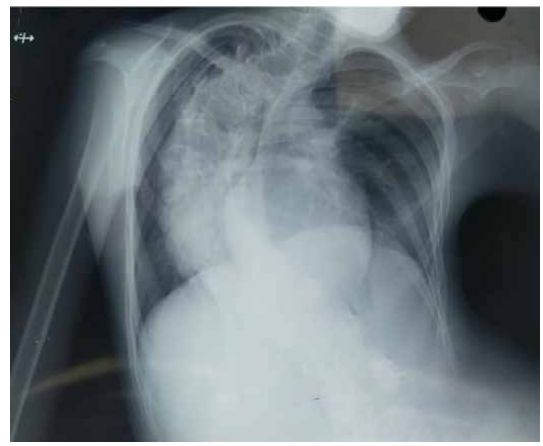

Figure 2.
Adolescent girl with unrepaired TOF and severe kyphoscoliosis.

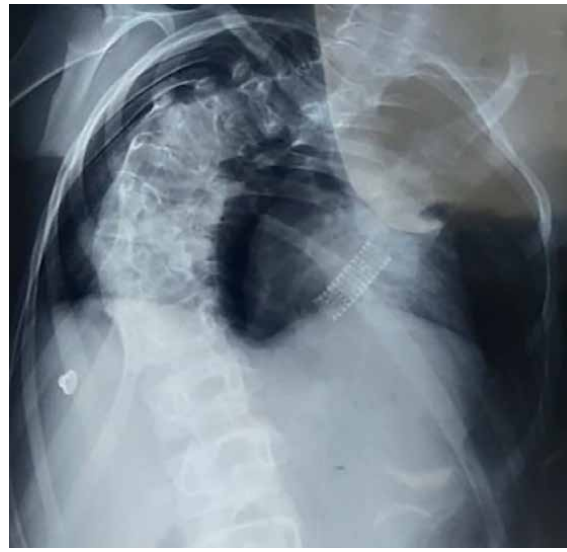

Figure 3.
Same patient who underwent RVOT stenting despite the anatomy being suitable for complete repair, due to technical challenges posed by kyphoscoliosis during surgical repair.

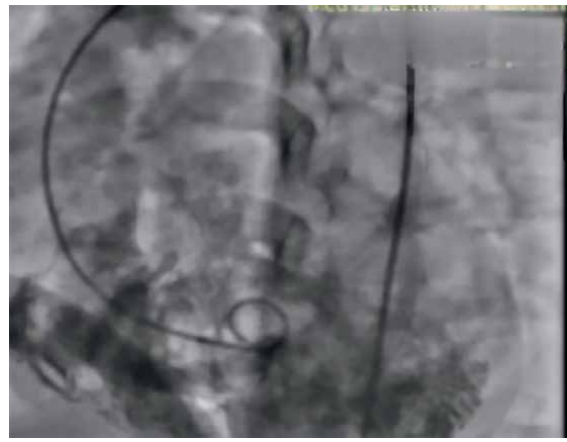

Figure 4.
15 years old boy with profound desaturation and severe symptoms having a single ventricle with TOF physiology, D malposed great arteries, not suitable for surgery. SV angiogram done via retrograde route.

Miscellaneous conditions.

Complicated cardiac anatomy with single ventricle physiology where Fontan completion surgery is not feasible due to advanced age (final palliation to improve quality of life)—**Figures 4** and **5**.

3. Procedure

In contrast to the methodology outlined by Quandt and Stumper et al. [7], which is typically conducted under general anesthesia and mechanical ventilation due to the

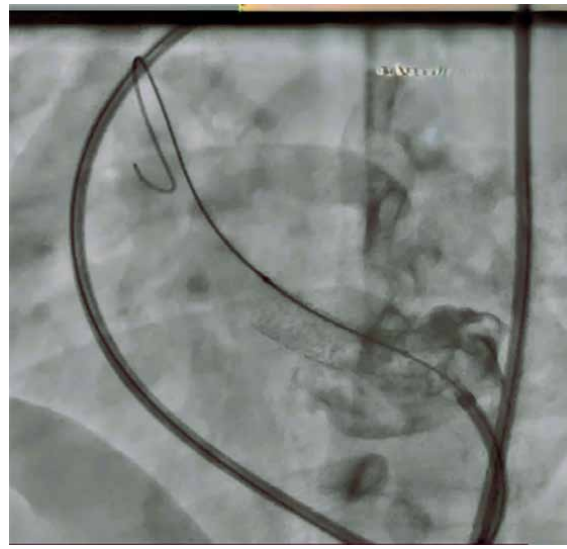

Figure 5.
Severe PS noted on angiogram (LVOTO), as a final palliation LVOT stenting done through retrograde route, patient improved significantly.

common hypoxic and debilitated state of pediatric patients prior to the procedure, our protocol generally employs mild sedation in most instances. This approach can be attributed to the increased cooperation observed in this age group, as well as the reduced duration of procedures and the accumulation of procedural expertise. Access is predominantly achieved via the right femoral vein; however, an internal jugular venous approach may be recommended in cases in which crossing the right ventricular outflow tract (RVOT) proves challenging from the femoral route or when such technical difficulties are anticipated (**Figure 6**).

A cannula is inserted into the right femoral artery to facilitate continuous blood pressure monitoring and blood gas analysis. Following the insertion of a right femoral venous sheath, typically 5F in size, an intravenous administration of 50–100 IU/Kg of heparin is performed. Additionally, the patient is given a pre-procedural antibiotic, such as IV Cefazolin or IV Amoxicillin combined with Clavulanic acid, based on

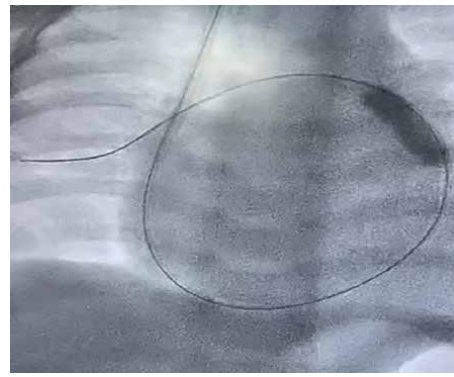

Figure 6.
Crossing of RVOT and deploying stent through RIJV approach.

body weight, to prevent infective endocarditis. A right ventricular cine-angiogram is conducted using an NIH or another diagnostic catheter equipped with a side hole positioned at the apex of the right ventricle. Standard imaging angles include a 30° right anterior oblique (RAO), 30° left anterior oblique (LAO) with a 20° cranial tilt, and lateral projections to visualize the right ventricle (RV), right ventricular outflow tract (RVOT), and branch pulmonary arteries (PAs). Some institutions may opt for deep LAO views for angiograms instead of lateral views. The diameter of the stent is determined based on RVOT measurements at potential landing zones, typically ranging from 60–70% of the estimated full size derived from Kirklin's tables, which are calculated according to the patient's body weight, the length of the infundibulum, and stent availability. Generally, the stent diameter is 1–2 mm larger than the measured infundibulum during diastole, and its length should encompass the distal muscular section of the RVOT, the pulmonary valve, and/or the main branch of the pulmonary artery prior to bifurcation, particularly in cases where valve preservation is not intended. This strategy enhances two-point fixation and stability. An echocardiographic assessment is typically conducted before the procedure to accurately measure the RVOT length and diameter, the pulmonary valve annulus, and the dimensions of the branch pulmonary arteries, thereby minimizing discrepancies that may arise from relying solely on RV angiograms, which could lead to under-sizing due to reduced Qp and underflow conditions. The selection of the stent size and type for implantation is influenced by the patient's size, the dimensions of the outflow tract, and the expected duration of palliation before corrective intervention (**Figure 7A–C**).

In cases of membranous pulmonary atresia, the atretic pulmonary valve may be perforated using the sharp end of PTCA wires or Teflon wire. In rare instances, perforation can also be achieved through electrocautery or radiofrequency energy delivered via a metallic wire or a broken borough needle positioned within a long sheath, with its tip located just caudal to the atretic valve. A bare metal pre-balloon mounted peripheral vascular stent, such as the Cook Formula TM 414 or 418 stent, can be deployed across the right ventricular outflow tract (RVOT). The primary advantage of the Cook Formula stent is its ability to be post-dilated in subsequent procedures, thereby facilitating long-term palliation. Alternatively, other peripheral stents, such as Myra BMS stents and RX Herculink Elite renal and biliary stents, may also be utilized. Balloon-mounted stents are generally favored over self-expanding varieties; however, the deployment of these stents may necessitate the use of a stiffer wire (greater than 0.035 inches), such as the Amplatzer super stiff wire, for effective stent delivery. Once the stent is selected, the appropriate delivery sheath or guide catheter is advanced along the wire across the RVOT and positioned in the main pulmonary artery, ensuring it is de-aired. Cook Formula stents are typically tracked using either 6 or 7 French Flexor sheaths, although a Mullins sheath may be required for wider peripheral stents. A notable drawback of utilizing stiffer or braided sheaths is their difficulty in navigating the constricted infundibular region, particularly in older children with significantly hypertrophied RVOT muscle bands. In such cases, the sheath is positioned just below the constricted area, with multiple side arm injections confirming the tip's location; the stent's position is then adjusted accordingly, with the sheath tip marked as the upper limit of the RVOT stent to avoid encroaching on the pulmonary annulus. However, if the annulus is hypoplastic or if there is supra-valvular pulmonary artery narrowing, the stent may be placed across the pulmonary valve, achieving a two-point fixation at the infundibulum caudally and at the annulus level cranially, which may necessitate future interventions (**Figure 8**).

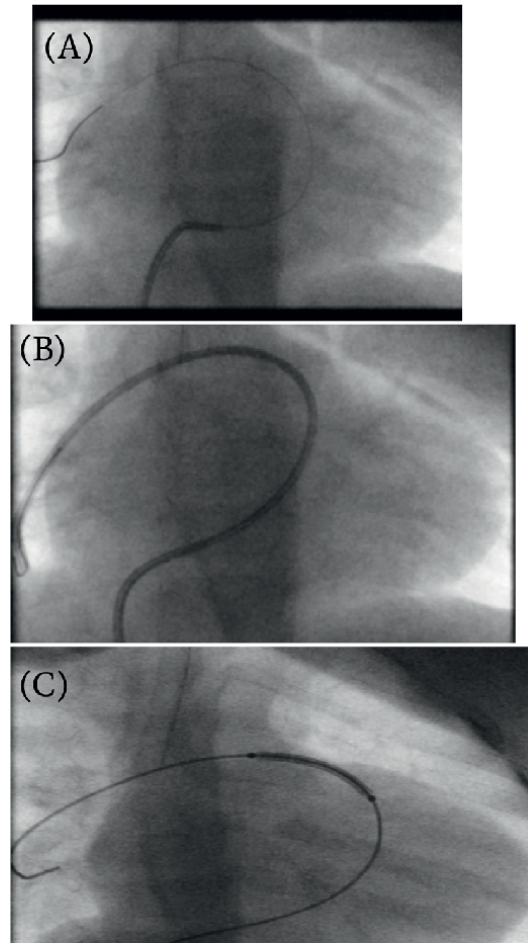

Figure 7.
A. Crossing RVOT with coronary wire. B. JR catheter taken over wire to distal RPA. C. Coronary wire exchange to Amplatzer super stiff wire.

The final angiogram captures the positioning of the stent, the opacification of the branch pulmonary arteries, and the movements of the pulmonary valve. Echocardiography is subsequently conducted to verify the stent's position and blood flow, assess ventricular and tricuspid valve function, and check for any signs of pericardial effusion. A repeat blood gas analysis is performed, showing an improvement in PaO2 levels. Once the desired stent position is confirmed, the super stiff wire and delivery sheath are removed under fluoroscopic guidance, followed by achieving hemostasis at the local site through manual compression or a figure-of-eight suture if a large delivery sheath was utilized. Patients are then transferred to the post-procedure cardiac care unit for monitoring of vital signs. In accordance with unit protocols, a heparin infusion at a rate of 10–20 units/kg/hour is initiated and maintained for the first 24 hours to prevent stent thrombosis. Oral antiplatelet therapy with aspirin, at a dosage of 4 to 5 mg/kg, may commence the following day. A chest X-ray is routinely performed post-procedure to evaluate pulmonary blood flow and identify any signs of pulmonary overcirculation. A peak-to-peak gradient of up to 40 mm Hg across the right ventricular outflow tract (RVOT) on Doppler echocardiography following

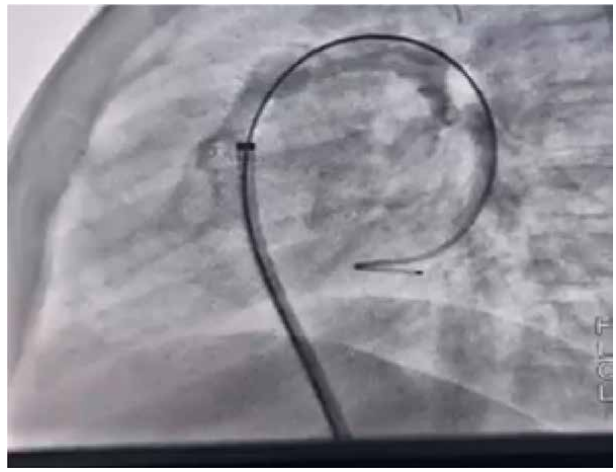

Figure 8.
Confirming the position with RV angiogram via the side arm of long sheath in lateral view to assess length of RVOT.

stenting is considered acceptable, attributed to the resistance posed by the RVOT muscle bands.

4. Technical tips

Comprehensive echocardiography, particularly through subcostal and parasternal short-axis views, plays a crucial role in assessing the relative contributions of various obstruction levels. It is instrumental in understanding the hemodynamic implications of sub-valvular, valvular, and supra-valvular stenosis components on overall obstruction, as well as in evaluating the anatomy of the branch pulmonary arteries in neonates and infants. The utility of echocardiograms for pre-procedural planning is limited in older children and adults due to suboptimal imaging windows. Therefore, it is advisable to incorporate additional diagnostic modalities, such as cardiac CT scans, during pre-assessment. In instances where a CT scan is not performed for any reason, diagnostic angiography can be beneficial in conjunction with echocardiography for case planning. CT imaging provides critical information regarding the precise dimensions of the pulmonary valve, the sizes of the branch pulmonary arteries, the length of the right ventricular outflow tract (RVOT), any supravalvular pulmonary stenosis components, and the size and quantity of major aortopulmonary collaterals (MAPCAs). This information is vital for selecting the appropriate stent size, which is essential for the successful planning and execution of the percutaneous procedure. Patients in the older age group typically exhibit greater hemodynamic stability compared to neonates. Most procedures for these patients are elective, in contrast to the emergency nature of interventions required for newborns and infants. In the latter group, coronary stenting is often necessary, and the use of a long sheath is generally minimal; instead, a guiding JR catheter is predominantly employed. The long sheath technique, as described by Quandt et al., is primarily utilized to reduce the risk of injury to the tricuspid valve apparatus and to ensure a stable stent position through repeated test angiograms. Linnane et al. have reported using a periventricular approach in four patients weighing 2 kg or less, employing a small subxiphoid

incision. This method offered a more direct access route to the RVOT, with stent deployment guided by trans thoracic echocardiography (TTE). Additionally, Linnane et al. have outlined a technique to avoid the use of a long delivery sheath during stent deployment by navigating an angled glide catheter across the tricuspid valve and RVOT.

5. Complications and their management

Complications can be classified as:
Stent related:

1. Stent migration and embolization: Malposition or migration of the stent may occur due to more proximal deployment of the stent. If the stent does not achieve two-point fixation, it remains unstable. The commonest site of embolization is descending aorta. Sometimes, distal deployment of the stent can lead to migration of stent in to branch pulmonary arteries. The use of a long delivery sheath can help in confirming the position and preventing the slippage of the stent.

2. Stent fracture: Over time, repetitive heart motion can cause fractures, potentially leading to embolization or obstruction

3. Incomplete expansion: Suboptimal placement or incomplete deployment may cause this.

4. In stent thrombosis: Intimal hyperplasia or neointimal proliferation can narrow the stent, reducing blood flow.

5. Thrombosis: Clot formation within or around the stent may obstruct the blood flow and require anticoagulation therapy.

Hemodynamic complications

1. Residual cyanosis: under sizing of stent diameter, suboptimal placement, and sparing significant infundibulum/pulmonary valve annulus area can lead to residual cyanosis.

2. Over circulation to the lungs: over sizing of stents can lead to this situation specially in neonates or infants resulting in pulmonary edema, and most of the time this is simple to treat medically with diuretics.

Rhythm-related complications.
RVOT stent irritates cardiac tissue, potentially causing arrythmias such as:

1. Ventricular tachycardia

2. Premature ventricular contractions

3. Atrioventricular block in rare cases.

Procedure-related complications

1. Vascular injury: damage to arteries or veins during procedure

2. Perforation: RVOT, MPA, any heart chamber which may end up in cardiac tamponade

3. Bleeding and hematomas at puncture site, more risk with associated coagulopathy

4. Infections: risk of IE, localized infection is always there.

Long-term complications

1. RVOT dysfunction: Scarring or narrowing at the stent can lead to RVOT obstruction.

2. Impact on future surgeries: The presence of stent can complicate later definitive surgeries.

Best way to treat complications is to prevent them, these following strategies can help in preventing the above-mentioned complications:

1. Anticoagulation therapy: to prevent or treat thrombosis

2. Timely re-intervention: for stent migration, stenosis, or residual cyanosis

3. Careful planning for definitive repair.

6. Challanges and pitfalls

The primary objective of any palliation achieved through either transcatheter stenting or surgically created shunts is to facilitate a substantial and balanced enhancement of pulmonary blood flow, thereby improving systemic arterial saturation and replicating the physiological pattern of pulmonary blood flow. RVOT stenting accomplishes this goal by promoting pulmonary blood flow exclusively during systole, ensuring an even distribution of pulmonary blood flow across both branches of the pulmonary artery, provided there is no pre-existing stenosis in the branch pulmonary arteries. Furthermore, the dimensions of the stent are significantly influenced by the anatomy of the right ventricular outflow tract (RVOT) and the size of the pulmonary valve annulus. The rhythmic contraction of the muscle bands within the right ventricular infundibulum can ultimately lead to fractures in the stent struts, potentially resulting in an early recurrence of RVOT obstruction. Stent fractures are a common occurrence in the lifespan of a stent due to the dynamic forces at play (**Figures 9** and **10**).

The procedure presents significant technical challenges, primarily due to pre-existing hemodynamic issues, and involves an initial learning curve, making it relatively difficult to implement in a new program. Right ventricular outflow tract (RVOT) stenting frequently results in metallic remnants being left within

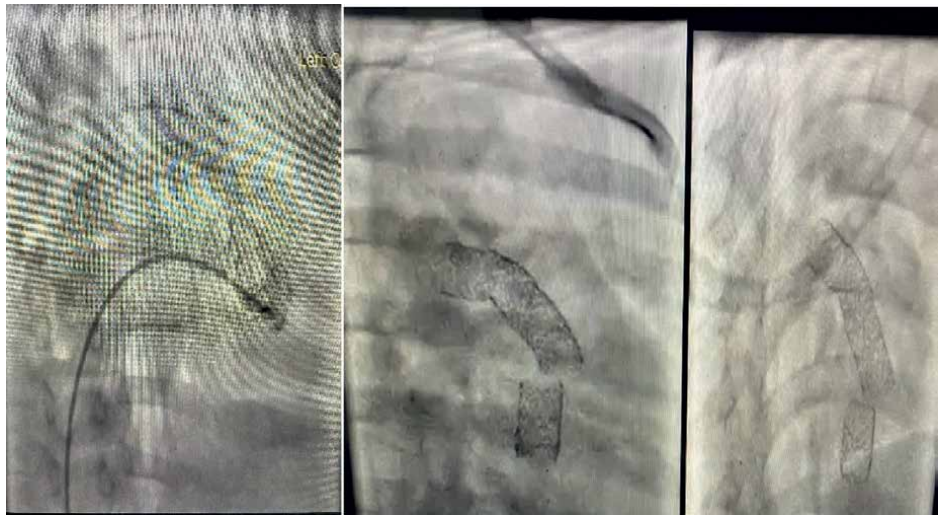

Figure 9.
RAO 30-degree view and LAO 30-degree view of a long standing RVOT stenting patient who had lost to follow up, presented with stent fracture at multiple places, patient underwent corrective surgery successfully.

the RVOT myocardium, which can only be partially removed during surgical repair. The potential risks associated with these retained stent fragments, such as the possibility of inducing focal ventricular arrhythmias or infections, remain uncertain. While the removal of the stent may prolong the surgical repair process, the duration of cardiopulmonary bypass appears to be comparable to that of trans-annular patch repairs in patients who have not undergone stenting. The extraction of the stent can be complex, potentially leading to increased cardiopulmonary bypass time; in some cases, the posterior portion of the stent may be left in place, raising concerns about possible damage to adjacent structures, such as the aortic and tricuspid valves, which could complicate postoperative recovery. There remains a lack of long-term data following RVOT stenting, particularly concerning its impact on right ventricular remodeling, the incidence of arrhythmias, the growth of branch pulmonary arteries, and the necessity for future re-interventions.

7. Outcomes

The immediate results for patients undergoing RVOT stenting are generally positive, with oxygen saturation levels showing immediate improvement post-procedure, except in cases related to transposition physiology. According to yet-to-be-published data from the same researchers, over 30 children, predominantly older than 1 year, have received RVOT stenting. This cohort exhibited a notable enhancement in saturation levels, allowing for their transfer from the intensive cardiac care unit within 24 hours. During the initial learning phase, there were two occurrences of stent embolization; however, there were no recorded in-hospital fatalities. The children were discharged with antiplatelet therapy. Additionally, one case of complex fractures of the RVOT stent was reported 8 months following implantation, but no instances of stent thrombosis were observed during follow-up.

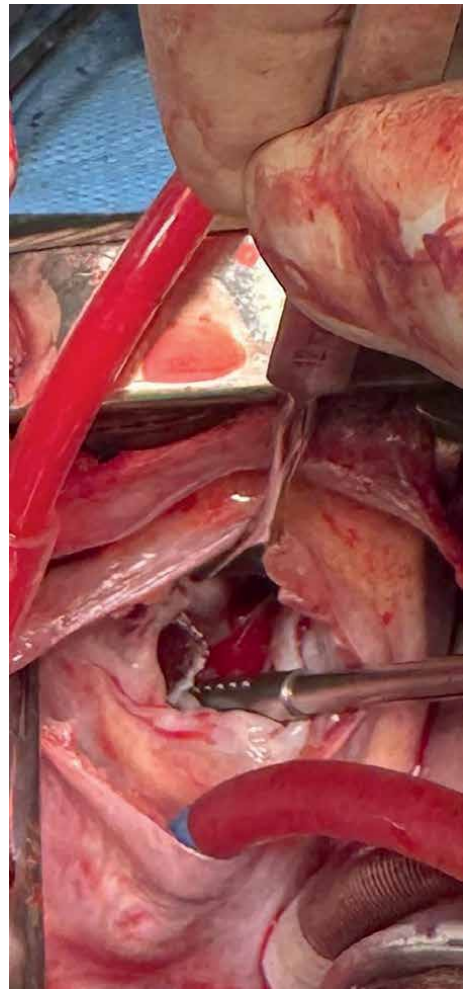

Figure 10.
Same patient with fractured stent taken up for ICR with TAP showing displaced stent adhered to tricuspid valve chordae.

8. Summary

To summarize, RVOT stenting may represent a superior alternative for adult patients with unrepaired tetralogy of Fallot (TOF) or other complex congenital heart defects (CCHDs) characterized by ventricular septal defect (VSD) and pulmonary stenosis (PS) physiology, compared to surgical palliation. This approach is supported by notable enhancements in oxygen saturation levels, exercise capacity, and biventricular function. Although the initial procedural success and ease have been observed following the learning curve, further long-term studies are necessary to evaluate the need for re-interventions in adults with RVOT stents for VSD and PS palliation. The development of a specialized stent designed for these conditions, featuring increased tensile strength, and resistance to shear forces could lead to improved long-term outcomes. Presently, peripheral stents intended for other vascular locations are being utilized in the RVOT, an area subjected to various hemodynamic forces, rather than

in vessels that experience only radial stresses. Given that these regions, such as the RVOT infundibulum, are hypercontractile, a more robust and durable dedicated stent could significantly alter treatment outcomes. Additional research is imperative, particularly long-term data, which may be challenging to acquire since definitive or corrective surgeries are typically conducted within 6 to 12 months post-palliation, during which hemodynamics and anatomy may improve. Transcatheter RVOT stenting is increasingly preferred over other surgical palliative techniques, as aorto-pulmonary shunts often exhibit unpredictable postoperative courses, particularly in neonates, regarding the regulation of pulmonary blood flow. The potential risks of shunt thrombosis or excessive pulmonary circulation can adversely affect postoperative recovery. Furthermore, alterations in the pulmonary arteries following shunt placement can considerably influence the success of definitive repair. RVOT stenting promotes a more physiological flow to the pulmonary arteries and fosters the bilateral growth of smaller pulmonary arteries, thereby providing a more favorable surgical substrate for future repairs.

9. Conclusions

In conclusion, RVOT stenting is a viable option for adults with TOF, leading to notable enhancements in their oxygen saturation and left ventricular ejection fraction (LVEF). As expertise and techniques advance, RVOT stenting is becoming a more secure alternative to other palliative interventions and is likely to receive increasing acceptance among adults seeking palliative care. Furthermore, this procedure offers hope to patients in low- or middle-income countries who have limited access to surgical facilities and are considered at higher risk for total repair as a last-resort intervention. Nonetheless, further long-term studies are essential to draw more definitive conclusions.

Conflict of interest

The authors declare no conflict of interest.

Acronyms and abbreviations

RVOT	right ventricular outflow tract
mBTs	modified Blalock Tausig shunt
LVOT	left ventricular outflow tract
TOF	tetralogy of Fallot

DOI: http://dx.doi.org/10.5772/intechopen.1009223

Author details

Mirza Mohammad Kamran
Metromed International Cardiac Centre, Calicut, Kerala, India

*Address all correspondence to: kamran16paeds@gmail.com

IntechOpen

References

[1] Ghaderian M, Ahmadi A, Sabri MR, et al. Clinical outcome of right ventricular outflow tract stenting versus Blalock-Taussig shunt intetralogy of Fallot: A systematic review and meta-analysis. Current Problems in Cardiology. 2021;**46**(3):1-14

[2] Prakoso R, Agita Sembiring A, Dwisepto Aulia Sakti D, Mendel B, Lilyasari O. Double stenting in 19-year-old patient with tetralogy of Fallot with prior fractured stent. JACC Case Reports. 2022;**4**(20):1375-1378

[3] Baumgartner H, Backer JD, Babu-Narayan SV, et al. 2020 ESC guidelinesforthe management of adult congenital heart disease. European Heart Journal. 2021;**42**:563-645

[4] Stout KK, Daniels CJ, Aboulhosn JA, et al. 2018 AHA/ACC guideline for the management of adults with congenital heart disease: A report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. Journal of the American College of Cardiology. 2019;**73**(e81):e192

[5] Gibbs JL, Uzun O, Blackburn ME, et al. Right ventricular outflow stent implantation: An alternative to palliative surgical relief of infundibular pulmonary stenosis. Heart. 1997;**77**:176-179

[6] Dohlen G, Chaturvedi RR, Benson LN, Ozawa A, Van Arsdell GS, Fruitman DS, et al. Stenting of the right ventricular outflow tract in the symptomatic infant with tetralogy of Fallot. Heart. 2008;**95**:142-147

[7] Quandt D, Ramchandani B, Penford G, Stickley J, Bhole V, Mehta C, et al. Right ventricular outflow tract stent versus BT shunt palliation in tetralogy of Fallot. Heart. 2017;**103**:1985-1991

[8] Abumehdi M, AlNasef M, Mehta C, Botha P, McMahon C, Oslizlok P, et al. Short to medium term outcomes of right ventricular outflow tract stenting as initial palliation for symptomatic infants with complete atrioventricular septal defect with associated tetralogy of Fallot. Catheterization and Cardiovascular Interventions. 2020;**96**:1445-1453

[9] Ng LY, Al-Alawi K, Breatnach C, Nolke L, Redmond M, McCrossan B, et al. Hybrid subxiphoid perventricular approach as an alternative access in neonates and small children undergoing complex congenital heart interventions. Pediatric Cardiology. 2020;**42**:526-532

[10] Sandoval JP, Chaturvedi RR, Benson L, Morgan G, Van Arsdell G, Honjo O, et al. Right ventricular outflow tract stenting in tetralogy of Fallot infants with risk factors for early primary repair. Circulation: Cardiovascular Interventions. 2016;**9**:e003979

[11] Dohlen G, Chaturvedi RR, Benson LN, Ozawa A, Van Arsdell GS, Fruitman DS, et al. Stenting of the right ventricular outflow tract in the symptomatic infant with tetralogy of Fallot. Heart. 2009;**95**:142-147. DOI: 10.1136/hrt.2007.135723

[12] Barron DJ, Ramchandani B, Murala J, Stumper O, De Giovanni JV, Jones TJ, et al. Surgery following primary right ventricular outflow tract stenting for Fallot's tetralogy and variants: Rehabilitation of small pulmonary arteries. European Journal of Cardio Thoracic Surgery. 2013;**44**:656-662. DOI: 10.1093/ejcts/ezt188

[13] Kirsch RE, Glatz AC, Gaynor JW, Nicolson SC, Spray TL, Wernovsky G, et al. Results of elective repair at 6

months or younger in 277 patients with tetralogy of Fallot: A 14-year experience at a single center. The Journal of Thoracic and Cardiovascular Surgery. 2014;**147**:713-717

[14] Gladman G, McCrindle BW, Williams WG, Freedom RM, Benson LN. The modified Blalock-Taussig shunt: Clinical impact and morbidity in Fallot's tetralogy in the current era. The Journal of Thoracic and Cardiovascular Surgery. 1997;**114**:25-30

[15] Kanter KR, Kogon BE, Kirshbom PM, Carlock PR. Symptomatic neonatal tetralogy of Fallot: Repair or shunt? The Annals of Thoracic Surgery. 2010;**89**:858-863. DOI: 10.1016/j. athoracsur. 2009.12.060

[16] Nakashima K, Itatani K, Oka N, Kitamura T, Horai T, Hari Y, et al. Pulmonary annulus growth after the modified Blalock-Taussig shunt in tetralogy of Fallot. The Annals of Thoracic Surgery. 2014;**98**:934-940

[17] Petrucci O, O'Brien SM, Jacobs ML, Jacobs JP, Manning PB, Eghtesady P. Risk factors for mortality and morbidity after the neonatal Blalock-Taussig shunt procedure. The Annals of Thoracic Surgery. 2011;**92**:642-651

[18] Linnane N, Walsh KP, McGuinness J, Kenny D. Evolution of approach to right venticular outflow tract stenting in infants ≤2 Kgs. Structural Heart Disease. 2018;**4**(2):50-55

Chapter 3

Interventional Closure of Ventricular Septal Defects: A Focus on Pediatric Population

Aso F. Salih

Abstract

Ventricular septal defects (VSDs) are the most common congenital heart defects in children. Transcatheter closure has emerged as a less invasive alternative to surgery. This chapter reviews the current literature on interventional catheterization closure of VSDs in the pediatric population. A comprehensive review of relevant studies and literature was conducted, focusing on indications, patient selection, procedural techniques, device options, and outcomes of transcatheter VSD closure. Transcatheter VSD closure has high success rates and favorable short- and long-term outcomes in appropriately selected patients. Advantages include reduced invasiveness and recovery time compared to surgery. However, potential complications include device embolization, valve dysfunction, and residual shunts. Interventional catheterization closure offers a safe and effective alternative to surgery for many children with VSDs. A multidisciplinary team approach is crucial to determine the optimal treatment strategy based on individual patient factors.

Keywords: ventricular septal defect, VSD, transcatheter closure, interventional catheterization, pediatric, congenital heart disease

1. Introduction

The first septation in the heart during embryogenesis normally results in the separation of the right ventricle from the left ventricle. Ventricular septal defects (VSDs) are one of the most common congenital heart defects and the overall prevalence of VSD is 1% of all live births [1]. The location, size, and number of defects in the ventricular septum can bring about a variety of hemodynamic consequences, ranging from being silent to producing severe consequences. A balance of the pulmonary-to-systemic flow ratio, ventricular muscle function, and pulmonary vascular resistance are the major determinants of the initial symptoms and progression of VSDs. More than 50% of small muscular VSDs will close spontaneously in the first few years of life. As in many disease processes, early detection and timely interventions are key for the optimal management of patients with VSD. The pediatric population with VSD needs to be continuously monitored, and the immediate

and long-term management goals need to be set individually. Over the last two decades, there have been remarkable advancements in the field of medicine, resulting in the evolution of interventional treatment approaches. Interventional catheterization has gained special attention and appreciation in many of these disease processes, including VSDs. Over the past few years, various treatment methods and guidelines for intervention have been proposed to ensure better outcomes for these sick children. The aim is to review these techniques and guidelines that are to be adopted for the management and treatment of patients with VSD—both recently and not-so-recently described.

1.1 Overview and incidence of ventricular septal defects

Ventricular septal defects (VSDs) are among the most common congenital heart defects, frequently identified in infants, particularly within the first few days or weeks of life. The classification and description of VSDs have evolved, with recent classifications highlighting the geographical and ethnic variations in incidence. Notably, there is a higher occurrence of doubly committed VSDs in Asian populations and larger defects in Western populations [1].

The natural progression of VSDs is not extensively documented, but they can be categorized based on size—typically classified as moderate to large. Most small VSDs are asymptomatic and do not pose significant health risks, resolving spontaneously as the child grows. These small defects are generally considered hemodynamically inconsequential, posing a low risk for serious complications such as heart failure, death, or irreversible pulmonary vascular disease.

To better understand the incidence and management trends of VSDs, further epidemiological research is essential. The socioeconomic implications of VSDs are significant, especially in developing countries where healthcare systems may struggle with the burden of these defects. Families affected by VSDs often face challenges, including poor maternal weight gain and increased morbidity for both the mother and fetus.

Early surgical intervention or other treatment options are crucial for preventing severe complications, such as heart failure, aspiration pneumonia, pulmonary arterial hypertension, and impaired growth and development. When VSDs are detected during routine medical assessments or soon after birth due to signs of heart failure or pulmonary overcirculation, a comprehensive diagnostic evaluation is necessary.

The characteristics of VSDs can vary widely, ranging from small openings that may close on their own to significant defects that lead to substantial hemodynamic impacts. Fortunately, trained heart surgeons and pediatric interventional cardiologists possess the expertise to effectively close nearly all congenital heart defects, including VSDs.

1.2 Classification of ventricular septal defects

Variability of ventricular septal defects, or VSDs, has deteriorated the classification and terminology agreement. Research has shown that abnormal morphological features of VSDs, such as complex shapes and the presence of associated coexisting additional anatomical structures in a considerable number of patients, are responsible for inaccurate classification. Ventricular septal defects are usually classified, in determining eligibility for most interventional procedures and transcatheter device

closure, on the basis of echocardiography and/or angiographically determined defect size. A new classification or ordering agreement of VSDs according to newer, more precise information, anatomically and pathophysiologically more correct, is necessary for a shorter, clearer, and more precise understanding of VSDs. In everyday practice, interventionists prefer the simpler two groups and two types of VSDs.

VSD classification is rarely used by interventional cardiologists. A classical classification, based on the anatomical relation of two ventricles and defect localization, refers to membranous and muscular types of VSDs. Children with VSDs have symptoms that depend on the size of the VSDs and the associated conditions [2, 3].

The classification showed the six most common VSDs in the pediatric population and their occurrence, as well as the proposed treatment guidelines.

2. Management strategies for ventricular septal defects

Ventricular septal defect (VSD) is the most common congenital heart defect. Although treatment of small VSD is not currently recommended, evaluation is necessary in newborns and infants. The selection of management strategies depends upon the shunt size, pulmonary artery pressure, and other comorbidities such as associated mitral valve regurgitation. In patients with moderate or large VSD, international guidelines for the management of VSD patients were stated to consider three treatment strategies according to the shunt and pressure features. Early intervention before 1 year may be reasonable in patients with an increased shunt prompting severe or moderate pulmonary hypertension.

Several studies on small VSDs with high PVR and low Qp: Qs showed a potential decrease in left-to-right shunt with the use of pulmonary servo-controlled vasodilators: sildenafil. The hemodynamic change after pulmonary vasodilation depends on PVR reduction, and it is normal to have a more relevant reduction in pulmonary pressures in large shunts after pulmonary vasodilation.

However, certain clinicians believe that the mentality of classifying VSDs correlates significantly with the transcatheter device vulnerability for embolization, the degree of infective endocarditis, and the possibility of future left ventricular outflow obstruction and surgical repair. In addition, there is an idea that even a VSD using less than five to six physiological lung resistance units in circulation might not have early left ventricular dysfunction and poor exercise performance. The objective assessment of the VSD and the proper treatment procedures depend completely on a thorough understanding of VSDs.

In additional studies, there is agreement about the relation of the degree of tricuspid regurgitation to the mean PCWP and mean PAP, development of primary PAP, and the possibility of VSD diameter.

2.1 Pharmacological approaches to treating ventricular septal defects

There are currently no pharmacological agents available specifically for the management of VSDs. However, symptomatic patients can start on medications to help alleviate their symptoms and improve ventricular function. Diuretics help reduce signs of heart failure when there is fluid overload, cough, and difficulty in breathing. Urine output and plasma creatinine should be monitored. Diuretics are useful in children waiting for further procedures. Sildenafil is the most commonly used agent. Other PAH agents may also be used. Some patients with significant

left-to-right shunts will have ventricular dilation, indicative of volume overload. Anti-hypertensives, particularly angiotensin-converting enzyme inhibitors and/or angiotensin receptor blockers, have been used as adjunctive therapy. At present, the use of β-blockers to control ventricular function in non-severe cases is being evaluated. Other medications that have been used include digoxin for inotropic support.

The limitations of pharmacotherapy are that they are purely a support strategy and are not anticipated to reverse ventricular dilatation. Large VSDs usually require intervention or surgery rather than medication, and the timing of medications in relation to "down-staging" to a stable patient for intervention is critical. Since there are no specific criteria guiding the use of medications for the management of VSD patients, the context in which these drugs are used would need to be individualized according to the clinical picture. However, these medications can often be started to support a patient in heart failure due to a large VSD and continue until VSD closure.

2.2 Complementary approaches to management

There are other complementary approaches beyond conventional pharmacological treatment with which we might be able to provide comprehensive care for ventricular septal defects (VSD) in higher percentages. Nutritional counseling should be administered to the patient and their relatives by an expert. It should include hypocaloric diets for patients particularly susceptible to becoming overweight, and protein-rich diets in conditions of hemodynamic overload. Physical therapy for thoracic cage mobility improvement, endurance training, and muscular strengthening should be considered according to the clinical conditions supported by physical therapy professionals. Psychological support for both the patient and the family is important to resolve concerns, psychological discomfort, or discomfort due to social embarrassment.

At the same time, experts should support a multilevel collaboration among team members able to integrate complementary approaches if there is a clinical benefit proven scientifically.

3. Surgical closure versus catheter-based intervention

Treatment of ventricular septal defects (VSD) with a significant left-to-right shunt is pursued with a combination of surgery, catheterization, and medications. Initially, surgical closure was the gold standard, and it still has several applications in specific patient groups. The technical differences between surgery and intervention are obvious. On the one hand, surgery provides direct visual and manual control over the defect. However, surgical options may become limited by the presence of additional risk factors. Catheter-based interventions, initially used as palliative measures, became a true arterio-septal defect occlusion following significant technological advancements. Newer devices and new deployment techniques have led interventional therapy to stand alone against surgical management in certain locations.

The decision on how to intervene should be based primarily on the patient's anatomy and related technical prowess. In certain instances, especially with small defects, patients are sent for catheterization without prior surgery. With increasing experience and the development of newer devices, catheter intervention will potentially prove as efficacious as surgery. The effect on the left ventricular volume is not uniform. Age and anatomic characteristics are important for the choice of intervention. Since each

case has distinct anatomical characteristics and the availability of devices and experience varies among centers, the right choice depends on individualized planning.

3.1 Surgical closure effectiveness

Surgical closure remains the gold standard for VSD management, particularly in infants, with low mortality rates and minimal complications [4].

Long-term follow-ups show that most patients maintain good health and quality of life post-surgery [5].

3.2 Catheter-based interventions

While catheter-based interventions are less invasive, they carry risks such as heart block, particularly in perimembranous VSDs [6].

Comparative studies suggest that both surgical and catheter-based methods can be effective, but the choice often hinges on the specific clinical scenario and available resources [6, 7].

3.3 Considerations for treatment

The decision-making process for VSD treatment should consider the patient's age, defect type, and the healthcare facility's capabilities [4].

Despite the advantages of less invasive techniques, surgical closure remains a preferred option for many cases due to its established success rates.

In contrast, some argue that advancements in catheter-based techniques may offer comparable outcomes with reduced recovery times, suggesting a potential shift in treatment paradigms as technology continues to evolve.

4. Pros and cons of surgical versus catheter-based closure methods

The choice between surgical and catheter-based closure methods for ventricular septal defects (VSD) significantly impacts the overall cost of treatment and healthcare resource utilization. Catheter-based approaches, such as transcatheter closure, generally offer advantages in terms of reduced hospital stays and lower associated costs, although the initial procedural costs can be higher. Surgical methods, while effective, often involve longer recovery times and higher costs related to hospitalization and postoperative care.

Cost efficiency: Catheter-based closure methods tend to have lower total medical costs compared to surgical methods, primarily due to reduced hospital stays and less need for postoperative care. For instance, in the case of perimembranous VSD, the total medical cost for percutaneous closure was significantly lower than surgical closure [8]. Surgical closure often incurs higher initial costs due to the need for cardiopulmonary bypass and longer hospital stays [9, 10].

4.1 Reduced bed occupancy

Interventional VSD closure has been associated with a high success rate and minimal complications, which translates to shorter hospital stays and reduced bed occupancy [11].

Lower bed occupancy can mitigate emergency department crowding, which is linked to improved patient safety and reduced hospital mortality [12].

Clinical outcomes: Transcatheter closure is associated with high success rates and fewer complications, such as the avoidance of thoracotomy and general anesthesia, which contribute to its cost-effectiveness [13, 14].

Long-term effectiveness: While surgical methods are well-established and effective, they are associated with higher morbidity and longer recovery periods, which can increase overall healthcare costs [10, 15].

Complex cases: Surgical closure remains a preferred option for more complex VSD cases, where catheter-based methods may not be feasible [16].

4.2 Impact on healthcare resource utilization

Resource allocation: The choice of closure method affects the allocation of healthcare resources, with catheter-based methods allowing for more efficient use of hospital facilities and personnel [8, 17].

Economic considerations: In some regions, the cost of catheter-based devices can be higher, but the overall economic benefits, including reduced societal costs, often outweigh these initial expenses [9, 16].

While catheter-based closure methods offer significant advantages in terms of cost and resource utilization, they may not be suitable for all patients, particularly those with complex VSDs. Surgical methods, despite their higher costs, provide a reliable alternative for such cases.

5. Age-related preferences in treatment modalities

The treatment strategies for ventricular septal defects (VSDs) in different age groups were progressively clarified, and decisions about the timing of the procedure and the choice of intervention are made based on the specific characteristics of the affected patients.

In general, the most common reason given for avoiding catheter-based closure is that neonates and infants have a specific period in which the systemic vascular bed, pulmonary vascular bed, and the underlying pathophysiology favor the surgical approach.

Treatment should provide a functional and anatomical cure for the particular age of the child.

Catheter-based closure of ventricular septal defects (VSD) demonstrates varying outcomes based on patient age, influencing both procedural success and complication rates. The age-related modalities in VSD closure highlight the effectiveness of transcatheter techniques across different age groups, particularly in infants and young children, where the procedure is increasingly recognized for its safety and efficacy.

Infants and young children: Studies indicate that transcatheter closure is feasible in patients weighing as little as 5 kg, with success rates around 86% [18].

Older children and adults: The median age for successful procedures is reported at 6.2 years, with an overall closure rate of 86.2% [11].

5.1 Complications and outcomes

Complications: Common complications include arrhythmias and residual shunts, with arrhythmias occurring in 62.96% of cases during transcatheterization [19].

Long-term outcomes: Long-term follow-up shows favorable outcomes, with only a 0.7% incidence of complete atrioventricular block [11].

In contrast, while transcatheter VSD closure is generally safe, some studies suggest that older patients may experience higher rates of complications, necessitating careful monitoring [20].

6. Methods for catheter-based closure of ventricular septal defects

The process of choosing a patient for a suitable closure during an interventional VSD procedure is of paramount importance. Initial patient evaluation generally focuses on determining the feasibility of catheter intervention, as well as patient suitability for device therapy based on anatomic and physiologic considerations. Such evaluations usually require cardiac catheterization, including hemodynamic assessment of the defect and angiographic and/or echocardiographic assessment of both the left heart and aortic arch.

Moderate or severe pulmonary hypertension, left ventricular outflow obstruction, and other substantial side-branch compromises should be avoided in ideal candidates. The importance of imaging in guiding the procedures cannot be overemphasized, in particular for devices placed across the septum.

A variety of techniques can be used to further aid VSD closure percutaneously. These are usually performed with arterial access in the cath lab, depending on patient factors and operator preference. Many VSD closure antegrade procedures have been described and can be highly effective, with high success rates, but the retrograde aortic approach has been the preferred methods for many due to its ability to allow two operators to work simultaneously and to directly visualize the VSD by turning the aortogram into a left ventriculogram. This can simplify device delivery, especially when using wire-reinforced delivery systems.

A variety of devices are being used since there is no pediatric-specific market. The size and type of VSD is a major determinant of device selection. Large or heavy devices should be avoided since they may cause erosion or arrhythmia. Multiple devices, including various muscular and perimembranous VSD devices, have been used safely and effectively for the perimembranous VSD. A cinching technique, whereby a constrictive wire is placed inside the VSD through a venous catheter, has been described to downsize the minimal diameter of the device, allowing for satisfactory attachment and successful closure.

7. Criteria for device selection and sizing

Device selection and sizing for VSD closure are crucial for successful outcomes and depend on several factors, including the type of VSD, its size and morphology, and patient-specific characteristics. Here is a more detailed explanation:

Types of VSDs and device options:

Perimembranous VSDs: These are the most common type of VSD. Device options include the Amplatzer Duct Occluder II (ADO II), especially for smaller defects with specific anatomy, and asymmetric or eccentric double-disc devices. The ADO II is known for its softness, flexibility, and faster implantation.

Muscular VSDs: For these VSDs, the Amplatzer Muscular VSD Occluder (AMO) is commonly used. The AMO comes in various sizes with waist diameters ranging from 4 mm to 18 mm.

Other VSD types: Other devices, sometimes used off-label, include nitinol or vascular coils, double-umbrella devices, buttoned devices, and Starflex devices.

The choice of device should be based on the size of the ventricular septal defect and marginal sinus size, as well as aortic and aortic cusp malalignment, valve disease, and aortic regurgitation. The next step is to cross-select categories of devices that are specific to the defect anatomy: muscular VSDs – screw moving away; membranous VSDs – screw moving toward; these materials are friendly for the young age group.

Oversizing carries potential hemolysis, hemodynamic abnormality, device migration, endothelial damage, and carditis, while undersizing can result in aortic or tricuspid valve dysfunction, coronary artery obstruction, and left ventricular or VSD obstruction. Moreover, device failure can be more likely in a regularly shaped sinus; hence, the accurate measurement should be triple-checked in such defects.

7.1 Age and success rates

The success rate of transcatheter VSD closure is generally high across different age groups. For instance, a study reported an 88.9% success rate in patients with a mean age of 4.48 years [19].

In older patients, the success rate remains favorable, with a reported closure rate of 86.2% at the last follow-up in a cohort with a median age of 6.2 years [11].

7.2 Complications and age

Younger patients, particularly those weighing 5 kg or less, can undergo successful transcatheter VSD closure, although the procedure may be more challenging. Complications such as device embolization and tricuspid regurgitation have been noted but are generally manageable [18].

In older patients, complications like complete atrioventricular block (cAVB) and residual shunting are concerns, although they occur infrequently. For example, only one case of cAVB was reported in a study involving patients with a median age of 6.2 years [11].

7.3 Device selection and age

The choice of device can vary based on the patient's age and the specific characteristics of the VSD. Devices like the Nit-Occlud® Le VSD coil have shown high success rates and minimal adverse effects in patients with perimembranous VSDs, which are common in both pediatric and adult populations [21, 22].

The findings suggest that the Amplatzer™ Duct Occluder II (ADOII) and MFO should be considered complementary devices, as ADOII is limited to smaller defects while MFO can accommodate larger defects, allowing for a broader range of pmVSD anatomies to be treated effectively [23].

Device sizing:

General principles: The device should be large enough to effectively close the defect but not so large that it interferes with surrounding structures, such as heart valves. Oversizing can lead to complications like atrioventricular block or valve issues.

Sizing guidelines:

For symmetric and eccentric occluders, the device size is typically chosen to be 2–4 mm larger than the defect diameter measured by angiography.

For the ADO II, the device size is usually 1–2 mm larger than the defect diameter.

In the case of perimembranous VSDs, the distal diameter of the device should be at least twice the minimal diameter of the VSD on the right ventricular side and 1–2 mm greater than the diameter of the VSD on the left ventricular side.

Oversizing can lead to complications like atrioventricular block or valve issues. Therefore, careful assessment and device selection are crucial [24].

Echocardiography: Echocardiography is essential for accurate sizing. It helps determine the defect's diameter, which guides device selection. For perimembranous VSDs, the device's distal diameter should be at least twice the defect's minimal diameter on the right ventricular side and 1–2 mm larger than the diameter on the left ventricular side.

Angiography: Angiography can also be used to assess the defect's size. Generally, the device is chosen to be 2–4 mm larger than the defect diameter measured by angiography for symmetric and eccentric occluders and 1–2 mm larger for the ADO II.

7.4 Long-term outcomes

Long-term outcomes are generally positive, with most patients experiencing significant improvements in heart function and a low incidence of severe complications. However, the risk of arrhythmias and other cardiac issues may persist, particularly in older patients [11, 21].

8. Techniques and catheters for vascular access in retrograde and Antegrade approaches

The techniques and catheters necessary for obtaining vascular access in several locations during the performance of a catheter-based closure of ventricular septal defects are extensive and vary according to the age, size, and weight of the pediatric patient. There are two types of techniques for catheter-based closure of ventricular septal: retrograde access in the venous system and antegrade arterial access, depending on the clinical and morphological situation and the morphology of the septal defect to be closed, and ability to cross from right, which may not allow the use of the retrograde technique.

The antegrade access in a transarterial technique is a hydrophilic tip ultra-soft wire to go through the aortic arch to the heart, especially in children with less than 10 kg body weight. The use of micropuncture kits allows percutaneous puncture of an arterial or venous vessel. Several catheters can be used with different guiding and supporting devices. Then, ventriculography was performed using a pigtail catheter to clearly visualize the defect located in the left anterior oblique (LAO) position with cranial angulation. The diameter of VSD and its relation to the aortic valve were confirmed. VSD diameter was determined using transthoracic echo (TTE) and/or transesophageal echo (TEE) and angiography images. The defect was passed with an exchangeable 0.035-inch angulated floppy hydrophilic guide wire (Radiofocus, Terumo cooperation, Tokyo, Japan) from the left ventricle through a diagnostic coronary artery catheter (mostly Judkins right, Amplatz right catheter, Medtronic, Minnesota, USA). The catheter was advanced to the pulmonary artery (PA) or superior vena cava (SVC) or, less frequently, to the inferior vena cava using a hydrophilic wire, then started from the venous side, and then the loop was completed.

Eventually, the looping is made with the catheter, then, stiff wire introduces from the right side to the left side through the femoral artery and the only stiff wire left

eventually, the long sheath for the device introduced from the right side by cross the defect from right either to aorta or left ventricle (LV) directly then the device will be advanced through the long sheath eventually the left disc with be opened in left side then right disc on the right for securing the device in place (**Figure 1**).

The retrograde technique for closing a ventricular septal defect (VSD) is a specialized procedure used when traditional methods are not appropriate. It starts similarly to other catheter-based approaches, typically gaining access through the femoral vein. However, in this technique, the catheter is advanced through the heart and crosses the VSD from the right ventricle into the left ventricle. Once in position, the catheter tip can be placed in one of two locations: LV Apex: The tip is positioned at the apex, which is the bottom point of the left ventricle. Ascending Aorta: The catheter can be advanced further across the aortic valve and positioned in the ascending aorta, the large blood vessel that exits the left ventricle. For added stability, the tip may be maneuvered further into the descending aorta, the part of the aorta that curves downward. After securing the catheter tip in the desired location, a stiff guidewire is inserted through it, eliminating the need for a snare, which is a small loop typically used to capture and guide wires within the heart. This guidewire provides support and allows for the advancement of a long sheath and dilator over it, creating a stable pathway for delivering the VSD closure device. Finally, the device is deployed. The left disc of the device opens first, either in the ascending aorta or at the apex of the left ventricle, depending on the catheter's position. The right disc then opens on the right side of the ventricle, effectively sandwiching the VSD between the two discs and closing the defect (**Figures 2** and **3**).

8.1 Advantages of retrograde approach

Device compatibility: The retrograde approach is compatible with devices like the Amplatzer Vascular Plug II, which is effective for large perimembranous VSDs with inlet-to-outlet extension [25].

Success rates: Retrograde closure has shown high success rates in specific cases, such as perimembranous VSDs, with devices like the Amplatzer Duct Occluder II and the KONAR-MF™ VSD occluder achieving high implantation success [23].

8.2 Limitations of retrograde approach

Procedural complexity: The retrograde approach often involves longer procedural times and increased use of fluoroscopy and contrast dye, which can lead to higher radiation exposure and potential renal complications [26].

Technical challenges: It may be technically challenging in cases with deficient subaortic rims, limiting its applicability in certain anatomical configurations [23].

8.3 Advantages of antegrade approach

Higher success rates: The antegrade approach has demonstrated higher technical and procedural success rates compared to the retrograde approach, with a 5% higher likelihood of technical success and 14% higher odds of procedural success [27].

Lower risk of adverse events: It is associated with lower risks of major adverse cardiac events, all-cause mortality, and myocardial infarction [27].

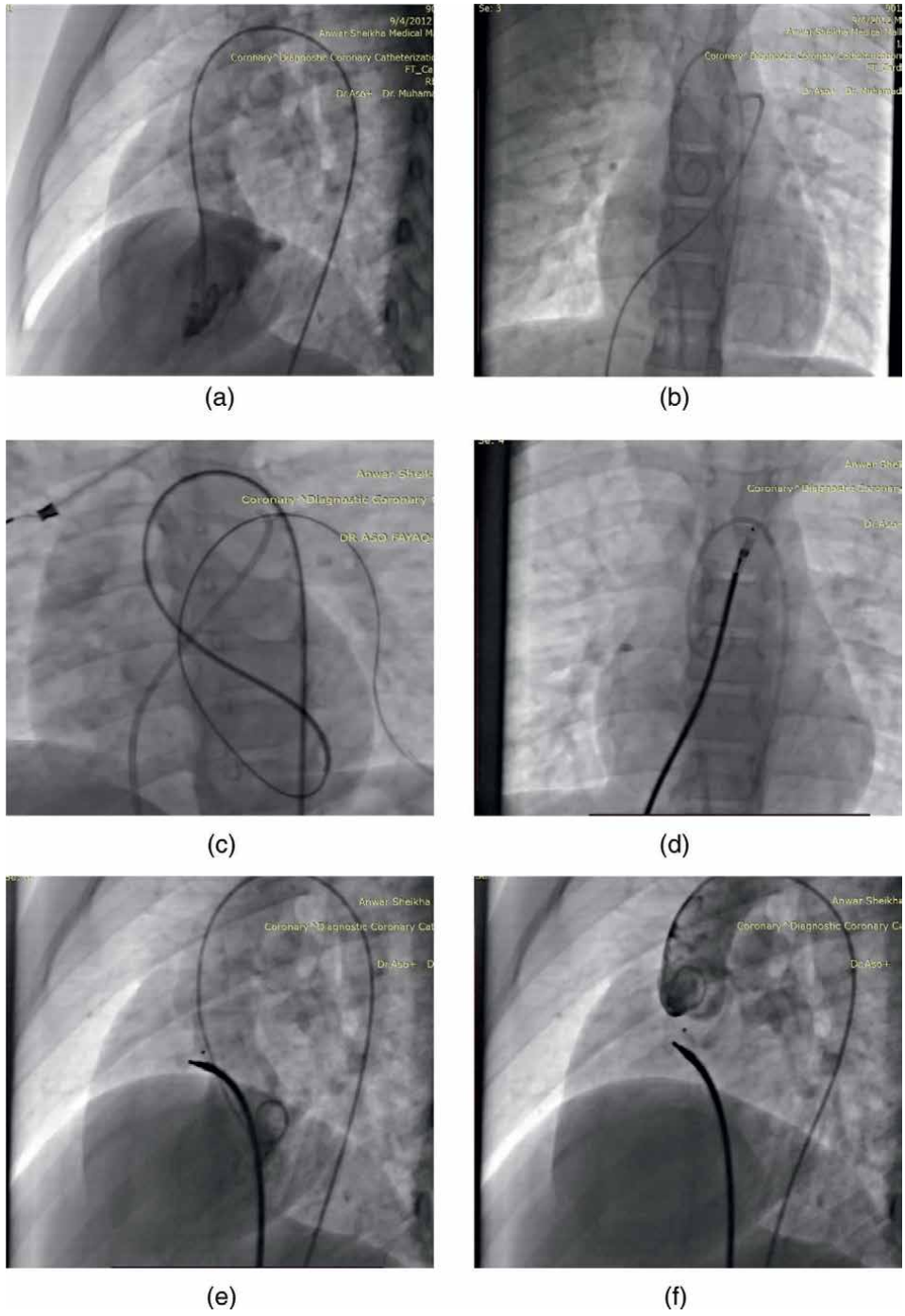

Figure 1.
Stepwise percutaneous VSD closure technique VSD occluder. (a) LV angiography showing subaortic VSD. (b) Crossing the PA and putting the catheter in the pulmonary artery. (c) Snaring the pulmonary wire via *venous access. Making the AV loop from arterial and venous access. (d) Crossing the VSD by a long sheet and into the descending aorta. (e) Releasing the first disc of the device with LV angio. (f) Performing aortogram to check for the aortic valve state.*

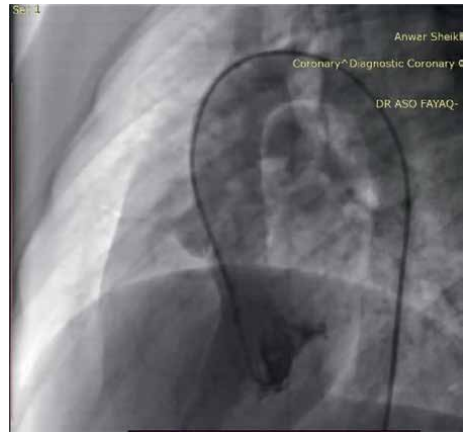

Figure 2.
LV angio for the VSD.

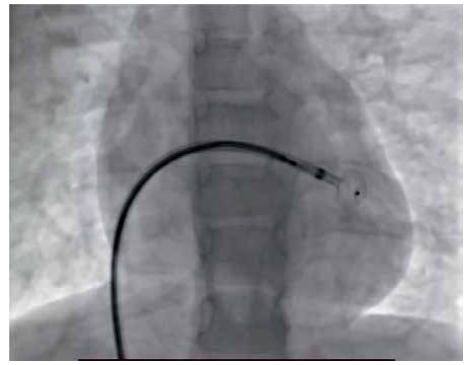

Figure 3.
Crossing from right side to apex of the LV.

8.4 Limitations of antegrade approach

Anatomical limitations: The antegrade approach may not be suitable for all anatomical variations, particularly in complex lesions where the retrograde approach is preferred [25, 27].

While the retrograde approach offers advantages in handling complex lesions and specific device compatibility, it is often limited by procedural complexity and anatomical challenges. Conversely, the antegrade approach provides higher success rates and safety but may not be suitable for all anatomical configurations. The choice between these approaches should be guided by the specific clinical scenario, patient anatomy, and available resources.

9. Clinical outcomes and risk assessment

Catheter-based closure for VSD has shown promising outcomes. The successful closure rate approaches 100%. Several studies have demonstrated its efficacy in increasing O_2 saturation in the lower chamber and reducing left-to-right shunt,

subsequently normalizing the PVR for open-heart surgery before complete repair with closure of VSD. In comparison to surgical closure, both its short- and long-term prognosis, even in adults, are now very favorable. Several previous reports have shown "minimal" to "no" or "rare" mortality associated with OHS or device occlusion procedures. A study states minimal procedural mortality of 1.3% and zero OHS mortality from 9.1 years of follow-up [26].

The MODULATE trial focuses on the interventional closure of ventricular septal defects (VSDs), particularly perimembranous VSDs, using various transcatheter techniques. This approach has gained traction due to its minimally invasive nature, which contrasts with traditional surgical methods that involve significant risks and recovery times. The trial highlights the effectiveness and safety of these interventions, showcasing promising outcomes.

9.1 Short-term prognosis

Success rates: Device closure of VSDs has shown high success rates, with studies reporting successful closure in 87–100% of cases [14, 28, 29]. The use of the Nit-Occlud® Lê VSD coil system demonstrated a high success rate, achieving complete closure in 98.6% of patients at 5 years [21]. Transcatheter closure of perimembranous VSDs with PDA I device showed a 92.6% success rate with minimal complications [30].

Amplatzer PIVSD Occluder and Konar-MF Occluder have shown high success rates in closing VSDs, with reported closure rates of 93 and 98.6%, respectively [31, 32].

Complications: Short-term complications are generally minor, including transient arrhythmias, residual leaks, and device embolization, with major complications being rare [14, 29]. Long-term complications such as valve regurgitation or rhythm disturbances are rare, and most patients do not experience significant issues [31].

Serious adverse events were reported at a rate of 3.5%, with no permanent atrioventricular block observed [21].

The MIPDO method exhibited comparable safety to surgical closure, with reduced procedural duration and hospitalization costs [33].

Device embolization occurs in less than 2% of cases [17, 32].

Recovery: Patients typically experience quick recovery times, with short ICU stays and minimal need for inotropic support or blood transfusions [28].

9.2 Long-term prognosis

Residual shunts: Long-term follow-up shows a reduction in residual shunts, with some studies reporting complete occlusion in the majority of patients [30].

Survival rates: The mortality rate post-procedure remains low, emphasizing the safety of transcatheter methods [17].

9.3 Factors influencing prognosis

Device type: The choice of device can influence outcomes, with some devices associated with higher complication rates in certain patient groups [14].

VSD size: Larger VSDs are more likely to result in residual shunts post-procedure, impacting long-term outcome [34].

10. Examples of challenging case approaches

Challenging cases approached in ventricular septal defects (VSD) closure are numerous in the literature. A recent review of VSD device closure showed that fewer than 1700 cases can be considered difficult or extremely challenging worldwide. Historical data on interventional VSD closure (IVSDC) report a mortality rate for the procedure of 2.7%. Given the wide range and variety of VSDs, it is impossible to standardize the procedure. Knowledge of the complications is mandatory, as is the learning curve, of which continuing education is an integral part.

10.1 Advanced techniques in VSD closure

10.2 "Peanut approach"

The "peanut approach" is a technique used in VSD closure where the device is maneuvered through the defect with a twisting motion, resembling the shape of a peanut. This approach can be helpful in challenging cases where the device needs to navigate around anatomical obstacles.

10.2.1 Aortic root catheter manipulation

Aortic root catheter manipulation is an advanced technique used to exchange devices or reposition catheters during VSD closure. This technique allows for greater flexibility and precision in complex cases. For instance, in cases of VSD with aortic valve prolapse, the Amplatzer Duct Occluder can be utilized with this technique. Before detaching the device, it is crucial to evaluate its position relative to the free atrial wall and the aortic root using echocardiography to ensure proper placement and avoid complications.

10.3 Strategies for addressing prolapsed aortic cusp during ventricular septal defect closure

In patients with large VSDs, attempts to close the hole can cause prolapse of the non-coronary commissure of the aortic valve, resulting in acute severe aortic regurgitation and hemodynamic compromise. This is an important clinical problem that is often unrecognized. Larger VSDs present with prolapse of the aortic cusp. Pacing maneuver is important to gauge the effect of closure and plan accordingly. Abdominal breathing is often seen to reduce cusp-related issues intra-procedurally.

A 14-year-old male with a known moderate perimembranous ventricular septal defect (VSD) and mild aortic valve prolapse presented with mild exercise-induced dyspnea but was otherwise asymptomatic. Examination revealed a holosystolic murmur, and investigations confirmed a 6 mm VSD with a left-to-right shunt and mild aortic regurgitation.

Management: Percutaneous closure was chosen, which is a minimally invasive procedure compared to open-heart surgery.

Device: Amplatzer Vascular Plug II. This is a commonly used device for closing VSDs.

Procedure: Performed under general anesthesia with fluoroscopic and transesophageal echocardiographic guidance to ensure accurate device placement.

Outcome:

Successful closure: The VSD was completely closed with no residual shunt.

Preservation of aortic valve function: The procedure did not worsen the aortic valve prolapse or regurgitation.

Symptom resolution: The patient's exertional dyspnea resolved.

Good follow-up: Echocardiograms at 1 and 3 months confirmed the device's stability and normal heart function.

Teaching points:

This case highlights the effectiveness of percutaneous closure for suitable VSDs.

It emphasizes the importance of careful patient selection and meticulous technique to avoid complications, especially in cases with associated valve abnormalities.

The case also demonstrates the value of echocardiography in diagnosis and follow-up.

This case report provides a good example of a successful intervention for a case with VSD, prolapsed coronary cusp, and is regarded as a difficult case to manage (**Figures 4** and **5**).

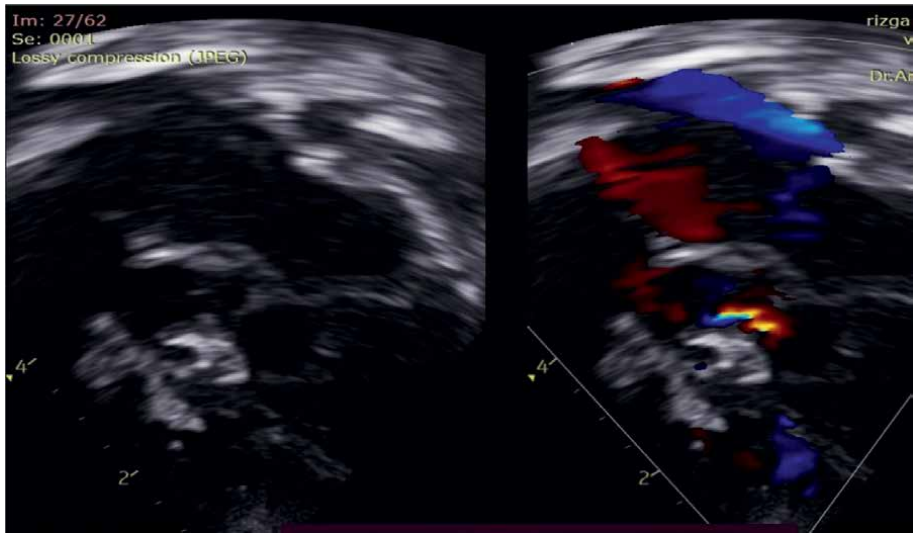

Figure 4.
Subcostal echocardiography shows the device in place with mild aortic incompetence.

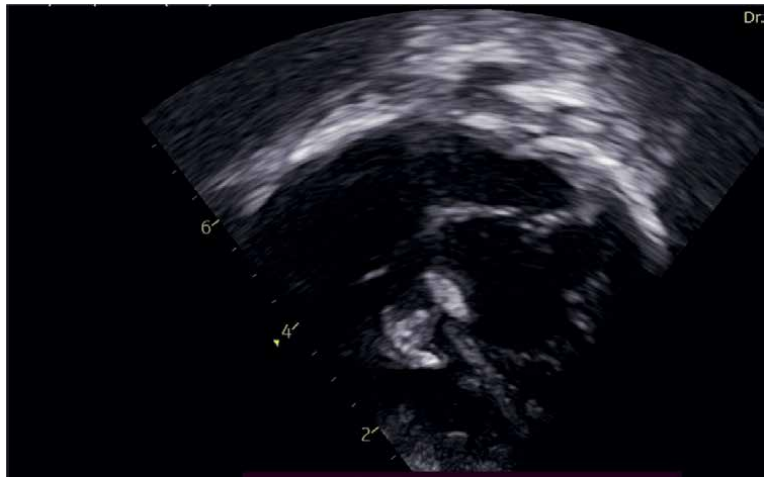

Figure 5.
Subcostal view showing PDA II Amplatzer device in place.

Author details

Aso F. Salih[1,2]

1 Clinical Science Department, College of Medicine, University of Sulaimani, Al-Sulaymaneyah, Iraq

2 Anawar Shexa Medical City, High Quality Hospital, Al-Sulaymaniyah, Iraq

*Address all correspondence to: aso.salih@univsul.edu.iq

IntechOpen

References

[1] Salih A, Othman N, Kamal N. Incidence and types of congenital heart diseases among children in Sulaimani governorate. Kurdistan Journal of Applied Research. 2017;**2**(2):106-111

[2] Salih A. Effects of ventricular septal defect on children's growth pattern in Slemani pediatric teaching hospital. Pediatrics & Therapeutics. 2015;**5**(4):1-4

[3] Rathod RH, Powell AJ. Congenital heart disease: Indications, patient preparation, and simple lesions. In: Kwong RY, Jerosch-Herold M, Heydari B, editors. Cardiovascular Magnetic Resonance Imaging. New York, NY: Springer New York; 2019. pp. 359-379

[4] Dawood AK. Review of surgery of VSD in Ibn Al-Nafees teaching hospital. Journal of the Faculty of Medicine Baghdad. 2015;**57**(2):99-102

[5] Kuribayashi R, Sekine S, Aida H, Seki K, Meguro A, Shibata Y, et al. Long-term results of primary closure for ventricular septal defects in the first year of life. Surgery Today. 1994;**24**(5):389-392

[6] Holzer RJ, Ahmad S, Hijazi ZM. Surgical strategies and novel alternatives for the closure of ventricular septal defects. Expert Review of Cardiovascular Therapy. 2016;**14**(7):831-834

[7] Banday MJ, Bansal D, Bhushan R, Jhajhria NS, Grover V, Gupta V. Surgical closure of VSD in infants: Results in our Centre over 4 years. Journal of Medical Science And clinical Research. 2019;**7**

[8] Suxuan L, Feng C, Xueyan D, Zhenzhen Z, Wen K, Yan Y, et al. Comparison of results and economic analysis of surgical and transcatheter closure of perimembranous ventricular septal defect. Eur J Cardiothorac Surg. 2012;**42**(6):e157-e162

[9] Jessica NS, Michael DS. Lower hospital charges and societal costs for catheter device closure of atrial septal defects. Pediatric Cardiology. 2017;**38**(7):1365-1369

[10] Anton M, Doss M, Dogan S, Aybek T, Wimmer-Greinecker G. Interventional versus surgical closure of atrial and ventricular septal defects: Advantages and limitations of the catheter-based approach. Journal of Interventional Cardiology. 2000;**13**(4):235-244

[11] Bergmann M, Germann CP, Nordmeyer J, Peters B, Berger F, Schubert S. Short- and long-term outcome after interventional VSD closure: A single-center experience in pediatric and adult patients. Pediatric Cardiology. 2020;**41**(5):1087-1096

[12] Goodacre S, Campbell M. Lowering Bed Occupancy: A Life-Saving Intervention? BMJ Publishing Group Ltd and the British Association for Accident. London, UK; 2016. p. 84

[13] Horst S. Interventional versus surgical closure of atrial and ventricular septal defects: Advantages and limitations of the catheter-based approach. Journal of Interventional Cardiology. 2000;**13**(6):493-501

[14] Abdel-Latif D, Mamdouh N, El-Sayed E. Device closure of ventricular septal defect: A retrospective study at pediatric cardiac unit, pediatrics hospital. Ain Shams University. QJM. 2024;**117**(4):289-294

[15] Alizadehasl A, Sadeghpour A. Transcatheter Closure of the Ventricular Septal Defects. Boston, US: Springer; 2013

[16] Akbar ZA, Meraji SM, Zanjani KS, Aghayan MRM. Device occlusion versus surgery for closure of congenital heart defects: Cost issues in Iran. The Journal of Tehran University Heart Center. 2007;**3**(3):141-144

[17] Abdelmohsen G, Gabel H, Al-Ata J, Bahaidarah S, Alkhushi N, Abdelsalam M, et al. Percutaneous closure of postoperative residual ventricular septal defects, including dehiscence of surgical patches. Cardiovascular Diagnosis and Therapy. 2023;**13**(4):1014-1022

[18] Mirza MK, Abqari S, Haseen A, Yadav M. Transcatheter closure of ventricular septal defects: Preliminary results in children weighing 10 kg or less. Cardiology in the Young. 2023;**33**(4):539-545

[19] Salsabila NN, TSN H, Lefi A. Characteristics of patients with ventricular septal defect that had been closed with transcatheter in Dr. Soetomo general hospital from January 2019 to December 2021. International Journal of Research Publications. 2022;**114**(1):121-125

[20] Muroke V, Jalanko M, Pihkala J, Hartikainen J, Tahvanainen A, Airaksinen J, et al. Outcome of device atrial septal defect closure in different age groups: A nationwide cohort study. European Heart Journal. 2022;**43**:4124-4131

[21] Kozlik-Feldmann R, Lorber A, Sievert H, Ewert P, Jux C, Müller G, et al. Long-term outcome of perimembranous VSD closure using the nit-Occlud® Lê VSD coil system. Clinical Research in Cardiology. 2021;**110**:1447-1457

[22] Tamimi MM, Al-Mutairi M, Alomrani A. Outcome of ventricular septal defect closure with the nit-Occlud® Le VSD-coil: Single centre experience. Sudanese Journal of Paediatrics. 2021;**21**(2):172-178

[23] Haddad RN, Saliba ZS. Comparative outcomes of two competitive devices for retrograde closure of perimembranous ventricular septal defects. Frontiers in Cardiovascular Medicine. 2023;**10**:1215397

[24] Wang F, Wang W, Wu Q, Cao Y, Huang H, Tao E, et al. Summary of the experiences and results of transesophageal ultrasound-guided ventricular septal defect and atrial septal defect closure operation. The Heart Surgery Forum. 2022;**25**(5):E638-Ee44

[25] Piccinelli E, Bautista-Rodriguez C, Fraisse A. Transcatheter closure of large perimembranous ventricular septal defects with inlet to outlet extension with the Amplatzer vascular plug-II. Cardiology in the Young. 2023;**33**(6):1018-1022

[26] Abdelaziz A, Hafez A, Atta K, Elsayed H, Elaraby A, Ibrahim A, et al. Antegrade approach versus retrograde approach percutaneous coronary intervention for chronic total occlusion: An updated meta-analysis. Current Problems in Cardiology. 2024;**49**(12):102832

[27] Tabowei G et al. Comparison of clinical outcomes between antegrade and retrograde techniques for chronic total occlusion revascularizations: A systematic review and meta-analysis. Cureus. 2024;**16**(8):e66213

[28] Omelchenko O, Shah N, Jha N, Girgius A, Montiel J, Rajkumar B. Safety and efficacy of perventricular device closure of ventricular septal defects in children. European Heart Journal. 2024;**45**(48):4761-4769

[29] Imtiaz S, Rafique S, Akhtar K, Mehmood A, Akbar H, Ara A, et al. Short term outcomes of transcatheter ventricular septal defect device closure at tertiary cardiac care center. Pakistan Armed Forces Medical Journal. 2023;**73**(Suppl. 3):10661

[30] Nguyen C. Transcatheter closure of perimembranous ventricular septal defects by coils. Vietnamese Journal of Cardiothoracic and Vascular Surgery. 2023;**43**(1):1032

[31] Laha S, Gangopadhyay D, Roy M, Singh A, Nandi D, Dutta J. Procedural outcomes of percutaneous closure of perimembranous and other ventricular septal defects using Konar-MF occluder and short-term follow-up. Annals of Pediatric Cardiology. 2024;**17**(2):101-108

[32] Ghosh B, Sahai I, Agrawal G, Khadase S, Rao T, Lohakare A, et al. Experience of percutaneous closure of ventricular septal defects in 140 patients with different duct occluders in a tertiary care rural hospital in Central India. Cureus. 2023;**15**(12):e42591

[33] Lu W, Zhang F, Fan T, Zhao T, Han Y, Hu X, et al. Minimally-invasive perventricular device occlusion versus surgical closure for treating perimembranous ventricular septal defect: 3-year outcomes of a multicenter randomized clinical trial. Journal of Thoracic Disease. 2021;**13**(11):6871-6881

[34] Ouf R, Abdallah D. Predictors of residual VSD after surgical versus transcatheter closure. Journal of Medical Science Research. 2024;**7**(1):12

Chapter 4

Echocardiographic Strain Imaging in Pediatrics

Teja Senekovič Kojc and Nataša Marčun Varda

Abstract

Recent advances in cardiac imaging have enabled a more detailed and comprehensive evaluation of myocardial performance in the pediatric population, which allows the identification of early heart damage that was not identified by traditional echocardiographic methods. Strain imaging represents an innovative, quantitative echocardiographic method that facilitates the assessment of both global and regional myocardial functions with enhanced precision. Furthermore, this technique holds significant potential for the early detection of ventricular dysfunction, particularly in clinical scenarios where traditional imaging methods may lack reliability. Notably, strain imaging does not depend on geometric assumptions, thereby enabling accurate quantification of both regional and global ventricular functions. In the past, echocardiographic strain imaging has been used mainly as a research tool in interrogating early subclinical impairment of the systemic left ventricle. Due to the possibility of widespread use in patients with congenital heart disease and in patients with other chronic diseases potentially affecting the heart, there are growing opportunities for clinical use. It is time for pediatric cardiologists to consider incorporating echocardiographic strain imaging into the clinical management algorithm. In conclusion, we present the possibilities of using echocardiographic strain imaging in pediatrics.

Keywords: echocardiography, strain imaging, pediatrics, congenital heart disease, heart failure, cardiomyopathy, hypertension

1. Introduction

Strain imaging (SI) is an echocardiographic method used to assess the deformation (strain) of the heart muscle during its contraction and relaxation. This method provides valuable insights into the heart's function, especially in cases where traditional methods with ejection fraction (EF) might not give a complete picture of cardiac condition [1, 2]. SI is a noninvasive method of evaluating myocardial function using speckle-tracking imaging (STI), also known as speckle-tracking echocardiography (STE), which analyzes the movement of speckles within the heart muscle during the cardiac cycle [2]. It tracks how the heart muscle fibers shorten, lengthen, and twist as the heart pumps blood. With the resulting data, we could assess the strain (the amount of deformation) of the myocardial tissue. Strain values provide an understanding of the heart's

performance, even in cases where traditional parameters might appear in the normal range, but subtle functional abnormalities are present. Detecting early signs of heart disease with quantitative information about cardiac strain makes this method extremely valuable in assessing cardiac function, monitoring disease progression, and evaluating treatment outcomes [1, 2]. The main types of myocardial strain are longitudinal strain (measures deformation along the long axis of the heart, from base to apex), radial strain (measures deformation in the radial direction, toward or away from the center of the heart), and circumferential strain (measures deformation in the circumferential direction, around the heart) [2, 3].

2. Speckle-tracking imaging

STI is an echocardiographic technique that follows the movement of speckles, which results in measuring the strain, correlating well with the structural changes of the heart muscle. The speckles are small acoustic markers that appear in ultrasound images due to the scattering of sound waves by tissues in the heart. These speckles are granular patterns unique to the tissue being imaged. We can obtain valuable information about cardiac function by tracking their movement throughout the cardiac cycle. Specific software systems can calculate how much the heart muscle deforms during the cardiac cycle. The strain is often measured in longitudinal, circumferential, and radial directions. Global longitudinal strain (GLS), as a new global parameter of left ventricular longitudinal deformation, demonstrates superior sensitivity for the early detection of myocardial dysfunction compared to conventional echocardiographic parameters of systolic function. Myocardial deformation parameters possess both diagnostic and prognostic utilities across a broad spectrum of cardiac pathologies, enhancing clinical decision-making and risk stratification [2, 4].

The main technical stages of STI:

- Speckles

  When an ultrasound pulse is directed at the heart muscle, the resulting image contains tiny patterns (speckles) that are caused by the interference of the ultrasound waves with tissue. These speckles are used as markers that represent the movement of the heart muscle during the cardiac cycle.

- Tracking

  The software used in speckle tracking follows the movement of the speckles frame by frame, from one point in the heart muscle to the next, throughout the systole (contraction) and diastole (relaxation). This data allows the calculation of myocardial deformation.

- Deformation (strain)

  The main output from speckle tracking is strain, which refers to how much the myocardial fibers stretch or shorten during each heart cycle. Positive strain indicates stretching (typically seen in the endocardial layer), and negative strain indicates shortening (typically seen in the epicardial layer) [1, 2].

Key parameters of STI:

- Longitudinal strain

  Longitudinal strain measures the deformation along the long axis of the heart (from the base to the apex of the heart). It correlates well with changes in myocardial function; therefore, it is commonly used in clinical practice.

- Radial strain

  Radial strain measures the change in thickness of the myocardial wall. It assesses how the heart muscle expands and contracts in a direction perpendicular to the wall.

- Circumferential strain

  Circumferential strain measures the deformation in a direction around the heart, assessing how the muscle fibers contract and relax in a circular motion.

- Strain rate

  This is the rate at which strain changes over time. It provides a dynamic picture of myocardial motion during the cardiac cycle.

- Twist and torsion

  Speckle tracking can also be used to assess the rotational motion of the heart, which involves how the left ventricle twists during contraction and untwists during relaxation. This is important in assessing global myocardial function [5, 6].

- Global longitudinal strain (GLS)

  GLS value is defined as the average peak longitudinal strain of the left ventricle as a measure of global left ventricular function [5, 6]. Standard apical two-, three-, and four-chamber echocardiographic views are used for measuring GLS. The timing of end-systole is determined by the point of aortic valve closure, ensuring accurate temporal alignment for strain analysis [2]. Normal GLS in healthy individuals is reported between 18% and 25% for most echocardiographic systems; a variation may be explained by inter-software and inter-vendor variability [2, 3, 7, 8].

3. Advantages of strain imaging

SI has many advantages that stimulate wider clinical use. Firstly, it provides a noninvasive way to monitor heart function, which is ideal for children who may not tolerate invasive tests or require general anesthesia to perform some cardiac diagnostic tests. In the context of clinical decisions, the main advantage of this method is high sensitivity in the early detection of myocardial dysfunction. Unlike traditional echocardiographic methods, which do not always detect subtle changes, SI can identify

myocardial dysfunction early, even without changes in EF or other conventional echocardiographic parameters. Moreover, SI provides objective, reproducible, and quantitative data on myocardial deformation, making it a valuable tool for clinical decisions. At the same time, it enables a detailed assessment of myocardial mechanics. Measuring strain in multiple directions (longitudinal, circumferential, and radial) offers a comprehensive picture of myocardial performance, which helps recognize the affected areas of the heart. Ultimately, all of the above influence clinical decisions regarding additional diagnostic tests and treatment options. The extra value of SI is its reproducibility and use as a bedside test. Therefore, it is often used to monitor disease progression and response to therapy over time [1, 6, 9, 10].

4. Limitations of strain imaging

The most evident obstacles to widespread use of SI are technical limitations. While SI is becoming increasingly used, the technique requires advanced equipment and skilled operators to obtain reliable data. Not all medical centers, especially those in low-income countries, may have the advanced echocardiographic equipment necessary to perform SI. It requires highly skilled operators and advanced software to ensure accurate measurements. Inaccurate tracking of speckles or improper analysis can lead to unreliable results. In pediatrics, some age-related conditions that affect the interpretation of echocardiographic measurements are especially challenging. Infants and very young children have smaller, faster-beating hearts that can make accurate measurements more difficult. SI requires high-quality echocardiographic images and appropriate settings. Furthermore, movement and cooperation are also challenging in young children. Not all pediatric patients can remain still during the echocardiographic procedure, making it harder to get accurate strain measurements. Finally, a lack of age-related norms can make clinical decisions difficult. While SI is increasingly being used in pediatric cardiology, age-specific reference values for strain and strain rates are still being developed. Therefore, getting accurate strain reference values for different age groups in children is an ongoing area of research. Pediatric strain norms are less well-established than those in adults, which can make interpretation of results challenging [3, 11, 12].

GLS, as a main parameter of left ventricular function, may be subject to various limitations. These include dependency on geometric assumptions, suboptimal

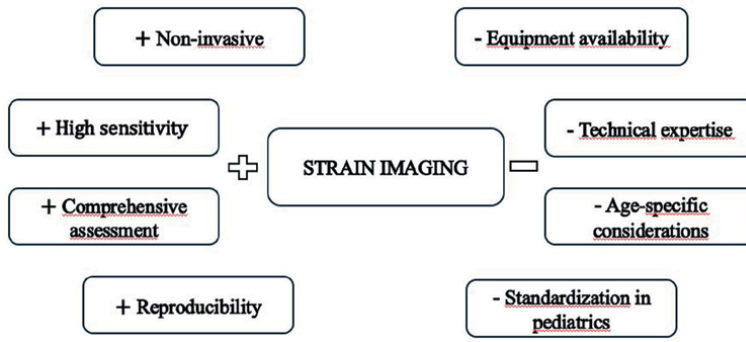

Figure 1.
The advantages and limitations of SI in pediatrics.

acoustic windows, measurement inaccuracies resulting from inadequate image optimization, and errors in myocardial tracking throughout systole. Additionally, GLS values can vary with patient-specific factors such as age, sex, and hemodynamic loading conditions. Minor discrepancies also exist between different ultrasound vendors; consequently, updated software versions have been developed to enhance inter-vendor consistency and improve standardization of GLS measurements [10, 13]. The main advantages and limitations of SI are presented in **Figure 1**.

5. Clinical applications of strain imaging in pediatrics

SI allows wide clinical use as long as the operator is sufficiently skilled in technical performance and interpretation of the results. The most used clinical application of SI is the assessment of cardiac function, with the extra benefit of detecting early signs of myocardial dysfunction before noticeable changes in traditional measurements such as EF [3]. This is especially useful for children with congenital heart disease (CHD), cardiomyopathies (congenital or acquired), post-cardiac surgery follow-up, and chemotherapy-related cardiotoxicity. SI can help monitor the progression of conditions like heart failure (HF), where changes in myocardial strain can be detected early before traditional measurements show changes. In conditions like HF or myocarditis, SI can be a prognostic tool, offering insights into how well the heart will function in the future. Therefore, SI is not only used for monitoring disease progression but also for predicting outcomes [2]. In pediatrics, the noninvasive evaluation of cardiac function and assessment of cardiac mechanics are extremely valuable for clinical praxis. With appropriate knowledge of SI, we can avoid time-consuming invasive procedures and general anesthesia with possible medical complications.

Applications for SI in clinical practice:

5.1 Congenital heart disease (CHD)

Children with CHD can benefit from SI by monitoring subtle changes in cardiac function that may not be detectable with conventional echocardiography. This is particularly important in children who have undergone cardiac surgery or have complex congenital defects like Tetralogy of Fallot (TOF) or transposition of the great arteries (TGA). For patients with CHD or those with repaired CHD, SI offers insights into myocardial function that might be difficult to evaluate with traditional methods. While EF is a common measure of cardiac function, it does not always detect subtle abnormalities in cardiac function. SI can detect changes in strain even when EF is still normal, allowing early detection of dysfunction. Post-surgical assessment of myocardial function is often difficult. Therefore, SI is a valuable additional echocardiographic tool to provide an accurate evaluation of ventricular function and the heart's recovery over time [2, 3]. SI has been increasingly utilized to evaluate myocardial performance across pediatric, adolescent, and adult populations with a wide range of congenital and acquired cardiovascular diseases. Its application provides valuable insights into myocardial mechanics beyond those offered by conventional echocardiographic assessments. Two-dimensional STI has emerged as the technology of choice for assessing myocardial strain in various CHDs [3].

SI is commonly used in patients with TOF to assess ventricular function. Dysfunction of both the right and left ventricles remains a significant concern even after surgical repair. Adverse remodeling of the right ventricle, often secondary to

chronic pulmonary regurgitation, the placement of a transannular patch, electromechanical dyssynchrony, or myocardial fibrosis, can lead to progressive impairment of right ventricular function. Furthermore, interventricular dependence (commonly referred to as ventricular-ventricular interaction) may exacerbate this condition by contributing to subsequent left ventricular dysfunction, thereby amplifying the overall hemodynamic compromise [3]. Data on using SI to assess cardiac mechanics, as well as its clinical and prognostic value, are steadily increasing. Numerous studies have explored the application of SI in evaluating ventricular mechanics. This includes the interplay between right and left ventricular deformation, alterations in ventricular strain parameters following pulmonary valve replacement, and the associations between biventricular deformation metrics and clinical outcomes in patients with repaired TOF. Understanding these relationships is critical for risk stratification, timing of intervention, and long-term management in this patient population [14]. Scientific evidence has demonstrated a significant reduction in both global and regional right ventricular systolic strain and strain rates in patients with repaired TOF [15–18]. Impairment of right ventricular deformation has been associated with reduced right ventricular EF, ventricular dyssynchrony, and greater severity of pulmonary regurgitation [19, 20]. There is also a notable reduction in left ventricular systolic longitudinal, circumferential, and radial strain in patients with repaired TOF [3, 19, 20]. Correlations between left and right ventricular strain parameters provide compelling evidence of ventricular-ventricular interaction in these patients. Dysfunction in one chamber can adversely affect the performance of the other, further complicating the overall cardiac function and influencing clinical outcomes. However, there are inconsistent results of the impact of pulmonary valve replacement on right and left ventricular strain [21, 22]. Some studies have found associations between left ventricular GLS and right ventricular free wall longitudinal strain and adverse cardiovascular outcomes, including sudden cardiac death, HF, and life-threatening ventricular arrhythmia [3, 23].

In patients with pulmonary atresia with intact ventricular septum (PAIVS) and severe pulmonary stenosis, the hypertrophied myocardium, coupled with varying degrees of endocardial fibroelastosis, may serve as anatomical substrates that contribute to restrictive right ventricular physiology. The studies have shown impairment of right ventricular systolic and diastolic strain in patients after biventricular repair of PAIVS [24]. Patients with a restrictive right ventricular physiology had lower right ventricular GLS and lower right ventricular systolic and early diastolic strain rates compared to those without restrictive right ventricular physiology. These findings suggest that assessing the right ventricular diastolic strain may be a valuable tool in evaluating diastolic function, providing additional insights into right ventricular performance [24, 25].

Dysfunction of the systemic right ventricle is an important concern in patients after the Senning/Mustard procedure for complete TGA [26]. Anatomic, hemodynamic, and surgical factors and the fibrotic myocardium may contribute to systemic right ventricular dysfunction. Systemic right ventricular longitudinal strain and strain rate were found to correlate with cardiac magnetic resonance-derived systemic right ventricular EF [27]. Furthermore, only systemic right ventricular GLS, but not EF, showed a significant correlation with functional capacity as measured by peak oxygen uptake during exercise testing [28]. SI can also help to define the magnitude of intra-systemic right ventricular and inter-ventricular mechanical delay [28, 29], which may negatively influence systemic right ventricular EF and exercise tolerance with overall functional capacity [29]. Additionally, SI studies have revealed an unfavorable systolic

and diastolic interaction between the subpulmonary left ventricle and the systemic right ventricle. This maladaptive ventricular interaction contributes to altered hemodynamics [29]. The systemic right ventricular GLS is increasingly utilized as a prognostic marker to predict the adverse clinical outcomes in patients following atrial switch operations. It has been shown to correlate with the symptomatic progression to worse functional classes, the development of cardiac arrhythmias, and increased mortality, thus serving as a valuable tool for risk stratification and long-term management [30].

Patients with coarctation of the aorta or other pathology of the aortic arch may also benefit from SI performed before and after the surgery. Structural changes of the aorta and stiffening of the central arteries persist despite successful interventions for coarctation of the aorta [31]. In these patients, increased afterload may detrimentally affect ventricular-arterial coupling, leading to impaired hemodynamic efficiency. Previous studies have demonstrated a reduction in systolic longitudinal and radial strain, while circumferential strain appears relatively preserved. This strain pattern likely reflects adaptive remodeling mechanisms aimed at maintaining ventricular function despite chronic pressure overload [32]. Obese patients were found to exhibit greater impairment in left ventricular myocardial deformation across the longitudinal, radial, and circumferential dimensions [33].

Impairment of myocardial strain was visible in patients with functional single ventricles of either the right or left ventricular morphology [34]. After the Fontan procedure, there is characteristic systolic and diastolic ventricular dysfunction of the functional single ventricle [35]. In patients after the Fontan procedure due to tricuspid atresia, reduction of global systemic left ventricular longitudinal, circumferential, and radial strain and systolic and diastolic strain rates was documented. Also, evidence of mechanical dyssynchrony was found in about half of Fontan patients with tricuspid atresia [36]. Mechanical dyssynchrony of the systemic right ventricle was also found in children with hypoplastic left heart syndrome [37]. The preoperative circumferential strain rate was independently associated with the length of hospital stay in patients with a functional single ventricle who were undergoing total cavopulmonary connection, which suggests that strain assessment may improve preoperative risk stratification [38].

In patients with septal defects, studies have reported significant differences in atrial strain parameters between children who undergo surgical repair and those treated with transcatheter closure of an atrial septal defect [39]. The peak right and left atrial strain and strain rate have been found to be significantly reduced in the surgical group compared to both the catheter-based intervention group and healthy controls. These findings suggest greater atrial functional impairment following surgical closure. Among patients with various types of ventricular septal defects, worse left ventricular systolic deformation was found in patients after surgical repair of subarterial defects compared with those after patch closure of perimembranous defects [39, 40].

5.2 Cardiomyopathies

Cardiomyopathies can be more accurately assessed using SI. Dilated cardiomyopathy (DCM) and hypertrophic cardiomyopathy (HCM) are rare but potentially severe conditions that can affect children, with other types of cardiomyopathies being even less common. SI can detect early functional abnormalities in the heart muscle, which may precede visible structural changes. In DCM, where the heart becomes enlarged

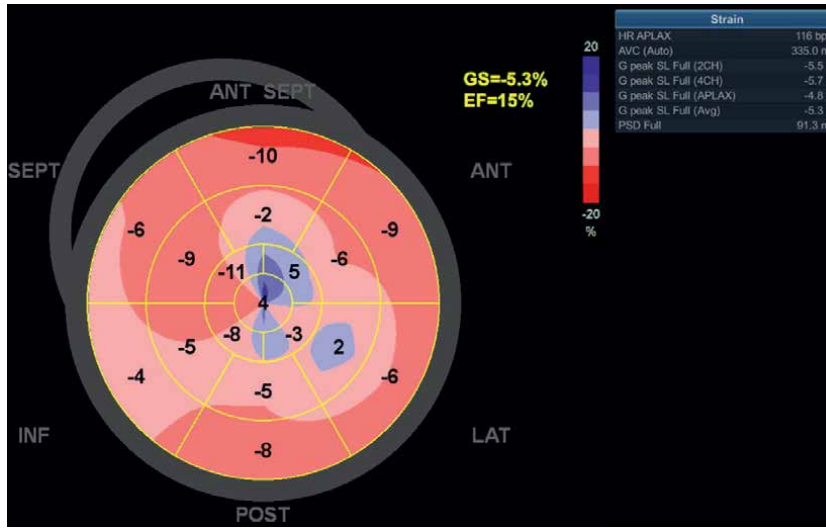

Figure 2.
Significantly reduced GLS in patient with DCM and HF with severely reduced EF.

and weakened, and in HCM, where the heart muscle thickens, SI offers sensitive markers of early myocardial dysfunction, facilitating improved monitoring and management of disease [41]. Significantly reduced GLS in patients with DCM and HF, portrayed in the segment model or bull's-eye, is presented in **Figure 2**.

GLS may be a useful echocardiographic parameter of myocardial function and may predict clinical outcomes in patients with cardiomyopathies. Some studies have manifested the potential use of myocardial strain phenotyping to monitor disease progression and potentially predict clinical outcomes in genetic cardiomyopathies [41]. It has been demonstrated that SI is significantly reduced in patients with HCM, even in the presence of a normal left ventricular EF [41, 42]. Additionally, GLS can serve as a valuable diagnostic tool in differentiating between various etiologies of left ventricular hypertrophy. Beyond its established role in sarcomeric HCM, GLS has demonstrated utility in identifying phenocopies such as Danon disease, Anderson-Fabry disease, Pompe disease, and Friedreich ataxia. It is also effective in distinguishing physiological left ventricular hypertrophy from other conditions like hypertensive heart disease and aortic stenosis. However, studies evaluating SI in genetic cardiomyopathies remain limited [41].

5.3 Heart failure

HF is a complex pathophysiological condition characterized by clinical signs and symptoms resulting from impaired cardiac function. It manifests either as the heart's inability to generate sufficient cardiac output to meet the metabolic demands of peripheral tissues or as elevated left ventricular filling pressure despite preserved systolic function. HF is classified based on the left ventricular systolic function [43].

Prognosis does not significantly differ between various left ventricular EF groups [44], highlighting the limited role of EF measured by echocardiography. Left ventricular EF is influenced by preload and afterload, and its measurement is subject to substantial intra- and inter-observer variability, which can impact reproducibility.

Additionally, the accuracy of EF assessment is also dependent on the expertise of the operator [10, 45].

Moreover, segmental abnormalities of myocardial contractility are frequently underrecognized in patients with preserved EF, as compensatory hypercontractility in unaffected myocardial regions may mask regional dysfunction. Consequently, reliance solely on geometric assumptions is insufficient for accurately diagnosing HF, particularly in cases of HF with preserved EF. This underscores the need for more sensitive and region-specific imaging modalities, such as myocardial SI, to detect subclinical myocardial dysfunction [43].

After myocardial injury, a reduction of longitudinal contraction is first affected, which is not reflected in changes of EF [46]. Advanced imaging techniques, most notably the assessment of longitudinal myocardial strain using GLS, have been integrated into routine clinical practice to address these limitations. GLS quantifies the degree of longitudinal myocardial fiber shortening as a percentage, offering a sensitive and reproducible measure of systolic function. The longitudinal shortening of the left atrium and right ventricle was also studied for better stratification of patients with HF [10].

In pediatric HF, especially in those patients with systolic dysfunction or diastolic dysfunction, SI can identify myocardial impairment before EF drops below normal levels. This allows earlier intervention, which is often crucial for the progression of the disease. In children with HF, SI can be utilized to monitor changes in cardiac function, providing valuable insights that can guide the adjustment of treatment strategies as needed. GLS can serve as a valuable clinical tool to enhance risk stratification in patients with HF. This parameter has a strong correlation with the severity of HF and can help identify distinct cardiomyopathy phenotypes, suggesting disease causes and severity [10].

5.4 Myocarditis

Myocarditis is an inflammatory disorder of the myocardium, precipitated by a diverse array of etiological factors, including infectious agents (most commonly viral pathogens), autoimmune responses, and exposure to certain drugs or cardiotoxic substances. Myocarditis has a highly variable presentation, natural history, and prognosis [47].

Over the last years, cardiac magnetic resonance (CMR) has emerged as the primary modality for diagnosis and risk stratification of myocarditis. CMR plays a pivotal role in the diagnosis of myocarditis and is typically guided by a clinical presentation suggestive of myocardial inflammation. The diagnostic criteria most often rely on the presence of late gadolinium enhancement (LGE) in characteristic nonischemic distribution patterns, indicative of myocardial injury or fibrosis, in conjunction with evidence of myocardial edema identified on T2-weighted imaging [47, 48]. The natural history and prognosis of myocarditis are highly heterogeneous, ranging from complete clinical and functional recovery to progression toward severe DCM or sudden cardiac death. Given this variability, there is substantial clinical interest in advanced imaging modalities that can enhance risk stratification and improve the prediction of future adverse outcomes. LGE has proven to be a powerful prognostic tool for patients with myocarditis [47].

Several studies have shown abnormalities of strain in patients with myocarditis using both STE and feature-tracking techniques [49]. Moreover, an association between impaired GLS and adverse cardiac events was also suggested.

Feature-tracking GLS is independently associated with adverse cardiac outcomes. Abnormalities of GLS reflect functional disturbance of longitudinal left ventricular function [47]. GLS can detect subtle myocardial injury even in the absence of LGE [50]. In patients with myocarditis, SI is mainly used for evaluation of ventricular function, especially when left ventricular EF is preserved, and for evaluation of regional myocardial dysfunction [49].

5.5 Chemotherapy-induced cardiotoxicity

The growing population of long-term childhood cancer survivors is confronted with a substantial burden of cardiovascular sequelae, with the highest risk associated with prior exposure to anthracyclines and chest radiation. These treatments, while effective in oncological care, can induce a range of cardiovascular complications, including HF, arrhythmias, and vascular damage. Although longitudinal cardiovascular surveillance is universally recommended for childhood cancer survivors, the ideal methodologies, frequency, and timing for such monitoring remain inadequately defined [51].

Pediatric patients who undergo chemotherapy are at risk for chemotherapy-induced cardiotoxicity, which can lead to HF. Speckle tracking can detect subtle changes in myocardial function early on, even before traditional markers like EF show abnormalities. This allows for early intervention to prevent further cardiac damage. SI is also used for monitoring therapy and disease progression [51, 52].

Anthracycline-induced cardiotoxicity represents a significant contributor to both morbidity and mortality among childhood cancer survivors. While echocardiographic myocardial SI is routinely used in adult oncology patients, its diagnostic value in pediatric patients remains part of ongoing research [52].

The studies demonstrate the feasibility of left ventricular strain assessment in most echocardiographic evaluations. Based on the results of impaired longitudinal strain (LS) during anthracycline treatment for childhood sarcoma, the integration of LS measurement into pediatric echocardiographic surveillance protocols is suggested [51].

5.6 Pulmonary hypertension and right heart function

In children with pulmonary hypertension due to various causes like CHD or chronic lung disease, STE can evaluate the function of the right ventricle, which is critical in understanding the overall function of the heart. STE can evaluate both left and right ventricular functions, which is important in a variety of clinical conditions. On the other hand, STE can also help monitor the changes in cardiac function and guide the treatment of pulmonary arterial hypertension (PAH). Right ventricular LS offers critical reference data that can enhance clinical decision-making regarding the status and severity of the disease in affected children [53].

Right ventricular function has been recognized as a critical prognostic indicator in pediatric patients with PAH. Two-dimensional STE serves as a valuable noninvasive modality for assessing the right ventricular function in children with advanced PAH. It facilitates not only clinical prognosis but also enables segmental analysis of right ventricular myocardial performance in these patients. The studies have tried to evaluate the deformation pattern and prognostic significance of right ventricular LS. Right ventricular free wall LS and strain rate were significantly lower in children with PAH compared with controls. Furthermore, there was a more expressed decrease of

the basal than the apical region of the right ventricular free wall LS in PAH patients compared with the control group [54].

5.7 Post-cardiac surgery

After heart surgeries, STE can monitor myocardial function to assess the heart's recovery. This is especially useful in assessing subtle changes in heart function that may not be evident with traditional echocardiographic methods. After procedures like cardiac surgery, SI can assess the effectiveness of the surgery in improving cardiac function [55–57].

STE has gained increasing value in the evaluation of CHD. However, its use in pediatric cardiac surgery is still limited. Some studies using STE analysis were performed to evaluate left ventricular systolic impairment after biventricular pediatric cardiac surgery. STE analysis demonstrated significant left ventricular systolic dysfunction immediately following surgery, with subsequent improvement, though incomplete normalization at discharge. Notably, base-apex differences were observed, with apical segments exhibiting relative hypercontractility after surgery, in contrast to other myocardial regions. The more gradual recovery of SI values, compared to left ventricular EF, suggests that STE analysis may offer superior sensitivity for monitoring mild left ventricular dysfunction in the post-surgical period [55].

STE is becoming increasingly used in the evaluation of a wide range of cardiovascular conditions, including patients following heart transplantation. Alterations in myocardial strain measured by STE have been observed in the context of allograft rejection and cardiac allograft vasculopathy [58, 59]. It is valuable for the noninvasive assessment of left ventricular diastolic dysfunction [60]. In pediatric heart transplant recipients, there is an initial deterioration in both longitudinal systolic and diastolic strain during the early post-transplant period, accompanied by an increase in circumferential strain parameters. These changes generally normalize by 1-year post-transplant and remain stable thereafter, in the absence of clinically significant rejection or cardiac allograft vasculopathy. Consequently, a notable deviation from baseline strain values requires further clinical investigation [58].

5.8 Risk stratification for HF and sudden cardiac death in children with a systemic disease

Left ventricular GLS is a sensitive and clinically significant marker of myocardial dysfunction. Early detection of ventricular dysfunction with SI is becoming a more and more promising tool in patients with arterial hypertension, diabetes mellitus, metabolic syndrome, chronic kidney disease, and neuromuscular diseases. SI can assist regarding the potential need for further diagnostic evaluation; timely treatment decisions are crucial to ensure the best outcomes for the patients [61, 62].

Established risk factors for atherosclerosis, such as dyslipidemia, hypertension, obesity, and hyperglycemia, have been associated with subclinical myocardial dysfunction. Studies evaluated myocardial strain in pediatric patients with atherosclerotic risk factors using three-dimensional STE. The findings revealed that left ventricular GLS and global circumferential strain were significantly reduced in children with isolated dyslipidemia, isolated hypertension, and isolated obesity/overweight, and in those with multiple risk factors, compared to healthy controls. Notably, the extent of myocardial strain deterioration was directly proportional to the number of risk factors present in each individual [61].

Diabetic cardiomyopathy results in pathological alterations in myocardial structure and function, occurring in the absence of traditional cardiac risk factors. However, screening during the preclinical phase remains inadequately defined. GLS has emerged as a significant echocardiographic parameter for evaluating asymptomatic patients. Studies have shown that GLS can serve as a potential early biomarker for detecting left ventricular changes in individuals with type 2 diabetes mellitus [63].

Children with type 1 diabetes mellitus may experience subclinical myocardial damage, although there is considerable variability in the findings across studies. The comparison of left ventricular myocardial strain values was made between pediatric patients with type 1 diabetes mellitus without cardiac disease and a healthy control group. Subclinical left ventricular dysfunction was observed in type 1 diabetes mellitus patients, even in the absence of a reduction in EF. While longitudinal cardiac function was impaired, circumferential strain remained unaffected. GLS was identified as a valuable tool for detecting subclinical left ventricular systolic dysfunction in pediatric patients with type 1 diabetes mellitus [64].

A reduction in left ventricular GLS is commonly observed in adults with chronic kidney disease (CKD) and hypertension, and it is correlated with adverse cardiovascular outcomes. Although left ventricular GLS may serve as a biomarker for CKD-associated myocardial dysfunction in children, data in this population remains limited. The research found that systolic and diastolic hypertension were linked to reduced left ventricular GLS. Notably, only diastolic hypertension detected through ambulatory blood pressure monitoring was significantly associated with lower left ventricular GLS [65]. A limit value of GLS in patients with arterial hypertension and preserved EF is presented in **Figure 3**.

Cardiomyopathy is the primary cause of mortality in individuals with Duchenne muscular dystrophy (DMD). While DMD-related cardiomyopathy can progress rapidly and fatally in some patients during their teenage years, others may remain

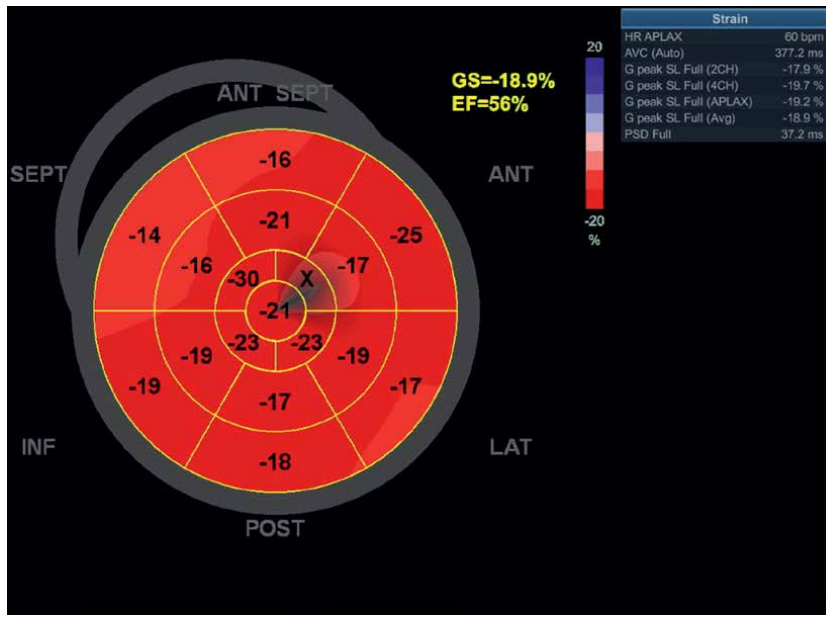

Figure 3.
Limit value of GLS in patient with arterial hypertension and preserved EF.

relatively symptom-free well into adulthood. Given the heterogeneous progression of cardiomyopathy in DMD, there is an urgent need for biomarkers to detect early onset and assess the rate of progression. Despite advances in imaging, reliable methods to identify the onset or track the progression of DMD-related cardiomyopathy remain lacking. Cardiac SI has emerged as a promising tool, demonstrating substantial value in evaluating DMD cardiomyopathy. A recent study involving boys with DMD found that 9% of them exhibited reduced GLS on two-dimensional STE before clinical signs of cardiac dysfunction became evident [66].

5.9 Cardiac ischemia and infarction

SI can be effectively used in the diagnosis of myocardial ischemia by identifying a reduction in peak systolic strain, reflecting impaired contractile function. Equally important is the detection of abnormal deformation patterns, specifically systolic lengthening and post-systolic shortening, which are hallmark features of ischemic myocardium. Systolic lengthening indicates paradoxical myocardial stretching during systole, while post-systolic shortening reflects delayed contraction beyond aortic valve closure. These deformation abnormalities, often missed by conventional echocardiographic parameters, provide sensitive and early indicators of regional ischemic dysfunction [2, 67]. Speckle tracking can identify regional myocardial dysfunction after cardiac ischemia, even if the EF is preserved. Assessing the extent of the ischemic myocardium and evaluating ventricular function are key steps in determining the most effective treatment approach. Furthermore, the additional diagnostic insights offered by SI can be valuable when other noninvasive tests give inconclusive results [2].

5.10 Cardiac resynchronization therapy

Cardiac resynchronization therapy (CRT) can improve cardiac function in children with heart failure. SI is used to quantify abnormalities in the timing of mechanical activation of the left ventricle to select patients suitable for CRT [2]. More recent studies have focused on the abnormal wall motion patterns, typical for left bundle branch block, to predict response to CRT [68, 69]. Furthermore, in patients with the left bundle branch block in ECG, the absence of a typical contraction pattern using SI is associated with an increased risk of adverse events after CRT. This characteristic contraction pattern, often observed in the setting of ischemia or dyssynchrony, involves early systolic shortening followed by rebound stretch in the interventricular septum, coupled with early systolic lengthening and delayed peak shortening, occurring after aortic valve closure in the left ventricular lateral wall. This asynchronous myocardial deformation reflects mechanical inefficiency and impaired electromechanical coupling. SI enables the precise temporal and spatial characterization of these abnormalities, enhancing diagnostic accuracy and informing therapeutic decision-making [69].

In the subgroup of patients who do not exhibit the typical strain pattern of mechanical dyssynchrony, QRS complex widening is likely attributable to myocardial hypertrophy and diffuse interstitial fibrosis. In such cases, the mechanical inefficiency is not primarily due to asynchronous activation but rather to intrinsic myocardial structural abnormalities. As a result, these ventricles may respond suboptimally to pacing therapy, such as CRT, highlighting the importance of advanced imaging, particularly strain analysis [2].

Speckle-tracking analysis appears to be successful in the live, on-site optimization of CRT in children. STE is a simple and sensitive way to evaluate dyssynchrony leading to impaired hemodynamics in children with CHD post-operatively. However, STE has not been used in combination with CRT in the long-term, outpatient management of children.

Precise assessment of synchrony allowed fine adjustments of ventricular delay. This led to improved long-term clinical parameters, including improved ventricular function, decreased QRS duration, and improved growth. Accurate assessment of ventricular synchrony has enabled refined optimization of interventricular and intraventricular pacing delays, resulting in significant improvements in long-term clinical outcomes. These include enhanced ventricular function, reduction in QRS duration, and notably improved somatic growth. Further studies are needed to determine whether optimization of CRT needs to be periodically repeated to maintain these improvements [70].

Three-dimensional STE serves well as an activation imaging modality capable of visualizing the propagation of regional myocardial contraction across both the left and right ventricles. An advanced activation imaging system has recently been developed to enable integrated visualization of biventricular contraction dynamics.

Compared to two-dimensional STE, three-dimensional STE offers several significant advantages. First, it is not constrained by the three-dimensional motion of the heart, thereby providing a more accurate representation of myocardial deformation. Second, the acquisition of full-volume datasets for both the left and right ventricles overcomes the inherent limitation of plane dependency associated with two-dimensional imaging [71].

Using a three-dimensional STE-derived activation imaging system, interventricular dyssynchrony was successfully visualized in a patient with repaired TOF presenting with pacing-induced left ventricular dysfunction. This advanced imaging modality allows for the dynamic visualization of electromechanical activation patterns across both ventricles, enabling precise identification of dyssynchrony. Furthermore, it facilitates the assessment of mechanical resynchronization following CRT, making it a valuable tool for evaluating electromechanical disturbances [72].

Patients with D-loop transposition of the great arteries (D-TGA) and ventricular septal defect (VSD) are at risk of developing left ventricular dysfunction following an arterial switch operation (ASO), primarily due to the occurrence of surgically induced heart block. In this context, epicardial pacing leads are often implanted on the right ventricular free wall. However, follow-up evaluations at a median of 6-month post-implantation have shown that approximately two-thirds of these patients exhibit significant deterioration in left ventricular function. Chronic right ventricular pacing has been consistently associated with adverse effects on left ventricular performance, not only in individuals with congenital complete heart block but also in those with various forms of CHD [73]. This dysfunction is thought to be mediated by dyssynchronous electrical activation, which promotes maladaptive left ventricular remodeling, particularly when pacing originates from the right ventricular free wall [74]. CRT has emerged as a viable strategy to restore ventricular function in patients for whom long-term pacing is unavoidable. Clinical evidence suggests that the beneficial effects of CRT can become evident within the first 3–6 months following system upgrade, with CHD patients who are likely to respond within 3 months of therapy [73, 75]. In patients who have undergone an arterial switch operation with VSD closure, the development of complete heart block and subsequent chronic right ventricular pacing

may be associated with the onset of left ventricular dysfunction. This dysfunction is thought to result from pacing-induced ventricular dyssynchrony. In such cases, CRT, either *via* a biventricular pacing system or with targeted left ventricular lead placement, may be considered as the primary pacing strategy. This approach aims to preserve or restore ventricular synchrony and prevent the progression of pacing-induced cardiomyopathy [76].

Finally, inter-vendor variability must be considered when assessing strain or synchrony values. Data suggests that reliable comparisons between different settings may be appropriate, but clinicians and researchers should use these tools cautiously. Synchrony values varied substantially among all software packages in children. Also, strain values varied widely. Quantification smoothness settings led to only minimal variability in strain measurements, indicating that post-processing adjustments exert a limited effect on the overall accuracy of deformation analysis. Notably, significant differences in strain values between low and high frame rates were observed exclusively in a subset of patients characterized by a flattened interventricular septum. This suggests that while strain analysis is generally robust across varying acquisition parameters, specific anatomical alterations, such as septal flattening, may introduce sensitivity to frame rate, warranting careful consideration during image interpretation [77].

The main clinical applications of SI are summarized in **Table 1**.

Area of use	Clinical applications
CHD	• Early detection of myocardial dysfunction • The effects of valvular disease on myocardial function • Understanding of the diastolic ventricular function • Timely treatment decisions • Post-surgical assessment
Cardiomyopathies	• Early detection of ventricular dysfunction • Potential need for additional diagnostics • Timely treatment decisions
Heart failure	• Early detection of dysfunction • Monitoring disease progression • Timely treatment decisions
Myocarditis	• Evaluation of ventricular function in patients with preserved LVEF • Evaluation of regional myocardial dysfunction
Cardiotoxicity	• Detecting subclinical damage • Early intervention and adjustment of therapy
Pulmonary hypertension and right heart function	• Assessment of right ventricular function • Prognosis and monitoring of disease
Post-cardiac surgery	• Recovery of the heart's function
Risk stratification for heart failure and sudden cardiac death in children with a systemic disease	• Early detection of ventricular dysfunction in patients with arterial hypertension, diabetes mellitus, metabolic syndrome, chronic kidney disease, neuromuscular diseases • Potential need for additional diagnostics • Timely treatment decisions

Area of use	Clinical applications
Cardiac ischemia and infarction	• Extent of the ischemic myocardium • Assessing ventricular function, especially in patients with preserved LVEF
Cardiac resynchronization therapy	• Quantify abnormalities in the timing of mechanical activation of the left ventricle

CHD, congenital heart disease; LVEF, left ventricular ejection fraction.

Table 1.
Clinical applications of SI in pediatrics.

6. Conclusions

SI is a powerful tool for evaluating myocardial function, particularly in children with congenital or acquired heart conditions. It offers detailed insights into cardiac function that may be overlooked by traditional imaging methods, enabling earlier detection of abnormalities and more informed clinical decisions. As a result, myocardial strain has gained increasing utility in the assessment of cardiovascular disorders due to its capacity to detect subclinical myocardial dysfunction. Unlike EF, which does not directly measure myocardial contractility and has limited predictive value for clinical outcomes, SI offers a more sensitive and comprehensive evaluation of myocardial function. Therefore, reliable and precise tools for measuring myocardial function are needed to ensure appropriate treatment and improve clinical outcomes. GLS, as a main parameter of global left ventricular function, measured by STE, offers a more accurate measure of myocardial function. Besides that, SI also provides a better insight into cardiac mechanics. GLS can identify cardiac pathology before clinical symptoms or a reduction in EF. Moreover, it has been well validated as a prognostic marker in HF, myocardial infarction, chemotherapy cardiotoxicity, and cardiomyopathies. In addition, GLS may help differentiate causes of left ventricular hypertrophy. However, SI requires expertise and high-quality imaging to interpret the results accurately, particularly in younger children with smaller and faster hearts. Additionally, inter-vendor differences and the lack of standardization in pediatric applications continue to limit its broader clinical use. As technology advances, SI is expected to play an increasingly important role in clinical practice.

Conflict of interest

The authors declare no conflict of interest.

Notes/thanks/other declarations

None.

DOI: http://dx.doi.org/10.5772/intechopen.1011362

Author details

Teja Senekovič Kojc[1*] and Nataša Marčun Varda[1,2]

1 University Medical Centre Maribor, Maribor, Slovenia

2 Medical Faculty, University of Maribor, Maribor, Slovenia

*Address all correspondence to: teja.senekovic@gmail.com

IntechOpen

References

[1] Amundsen BH, Helle-Valle T, Edvardsen T, Torp H, Crosby J, Lyseggen E, et al. Noninvasive myocardial strain measurement by speckle tracking echocardiography: Validation against sonomicrometry and tagged magnetic resonance imaging. Journal of the American College of Cardiology. 2006;**47**(4):789-793. DOI: 10.1016/j.jacc.2005.10.040

[2] Smiseth OA, Torp H, Opdahl A, Haugaa KH, Urheim S. Myocardial strain imaging: How useful is it in clinical decision making? European Heart Journal. 2016;**37**(15):1196-1207. DOI: 10.1093/eurheartj/ehv529

[3] Cheung Y-F. Echocardiographic strain imaging: What do paediatric cardiologists need to know? Pediatric Medicine. 2021;**5**:38. DOI: 10.21037/pm-21-39

[4] Kalam K, Otahal P, Marwick TH. Prognostic implications of global LV dysfunction: A systematic review and meta-analysis of global longitudinal strain and ejection fraction. Heart. 2014;**100**:1673-1680. DOI: 10.1136/heartjnl-2014-305538

[5] Seo Y, Ishizu T, Enomoto Y, Sugimori H, Yamamoto M, Machino T, et al. Validation of 3-dimensional speckle tracking imaging to quantify regional myocardial deformation. Circulation. Cardiovascular Imaging. 2009;**2**(6):451-459. DOI: 10.1161/CIRCIMAGING.109.858480

[6] Leitman M, Lysyansky P, Sidenko S, Shir V, Peleg E, Binenbaum M, et al. Two-dimensional strain—A novel software for real-time quantitative echocardiographic assessment of myocardial function. Journal of the American Society of Echocardiography. 2004;**17**(10):1021-1029. DOI: 10.1016/j.echo.2004.06.019

[7] Tanaka H, Hara H, Saba S, Gorcsan J. Usefulness of three-dimensional speckle tracking strain to quantify dyssynchrony and the site of latest mechanical activation. The American Journal of Cardiology. 2010;**105**:235-242. DOI: 10.1016/j.amjcard.2009.09.010

[8] Gorcsan J, Tanaka H. Echocardiographic assessment of myocardial strain. Journal of the American College of Cardiology. 2011;**58**:1401-1413. DOI: 10.1016/j.jacc.2011.06.038

[9] Reisner SA, Lysyansky P, Agmon Y, Mutlak D, Lessick J, Friedman Z. Global longitudinal strain: A novel index of left ventricular systolic function. Journal of the American Society of Echocardiography. 2004;**17**(6):630-633. DOI: 10.1016/j.echo.2004.02.011

[10] Pastorini G, Anastasio F, Feola M. What strain analysis adds to diagnosis and prognosis in heart failure patients. Journal of Clinical Medicine. 2023;**12**(3):836. DOI: 10.3390/jcm12030836

[11] Crosby J, Amundsen BH, Hergum T, Remme EW, Langeland S, Torp H. 3-D speckle tracking for assessment of regional left ventricular function. Ultrasound in Medicine & Biology. 2009;**35**(3):458-471. DOI: 10.1016/j.ultrasmedbio.2008.09.011

[12] Takeguchi T, Nishiura M, Abe Y, Ohuchi H, Kawagishi T. Practical considerations for a method of rapid cardiac function analysis based on three-dimensional speckle tracking in a three-dimensional diagnostic ultrasound

system. Journal of Medical Ultrasonics (2001). 2010;**37**(2):41-49. DOI: 10.1007/s10396-009-0249-8

[13] Yang H, Marwick TH, Fukuda N, Oe H, Saito M, Thomas JD, et al. Improvement in strain concordance between two major vendors after the strain standardization initiative. Journal of the American Society of Echocardiography. 2015;**28**(6):642-8.e7. DOI: 10.1016/j.echo.2014.12.009

[14] Li VW, Yu CK, So EK, Wong WH, Cheung YF. Ventricular myocardial deformation imaging of patients with repaired tetralogy of Fallot. Journal of the American Society of Echocardiography. 2020;**33**(7):788-801. DOI: 10.1016/j.echo.2020.03.017

[15] Menting ME, van den Bosch AE, McGhie JS, Eindhoven JA, Cuypers JA, Witsenburg M, et al. Assessment of ventricular function in adults with repaired tetralogy of Fallot using myocardial deformation imaging. European Heart Journal Cardiovascular Imaging. 2015;**16**(12):1347-1357. DOI: 10.1093/ehjci/jev090

[16] Friedberg MK, Fernandes FP, Roche SL, Grosse-Wortmann L, Manlhiot C, Fackoury C, et al. Impaired right and left ventricular diastolic myocardial mechanics and filling in asymptomatic children and adolescents after repair of tetralogy of Fallot. European Heart Journal Cardiovascular Imaging. 2012;**13**(11):905-913. DOI: 10.1093/ehjci/jes067

[17] Yim D, Hui W, Larios G, Dragulescu A, Grosse-Wortmann L, Bijnens B, et al. Quantification of right ventricular electromechanical dissynchrony in relation to right ventricular function and clinical outcomes in children with repaired tetralogy of Fallot. Journal of the American Society of Echocardiography. 2018;**31**(7):822-830. DOI: 10.1016/j.echo.2018.03.012

[18] Bhatt SM, Wang Y, Elci OU, Goldmuntz E, McBride M, Paridon S, et al. Right ventricular contractile reserve is impaired in children and adolescents with repaired tetralogy of Fallot: An exercise strain imaging study. Journal of the American Society of Echocardiography. 2019;**32**(1):135-144. DOI: 10.1016/j.echo.2018.08.008

[19] Toro KD, Soriano BD, Buddhe S. Right ventricular global longitudinal strain in repaired tetralogy of Fallot. Echocardiography. 2016;**33**(10):1557-1562. DOI: 10.1111/echo.13302

[20] Friedberg MK, Fernandes FP, Roche SL, Slorach C, Grosse-Wortmann L, Manlhiot C, et al. Relation of right ventricular mechanics to exercise tolerance in children after tetralogy of Fallot repair. American Heart Journal. 2013;**165**(4):551-557. DOI: 10.1016/j.ahj.2012.06.029

[21] Yim D, Mertens L, Morgan CT, Friedberg MK, Grosse-Wortmann L, Dragulescu A. Impact of surgical pulmonary valve replacement on ventricular mechanics in children with repaired tetralogy of Fallot. The International Journal of Cardiovascular Imaging. 2017;**33**(5):711-720. DOI: 10.1007/s10554-016-1046-2

[22] Knirsch W, Dodge-Khatami A, Kadner A, Kretschmar O, Steiner J, Böttler P, et al. Assessment of myocardial function in pediatric patients with operated tetralogy of Fallot: Preliminary results with 2D strain echocardiography. Pediatric Cardiology. 2008;**29**(4):718-725. DOI: 10.1007/s00246-008-9227-y

[23] van Grootel RWJ, van den Bosch AE, Baggen VJM, Menting ME, Baart SJ,

Cuypers JAAE, et al. The prognostic value of myocardial deformation in adult patients with corrected tetralogy of Fallot. Journal of the American Society of Echocardiography. 2019;**32**(7):866-875. e2. DOI: 10.1016/j.echo.2019.03.014

[24] Liang XC, Lam WW, Cheung EW, Wu AK, Wong SJ, Cheung YF. Restrictive right ventricular physiology and right ventricular fibrosis as assessed by cardiac magnetic resonance and exercise capacity after biventricular repair of pulmonary atresia and intact ventricular septum. Clinical Cardiology. 2010;**33**(2):104-110. DOI: 10.1002/clc.20711

[25] To AH, Lai CT, Wong SJ, Cheung YF. Right atrial mechanics long-term after biventricular repair of pulmonary atresia or stenosis with intact ventricular septum. Echocardiography. 2016;**33**(4):586-595. DOI: 10.1111/echo.13121

[26] Roos-Hesselink JW, Meijboom FJ, Spitaels SE, van Domburg R, van Rijen EH, Utens EM, et al. Decline in ventricular function and clinical condition after mustard repair for transposition of the great arteries (a prospective study of 22-29 years). European Heart Journal. 2004;**25**(14):1264-1270. DOI: 10.1016/j.ehj.2004.03.009

[27] Chow PC, Liang XC, Cheung EW, Lam WW, Cheung YF. New two-dimensional global longitudinal strain and strain rate imaging for assessment of systemic right ventricular function. Heart. 2008;**94**(7):855-859. DOI: 10.1136/hrt.2007.131862

[28] Ladouceur M, Redheuil A, Soulat G, Delclaux C, Azizi M, Patel M, et al. Longitudinal strain of systemic right ventricle correlates with exercise capacity in adult with transposition of the great arteries after atrial switch. International Journal of Cardiology. 2016;**217**:28-34. DOI: 10.1016/j.ijcard.2016.04.166

[29] Chow PC, Liang XC, Lam WW, Cheung EW, Wong KT, Cheung YF. Mechanical right ventricular dyssynchrony in patients after atrial switch operation for transposition of the great arteries. The American Journal of Cardiology. 2008;**101**(6):874-881. DOI: 10.1016/j.amjcard.2007

[30] Kalogeropoulos AP, Deka A, Border W, Pernetz MA, Georgiopoulou VV, Kiani J, et al. Right ventricular function with standard and speckle-tracking echocardiography and clinical events in adults with D-transposition of the great arteries post atrial switch. Journal of the American Society of Echocardiography. 2012;**25**(3):304-312. DOI: 10.1016/j.echo.2011.12.003

[31] de Divitiis M, Pilla C, Kattenhorn M, Zadinello M, Donald A, Leeson P, et al. Vascular dysfunction after repair of coarctation of the aorta: Impact of early surgery. Circulation. 2001;**104**(12 Suppl. 1):I165-I170. DOI: 10.1161/hc37t1.094900

[32] Kowalski M, Kowalik E, Kotliński K, Szymański P, Kuśmierczyk M, Rózański J, et al. Regional left ventricular myocardial shortening in normotensive patients late after aortic coarctation repair—Normal or impaired? Ultrasound in Medicine & Biology. 2009;**35**(12):1947-1952. DOI: 10.1016/j.ultrasmedbio.2009.08.002

[33] Di Salvo G, Gala S, Castaldi B, Baldini L, Limongelli G, D'Andrea A, et al. Impact of obesity on left ventricular geometry and function in pediatric patients after successful aortic coarctation repair. Echocardiography. 2011;**28**(8):907-912. DOI: 10.1111/j.1540-8175.2011.01449.x

[34] Singh GK, Cupps B, Pasque M, Woodard PK, Holland MR, Ludomirsky A. Accuracy and reproducibility of strain by speckle tracking in pediatric subjects with normal heart and single ventricular physiology: A two-dimensional speckle-tracking echocardiography and magnetic resonance imaging correlative study. Journal of the American Society of Echocardiography. 2010;**23**(11):1143-1152. DOI: 10.1016/j.echo.2010.08.010

[35] Rychik J, Atz AM, Celermajer DS, Deal BJ, Gatzoulis MA, Gewillig MH, et al. Evaluation and management of the child and adult with Fontan circulation: A scientific statement from the American Heart Association. Circulation. 2019;**140**(6):e234-e284. DOI: 10.1161/CIR.0000000000000696

[36] Ho PK, Lai CT, Wong SJ, Cheung YF. Three-dimensional mechanical dyssynchrony and myocardial deformation of the left ventricle in patients with tricuspid atresia after Fontan procedure. Journal of the American Society of Echocardiography. 2012;**25**(4):393-400. DOI: 10.1016/j.echo.2012.01.003

[37] Friedberg MK, Silverman NH, Dubin AM, Rosenthal DN. Right ventricular mechanical dyssynchrony in children with hypoplastic left heart syndrome. Journal of the American Society of Echocardiography. 2007;**20**(9):1073-1079. DOI: 10.1016/j.echo.2007.02.015

[38] Park PW, Atz AM, Taylor CL, Chowdhury SM. Speckle-tracking echocardiography improves pre-operative risk stratification before the total cavopulmonary connection. Journal of the American Society of Echocardiography. 2017;**30**(5):478-484. DOI: 10.1016/j.echo.2017.01.008

[39] Di Salvo G, Drago M, Pacileo G, Rea A, Carrozza M, Santoro G, et al. Atrial function after surgical and percutaneous closure of atrial septal defect: A strain rate imaging study. Journal of the American Society of Echocardiography. 2005;**18**(9):930-933. DOI: 10.1016/j.echo.2005.01.029

[40] Kwok SY, Yeung SS, Li VW, Cheung YF. Ventricular mechanics after repair of subarterial and perimembranous VSDs. European Journal of Clinical Investigation. 2017;**47**(12):e12852. DOI: 10.1111/eci.12852

[41] Bui QM, Hong KN, Kraushaar M, Ma GS, Brambatti M, Kahn AM, et al. Myocardial strain and association with clinical outcomes in Danon disease: A model for monitoring progression of genetic cardiomyopathies. Journal of the American Heart Association. 2021;**10**(23):e022544. DOI: 10.1161/JAHA.121.022544

[42] Serri K, Reant P, Lafitte M, Berhouet M, Le Bouffos V, Roudaut R, et al. Global and regional myocardial function quantification by two-dimensional strain: Application in hypertrophic cardiomyopathy. Journal of the American College of Cardiology. 2006;**47**(6):1175-1181. DOI: 10.1016/j.jacc.2005.10.061

[43] Longobardo L, Suma V, Jain R, Carerj S, Zito C, Zwicke DL, et al. Role of two-dimensional speckle-tracking echocardiography strain in the assessment of right ventricular systolic function and comparison with conventional parameters. Journal of the American Society of Echocardiography. 2017;**30**(10):937-946.e6. DOI: 10.1016/j.echo.2017.06.016

[44] Bozkurt B, Coats AJ, Tsutsui H, Abdelhamid M, Adamopoulos S, Albert N, et al. Universal definition

and classification of heart failure: A report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure. Journal of Cardiac Failure. 2021;**S1071-9164**(21):00050-00056. DOI: 10.1016/j.cardfail.2021.01.022

[45] Hoffmann R, Barletta G, von Bardeleben S, Vanoverschelde JL, Kasprzak J, Greis C, et al. Analysis of left ventricular volumes and function: A multicenter comparison of cardiac magnetic resonance imaging, cine ventriculography, and unenhanced and contrast-enhanced two-dimensional and three-dimensional echocardiography. Journal of the American Society of Echocardiography. 2014;**27**(3):292-301. DOI: 10.1016/j.echo.2013.12.005

[46] Wang J, Khoury DS, Yue Y, Torre-Amione G, Nagueh SF. Preserved left ventricular twist and circumferential deformation, but depressed longitudinal and radial deformation in patients with diastolic heart failure. European Heart Journal. 2008;**29**(10):1283-1289. DOI: 10.1093/eurheartj/ehn141

[47] Farzaneh-Far A, Romano S. Imaging and impact of myocardial strain in myocarditis. JACC: Cardiovascular Imaging. 2020;**13**(9):1902-1905. DOI: 10.1016/j.jcmg.2020.05.028

[48] Ferreira VM, Schulz-Menger J, Holmvang G, Kramer CM, Carbone I, Sechtem U, et al. Cardiovascular magnetic resonance in nonischemic myocardial inflammation: Expert recommendations. Journal of the American College of Cardiology. 2018;**72**(24):3158-3176. DOI: 10.1016/j.jacc.2018.09.072

[49] Fung G, Luo H, Qiu Y, Yang D, McManus B. Myocarditis. Circulation Research. 2016;**118**(3):496-514. DOI: 10.1161/CIRCRESAHA.115.306573

[50] Lagan J, Schmitt M, Miller CA. Clinical applications of multi-parametric CMR in myocarditis and systemic inflammatory diseases. The International Journal of Cardiovascular Imaging. 2018;**34**(1):35-54. DOI: 10.1007/s10554-017-1063-9

[51] Alpman MS, Jarting A, Magnusson K, Manouras A, Henter JI, Broberg AM, et al. Longitudinal strain analysis for assessment of early cardiotoxicity during anthracycline treatment in childhood sarcoma: A single center experience. Cancer Reports (Hoboken, N.J.). 2023;**6**(9):e1852. DOI: 10.1002/cnr2.1852

[52] Slieker MG, Fackoury C, Slorach C, Hui W, Friedberg MK, Fan CS, et al. Echocardiographic assessment of cardiac function in pediatric survivors of anthracycline-treated childhood cancer. Circulation. Cardiovascular Imaging. 2019;**12**(12):e008869. DOI: 10.1161/CIRCIMAGING.119.008869

[53] Liu Q, Hu Y, Chen W, Yao T, Li W, Xiao Z, et al. Evaluation of right ventricular longitudinal strain in pediatric patients with pulmonary hypertension by two-dimensional speckle-tracking echocardiography. Frontiers in Pediatrics. 2023;**11**:1189373. DOI: 10.3389/fped.2023.1189373

[54] Muntean I, Benedek T, Melinte M, Suteu C, Togãnel R. Deformation pattern and predictive value of right ventricular longitudinal strain in children with pulmonary arterial hypertension. Cardiovascular Ultrasound. 2016;**14**(1):27. DOI: 10.1186/s12947-016-0074-3

[55] Cantinotti M, Marchese P, Scalese M, Medino P, Jani V, Franchi E, et al. Left

ventricular systolic impairment after pediatric cardiac surgery assessed by STE analysis. Healthcare (Basel). 2021;**9**(10):1338. DOI: 10.3390/healthcare9101338

[56] Colquitt JL, Pignatelli RH. Strain imaging: The emergence of speckle tracking echocardiography into clinical pediatric cardiology. Congenital Heart Disease. 2016;**11**(2):199-207. DOI: 10.1111/chd.12334

[57] Karsenty C, Hadeed K, Dulac Y, Semet F, Alacoque X, Breinig S, et al. Two-dimensional right ventricular strain by speckle tracking for assessment of longitudinal right ventricular function after paediatric congenital heart disease surgery. Archives of Cardiovascular Diseases. 2017;**110**(3):157-166. DOI: 10.1016/j.acvd.2016.09.003

[58] Godown J, Dodd DA, Stanley M, Havens C, Xu M, Slaughter JC, et al. Changes in left ventricular strain parameters following pediatric heart transplantation. Pediatric Transplantation. 2018;**22**(5):e13166. DOI: 10.1111/petr.13166

[59] Podrouzkova H, Bedanova H, Tretina M, Korinek J, Stepanova R, Hruskova J, et al. Decrease in longitudinal strain in heart transplant recipients is associated with rejection. Biomedical Papers of the Medical Faculty of the University Palacky, Olomouc, Czech Republic. 2015;**159**(4):601-606. DOI: 10.5507/bp.2015.020

[60] Buddhe S, Richmond ME, Gilbreth J, Lai WW. Longitudinal strain by speckle tracking echocardiography in pediatric heart transplant recipients. Congenital Heart Disease. 2015;**10**(4):362-370. DOI: 10.1111/chd.12263

[61] Zhang P, Li D, Su Y, Wang X, Sun J, Xu Y, et al. Assessment of myocardial strain in children with risk factors for atherosclerosis with use of 3D speckle tracking echocardiography. Echocardiography. 2018;**35**(4):487-493. DOI: 10.1111/echo.13806

[62] Pieruzzi F, Antolini L, Salerno FR, Giussani M, Brambilla P, Galbiati S, et al. The role of blood pressure, body weight and fat distribution on left ventricular mass, diastolic function and cardiac geometry in children. Journal of Hypertension. 2015;**33**(6):1182-1192. DOI: 10.1097/HJH.0000000000000552

[63] Saran AC, Tormin SC, Vogel J, Krakauer R, Salles JEN. Left ventricular global longitudinal strain: An early marker of diabetic cardiomyopathy. Arquivos Brasileiros de Cardiologia: Imagem Cardiovascular. 2025;**38**(1):e20240082. DOI: 10.36660/abcimg.20240082i

[64] Gupta A, Jeyaprakash P, Ghoreyshi-Hefzabad SM, Pathan F, Ozawa K, Negishi K. Left ventricular longitudinal systolic dysfunction in children with type 1 diabetes mellitus: A systematic review and meta-analysis. Journal of Diabetes and its Complications. 2023;**37**(8):108528. DOI: 10.1016/j.jdiacomp.2023.108528

[65] Kula AJ, Xu Y, Hill GD, Furth SL, Warady BA, Ng DK, et al. Hypertension and left ventricular strain in pediatric chronic kidney disease. Hypertension. 2024;**81**(10):2181-2188. DOI: 10.1161/HYPERTENSIONAHA.124.23167

[66] Earl CC, Soslow JH, Markham LW, Goergen CJ. Myocardial strain imaging in Duchenne muscular dystrophy. Frontiers in Cardiovascular Medicine. 2022;**9**:1031205. DOI: 10.3389/fcvm.2022.1031205

[67] Kukulski T, Jamal F, Herbots L, D'hooge J, Bijnens B, Hatle L, et al.

Identification of acutely ischemic myocardium using ultrasonic strain measurements. A clinical study in patients undergoing coronary angioplasty. Journal of the American College of Cardiology. 2003;**41**(5):810-819. DOI: 10.1016/s0735-1097(02)02934-0

[68] Leenders GE, De Boeck BW, Teske AJ, Meine M, Bogaard MD, Prinzen FW, et al. Septal rebound stretch is a strong predictor of outcome after cardiac resynchronization therapy. Journal of Cardiac Failure. 2012;**18**(5):404-412. DOI: 10.1016/j.cardfail.2012.02.001

[69] Risum N, Tayal B, Hansen TF, Bruun NE, Jensen MT, Lauridsen TK, et al. Identification of typical left bundle branch block contraction by strain echocardiography is additive to electrocardiography in prediction of long-term outcome after cardiac resynchronization therapy. Journal of the American College of Cardiology. 2015;**66**(6):631-641. DOI: 10.1016/j.jacc.2015.06.020

[70] Madriago E, Sahn DJ, Balaji S. Optimization of myocardial strain imaging and speckle tracking for resynchronization after congenital heart surgery in children. Europace. 2010;**12**(9):1341-1343. DOI: 10.1093/europace/euq169

[71] Seo Y, Ishizu T, Kawamura R, Yamamoto M, Kuroki K, Igarashi M, et al. Three-dimensional propagation imaging of left ventricular activation by speckle-tracking echocardiography to predict responses to cardiac resynchronization therapy. Journal of the American Society of Echocardiography. 2015;**28**(5):606-614. DOI: 10.1016/j.echo.2015.02.003

[72] Ishizu T, Seo Y, Komatsu Y, Ohte N, Ieda M. 3-dimensional speckle-tracking echocardiography-derived interventricular activation imaging in a patient with repaired tetralogy of Fallot. JACC: Case Reports. 2020;**2**(10):1575-1577. DOI: 10.1016/j.jaccas.2020.06.021

[73] Dubin AM, Janousek J, Rhee E, Strieper MJ, Cecchin F, Law IH, et al. Resynchronization therapy in pediatric and congenital heart disease patients: An international multicenter study. Journal of the American College of Cardiology. 2005;**46**(12):2277-2283. DOI: 10.1016/j.jacc.2005.05.096

[74] Gebauer RA, Tomek V, Salameh A, Marek J, Chaloupecký V, Gebauer R, et al. Predictors of left ventricular remodelling and failure in right ventricular pacing in the young. European Heart Journal. 2009;**30**(9):1097-1104. DOI: 10.1093/eurheartj/ehp060

[75] Horwich T, Foster E, De Marco T, Tseng Z, Saxon L. Effects of resynchronization therapy on cardiac function in pacemaker patients "upgraded" to biventricular devices. Journal of Cardiovascular Electrophysiology. 2004;**15**(11):1284-1289. DOI: 10.1046/j.1540-8167.2004.04279.x

[76] Mah DY, Alexander ME, Banka P, Abrams DJ, Triedman JK, Walsh EP, et al. The role of cardiac resynchronization therapy for arterial switch operations complicated by complete heart block. The Annals of Thoracic Surgery. 2013;**96**(3):904-909. DOI: 10.1016/j.athoracsur.2013.05.082

[77] Ferraro AM, Adar A, Ghelani SJ, Sleeper LA, Levy PT, Rathod RH, et al. Speckle tracking echocardiographically-based analysis of ventricular strain in children: An intervendor comparison. Cardiovascular Ultrasound. 2020;**18**(1):15. DOI: 10.1186/s12947-020-00199-x

Chapter 5

Aerobic Fitness and Leg Muscle Power in Relation to Arterial Blood Pressure in Adolescents

Danladi Musa, Tavershima Kparev, Oluwatoyin Toriola and Juliah Githang'a

Abstract

Hypertension (HTN) is a modifiable risk factor for cardiovascular morbidity and mortality that affects all population groups, including adolescents. This study investigated the independent associations of aerobic fitness (AF) and leg muscle power (LP) with resting arterial blood pressure (BP) among Nigerian adolescents. This cross-sectional study comprised 2047 adolescents aged 12–15 years from secondary schools in North-Central Nigeria. Participants were assessed for AF, LP, systolic blood pressure (SBP), and diastolic blood pressure (DBP). Multivariate regression models, adjusted for age, maturity status, waist circumference, and 1-minute post-exercise SBP and DBP, examined the relationships between the independent variables and the HTN risk. The results indicated that LP was independently associated with SBP in both sexes (girls: $\beta = 0.148$, $p = 0.032$; boys: $\beta = 0.205$, $p = 0.009$). However, AF did not turn up significant results with BP ($p > 0.05$). In boys, LP was significantly associated with DBP ($\beta = 0.202$; $p < 0.001$), while there was no significant association in girls. LP, but not AF, was significantly associated with the HTN risk in Nigerian adolescents. This relationship was more pronounced in boys. Incorporating weight-bearing exercises alongside aerobic exercises is important in mitigating the risk of HTN among Nigerian adolescents.

Keywords: adolescents, cardiovascular health, fitness, lower body anaerobic power, ROC curves

1. Introduction

Hypertension (HTN) is a significant modifiable risk factor for cardiovascular disease (CVD) and a leading contributor to global morbidity and mortality. It exacerbates the burden of CVD, stroke, and other related comorbidities [1]. Globally, HTN ranks as the third leading cause of death and is the most prevalent risk factor for non-communicable diseases (NCDs), accounting for approximately 9.4 million of the 17.7 million annual CVD-related deaths [2, 3]. Once considered rare in Africa,

the prevalence of HTN in the region has risen sharply, driven by factors such as unhealthy diets, obesity, and reduced physical activity [4, 5].

Although HTN is less common in younger populations, its increasing prevalence among adolescents is alarming. This rise is concerning not only for immediate health implications but also due to evidence suggesting its tracking from childhood to adulthood [3]. Moreover, childhood HTN is associated with serious cardiovascular complications, including carotid intima-media thickening, kidney dysfunction, left ventricular hypertrophy, and coronary atherosclerosis [6, 7]. Early diagnosis and management of childhood HTN are therefore essential to improving long-term hypertension-related cardiovascular outcomes.

The etiology of HTN is multifactorial, with poor lifestyle choices, such as physical inactivity and obesity, identified as major predisposing factors [8, 9]. Components of physical fitness, including aerobic fitness (AF), muscular strength, muscular power, body composition, and flexibility, have been implicated in adolescent HTN [10]. For example, low AF is associated with increased sympathetic activity and impaired baroreflex function, while reduced muscle strength and power correlate with arterial stiffness, contributing to elevated blood pressure [11, 12]. Musculoskeletal fitness (MSF), encompassing muscular strength, endurance, and power, is a vital aspect of health-related fitness [13]. It is increasingly recognized for its role in promoting bone and cardiometabolic health in youth [8, 14].

Despite the available evidence linking AF and MSF with cardiometabolic health in youth [10, 15, 16], the findings remain inconsistent. Studies involving Brazilian youth [10] and Northern Irish youth [15] reported significant associations between both AF and MSF and BP risk, including blood pressure (BP). However, AF demonstrated a stronger association with BP risk than MSF. Conversely, a study on Korean adolescents [17] found AF but not muscular fitness to be associated with cardiometabolic (CMD) risk. Yet another study in Scottish adolescents [16] found that muscular fitness and cardiorespiratory fitness (CRF) were independently and significantly associated with CMD risk, including hypertension. Supporting this, a systematic review and meta-analysis reported a positive association between muscular fitness, CRF, and overall cardiometabolic health in children and adolescents [14]. Given these mixed results, further investigation is imperative.

While the relationship between physical fitness and cardiovascular outcomes is well-documented [18, 19], the specific contributions of AF and MSF (herein referred to as fitness and leg power-LP, respectively) to adolescent HTN remain unclear. Furthermore, available studies investigating the associations of these two physical fitness components with cardiometabolic health used a continuous CVD or metabolic risk score [15, 16, 20]. Additionally, most studies have employed the standing broad jump rather than the vertical jump test (VJT) despite the latter's robust predictive capabilities [16, 21].

Understanding the relative effects of these two physical fitness components in adolescents is crucial for informing interventions aimed at reducing HTN risk through improved fitness. This study aims to examine the association between AF, LP, and arterial BP in adolescents from Benue State, Nigeria. It characterized participants' CVD profiles using their HTN risk status. It also seeks to establish population-specific thresholds for these fitness components that indicate HTN risk. It was hypothesized that adolescents with low AF and LP would demonstrate higher HTN risk. Findings from this study may inform public health strategies to promote fitness and mitigate HTN risk in youth.

2. Methods

2.1 Study design and sample

This cross-sectional, observational study involved 2047 school-going adolescents aged 12–16 years from seven secondary schools in Benue State, Nigeria. Sample size determination followed the Lorenz formula [22], with a systolic HTN prevalence of 5% from prior studies in the region [3]. A minimum of 126 participants was required (95% confidence level, 5% margin of error), but the sample size was increased to 2100 to account for dropouts and ensure representativeness. Detailed descriptions of the study setting, sampling procedures, inclusion and exclusion criteria, and pilot testing have been published elsewhere [23]. The study purpose and test procedures were explained to participants after permission was obtained from the heads of the participating schools. The testing team made two visits to the participating schools. The first was to measure participants' physical characteristics and familiarize them with the physical fitness protocols. Blood pressure measurement and physical fitness testing required one additional visit.

Ethical approval was obtained from the Benue State University Health Research Ethics Committee (Ref. No. BSUTHMKD/HREC/2013/017). Written informed consent was obtained from parents/guardians, and participants provided assent before data collection—study procedures adhered to the ethical standards of the Declaration of Helsinki [24].

2.2 Anthropometric measurements

Physical characteristics were assessed using standardized procedures [25]. Body mass and stature were measured using a digital scale and stadiometer (Seca Models 880 and 206, Birmingham, UK) to the nearest 0.1 kg and 0.1 cm, respectively. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2) and used to classify participants as healthy weight or overweight based on FitnessGram thresholds [26]. Body fat percentage was estimated using triceps and medial calf skinfold measurements, taken with Harpenden calipers (Creative Health Products, Ann Arbor, MI, USA). Measurements were taken three times on the right side of a participant's body, and the median was recorded. The revised regression equations for black children were used to estimate the percent body fat [27]. Waist circumference (WC), a marker of abdominal fat, was measured with a Lufkin anthropometric tape (W606PM Rosscraft, Canada) to the nearest 0.1 cm. The threshold for abdominal obesity of the 90th percentile for age and sex was determined as recommended by the International Diabetes Federation (IDF) [28]. An ISAK-certified anthropometrist conducted all measurements.

2.3 Fitness testing

Aerobic fitness was assessed using the progressive aerobic cardiovascular endurance run (PACER) test, a 20-m multistage shuttle run that progresses in intensity. Participants ran back and forth between two lines drawn 20 m apart. Participants were instructed to run until exhaustion, while they were motivated through verbal encouragement. Participants who failed to complete two successive shuttles were withdrawn from the test. The maximum running speed was used to predict AF, that is, peak $\dot{V}O_2$ ($ml.kg^{-1}.min^{-1}$) using the regression equation of Leger et al. [29].

Details of the administrative procedure of this test and the classification of participants into high fitness and low fitness based on FitnessGram revised data have been described [26].

$$\dot{V}O_2\,\max(\text{ml.kg}^{-1}\,\text{min}^{-1}) = 31.025 + 3.238\,(\text{max speed}) - 3.248\,(\text{Age}) + 0.1536\,(\text{Max speed} * \text{Age}) \quad (1)$$

Leg muscle power, a key component of muscle fitness, was assessed using the vertical jump test (VJT). The test was conducted indoors on a flat, smooth surface adjacent to a wall, following the countermovement jump (CMJ) protocol. In this protocol, participants stood with their dominant shoulder close to the wall and both feet flat on the floor. They reached upward with their dominant hand to make a chalk mark on the wall, representing their standing reach height. Next, they bent their knees and hips into a squat position, then jumped as high as possible while swinging their arms, making a second chalk mark at the peak of their jump.

The vertical jump score was calculated as the vertical distance between the two chalk marks, that is, the vertical jump height (VJH). These scores were then converted into vertical jump power (VJP) values using a prediction equation [21]:

$$\text{VJP}(\text{watt}) = -1354.820 + (35.445 \times \text{vertical jump}[\text{cm}]) + (43.942 \times \text{body mass}[\text{kg}]) \quad (2)$$

Each participant performed two trials, with the highest score recorded to the nearest centimeter. A detailed description of the protocol is available elsewhere [30]. Participants were categorized into high and low power groups based on sex-specific VJP receiver operating characteristic (ROC) cut-off values.

2.4 Blood pressure measurements

Resting systolic (SBP) and diastolic blood pressure (DBP) were measured using an automated device (Omron HEM-705 CP, Tokyo, Japan). Measurements were taken in the morning while participants were in a sitting position after 10 minutes of rest, according to the protocol of Buchan et al. [16]. Measurements were taken thrice at 2-minute intervals, with the average used for analysis. Systolic and diastolic BP values were obtained from a sub-sample of 454 participants during a 1-minute recovery from the PACER test using the same measurement protocol. It has been reported that delayed recovery BP after exercise is associated with an increased risk of HTN [31]. Blood pressure thresholds for HTN classification followed the Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents 2004 [32].

2.5 Statistical analysis

Data were analyzed using IBM SPSS (Version 20, IBM Corporation, Armonk, NY, USA). Descriptive statistics were calculated as means and standard deviations for continuous variables and frequencies and percentages for categorical data. Gender differences were analyzed using independent t-tests, or Mann-Whitney U tests as appropriate. Relationships between variables were assessed using zero-order correlations. Multivariate regression models determined the associations between AF, LP, and BP, adjusted for age, WC, SBP_1, DBP_1, and sexual maturation, with the

latter estimated from stature and age using the prediction equation of Moore and Colleagues [33]. Maturity offset (MO) was estimated directly from the formula. Then, age at peak height velocity (APHV) was estimated as the difference between MO and age. These covariates are known to affect both fitness and BP scores [31, 34]. The independent association of AF and LP with BP was determined with the logistic regression model. Separate analyses were conducted for girls and boys. Benchmarks for identifying risks of systolic and diastolic HTN were evaluated through the receiver operating characteristic curves (ROCs) using values of area under curve (AUC), sensitivity, and specificity. The AUC values were interpreted as recommended by Swets [35].

3. Results

3.1 General characteristics of participants

Participants' general characteristics are summarized in **Table 1**. Boys exhibited significantly better endurance run performance ($p < 0.001$), peak $\dot{V}O_2$ ($p < 0.001$), and APHV ($p < 0.001$) than girls. However, age, VJP, and DBP were similar between sexes. Conversely, girls were significantly heavier ($p < 0.001$) and taller ($p = 0.032$), and had higher BMI ($p = 0.021$), body fat percentage ($p < 0.001$), WC ($p < 0.001$), and SBP ($p < 0.001$) than boys. The prevalence of combined HTN risk was 9.8% for systolic hypertension and 8.9% for diastolic hypertension. Sex-specific rates are

Variables	Combined (n = 2047)	Girls (n = 1087)	Boys (n = 960)	t-Value	*p*-Value
Age (y)	13.6 ± 1.3	13.6 ± 1.3	13.6 ± 1.3	0.786	0.432
APHV (y)	13.4 ± 1.1	12.6 ± 0.7	14.2 ± 0.7	50.075	<0.001
Stature (cm)	150.3 ± 11.6	150.8 ± 11.0	149.7 ± 12.2	2.149	0.032
MO (y)	0.2 ± 1.4	1.0 ± 1.0	−0.6 ± 1.0	33.6	<0.001
Body mass (kg)	43.5 ± 9.0	44.2 ± 8.7	42.6 ± 9.3	3.931	<0.001
BMI (kg m^{-2})	19.3 ± 3.8	19.5 ± 3.7	19.1 ± 3.9	2.319	0.021
Body fat (%)	16.0 ± 6.5	18.4 ± 5.6	13.4 ± 6.4	18.597	<0.001
WC (cm)	66.2 ± 8.4	67.1 ± 8.2.	65.1 ± 8.5	5.460	<0.001
LBM (kg)	36.4 ± 7.4	35.9 ± 6.5	36.9 ± 8.3	2.935	0.003
VJH (cm)	23.8 ± 7.6	22.7 ± 7.1	25.0 ± 7.9	6.774	<0.001
VJP (w)	1397.9 ± 507.9	1392.6 ± 481.7	1403.9 ± 536.2	0.501	0.617
SBP (mmHg)	113.6 ± 17.4	115.5 ± 18.1	111.5 ± 16.4	5.174	<0.001
DBP (mmHg)	69.2 ± 13.7	68.8 ± 13.7	69.7 ± 13.7	1.465	0.143
20MST (lap)	34.7 ± 17.8	32.1 ± 18.3	37.7 ± 16.7	7.161	<0.001
Peak $\dot{V}O_2$ (ml kg^{-1} min^{-1})	42.7 ± 6.4	41.7 ± 6.6	43.7 ± 6.0	7.227	<0/001

Table 1.
General characteristics of participants stratified by gender (n = 2047).

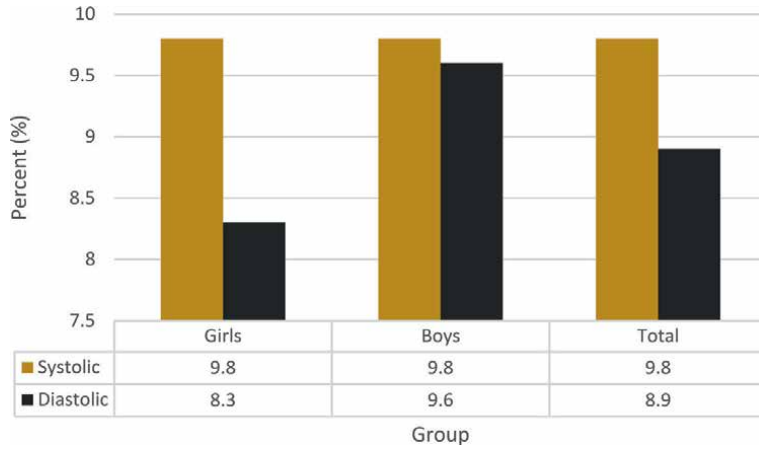

Figure 1.
Prevalence of hypertension in participants.

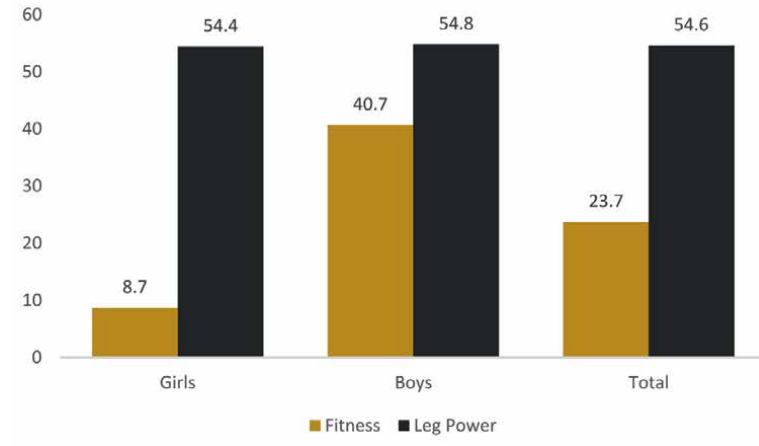

Figure 2.
Physical fitness status of participants.

shown in **Figure 1**. The prevalence of low AF was 23.7%, while 54.6% of participants exhibited weak LP. Detailed sex-specific rates are illustrated in **Figure 2**.

3.2 Cardiovascular disease characteristics of participants

When participants at risk of systolic HTN were compared with those without risk (**Table 2**), the former group was significantly ($p < 0.05$) older, heavier, and fatter, and displayed greater BMI, WC, SBP, DBP, SBP_1, and DBP_1 in both sexes. Except for VJH ($p < 0.001$) in girls, there were no significant differences ($p > 0.05$) in the physical fitness tests. The differences were all in favor of the groups without risk in both sexes. Overall, girls were more disadvantaged compared to boys. However, with the exception of aerobic fitness, in which boys were disproportionately more vulnerable, the proportions of participants at risk of other health indicators were similar

	Girls (n = 1087)			Boys (n = 960)		
Variables	**No risk (n = 875)**	**Risk (n = 212)**	**t-Value**	**No risk (n = 839)**	**Risk (n = 121)**	**t-Value**
Age (y)	13.5 ± 1.3	14.0 ± 1.3	4.641**	13.5 ± 1.3	14.0 ± 1.2	4.163**
Body mass (kg)	43.0 ± 8.5	49.3 ± 8.1	9.823**	41.8 ± 8.8	48.6 ± 10.0	10.772**
BMI (kg m^{-2})	19.2 ± 3.6	20.5 ± 4.3	4.606**	19.0 ± 3.9	19.8 ± 4.1	2.202*
WC (cm)	66.5 ± 8.3	69.9 ± 7.2	5.996**	64.6 ± 8.0	68.6 ± 10.5	4.876**
Body fat (%)	17.9 ± 5.4	20.2 ± 5.7	5.424**	13.2 ± 5.9	15.2 ± 9.0	2.381*
SBP (mmHg)	102.0 ± 13.0	142.1 ± 9.9	40.801**	107.2 ± 11.9	141.1 ± 12.0	29.296**
DBP (mmHg)	66.9 ± 12.7	76.6 ± 15.1	8.601**	67.9 ± 12.0	82.3 ± 17.7	8.704**
SBP_1	144.4 ± 17.6	169.1 ± 14.2	8.428**	142.1 ± 17.6	153.7 ± 20.5	2.917*
PACER	32.0 ± 18.6	32.6 ± 16.9	0.409	37.3 ± 16.5	40.2 ± 18.0	1.787
VJH	22.2 ± 7.0	24.8 ± 7.3	4.802**	24.8 ± 7.8	26.0 ± 8.4	1.582

*$p < 0.05$.
**$p < 0.001$.

Table 2.
Characteristics of participants according to level of CVD risk (n = 2047).

gender-wise. There were more adolescents at risk of fitness and leg power than any other risk factor. Notably, the levels of CVD risks, even among adolescents at risk of HTN, are within acceptable health standards [28].

3.3 Associations between variables

Partial correlations among measures of AF, LP, and blood pressure are summarized in **Table 3**. Weak negative associations were observed only between leg power and SBP in both sexes. Aerobic fitness showed no significant associations with any independent variables in either sex. Multivariate regression analyses (**Table 4**) revealed that aerobic fitness was not significantly associated with the dependent variables in either sex ($p > 0.05$). However, leg power demonstrated significant and independent associations with both SBP ($p = 0.013$) and DBP ($p < 0.001$) in boys and only with SBP ($p = 0.032$) in girls. These associations persisted even after adjusting for AF, suggesting that the relationships between LP and BP are independent of AF. Notably, these relationships were stronger in boys.

	SBP		DBP	
Group	**AF**	**LP**	**AF**	**LP**
Girls	−0.048	−0.146*	−0.085	−0.096
Boys	−0.110	−0.229*	−0.050	−0.020

*$p < 0.05$.

Table 3.
Partial correlation coefficients assessing the relationships among AF, LP, and blood pressure after controlling for age, MO, WC, and 1-minute post exercise BP.

	Girls				Boys			
	Aerobic fitness		Leg power		Aerobic fitness		Leg power	
Variables	Crude	adjusted	Crude	Adjusted	Crude	Adjusted	Crude	Adjusted
SBP	−0.094	−0.107	−0.133	−0.148*	−0.040	−0.063	−0.195*	−0.205**
DBP	0.009	0.011	−0.029	−0.030	−0.008	−0.033	−0.202**	−0.208**

Crude: correcting for age, MO, WC and SBP_1 and DBP_1; Adjusted: also correcting for either AF or LP.
$p < 0.05$.
**$p < 0.01$.*

Table 4.
Standardized regression coefficients on the associations between BP and the independent variables after controlling age, MO, WC, and 1-minute post-exercise BP.

For the SBP model, LP accounted for 1.2% of the variation in girls' SBP, while 37% of the variation was explained by covariates, particularly SBP_1. Additionally, a unit increase in VJH in girls was associated with a 2.6 mmHg reduction in SBP. In boys, leg power was negatively associated with both SBP and DBP, accounting for 2.6% and 2.8% of the variations, respectively. Similar to girls, a significant portion of the variations in SBP and DBP in boys (16–69%) were attributed to covariates, notably 1-minute post-exercise blood pressure measurements. Furthermore, a unit increase in VJH was associated with 3.2 mmHg and 2.8 mmHg reduction in SBP and DBP, respectively. Therefore, the major determinants of resting arterial BP were the 1-minute post-exercise SBP and DBP.

Logistic regression models adjusted for covariates indicated significant predictors for blood pressure outcomes. In girls, leg power ($p = 0.033$), age ($p = 0.002$), and SBP_1 ($p < 0.001$) significantly affected SBP with corresponding odds ratios of 1.0, 3.6, and 1.1. For boys, waist circumference ($p = 0.004$) and SBP_1 ($p = 0.015$) were significant predictors of SBP with odds ratios of 5.0 and 1.0, respectively. Regarding the DBP model, only DBP_1 showed a significant effect in girls ($p = 0.001$) with an odds ratio of 1.7. Detailed results are presented in **Table 5**.

3.4 Predictive values of AF and LP for HTN risk

Results of the ROC analyses are presented in **Table 6**, **Figures 3** and **4**. The AUC for LP was significant for predicting SBP in both sexes ($p < 0.001$). For DBP, only

Group	Predictor	Odds ratio	95% CI	*p*-Value
Girls	Age	3.58	1.61–7.94	0.002
	SBP_1	1.09	1.07–1.13	<0.001
	LP	1.00	1.00–1.02	0.033
Boys	WC Healthy weight Overweight	1 4.95	1.66–14.74	0.004
	SBP_1	1.04	1.00–1.06	0.015

Table 5.
The odds of risk of systolic hypertension in participants (n = 2047).

Variables	Group	Variable	AUC	95% CI	Cut-point	Se	SP	*p*-Value
SBP	Girls	AF	0.488	.445–.531	39.9	0.486	0.545	0.601
		LP	0.719	.681–.706	1460.6	0.722	0.360	<0.001
	Boys	AF	0.518	.462–.575	43.4	0.504	0.491	0.515
		LP	0.676	.622–.730	1405.8	0.678	0.430	<0.001
DBP	Girls	AF	0.543	.491–.595	40.3	0.535	0.495	0.098
		LP	0.544	.494–.595	1379.6	0.542	0.483	0.087
	Boys	AF	0.571	.516–.627	44.1	0.573	0.434	0.008
		LP	0.538	.483–.592	1335.1	0.542	0.498	0.165

Table 6.
ROC curve analysis for risk of BP among participants (n = 2047).

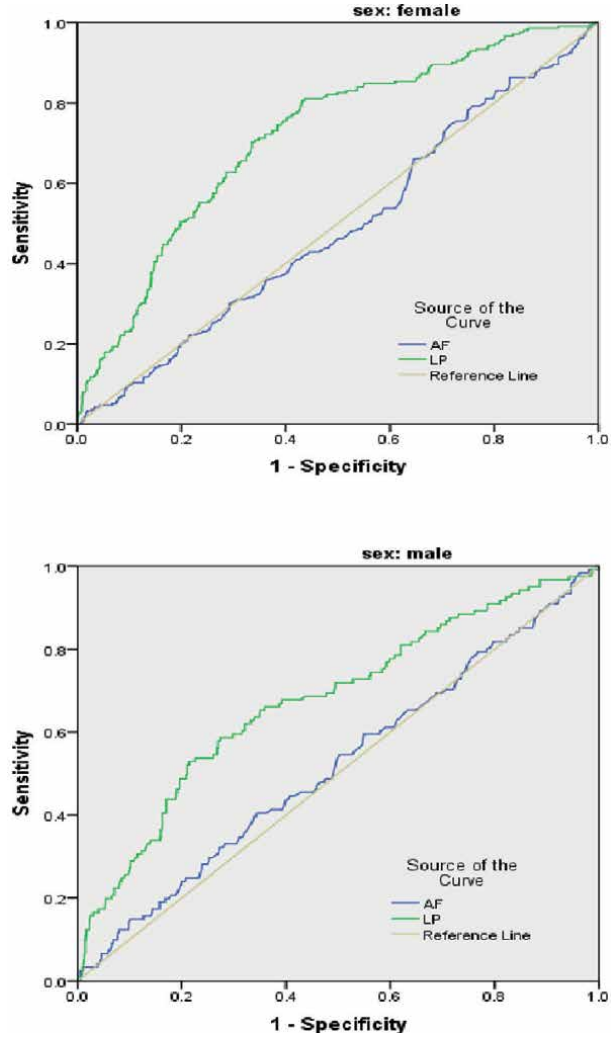

Figure 3.
Sex-specific areas under the ROC curves of aerobic fitness and leg power for SBP in girls and boys.

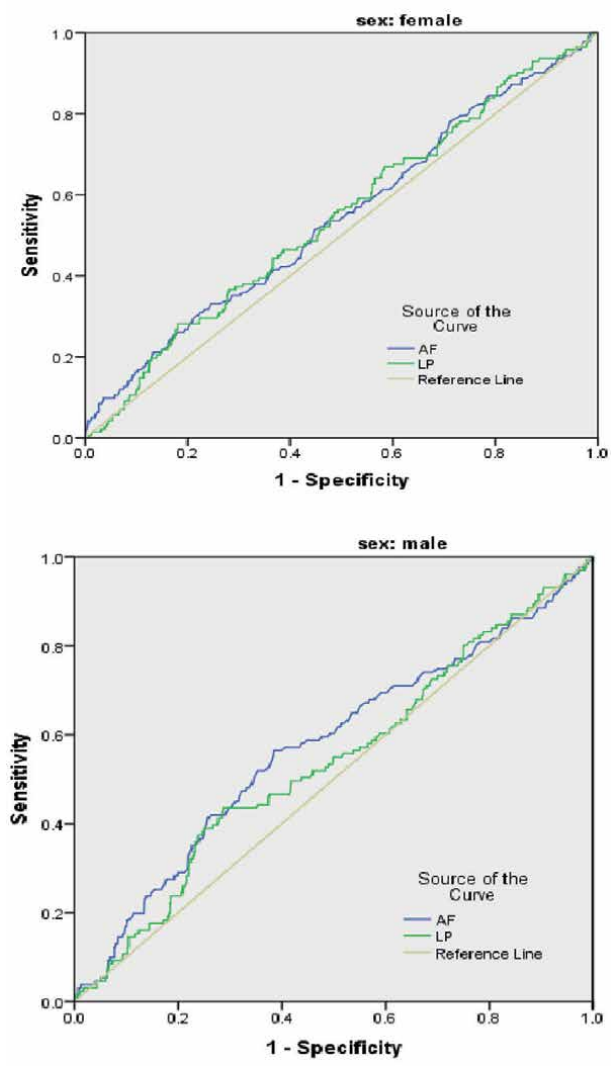

Figure 4.
Sex-specific areas under the ROC curves of aerobic fitness and leg power for DBP in girls and boys.

the AUC for AF was significant in boys (p = 0.008). Detailed results are provided in **Table 6**. The LP thresholds for detecting systolic HTN risks in girls and boys were 1460.6 W and 1405.8 W, respectively.

4. Discussion

Two major components of health-related physical fitness—AF and LP, were examined alongside resting arterial blood pressure, a key cardiovascular health risk. Major findings from this study include: The risk of HTN exists among adolescents, with the prevalence of SBP (9.8%) higher than DBP (8.9%). The prevalence was similar in both sexes. Health indicators were more favorable among adolescents with lower HTN risk. Only LP was negatively associated with SBP in both sexes, while AF showed no

significant relationship with the dependent variables in either sex. Multiple regression models indicated no association between AF and the dependent variables in both sexes. Conversely, LP demonstrated significant and independent associations with both SBP and DBP in boys and with only SBP in girls, with the relationships more pronounced in boys. Only LP demonstrated diagnostic capacity to detect HTN risk in both sexes.

4.1 Cardiovascular disease attributes of participants

The prevalence of systolic HTN risk observed in this study (9.8%) is consistent with the findings from prior research on Eastern Nigerian children, which reported a prevalence of 10.2% [36]. However, the diastolic HTN risk identified in this study (8.9%) is significantly higher than the 3.5% prevalence documented in earlier research. Furthermore, the rates of 3.6% and 19.0% for systolic and diastolic HTN risk reported by Dewi and co-workers [37] differ significantly from the current findings. The mean values of all health indicators, except LP, were significantly more favorable in adolescents without HTN risk, corroborating previous studies [19, 38]. However, girls appeared more disadvantaged in terms of the number of risks. This may be attributed to the fact that many girls in this study were early maturers, who typically have higher CVD risks compared to boys [39].

Regarding the vulnerability of adolescents to CVD risk, a significant proportion of participants exhibited an increased risk of weak leg power and low fitness (**Figure 2**). This finding emphasizes that low physical fitness, particularly lower extremity power, poses a more serious health problem than weight disorders and blood pressure abnormalities in this cohort.

4.2 Associations between fitness and HTN risk

This study's findings indicated that only LP was negatively associated with SBP in both sexes, while AF showed no significant relationship with the dependent variables in either sex. This highlights the importance of lower body anaerobic power in this cohort and suggests that LP is a more critical determinant of systolic HTN risk. Leg power also displayed significant independent associations with both SBP and DBP in boys and with only SBP in girls, with the relationships more pronounced in boys. These findings align with research among 709 European adolescents aged 12–18 [20], which documented an independent association between muscular fitness and metabolic risk (including BP), with muscular fitness showing a stronger association. Potential explanations for the lack of significant impact of AF on HTN risk, especially in girls, could include the higher fitness levels observed in this group, which are associated with better cardiovascular health and BP regulation [40]. However, these results contradict other studies. For example, Nunes et al. [10] found significant associations between fitness components and BP among 1117 Brazilian adolescents, with aerobic fitness being a stronger predictor of SBP in boys and DBP in both sexes. Similarly, Zaqout et al. [41], in a 2-year prospective study involving 1635 European children aged 6–11 years, identified CRF and lower limb strength as key determinants of cardiometabolic risk factors, though BP was not well-predicted. These inconsistencies may stem from variations in sampling, participant age, and measurement protocols.

Findings from this study clearly demonstrate that the joint contribution of AF and LP to resting BP was minimal, accounting for only 1–3% of the variance in both

dependent variables. The primary predictors of resting BP were recovery SBP_1 and DBP_1 which explained between 16% and 69% of the variance in the dependent variables. These results have significant public health implications. Delayed BP recovery following exercise in otherwise normotensive individuals has been associated with a two- to threefold increased risk of future HTN, endothelial dysfunction, and a higher prevalence of left ventricular hypertrophy [7, 42, 43]. Some of the proposed factors contributing to these conditions include low physical fitness, increased stroke volume, and elevated vascular resistance [44]. Consequently, interventions to prevent and manage pediatric HTN should emphasize improving physical fitness, reducing sedentary behavior, and promoting healthy lifestyle habits among adolescents. These strategies are well-documented to mitigate HTN risk [32]. Given the challenges associated with successfully treating and managing HTN and its associated burden, primary prevention through lifestyle modifications has been widely advocated as a critical priority by health stakeholders.

The stronger association of LP with the dependent variables in this study may be linked to the prevalence of weak LP among participants (**Figure 2**). This underscores that weak LP is a more critical health problem than AF or other CVD risk factors in this cohort. Consequently, stakeholders in pediatric health should promote participation in muscle-strengthening activities as recommended by current physical activity guidelines for youth [32, 45] to enhance musculoskeletal fitness and reduce HTN risk.

4.3 Diagnostic utility of leg power

This study indicates that LP is the only fitness component with a diagnostic capacity to identify HTN risk in both sexes. A previous study from our lab examining the association of physical fitness with adipose tissue [23] documented similar findings. This consistently strong diagnostic capacity of LP underscores its potential utility as a screening tool in pediatric health and clinical settings. Future studies and public health policies should incorporate LP assessment into routine health surveillance for adolescents, particularly in school-based settings and societies with increasingly sedentary lifestyles.

4.4 Public health implications

In this study, a unit increase in VJH resulted in a mean reduction of over 2 mmHg in both SBP and DBP. Similar findings were documented among Brazilian adolescents [10]. These results highlight the public health importance of engaging in and maintaining a physically active lifestyle, particularly through regular muscle-strengthening activities, to mitigate blood pressure levels. Previous research has consistently demonstrated that muscle fitness is strongly linked to cardiometabolic health in children and adolescents [8, 46]. Additionally, public health policies should include provisions for routine health screening to identify CVD risk factors, with particular attention to BP levels among students. This approach will help identify adolescents at risk, enabling early intervention to prevent the onset of HTN and other CVD risk factors.

4.5 Limitations and strengths

The cross-sectional design of this study limits causal inferences. Additionally, the exclusive focus on school-going adolescents, excluding those without formal education, introduces sampling bias, restricting the generalizability of findings. The use of

field methods to estimate AF and LP may also be less precise than laboratory-based measurements, such as maximal oxygen uptake and force platform assessments. Despite these limitations, the study has notable strengths, including the use of health-related CRF and BMI cut-points, which showed that participants meeting health standards had better BP profiles. Furthermore, direct measurement of participants provided more reliable data compared to self-reported measures.

5. Conclusion

This study underscores the presence of HTN risk among Nigerian adolescents. While leg power, but not aerobic fitness, was independently associated with HTN risk, the relationship between LP and HTN risk was more pronounced in boys than girls. Although the joint contribution of LP in predicting HTN risk was relatively weak, 1-minute post-exercise SBP and DBP emerged as the major determinants of the outcome measures in this population. Health-promoting strategies aimed at maintaining healthy BP levels should prioritize regular physical activity, particularly weight-bearing exercises. Such interventions are crucial for reducing HTN risk and fostering long-term cardiovascular health among adolescents. Future prospective studies will provide better insights into the roles of AF and LP in predicting HTN risk in youth.

Acknowledgements

The authors gratefully thank the principal, tutorial staff, and students of the participating schools for their cooperation during the data collection period. The efforts of the research assistants who facilitated data collection is gratefully acknowledged.

Conflict of interest

The authors have no conflict of interest.

Author details

Danladi Musa[1*], Tavershima Kparev[2], Oluwatoyin Toriola[3] and Juliah Githang'a[4]

1 Department of Human Kinetics and Health Education, Kogi State University, Anyigba, Nigeria

2 Department of Human Kinetics and Health Education, Benue State University, Makurdi, Nigeria

3 Prince Sultan University, Riyadh, Kingdom of Saudi Arabia

4 Department of Physical Education and Exercise Science, Kenyatta University, Nairobi, Kenya

*Address all correspondence to: dimusa55@gmail.com

IntechOpen

References

[1] Lurbe E, Agabiti-Rosei E, Cruickshank JK, Dominiczak A, Erdine S, Hirth A, et al. European Society of Hypertension Guidelines for the management of high blood pressure in children and adolescents. Journal of Hypertension. 2016;**34**:1887-1920

[2] WHO. World Health Statistics. Monitoring Health for the SDGs, Sustainable Development Goals. 2017. Available from: https://www.who.int/ghopublications/world_health_statistics/2017/en/ [Accessed: June 12, 2020]

[3] Ejike CECC. Prevalence of hypertension in Nigerian children and adolescents: A systematic review and trend analysis of data from the past four decades. Journal of Tropical Pediatrics. 2017;**63**:229-241

[4] Non-Communicable Disease Risk factor collaboration—NCD-RisC. Worldwide trend s in blood pressure from 1975 to 2015: A pooled analysis of 1479 population-based measurement studies with 19.1 million participants. Lancet. 2017;**389**:37-55

[5] Hardy ST, Urbina EM. Blood pressure in childhood and adolescence. American Journal of Hypertension. 2021;**34**(3):242-249

[6] Li S, Chen W, Srinivasan SR, et al. Childhood cardiovascular risk factors and carotid vascular changes in adulthood. The Bogalusa Heart study. Journal of the American Medical Association. 2003;**290**:2272-2276

[7] Litwin M, Niemirska A, Sladowska-Kozlowska J, et al. Regression of target organ damage in children and adolescents with primary hypertension. Pediatric Nephrology. 2010;**25**:2489-2499

[8] Janz KF, Baptista F, Ren S, Zhu W, Laurson KR, Mahar MT, et al. Association among musculoskeletal fitness assessments and health outcomes: The Lisbon study for the development and evaluation of musculoskeletal fitness standards in youth. Measurement in Physical Education and Exercise Science. 2021;**26**(4):297-305. DOI: 10.1080/1091367x.2021.2000414

[9] Musa DI, Dominic OL. Predictive capacity of anthropometric indicators of body fat in in identifying hypertension in adolescents. Annals of Pediatric Cardiology. 2021;**14**(4):465-470

[10] Nunes HEG, Alves CAS Jr, Concalves ECA, Silva DAS. What physical fitness is most commonly associated with adolescents' blood pressure? Perceptual and Motor Skills. 2017;**124**(6):1107-1120

[11] Awotebi A, Monyeki MA, Moss SJ, Strydom GL, Armstrong M, Kemper HCG. Relationship of adiposity and CRF with resting blood pressure of South African adolescents: The PAHL study. Journal of Human Hypertension. 2016;**30**:245-257

[12] Silva DAS, Lima LRA, Dellagana RA, Bacl EDA, Rech CR. High blood pressure in adolescents: Prevalence and associated factors. Revista Ciência & Saúde Coletiva. 2013;**18**:3391-3400

[13] Pate RR, Daniels S. Institute of Medicines report on fitness measures and health outcomes in youth. JAMA Pediatrics. 2013;**167**(3):221-222

[14] Garcia-Hermoso A, Ramirez-Campillo R, Izquirok M. Is muscular fitness associated with future health benefits in children and adolescents?

A systematic review and meta-analysis of longitudinal studies. Sports Medicine. 2019;**49**:1079-1094. DOI: 10.1007/340179-019-01098

[15] Hoekstra T, Boreham CA, Murray LJ, Troisk WR. Associations between aerobic and muscular fitness and cardiovascular disease risk: The Northern Ireland Young Hearts Study. Journal of Physical Activity and Health. 2008;**5**:815-829

[16] Buchan DS, Boody IM, Young JD, Cooper SM, Noakes TD, Mahoney C, et al. Relationships between cardiorespiratory and muscular fitness with cardiometabolic risk in adolescents. Research in Sports Medicine. 2015;**23**:227-239

[17] An KY, Kims OHM, Lee HS, Yang HI, Pork H. Cardiopulmonary fitness but not muscular fitness associated with visceral adipose tissue mass. Archives of Physiology and Biochemistry. 2021;**127**(3):717-222

[18] Boony E, Ferguson G, Smith-Engelsman B. Relationship between body mass index, cardiorespiratory and musculoskeletal fitness among South African adolescent girls. International Journal of Environmental Research and Public Health. 2018;**15**:1087

[19] Musa DI, Goon DT, Okuneye RO, Onoja-Alexander MO, Momoh JI, Angba TO. Visceral adiposity index, fitness and clustered cardiovascular disease risk in adolescents. African Journal of Primary Health Care & Family Medicine. 2024;**1691**:a4474. DOI: 10.4102/phcfm.v16i1.4474

[20] Artero EG, Ruiz JR, Ortega FB, et al. Muscular and cardiorespiratory fitness are independently associated with metabolic risks in adolescents: The HELENA Study. Pediatric Diabetes. 2011;**12**:704-712. DOI: 10.1111/j.1399-5448.2011.00769.x

[21] Mahar MT, Welk GJ, Janz KF, Laurson K, Zhu W, Baptista F. Estimation of lower body muscle power from vertical jump in youth. Measurement in Physical Education and Exercise Science. 2022;**26**(4):324-334. DOI: 10.1080/1091367x.2022.2041420

[22] Pourhosengholi MA, Vahedi M, Rahizadeh M. Sample size calculation in medical studies. Gastroenterology and Hepatology from Bed to Bench. 2013;**6**(1):14-17

[23] Musa DI, Toriola OO, Abubakar MN, Jonathan SU, Iornyor D, Agbana BE. Cardiorespiratory fitness and leg muscle power in relation to abdominal adipose tissue in adolescents. International Journal of Kinesiology and Sports Science. 2023;**11**(1):53-59

[24] World Medical Association. World medical association declaration of Helsinki ethical principles for medical research involving human subjects. Journal of the American Medical Association. 2013;**310**(20):2191-2194

[25] Marfell-Jones M, Stweart AD, de Ridder JH. International Standards for Anthropometric Assessment. Wellington, New Zealand: International Society for the Advancement of Kinantropometry; 2012. pp. 32-89. Available from: http://hdl.handle.net/11072/1510

[26] The Cooper Institute. FITNESSGRAM Test Administration Manual. 5th ed. Champaign, IL: Human Kinetics; 2017. pp. 39-64

[27] Gibson AL, Wagner DR, Heyward VH. Advanced Fitness Assessment and Exercise Prescription. 9th ed. Champaign, IL: Human Kinetics; 2025

[28] Zimmet P, Alberti KG, Kaufman F, Tajima N, Silink M, Arslanian S, et al.

The metabolic syndrome in children and adolescents—An IDF consensus report. Pediatric Diabetes. 2007;**8**:299-306. DOI: 10.1111/j.1399-5448.2007.00271.x

[29] Leger LA, Mercier D, Gadoury C, Lambert J. The multistage 20 metre shuttle run test for aerobic fitness. Journal of Sports Sciences. 1988;**6**:93-101. DOI: 10.1080/02640418808729800

[30] Mcguigan M. Administration, scoring and interpretation of selected tests. In: Halt GG, Triplet NT, editors. Essentials of Strength Training and Conditioning. 4th ed. Champaign, IL: Human Kinetics; 2015

[31] Singh JP, Larson MJ, Manolio TA, et al. Blood pressure during treadmill testing as a risk factor for new-onset hypertension: The Framingham Heart Study. Circulation. 1999;**99**:1831-1836

[32] National High Blood Pressure Education Working Group on High Blood Pressure in Children and Adolescents. The fourth report on the diagnosis, evaluation and treatment of high blood pressure in children and adolescent. Pediatrics. 2004;**114**:555-576

[33] Moore SA, McKay HA, Macdonald H, Nettlefold L, Baxter-Jones AD, Cameron N, et al. Enhancing somatic maturity prediction model. Medicine and Science in Sports and Exercise. 2015;**47**(8):1755-1764. DOI: 10.1249/MSS.0000000000000588

[34] Baxter-Jones ADG, Eisemann JC, Shera LB. Controlling for maturation in pediatric exercise science. Pediatric Exercise Science. 2005;**17**:18-30

[35] Swets JA. Measuring the accuracy of diagnostic systems. Science. 1988;**240**(4857):1285-1293. DOI: 10.1126/science.3287615

[36] Uwaezueke SN, Okoli CV, Ubesie AC, Ikefuna AN. Primary hypertension among a population of Nigerian secondary school adolescents: Prevalence and correlation with anthropometric indices: A cross-sectional study. Nigerian Journal of Clinical Practice. 2016;**19**:649-654

[37] Dewi R, Ramayati R, Rosdiana N, Ramayani OR, Siregar R, Siregar B. Waist circumference, body mass index and skinfold thickness as potential risk factors for high blood pressure among adolescents. Paediatrica Indonesiana. 2019;**59**:79-86

[38] Resaland GK, Mamen A, Boreham C, Anderssen SA, Andersen LB. Cardiovascular risk factor clustering and its association with fitness in nine-year-old rural Norwegian children. Scandinavian Journal of Medicine & Science in Sports. 2010;**20**:e112-e120. DOI: 10.1111/j.1600-0838.2009.00921.x

[39] Werneck AO, Silva DR, DG SMFC, Tomeleri CM, Fernandes RA, et al. Correlates of blood pressure according to early ontime, and late maturation in adolescents. The Journal of Clinical Hypertension (Greenwich). 2016;**18**:424-430

[40] Myers J, Vanishelbolm B, Kamil-Rosenberg S, Chan K, Kokkinos P. Physical activity, CRF and population attributable risk. Mayo Clinic Proceedings. 2021;**96**:342-349

[41] Zaqout M, Michel N, Baminaun K, Aherus W, Sprengeler O, Mohnarsd S, et al. Influence of physical fitness on cardio metabolic risk factors in European children. The IDEFICS study. International Journal of Obesity. 2016;**40**:1119-1125. Available from: www.nature.comlijo

[42] Rongling L, Alpert SB, Walker AA, Somes GW. Longitudinal relationship of

parental hypertension with body mass index, blood pressure and cardiovascular reactivity in children. The Journal of Pediatrics. 2007;**150**:498-502

[43] Stewart KJ, Sung J, Silbar HA, et al. Exaggerated exercise blood pressure is related impaired endothelial vasodialator function. American Journal of Hypertension. 2004;**17**:314-320

[44] Moller NC, Gronued A, Wedderkopp N, et al. Cardiovascular disease risk factors and blood pressure response during exercise in healthy children and adolescents: The European Youth Hearth study. Journal of Applied Physiology. 2010;**109**:1125-1132

[45] Welk GJ, Janz K, Laurson K, Mahar MT, Zhu W, Paulovic A. Development of criterion- reference standards for musculoskeletal fitness in youth: Considerations and approaches by the FitnessGram Scientific Advisory Board. Measurement in Physical Education and Exercise Science. 2022;**26**(4):276-288. DOI: 10.1080/1091367x.2021.2014331

[46] Baptista F, Zymbal V, Janz KF. Predictive validity of handgrip strength, vertical jump power and plank time in the identification of pediatric sarcopenia. Measurement in Physical Education and Exercise Science. 2021;**26**(4):361-370. DOI: 10.1080/1091307x.2021.1987242

Chapter 6

Transesophageal Electrophysiological Study for Pediatric Arrhythmias

Gabriel Cismaru, Puriș Cătălina-Maria, Voicu Răzvan Gabriel, Rus Oana, Țăpîrdea Andrada Olivia, Popescu Ioana Georgiana, Șonea Ștefan, Reuț Anca and Bârsu Cristian

Abstract

Since the nineteenth century, the intimate anatomical relationship between the esophagus and the heart has been highlighted, motivating research into cardiac stimulation through the esophagus. In 1980s, the technique of transesophageal pacing was refined using impulse duration of 10 ms and amplitudes of 15–25 mA, which was successful in the majority of patients. The technique can be used for measuring sinus node recovery time, revealing latent antegrade preexcitation, providing temporary treatment for bradyarrhythmias caused by sinus node dysfunction or AV block, inducing and terminating supraventricular tachycardias, inducing atrial fibrillation in patients with preexcitation and measuring the shortest RR interval, converting atrial flutter to sinus rhythm, regulating high-rate atrial fibrillation to a slower ventricular response, demonstrating capture and fusion in patients with ventricular tachycardia, and evaluating the efficacy of antiarrhythmic medications for atrial or ventricular arrhythmias.

Keywords: esophagus, pacing, electrophysiological study, pediatric, WPW syndrome, arrhythmia

1. Introduction

Since the nineteenth century, the close anatomical relationship between the esophagus and the heart has been highlighted, raising the question of the stimulation of the heart through the esophagus. This relationship is valid only in humans, in other animals; the distance between the esophagus and the heart is greater.

Augustus Waller (1856–1922), a British physiologist, who recorded for the first time the human electrocardiogram using a capillary electrometer in 1887, was also the first to record in 1889 the cardiac electrogram from the esophagus [1]. Later in 1906,

the German physiologist Max Cremer (1865–1935) recorded a transesophageal cardiac electrogram using an electrode ingested by a sword swallower under fluoroscopic guidance [2]. In 1934, Lieberson and Liberson introduced an esophageal electrode in 6 patients and confirmed its position using X rays. In 1936 WB Hurst [3] refined the technique, and calculated the distance from the teeth to posterior wall of the left atrium finding a value of 35 to 37 cm. It can also be calculated using the formula 1.33 x distance between thyroid to inferior sternum. This value was derived from fluoroscopic measurements and calculations of body surface distances.

Brody and Copeland further clarified the technique of transesophageal unipolar and bipolar recording in 1959 [4]. In 1952, Paul M Zoll reported the experimental application of transesophageal pacing combined with subcutaneous pacing of the ventricle in dogs. The method was used in 2 human patients with Adams Stokes syncope to stimulate the ventricles [5].

McNally et al. [6] reported in 1966 that cardioversion of atrial fibrillation in 8 human patients using one electrode in the esophagus and the second one in precordial position. In a preliminary study, they used the same method on 6 dogs with good success rate.

In 1965, Bernard Burack and Seymour Furman [7] tried transesophageal ventricular pacing on dogs, without any success. The distance between the esophagus and the ventricle is considerable; therefore, high amplitude stimulation with 25 jouls was ineffective in obtaining ventricular capture. After sewing the posterior wall of the ventricle to the esophagus, ventricular stimulation was possible. In 1969, they used the same method on a patient foe 36 hours, without any local complication at the level of the esophagus.

In 1972, Serge Barold managed to filter bipolar esophageal electrograms using 5818 Medtronic catheters obtaining signals comparable to intracardiac electrograms [8].

In the same year, Stopczyc and Zochowski [9] reported transesophageal atrial pacing in a 57-year-old female patient with repeated episodes of sinus arrest.

In 1973, Julio Montoyo [10] from Barcelona Spain reported the possibility to stop atrial arrhythmias by using transesophageal pacing. In 22 patients with different types of atrial arrhythmias: paroxysmal supraventricular tachycardia, atrial flutter, atrial fibrillation, and nonparoxysmal atrioventricular junctional tachycardia, the technique was effective only in patients with PSVT and NPAVJT.

In 1978, Rocchi and Santini [11] used transesophageal pacing to measure the sinus node recovery time. In 1982, John Gallagher [12, 13] refined the technique of transesophageal pacing using impulse duration of 10 ms and amplitudes of 15–25 mA, which was successful in the majority of patients. The technique was used to induce and to stop supraventricular arrhythmias. The unipolar signals were filtered at 0.1–1 kHz and the bipolar signals at 50–1 kHz.

The proposed indications for transesophageal pacing are (1) measurement of sinus node recovery time, (2) unmask latent antegrade preexcitation, (3) temporary treatment of bradyarrhythmias due to sinus node dysfunction or AV block, (4) induction and termination of supraventricular tachycardias, (5) induction of atrial fibrillation in patients with preexcitation with measurement of shortest RR interval, (6) conversion of atrial flutter to sinus rhythm or (7) transformation of high rate atrial fibrillation to a slower ventricular response AFib, (8) demonstration of capture and fusion in patients with ventricular tachycardia, and (9) assessment of the efficacy of antiarrhythmic drugs for atrial or ventricular arrhythmias (**Figure 1**) [14–40].

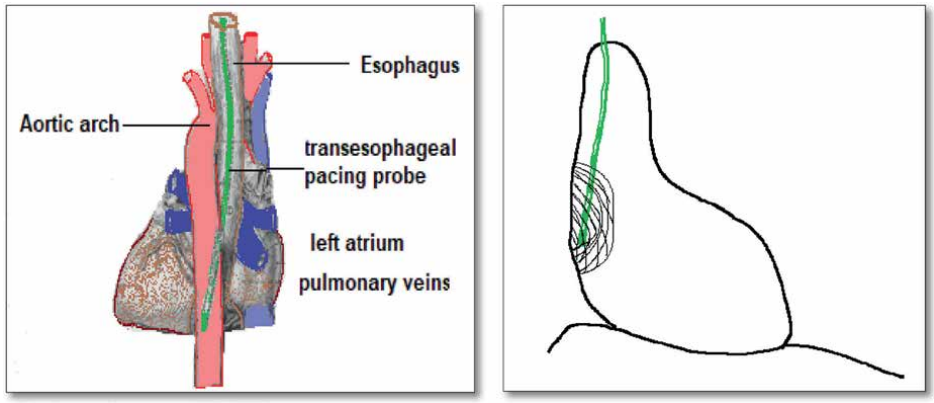

Figure 1.
(A) In transesophageal pacing, the probe is inserted inside the mid-esophagus that is in contact with the posterior wall of the left atrium. (B) Stimulating the esophagus the electrical field produces contraction of the atrium.

2. Technique of TTEPS in children

1. Prior to the procedure, the physician has to identify any contraindications to performing the transesophageal electrophysiological examination. Absolute contraindications include esophageal problems such as recent surgical interventions on the esophagus, esophageal strictures, esophageal perforation, or large diverticula with a risk of perforation, as well as the presence of an esophageal or gastric active bleeding. There are also contraindications that are relative, such as hiatal hernia, clotting disorders that could predispose to esophageal bleeding, and chest irradiation that could affect the esophagus [41–50].

2. Children aged >12 years generally tolerate well the transesophageal examination, without requiring analog-sedation. The pain felt during stimulation with 20 A is not very intense and is bearable. In pediatric patients under 12 years of age, analgosedation is favored due to their heightened anxiety, emotional instability, propensity to cry, and tendency to move during procedures, which may result in the loss of atrial capture. The procedure cannot be performed in uncooperative children with severe agitation. Consequently, the examination is conducted following the administration of Propofol and Midazolam, under the supervision of a specialized anesthesiologist. The pharmacological effects are transient, allowing for quick recovery; typically, the child can be discharged from the hospital within approximately 30 minutes and return home.

3. The preliminary step involves preparing the device: the stimulator is switched on and the esophageal stimulation probe is attached. This specialized probe features a significant inter-electrode distance, enabling the recording of atrial signals through the esophagus wall. A 12-lead electrocardiograph capable of capturing images at various coupling intervals during stimulation should be ensured.

4. Local anesthesia is performed with 1–2% Lidocaine spray, and the esophageal probe is lubricated with gel.

5. The probe is introduced to the esophageal level, using the distance from the ear to the xiphoid process as a reference, while monitoring for an atrial electrical signal.

6. Stimulation begins upon the appearance of an electrical atrial signal on the screen. Stimulation is not recommended in the absence of the atrial signal, as it confirms the accurate placement of the probe close to the left atrium.

7. Adjust the stimulator to a high amplitude of 20–25 A and a long pulse duration of 10 milliseconds. A stimulator capable of delivering long pulses is required for this purpose.

8. Stimulation is initiated, and the presence of atrial capture is assessed on the surface ECG. The necessary measurements on the surface ECG recordings are conducted.

9. The esophageal probe is removed, terminating the procedure.

3. Diagnostic utility

3.1 TEEPS for palpitations of unknown origin

Children with palpitations that are suggestive of paroxysmal tachycardia may benefit from TEEPS. The arrhythmia can be inducible by programmed atrial stimulation and may be stopped by burst atrial pacing. Accurate diagnosis of palpitations of unknown origin is crucial for preventing cardiac complications. In the study of Yang et al. [51], the authors aimed to evaluate the diagnostic efficacy of combining wearable Patch ECG monitors with transesophageal electrophysiological studies in diagnosing palpitations of unknown origin. The study was conducted between October 2021 and July 2023 and included 569 patients, of whom 467 completed the study. The inclusion criteria were recurrent paroxysmal palpitations with or without associated symptoms (e.g., dizziness, syncope) and negative results from initial comprehensive evaluations. Exclusion criteria included significant esophageal or cardiac conditions, severe hypertension, and inability to continue Patch ECG monitoring. TEEPS was used to detect arrhythmias in the study population. Of the 467 patients, 342 (73.2%) had arrhythmias consistent with clinical symptoms, with supraventricular arrhythmias being the most common (72.38%). The diagnostic performance of TEEPS showed an accuracy of 91.65%, sensitivity of 89.97%, specificity of 98.86%, a positive predictive value (PPV) of 99.71%, and a negative predictive value (NPV) of 69.60%. For patients who did not exhibit arrhythmias on TEEPS, Patch ECG monitors were used for 2 to 6 weeks. Among 125 patients, 37 (29.6%) showed arrhythmias consistent with their clinical symptoms, with Patch ECG monitors demonstrating an accuracy of 99.2%, sensitivity of 97.37%, specificity and PPV of 100%, and NPV of 98.86%. The combined diagnosis method significantly improved diagnostic accuracy. The combined method showed an accuracy of 99.57%, sensitivity of 99.74%, specificity of 98.86%, PPV of 99.74%, and NPV of 98.86%. This dual approach helped detect arrhythmias, such as autonomic atrial tachycardia and inappropriate sinus tachycardia, which were missed by TEEPS alone. Patch ECG monitoring also detected arrhythmias such as paroxysmal atrial fibrillation and atrial flutter, providing a more

comprehensive diagnostic tool and reducing the risk of missed diagnoses. In conclusion, the study demonstrates that the combined diagnosis method enhanced the diagnostic efficiency for palpitations of unknown origin. The study suggests that this dual diagnostic approach can help identify arrhythmias that might be missed with TEEPS alone, ultimately improving patient outcomes.

3.2 TEEPS for pediatric tachyarrhythmias

Transesophagial pacing may be used for the diagnosis and treatment of paroxysmal supraventricular tachycardias. In the retrospective observational study of Manickavasagam et al. [52], the authors evaluated the diagnostic and safety profiles of Transesophageal Electrophysiological Study in pediatric patients with Supraventricular Tachycardia (SVT). Conducted at an Indian institution between January 2014 and December 2020, it aimed to assess the negative predictive value (NPV) of non-inducibility of tachycardia and the overall safety of TEEPS. The procedure involved stopping antiarrhythmic medications for at least five half-lives before testing tachycardia inducibility. An esophageal catheter was inserted, and pacing was performed to assess arrhythmia (including burst pacing, incremental pacing to the AV Wenckebach point, programmed extrastimuli pacing with up to three extrastimuli to induce tachycardia). Patients were monitored post-procedure for 2 hours and discharged within 24 hours, with no complications reported. The study comprised 18 children (8 males and 10 females), with a total of 22 TEEPS procedures. The children had a range of SVT mechanisms, including orthodromic AVRT, atrial tachycardia, and fetal tachyarrhythmia. Of the 22 procedures (3 children underwent more than one procedure), 16 aimed to evaluate tachycardia inducibility, with 6 children showing inducible tachycardia. Non-inducibility was observed in 9 children, and the negative predictive value of non-inducible tachycardia was 88.89%. In these cases, no recurrence of SVT was observed during follow-up. In contrast, 6 children with inducible tachycardia continued medications, and one had a clinical recurrence despite treatment. Four procedures were conducted to terminate incessant tachycardia, with some success in acute termination using sedation or intravenous adenosine. TEEPS was determined to be safe and effective for assessing arrhythmia mechanisms and evaluating the efficacy of medications in managing SVT. The high NPV suggests that non-inducibility on TEEPS is a reliable indicator of reduced arrhythmia recurrence. This is particularly useful in pediatric patients with conditions like Wolff–Parkinson–White Syndrome, where SVT may resolve with age, allowing for medication discontinuation when non-inducibility is confirmed. In conclusion, this study confirms that TEEPS is a safe and reliable procedure for diagnosing and managing SVT in children. It provides valuable information for decision-making, particularly regarding the continuation of antiarrhythmic medications, with a high negative predictive value supporting its use in guiding clinical management and improving patient outcomes.

In children with paroxysmal supraventricular tachycardia and without signs of ventricular preexcitation, TEEPS can elucidate the mechanism of the arrhythmia. In 2013, Brembilla-Perrot et al. [53] published a retrospective study that evaluated the clinical utility of transesophageal electrophysiological studies (TEEPS) for a period of 15 years (1996–2012) in a cohort of 140 pediatric patients referred for documented or suspected supraventricular tachycardia (SVT) and normal ECG in sinus rhythm. The study aims to assess the diagnostic yield of TEEPS as a less-invasive procedure for identifying the origins of arrhythmia and its impact in guiding further management, particularly radiofrequency ablation (RFA). The target population was represented

by patients aged from 5 to 19 years old with a history of SVT episodes and without preexcitation in sinus rhythm documented on surface ECG. TEEPS was performed using standard esophageal electrode catheters positioned in the mid-esophagus for atrial stimulation. Both before and after isoproterenol administration, incremental atrial pacing, and programmed extrastimulation protocols were used to define the nature of the induced arrhythmia and also the conduction properties. The procedure-associated negative effects were minimal and mostly linked to the insertion of the esophageal probe. The tachycardia induction rate was high, with atrioventricular nodal reentrant tachycardia (AVNRT) occurring in 81 patients (53% typical and 6% atypical) and atrioventricular reentrant tachycardia (AVRT) in 52, both concealed (23,5%) and manifest (13,5%) accessory pathways (AP) conduction. Among patients with AVRT, TEEPS effectively identified masked preexcitation in sinus rhythm with also two potentially malignant forms. Younger patients generally received oral antiarrhythmic medication unless very symptomatic, the catheterization with RFA being postponed until the age of 12–15 years old. Through TEEPS, this younger subpopulation was deprived of highly invasive intracardiac catheterization that would have not added any benefit to the diagnostic and therapeutical management. In older patients, the added value was the noninvasive selection of ablation candidates. The limitations of the technique referred to the fact that TEEPS cannot always differentiate between AVRT and AVNRT. However, invasive confirmation *via* intracardiac study can be indicated. Nevertheless, the procedure-related complications were minimal and manageable in the outpatient clinic, occurring mostly in younger patients. This study concluded that TEEPS is both a safe and effective tool for the noninvasive diagnosis of younger pediatric patients with SVT who are not very symptomatic. In teenagers, its benefit diminishes due to the high rate of ablation procedures that could be performed right during the diagnostic intracardiac catheterization. However, TEEPS seems to be an overall promising step in guiding the therapy for these patients.

Kayali et al. [54] from Turkey demonstrated the value of transesophageal pacing for the mechanism of supraventricular tachycardia in pediatric patients. The main objective of the study was to assess the effectiveness, indications, and diagnostic value of TEEPS in children presenting with symptoms suggestive of arrhythmias, those diagnosed with Wolf-Parkinson-White (WPW) syndrome, and patients with previously documented SVT. The study involved 132 children (49 males, 83 females) aged between 4.7 and 18 years, who underwent TEEPS between January 2010 and February 2015. Patients were divided into three groups based on the indication: (1) the Symptom group (91 patients—68.9%) with unexplained palpitations, syncope, or chest pain; (2) the WPW group (18 patients—13.6%) with no previously documented tachycardia; and (3) the Tachycardia group (23 patients—17.4%) with previously confirmed SVT. Standard ECG identified dysrhythmias in only 19 cases; Holter monitoring and exercise testing offered limited additional diagnostic value, highlighting the challenge of detecting arrhythmias with conventional noninvasive methods in pediatric patients. TEEPS was performed under fasting conditions using a quadripolar electrode inserted trans-nasally into the esophagus, with or without midazolam sedation, depending on the case (18 patients). Tachycardia was induced using programmed atrial stimulation, and if necessary, isoproterenol infusion. Tachycardia was successfully induced in 40 out of 132 patients (30.3%). Specifically, inducibility was 14.3% in the Symptom group, 38.9% in the WPW group, and 86.9% in the Tachycardia group. In the Symptom group, most patients presented with isolated palpitations, while only a minority had additional symptoms like chest pain or syncope; tachycardia was induced in 19.7% of those with palpitations alone and

was primarily AVNRT (atrioventricular nodal reentrant tachycardia). In the WPW group, 38.9% had inducible tachycardia, mostly AVRT (atrioventricular reentrant tachycardia), with two patients showing APERP (accessory pathway effective refractory period) values shorter than 250 ms. The majority of WPW patients were asymptomatic. In the Tachycardia group, inducibility was 86.9%, predominantly AVRT and AVNRT forms. The study demonstrated diagnostic accuracy with sensitivity of 86.9% and specificity 81.6%. The authors conclude that TEEPS is a safe, semi-invasive, and effective method for diagnosing SVT in children. It is especially useful in cases where noninvasive tests like ECG or Holter monitoring are inconclusive. Additionally, TEEPS can help stratify risk in asymptomatic WPW patients by assessing APERP.

The transesophageal method can also be used in neonates, with smaller TE probes provided by the same companies that deliver pediatric probes. The transesophageal electrophysiological study enables the detection of any potential persistence of the arrhythmia beyond the first year of life. The Italian team from Bari [55] described the use of TE pacing for neonates with paroxysmal supraventricular tachycardia that is the most prevalent arrhythmia in neonates. The authors evaluated the reliability of transesophageal electrophysiological study in the follow–up of these patients. A retrospective observation was conducted on 8 patients who presented with PSVT during the neonatal period. All patients underwent echocardiography and Holter monitoring and were discharged with an effective drug regimen for rhythm control, using one or two medications. Follow-up involved Holter monitoring every three months while on drug therapy. Once the patients reached one year of age, antiarrhythmic therapy was discontinued, and a transesophageal electrophysiological study was performed. This study included atrial stimulation at increasing frequencies and programmed atrial stimulation with single, double, and triple extra stimuli. If PSVT was inducible, therapy was resumed, and the study was repeated one year later following a washout period. Eight patients who presented with PSVT during the neonatal period were observed. Seven of these patients had structurally normal hearts, while one patient had aortic coarctation, which was corrected through aortoplasty. After one year of therapy, four patients (50%), half of whom were receiving dual therapy (flecainide combined with beta-blocker and/or amiodarone), were non-inducible. These patients, whose therapy was permanently discontinued, no longer experienced arrhythmic episodes during follow-up. The remaining four patients resumed therapy (with double therapy in half of the cases) for another year and then repeated the study after a washout period. One patient continued to present arrhythmias (the patient with corrected aortic coarctation), while the other three were non-inducible. During subsequent follow-up, arrhythmia recurred in only one of these three patients. Authors conclude that transesophageal electrophysiological study is a straightforward, minimally invasive, and reliable method for identifying neonates at risk of PSVT recurrence. In this study, the persistence of arrhythmia was found to be independent of the pharmacological treatment, whether administered as mono or dual therapy. It was also observed that in case of positivity after one year of therapy, the study can be repeated later allowing therapy to be interrupted at a later time.

3.3 TEEPS for children with ventricular preexcitation

The Italian group conducted by professor Drago [56] evaluated pediatric athletes with ventricular preexcitation by means of transesophageal pacing. The research investigated how somatic growth influences the electrophysiological properties of the heart by retrospectively analyzing 44 pediatric athletes (mean age at baseline:

10 years), each undergoing two electrophysiological assessments at a minimum interval of two years. Although both transoesophageal and intracardiac methods were employed, TEEPS was used in the majority of cases due to its noninvasive nature and favorable safety profile in children. The TEEPS procedure involved the insertion of a specialized catheter into the esophagus to deliver atrial stimulation and assess key conduction parameters—both at rest and under adrenergic stress (via isoproterenol infusion or exercise testing). This approach enabled detailed evaluation of the accessory pathway's effective refractory period (APERP), 1:1 conduction capacity, and arrhythmia inducibility, without the need for general anesthesia or vascular access. The results revealed that, over time, the accessory pathway demonstrated enhanced conduction capacity, indicated by a significant reduction in APERP and 1:1 conduction time at rest. Under adrenergic stress, the shortest preexcited R-R interval during atrial fibrillation also decreased significantly, suggesting an increased arrhythmic risk with growth. The inducibility of atrial fibrillation (AF) rose from 15.9% to 36.4% ($p = 0.05$), while atrioventricular reentry tachycardia (AVRT) increased from 20.5% to 31.8% ($p = 0.33$), though the latter was not statistically significant. Notably, six patients (13.6%) changed their electrophysiological risk category during the study: four transitioned from low- to high-risk, and two from high- to low-risk. These findings highlight the dynamic evolution of VPE during growth and the need for continued electrophysiological monitoring. The authors conclude that repeated evaluation using the transoesophageal approach is both feasible and clinically valuable in the long-term management of pediatric athletes with VPE. Given its diagnostic precision and minimal invasiveness, TEEPS represents a reliable tool for tracking changes in accessory pathway behavior, guiding the timing of catheter ablation, and supporting risk-based decisions regarding sports eligibility to minimize the potential for adverse cardiac events.

Hoyt et al. [57] tested the inducibility of atrial fibrillation by transesophageal pacing in children with asymptomatic ventricular preexcitation. They included 26 patients with an average age of 12 years, weight of 49 kg, and height of 149 cm. Atrial fibrillation could be induced by transesophageal pacing in 23 patients (88.5%) of whom 17 had a short RR interval < 250 ms and 6 had a long RR interval > 250 ms. The technique used by the authors included high voltahe, long duration impulses of 25 mV and 10 ms for a duration of up to 30 seconds with 140 ms cycle length. The method was effective in 88.5% of patients.

On a retrospective study, Koca et al. [58] evaluated 71 pediatric patients, of which 43 (60.6%) were male, with a median age of 14 (11–16) years, between November 2008 and January 2015. The means of the evaluation consisted of transthoracic echocardiography, ambulatory Holter monitoring, exercise stress test (EST), and TEEPS. An Invasive electrophysiological study was performed on 43 patients who were stratified as high-risk through TEEPS. Key findings showed that noninvasive tests, such as Holter monitoring and EST, have some capacity to predict high values of the accessory pathway effective refractory period (APERP), a risk indicator for WPW pattern. However, noninvasive tests were not as effective as TEEPS in accurately identifying high-risk cases. Specifically, 23 (39.1%) patients were considered low-risk by Holter monitoring and 26 (30.8%) of those considered low-risk by EST were classified as high-risk by TEEPS. TEEPS demonstrated a strong correlation with EPS. EPS was performed in 42 (59.2%) of the 71 patients. The median APERP was measured by EPS (230; 228–250), which was statistically lower than the median APERP measured by TEEPS (245, 239–260) ($p = 0.002$). Atrial fibrillation was induced in 5 (11.9%) patients during EPS, while none was induced during TEEPS. In regard to EPS, TEEPS

displayed the following values se = 100%, sp. = 16.7%, vpp = 87.8%, and vpn = 100%. Several limitations were noted in the study. Firstly, EPS data was not available for all participants, which limited the comparison of electrophysiological characteristics for low-risk accessory pathways. Secondly, the unavailability of isoproterenol, a drug used to provoke arrhythmias, for patients with low-risk accessory pathway conduction properties was a significant limitation. Lastly, the study population had a high proportion of asymptomatic patients (60%) that may limit the generalizability of the findings. In conclusion, the study suggests that noninvasive tests may underestimate risk in some pediatric patients with WPW pattern. The authors recommend using TEEPS as an initial screening tool, with EPS reserved for patients identified as high-risk by TEEPS.

4. Therapeutic use of TEEPS

Numerous investigations have shown the efficacy of transesophageal pacing in terminating supraventricular reentrant arrhythmias. Doni et al. [59] demonstrated 53% efficacy in interrupting atrial flutter without any antiarrhythmic drugs and 87% if propafenone 600 mg is added to transesophageal pacing. The same authors described 5 years later different protocols for interrupting atrial flutter and demonstrated that longer bursts of 30 seconds are more effective than shorter bursts of 5 seconds pacing. Hessling et al. [60] used this technique to stop atrial reentrant tachycardias in children that presented arrhythma after surgery for congenital heart disease. The success rate was 81% (50 out of 62 patients). Chen et al. [61] used the technique for other reentrant arrhythmis: 15 neonates with atrioventricular reentrant tachycardia using an accessory pathway, 3 with sinus tachycardia, 3 with ventricular tachycardia, 2 with slow-fast atrioventricular node reentrant tachycardia, and 2 with atrial tachycardia. For 22 neonates, overdrive suppression was used, with 18 successful transition to sinus rhythm. Four patients failed to convert to sinus rhythm: 2 with atrial tachycardia and 2 with ventricular tachycardia. This study's concern is that patients with typical atrial flutter and postoperative atrial reentrant tachycardias constitute a highly heterogeneous cohort. Hessling et al. [60] combined these patient types; nonetheless, the response to pacing varies between typical counterclockwise flutter and left atrial flutter, as well as postoperative microreentrant atrial tachycardias. Thus, averaging the response to pace in these arrhythmias is untenable.

5. Follow-up after catheter ablation

The success rate of catheter ablation is high in children; however, recurrences are still possible. A noninvasive method to demonstrate recurrences is the transesophageal EP study. Gulgun et al. [62] aimed to evaluate the efficiency of transesophageal electrophysiologic study on follow-up of children who underwent radiofrequency ablation (RFA) of supraventricular tachycardia (SVT). TEEPS is an alternative to other investigations used to evaluate patients after successful SVT ablation: clinical evaluation, exercise testing, or Holter monitoring, which are more difficult to perform in children because they cannot describe their symptoms accurately or they tend to not complete the entire exercise stages. A total of 66 patients were included in the study, out of 265 who underwent RFAs for SVT between June 2007 and September 2012. There were 24 (36.4%) boys and 42 (63.6%) girls, and also,

41 were asymptomatic and 25 still had symptoms. Mean age at the time of TEEPS was 11.8 years. They were monitored for an average period of 44.1 months, and the interval between the RFA procedure and subsequent TEEPS was 5.2 months. During the procedure, SVT (AVRT and AVNRT) was induced in 5 out of 41 (12.1%) asymptomatic patients and in 2 out of 25 (8%) symptomatic, without any other arrhythmia being observed. SVT inducibility rates were 5.5% for AVRT patients and 12.7% for those with AVNRT. 85.7% of these recurrences occurred within 3.5 months post-RFA. Individuals that were symptomatic (chest pain and palpitations) were identified in the first month after the procedure, and those asymptomatic were detected within 3.5 to 15 months. The limitations of this study were: not all patients who underwent RFA were included due do difficulties in accessing data, as some of them did not come back to the same hospital and were treated by their local cardiologist. Also, it only evaluated the mid-term effectiveness of TEEPS and there was no long-term follow-up. The findings suggest that TEEPS is a valuable diagnostic tool for identifying SVT recurrences in both symptomatic and asymptomatic pediatric patients following successful RFA. The study emphasizes the importance of monitoring for recurrences, particularly within the initial four months after the ablation procedure.

6. Conclusions

An electrophysiology study is an invasive percutaneous cardiac intervention used for the diagnosis and treatment of certain arrhythmias. The noninvasive form is the transesophageal EP study, performed with the use of a flexible thin transesophageal probe. The aims of the TEEPS are to identify the mechanism of the arrhythmia, risk stratification, and determine the response to antiarrhythmic therapy. Decremental atrial pacing and atrial extrastimulus testing permits identification of an accessory pathway, dual nodal conduction pathway, and induce a specific arrhythmia: fibrillation, flutter, or tachycardia [63–66].

The field of electrophysiology has significantly advanced in recent decades. The application of EP research in clinical practice has markedly improved. Electrophysiological studies remain an invasive procedure with restricted applicability in specific niche purposes, while they can yield important insights in particular arrhythmias. Clinicians need to understand the importance and utility of noninvasive electrophysiological tests using the transesophageal approach and recommend patients for this noninvasive examination judiciously, adhering to the principles of high-value care.

DOI: http://dx.doi.org/10.5772/intechopen.1012524

Author details

Gabriel Cismaru[1*], Puriș Cătălina-Maria[2], Voicu Răzvan Gabriel[2], Rus Oana[2], Țăpîrdea Andrada Olivia[2], Popescu Ioana Georgiana[2], Șonea Ștefan[2], Reuț Anca[2] and Bârsu Cristian[3]

1 4th Department of Internal Medicine, Cardiology Rehabilitation, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

2 Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

3 Department of Abilities - Humanistic Sciences, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

*Address all correspondence to: gabi_cismaru@yahoo.com

IntechOpen

References

[1] Waller A. On the electromotion changes connected with the beat of the mammalian heart and the human heart in particular. Philosophical Transactions of the Royal Society. 1989;**180**:169

[2] Cremer M. Uber die direkte ableitung der aktionsstrome des menslichen herzens vom esophagus und uber das elektrokardiogramm des fetus. Münchener Medizinische Wochenschrift (1950). 1996;**53**:811

[3] Hurst BW. A study of the esophageal lead in clinical electrocardiography: Part I. The application of the esophageal lead to the human subject with observations on the Ta wave, extrasystoles, and bundle branch block. American Heart Journal. 1936;**12**(1):20

[4] Brody DA, Copeland GD. The principles of esophageal electrocardiography. American Heart Journal. 1959;**57**:3

[5] Zoll PM. Resuscitation of the heart in ventricular standstill by external electric stimulation. The New England Journal of Medicine. 1952;**247**:768

[6] McNally EM, Meyer EC, Langendorf R. Elective countershock in unanesthetized patients with use of an esophageal electrode. Circulation. 1966;**33**:124

[7] Burack B, Furman S. Transesophageal cardiac pacing. The American Journal of Cardiology. 1969;**23**:469

[8] Barold SS. Filtered bipolar esophageal electrocardiography. American Heart Journal. 1972;**83**:431

[9] Stopczyc MJ, Zochowski RT. P wave-triggered permanent atrial pacing in a case of transient sinus arrest. British Heart Journal. 1972;**34**:318

[10] Montoyo JV, Angel J, Valle V, Gausi C. Cardioversion of tachycardias by transesophageal atrial pacing. The American Journal of Cardiology. 1973;**32**:85

[11] Santini M, Rocchi M, Masini M. Study of sinus node recovery time by means of transesophageal atrial pacing. In: Meere C, editor. Proceedings of the Sixth World Symposium on Cardiac Pacing. Montreal: Pacesymp; 1979

[12] Gallagher JJ, Smith WM, Kassel J. Use of the esophageal lead in the diagnosis of mechanism of reciprocating supraventricular tachycardia. PACE. 1980;**3**:440

[13] Gallagher JJ, Smith WM, Kerr CR. Esophageal pacing: A diagnostic and therapeutic tool. Circulation. 1982;**65**:336. 350 U. Simoncelli et al

[14] Crawford W, Plumb VJ, Epstein AE, Kay GN. Prospective evaluation of transesophageal pacing for termination of atrial flutter. The American Journal of Medicine. 1989;**86**:663

[15] Blomstrom-Lundqvist C, Evardsonn N. Transesophageal versus intracardiac atrial stimulation in assessing electro physiologic parameters of the sinus and a V nodes and of the atrial myocardium. PACE. 1987;**10**:1081

[16] Chung DC, Kerr CR. Cooper 1. Termination of spontaneous atrial flutter by transesophageal pacing. PACE. 1987;**10**:1147

[17] Delise P, D'Este D, Raviele A. Stimolazione transesofagea e

vulnerabilita atriale. In: Disertori M, Marconi P, editors. La Stimolazione Cardiaca Transesofagea. Rome: CIC Ed. Internazionali; 1987. p. 51

[18] Moquet B, Cosnay P, Fauchier JP, Rouesnel P, Mannara R, Rioux P, et al. Interet de la stimulation oesophagienne pour la reduction du flutter auriculaire. Annals of Cardiology Angiography. 1988;**37**:53

[19] Vergara FF, Disertori M, Bettini R, Stivpe E, Inama G, Guarnerio M, et al. La valutazione elettrofisiologica degli atleti con Wolff-Parkinson-White: Induzione di tachiaritmia sopraventricolare di base e sotto sforzo con elettrostimolazione atriale transesofagea. Giornale Italiano di Cardiologia. 1986;**16**:625

[20] Wellens HJJ, Durrer D. Wolff-Parkinson-white syndrome and atrial fibrillation: Relation between refractory period of the accessory pathway and ventricular rate during atrial fibrillation. The American Journal of Cardiology. 1974;**34**:777

[21] Merkulova IN, Khakimov AG, Chikvashvili DI, Karpov I. Evaluation of the informative value and safety of the transesophageal atrial electric stimulation test in patients with unstable stenocardia and myocardial infarction. (Data of 24 hours Holter monitoring.) Kardiologia. 1987;**27**(10):69

[22] Doni F, Della Bella P, Kheir A, Manfredi M, Piemonti C, Staffiere E, et al. Atrial flutter termination by overdrive transesophageal pacing and the facilitating effect of oral propafenone. The American Journal of Cardiology. 1995;**76**(17):1243

[23] Dick M, Scott AW, Serwer GS, Vergara G, Inama G, Disertori M. Acute termination of supraventricular tachyarrhythmias in children by trans esophageal atrial pacing. The American Journal of Cardiology. 1988;**61**:925

[24] La DM. stimolazione atriale transesofagea nel trattamento del flutter atriale: Utilita e limiti. Giornale Italiano di Cardiologia. 1993;**23**:281

[25] Gallay P, Bertichant JP, Lehujer C, Erreva J, Leenhardt A, Grolleau R, et al. La stimulation transoesophagienne dans Ie traitement du flutter de la tachysistolie auriculaire. Archives des Maladies du Coeur et des Vaisseaux. 1987;**78**:311

[26] Gallo G, Maggi A, Gei P. Induzione di fibrillazione ventricolare tramite pacing transesofageo in soggetti con flutter atriale e funzionalita' ventricolare sinistra compromessa. Giornale Italiano di Cardiologia. 1993;**23**:279

[27] Lambertz H, Kreis A, Trumper H, Hanvath P. Simultaneous transesophageal atrial pacing and transesophageal two dimensional echocardiography: A new method of stress echocardiography. JACC. 1990;**16**:1143

[28] Girardot C, Diebold P, Morelon P, Dentan G, Fraisson M, Eicher JC, et al. La stimulation transoesophagienne dans Ie traitement du flutter e de la tachysistolie auriculaire: Factor influencant Ie resultats immediate. Archives des Maladies du Coeur et des Vaisseaux. 1988;**81**:1379

[29] Don Michael TA, Rao G, Balasingam S. Accuracy and usefulness of atrial pacing in conjunction with transesophageal echo cardiography in the detection of cardiac ischemia (a comparative study with scintigrafic tomography and coronary arteriography). The American Journal of Cardiology. 1995;**75**:563

[30] Simoncelli U, Marchetti A, Sorgato A. Terapia elettrica transesofagea delle tachiaritmie sopraventricolari

parossistiche: fattori predittivi dell'efficacia. In: Disertori M, Marconi P, editors. Atti de La Stimolazione Cardiaca Transesofagea e L'elettrocardiografia ad Alta Risoluzione. New York, NY: Springer; 1993. p. 291. ISBN 978-1-4612-7261-8

[31] Raczack G, Swiatecka G, Lubinski A, et al. Transesophageal atrial pacing complications in patients suspected of tachy-Brady syndrome. PACE. 1990;**13**:2048

[32] Guarnerio M, Furlanello F, Del Greco M, Vergara G, Inama G, Disertori M. Transesophageal atrial pacing: A first choice technique in atrial flutter therapy. American Heart Journal. 1989;**117**:1241

[33] Kantharia BK, Mookherejee S. Clinical utility and the predictors of outcome of overdrive transesophageal atrial pacing in the treatment of atrial flutter. The American Journal of Cardiology. 1995;**76**(3):144

[34] Mandel W, Hayakowa H, Danzig R, Marcus HS. Evaluation of sino-atrial node function in man by overdrive suppression. Circulation. 1971;**44**:59

[35] Don Michael TA, Antonescu A, Bhambi B, Balasingam S. Accuracy and usefulness of atrial pacing in conjunction with transthoracic echocardiography in the detection of cardiac ischemia. The American Journal of Cardiology. 1996;**77**:187

[36] Santinelli V, Chiariello M, Clarizia M, et al. Esophageal ambulatory ECG monitoring: A new technique for detecting and differentiating supraventricular and ventricular arrhythmias. European Heart Journal. 1984;**5**(1):246

[37] Santini M, Ansalone G, Cacciatore G, Turitto G. Transesophageal pacing. PACE. 1990;**13**:1298

[38] Samson RA, Deal BJ, Strasburger JF, Benson DW. Comparison of transesophageal and intracardiac electrophysiologic studies in characterization of supraventricular tachycardia in pediatric patients. Journal of the American College of Cardiology. 1995;**26**:159

[39] Rhodes LA, Walsh EP, Saul JP. Conversion of atrial flutter in pediatric patients by transesophageal atrial pacing: A safe, effective, minimally invasive procedure. American Heart Journal. 1995;**130**(2):323

[40] Mangieri E, Greco C, Barilla' F, Critelli G. A complex arrhythmia defined by an esophageal lead. PACE. 1996;**19**:1122

[41] Disertori M, Vergara G, Inama G, Guarnerio M, Furlanello F. Protocollo per l'impiego della stimolazione cardiaca transesofagea nella diagnostica e nel trattamento delle aritmie. Giornale Italiano di Cardiologia. 1984;**141**(II):958

[42] Falk RH, Werner M. Transesophageal atrial pacing using a pill electrode for the termination of atrial flutter. Chest. 1987;**92**:111

[43] Kerr CR, Chung DC, Wickham G, Jameson M, Vordesbrugge S. Impedance to trans esophageal atrial pacing: Significance regarding power sources. PACE. 1989;**12**:930

[44] Woodrow Benson D, Jr JH, Strasburger JF. Utility of a stimulus artifact suppressor for transesophageal pacing. The American Journal of Cardiology. 1990;**65**:393

[45] Woodrow Benson D. Transesophageal electrocardiography and cardiac pacing: State of the art. Circulation. 1987;**75**(III):86

[46] Nishimura M, Katoh T, Hanai S, Watanabe Y. Optimal mode of transesophageal atrial pacing. The American Journal of Cardiology. 1986;**57**:791

[47] Kamp O, De Cock C, Funke Kupper A, Roos JP, Visser CA. Simultaneous trans esophageal two dimensional echocardiography and atrial pacing for detecting coronary artery disease. The American Journal of Cardiology. 1992;**69**:1412

[48] Favale S, Di Biase M, Rizzo U, Minafra F, Rizzoni P. Ventricular fibrillation induced by transesophageal atrial pacing in hypertrophic cardiomyopathy. European Heart Journal. 1987;**8**:912

[49] Jenkins JM, Wu D, Arzabaecher RC. Computer diagnosis of supraventricular and ventricular arrhythmias: A new esophageal technique. Circulation. 1979;**60**:977

[50] Arzbaecher R, Jenkins JM. A review of the theoretical and experimental bases of transesophageal atrial pacing. Journal of Electrocardiology. 2002;**35**(Suppl.):137-141. DOI: 10.1054/jelc.2002.37171

[51] Yang R, Yang L, Zhang Q, Wang S, Xu J. Wearable patch ECG monitors and transesophageal electrophysiological study for diagnosing palpitations of unknown origin. Frontiers in Cardiovascular Medicine. 2024;**11**:1469108. DOI: 10.3389/fcvm.2024.1469108

[52] Manickavasagam A, Patloori SCS, Perla HT, Chase D, Roshan J. Impact of transesophageal electrophysiological study on midterm management of pediatric tachyarrhythmias. Annals of Pediatric Cardiology. 2022;**15**(5-6):453-458. DOI: 10.4103/apc.apc_25_22. Epub 2023 Mar 1

[53] Brembilla-Perrot B, Moulin-Zinsch A, Sellal JM, Schwartz J, Olivier A, Zinzius PY, et al. Impact of transesophageal electrophysiologic study to elucidate the mechanism of arrhythmia on children with supraventricular tachycardia and no preexcitation. Pediatric Cardiology. 2013;**34**(7):1695-1702. DOI: 10.1007/s00246-013-0703-7. Epub 2013 Apr 23

[54] Kayali Ş, Ertuğrul I, Doğan V, Özgür S, Örün UA, et al. A valuable tool to determine supraventricular tachycardia in children: Trans-esophageal electrophysiological study. International Journal of Pediatric Research. 2016;**2**:023. DOI: 10.23937/2469-5769/1510023

[55] Catucci S, Lombardi M, Maiorano A, Massari E, Meliota G, Pirolo T, et al. Transesophageal electrophysiological study for follow up of neonatal paroxysmal supraventricular tachycardia. European Heart Journal Supplements. 2023;**25**(Suppl. D):D111

[56] Raimondo C, Flore F, Alberio AMQ, Garibaldi S, Campisi M, Tamburri I, et al. Impact of growth on electrophysiological properties of ventricular pre-excitation in paediatric athletes. Cardiology in the Young. 2025;**35**(2):261-266

[57] Hoyt WJ Jr, Thomas PE, DeSena HC, Steinberg JS, Harmon DE, Snyder CS. Atrial fibrillation induction by transesophageal electrophysiology studies in patients with asymptomatic ventricular preexcitation. Congenital Heart Disease. 2013;**8**(1):57-61. DOI: 10.1111/j.1747-0803.2012.00689.x. Epub 2012 Jun 21

[58] Koca S, Pac FA, Kavurt AV, Cay S, Mihcioglu A, Aras D, et al. Transesophageal and invasive electrophysiologic evaluation in children with Wolff-Parkinson-white pattern. Pacing and Clinical Electrophysiology.

2017;**40**(7):808-814. DOI: 10.1111/pace.13100. Epub 2017 Jun 1

[59] Doni F, Manfredi M, Piemonti C, Staffiere E, Todd S, Rimondini A, et al. New onset atrial flutter termination by overdrive transoesophageal pacing: Effects of different protocols of stimulation. Europace. 2000;**2**(4):292-296. DOI: 10.1053/eupc.2000.0126

[60] Brockmeier K, Ulmer HE, Hessling G. Termination of atrial reentrant tachycardias by using transesophageal atrial pacing. Journal of Electrocardiology. 2002;**35**(Suppl.):159-163. DOI: 10.1054/jelc.2002.37174

[61] Chen M, Qin JH, Tan XL, Huang J, Ma LZ, Zhang XM, et al. Value of transesophageal atrial pacing in neonates with tachyarrhythmia. Zhongguo Dang Dai Er Ke Za Zhi. 2018;**20**(9):734-736. Chinese. DOI: 10.7499/j.issn.1008-8830.2018.09.008

[62] Gülgün M, Özer S, Karagöz T, Akın A, Aykan HH, Özkutlu S, et al. Is transesophageal electrophysiologic study valuable in children with successful radiofrequency ablation of supraventricular tachycardia on follow-up for recurrence? Anatolian Journal of Cardiology. 2016;**16**(2):126-130. DOI: 10.5152/akd.2015.5895. Epub 2015 Mar 4

[63] Bongiorni MG, Soldati E, Paperini L, Pozzolin A, Levorato D, Arena G, et al. Evaluation of rate-responsive pacemakers by transesophageal Holter monitoring of spontaneous atrial rate. PACE. 1990;**13**:1755

[64] Critelli G, Monda V, Scherillo M, Coltorti F, Greco C, Reale A. The automatic implantable cardioverter/defibrillator: Transesophageal atrial pacing discloses the potential for erroneous discharge. PACE. 1988;**11**:419

[65] Favale S, Minafra F, Massari V, Tritto M, Rizzon P. Transesophageal versus intracardiac atrial stimulation in assessing anterograde conduction properties of the accessory pathway in Wolff-Parkinson-white syndrome. International Journal of Cardiology. 1991;**30**:209

[66] Tucker KJ, Wilson C. A comparison of transesophageal atrial pacing and direct current cardioversion for the termination of atrial flutter: A prospective, randomised clinical trial. British Heart Journal. 1993;**69/6**:530

Edited by Gabriel Cismaru

Pediatric cardiology has developed into a specialism within both pediatrics and cardiology over the past few decades. It covers cardiac disorders in developing children, from the fetal stage through young adulthood. Lifelong monitoring is sometimes necessary for children with congenital cardiac conditions, regardless of whether they have undergone surgery. The modern therapy of congenital heart disorders has led to a normal or almost normal life during childhood and adulthood. Diagnostic techniques and treatment methods have made significant progress in pediatric cardiology, leading to innovative procedures with higher success rates and improved quality of life. Advanced imaging techniques for pediatric patients encompass echocardiography, cardiac MRI, computed tomography, angiography, and electrophysiological examinations with three-dimensional mapping. Catheter procedures have evolved from atrial balloon septostomy to the innovation of novel occluders for atrial and ventricular septal defects. The improvement in stent quality has enabled better long-term outcomes with fewer complications. Over the last twenty years, pediatric invasive and semi-invasive electrophysiology has emerged as a standard component of treatment strategies. Transesophageal procedures can be performed in newborns and young children without the risks associated with invasive techniques. The pharmacist now exerts a greater influence in the routine practice of pediatric cardiology. Pediatric patients utilize the identical medications as adult cardiac patients; yet, drugs have infrequently received thorough evaluation in children via large-scale studies. The pharmacist's support facilitates a more customized, pediatric-oriented treatment.

Kaan Kırali,
Cardiology and Cardiovascular Medicine Series Editor

ISSN 3033-361X
ISBN 978-1-83634-459-9
9 781836 344599

Published in London, UK

IntechOpen