A RETROSPECTIVE REVIEW OF PATIENTS WITH TRANSPOSITION OF THE GREAT ARTERIES COMPLEX (TGA) THAT UNDERWENT SURGICAL REPAIR AT A REGIONAL CARDIAC REFERRAL CENTRE IN SOUTH AFRICA

By

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Submitted in partial fulfilment of the academic requirements
for the degree of MMed
in the Department of Cardiothoracic Surgery
School of Clinical Medicine
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Durban
2024

As the candidate's supervisor I have/have not approved this thesis for submission.

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Declaration

I, YASTEEL RAJENDRA MOHANPERSADH MAHARAJ, declare that

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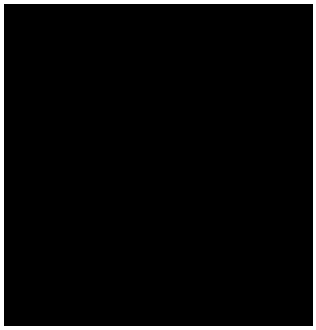
Signed:  Date: _2025/02/06 _

Dedication

To my parents, Rajendra Kumar and Jayshree Maharaj, whose wisdom and resilience have instilled in me the importance of hard work and determination. Your guidance has been a beacon of light throughout my academic endeavors, reminding me to pursue my passions relentlessly. Thank you for being a constant source of inspiration.

To my brother, Pavit, and sister, Juhi Kiara, who have always motivated me and provided a safe space for laughter and support. Your camaraderie and playful competitiveness fueled my drive to excel, and our shared experiences have made this journey more enjoyable. The love we share as siblings has and always will be unwavering.

To my supervisor, Dr Darshan Reddy, whose guidance has been pivotal in shaping this thesis. Thank you for your mentorship, constructive feedback, and encouragement throughout this process. Your expertise instilled in me a deeper understanding of Cardiothoracic Surgery.

To my head of department, Dr Rajhmun Madansein, thank you for your leadership and vision. Your commitment to fostering academic excellence has greatly impacted my training, and your support has encouraged me to strive for personal and professional growth.

To my senior colleague, Dr Manogran Moopanar, whose nurturing has shaped my character and values. Your infinite encouragement and faith in my potential have inspired me to strive for excellence as a surgeon. I am eternally grateful for your guidance during this journey.

To my dearest grandmother, the late Mrs Leelamathi Singh, thank you for always inspiring me to go for my dreams. I know you will be smiling down at your eldest grandchild fulfilling his childhood aspiration. You will forever live on in my memory with the utmost gratitude.

To my inspiration, role model and bigger brother, the late Dr Araj Hannooman. You mentored me in becoming not just a doctor but now a specialist surgeon too. Even if I only end up being an eighth of the surgeon you were, I would see my surgical career as a sterling success.

Lastly and by no means least, to my wife, Revashnee Maharaj. Your unconditional support, patience, and love have been my ultimate source of strength. Your belief in my abilities kept me going, and your sacrifices have been instrumental in this journey. Thank you for standing by my side during late nights and long weekends. Your understanding has meant the world to me.

As I reflect on this heartfelt journey, I realize that completing this thesis is as much a collective effort as it is an individual achievement. I am indebted to each of you for your contributions to my growth as an individual and as a scholar. This work is dedicated to you, with all my love, gratitude, and appreciation.

Acknowledgements

As I reach the culmination of my academic journey with the completion of this master's thesis, I would like to take a moment to express my profound gratitude to all the individuals and institutions that have supported me throughout this undertaking. The process of researching and writing this thesis has not only enriched my knowledge in my field of study but has also been a transformative experience, made possible through the guidance, encouragement, and assistance of many remarkable people.

First and foremost, I would like to extend my heartfelt thanks to my thesis supervisor, Dr Darshan Reddy. Your unwavering support, insightful feedback, and patience throughout this process have been invaluable. Your expertise and guidance have not only shaped my research but have also inspired me to pursue excellence in my academic endeavors. Thank you for challenging me to think critically and for believing in my potential.

I am also grateful to Mrs Selverani Naidoo, who assisted me unconditionally in my data collection and collaboration. The time dedicated by you to this project saved me many hours and allowed me to continue my clinical training as a surgeon. For that, you have my sincerest gratitude.

I express my gratitude to my sister, Dr Juhi Kiara Maharaj, who assisted in collating and capturing my data used for my thesis. Your thorough and meticulous work will serve you well in any research you may undertake in the future.

My heartfelt thanks go to Dr Gill Hendry, who provided me with the statistical analysis and data interpretation for this master's thesis. Your analytical acumen has aided in making us all better understand the outcomes of this thesis.

I would also like to express my appreciation to the Department of Health in KwaZulu Natal, Medical Management and Department of Cardiothoracic Surgery of Inkosi Albert Luthuli Central Hospital as well as the University of KwaZulu-Natal School of Clinical Medicine for allowing me to undertake this study and make this thesis possible. I hope that this project contributes to better patient outcomes and management in the future.

To my family and friends, your unwavering belief in me has been my anchor during moments of doubt. Thank you for your encouragement and understanding. Your love and support have provided me with the strength to persevere, even when faced with challenges.

In closing, this thesis is a product of the collective efforts and support of many, and I am deeply thankful to each person who has contributed to this journey, no matter how big or small. I hope that this work reflects the wisdom imparted to me and that it contributes meaningfully to the field of Cardiothoracic Surgery.

OVERVIEW OF THESIS

Transposition of the great arteries (TGA) is a complex congenital heart defect that is encountered globally, with established corrective surgical outcome data from the developed world.

TGA is anatomically characterised by the aorta arising primarily from the morphologic right ventricle, with the pulmonary artery arising from the morphological left ventricle. TGA physiology is present when the pulmonary artery saturations are higher than aortic saturation. TGA can be classified on a spectrum from simple to complex based on associated cardiac anomalies such as the presence of a ventricular septal defect or aortic arch obstruction.

The surgical treatment of simple TGA has evolved from historical physiological corrective procedures in the form of the atrial switch (Senning or Mustard operations) to the current global standard of anatomical repair in the form of the neonatal arterial switch operation. This highly technical procedure currently has survival rates of over 90% in experienced high-volume centres and appears to be a useful benchmark operation in paediatric cardiac surgery. In contrast, complex forms of TGA necessitate a variety of surgical procedures, and the approach to these anomalies varies from centre to centre.

The low mortality rate for the arterial switch operation in the developed world is not solely attributed to improvements in surgical technique – outcomes for complex congenital cardiac surgery procedures are related to the overall advances in quality of diagnostic imaging, neonatal intensive care, catheter interventions, anaesthesia and perfusion services, and post-surgical intensive care facilities and staffing.

Little to no published data exists on the morphological features, surgical management and outcomes data for patients with TGA undergoing surgery in Sub-Saharan Africa. This study is a retrospective review of patients that underwent surgical correction of TGA at a regional cardiac referral centre in Durban South Africa between January 2015 and December 2023. The data has been analysed and reported using internationally accepted standards and norms for the purposes of comparison and applicability to the existing published developed world data.

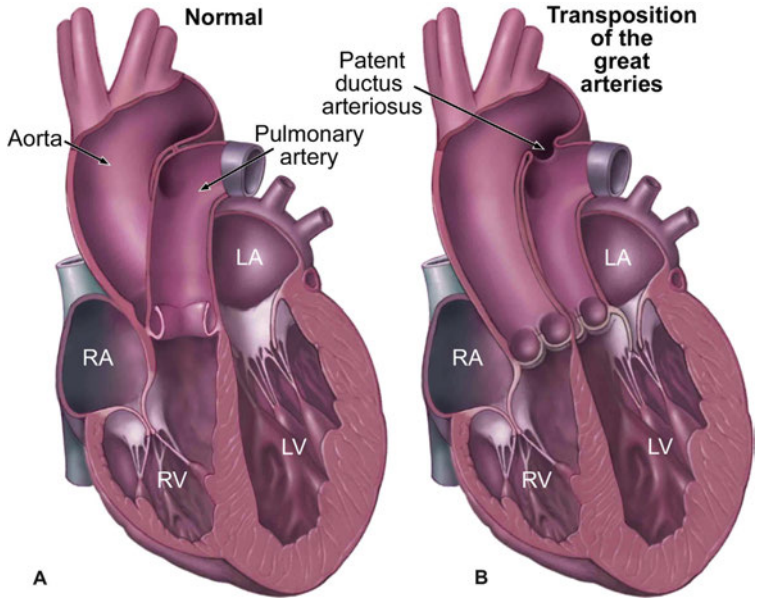
We believe that analysis of the surgical outcome data for TGA is a bellwether of the status of paediatric cardiac surgical services, and in particular neonatal cardiac surgery resources, in Sub-Saharan South Africa.

Part 1: The Review of Literature

LITERATURE REVIEW

Introduction

Transposition of the great arteries (TGA) refers to a condition where the heart has concordant atrioventricular connections but discordant ventriculoarterial connections. In TGA, there exists a cardiovascular malformation in which the morphologically right ventricle connects to the aorta and the morphologically left ventricle connects to the pulmonary trunk.[1, 2] This results in, the pulmonary and aortic circulations running in parallel instead of in series. Without adequate mixing of these circulations, through either a ventricular septal defect (VSD), a patent foramen ovale or patent ductus arteriosus (PDA), this lesion is not compatible with survival.[3] It is a critical cyanotic congenital heart defect comprising of 5% to 7% of all congenital heart disease and occurs in 3 per 10000 live births.[1, 2, 3] If left untreated, a mortality approaching more than 85% in the first year of life in those with untreated TGA. In the developed world, surgical management is well established, with the usual practice being an arterial switch operation (ASO). This is a single- stage anatomic repair, most commonly done within the first week of life following diagnosis.



(A) A heart with normally related great arteries with the pulmonary artery arising from the right ventricle and the aorta arising from the left ventricle. (B) A heart with TGA with the aorta arising from the right ventricle and the pulmonary artery arising from the left ventricle. Note that the great arteries in TGA are parallel to each other rather than in a spiral relationship. LA, Left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle. *(Cohen MS et al. Multimodality Imaging Guidelines of Patients with Transposition of the Great Arteries: A Report from the American Society of Echocardiography Developed in Collaboration with the Society for Cardiovascular Magnetic Resonance and the Society of Cardiovascular Computed Tomography. Journal of the American Society of Echocardiography. 2016 Jul;29(7):571–621)*

North America and Europe demonstrate a 30-day mortality of <3% with long-term 20-year survival approaching 90%. Despite these promising statistics, less is known regarding the outcomes of surgery in the developing world,[4] including South Africa.
One needs to bear in mind that the global demand for cardiac surgery is critical, with over 6 billion individuals in non-industrialized nations lacking access to necessary healthcare facilities. Cardiac surgery rates vary widely, ranging from 200 to over 1,000 operations per million people across different income brackets. Access remains limited, especially in Africa, which has only 22 cardiac centers outside South Africa.[5, 6]

Embryology

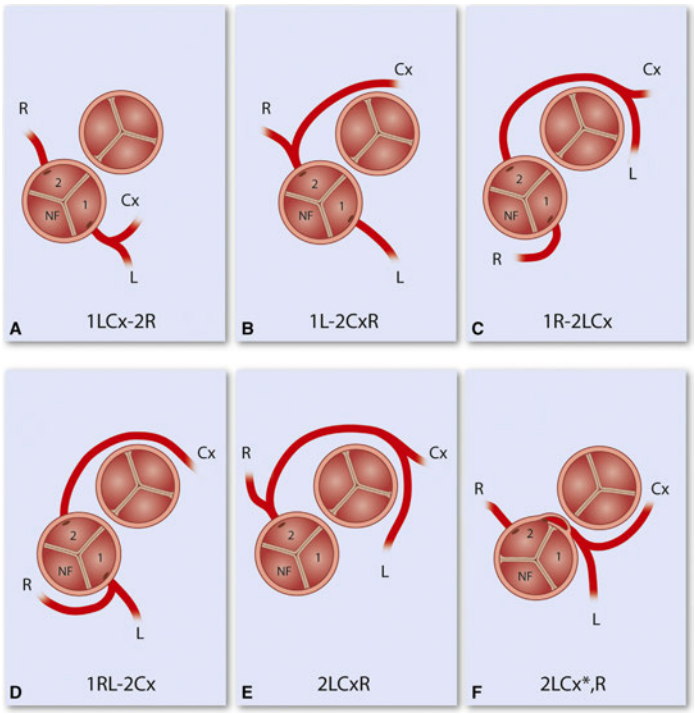
Two prominent theories explain the development of TGA. The first theory, formulated by Goor and Edwards, suggests that a lack of the normal clockwise rotation of the aorta towards the left ventricle results in TGA. Normal absorptions of the bulboventricular ledge allows the aorta to rotate to the left during normal development of the heart and become orientated over the left (or primitive) ventricle. Therefore, TGA is an extreme case of dextroposition of the aorta. This ranges from various forms of double outlet right ventricle (DORV), through Tetralogy of Fallot, up to malaligned ventricular septal defects (VSDs). If this absorption does not occur, there is perisistence of a subaortic conus, underdevelopment of the subpulmonary conus and dextroposition of the aorta occurs. A second theory by del la Cruz and colleagues proposes that TGA results from abnormal spiraling of the aorto-pulmonary septum. Here it is implied that there is no rotation during embryogenesis and that TGA is due to a linear, as opposed to normal, spiraling of the aortopulmonary septum. This results in the fourth aortic arch remaining (the future aorta) in contact with the anterior conus, situated on the right ventricle.[7]

Associated Anomalies

There are two types of TGA: the simple form, in which there is ventriculoarterial discordance without other associated cardiac anomalies, and the complex forms, which are further complicated by the presence of ventricular septal defects (VSD), ventricular outflow tract obstruction and/or coarctation of the aorta (CoAo).[8]
Ventricular septal defects (VSDs) are found in more than 40% of all patients diagnosed with TGA. A VSD can be simple type (perimembranous or muscular) or more complex type (malaligned, doubly committed subarterial, or inlet).
Anterior displacement of the septum results in hypoplasia of the right ventricular outflow tract (RVOT) is associated with coarctation, hypoplastic aortic arch, and interrupted aortic arch. Posterior malalignment of the outlet septum results in LV outflow tract obstruction (LVOTO) with pulmonary valve and subpulmonary stenosis.[9]

Aortic arch obstruction is more common in TGA with VSD, particularly in cases with double outlet right ventricle with subpulmonary VSD (Taussig–Bing anomaly) in which the incidence of aortic arch obstruction is approximately 50%.[9, 10] Some patients with associated hypoplastic arch as well interrupted aortic arch (IAA) also have associated DiGeorge syndrome (22q11.2 deletion syndrome). These patients have a higher morbidity due to depressed immunological status, hypocalcemia, bronchomalacia and bleeding tendencies.[11]

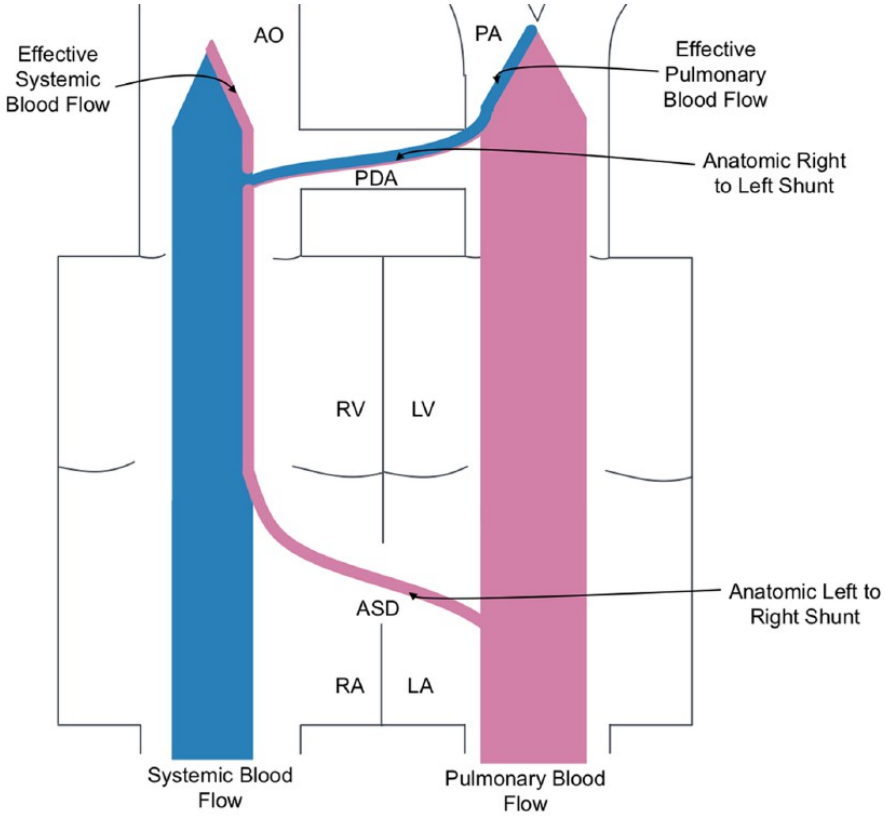
Coronary artery variations are associated with TGA, with almost all cases the coronary arteries arising from the aortic sinuses facing, or adjacent to the pulmonary artery. Leiden convention is the most commonly used classification system for describing coronary anatomy in TGA. Most coronary artery patterns can undergo an ASO with relatively low risk, but the presence of a single coronary ostium or an intramural coronary artery have both been shown to increase mortality risk.[12,13]



Variations in coronary anatomy in TGA, view from above. A, The most common form. B-D, Variations with a double sinus origin. E, Example of a single sinus 2 origin. F, The clinically most hazardous form is shown with the LCx taking off directly behind the facing commissure from sinus 2 and thereafter taking an interarterial/intramural course to the anterior aspect of the heart (indicated by an asterisk in the coding). The combination of L and Cx thereafter courses over the right ventricular outflow tract crossing anteriorly to the pulmonary orifice. R, Right; NF, nonfacing; Cx, circumflex; L, left. *(Gittenberger-de AC, Wilke, Bartelings MM, Bökenkamp R, DeRuiter MC, Hazekamp MG, et al. Coding of coronary arterial origin and branching in congenital heart disease: The modified Leiden Convention. 2018 Dec 1;156(6):2260–9)*

Pathophysiology

TGA is a contruncal abnormality in which there is ventriculoarterial discordance. This implies that the systemic venous return of deoxygenated blood flows from the right atrium (RA) through the right AV valve (tricuspid valve) to the right ventricle (RV) and to the aorta. In turn, the oxygenated pulmonary venous return flows into the left atrium (LA), through the left AV valve (mitral valve) into the left ventricle (LV) and then to the pulmonary artery (PA).
These systemic and pulmonary circulations act as two closed circuits running in parallel to each other. This is the basis for transposition physiology i.e., there is a higher oxygen saturation in the main PA than in the aorta. For a patient to survive, they require adequate systemic oxygen delivery.[3, 7, 9]



Schematic demonstrating the circulation of transposition of the great arteries with intact ventricular septum, with intercirculatory mixing at the atrial and great artery levels. The majority of the systemic and pulmonary blood flow is recirculated within the parallel circulations and is ineffective. An anatomical left-to-right shunt is seen at the atrial level, which ultimately enters the systemic circulation as effective, oxygenated systemic blood flow. An equal volume passes from the aorta to the pulmonary artery as effective pulmonary blood flow. As seen in the shunt at the PDA, a small portion of the anatomical shunt is derived from the pulmonary circulation; thus, the anatomical shunt may be greater than the effective pulmonary blood flow. This concept is important when understanding bidirectional shunting. Abbreviations: AO, aorta; ASD, atrial septal defect; LA, left atrium; LV, left ventricle; PA, pulmonary artery; PDA, patent ductus arteriosus; RA, right atrium; RV, right ventricle. *(Files MD, Arya B. Preoperative Physiology, Imaging, and Management of Transposition of the Great Arteries. Seminars in Cardiothoracic and Vascular Anesthesia. 2015 Apr 21;19(3):210–22)*

Clinical presentation

The clinical presentation varies greatly based on the degree of mixing at ductal, atrial, and ventricular levels. Neonates will demonstrate cyanosis to some degree but to varying degrees. Cyanosis and hypoxemia can range from very subtle to rapidly progressive cyanosis and hypoxemia that may become life-threatening within an hour of birth. The latter may collapse and require urgent resuscitation. Patients will also present with poor feeding after birth. On auscultation, S2 is single and loud. No heart murmur is heard in infants with an intact ventricular septum, but a continuous murmur in keeping with a closing PDA may be present. The presence of an early or holosystolic murmur of VSD may be audible in less cyanotic infants with associated VSD, while a mid-systolic murmur of pulmonary stenosis (PS or LVOT obstruction) may also be evident.[1, 3, 7]

Diagnosis

Chest radiograph: the classic description of TGA is that of increased pulmonary vascularity as well as of an egg-shaped or egg-on-a-string regarding the cardiac silhouette. This is due to the heart being globular in appearance as well as the narrow superior mediastinum and small thymus. However it is not uncommon for patients to present with a normal chest radiograph.[1, 3]

Electrocardiogram (ECG): Findings typically show right ventricular hypertrophy (RVH) as well as rightward QRS axis (i.e., +90 to +200 degrees). Some patients may also demonstrate normal ECG findings.[1, 3]

Transthoracic Echocardiography (TTE): In a newborn who presents with cyanosis with tachypnoea with suspected underlying congenital heart disease, an urgent transthoracic echo is required for further scrutiny. 2-D TTE has been the primary diagnostic imaging modality in patients with TGA for almost 40 years. TTE is safe, non-invasive, readily and widely available, relatively inexpensive and portable. It provides the ability to evaluate the anatomic and haemodynamic abnormalities in patients with TGA. This would include levels of shunting, assessment of the atrial communication and the PDA, severity of outflow tract obstruction, AV and semilunar valve function, assessment of the VSD, relationship of the great vessels and arch, qualitative assessment of ventricular function, and the presence of additional intrathoracic abnormalities. Coronary artery anatomy can also be assessed using a combination 2D and colour flow Doppler. TTE also guides interventional procedures such as balloon atrial septostomy (BAS) as well as closure or stenting of baffle leaks following atrial switch procedures.[3, 9]

Foetal ultrasound and Prenatal diagnosis of TGA: Prenatal diagnosis of TGA is becoming increasingly more common and with a high degree of accuracy. Dominguez et al demonstrated an accuracy rate between the prenatal and the postnatal diagnosis improving during pregnancy

from 84%, when considering the first diagnosis, to 93.6% with the last foetal diagnosis. From initial foetal ultrasound to final assessment before delivery, foetal ultrasound provides a detailed extracardiac structural survey as well as a complete echocardiography, cardiac dimensions, colour doppler to assess the septum for a suspected VSD, as well as colour Doppler assessment of the flow at the aortic arch can also be recorded and assessed. 2-D assessment of the spatial relationship between the great arteries is used to identify cases at high risk of having coronary anomalies such as an intramural course or single coronary artery. There may be non-cardiac abnormalities that require need addressing as well. Although the majority of cases are diagnosed post-natally, accuracy of antenatal diagnosis is increasing and can help in planning immediate management post-partum. The benefits of foetal ultrasound include optimal planning for delivery, postnatal care as well as offering prenatal counselling to parents.[8]

Medical and pre op management

An inadequately oxygenated patient will demise unless there is mixing of blood at either an atrial, ventricular or ductal level. As a results, not only will most patients die within the first few hours or days of life, but a multidisciplinary team approach is required for TGA patients even prior to definitive management. Patients require stabilization in neonatal ICU and subsequent transfer to a tertiary level centre where surgical care is available. Arterial blood gas should be routinely done and any electrolyte abnormalities (e.g. hypocalcemia or hypoglycemia) or metabolic acidosis should be corrected. In the patients who are severely hypoxic, oxygen should be administered either via nasal cannula, face-mask, CPAP or if required mechanical ventilation. Oxygen administration will help lower the PVR and increase the PBF, which will result in an increase in systemic arterial oxygen saturation. Concurrently, the patient would be commenced on a high dose prostaglandin (PGE_1) infusion (0.1mcg/kg/min) to reopen a closing PDA and also improve oxygen saturation. PGE_1 is continued throughout cardiac catheterization and septostomy, until definitive surgical repair. Other adjuncts to assist patients in congestive cardiac failure (CCF) include digoxin and diuretics. [3, 14, 15]

Prostaglandin (PGE_1)

Intravenous prostaglandin (PGE_1) has become one of the mainstays of medical treatment for hypoxic TGA patients. PGE_1 is particularly useful as part of the stabilization of patients whilst awaiting transfer to the appropriate referral centre or until definitive surgical repair. It is used to maintain patency of the PDA. This increases pulmonary blood flow, increasing pulmonary venous return and increase in left atrial pressure. This may enlarge the foramen ovale which promotes left to right flow at atrial level. However should the foramen ovale be restrictive, the increased pulmonary blood flow from the PDA may result in pulmonary congestion and low cardiac output

state.[3, 14] Other side effects include apnoea, bradycardia, fever with cortical hyperostosis observed in long-term use.[1, 16]

Balloon Atrial Septostomy (BAS)

Balloon Atrial septostomy is a safe and routine procedure indicated for patients with TGA complex that are persistently hypoxic and cyanotic despite initiation of PGE_1. It may also be required to be undertaken despite the presence of a VSD if there is still inadequate mixing. It can be undertaken at either the patient's bedside using echographic guidance or in the cardiac catheterization suite. Following a successful BAS, oxygen saturation should be dramatically improved within minutes. This also results in clinical and haemodynamic improvement in the patient. Associated risks and complications of BAS include vascular trauma, complete heart block, atrial arrhythmias, cardiac tamponade as well as a risk of stroke. There is an occasional transient hypotensive episode, most likely due to relief of left atrial hypertension and PDA shunting.[3, 16, 17]

Surgical management

Atrial Switch Operations

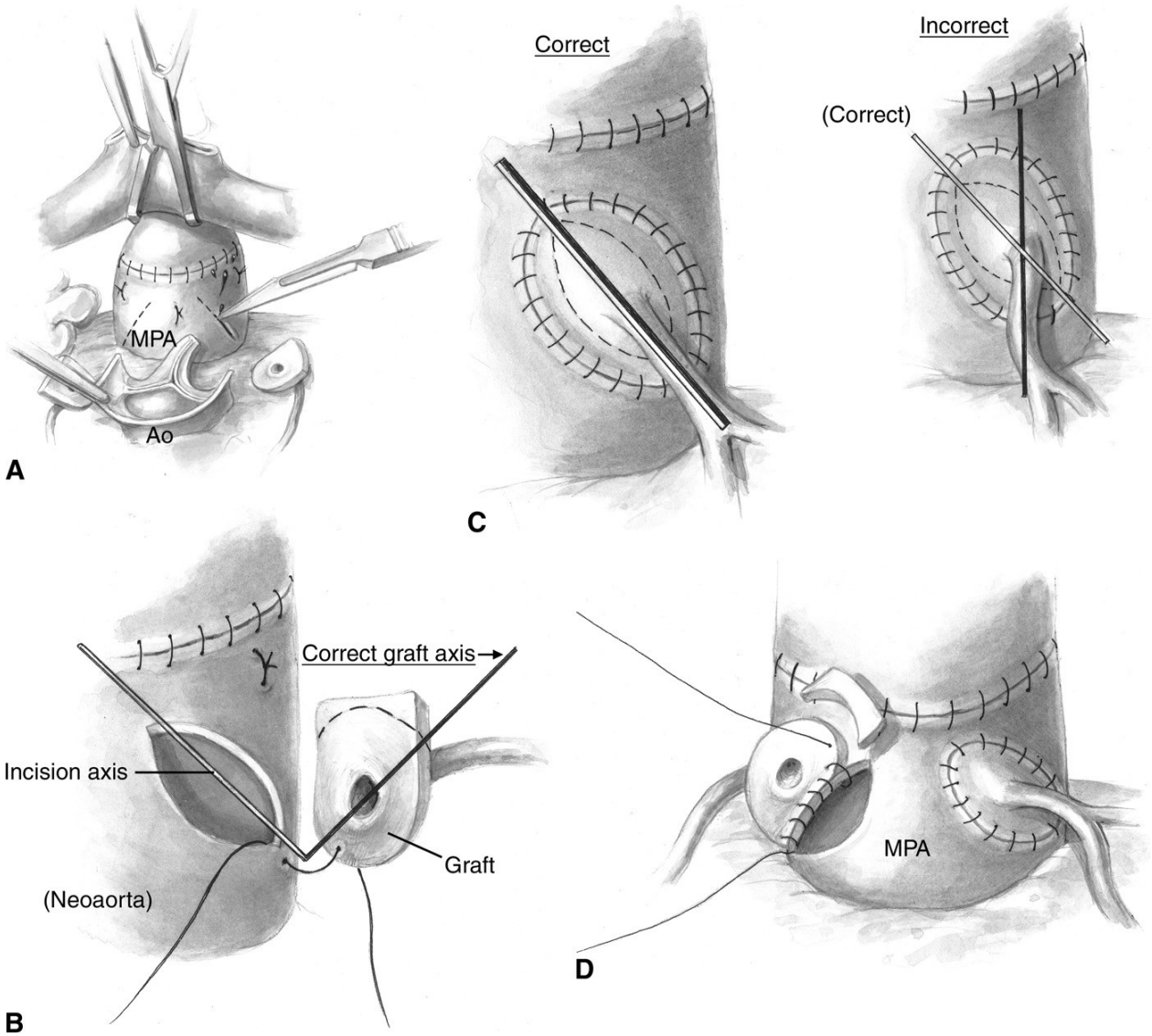
The 1950s saw the Mustard and Senning operations, which were the first successful surgical procedures for the management of TGA.[18] Atrial switch procedures are physiological corrections of TGA and involve redirection of blood flow at the atrial level – systemic venous flow to the mitral valve, the LV and the PAs. Concurrently, pulmonary venous flow to the tricuspid valve, the RV and the aorta. The Mustard procedure involves excision of the atrial septum and the use of autologous pericardium to form an intra-atrial baffle, whereas the Senning creates these pathways by cutting and folding of native atrial tissue. The ASO has almost entirely replaced these procedures, with the only indications being for congenital corrected TGA (ccTGA) or for late presentation TGA. Complications of these include systemic RV dysfunction, baffle obstruction, and arrhythmias. [19,, 20, 21]

The Arterial Switch Operation

The procedure of choice for patients diagnosed with TGA remains the arterial switch operation (ASO). Generally undertaken during the first days to 3 weeks of life, successful ASO demonstrates excellent early and long-term survival for a lesion that was considered fatal 50 years ago.[14, 18, 22, 23] The ASO is undertaken via median sternotomy and autologous pericardium is harvested and placed in glutaraldehyde for later use. This is followed by institution of cardiopulmonary bypass (CPB). Cannulation strategy involves aortic cannulation into the distal ascending aorta and bicaval venous cannulation into the SVC and IVC with snares. Systemic cooling of the patient to 18^{o}C is commenced, during which time the PDA is divided and the MPA and its branches are mobilized. Once target temperature is achieved, the aortic crossclamp is applied and a dose of cold crystalloid cardioplegia is administered through the aortic root. Following detachment of the aorta, both coronary ostia are visualized and coronary artery buttons are fashioned. Once the pulmonary artery is transected, coronary transfer is undertaken to the neoaorta. Thereafter, a Lecompte manoeuvre is performed and the distal ascending aorta is anastomosed to the neoaorta. Following reconstruction of the neopulmonary artery root with the treated autologous pericardium, closure of the VSD, ASD or septostomy is undertaken through the right atrium during a brief period of circulatory arrest. Once the atrium is closed, rewarming is commenced and the distal pulmonary artery is anastomosed to the neopulmonary artery root. The patient is then weaned off CPB and chest closed (if tolerated) and transferred to ICU ventilated on inotropic support. Failure of inability to wean from CPB may require the use of extracorporeal life support (ECLS).[15, 24, 25]

Coronary Transfer Techniques

Once the harvesting of the coronary buttons is undertaken, they are transferred to the neoaortic root. This can be done with one of two transfer techniques: the “open” or “closed” technique. These techniques describe undertaking the coronary transfer before or after neoaortic construction. The aim of the transfer is to do so torsion-free and with no tension.[12, 26] The closed coronary transfer is useful when there is only a single coronary present or if the great vessels lie side by side. In the open technique, the buttons are anastomosed to the medially created trapdoor incisions on the neoaortic root. This is prior to the distal ascending aorta being anastomosed to the neoaortic root.[10, 27, 28] Whilst there has been no superiority of the coronary transfer technique undertaken,[14, 16] there has been recent evidence that the “closed” technique offers better results regarding mortality and peri-operative complications, all without increasing the risk of post-operative neoaortic valve regurgitation.[29]



After removing the cross-clamp, distending the root, and closing the neo-aortic valve, the incision for the left coronary button is made within the facing sinus of Valsalva (A). The oblique orientation helps in achieving the proper orientation of the coronary artery (B, C), avoiding kinking of the vessel. The right coronary artery button is transferred using the same technique (D). Ao aorta; MPA main pulmonary artery. *(Bove EL. The Arterial Switch Procedure: Closed Coronary Artery Transfer. Operative Techniques in Thoracic and Cardiovascular Surgery. 2009 Jan 1;14(4):309– 16)*

TGA with Arch Hypoplasia and Ventricular Septal Defect

Concomitant aortic arch anomalies (either hypoplasia or interrupted aortic arch (IAA)) can be found in almost 10% of patients with TGA and even more common in Taussig-Bing anomaly. These patients are associated with higher morbidity and mortality.[10] A single stage primary repair has largely replaced the staged repair. In the single complete repair, the arch is repaired using deep hypothermic circulatory arrest or continuous antegrade cerebral perfusion. Additional cannulation of the PDA may be required in the cases of IAA. The VSD can be closed either through

the tricuspid valve or right ventriculotomy. Repair and arch augmentation is done with the use of a patch and the ASO is undertaken routinely. These patients tend to also have a longer CPB time as well as delayed closure of the sternum.[30 - 33]

TGA with Left Ventricular Outflow Tract Obstruction (LVOTO) – Rastelli, REV (Réparation à l'Etage Ventriculaire) and Nikaidoh techniques

TGA with LVOTO poses a unique difficulty as this precludes the use of the pulmonary valve as the neoaortic valve in some patients. Repair options include the Rastelli, REV or Nikaidoh procedures. The Rastelli procedure involves rerouting or baffling the LV outflow through the VSD with a tunnel patch to the aorta. This is done in combination with a RV to PA connection, using either a direct connection or a valved conduit. The REV procedure is similar to the Rastelli but differs in a key technical aspect – regarding restoration of RV to PA continuity, it is done so using a patch, which is also used to repair the RVOT, enlarge the PA stenosis and restore competence of the neopulmonary valve.[34 - 37]

In the Nikaidoh procedure, the aortic root is excised and translocated posteriorly into the stenotic LVOT following enlargement of the VSD. This is followed by a Lecompte manoeuvre and anastomosis of the MPA to the right ventricle with a patch. The Nikaidoh is seen as a suitable option for patients with moderate degrees of pulmonary annular hypoplasia.[37, 38, 39]

Timing of Surgery for ASO & Late Presentation of TGA

The timing of undertaking an ASO should be within the first 3 weeks of life. This is due to the progression of deconditioning of the LV as the PVR drops and the pressures generated by the LV deteriorate. It is therefore recommended that ASO can be undertaken until 60 days of life, provided that there is ECLS present as a support back-up.[14] In patients where the VSD is non- restrictive and without the presence of obstruction to systemic or pulmonary blood flow, surgery can be safely delayed up to 90 days of age.[40] For patients with ductal-dependent systemic or PA blood flow, as well as those with arch anomalies, neonatal intervention is required.[10] For patients with TGA +VSD+LVOTO, the timing of repair depends on the degree of cyanosis. Mild degrees of LVOTO allow surgical repair to be deferred beyond the neonatal period, whereas those with severely restricted pulmonary blood flow will require intervention as neonates. This would imply a systemic to PA shunt, whilst those undergoing definitive repair is based on institutional and surgeon preference.[34 - 37]

It is not uncommon for patients to present with a diagnosis of TGA beyond 3 weeks of age. Although common in the developing world,[6] it can occur on occasion in the developed world. It has been demonstrated that ASO can be undertaken up to 10 weeks of life safely and with comparable outcomes to neonatal ASO repairs.[15, 41, 42] This is instead of a rapid 2-stage that is advocated in most units, or repairs at an atrial level (Senning or Mustard). The rapid 2-stage

involved PA banding, an aortopulmonary shunt was fashioned proximal to the band, and subsequent anatomic repair was performed 6 months later.[43, 44, 45] Thus the need for mechanical circulatory support should be available as a rescue form of management.[15, 46]

Post op management

Postoperative Critical Care Management

Prior to transferring to the ICU, a transoesophageal echocardiogram (TOE) should be used to assess the presence of any residual lesions following the surgical repair. Patients should be transferred with standard monitoring comprising of continuous ECG, invasive arterial and central venous pressure (CVP), pulse oximetry and capnography.[16] The surgeon may also wish to insert a peritoneal dialysis catheter intraoperatively to aide in diuresis when needed. Upon arrival to the ICU, a 12-lead ECG and chest radiograph should be obtained. Providing adequate tissue perfusion is critical, maintaining acceptable mean arterial pressures (MAPs) of 35–45mmHg for newborns following an ASO. Patients should be transferred on milrinone (0.5-1.0 mcg/kg/min) and dopamine (3–5 mg/kg/min) or adrenaline (0.01–0.05 mg/kg/min) for additional LV support. Calcium chloride (10%) infusions at 5–15 mg/kg/h may also be helpful. In addition to milrinone, systemic afterload reduction can also be achieved with sodium nitroprusside.[10] Low-dose vasopressin, norepinephrine and phenylephrine are useful to optimize organ perfusion and urine output, especially if vascular tone is compromised. As such, it also assists in reducing a fluid overloaded state. Patients should be fully sedated and mechanically ventilated with nitric oxide available for usage in the ICU.[10, 14]

Low Cardiac Output Syndrome and Left Ventricular Dysfunction

Low cardiac output syndrome can occur after any procedure requiring cardiopulmonary bypass and cardioplegic arrest. It is multifactorial relating to inadequate myocardial preservation, long ischaemic time, post-inflammatory effects of CPB and coronary manipulation.[14, 47] In TGA, a neonate undergoing ASO may experience LV dysfunction and mitral regurgitation. Improvement of contractility is aided with inotropes, as well as afterload-reducing agents such as milrinone. These drugs aim to maximize systemic output. If the TTE or TOE shows decreased systolic function along with regional wall motion abnormalities, evaluation of the coronary arteries using cardiac catheterization is necessary. Other routine measures of cardiac output include urine output, blood gas evaluation, lactate level trend and near-infrared spectroscopy.[14]

Pulmonary hypertension

Although acute pulmonary hypertension (PHTN) following cardiac surgery in the current era has become less common, it can very rapidly escalate to a full-blown pulmonary hypertensive crisis resulting in cardiac arrest. PHTN is defined as a systolic pulmonary arterial pressure (PAP) of more than 35 mm Hg or a mean PAP of more than 25 mm Hg. It occurs in the postoperative period due to the physiologic consequences of RV pressure overload and ventricular dysfunction. Early signs of elevated PAP include hypotension, bradycardia and pallor due to drop in cardiac output. An increase in the arterial to end-tidal CO_2 gradient indicates decrease in pulmonary blood flow. Identification of these signs are essential as early intervention is necessary to prevent ischaemia of the right ventricle due to decreased coronary artery blood flow.[14, 48]

The principles of prevention and acute management of PHTN are that of reduction of sympathetic stimulation and lowering pulmonary vascular resistance (PVR). Stimulation is reduced by maintaining normothermia as well as full sedation and adequate analgesia. Premedication with muscle relaxants prior to noxious stimuli such as endotracheal tube suctioning can also be considered. Lowering of pulmonary vascular resistance involves correcting any metabolic or respiratory alkalosis/acidosis, mechanical ventilation to maintain adequate functional residual capacity and the use of vasodilating drugs. Examples of these would be inhaled nitric oxide, inhaled iloprost, nitroprusside and phosphodiesterase inhibitors such as milrinone and sildenafil. These measures should be continued for at least up to 24 hours post- operatively. [10, 14, 48]

Timing of Extubation

Patients who have undergone ASO should ideally be weaned from ventilatory support over 6 to 24 hours following surgery. However, those neonates complicated with ongoing bleeding, haemodynamic instability, rhythm abnormalities and delayed closure of the sternum should preferably remain mechanically ventilated. [14, 16] In a cohort by Varghese et al, it was demonstrated that 56% of their patients safely underwent immediate extubation following ASO. The predictors associated with a lesser likelihood of immediate extubation were patients who had a greater CPB and cross-clamp time, as well as those who underwent surgery with the lowest temperature on CPB being <30.4^{o}C. Immediate extubation was in turn associated with a shorter ICU length of stay and eventual drop in ICU costs and expenses.[49]

Outcomes

Mortality

Results following arterial switch operation, with or without the presence of VSD, in the developed world demonstrate mortality rates of less than 5% along with excellent early survival and long-term outcomes.[24] The presence of associated abnormalities including VSD, aortic arch repair, LVOTO, and intramural or single coronary anatomy are associated with higher mortality rates.[26, 50] Late ASO repair (>1 month), weight less than 3kg, and those requiring perioperative for ECMO are also associated with an increase in mortality risk.[51, 52] The most common cause of death is due to myocardial ischemia. Patients who have undergone other methods of repair for the spectrum of TGA complex such as the Rastelli, REV, and Nikaidoh also demonstrate less than 5% mortality risk. Regarding the developing world, an overall mortality rate approaches 15%.[4] Lack and limitation of resources, equipment, trained personnel, and appropriate referral patterns make achieving comparative results with the developed world challenging. A lack of available data adds increased difficulty regarding intermediate and long-term outcomes. It should be noted that the mortality rates of rapid 2-stage is higher than in those who presented for a late primary ASO.[4, 15]

Long-term outcomes following arterial switch operation

Whilst long-term outcomes demonstrate survival rates of more than 90%, reinterventions are sometimes required should certain complications occur. These would include RVOT obstruction, neoaortic valve regurgitation and coronary artery obstruction.[53, 54, 55]

Right Ventricular Outflow Tract Obstruction.

The occurrence of right ventricular outflow tract obstruction (RVOTO) after the arterial switch operation (ASO) ranges from 7% to 40%, positioning it as the predominant reason for late reoperations. While RVOTO can manifest as multilevel obstructions, the most commonly impacted areas are the main pulmonary trunk and the right pulmonary artery (PA) branch. Other potential sites of obstruction include the pulmonary bifurcation, the left pulmonary branch artery, and the infundibulum of the right ventricle. Notably, valvar stenosis is comparatively rare, affecting only 7.7% of patients. Various factors contribute to the risk of RVOTO, particularly techniques used during the reconstruction of the neopulmonary root, such as the excision of coronary buttons and potentially the Lecompte manoeuvre. The effects of previous PA banding remain inconclusive. Interventional options for managing this obstruction comprise balloon valvuloplasty with or without stenting, patch enlargement, or replacement of the PA with a

valved conduit. Rates of freedom from further interventions stand at 68% at one year, declining to 42% at five, ten, and fifteen years.[41, 56]

Neoaortic Root Dilation and Neoaortic Valve Regurgitation

In more than two thirds of patients, following ASO, there is some degree of neoaortic root dilation one can observe. This in turn is a significant risk factor for the development of neoaortic valve regurgitation. Neoaortic root dilation risk factors include Taussig-Bing anatomy, history of PA banding or aortic arch obstruction. The probability of remaining free from neoaortic root dilation decreases progressively over the years.[56, 63] The optimal timing for valve repair should ideally occur prior to the onset of severe aortic regurgitation, allowing the possibility of performing a valve-sparing root replacement; conversely, valve replacement is advised once severe regurgitation develops. [63] Long-term follow-up efforts should prioritize monitoring the progression of the left ventricular outflow tract (LVOT), with regular echocardiograms performed every one to two years. Surgical intervention is indicated upon the manifestation of symptomatic neoaortic regurgitation and/or progressive left ventricular dilation. [30, 31, 54, 55]

Coronary Artery Obstruction

The presence of coronary obstruction has been observed in 5% to 7% of late survivors. The incidence of myocardial ischemia, infarction, or mortality linked to coronary issues diminishes significantly after the first three months post-surgery, with an 88% rate of freedom from coronary events at 20 years.[12, 16] In light of the possibility of coronary obstruction, routine coronary angiographic evaluation of the coronary arteries within the first 2—3 years after repair is advocated. This is predominately done to maximise the potential for revascularization.[26, 57, 58] These patients would require surgical angioplasty of the obstructed main coronary arteries, which can be undertaken safely with satisfactory outcomes.[59, 60]

Arrhythmias

The occurrence of arrhythmias following ASO is relatively low, with over 94% of patients remaining arrhythmia-free for up to 25 years of follow-up. Late arrhythmias, arising beyond 30 days post-operation, affect 2.4% to 9.6% of patients and are typically associated with residual hemodynamic lesions or coronary artery occlusion.[16] In contrast to patients post-ASO, those who have undergone the atrial switch procedure (Mustard/Senning) face a significantly heightened risk of arrhythmias. Atrial arrhythmias often arise from intra-atrial baffle placement and resultant scarring. Medical therapy and cardioversion are the primary treatments for maintaining normal

sinus rhythm. However, these patients will inevitably require pacemaker insertion due to eventual low cardiac output from RV dysfunction, rather than for control of arrhythmias. [20, 21, 61]

Outcomes Specific to the Rastelli, REV and Nikaidoh Procedures

Following the Rastelli procedure, patients are susceptible to reoperation due to issues such as RV to PA conduit stenosis and left ventricular outflow tract obstruction stemming from stenosis of the LV to aortic baffle site. Other less frequent causes for reintervention include tricuspid regurgitation and residual aortic arch obstruction. Factors that elevate the risk of late intervention encompass a history of ventricular septal defect (VSD), aortic arch obstruction, prolonged cardiopulmonary bypass times, and postoperative neoaortic stenosis or regurgitation at discharge. Patients who also present with Taussig-Bing anatomy, show a markedly poorer rate of freedom from reintervention. [47, 48, 61] Due to mobilization and reimplantation, there is added risk of coronary insufficiency in those undergoing aortic root translocation. Other concerns include residual VSD, conduction abnormalities, LVOTO, and RVOTO. Late intervention is required regardless of surgical procedure for either valve regurgitation or conduit stenosis.[34, 35, 57]

Neurodevelopmental Outcomes

Neurodevelopmental impairment is frequently described in ASO survivors. Infants diagnosed prenatally who receive prompt resuscitation and quick initiation of prostaglandin infusion display markedly higher performance in executive functioning and social cognition assessments compared to those diagnosed after birth. Conversely, those who go undiagnosed at birth are at an elevated risk for complications such as ductal closure, acidosis, and hypoxia, which can lead to hypoxic-ischemic injury. Common deficits following ASO include visual-spatial skills, carrying out executive functions, and memory. Also, there is a higher incidence of depression and anxiety disorders. Predictors of long-term outcomes include gender and parental socioeconomic and educational status. Evaluation of long-term neuropsychological issues in early adulthood is a critical component to long-term success and is a major driver in the adoption of treatment strategies.[45, 56, 62]

Part 2: A submission ready manuscript.

TITLE

Surgery for transposition of the great arteries complex at a regional referral centre in South Africa

ABSTRACT

Background: This study describes the surgical treatment of transposition of the great arteries (TGA) at a regional referral centre in South Africa over a nine year period

Methods: A single centre retrospective observational analysis of patients that underwent surgical repair of TGA between January 2015 and December 2023 at Inkosi Albert Luthuli Central Hospital in Durban, South Africa.

Results: A total of 37 consecutive patients that underwent surgical repair of TGA during the study period were included,15 (40.6%) patients with intact ventricular septum (TGA-IVS), 17 (45.9%) with ventricular septal defect (TGA-VSD), and 5 (13.5%) patients with aortic arch hypoplasia or pulmonary stenosis (TGA-complex). There were 4 (10.8%) early (< 30 day) deaths and 1 late (> 90 days) death with a median follow-up of 20 months. One (2.7%) patient underwent surgical reintervention for coronary artery button revision. There were no catheter based reinterventions.

Conclusions: Surgery for TGA may be undertaken in low-volume resource constrained centres in Sub-Saharan Africa with acceptable surgical outcomes and low rates of surgical and catheter reinterventions.

KEYWORDS

Aortic arch, Arterial switch operation, Transposition of the great arteries, Ventricular septal defect, Neonate

Introduction

Transposition of the great arteries (TGA) is a cyanotic congenital heart defect characterized by concordant atrioventricular connections and discordant ventriculoarterial connections. TGA accounts for 5 - 7% of all congenital heart disease cases, with an estimated incidence of 3 cases per 10,000 live births. The surgical correction of TGA remains one of the most successful and historically important interventions in the field of congenital cardiac surgery, with virtually every variation in morphology now amenable to either anatomical or physiological correction. Untreated, the condition is uniformly fatal. In Sub-Saharan Africa, early diagnosis and access to complex congenital cardiac surgery remains a significant challenge, and little data exists on the morphology and surgical management of patients with TGA. This paper analysed the morphological characteristics, surgical management and clinical outcomes of patients that underwent surgical repair of TGA at a regional cardiac referral centre in South Africa between January 2015 and December 2023.

Patients and Methods

Ethics statement

Ethical approval for this study was granted from the Biomedical Research Ethics Committee of the University of KwaZulu Natal (BREC/00001370/2020). Institutional permission was granted from the Health Research Committee of the Department of Health and Inkosi Albert Luthuli Central Hospital management for the publication of all de-identified patient data including images.

Study population

A single-centre retrospective, observational analysis of consecutive patients undergoing surgical correction of Transposition of the Great Arteries (TGA) between January 2015 and December 2023 in the Department of Cardiothoracic Surgery at Inkosi Albert Luthuli Central Hospital in Durban, South Africa were included. Patients that underwent isolated palliative procedures such as systemic to pulmonary artery shunts or pulmonary artery banding were excluded. Patients undergoing an arterial switch operation for anomalies other than TGA, such as the Taussig-Bing anomaly or congenitally corrected transposition of the great arteries (ccTGA) were excluded.

Patients undergoing an atrial switch procedure for isolated ventricular inversion were also excluded from the study population.

Study design

Data was assembled from electronic patient records that detailed diagnoses, echocardiographic and radiographic imaging, detailed surgical reports, perfusion charts and follow-up records. Sub- group analysis was based on morphological features and surgery undertaken. Follow-up data (where available) was included in the analysis. This study was primarily descriptive. The variables investigated in this study included age at surgical correction, associated cardiac and non-cardiac anomalies, technical aspects of surgery, early and late surgical outcomes, and the need for surgical or catheter-based reintervention. A consecutive sampling strategy from IALCH records was compiled using non-probability, purposive sampling techniques. Sample size comprised of patients who have undergone cardiac surgery for TGA complex at IALCH between January 2015 to December 2023.

Clinical variables

The term TGA complex was used as an overarching term to describe patients with a primary diagnosis of TGA, with or without associated anomalies. For the purpose of data analysis and consistency with existing literature, the patient cohort was divided into three groups:

- **TGA-IVS:** TGA with intact ventricular septum
- **TGA-VSD:** TGA with a ventricular septal defect (VSD), including patients with small, restrictive muscular VSD's not closed at surgery.
- **TGA-complex:** TGA associated other significant anomalies such as aortic arch hypoplasia, or valvar pulmonary stenosis.

Surgical pathways

Neonates with TGA-IVS are commenced on intravenous Prostaglandin (PGE) at a dose of 0.1 mcg/kg/min to maintain ductal patency and facilitate stabilisation during transfer to the referral centre. Echocardiogram is undertaken and the interatrial communication is assessed. Balloon atrial septostomy is used selectively in patients with a restrictive patent foramen ovale.

Once an unrestrictive atrial septal defect has been established, the PGE dose is reduced to 0.01mcg/kg/min with the goal of discontinuation to avoid congestive cardiac failure from left atrial hypertension. Arterial switch is scheduled on the next available operative list, or as an emergency in an unstable patient.

Late presenting TGA-IVS patients with cyanosis and the echocardiographic features of left ventricular involution undergo an atrial switch procedure, with the Senning operation our preference. Patients with TGA-VSD undergo an elective arterial switch, ideally within 6 weeks of age. Patients with TGA-complex and aortic arch hypoplasia undergo concomitant arterial switch operation and aortic arch reconstruction. Patients with TGA-complex and severe valvar pulmonary stenosis undergo a Rastelli operation.

Operative technique

The preferred technique of performing the arterial switch operation has remained unchanged for the duration of the study period.

Via median sternotomy, the thymus is subtotally excised and a patch of anterior pericardium is harvested and placed in a saline-soaked gauze swab. No glutaraldehyde is used. Following systemic heparinisation, the distal ascending aorta is cannulated. For venous return, our preference in neonates is a single straight venous cannula in the right atrial appendage. In older infants, bicaval cannulation is undertaken using right angled metal-tipped venous cannulae. A vent is placed in the left atrium via the right superior pulmonary vein in older infants. In neonates with a large interatrial communication, no additional vent is used.

Once the activated clotting time (ACT) exceeds 400 seconds, cardiopulmonary bypass (CPB) is instituted with cooling to 20 degrees Centigrade over a 30 minute interval.

The branch pulmonary arteries are isolated using silastic vessel loops and the ductus arteriosus is isolated and divided between suture ligatures, with care taken to avoid injury to the left recurrent laryngeal nerve. The branch pulmonary arteries are mobilised to the first order hilar branches, with care taken to avoid electrocautery injury to the phrenic nerves.

The aortic cross clamp is applied high and a single induction dose of cold crystalloid St Thomas 2 cardioplegia is infused into the aortic root. In patients with TGA-VSD, the VSD closure is undertaken via right atriotomy and a second dose of cardioplegia administered prior to arterial switch.

The ascending aorta is transected high, approximately 5mm above the level of the pulmonary artery bifurcation. The coronary artery origins are confirmed, and the coronary arteries are excised as buttons. The rectangular untreated autologous pericardial patch is used to augment the neopulmonary root, and the neo-pulmonary valve commissure between the excised coronary buttons is resuspended on the patch.

The main pulmonary artery is then transected at the bifurcation, and a Lecompte manoeuvre undertaken. The neoaortic valve is then inspected and the commissures are marked externally. In patients with TGA-VSD and a markedly dilated main pulmonary artery a limited plication of the posterior sinus is undertaken. The aorta is reconstructed, maintaining alignment of the anterior commissure between the proposed site of coronary reimplantation. The aortic cross clamp is briefly released and the neoaortic root pressurised to allow for accurate identification of the site of coronary artery implantation. An incision is made in the aortic root at the site of contact with the coronary button and the aorta reclamped. The incision is carefully extended in alignment with the axis of the coronary artery trunk, with care taken to avoid injury to the neoaortic valve leaflets and commissural post, and the coronary artery buttons are reimplanted on the neoaortic root. Prior to completion of the right coronary artery anastomosis, a short period of circulatory arrest is used to close the atrial septal defect via right atriotomy. Deairation is undertaken via the right coronary artery button and the aortic cross clamp is released, confirming satisfactory coronary artery filling and perfusion of all myocardial segments.

The pulmonary artery is reconstructed during rewarming with the heart beating. At a core temperature of 35 degrees Centigrade, the patient is separated from CPB on a milrinone infusion at 0.5mcg/kg/min. An epicardial pacing wire is placed in the right ventricle. Left atrial pressure monitoring lines are not used. Transoesophageal or epicardial echo is used to confirm a satisfactory repair. Following reversal of anticoagulation, the heart is decannulated and haemostasis secured. Topical glue is avoided, as is the use of indwelling topical haemostatic packing that may expand and result in coronary compression. In neonates, a peritoneal dialysis catheter is placed in the abdomen to facilitate post operative fluid management. Chest closure is undertaken primarily. Extracorporeal membrane oxygenation (ECMO) was not available at our institution during the study period.

Video *– 4min 22sec video will be included in the journal article submission demonstrating the key steps of the neonatal arterial switch operation. Emphasis is placed on the techniques of coronary artery transfer and neo-pulmonary root patch reconstruction, which we believe decrease the incidence of late aortic root dilation and pulmonary stenosis respectively.*

Statistical analysis

Data was extracted from the patient records stored on the Inkosi Albert Luthuli Central Hospital (IALCH) Meditech system and entered into a Microsoft Excel data capture sheet. Data was de- identified and detail coding and standardization of numerical values was used. Data was captured using Microsoft Excel were entered on SPSS version 26 (IBM Corp., USA). Descriptive statistical analysis of the data (means, standard deviations, ranges, frequencies and percentages) was conducted prior to the $\chi 2$ test of association between categorical variables; $p<0.05$ was considered statistically significant.

Results

Patient characteristics

During the study period, a total of 37 patients with TGA underwent surgery, of which 21 (56.8%) were male. This included 14 (37.8%) neonates, 19 (51.4%) infants and 4 (10.8%) children over a year of age (Table 1).

Table 1: Patient characteristics

Characteristic	TGA-IVS n = 15 (40.6%)	TGA-VSD n = 17 (45.9%)	TGA-complex n = 5 (13.5%)	p-value
Age (days), median (IQR)	31 (10-127)	58 (25-112.5)	354 (26.5-2781)	
Weight (kg), median (IQR)	3.9 (3.3-4.93)	4.7 (3.37-5.2)	4.6 (3.65-19.4)	
Male, n (%)	7 (50)	11 (64.7)	3 (60)	
Syndrome, n (%)				
- 22q11 deletion	2 (13.3)	-	-	
Associated anomalies				
- VSD	-	17	5	
- Aortic arch hypoplasia	-	-	3	
- Sub-valvar pulmonary stenosis	-	2	-	
- Valvar pulmonary	-	-	2	
Surgical procedure				
- ASO	11	-	-	
- ASO + VSD	-	16	-	
- ASO + PA band	-	1	-	
- ASO + VSD + arch	-	-	1	
- ASO + arch + PA band	-	-	2	
- Atrial switch (Senning)	4	-	-	
- Rastelli operation	-	-	2	
CPB time (min), mean (SD)	192.3 (46.5)	212.9 (63.3)	295 (41.3)	*p = 0.008*
AXR time (min), mean (SD)	133.3 (34.4)	147.8 (52.8)	173 (54.3)	*p = 0.299*
Delayed sternal closure, n (%)	4 (26.7)	0	0	
Ventilation duration (days), median (IQR)	7 (5-11)	6 (4-6)	5.5 (2-21)	*p = 0.319*
ICU duration (days), median (IQR)	10 (6.7-14.2)	7 (5.2-10.7)	8 (4.7-23.2)	*p = 0.223*
30-Day mortality, n (%)	1 (6.7)	2 (11.7)	1 (20)	
Late > 30-day mortality, n (%)	1 (6.7)	0	0	
Follow up (months), median (IQR)	33 (10-61)	16.5 (6.75-42.75)	19 (9.7-27.5)	*p = 0.238*
Surgical reintervention, n (%)				
- Coronary artery revision	1 (6.7)	-	-	
- Pulmonary artery revision	-	-	-	
- Baffle revision post Senning	-	-	-	
Catheter reintervention, n (%)				
- Pulmonary artery balloon / stent	-	-	-	
- Aortic arch balloon / stent	-	-	-	

TGA, transposition of the great arteries; *TGA-IVS*, TGA with intact ventricular septum; *TGA-VSD*, with a ventricular septal defect; *IQR*, interquartile range; *kg*, kilogram; *ASO*, arterial switch operation; *PA*, pulmonary artery; *CPB*, cardiopulmonary bypass; *SD*, standard deviation; *AXR*, aortic cross-clamp; ICU, intensive care unit

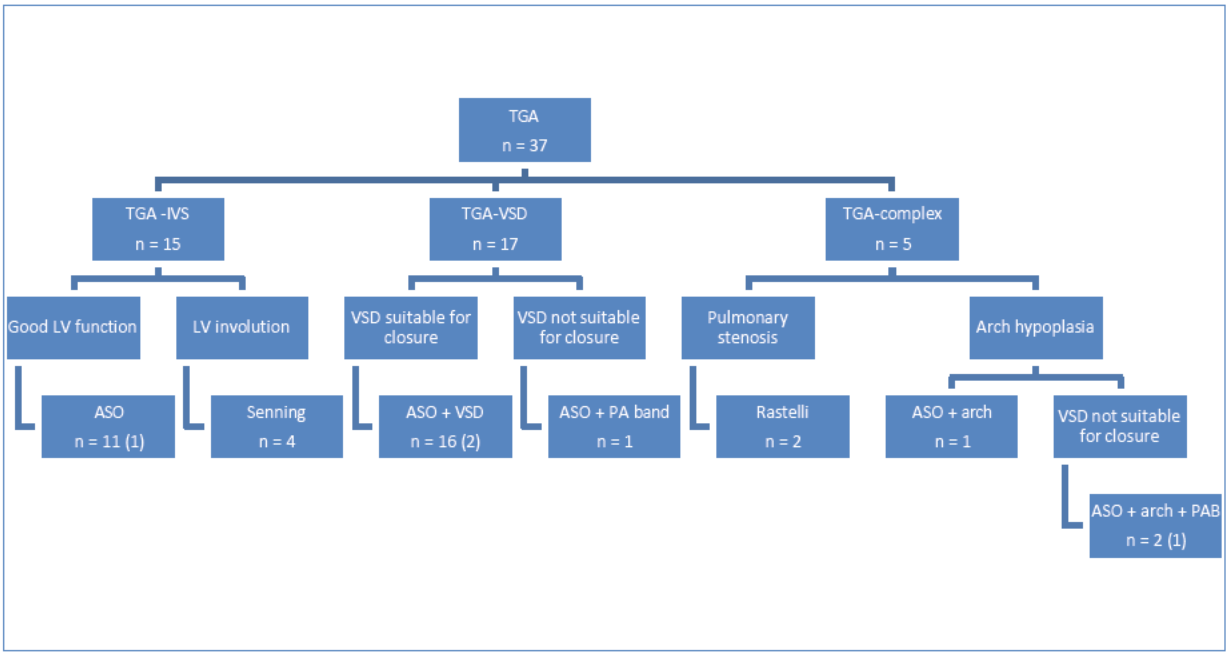
Morphology

15 (40.5%) patients presented with TGA-IVS, 17 (45.9%) patients with TGA-VSD and 5 (13.6%) patients with complex forms of TGA. Two patients with TGA-IVS were confirmed positive for DiGeorge syndrome (22q11.2 deletion syndrome). Six patients underwent BAS (4 TGA-IVS and 2 TGA-VSD) for inadequate mixing. Four (26.7%) patients in the TGA-IVS group presented late (age range 127-1025 days) with echocardiographic features of left ventricular involution and were not suitable for anatomical repair. Coronary artery origin and course was noted intraoperatively in all patients undergoing ASO, with the usual coronary pattern (1LCx-2R) confirmed in 17 (54.8%) patients, 1L-2CxR in 11 (35.5%) patients, a single coronary origin in two (6.5%) and inverted 1RL-2Cx in one (3.2%) patient. The TGA-complex group consisted of 3/5 (60%) of patients with aortic arch hypoplasia and 2/5 (40%) of patients with pulmonary stenosis.

Surgical results

In the TGA-IVS group, 11/15 (73.3%) of patients underwent an arterial switch operation and 4/15 (26.7%) of patients underwent an atrial switch procedure. In the TGA-VSD group, 17/17 (100%) of patients underwent arterial switch operation with VSD closure in 15/17 (88.2%) of patients and pulmonary artery banding in 1/17 (5.9%). In the TGA-complex group, 3/5 (60%) of patients with aortic arch hypoplasia underwent arterial switch operation, VSD closure and aortic arch reconstruction and 2/5 (40%) of patients with pulmonary stenosis underwent a Rastelli operation.

Figure 1: Patient treatment pathways



Early outcomes

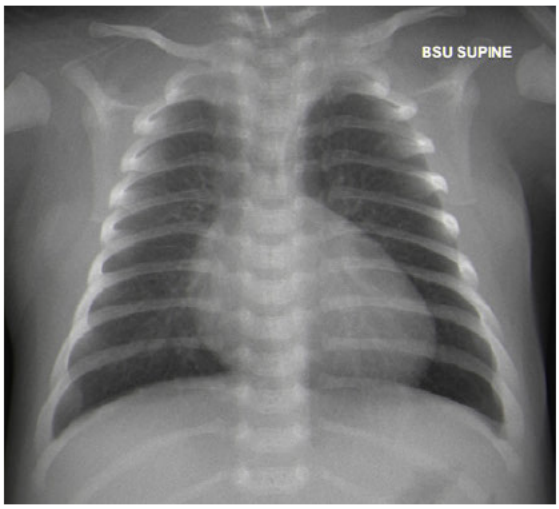
In the TGA-IVS group, there was one death within 30 days of surgery with a mortality rate of 6.6%. One patient in the TGA-IVS group required early mediastinal exploration for post-operative bleeding following ASO. The median duration of post-operative ventilation for TGA-IVS was 7 (IQR 5-11) days and the median duration of ICU stay was 10 (IQR 6.7-14.2) days. In the TGA- VSD group, there were two early mortalities with a mortality rate of 11.7%. One patient in the TGA-VSD group required early mediastinal exploration for post-operative bleeding following ASO. The median duration of post-operative ventilation for TGA-VSD was 6 (IQR 4-6) days and the median duration of ICU stay was 7 (IQR 5.2-10.7) days. In the TGA-complex group there was one mortality resulting in a mortality rate of 20%. The median duration of post-operative ventilation in this group was 5.5 (IQR 2-21) days and the median duration of ICU stay was 8 (IQR 4.7-23.2) days.

Reinterventions

In the TGA-IVS group, one patient (6.7%) underwent revision and patch plasty of the left anterior descending coronary artery button four months after arterial switch and made an excellent recovery (Figure 2). There were no surgical or catheter based pulmonary artery reinterventions in patients that underwent the arterial switch operation across all groups. There were no surgical or catheter based aortic arch reinterventions in patients that underwent Norwood-style aortic arch patch reconstruction in the TGA-complex group.

One neonate with TGA-IVS and a single coronary artery origin developed progressive left ventricular dysfunction and cardiomegaly two weeks after ASO (Figure 2). Cardiac catheterisation demonstrated an obstructed left anterior descending artery, and the patient underwent coronary artery revision and patch plasty at 4 months of age and remains asymptomatic at 8-year follow up.

Figure 2



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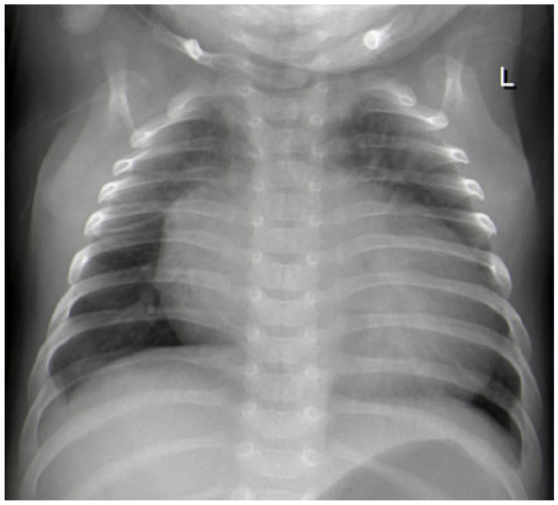

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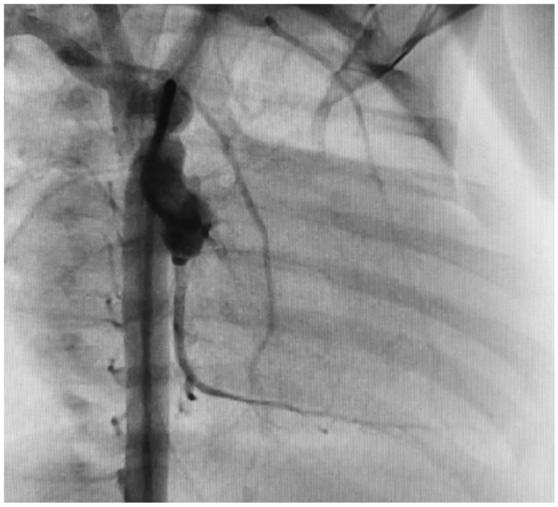

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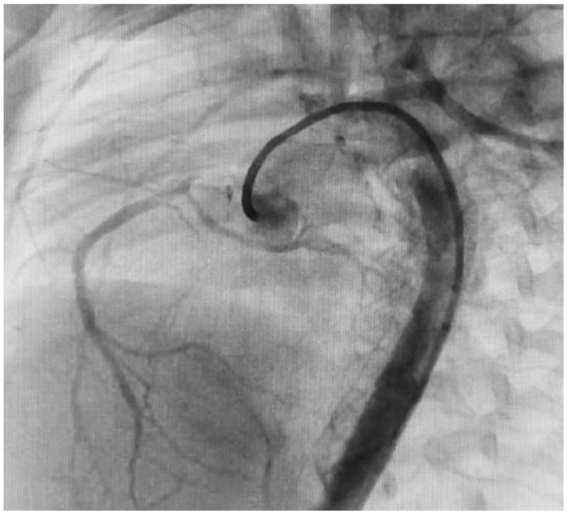

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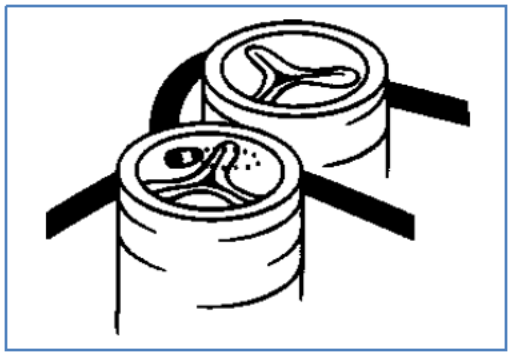

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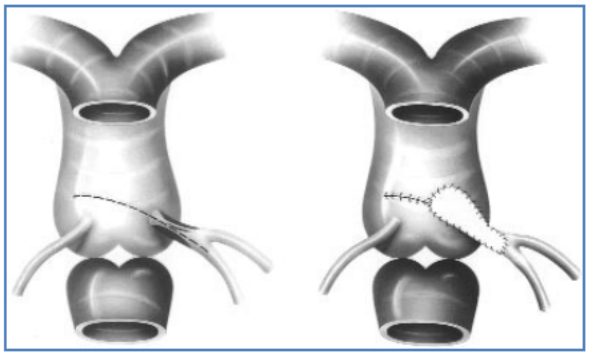

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Figure 2

Demonstrates the early (A) and late (B) postoperative chest radiographic images of a neonate that underwent arterial switch operation (ASO) for simple transposition of the great arteries (TGA). The increase in cardiac dimensions and left ventricular dilatation on echocardiography prompted cardiac catheterization, and the aortic root injection (C and D) demonstrated no filling of the left anterior descending artery (LAD) territory. At ASO the coronary artery branching pattern was noted to be complex with a single composite coronary origin and an intramural course of the LAD (E). The child underwent repeat surgery at 4 months of age, and patch plasty of the LAD was undertaken (F). The child remains asymptomatic at 8 year follow up.

References:

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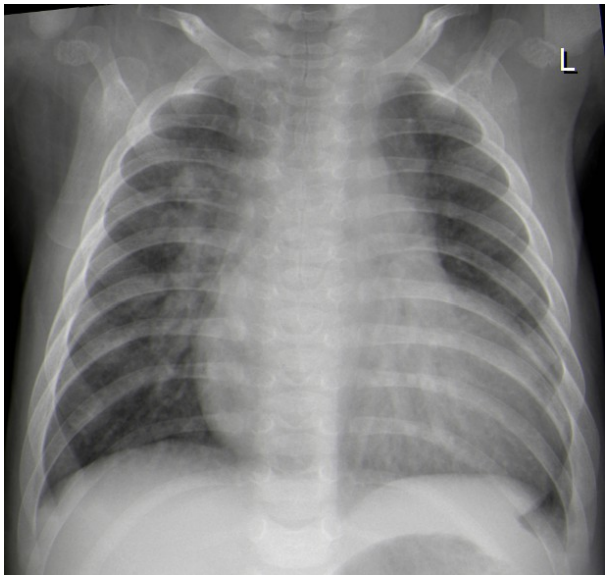
1F - Bergoënd E, Raisky O, Degandt A, Tamisier D, Sidi D, Vouhé P. Myocardial revascularization in infants and children by means of coronary artery proximal patch arterioplasty or bypass grafting: a single-institution experience. J Thorac Cardiovasc Surg. 2008 Aug;136(2):298-305.

Figure 3 demonstrates a 6-month-old child at first presentation with TGA-IVS and LV involution. The child remains asymptomatic at 9-year follow-up.

Figure 3



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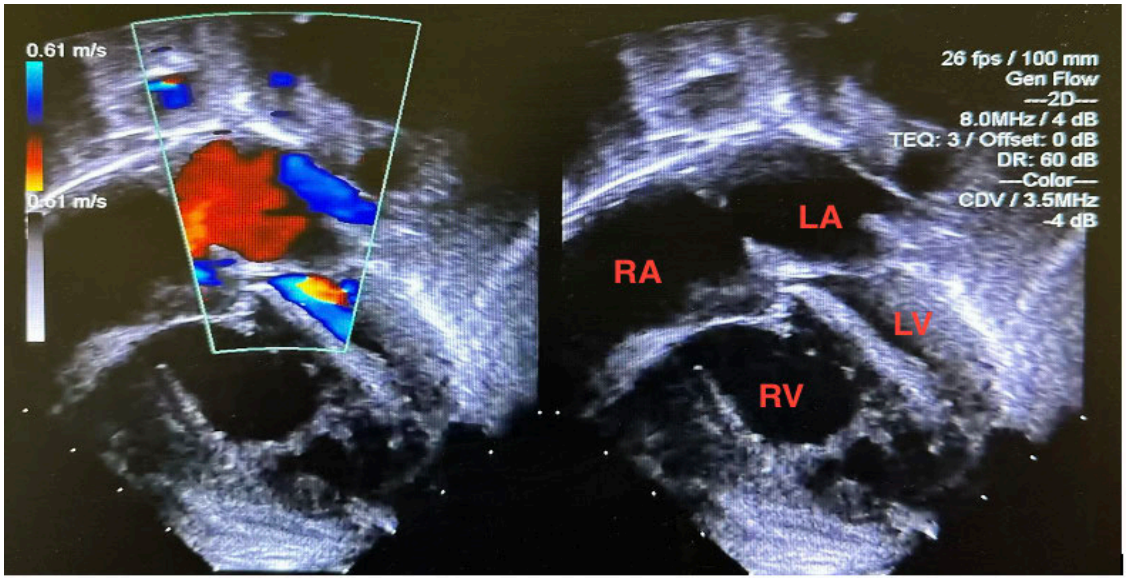


3b

Figure 3

The plain chest radiograph (A) of a child with simple transposition of the great arteries (TGA) at first presentation at 6 months of age. Echocardiography (B) demonstrated involution of the left ventricle. This

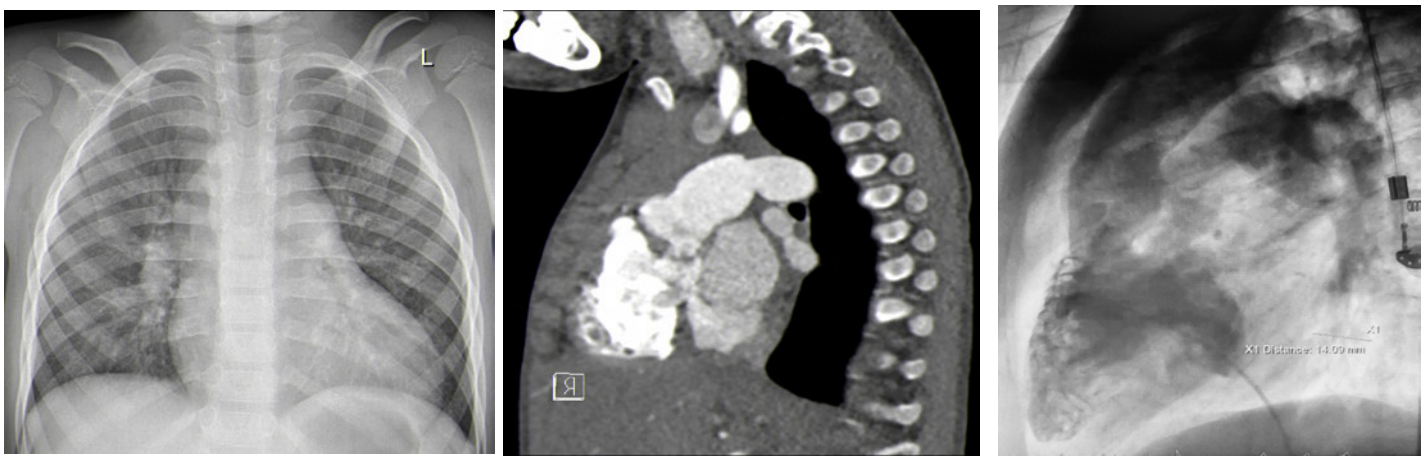
patient underwent an atrial switch (Senning) operation and remains well with good right ventricular function at 9-year follow up. *Right atrium (RA), right ventricle (RV), left atrium (LA), left ventricle (LV)*

In patients with TGA-VSD, surgery is generally undertaken within the first 6 weeks of life, and this is reflected in the median age of ASO with VSD closure of 58 days in this study. Our preference has recently shifted toward surgery within the first 2-4 weeks of life to prevent the development of cardiac failure as the pulmonary vascular resistance (PVR) drops and to minimize the aorto- pulmonary mismatch at ASO. In 3/15 (33%) of patients with TGA-VSD and unrestricted pulmonary blood flow, plication of the non-coronary sinus of the neoaortic root was undertaken to accommodate the size mismatch between the pulmonary artery and ascending aorta.

Two early deaths occurred in the TGA-VSD group. A 27-day-old neonate underwent ASO and VSD closure and following coronary transfer (coronary branching pattern 1L-2CxR) the right coronary artery territory appeared ischaemic and required revision. The patient failed to separate from CPB due to left ventricular dysfunction and the patient demised as ECMO was not available at the institution. The second death in this group was a 39-day old patient that underwent uneventful ASO and VSD closure and had a severe pulmonary hypertensive crisis 12 hours post- surgery and was unable to be resuscitated.

Two patients with TGA-VSD and subvalvar pulmonary stenosis due to muscular obstruction or accessory tricuspid valve tissue underwent ASO with VSD closure and relief of the subpulmonary stenosis at ages of 21 months and 8 years old. Preoperative echocardiography in these late presenting patients demonstrated a competent pulmonary valve suitable for ASO, however the substrate for subsequent neo-aortic root dilation and neo-aortic valve regurgitation is highlighted in Figure 4.

Figure 4



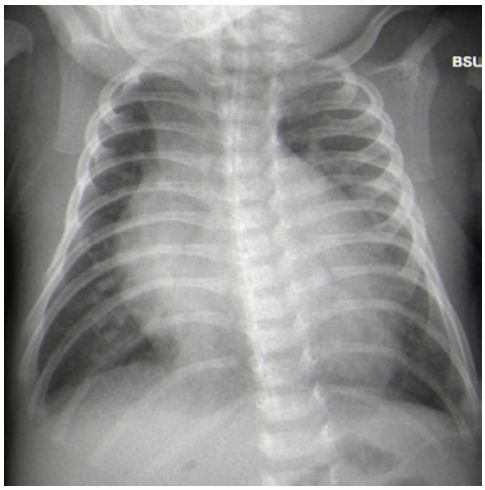
4a 4b 4c

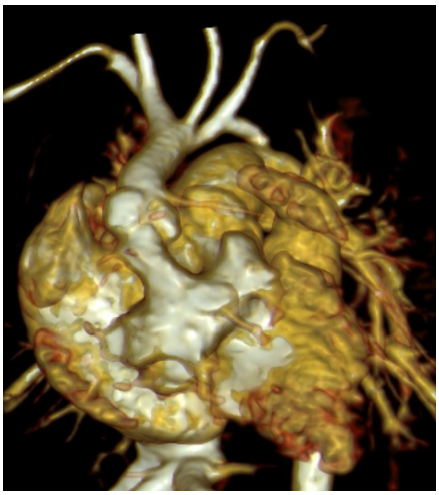
Figure 4

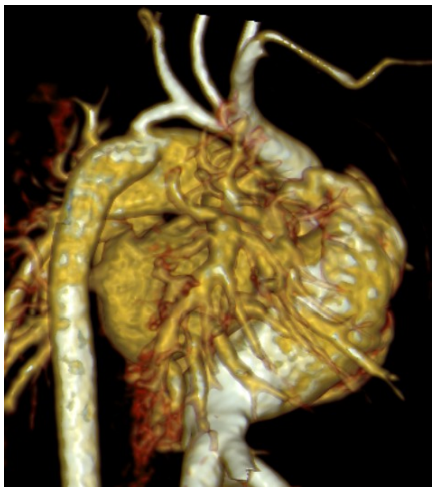
The plain chest radiograph (A), CT angiogram (B) and cardiac catherization study (C) of an 8- year-old child at first presentation with transposition of the great arteries (TGA) associated with a subpulmonary ventricular septal defect (VSD) and subvalvar pulmonary stenosis due to accessory tricuspid valve tissue. She underwent relief of the subpulmonary stenosis, VSD closure and arterial switch operation. The child remains asymptomatic at 4-year follow-up; however echocardiography demonstrates dilatation of the neo-aortic root and mild-moderate aortic regurgitation that may require future intervention.

The TGA-complex group consisted of two distinct morphological groups – severe pulmonary stenosis and aortic arch hypoplasia. Two patients with severe valvar pulmonary stenosis underwent a Rastelli operation - a 21-month-old patient previously palliated with a PDA stent and a 13-year-old that had undergone prior palliation with a 5mm right modified Blalock-Taussig shunt via thoracotomy. Homograft conduits are not readily available in South Africa and for this reason commercial bovine jugular vein conduits were used to establish RV to PA continuity. In the aortic arch hypoplasia group, two neonates underwent Norwood-style patch reconstruction of the aortic arch and concomitant ASO. In one patient straddling atrioventricular valve chordae precluded VSD closure and this patient underwent PA banding (Figure 5). One early mortality occurred in a 2-month-old patient with a large VSD and severe pulmonary hypertension that underwent Norwood style aortic arch reconstruction, ASO and PA banding and developed a low cardiac output state post operatively.

Figure 5







5a **5b** **5c**

Figure 5

The plain chest radiograph (A) and CT angiogram (B) of a neonate with transposition of the great arteries (TGA) associated with a large inlet ventricular septal defect (VSD) and a hypoplastic aortic arch and coarctation. This child underwent Norwood-style patch reconstruction of the aortic arch and arterial switch operation. Due to straddling atrioventricular valve chordae, the VSD was left open and an 8mm Goretex tube graft was interposed between the neo-pulmonary root and the pulmonary artery bifurcation as a pulmonary flow restrictor or "band". The child will be evaluated for biventricular repair at follow-up.

Table 2: Patients undergoing arterial switch operation (ASO)

Characteristic	ASO (n = 31)
Age (days), median (IQR)	39 (15-75)
Weight (kg), median (IQR)	3.8 (3.3-4.9)
Male, n (%)	18 (58)
Associated anomalies, n (%) - VSD - Aortic arch hypoplasia - Sub-valvar pulmonary stenosis	 19 3 2
Coronary artery pattern, n (%) - 1LCx-2R (Usual) - 1L-2CxR (Circumflex from RCA) - Single coronary orifice - 1RL-2Cx (Inverted)	 17 (54.8) 11 (35.4) 2 (6.5) 1 (3.2)
Great vessel relations, n (%) - Aorta anterior to PA - Side by side	 31 (100) 0
Additional procedures, n (%) - VSD closure - PA band - Aortic arch reconstruction - Relief of sub-valvar pulmonary stenosis	 15 3 3 2
LeCompte manoeuvre, n (%)	31 (100)
Coronary transfer technique, n (%) - Closed - Open	 26 (83.9) 5 (16.1)
Neoaortic root plication, n (%)	6 (19.3)
CPB time (min), mean (SD)	217.2 (60.1)
AXR time (min), mean (SD)	142.4 (45)
Delayed sternal closure, n (%)	4 (12.9)
Ventilation duration (days), median (IQR)	6 (5-9)
ICU duration (days), median (IQR)	8 (6.2-13.7)
30-Day mortality, n (%)	4 (12.9)
Late > 30-day mortality, n (%)	0
Follow up (months), median (IQR)	19 (9-46)
Surgical reintervention, n (%) - Coronary artery revision - Pulmonary artery revision	 1 (3.2) -
Catheter reintervention, n (%) - Pulmonary artery balloon / stent - Aortic arch balloon / stent	 - -

R, right coronary artery*; L,* left anterior descending coronary artery*; Cx*, left circumflex artery; *IQR*, interquartile range; *kg*, kilogram; *ASO*, arterial switch operation; *PA*, pulmonary artery; *CPB*, cardiopulmonary bypass; *SD*, standard deviation; *AXR*, aortic cross-clamp; ICU, intensive care unit

The analysis of all 31 patients that underwent ASO (Table 2) demonstrated a median age at surgery of 39 days with a median weight of 3.8kg. Similar reports from the developed world report a median age of ASO across all groups of 8 days, highlighting the challenges associated with postnatal diagnosis and late referral[51].

The coronary artery branching patterns encountered in this study are reflective of other reports[51], and we do not consider coronary artery variations a significant risk factor for ASO. Our belief is that, with the exception of a single ostium and intramural course, the course and looping of coronary artery branches are more critical than the origins from the aorta, a view shared by others[64].

A LeCompte manoeuvre was undertaken in all patients undergoing ASO, and is our routine in all situations when the aorta lies anterior to the pulmonary artery.

The closed coronary artery transfer technique was used in 26 / 31 (83.9%) of patients, and has been demonstrated to be a reproducible and "teachable" technique to avoid coronary artery kinking and tension with all coronary artery patterns [27]. This technique is particularly suitable for TGA-VSD when significant neo-aortic root dilatation may distort the anticipated position of coronary artery implantation. An exception to the use of the closed transfer technique is with side-by-side great vessels, when an open or combination of open/closed transfer techniques can be used.

Delayed sternal closure was using in 4 / 31 (12.9%) of patients, significantly lower than the reported rates of over 40% in other published series.[51] Our preference for primary sternal closure is based on the decreased risk of mediastinal sepsis, improved haemostasis and lack of an e- CPR service which may lower the threshold for chest closure in high risk patients.

Early (< 30 day) mortality in high volume units in the developed world demonstrate an overall mortality rate of < 5%, and this remains a challenge in low volume units in the developing world. The overall early mortality rate following ASO was 4 / 31 (12.7%) of patients in this study. The only early mortality in the TGA-IVS group occurred in February 2015, with no early or late mortalities over the past 10 years. Patients that died following surgery due to low cardiac output syndrome or severe pulmonary hypertension may have been salvaged if ECMO was available.

Following ASO, surgical and catheter-based reintervention rates vary between 4.3% – 15.8% in large series, with pulmonary artery reinterventions for pulmonary stenosis being the most

common.[51] We did not encounter any early or late pulmonary artery stenosis and believe that this is due to technical factors, including the use of a rectangular patch of fresh autologous pericardium for neo-pulmonary root reconstruction (rather than a glutaraldehyde soaked pantaloon shaped patch), as well as transection of the ascending aorta high to significantly shorten and "tuck back" the neo-aorta avoiding posterior compression of the MPA.

Reintervention following ASO was limited to one patient with a complex single coronary artery origin that underwent surgical revision and patch plasty of the LAD coronary artery button 4 months after ASO (Figure 2). This highlights the recommendation for routine coronary angiography in patients with complex coronary artery patterns following ASO. [64]

Follow-up

Following discharge, patients are reviewed at 2 weeks, 6 weeks, 6 months and thereafter annually as outpatients by the Department of Paediatric Cardiology. The median duration of follow-up across all groups was 20 (IQR 9-42) months. Patients were considered to be lost to follow-up if they were not seen a year after their previous clinic appointment. A total of 8 of the 32 surviving patients (25%) have been lost to long-term follow-up.

Discussion

This study highlights the surgical outcomes of a cohort of patients with TGA encountered at a referral centre in Sub-Saharan Africa. Despite the population of approximately 10 million inhabitants in the region, the diagnosis and surgical treatment of TGA was far below the expected incidence. None of the patients in this series were diagnosed antenatally, highlighting the deficiencies in maternal obstetric imaging services in Africa.

In the TGA-IVS group, neonates were often referred from remote hospitals with cyanosis and metabolic acidosis, and the presumptive diagnosis of a duct dependent cardiac lesion was made. In patients with a restrictive interatrial communication, balloon atrial septostomy (BAS) was undertaken to improve mixing and facilitate weaning of the PGE to 0.01mcg/kg/min to prevent congestive cardiac failure. In the absence of overt neonatal sepsis, surgical correction is undertaken on an urgent basis ideally within the first 2 weeks of life. This group consisted of 7 /11 (63.6%) of patients in our series. The remaining 4/11 (36.4%) of

patients that underwent ASO at ages 31 days, 47 days, 54 days and 55 days had preserved LV function on echocardiography, likely due to delayed PDA closure.

In patients with TGA-IVS undergoing ASO, the single early mortality occurred on the 14th postoperative day in a neonate with severe hypoxaemia due to intractable pulmonary hypertension despite inhaled nitric oxide (NO) ventilation.

In late presenting patients with TGA-IVS and left ventricular involution, our institutional preference has been the atrial switch (Senning) operation. Mechanical circulatory support in the form of extracorporeal membrane oxygenation (ECMO) or left ventricular assist device (LVAD) was not available at our institution during the study period, precluding late ASO. The alternative of LV retraining by a pulmonary artery band +/- systemic to pulmonary artery shunt was not considered appropriate in a patient population with a tenuous follow-up. Cardiac transplantation services are not available at our institution.

The single late mortality in this patient cohort occurred in a cyanotic child that underwent Senning operation at first presentation at the age of 21 months for TGA-IVS and LV involution. The patient developed progressive pulmonary hypertension and LV failure requiring home oxygen therapy and died 18 months after the atrial switch procedure.

The arterial switch operation (ASO) remains the mainstay of treatment for TGA, and this procedure serves as an important benchmark operation in the appraisal of any congenital cardiac surgery service. Improvement in surgical outcomes have largely been attributed to the technical aspects of the ASO, and in particular techniques of coronary artery transfer. However satisfactory outcomes following ASO require excellence in the following domains: -

- foetal imaging services and obstetric care
- neonatal intensive care
- diagnostic echocardiography
- interventional paediatric cardiology
- paediatric cardiac anaesthesiology
- perfusion services
- nursing care
- paediatric cardiac surgery
- cardiac intensive care
- paediatric cardiology outpatient services

Limitations

Limitations of this study are related to the inherent nature of a retrospective chart review, including reliance on electronic clinical data with varying degrees of data granularity. Incomplete follow-up data remains a challenge in the African patient population. The small data set may limit comparison with larger published series from high volume centres. Data was gathered from a single institution with > 85% of cases undertaken by a single surgeon, possibly limiting the applicability of the findings to other institutions.

Summary

Surgery for TGA may be undertaken in low-volume resource constrained centres in Sub-Saharan Africa with acceptable surgical outcomes and low rates of surgical and catheter reinterventions.

Acknowledgments

The authors would like to thank Ms Gill Hendry for assistance with the statistical analysis.

Statements and Declarations

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical considerations and permissions

Ethical approval for this study was granted from the Biomedical Research Ethics Committee of the University of KwaZulu Natal (BREC/00001370/2020). Institutional permission was granted from the Health Research Committee of the Department of Health and Inkosi Albert Luthuli Central Hospital management for the publication of all de-identified patient data including images.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Appendices

Appendices should be used for illustrative material which is not included in the main body of the thesis, or for material which interrupts the flow of the text, such as list of abbreviations, pertinent documents and extensive raw data. If several separate items are relegated to appendices, each one should form a separate appendix. If the appendices contain further references, a separate list should be included at the end of each appendix.

Appendix 1, 2 and 3 below are standard for all theses.

Appendix 1: Study Amendment Letter & Protocol

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YA KWAZULU -NATALI

28 October 2024

Mr Yasteel Rajendra Mohanpersadh Maharaj (205503676)
School of Clinical Medicine
Medical School

Dear Mr Maharaj,

Protocol reference number: BREC/00CEi1370/2020
Project title: A retrospective review of patients with Transposition of the Great Arteries complex and underwent cardiac surgical repair within the Department of Cardiothoracic Surgery at Inkosi Albert Luthuli Central Hospital during Che period of 28 February 2015 to 31 March 2020
Degree: Master of Medicine
NEW TITLE: A retrospective review of patients with transposition of the great arteries complex (TGA) that underwent surgical repair aC a regional cardiac referral centre in South Africa.

We wish to advise you that your application for amendments listed below received on 24 October 2024 for the above study has been noted and approved by a sub-committee of the Biomedical Research Ethics

- Please check that the study had been renewed annually after initial approval and if not please request a condonation of non-renewal /late renewal and submit a renewal for 2025 and annually until project is complete

Amendments noted and approved

i) New Tile
ii) Study period to be extended to December 2023.
iii) Patient sample size to be increased from approximately 30 to 48

The committee will be advised of the above at its next meeting to be held on 10 December 2024. Yours sincerely

Ms A Marimuthu
(for) Prof S Singh
Chair: Biomedical Research Ethics Committee

Biomedical Research Ethics Committee Chair:
Professor S Singh
UKZN Research Ethics Office Westville Campus, Govan Mbeki Building Pascal
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COPY OF PROTOCOL (with initial literature review and references)

Name of the investigator: ***Dr Yasteel Maharaj***

Student Number: ***205503676***

UKZN Department of Cardiothoracic Surgery

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UKZN Department of Cardiothoracic Surgery

Inkosi Albert Luthuli Central Hospital

Telephone: ***0312402114 / 0*** [redacted]

Email: [redacted]

Protocol approval number: BREC/00001370/2020

Title:

A retrospective review of patients with Transposition of the Great Arteries complex (TGA) who underwent cardiac surgical repair at a regional cardiac referral centre in South Africa.

Aim of this study:

The purpose of this study was to identify basic patient demographics, surgical interventions, and outcomes amongst patients who have undergone surgical repair for TGA complex within a regional cardiac referral centre in South Africa between January 2015 and December 2023.

Specific objectives:

a. To determine the modes of presentation and diagnosis of patients with Transposition of the Great Arteries complex who underwent surgical repair.

b. To examine the basic demographics amongst patients diagnosed with TGA complex.

c. To review the technical aspects of surgical repair, including the timing of surgery.

d. To determine the early and late postoperative outcomes of patients who have undergone surgical repair.

Summary of the proposed research

The project consists of a retrospective, observational study with the objective of analysing the inpatient and outpatient data of all patients with Transposition of the Great Arteries complex who have undergone surgical repair admitted to the Department of Cardiothoracic Surgery from January 2015 to December 2023. The data will be assembled from electronic file keeping and case records, including diagnoses, echographic imaging, surgical operation documentation and follow-up records. Sub-group analysis will be based on patient presentation, pre-operative investigations and technical aspects of the surgery undertaken. Follow-up data (where available) will be included in the investigation.

Background and Literature

INTRODUCTION

Transposition of the great arteries (TGA) is the most common cyanotic congenital heart defect making up 5% to 7% of all congenital cardiac disease.[1,2]

It occurs in 3 per 10,000 live births and without surgery, TGA is fatal. There is an associated mortality rate of 30% in the first week and up to 90% within the first year of life. There is ventriculoarterial discordance and when atrioventricular concordance is present, this anatomy results in cyanosis because the systemic and pulmonary circulations are in parallel. [7]. Some new-borns require emergent balloon atrial septostomy (BAS) and/or extracorporeal membrane oxygenation (ECMO) immediately after birth.[2]

Surgical care is rapidly evolving for congenital heart disease (CHD) in the developing world, enhancing chances of survival and improving quality of life for children with previously lethal cardiac malformations such as TGA. Although important progress is being made, the mortality associated with congenital heart disease and its surgical care remains challenging. Left

untreated, TGA is associated with mortality approaching 85% to 90%. Medical and surgical management of TGA is already well established in many North American and European countries, with the usual practice being single-stage anatomic repair with arterial switch operation (ASO) in the first week of life. As per statistics from these countries, ASO is associated with a 30-day mortality of <3%, and 20-year survival approaches 90%. However, less is known about surgery for TGA in the developing world[3]. Until three decades ago, atrial repair (Mustard or Senning procedures) was the only surgical option. On follow-up, long-term mortality and morbidity were considerable, most commonly due to progressive right systemic ventricular failure thus making arterial switch operation (ASO) the established method of surgical correction. The mid- and long-term follow-up studies are also encouraging; the oldest survivors of ASO at most centres are young adults.

ANATOMY AND EMBRYOLOGY

TGA is categorized as part of conotruncal defects. In normal embryology, absorption of the bulboventricular ledge allows a leftward rotation of the aorta during normal development of the heart and become oriented over the left (or primitive) ventricle.2,3 In TGA, there is abnormal rotation and septation of the truncus arteriosus, whereby the aorta is connected to the right ventricle via a subsemilunar valve muscular conus, and the pulmonary artery is connected to the left ventricle with mitral-pulmonary fibrous continuity. [2,5]

TGA refers to hearts with concordant atrioventricular connections but discordant ventriculoarterial (VA discordance).[1] In these patients, the morphologic right ventricle (RV) is primarily connected to the aorta, whereas the morphologic left ventricle (LV) is connected to the pulmonary artery (PA). TGA can be further subdivided on the basis of the if the morphologic right and left atria are connected to the morphologic right and left ventricles. When the atria are connected to the appropriate ventricles, they are said to have atrioventricular (AV) concordance. The atrium and ventricles usually have normal configuration, and the conduction system is also usually normal. In simple transposition, the atria are connected to the correct ventricles (AV concordance), but the RV is connected to the aorta, and the LV is connected to the main PA (VA discordance). Isolated VA discordance occurs in 50% of cases.1 Congenitally corrected transposition refers to both AV and VA discordance. [2,5]

In TGA, the pulmonary and aortic circulations run in parallel as opposed to in series, and this lesion is not compatible with survival without adequate mixing of these circulations.[5] A patent foramen ovale (PFO), a patent ductus arteriosus (PDA), and pulmonary stenosis are very common, and about 50% of patients have a ventricular septal defect (VSD). [6] These are necessary for survival in order to allow for mixing of the systemic and the pulmonary circulations. Coronary artery variations are also associated with TGA, and it is imperative to know the correct prior to undertaking corrective surgery.[8] In the current era, it appears that

most coronary artery patterns can undergo an ASO with acceptable risk, but the presence of a single coronary ostium or an intramural coronary artery has both been shown to contribute significantly to the risk of mortality. [2]

PATHOLOGY and CLINICAL PRESENTATION

As a result of the pulmonary and systemic circulations working in as two closed circuits (running in parallel as opposed to series), there is higher oxygen saturation in the main PA than in the aorta - Deoxygenated blood is pumped into the aorta from the right heart and out to the body, whilst oxygenated blood is returned from the lungs and pumped from the left heart into the pulmonary arteries[2,6]. this anatomy results in cyanosis[7] and can be identified in more than half of neonates within the first hour of life. [1] If a large VSD is present, cyanosis may be very mild and may be overlooked. By the 2nd to 6th week of life, signs of congestive heart failure (CHF), including tachypnoea and tachycardia develop due to a decrease of pulmonary vascular resistance falls and pulmonary blood flow increases. Murmurs found on auscultation include pansystolic murmur, a gallop, a mid-diastolic rumble, and a narrowly split second heart sound with a prominent pulmonary component. These may be amplified in the presence of worsening CHF. In the presence of inadequate mixing, potentially fatal parallel circulation can result in deep hypoxaemia, severe acidosis and death.[2,6]

INVESTIGATIONS

The diagnostic evaluation of patients with TGA has significantly improved over the past three decades due to the evolution and availability of imaging modalities made available to clinicians. The aims of these modalities are to gain accurate anatomic and haemodynamic information that enable medical and surgical planning. [2,5,7] These are also used to provide surveillance imaging to evaluate potential complications during the postoperative period. These investigations range from basic chest x-ray (CXR), electrocardiogram (ECG), echocardiography and cardiac catheterization to the more advanced cardiovascular magnetic resonance (CMR). CXR can be initially normal to the classic “egg on a string” (globular heart with mild or no cardiomegaly below a narrow mediastinal shadow due to the anteroposterior alignment of the great vessels). ECG findings are generally normal at birth to right axis deviation, RV hypertrophy in the first few weeks of life. Patients with pulmonary hypertension can demonstrate upright T waves in lateral leads.[6,7]

Echocardiography remains the primary diagnostic imaging modality of choice in TGA due to its widespread availability and portability. It is usually the only modality required for preoperative evaluation, providing accurate anatomical and haemodynamic assessment in the majority of patients with TGA. Echocardiography is routinely used postoperatively to evaluate any residual,

recurrent or new intracardiac pathology. It provides a comprehensive anatomic and hemodynamic evaluation in the majority of patients with TGA and is usually the only modality required for preoperative evaluation. For postoperative imaging, echocardiography is often used to assess for residual, recurrent or new pathology. Preoperative echo classically demonstrates (on the long-axis view) the two great vessels running in parallel rather than wrapping around each other in normal anatomy. [1,2,6]The "double-barrelled shotgun" appearance of the two semilunar valves can also be seen on the short-axis view (the aortic and pulmonary valves generally lie on different planes). Echocardiography can also visualize common associated lesions. These include VSDs (size and location), visualizing coronary anatomy and assess the patency of the atrial septum and ductus arteriosus. [5,7]

Cardiac Catheterization and Angiography is seldom used in the preoperative evaluation of TGA but is required when undertaking balloon atrial septostomy (BAS) to relieve cyanosis and improve mixing. There are some centres that undertake angiography more routinely to confirm coronary artery anatomy preoperatively or postoperatively to assess for stenosis following coronary artery reimplantation.[7]

Cardiovascular magnetic resonance (CMR) and multidetector computed tomography (CT) can be used to evaluate baffles, conduits, and extracardiac structures such as the branch pulmonary arteries and the aortic arch. CT can be used as an alternative in patients who cannot undergo CMR e.g. patients who have pacemakers.[7]

PREOPERATIVE MANAGEMENT

There is about a 50% mortality within the first month without any medical intervention. Strategies are employed to stabilize the patient prior to catheterization or a surgical procedure is carried out. Patients in shock and severe hypoxaemia should be managed appropriately as per neonatal advanced life-support algorithms. [1] Any electrolyte abnormalities or acidosis should be corrected and an infusion of prostaglandin E1 (PGE1) should be commenced. This is instituted to maintain ductal patency and to improve arterial oxygenation. Infusion of PGE1 should not be discontinued until angiography or surgery is undertaken. PGE1 is not without its own complications, more specifically prostaglandin-induced apnoea, and these patients may require intubation. Urgent postnatal echocardiograms are complete and all sites of inter-circulatory mixing have been evaluated. [1,2]

Usage of PGE1 may not suffice due to ductal shunting being inadequate in the presence of a restrictive interatrial communication. These patients warrant an emergent balloon atrial

septostomy under fluoroscopic or echocardiographic guidance. Even with a large VSD, atrial-level shunting is necessary as it is more effective than in the case of a VSD (this is because shunting occurs during systole and diastole rather than just systole). If there is satisfactory interatrial communication and the anatomic diagnosis of TGA is clear by echocardiographic examination, cardiac catheterization or septostomy is not required prior to surgical correction. [1,5,6]

SURGICAL MANAGEMENT

The first ASO was a single stage procedure, performed in the 1970s. During the same decade, a two-stage procedure was performed (the patient had TGA with intact ventricular septum) – the patient underwent a pulmonary artery banding followed by ASO.[7] The ASO is undertaken via median sternotomy and the commonly encountered anatomy is the anterior-posterior orientation of the great vessels. Visualizing the coronary anatomy is essential for the coronary transfer later in the operation and although there are various patterns, the most common is the left anterior descending and circumflex arising from the left facing sinus with the right coronary artery arising from the right facing sinus. Prior to proceeding with cannulation for cardiopulmonary bypass, the aorta is separated from the main pulmonary artery, and the branch pulmonary arteries are mobilized and freed to their first branches. The aortic cannulation suture is placed distally in the ascending aorta as far cephalad as possible provides the greatest exposure of the base of the heart.[3] Using a single venous cannula will decompress both the right and left atrium because of the presence of an ASD. [7] With the commencement of cardiopulmonary bypass the ductus arteriosus is ligated proximally and distally and then divided. A vent is placed into the left ventricle, and an antegrade cardioplegia cannula is placed in the ascending aorta. [3]Cooling to deep hypothermia is then commenced. After applying the aortic cross-clamp, single dose cardioplegia is administered. The aorta is divided midpoint opposite to the pulmonary bifurcation.

Transferring of the coronary buttons is a relatively straightforward rotation and is not necessary to place the button higher or lower than its original location (implantation should not be in the sinuses of Valsalva but should be above the sinotubular junction). The suture line must ensure the coronary ostia is patent and prevent creating a slit. The Lecompte manoeuvre brings the pulmonary bifurcation anterior to the ascending aorta. Division of the ductus and the prior mobilization of the branch pulmonary arteries ease the tension on the pulmonary artery anastomosis. An autologous pericardial patch is used to enlarge the “neopulmonary anastomosis”. The atrial septal defect (from preoperative septostomy) is then closed during a brief period of circulatory arrest. Following the release of the aortic cross-clamp and initiation of the rewarming process, the pulmonary anastomosis is begun, with gradual separation from

cardiopulmonary bypass and eventual further management in the intensive care unit (ICU) and beyond.

With a gradual experience of the arterial switch and learning of the various technical maneuverers, there has been a significant decreased in early mortality – with survival rates at 85% in developing countries.[4] Long term survival results have been as high as 96% as reported by Baruteau et al. [9]

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Study design:

A retrospective chart review study with observational analysis from data obtained from IALCH electronic inpatient and outpatient records.

Study population:

All patients with TGA complex who have undergone cardiac surgery admitted to the Department of Cardiothoracic Surgery at IALCH of from January 2015 to December 2023.

Sampling strategy:

The pre-existing registry from IALCH records is compiled through a consecutive sampling strategy. The sampling technique is non-probability, purposive sampling

Statistical planning (variables & confounders):

This study is primarily descriptive. The variables investigated in this study will be inclusive of gestational age, age of surgical correction, associated congenital abnormalities, the type of TGA, preoperative ventilation, the type of surgery undertaken, postoperative complications and the need for any reintervention. Confounders will not be taken into account, though the potential prevalence for said confounders will be prescribed.

Sample size:

Inpatients who have undergone cardiac surgery for TGA complex at IALCH between January 2015 to December 2023. (approximately 48 patients)

Inclusion & exclusion criteria:

Inclusion: All patients referred to the Department of Cardiothoracic Surgery at Inkosi Albert Luthuli Central Hospital for cardiac surgery for TGA complex between January 2015 to December 2023.

Exclusion: Patients not within the stipulated time period. Patients who underwent surgical correction of lesions that did not meet the IPCCC criteria for transposition of the great arteries. Patients with TGA who did not undergo cardiac surgery

Data collection methods and tools:

Data will be extracted from the patient records stored on the Inkosi Albert Luthuli Central Hospital Meditech system and entered into a Microsoft Excel data capture sheet. Detail coding and standardization of numerical values will be used as noted. The data will be assembled from electronic file keeping and case records, including radiological imaging, surgical operation documentation and follow-up records. Sub-group analysis will be based on patient presentation, pre-operative investigations and technical aspects of the surgery undertaken. Follow-up data (where available) will be included in the investigation.

Research instrument that will be used for data collection:

Addendum 1 – Data collection fields

Gestational age / Corrected gestational age	The corrected gestational age if the patient was born prematurely
Prem or not	If the child was born prematurely or not
Age at surgery	Patient age in weeks on the day of surgery
Gender	Male or Female.
Date of surgery	Date of surgery
Discharge Date	Date of discharge from IALCH
Post-op LOS	Length of stay between date of surgery and discharge. Will calculate using excel formula.
Height	Height in metres or NR (Not reported)
Weight	Weight in kilograms or NR (Not reported)

Associated congenital abnormalities	Does the patient have any associated congenital anomalies or syndromes
Major non-cardiac or chromosomal abnormalities	If there are any major non-cardiac or chromosomal anomalies present along with TGA
Atrial septostomy pre-op	If the patient required atrial septostomy prior to undergoing surgery
Pathology (the type of TGA)	The patient's pathology – TGA IVS (intact ventricular septum), TGA VSD, TGA DORV (double outlet right ventricle), TGA arch obstruction
Type of corrective surgery undertaken	If the patient underwent Arterial Switch Operation or Senning operation
Closure of the surgical wound	Was the surgical wound closed or was the chest left open? (covered by swabs and dressing film)
ICU LOS	Length of stay in ICU postoperatively
ICU ventilation	Length of patient requiring ventilatory support
Postop Complications	Complications the patient developed postoperatively if any.
Postop complication list	Please list all postop complications referred to above
Postop Death	Death following surgery. Please see patient discharge summary or progress notes to establish.
30-day mortality	Death occurring within 30 days of a defined event—e.g., hospital admission, diagnosis of an infection, surgery
Follow-up / re-intervention	If the patient required and further intervention on follow-up or postoperatively

Data analysis techniques:

The specific variables to be studied will be electronically captured using Microsoft Excel and then subjected to statistical analysis using SPSS. Usage of quantitative techniques will be implemented in the analysis of data.

Statistical analysis:

Descriptive statistical analysis of the study sample will be undertaken for objectives.

Study location:

This study will involve the use of data collected from IALCH, Durban, KwaZulu-Natal, South Africa

Study period:

January 2015 to December 2023.

Limitations of the study:

The potential lack or loss of follow-up review of the patient population. This study will contain data from a single hospital. However, IALCH is the only government facility in the province to perform surgery. This study is only limited to patients presenting between the period January 2015 to December 2023, which may limit the number of the disease profile. The aforementioned limitations will comprise part of the discussion section of the study with appropriate suggestions being mentioned on how to overcome said limitations

.

Ethical considerations:

Maintenance of patient confidentiality.

Benefits arising from this study:

Direct benefits to participants: *None*

Clinical care: *Establishing outcomes of the patient study group and to highlight the accepted surgical management for treatment of transposition of the great arteries.*

Public health: *In light of the high mortality of this condition without surgical intervention, the prompt diagnosis and appropriate referral should be sought for expedited surgical management*

Financial: *Re-emphasis of prompt referral and management is highlighted regarding efficacy and economy in the congenital cardiac population, especially the cost-effectiveness of unnecessary medical management*

Appendix 2: The Guidelines for Authorship for the Journal selected for submission of the manuscript

Journal: World Journal for Pediatric and Congenital Heart Surgery (WJPCHS) by Sage Journals Taken from: *https://journals.sagepub.com/author-instructions/PCH*

World Journal for Pediatric and Congenital Heart Surgery (WJPCHS) is a bi-monthly, peer reviewed, scientific publication dedicated to the advancement and dissemination of knowledge pertaining to congenital cardiac anomalies, pediatric heart diseases in general, and surgical management. WJPCHS is the official journal of the World Society for Pediatric and Congenital Heart Surgery (WSPCHS), the Congenital Heart Surgeons' Society (CHSS), and the European Congenital Heart Surgeons Association (ECHSA). WJPCHS publishes original reports of clinical and/or basic scientific investigations and observations relevant to the surgical and medical care and management of patients with congenital heart disease, as well as case reports, "how to do it" articles, image reports, new technology evaluations, review articles, historical reviews, invited editorials, correspondence, and commentary. Consistent with the mission of the journal's founding organization, WSPCHS, the journal serves as a forum for individuals and organizations interested in providing "the highest quality comprehensive cardiac care to all patients with pediatric and/or congenital heart disease, from the fetus to the adult, regardless of the patient's economic means, with an emphasis on excellence in education, research, and community service."

Preparing your manuscript for submission:
Your article must be within the scope of the journal and be of sufficient quality. If not, it will not be reviewed. The manuscript must be your original work, you must have the rights to the work, and you must have obtained and be able to supply all necessary permissions for the reproduction of any copyright works not owned by you, including figures, illustrations, tables, lengthy quotations, or other material previously published elsewhere.

Manuscripts should be typed double-spaced throughout with one (1) inch (2.5 cm) margins all around. Microsoft Word is the preferred software program. Manuscripts written in 12-point Arial or Times New Roman fonts are preferred and more reliably convert to PDF format during electronic submission. (Do not submit your manuscript in PDF format.) American rather than British spelling should be used throughout the manuscript, including within figures.

Original articles should not exceed 5000 words, inclusive of abstract, text, tables, figure legends, and up to 40 references. The combined total of figures and tables should not exceed 10.

The preferred format for your manuscript is Word. You do not need to follow a template, but please ensure your heading levels are clear, and the sections clearly defined.

Your article title, keywords, and abstract all contribute to its position in search engine results, directly affecting the number of people who see your work.

Title
Your manuscript's title should be concise, descriptive, unambiguous, accurate, and reflect the precise contents of the manuscript. A descriptive title that includes the topic of the manuscript makes an article more findable in the major indexing services.

Abstract
Please include a structured abstract between the title and main body of your manuscript that concisely states the purpose of the research, major findings, and conclusions. If your research includes clinical trials, the trial registry name and URL, and registration number must be included at the end of the abstract. Submissions that do not meet this requirement will not be considered.

Authors will also be asked on the submission form to provide a mini-abstract for inclusion in the journal's Table of Contents. This abstract should not exceed 60 words and should identify the type of study and convey the key findings and central message.

For clinical trials, the trial registry name and URL, and registration number must be included at the end of the abstract.

Keywords
Please include a minimum of 4 keywords, listed after the abstract. Keywords should be as specific as possible to the research topic.

Artwork, figures, and other graphics

- Format: TIFF, JPEG: Common format for pictures (containing no text or graphs).
- EPS: Preferred format for graphs and line art (retains quality when enlarging/zooming in).
- Placement: Figures/charts and tables created in MS Word should be included in the main text rather than at the end of the document.
- Figures and other files created outside Word (i.e. Excel, PowerPoint, JPG, TIFF and EPS) should be submitted separately. Please add a placeholder note in the running text (i.e. "[insert Figure 1.]")
- Resolution: Rasterized based files (i.e. with .tiff or .jpeg extension) require a resolution of at least 300 dpi (dots per inch). Line art should be supplied with a minimum resolution of 800 dpi.
- Colour: Please note that images supplied in colour will be published in colour online and black and white in print (unless otherwise arranged).

Figures supplied in colour will appear in colour online regardless of whether or not these illustrations are reproduced in colour in the printed version. If you have requested colour reproduction in the print version, we will advise you of the costs on receipt of your accepted

article. For journals that charge for colour in the print version - $800 for the first colour figure and $200 for each colour figure thereafter.

Statements and declarations
Please include a section with the heading ‘Statements and Declarations’ at the end of your submitted article, after the Acknowledgements section [and Author Contributions section if applicable] including each of the sub-headings listed below. If a declaration is not applicable to your submission, you must still include the heading and state ‘Not applicable’ underneath. Please note that you may be asked to justify why a declaration was not applicable to your submission by the Editorial Office.

Ethical considerations
Please include your ethics approval statements under this heading, even if you have already included ethics approval information in your methods section. If ethical approval was not required, you need to explicitly state this.

All papers reporting studies involving human participants, human data or human tissue must state that the relevant Ethics Committee or Institutional Review Board approved the study, or waived the requirement for approval, providing the full name and institution of the review committee in addition to the approval number. If applicable, please also include this information in the Methods section of your manuscript.

Declaration of conflicting interest
The journal requires a declaration of conflicting interests from all authors so that a statement can be included in your article. If no conflict exists, your statement should read: ‘The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article’.

Funding statement
All articles need to include a funding statement, under a separate heading, even if you did not receive funding.

Data availability
The Journal is committed to facilitating openness, transparency and reproducibility of research, and has the following research data sharing policy.

Subject to appropriate ethical and legal considerations, authors are encouraged to:

- Share your research data in a relevant public data repository
- Include a data availability statement linking to your data. If it is not possible to share your data, use the statement to confirm why it cannot be shared.
- Cite this data in your research

Reference style and citations

The journal follows the AMA Manual of Style. Every in-text citation must have a corresponding citation in the reference list and vice versa. Corresponding citations must have identical spelling and year. Authors should update any references to preprints when a peer reviewed version is made available, to cite the published research. Citations to preprints are otherwise discouraged. Identify references in the text using superscript Arabic numerals. Do not cite personal communications, manuscripts in preparation, or other unpublished data. Type references double-spaced after Acknowledgments, beginning on a separate page. Number consecutively in the order in which they appear in the text.

Appendix 3(i): Ethical approvals: BREC Expedited Application Approval Letter

UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

18 June 2020

Mr Yasteel Rajendra Mohanpersadh Maharaj (205503676)
School of Clinical Medicine
Medical School

Dear Mr Maharaj,

Protocol reference number: BREC/00001370/2020
Project title: A retrospective review of patients with Transposition of the Great Arteries complex and underwent cardiac surgical repair within the Department of Cardiothoracic Surgery at Inkosi Albert Luthuli Central Hospital during the period of 28 February 2015 to 31 March 2020
Degree Purposes: MMed

EXPEDITED APPLICATION: APPROVAL LETTER

A sub-committee of the Biomedical Research Ethics Committee has considered and noted your application.

The conditions have been met and the study is given full ethics approval and may begin as from 18 June 2020. Please ensure that outstanding site permissions are obtained and forwarded to BREC for approval before commencing research at a site.

This approval is subject to national and UKZN lockdown regulations dated 5th June 2020 which is available on the BREC website (http://research.ukzn.ac.za/Libraries/BREC/Proposed_UKZN_BREC_revision_to_research_constraints_anticipating_change_to_Level_3_lockdown.sflb.ashx).

This approval is valid for one year from 18 June 2020. To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2015), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx.

BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

The sub-committee's decision will be noted by a full Committee at its next meeting taking place on 14 July 2020.

Yours sincerely

[redacted]

Prof D Wassenaar
Chair: Biomedical Research Ethics Committee

Biomedical Research Ethics Committee
Chair: Professor D R Wassenaar
UKZN Research Ethics Office Westville Campus, Govan Mbeki Building
Postal Address: Private Bag X54001, Durban 4000
Email: BREC@ukzn.ac.za
Website: http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx

Appendix 3(ii): Approval from KwaZulu-Natal Department of Health

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

Physical Address: 330 Langalibalele Street, Pietermaritzburg
Postal Address: Private Bag X9051
Tel: 033 395 2805/ 3189/ 3123 Fax: 033 394 3782
Email: [redacted]
www.kznhealth.gov.za

DIRECTORATE:
Health Research & Knowledge Management

NHRD Ref: KZ_202005_028

Dear Dr Y. Maharaj (UKZN)

Approval of research

1. The research proposal titled **'A retrospective review of patients with Transposition of the Great Arteries complex and underwent cardiac surgical repair within the Department of Cardiothoracic Surgery at Inkosi Albert Luthuli Central Hospital during the period of 28 February 2015 to 31 March 2020'** was reviewed by the KwaZulu-Natal Department of Health (KZN-DoH).

   The proposal is hereby **approved** for research to be undertaken at Inkosi Albert Luthuli Central Hospital.

2. You are requested to take note of the following:
   a. *All research conducted in KwaZulu-Natal must comply with government regulations relating to Covid-19. These include but are not limited to: regulations concerning social distancing, the wearing of personal protective equipment, and limitations on meetings and social gatherings.*
   b. *Kindly liaise with the facility manager BEFORE your research begins in order to ensure that conditions in the facility are conducive to the conduct of your research. These include, but are not limited to, an assurance that the numbers of patients attending the facility are sufficient to support your sample size requirements, and that the space and physical infrastructure of the facility can accommodate the research team and any additional equipment required for the research.*
   c. *Please ensure that you provide your letter of ethics re-certification to this unit, when the current approval expires.*
   d. *Provide an interim progress report and final report (electronic and hard copies) when your research is complete to* ***HEALTH RESEARCH AND KNOWLEDGE MANAGEMENT, 10-102, PRIVATE BAG X9051, PIETERMARITZBURG, 3200*** *and e-mail an electronic copy to hrkm@kznhealth.gov.za*
   e. *Please note that the Department of Health shall not be held liable for any injury that occurs as a result of this study.*

For any additional information please contact Mr X. Xaba on 033-395 2805.

Yours Sincerely

[redacted]

Dr E Lutge
Chairperson, Health Research Committee
Date: 10/06/2020

Appendix 3(iii): Institutional Approval

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

DIRECTORATE:
Office of The Medical Manager
IALCH

Physical Address: 800 Bellair Road, Mayville, 4058
Postal Address: Private Bag X08, Mayville, 4058
Tel: 0312401059 Fax: 0312401050 Email: ursulanun@ ialch.co.za
www.kznhealth.gov.za

Reference: REC/00001370/2020
Enquiries: Medical Management

28 May 2020

Dr Y R M Maharaj (205503676)
School of Clinical Medicine
Medical School

Dear Dr Maharaj

RE: PERMISSION TO CONDUCT RESEARCH AT IALCH

I have pleasure in informing you that permission has been granted to you by the Medical Manager to conduct research on: **A retrospective review of patients with Transposition of the Great Arteries complex and underwent cardiac surgical repair within the Department of Cardiothoracic Surgery at Inkosi Albert Luthuli Central Hospital during the period of 28 February 2015 to 31 March 2020.**

Kindly take note of the following information before you continue:

1. Please ensure that you adhere to all the policies, procedures, protocols and guidelines of the Department of Health with regards to this research.
2. This research will only commence once this office has received confirmation from the Provincial Health Research Committee in the KZN Department of Health.
3. Kindly ensure that this office is informed before you commence your research.
4. The hospital will not provide any resources for this research.
5. You will be expected to provide feedback once your research is complete to the Medical Manager.

Yours faithfully

[redacted]

pp- **Dr L P Mtshali** Dr A. Harrichandprasad
Medical Manager

Fighting Disease, Fighting Poverty, Giving Hope

Appendix 3(iv): Provincial Health Research Committee Approval

health
Department:
Health
PROVINCE OF KWAZULU-NATAL

Physical Address: 800 Bellair Road, Mayville, 4058
Postal Address: Private Bag X08, Mayville, 4058
Tel: 0312401059 Fax: 0312401050 Email: ursulanun@ ialch.co.za
www.kznhealth.gov.za

DIRECTORATE:
Office of The Medical Manager
IALCH

28 May 2020

Dr Y R M Maharaj- (205503676)
School of Clinical Medicine
Medical School

Dear Dr Maharaj

Re: Approved Research: Ref No: REC/00001370/2020: A retrospective review of patients with Transposition of the Great Arteries complex and underwent cardiac surgical repair within the Department of Cardiothoracic Surgery at Inkosi Albert Luthuli Central Hospital during the period of 28 February 2015 to 31 March 2020.

As per the policy of the Provincial Health Research Committee (PHRC), you are hereby granted permission to conduct the above mentioned research once all relevant documentation has been submitted to PHRC inclusive of Full Ethical Approval.

Kindly note the following.

1. The research should adhere to all policies, procedures, protocols and guidelines of the KwaZulu-Natal Department of Health.
2. Research will only commence once the PHRC has granted approval to the researcher.
3. The researcher must ensure that the Medical Manager is informed before the commencement of the research by means of the approval letter by the chairperson of the PHRC.
4. The Medical Manager expects to be provided feedback on the findings of the research.
5. Kindly submit your research to:

   The Secretariat
   Health Research & Knowledge Management
   330 Langaliballe Street, Pietermaritzburg, 3200
   Private Bag X9501, Pietermaritzburg, 3201
   Tel: 033395-3123, Fax 033394-3782
   Email: hrkm@kznhealth.gov.za

Yours faithfully

[redacted]

pp **Dr L P Mtshali** Dr. A. Harrichandparsad
Medical Manager

Fighting Disease, Fighting Poverty, Giving Hope

Appendix 3(v): Approval from Academic Head of Department

UNIVERSITY OF
KWAZULU - NATAL
IN YUVESI
YA KWAZULU - NATAL I

Departnieiit of Cardiothoracic Siu'gery
Nelson R Mandela School of Medicine
Prin ate Bag 7
Cougella
4013
Kwazulti-Natal
South Africa
27 May 2020

Dea r Dr L Mtsha li
Senior Medica I Manager
In kosi AI bert Luth u li Centra I Hospita I

RE: **Protocol:** REC/00001370/2020

A retrospective review of patients wit h Trans position of the Great Arte]r ies com plex and underwent cardiac surgica I repair withi n the Department of Cardiothoracic Surgery at lnkosi AI bert Luth u li Central Hospita I during the pe riod of 28 Feb rua ry 2015 to 31 Ma rch 2020.

I give my approval for Dr Yasteel Ma haraj to collect data for the above study to be conducted in the Department of Card iothoracic Surge ry, lnkosi Albert Luthuli Hosp itaI.This is *for* his M Med. He has provisional BREC approval and protocol, attached. I wiII be grateful *for* IALCH and KwaZulu Natal, Department of Health permission for him ro extract data from our patient records.

Yours sincerely

[redacted]

Dr R Madansein
Hea d of Depa rtment: Cardiothoracic Surgery

De portment of Cordiothorocic Surgery
Surgical Disciplines
Sc hool of Clinical Me clicine
Postal Address: lnkosi AJ bert L uthuli Central Hospital, P/Bag XO3, Mayville, 4058, South Africa
Telephone: +27 (0) 31 2402114 Focsimilie: *27 (0) 31 2402 T T3 Website: vVwvv.ukzn.or.zm
Email: LeohGov6iolch.co.zo / thotharo@LJkzn.oc.za

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10G YEARS OF ACADEMIC EXCELLEN£tE

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Appendix 3(vi): Research Reviewer's Evaluation Form and Scientific Evaluation

NELSON R MANDELA SCHOOL OF MEDICINE
POSTGRADUATE EDUCATION COMMITTEE

RESEARCH REVIEWER'S EVALUATION FORM
SCIENTIFIC EVALUATION

APPLICANT: Dr Yasteel Maharaj ***DEGREE: MMed*** ***DEPT: Cardiothoracic surgery***
DATE: 08/04/2020

Title: A retrospective review of patients with Transposition of the Great Arteries complex and underwent cardiac surgical repair within the Department of Cardiothoracic Surgery at Inkosi Albert Luthuli Central Hospital during the period of 28 February 2015 to 29 February 2020.	
Category	**COMMENT**
Background Literature review	Satisfactory
Problem statement	Satisfactory
Research Question Hypothesis Objectives	Satisfactory
Scope of the project	Satisfactory
Study Population	Satisfactory
Methods/Procedures Materials	Satisfactory
Statistics and data analysis	Satisfactory
Research instruments	Satisfactory
Limitations	Satisfactory

NA = Not Applicable, E = Excellent, S = satisfactory, RC = Requires clarification, IC = Incomplete, US= Unsatisfactory,

RECOMMENDATIONS

Mark your selection below with X

1 Approve research proposal **as submitted** ..... ☐
2 Approve research proposal **with minor modifications** ..... ☒
3 Approve research proposal **subject to revisions (indicted above)**..... ☐
6 **Reject** the research proposal ..... ☐

COMMENTS :

Thank you for request to review.
Protocol is adequate for an MMed
Candidate must proof read to remove remaining minor grammatical errors.
Follow up period needs to be specified

Appendix 4: Data collection tools & Raw data

	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA
1	DOB	AG D	GEN	DATE O	CT	CT_Y	INDICATION FOR SURGERY	TG	INVOLUTED	M	N	P	TAUSSIG-B	CONDUIT STENO	DO	MG	PH	HYPOPLASTIC ARCH	PV OBSTRUCT	CH	DATE OF DISCHA	POST-OP FOLLOW-UP	LAST SEEN	TO ATTEND
2	07.01.2020	23	M	30.01.2020	NIL	N	TGA/VSD	TGA													19.02.2020	03.03.2020	DEFAULTED F/UP IN JULY 2020	UNABLE TO CONTACT
3	08.02.2020	5	M	13.02.2020	NIL	N	SIMPLE TGA	TGA													31.03.2020	14.04.2020	27.07.2020	CLINIC NOV 2020
4	02.06.2019	263	F	20.02.2020	NIL	N	SIMPLE TGA / INVOLUTED LV	TGA	INVOLUTED LV												02.03.2020	19.03.2020	08.06.2020	CLINIC OCT 2020
5	15.05.2017	1025	F	05.03.2020	NIL	N	TGA/IVS/PDA	TGA			IVS										24.03.2020	21.04.2020	23.06.2020	CLINIC SEPT 2020
6	09.07.2017	997	F	01.04.2020	15.04.2020	N	SEVERE MR (IE) ARTERIAL SWITCH /VSD CLOSURE		N	YES			TAUSSIG-BING		DORV						08.06.2020	14.07.2020		CLINIC NOV 2020
7	03.05.2014	1713	M	10.01.2019	NIL	N	TGA/VSD/PS (PREV RMBTS)	TGA				PS									18.01.2019	18.04.2019	POST-PONED DUE TO COVID	CLINIC MARCH 2021
8	07.02.2019	14	F	21.02.2019	20.02.2019	Y	DORV/TAUSSIG BING/HYPOPLASTIC ARCH						TAUSSIG BING		DORV			YES			EXPIRED	NONE	NONE	NONE
9	19.02.2019	29	F	20.03.2019	NIL	N	TGA/HYPOPLASTIC ARCH	TGA										YES			01.04.2019	30.04.2019	08.10.2019	CLINIC 10.09.2020
10	05.05.2019	11	M	16.05.2019	NIL	N	TGA/MUSCULAR VSD	TGA													28.05.2019	18.06.2019	22.10.2019	CLINIC 29.10.2020
11	03.05.2019	27	M	30.05.2019	NIL	N	TGA /MULTIPLE MUSCULAR VSD'S/LARGE PDA /ASD	TGA													EXPIRED	NONE	NONE	NONE
12	05.01.2006	4921	F	27.06.2019	12.06.2018	Y	TGA/VSD/PS (PREV RMBTS)	TGA				PS									04.07.2019	27.08.2019	20.02.2020	CLINIC FEB 2021
13	26.04.2006	4851	M	07.08.2019	29.03.2019	Y	TGA (PREV SENNING 2006) PV OBSTRUCTION	TGA											YES		14.08.2019	10.09.2019	16.01.2020	CLINIC JAN 2021
14	20.07.2019	54	M	12.09.2019	27.07.2019	Y	TAUSSIG-BING/HYPOPLASTIC ARCH						TAUSSIG-BING					YES			EXPIRED	NONE	NONE	NONE
15	30.08.2019	69	M	07.11.2019	05.09.2019	Y	TGA/VSD	TGA													19.11.2019	12.12.2019	02.07.2020	CLINIC MARCH 2021
16	06.10.2019	46	F	21.11.2019	NIL	N	TGA/VSD	TGA													02.12.2019	19.01.2020	CANCELLED DUE TO COVID 19	CLINIC AUG 2020
17	14.11.2017	55	F	08.01.2018	NIL	N	TGA	TGA													08.02.2018	20.03.2018	26.06.2018 LAST SEEN 26/9.2018	CLINIC OCT 2020
18	08.05.2018	9	M	17.05.2018	NIL	N	SIMPLE TRANSPOSITION OF THE GREAT VESSELS/LARGE ASD/PDA														07.06.2018	28.06.2018	17.08.2018	READMITTED OCT 2018
19	09.07.2017	333	F	07.06.2018	018 (PRE) 15.04.2020 (ches	Y	TAUSSIG-BING DORV						TAUSSIG-BING		DORV						03.07.2018	24.07.2018	09.10.2018	READMITTED NOV 2018
20	14.07.2018	412	F	30.08.2018	NIL	N	SIMPLE TGA	TGA													13.09.2018	04.10.2018	20.08.2019	CLINIC AUG 2020
21	10.12.2016	642	M	13.09.2018	20.01.2017	Y	DORV/MGV/VSD/PS					PS			DORV	MGV					28.09.2018	16.10.2018	03.03.2020	CLINIC MARCH 2021
22	10.01.2005	5043	M	01.11.2018	31.10.2018	Y	CONDUIT STENOSIS (PREV RASTELLI)							YES							EXPIRED	NONE	NONE	NONE
23	25.09.2018	58	M	22.11.2018	21.11.2018	Y	PULM HYPERTENSION TGA/VSD	TGA									YES				06.12.2018	10.01.2019	D JHB CHILD UNWELL ACCORDING	LOST TO FOLLOW-UP
24	03.12.2018	10	F	13.12.2018	NIL	N	TGA/IVS	YES			IVS										03.01.2019	24.01.2019	23.01.2020	CLINIC JAN 2021
25	05.12.2016	31	M	05.01.2017	NIL	N	SIMPLE TGA/ASD	YES													16.02.2017	16.03.2017	READMITTED 20.04.2017	
26	26.02.2017	39	M	06.04.2017	27.03.2017	Y	CHD/ASD/PDA	NO													03.05.2017	15.06.2017	CURRENTLY INPATIENT IN B2 EAST	
27	05.12.2016	476	M	25.04.2017	NIL	N	TGA (PREV ASO)	YES													31.05.2017	22.06.2017	27.02.2020	CLINIC AUG 2020
28	01.07.2017	54	M	24.08.2017	11.08.2017/05.09.2017	Y	TAUSSIG-BING DORV / ARCH HYPOPLASIA	NO					TAUSSIG-BING		DORV			YES			12.09.2017	26.09.2017	23.08.2018	LOST TO FOLLOW-UP
29	28.01.2016	595	M	14.09.2017	04.09.2017/27.11.2017	Y	TGA/VSD (TB)	YES													EXPIRED	NONE	NONE	NONE
30	06.09.2011	2254	F	07.11.2017	NIL	N	SIMPLE TGA ONLY DIAGNOSED AT 4 MONTHS WITH LV REGRESSION	YES													EXPIRED	NONE	NONE	NONE
31	17.07.2017	127	M	21.11.2017	NIL	N	TGA/ LATE PRESENTATION /SEVERE CYANOSIS/VENTILTED	YES													13.12.2017	12.06.2018	14.05.2020	CLINIC MAY 2021
32	26.11.2015	113	F	18.03.2016	17.02.2016	Y	TGA/VSD/ASD	YES													05.04.2016	19.05.2016	21.11.2019	CLINIC NOV 2020
33	08.04.2016	13	M	21.04.2016	03.05.2016 (Post)	Y	SIMPLE TGA/RESTRICTIVE SECUNDUM ASD	YES													09.05.2016	2016 SELF REFERAL FOR VOMITTING F/U 07.6	03.12.2019	CLINIC DEC 2021
34	09.03.2016	57	M	05.05.2016	22.04.2016	Y	TGA/VSD	YES													23.05.2016	21.06.2016	14.06.2018	LOST TO FOLLOW-UP
35	09.09.2016	81	M	29.11.2016	17.11.2016	Y	TGA/VSD	YES													22.12.2016	02.02.2017	19.03.2020	CLINIC JULY 2021
36	25.02.2015	13	F	10.03.2015	NIL	N	SIMPLE TGA	YES													EXPIRED	NONE	NONE	NONE
37	28.05.2015	7	F	04.06.2015	2019 (Post scan see compli	Y	SIMPLE TGA	YES													10.07.2015	16.07.2015	21.01.2020	CLINIC JAN 2021
38	05.10.2015	15	F	20.10.2015	2016 (Post scan see complic	Y	SIMPLE TGA/PDA	YES													09.11.2015	24.11.2015	18.07.2019	CLINIC MAY 2021
39	27.05.2015	181	M	24.11.2015	NIL	Y	SIMPLE TGA	YES													10.12.2015	15.12.2015	18.07.2019	CLINIC MAY 2021
40	20.08.2020	21	F	10.09.2020	NIL	Y	TGA WITH INLET VSD AND PDA, S/P BALLOON ATRIAL SEPTOSTOMY	YES													30.09.2020	16.10.2020	15.2.2022	06.06.2023
41	02.05.2020	75	M	16.07.2020	NIL	N	TGA/VSD/PHT	YES									PHT				24.07.2020	28.07.2020	15.09.2020	CLINIC 16.03.2021
42	09.06.2020	203	F	29.12.2020	14.12.2020	Y	TAUSSIG-BING	NO													EXPIRED	NONE	NONE	NONE
43	02.02.2020	354	M	21.01.2021	11.01.2021	Y	DORV/MGV/VSD/ARCH HYPOPLASIA	NO							DORV	MGV					EXPIRED	NONE	NONE	NONE
44	16.06.2020	259	M	02.09.2021	28.04.2021	Y	TGA/VSD/LVOTO	YES													14.09.2021	28.09.2021	12.07.2022	16.11.2023
45	10.01.2013	3219	M	03.11.2021	26.07.2017	Y	DORV/MGV/PS	NO								MGV					12.11.2021	30.11.2021	07.06.2022	06.06.2023
46	07.03.2022	360	M	31.03.2022	25.03.2022	Y	TGA/VSD/HYPOPLASTIC ARCH	YES													01.07.2022	25.08.2022	25.08.2022	22.11.2022
47	06.09.2021	269	F	02.06.2022	14.03.2022	Y	TGA/VSD/PDA	YES													30.06.2022	04.08.2022	04.08.2022	04.10.2022
48	07.08.2022	18	F	18.08.2022	NIL	N	TGA/VSD	YES													26.08.2022	13.09.2022	13.09.2022	16.02.2023
49	02.07.2022	54	M	25.08.2022	NIL	N	TGA	YES													19.09.2022	11.10.2022	11.10.2022	14.02.2023
50	03.02.2023	39	F	14.03.2023	16.02.2023	Y	TGA/VSD/ASD/PDA	YES													EXPIRED	NONE	NONE	NONE
51	19.09.2023	112	M	09.01.2024	08.12.2023	Y	TGA/OUTLET VSD/ASD	YES													02.02.2024	15.02.2024	15.02.2024	11.07.2024