Anesthesia in patients with congenital heart defects

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Anaesthesia in Patients with Congenital Heart Defects

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1.0 - Table of Abbreviations

Abbreviation	Definition	Abbreviation	Definition
ACHD	Adult Congenital Heart Defect	MDT	Multidisciplinary Team
AF	Atrial Fibrillation	NPPV	Non-PPV
ASD	Atrial Septal Defect	PA	Pulmonary Artery
ASO	Atrial Switch Operation	PAP	Pulmonary Arterial Pressure
BTS	Blalock-Taussig shunt	PBF	Pulmonary Blood Flow
CBP	Cardiopulmonary Bypass	PDA	Patent Ductus Arteriosus
CCT	Cardiac CT	PFO	Patent Foramen Ovale
CMR	Cardiac Magnetic Resonance	PH	Pulmonary Hypertension
CHD	Congenital Heart Defect	PPV	Positive Pulmonary Ventilation
CHF	Congestive Heart Failure	PVR	Pulmonary Vascular Resistance
CO	Cardiac Output	RBC	Red Blood Cells
CoAo	Coarctation Aorta	R-L	Right-to-Left
CPET	Cardiopulmonary Exercise Testing	RV	Right Ventricle
DIC	Disseminated Intravascular Coagulopathy	RVH	Right Ventricular Hypertrophy
GA	General Anaesthesia	RVOTO	Right Ventricular Outflow Tract Obstruction
GUCH	Grown up Congenital Heart Disease	SCD	Sudden Cardiac Death
HF	Heart Failure	SDI	Sociodemographic Index
HLHS	Hypoplastic Left Heart Syndrome	SVR	Systemic Vascular Resistance
IART	Interatrial re-entry tachycardia	TA	Truncus Arteriosus
IE	Infective Endocarditis	TGA	Transposition of Great Arteries
IPCCC	International Paediatric and Congenital Cardiac Code	ToF	Tetralogy of Fallot
JET	Junctional Ectopic Tachycardia	VF	Ventricular Fibrillation
L-R	Left-to-Right	VT	Ventricular Tachycardia
LV	Left Ventricle	VSD	Ventricular Septal Defect
MCS	Mechanical Circulatory Support		

2.0 - Table of Contents

3.0 – Summary

Title: Anaesthesia in Patients with Congenital Heart Defects

William Migo

Congenital Heart Disease (CHD) is the most common birth defects in humans affecting ~1% of live births worldwide. CHDs are structural abnormalities of the heart arising during fetal development leading to abnormal shunt formation and circulation of the pulmonary and systemic circulations. The exact causes of CHDs are not well understood, but a combination of genetic and environmental factors are thought to play a role. CHDs can range from simple defects that may not require treatment, to complex defects that can be life-threatening and require immediate surgical intervention.

Over recent decades, surgical and medical intervention has lead to >90% of children with CHD to reach adulthood defining a new population of adults with CHD (ACHD) previously known as Grown up CHD (GUCHD).

The anaesthetic management of adults with CHDs (ACHDs) presents a unique set of challenges for anaesthesiologists. The goal of anaesthetic management in CHD patients is to provide safe and effective anaesthesia while minimizing the risks associated with the patient's underlying cardiac defect. This requires knowledge of the patient's anatomy, physiology, and other specifics of their cardiac defect. Importantly, a multidisciplinary approach involving primary care physicians, cardiologists, cardiac surgeons, and anaesthesiologists with ACHD expertise is advised. These patients are at increased risk of morbidity and mortality with abnormal shunting and chronic hypoxemia. This leads to long term physiological changes and complications including haemodynamic instability, congestive heart failure (CHF), pulmonary hypertension (PH), dysrhythmias, threat of cyanotic spells, acid-base imbalances, coagulation defects, abscess induced seizures, meningitis and more.

This thesis explores recent developments in anesthetic management of patients with CHDs during non-cardiac surgery. As there is a growing ACHD population, anesthesiologists should be aware of their complex physiologies and subsequent anesthetic management as they encounter them during their clinical practice. This includes knowledge of their anatomy, physiology, and inherent CHD risk. During anaesthetic management they should carry out extensive medical histories and perioperative risk assessment.

Key words: Congenital Heart Disease; Anaesthesia; Management.

3.1 - Sažetak

Title: Anestezija u bolesnika s prirodenim srcanim greškama

William Migo

Kongenitalne srčane bolesti (CHD) su najčešće prirođene, pogađaju otprilike 1% novorođene djece diljem svijeta. CHD-ovi su strukturne abnormalnosti srca koje nastaju tijekom razvoja fetusa, rezultirajući abnormalnim preusmjeravanjem i cirkulacijom između plućne i sistemskih cirkulacija. Točni uzroci CHD-a nisu dobro istrazeni, ali smatra se da kombinacija genetskih i okolišnih čimbenika igra ulogu. CHD-ovi mogu varirati od jednostavnih mana koje možda ne zahtijevaju liječenje do složenih mana koje mogu biti opasne po život i zahtijevaju hitnu kiruršku intervenciju.

Tijekom posljednjih nekoliko desetljeća, kirurški i medicinski zahvati postigli su da preko 90% djece s CHD-om dostiglo odraslu dob, stvarajući novu populaciju odraslih osoba s CHD-om (ACHD), ranije poznatu kao Grown-Ups with Congenital Heart Disease (GUCHD).

Anestezijsko liječenje odraslih osoba s CHD-om (ACHD) predstavlja jedinstvene izazove za anesteziologe. Cilj anestezijskog upravljanja kod pacijenata s CHD-om je pružiti sigurnu i učinkovitu anesteziju uz minimiziranje rizika povezanih s osnovnom srčanom manom pacijenta. To zahtijeva razumijevanje anatomije, fiziologije i drugih specifičnosti pacijentove srčane mane. Važno je napomenuti da se savjetuje multidisciplinarni pristup koji uključuje liječnike primarne zdravstvene zaštite, kardiologe, srčane kirurge i anesteziologe s stručnim znanjem o ACHD-u. Ti pacijenti imaju povećani rizik od morbiditeta i smrtnosti zbog abnormalnog manevriranja i kronične hipoksemije. To dovodi do dugoročnih fizioloških promjena i komplikacija, uključujući nestabilnost hemodinamike, zatajenje srca (CHF), plućnu hipertenziju (PH), poremećaje srčanog ritma, cijanotske epizode, poremećaje kiselinsko-bazne ravnoteže, poremećaje zgrušavanja, napadaje izazvane apscesom, meningitis i još mnogo toga.

Ovaj rad istražuje najnovija postignuća u anestezijskom liječenju pacijenata s CHD-om tijekom nekardioloških zahvata.

Ključne riječi**:** kongenitalne srčane bolesti; anestezia; upravljanje.

4.0 - Introduction

CHDs are structural and functional heart defects present at birth, accounting for ~8-10/1000 live births(1). The Lancet report an increasing prevalence of ACHD globally (~20% worldwide since 1990) with the majority of deaths occurring in countries of low and middle socio-demographic index (SDI)(2). Increased fetal screening has prevented severe CHD while allowing adequate management for milder disease(3). Demographically, gender predilection varies according to type of CHD but in general appears equivalent(4,5). CHD incidence also varies by ethnicity and geographical location. For example, regions with highest infant CHD mortality reflect middle to low SDI regions (i.e Oceania, Africa and the Middle East, the Caribbean, and southeast Asia) while high SDI countries had vastly reduced death rates(2). CHDs are also associated with underlying genetic syndromes such as DiGeorges, Downs and Williams syndrome, though there are more(6). The fact that >90% of infants born with CHD now survive into adulthood makes it more prudent for anesthesiologists to be aware of their clinical presence.

CHDs are broadly classified into acyanotic and cyanotic defects. Acyanotic CHD is more prevalent and includes: atrial septal defects (ASD), ventricular septal defects (VSD), and patent ductus arteriosus (PDA). Cyanotic CHD, although less common is more severe, including: Tetralogy of Fallot (ToF), Transposition of the Great Arteries (TGA), and truncus arteriosus (TA). During this dissertation I will refer to European and American guidelines and classification systems(7,8). Since each CHD patient is unique, or can become more complex, the AHA/ACC classification is most appropriate (section 6.0).

The anaesthetic management of CHD patients is complicated by their pathophysiology and the potential for perioperative and long-term complications. Key problems are outlined below and will be discussed in subsequent sections:

Abnormalities in oxygenation and ventilation: Due to abnormal cardiac anatomy, presence of shunts, ventricular dysfunction, and increased PVR, CHD patients have poorer capacity for oxygenation and ventilation. This can exacerbate during anaesthesia, particularly if the patient is mechanically ventilated. Patients are more prone to hypoxia, hypercarbia, and acidosis, leading to increased pulmonary vascular

resistance (PVR) with subsequent shifts in intra/extra cardiac shunts resulting in cyanosis. Chronic underlying cyanosis lead to many consequences outlined below(9–11).

Hemodynamic instability: As described above, CHD patients have abnormal blood flow circulations making them more prone to hemodynamic instability and hypotension during anesthesia. Anaesthesiologists must be vigilant and monitor the patient's hemodynamic status (invasive or noninvasive) according to CHD risk stratification (see section 6.0).

Erythrocytosis, hemostasis and coagulopathy: Hemostatic abnormalities are an important cause of morbidity and mortality in CHD patients post-surgical intervention. It is now recognized to result from complex interactions between abnormal coagulation, thrombocytopenia, shortened platelet survival, deficiency of von Willebrand factor multimers and a plethora of clotting factor deficiencies(11). This increases bleeding risk during the perioperative period, especially if requiring cardiopulmonary bypass (CPB). The pathophysiology stems from chronic cyanosis to improve oxygen transport and delivery to tissues causing secondary erythrocytosis, a rightward shift of oxyhaemoglobin dissociation curve, and increase in cardiac output (CO). Compensated erythrocytosis reflects an equilibrium while decompensated erythrocytosis is a failure of equilibrium (excessive RBC/Hb increase and unstable, rising haematocrit with major hyperviscocity symptoms). Increased turnover of RBCs/Hb impairs urate filtration leading to hyperuricemia, excessive formation of unconjugated bilirubin increasing risk of gall stone formation and cholecystitis. Chronic hypoxemia, increased viscosity, and endothelial dysfunction impairs CO, microcirculation and autoregulation of visceral organs causing multiorgan dysfunction(12,13).

Risk of arrhythmias: Patients with CHD are at increased risk of arrhythmias due to their underlying cardiac defect. This risk is particularly high during periods of hemodynamic instability (during induction or cardiopulmonary bypass, CBP). Common arrythmias include atrial fibrillation (AF), re-entry atrial and ventricular tachycardias, heart block and sinus node dysfunction(14). They stem from cyanosis, chronic hemodynamic overload or superimposed surgical scarring, resulting in hypertrophy and fibrosis. Apart from the immediate effects of arrythmias (hemodynamic instability and hypoxia),

the effects of hyperviscosity and enhanced thrombi formation can lead to thromboembolic events. The subsequent need for antithrombotic drugs and pacemakers, results in frequent hospitalizations and further reduction in quality of life(15).

Neurological complications: Patients with CHD are at increased risk of neurological complications during and after surgery owing to the increased risk of emboli, microemboli and hemodynamic instability. The most frequent complications include embolic stroke, hemorrhagic stroke and, atherosclerotic cerebrovascular disease, the former being most common in structural defects such as transposition of great arteries (TGA) and tetralogy of fallot (ToF)(16). ACHDs are also far more likely to develop dementia and age related cognitive impairment owing to abnormal brain and cognitive reserve(17).

Anesthetic drugs and their effects: The choice of anesthetic drugs should be considered as they affect pulmonary and systemic vascular resistances (PVR, SVR), potentially worsening intra/extra cardiac shunts and subsequent oxygenation. Since CHD patients are high risk for noncardiac surgery the choice of anaesthetic drug is critical for maintaining hemodynamic stability and general habitus status. Specific anesthetic drugs are discussed in more detail in subsequent sections.

5.0 – Search Methods/ Methodology

To attain a general overview of this topic, several key words were used in an initial search on PubMed search database for publications on the anesthetic management of ACHDs. Key words included in each search were: “Anaesthesia”, “anaesthetic management”, and “congenital heart disease” AND/OR “defect”. Importantly, literature was limited to the last 10 years (September 2013 – January 2023), yielding 48 key articles – see figure 1 PRISMA diagram for completeness. Following initial searches on PubMed, we also conducted backward citation searching from relevant bibliographies to attain additional information previously not captured from our initial search. This included case studies and systematic review papers to support discussion points. This thesis focuses primarily on the anaesthetic management of common CHDs as well as a general overview of their anatomy and pathophysiology.

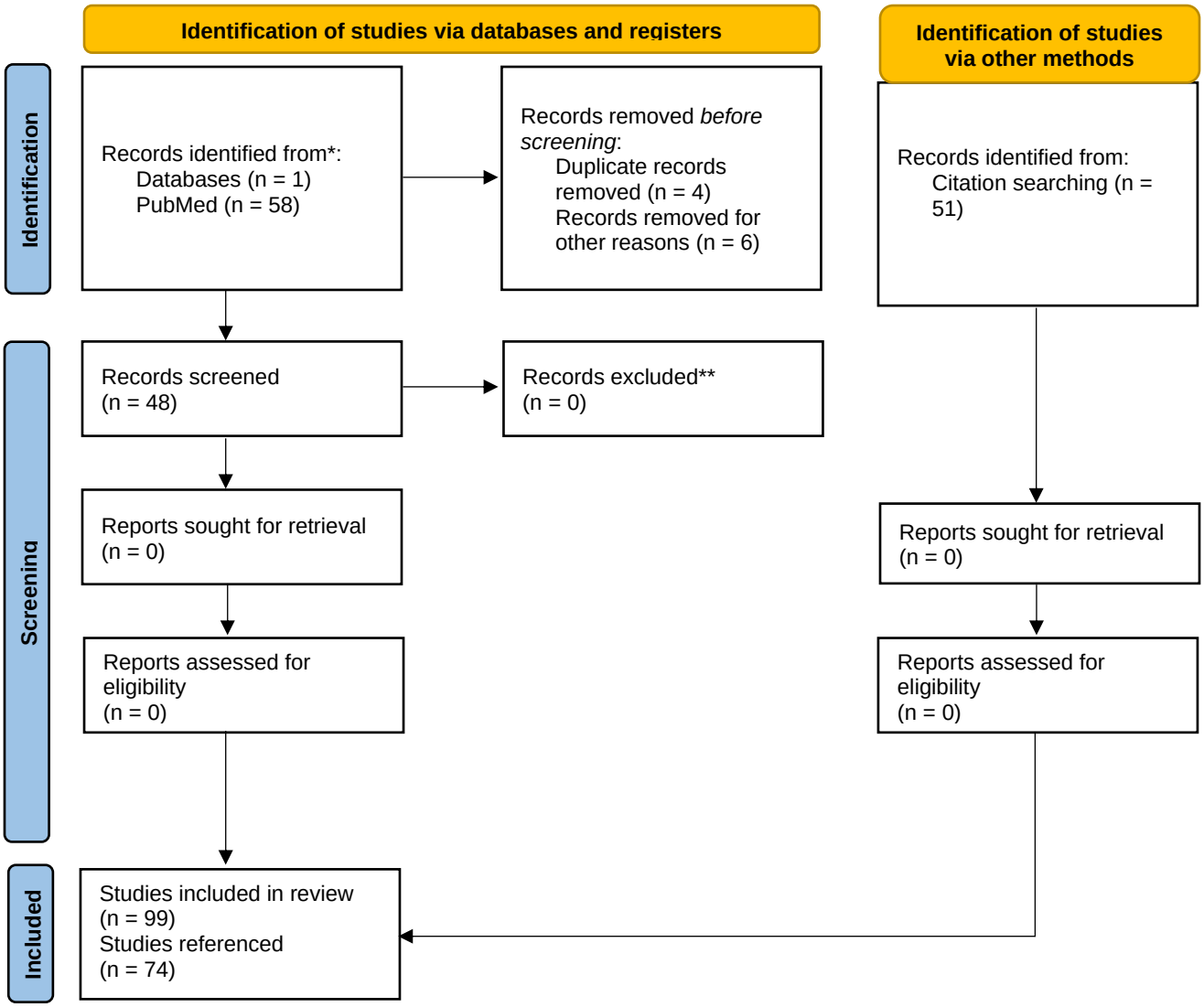

Figure 1: From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

6.0 - Classification of Congenital Heart Diseases

Historically, CHDs were classified according to their anatomy and physiological severity. However, due to the heterogenous nature of CHDs, the classification system has developed into a risk stratification classification, which has been revised over the years(7,8,12,18). Anatomic severity and resulting hemodynamic physiologies do not always correlate over the course of a patient's life. Therefore, the 2018 AHA/ACC guidelines for the Management of Adults with Congenital Heart Disease developed a classification based on native anatomy, state of surgical repair, the patients' physiology and functional status (shown in table 2)(7). Finally, I will be referring to the International Paediatric and Congenital Cardiac Code (IPCCC) nomenclature for anatomic lesions and repairs(19).

6.1 - Anatomical and Physiological classifications

An anatomic classification focuses on segmental analysis where the heart is split into 3 segments (atria, ventricles, and arterial trunks) connected by 2 junctions (atrioventricular and ventriculoarterial). This leaves us with 5 criteria to determine anatomical structures of the heart (see table 1)

Table 1 – Criteria to determine anatomical structures of the heart

Criteria	**Details**
Situs or Inversus	i.e Concordance with abdominal status, defined by position of right atrium (RA).
Concordance or disconcordance of each segment	i.e does one segment follow on to another in the correct order.
Segmental connections	i.e the atrioventricular canal and the infundibulum
Anatomical landmarks for each chamber	i.e LV defined by 2 papillary muscles, a mitral valve, and partially fibrous outlet. The RV is defined by 3 papillary muscles, one inserted on the septum; a tricuspid valve and a completely muscular outlet.
Assoc. abnormalities	i.e dysmorphic chamber structures, obstructive lesions or septal defects.

Physiological classification focuses on the hemodynamic abnormality and is divided into cyanotic and acyanotic heart defects. Cyanotic heart defects are characterized by abnormal blood flow between the two sides of the heart or between the heart and lungs leading to abnormal shunting and oxygenation that leads to cyanosis. These defects are more severe and can be life threatening. The most common cyanotic

heart conditions include Tetralogy of Fallot (ToF); Tricuspid atresia (TA); Transposition of Great Arteries (TGA); and Hypoplastic Left Heart Syndrome (HLHS).

Conversely, acyanotic heart defects are characterized by normal or near normal levels of oxygenation that do not result in cyanosis and are generally less severe. Acyanotic CHDs include: atrial septal defects (ASDs), ventricular septal defects (VSDs) and Patent Ductus Arteriosus (PDA).

Importantly CHDs are heterogenous and patients with the same CHD may have differing severity of disease and experience varying intensities of symptoms. It's important to distinguish these so anesthesiologists can administer appropriate perioperative care to minimize morbidity and mortality.

There have been many attempts to provide a comprehensive classification system for CHDs (7,18,20,21). The 2018 AHA/ACC guidelines for the management of ACHD proposed a new classification composed of 12 parameters: aortopathy, arrhythmia, concomitant valvular heart disease, end-organ dysfunction, exercise capacity, Eisenmenger syndrome, hypoxemia/cyanosis, NYHA functional classification, pulmonary hypertension, presence of a shunt, venous or arterial stenosis, and ventricular enlargement or dysfunction. This has allowed clinicians to stratify patients according to their inherent risk and is correlated with mortality(20).

6.2 – Risk Stratification Classification of CHDs

Table 2 shows the 2018 AHA/ACC classification of CHDs. This review will refer to this classification as it is the most documented and is utilized by European guidelines (8).

Table 2 - Classification of CHD according to severity and functional status split into mild, moderate and severe groups. *Adapted from AHA/ACC 2018 guidelines (Stout et al, 2018)*

Classification of CHD	AHA/ACC 2018 and ESC 2020 ACHD Classification
Mild	Isolated congenital aortic valve disease and bicuspid aortic disease Isolated congenital mitral valve disease (except parachute valve, cleft leaflet) Mild isolated pulmonary stenosis (infundibular, valvular, supravalvular) Isolated small ASD, VSD, or PDA Repaired secundum ASD, sinus venosus defect, VSD, or PDA without residuae or sequellae, such as chamber enlargement, ventricular dysfunction, or elevated PAP.

Moderate	Anomalous pulmonary venous connection (partial or total) Anomalous coronary artery arising from the PA Anomalous coronary artery arising from the opposite sinus Aortic stenosis - subvalvular or supravalvular AVSD, partial or complete, including primum ASD (excluding pulmonary vascular disease) ASD secundum, moderate or large unrepaired (excluding pulmonary vascular disease) Coarctation of the aorta Double chambered right ventricle Ebstein anomaly Marfan syndrome and related HTAD, Turner Syndrome PDA, moderate or large unrepaired (excluding pulmonary vascular disease) Peripheral pulmonary stenosis Pulmonary stenosis (infundibular, valvular, supravalvular), moderate or severe Sinus of Valsalva aneurysm/fistula Sinus venosus defect Tetralogy of Fallot repaired Transposition of the great arteries after arterial switch operation VSD with associated abnormalities (excluding pulmonary vascular disease) and/or moderate or greater shunt.
Severe	Any CHD (repaired or unrepaired) associated with pulmonary vascular disease (including Eisenmenger syndrome) Any cyanotic CHD (unoperated or palliated) Double-outlet ventricle Fontan circulation Interrupted aortic arch Pulmonary atresia (all forms) Transposition of the great arteries (except for patients with arterial switch operation) Univentricular heart (including double inlet left/right ventricle, tricuspid/mitral atresia, hypoplastic left heart syndrome, any other anatomic abnormality with a functionally single ventricle) Truncus arteriosus Other complex abnormalities of AV and ventriculoarterial connection (i.e. crisscross heart, heterotaxy syndromes, ventricular inversion).

7.0 - Physiology of Cyanotic and Acyanotic CHDs

CHDs form shunts and obstructive lesions leading to the clinical features seen in CHD patients. These lesions can result in volume overload (following left to right shunt and AV or semilunar valve insufficiency); pressure overload (following left sided obstruction, right sided obstruction); simultaneous volume and pressure overload (following single ventricle circulation) and pump failure (following ischemia and systemic right ventricle). Here we consider the most common acyanotic and cyanotic entities, describing their anatomical elements, shunting, and obstructive lesions. Finally, we discuss the effects of definitive and palliative surgical interventions in cyanotic CHDs. It is important to understand the physiologies of these lesions to manage these patients effectively. Furthermore, acyanotic lesions often contribute to the formation of cyanotic CHDs, therefore these are discussed first.

7.1 – Shunting Lesions

In normal cardiac physiology, the RV pushes deoxygenated blood to the lungs (Qp), while the LV pushes freshly oxygenated blood into the systemic circulation (Qs). These two circulations are separate and in series, maintaining a 1:1 volume ratio(10). Intracardiac shunting lesions are abnormal connections between the atria or ventricles. Left-to-right (L-R) shunts cause oxygenated blood to return to the pulmonary circulation, reducing oxygen delivery to the systemic circulation. Right-to-left (R-L) shunts cause deoxygenated blood to leak into the systemic circulation, bypassing oxygenation in the pulmonary circulation. In both cases, oxygenation is compromised leading to increased demand on the heart. We can quantify these shunts based on the Qp/Qs ratio, normally 1:1. >1:1 indicates pulmonary flow exceeds systemic flow and defines a L-R shunt. <1:1 indicates reduced pulmonary flow and a R-L shunt(12). Simultaneous shunting can occur in one patient and so it's possible for the shunts to cancel one another out.

7.2 - Acyanotic Heart Diseases

7.2.1 – Atrial Septal Defects

ASDs are a common type of CHD occurring in as many as 10% of live births(10). ASDs occur due to abnormal formation of the atrial septum and vary in size and severity. The main ASDs ranging from

most to least frequent are: patent foramen ovale (PFO), ostium secundum defect, ostium primum defect, sinusvenosus defect, and coronary sinus defect. Most patients with mild ASDs remain asymptomatic.

Flow across the ASD occurs in both systole and diastole, but is predominantly L-R owing to pressure differences between coronary and pulmonary circulations. Transient R-L shunts do occur, especially during Valsalva. Finally, during systole, depending on the size of the defect, a soft mid-systolic murmur can be identified.

Initially ASDs cause a L-R shunt, and patients may become symptomatic, experiencing shortness of breath on exertion. Theoretically, progressive overload of the right side of the heart can lead to an equalization of pressures between left and right systems. However, owing to the large capacitance of the pulmonary bed and the relatively smaller pressures seen in the atria, this is rare. When patients have concurrent pulmonary hypertension (PH) independent of cardiac anomaly, R-L shunting can occur.

Complications in ASD patients stem from ventricular hypertrophy, including arrythmias such as atrial fibrillation (AF). After surgical correction in children, chamber size normalizes while in adults it remains relatively fixed. This is the main reason why early intervention is paramount to avoid AF. Finally, ASD patients can develop paradoxical emboli although this is a rare occurrence(22).

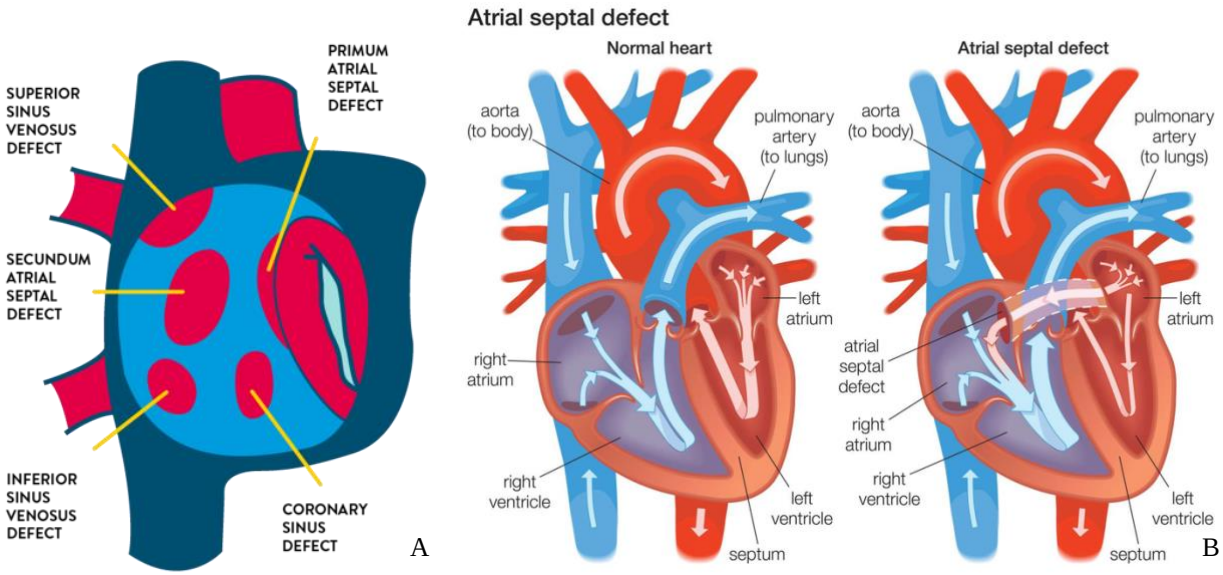

Figure 1 – Diagram to show Atrial Septal Defect and their main types. (A) Different types of ASDs differing in location. This includes: PFO, Ostium secundum ostium primum, sinusvenosus and coronary sinus defects. (B) Anatomy of ASDs and their principal shunts. Adapted from *Encyclopaedia Britannica* (2017).

7.2.2 – Ventricular Septal Defects

Ventricular Septal Defects (VSDs) are the most common CHD, accounting for 20% of cardiac malformations. The main types of VSDs are: perimembranous, muscular, inlet (AV canal type) and subpulmonary VSD (see figure 2) where perimembranous represents ~80% of VSD(10).

The hemodynamic effect of VSDs are different from ASDs. Blood from each ventricle has two possible systolic pathways: through the same sided outflow tract or the outflow tract of the opposite ventricle. This is dependent on the sum of PVR and SVR as well as the size of the defect. Specifically, a large defect results in reduced resistance and a larger shunt and vice versa(10).

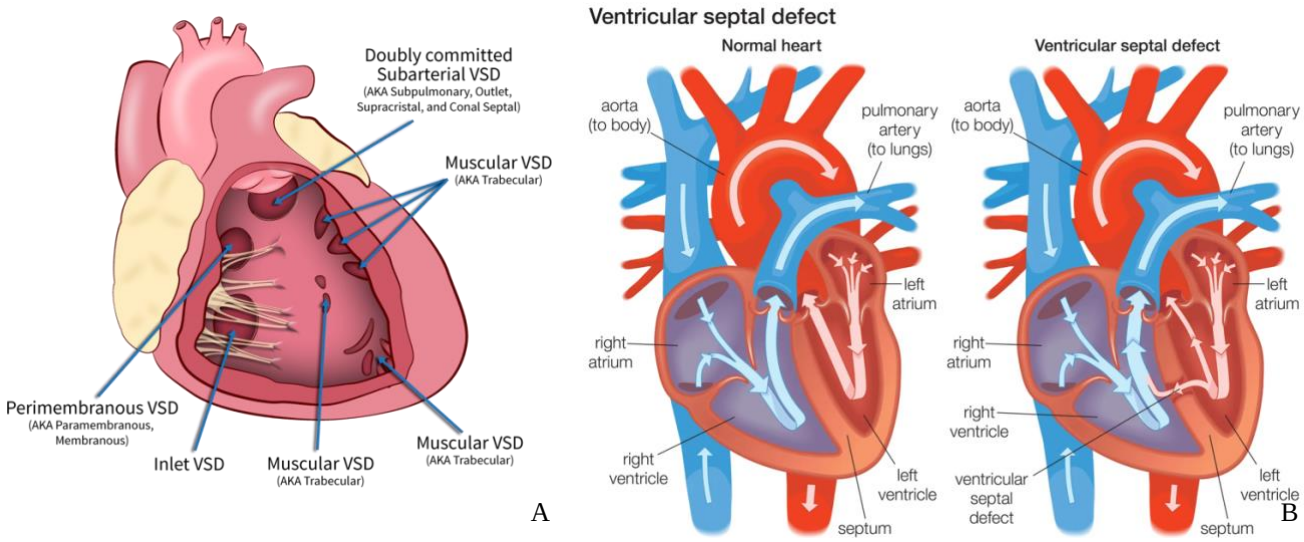

Figure 2 – Diagram to show Ventricular Septal Defect and their main types. (A) Different types of ASDs differing in location. This includes: perimembranous, muscular, inlet and subpulmonary (B) Anatomy of VSDs and their principal shunts. Adapted from *Encyclopaedia Britannica* (2017).

Normally, due to higher systemic pressures, an initial L-R shunt occurs. Overtime, this can lead to progressive overloading of the right system, causing PH and RV hypertrophy (RVH). Once pulmonary arterial pressure (PAP) overrides systemic blood pressure, flow reversal through the defect occurs, leading to Eisenmenger's syndrome. The difference between ASD and VSDs is the difference in pressures between pulmonary and systemic systems and flow across the defect occurring during systole, not diastole.

Small VSDs usually present with systolic murmur at birth, tend to remain asymptomatic and close by themselves. In those that persist into adulthood, the main concerns include infective endocarditis and aortic insufficiency. Both of which can be mitigated with prophylactic antibiotics and lifelong echocardiographic evaluation(23).

Large VSDs are more symptomatic presenting with congestive heart failure (CHF) symptoms. Left untreated Eisenmenger syndrome can develop and at this stage intervention is futile as closing the defect would lead to RV failure(23).

7.2.3 – Patent Ductus Arteriosus

Persistence of the Ductus Arteriosus at birth is known as Patent Ductus Arteriosus (PDA) and accounts for 5-10% of CHDs. Inutero this allows for blood flow from the main pulmonary artery to the aorta, usually obliterating within 72 hours after birth(24).

As with VSDs, PDA hemodynamics also depend on the relative resistance to flow in each pathway. Therefore, in most patients blood flows L-R (flowing into the PA). Patients with a large PDA have large LV end-diastolic volumes to compensate for the return of oxygenated blood to the pulmonary circulation while supplying normal CO. This increases LA filling pressures causing pulmonary venous congestion and subsequent exertional dyspnea. In contrast to VSDs, aortic blood returns to pulmonary circuitry directly. Also, if the diastolic “runoff” is large enough, it may impair coronary and splanchnic perfusion – a “steal” phenomenon(10).

The natural course of PDA is like VSDs in that those left unrepaired develop CHF symptoms and Eisenmenger physiology. The difference between them lies in the oxygen saturation preductally vs postductally. Preductally, the blood is fully oxygenated, while postductally it is mixed and saturations are reduced. This leads to near normal saturation in the upper body but hypoxemia in the lower body (identified by selective clubbing in the feet)(24).

Small PDAs are asymptomatic and require endarteritis prophylaxis. Larger PDAs are more symptomatic and should be treated early to avoid irreversible pathology.

7.3 - Cyanotic Heart Diseases

Cyanotic CHDs present with cyanosis and are far more severe owing to their complex anatomy pre and post correction. Physiologically, cyanotic CHDs cause chronic hypoxemia leading to the long-term sequelae as outlined in section 4.0.

7.3.1 - Tetralogy of Fallot

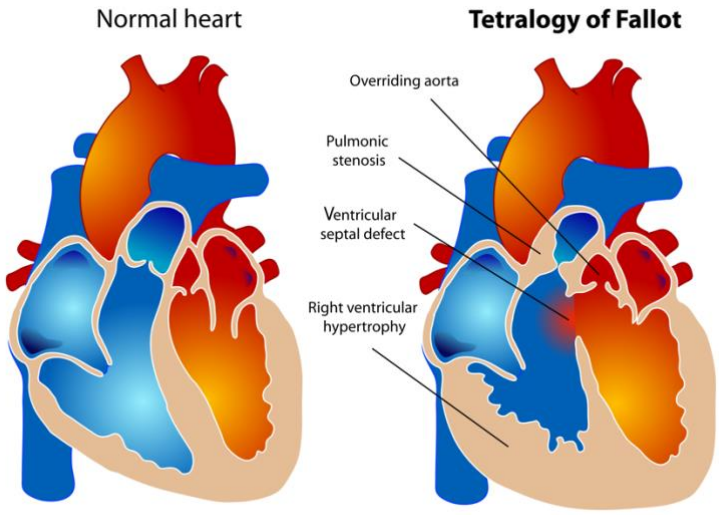

Figure 3 – Diagram to show Tetralogy of Fallot compared to normal heart anatomy. ToF contains four key features (1) Ventricular Septal Defect (2) Overriding of aorta (3) Pulmonary Stenosis (4) RVH. Diagram freely obtained from *google images* (2023).

ToF is one of the commonest cyanotic CHDs accounting for 7-10% of all CHDs with an incidence of 1 in 3500 births(25). It is classically characterized by the presence of a VSD, overriding aorta, right ventricular outflow tract obstruction (RVOTO) and right ventricular hypertrophy (RVH), see figure 3. ToF is associated with syndromes such as Down, DiGeorge, VACTERL and cardiovelofacial abnormalities. The severity of this condition is determined by the degree of RVOTO, the relative pressures in the right and left ventricles, and the degree to which the aorta overrides the VSD. This leads to a clinical spectrum of patients as depicted in figure 4.

The anatomy of ToF allows for the mixing of blood between pulmonary and systemic circulations, with a R-L shunt leading to cyanosis. Understanding the factors that worsen or improve the R-L shunt is key to the management of these patients.

RVOTO is due to sub-pulmonary valve muscle bundles. Infundibular spasms can occur following beta agonist administration, crying or various procedures, causing dynamic RVOTO a sudden increase in R-L shunting leading to profound hypoxemia known as hypoxic or "tet" spells.

Figure 4 – Diagram to illustrate clinical spectrum of ToF patients. ToF patients can be described as "pink" ToF with no or minimal RVOTO, little aortic override and essentially behaves like a VSD with L-R shunting; classic "blue" ToF with a degree of RVOTO and overriding; and "Profound Cyanosis" ToF with severe or complete RVOTO and overriding. Diagram adapted from Wilson et al (2019)

Reductions in SVR in the presence of RVOTO enhances R-L shunting. Therefore, increasing SVR forms the mainstay treatment for hypoxic spells and reductions in SVR during anesthesia induction should be avoided in these patients. Additionally, increases in PVR or RVOTO worsens R-L shunting. Importantly, once a tet spell initiates there tends to be a downward spiral consisting of: increasing R-L shunt, increasing hypoxia, acidosis and PaCO2, increasing PVR which worsens R-L shunt further.

Uncorrected ToF represent the most challenging subpopulation of patients as chronic hypoxemia and R-L shunting lead to significant morphological changes. This leaves them vulnerable to perioperative complications such as hemodynamic instability, cyanotic spells, CHF, acid inbalance, coagulation defects, meningitis and increased ICP(26). Surgically repaired patients with more normalized RV outflow must still avoid PVR/SVR altering anaesthesia owing to pulmonary vascular bed and RV muscle fiber changes that remain despite surgical correction.

7.3.2 - Transposition of the Great Arteries

TGA is a group of CHDs where the pulmonary artery arises from the morphological LV and the aorta arises from the morphological RV. According to anatomical classifications described earlier, this is known as ventriculoarterial *discordance*. The incidence of TGA is 1 in 3-5,000 live births and represents

5% of all cardiac malformations (2,3). TGA is frequently associated with other CHDs which complicates surgical intervention. There are three main subtypes of TGA relating to the spatial relationship between aorta and pulmonary trunk, including A-, D-, and L-transposition (27), figure 5.

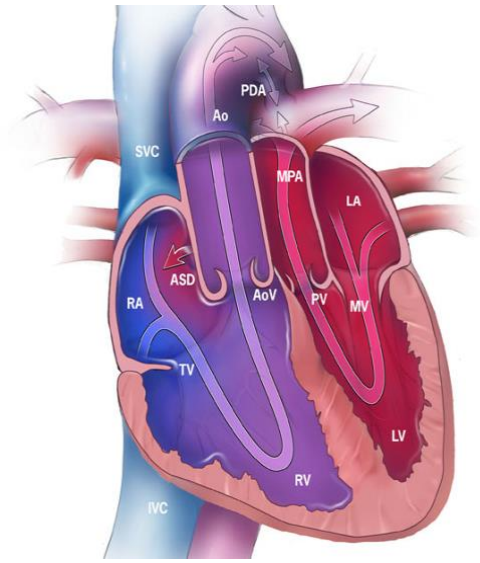

Figure 5 – Diagram to illustrate Transposition of Great Arteries CHD. RA, Right Atrium; RV, Right Ventricle; LA, Left Atrium; LV, Left Ventricle; SVC, Superior Vena Cava; IVC, Inferior Vena Cava; MPA, Main Pulmonary Artery; Ao, Aorta; TV, Tricuspid Valve; MV, Mitral Valve; AoV, Aortic Valve; ASD, Atrial Septal Defect; PDA, Patent Ductus Arteriosus. Diagram obtained and adapted from National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention (2023).

Physiologically, this CHD results in two parallel circulations as opposed to a normal series circulation between the heart and lungs. Hemodynamically, this does not allow for intra or extra cardiac mixing and without surgical intervention is almost universally fatal in early infancy. However, surgical intervention within the first few weeks of life (typically with introduction of ASD/ VSD or persistence of PDA allows for intracardiac mixing) and eventual corrective surgery (arterial switch operation, ASO), allows for up to 90% of patients to survive into adulthood(28). Surgical intervention can be definitive and/or palliative where patients with complex TGA often have palliative interventions. Finally, patients with complete ASO have less rhythm disturbance and incidence of RV failure. Long-term effects include, lifelong cardiac assessment is required, monitoring right and left ventricular outflow, pulmonary artery stenosis, ventricular dysfunction, arrythmias, and coronary insufficiency.

7.3.3 - Tricuspid Atresia

Tricuspid Atresia (TA) is a complex congenital heart disease presenting with cyanosis in the neonatal period. Incidence is 0.1 per 1000 live births and represents 1% of all CHD(29). As with other cyanotic

CHDs, TA is also associated with other conditions such as Down's syndrome, poorly controlled diabetes, excess alcohol consumption during pregnancy and a family history of CHD. Anatomically, the right atrium (RA) is separated from the hypoplastic RV. As a result, a PFO or ASD is required to allow for venous blood to enter the pulmonary circulation. Mixing of venous blood with newly oxygenated blood from the lungs therefore occurs in the left atrium (LA). Blood is then pumped to the systemic circulation via the LV, and to the pulmonary artery via VSD and RV. Importantly, the pulmonary valve may or may not be stenosed or dysplastic and should be evaluated as this will effect anesthetic management.

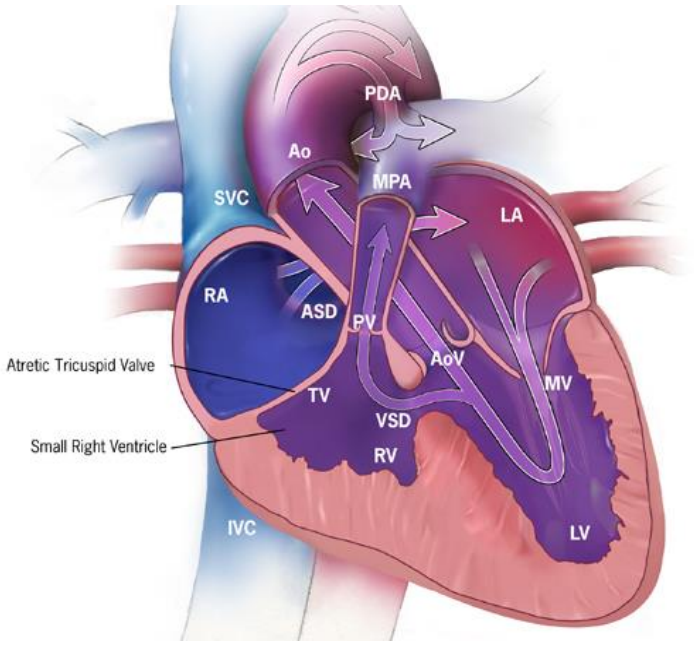

Figure 6 – Diagram to illustrate Tricuspid Atresia CHD, with atretic TV and small RV. RA, Right Atrium; RV, Right Ventricle; LA, Left Atrium; LV, Left Ventricle; SVC, Superior Vena Cava; IVC, Inferior Vena Cava; MPA, Main Pulmonary Artery; Ao, Aorta; TV, Tricuspid Valve; MV, Mitral Valve; PV, Pulmonary Valve; AoV, Aortic Valve; ASD, Atrial Septal Defect; PDA, Patent Ductus Arteriosus; VSD, Ventricular Septal Defect. Diagram obtained and adapted from National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention (2023).

As CO is mixed, oxygenation will be reduced but high enough to provide sufficient oxygenation to avoid cyanosis. As a result, pulmonary blood flow (PBF) dictates cyanosis in infants. PBF is determined by degree of pulmonary obstruction, the presence of VSD and/or PDA.

Corrective surgery involves the patient undergoing a Fontan procedure, whereby PBF is improved significantly. Fontan physiology consists of venous blood from the great veins passively entering the PA. Oxygenated blood then drains into the LA, into the single ventricle which pumps blood into the

systemic circulation. The transpulmonary gradient (difference between central venous pressure and systemic ventricular end-diastolic pressure) is the primary driving force for PBF and subsequently CO. Finally, as CVP is determined by intravascular volume it's important to keep these patients euvolemic. Hence, main factors driving Fontan circulation are SVP and volume, PVR, cardiac rhythm and LV function.

Fontan circulation survival outcomes of have been reported as high as 90% at age 1 month, 81% at 1 year, 70-90% at 10 years, and 60-80% at 20 years(30–32) with average life expectancy for patients undergoing Fontan procedure is now 35-40 years. Subsequently, long term complications are now being increasingly appreciated including: protein-losing enteropathy, thromboembolism, and arrythmias with most patients requiring cardiac transplantation(11). In fact, 70-80% of patients on the transplant register are those with univentricular hearts.

7.3.4 - Hypoplastic Left Heart Syndrome

Hypoplastic Left Heart Syndrome (HLHS) is the final considered cyanotic CHD. As one of the most severe CHDs it contributes ~20% of cardiac deaths during the first week of life. HLHS occurs in 0.16-0.36 per 1,000 live births, comprising 1.4-3.8% of CHDs(33). Structurally HLHS is defined as underdevelopment of the structures of the left side of the heart, including LV, subaortic structures, and ascending aorta (Figure 7). As a result, children are dependent upon blood pumped by the RV into the PA to supply blood to the systemic circulation and end organs via a PDA. As with other cyanotic CHDs, other defects may also be present, namely coarctation of the aorta (CoAo).

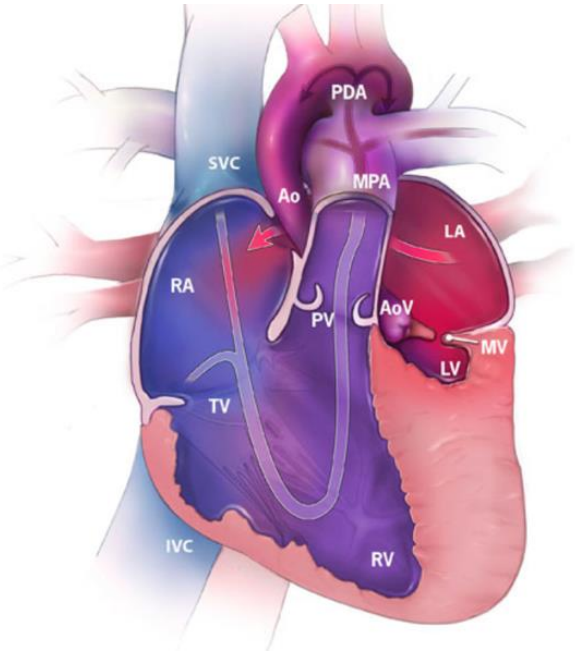

Figure 7 – Diagram to illustrate HLHS CHD with hypoplastic aorta, supraaortic vessels and LV. RA, Right Atrium; RV, Right Ventricle; LA, Left Atrium; LV, Left Ventricle; SVC, Superior Vena Cava; IVC, Inferior Vena Cava; MPA, Main Pulmonary Artery; Ao, Aorta; TV, Tricuspid Valve; MV, Mitral Valve; PV, Pulmonary Valve; AoV, Aortic Valve; ASD, Atrial Septal Defect; PDA, Patent Ductus Arteriosus. Diagram obtained and adapted from National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention (2023).

Patients with HLHS initially undergo Norwood procedure where the RV is used as the primary pumping system through a "neo-aorta" derived from the proximal end of the pulmonary artery (PA). Oxygenated pulmonary venous blood returning to the LA mixes with deoxygenated systemic venous blood returning to RA is subsequently mixed into the RV where it is pumped to systemic and pulmonary circulations simultaneously in a 1:1 ratio. PBF is dependent on a Blalock-Taussig shunt (BTS) connecting the innominate artery or right subclavian artery to the PA and the DA is ligated. The resulting arterial saturation ranges from 75-85%, which are well tolerated in these patients (33,34). However, this shunt doesn't come without its problems. Excessive PBF can lead to a "coronary steal" syndrome occurs. This leads to decreased cardiac function, malignant arrythmias and sudden cardiac death. Other morbid complications include acute shunt thrombosis (partial or complete) and subsequent life-threatening hypoxemia.

Furthermore, a modified Norwood procedure, utilizing a "Sano-shunt" whereby a RV-to-PA conduit has also gained recent popularity. The main advantage of this intervention is reduced diastolic run-off blood flow, improving coronary perfusion. However, the conduit requires a ventriculotomy and is non-valved in nature, leading to regurgitant flow. Complications include ventricular arrythmias, impaired systemic ventricular function and volume overload. Importantly, the Single Ventricle Reconstruction (SVR) Trial compared Norwood and modified Norwood procedures identified no significant difference in survival benefit between these two groups(35).

Importantly, children are required to be relatively stable to undergo a full Norwood procedure. Children that are not stable or too underdeveloped for such a drastic intervention can undergo a Hybrid procedure. This procedure is far less invasive and does not require CBP. Here, a stent is placed in the DA to maintain patency while bands are placed around the right and left pulmonary artery to restrict PBF, effectively balancing pulmonary and systemic circulations.

The resulting difference between Norwood and hybrid circulations is that of antegrade or retrograde cerebral and coronary profusions. The Hybrid system relies on retrograde coronary cerebral perfusion through the patent DA, while the Norwood procedure allows for antegrade profusion via the neo-aorta

or RV-PA conduit. Complications of the Hybrid system include DA obstruction (10-24% occurrence rate) and is associated with increased mortality. Owing to such complications, these children are monitored meticulously and can subsequently be converted to Norwood Anatomy if need be. Following primary Norwood procedure, as the child grows, a Fontan circulation is applied as with TA patients.

Given the complexity of these surgeries and interval anatomies, it's important for the anesthetist to be aware of them as to be able to assess the patients susceptibilities, complication risks given previous interventions and therefore the best options for anesthetic managements.

8.0 - Who should Provide Assessment/ Care to the ACHD patient?

The importance of who provides assessment and care to ACHD patients is critical as acute worsening of such conditions can be life-threatening. Accordingly, care is integrated, individualized, and planned. Previous 2020 ESC guidelines suggest patients be stratified into 3 categories:

1.) Patients who require exclusively specialist care
2.) Patients for whom shared care can be established with the appropriate general adult cardiac services
3.) Patients who can be managed in specialist clinics (with access to specialized care if required).

Guidelines also derive staff requirements for specialist centers (ref ESC 2020) and suggest that complexity of CHD not be the only criterion to assign patients to a certain level of care. Therefore, ACHD patients should be seen in a specialist center at least once to ascertain their risk stratification, appropriate level of care and follow-up intervals individually. Furthermore, it is prudent to organize end of life care as this also requires expert opinion. For patients with Fontan correction presenting with arrythmia, special attention is required as even supraventricular tachycardia arrythmias are poorly tolerated.

Transfer of ACHD care is important for continuity of care and assessment, there should be preparatory phases to account for adolescent patients moving into adult care. Specialist centers are advised to have specific staffing to qualify as specialist centres (outlined in 2018 AHA/ACC and 2020 ESC Guidelines).

Patients with CHD are not expected to travel long distances to reach specialist centers so it is recommended anesthesiologists have some knowledge of the patient's anatomy, physiology, the procedures impact on hemodynamics and potential complications associated. Overall, individual institutions should decide, based on multidisciplinary expertise, which patients can be managed and which should be referred to specialist centers.

9.0 - Risk Assessment and Therapeutic Considerations

9.1 – Risk assessment

Risk is divided into mild, moderate, and severe based on a combination of factors as mentioned in section 7.0.

Diagnostic methods are paramount to establish the level of risk individually. According to the 2010 ESC Guidelines for the management of grown-up congenital heart disease, diagnostic workup includes: Echocardiography, Cardiac MRI, CT and Cardiopulmonary exercise testing - discussed in section 10.1. Finally, cardiac catheterization is reserved for specific anatomical and physiological questions not answered from initial assessment.

9.2 – Therapeutic Considerations for Common Complications

This section discusses the main complications in ACHD patients and briefly how they are treated. We also highlight the physiological aspects for anesthesiologists to be aware of/ expect as it varies significantly in each ACHD patient. Furthermore, many of these complications should be evaluated in specialist centers in an MDT (multidisciplinary team) setting.

9.2.1 – Heart Failure

Although guidelines suggest utilizing normal heart failure (HF) treatment recommendations, the complex anatomies, and physiologies of ACHD patients (such as post Fontan, Mustard or Senning procedures) make it hard to extrapolate findings on HF studies. Specifically, whether these treatments are optimal for such patients and that these patients often cannot be stratified according to normal HF classification systems. Sabanayagam and Cavus et al (2018) summarize current medical and surgical

interventions in ACHD populations, including b-blockers, ACE inhibitors and ARB use in specific CHD pathology(15). Authors primarily suggest examining the underlying anatomy for lesions with possibility for intervention in treatable lesions followed by CHD and HF specialists. Secondly, mechanical circulatory support (MCS) and heart transplantation in CHD patients is more complex and are at a disadvantage in the current allocation system(36).

9.2.2 – Pulmonary Hypertension

Pulmonary hypertension (PH) is an important prognostic factor for ACHD and have a reported prevalence of 3.2%(37). Importantly, CHD women who choose to become pregnant are to be monitored meticulously(37). PH has a female predilection pre repair but normalizes after surgical intervention. PH-CHD patients can be subclassified according to 2020 ESC guidelines for the management of ACHD. Importantly, Fontan circulation patients often have pulmonary vascular disease and concurrent elevated PVR. Increases in pulmonary arterial pressure (PAP) often leads to increased post-capillary pressure (owing to increases in ventricular filling pressures and/or AV valve regurgitation) and subsequent pulmonary vascular changes. Low and intermediate risk patients with simple lesions and pre-capillary PH are recommended for initial oral combination therapy or sequential combination therapy. High risk patients are recommended to be treated with initial combination therapy including parental prostanoids. Those with Eisenmenger syndrome with reduced exercise capacity are initially treated similarly with a view for endothelin receptor antagonists(10).

Management of PH-CHD patients requires an MDT approach and advanced imaging with sequential follow-up. Continuous supplemental oxygen may also be required if arterial blood oxygen is consistently <60 mmHg (except Eisenmenger syndrome patients). L-R shunts cause endothelial shear which triggers PH. Theoretically, surgical repair may protect the pulmonary vasculature, however, there is no data to support this(37).

9.2.3 – Arrythmias

Arrhythmias are far more prevalent in the ACHD population owing to structural remodeling and occur at younger ages(14). There are many different types that can present due to the heterogenous nature of

CHDs. Arrythmias can form post-surgical repair, usually around the area of scarring or patch material. For example, right atrial incisions with cardiac remodeling from haemodynamic overload cause a high prevalence of atrial tachycardias. Most frequently is the late intra-atrial reentrant tachycardia (IART), namely atrial flutter with beats of 150-250 bpm(38). Importantly, arrythmias may lead to unstable hemodynamics, and sudden cardiac death (SCD)(14). Conversely, some arrythmias develop following progressive failure of left or right side of the heart. This leads to more complex electrophysiological changes involving channel remodeling, altered calcium handling and remodeling. In this scenario, fast polymorphic (VT) and ventricular fibrillation (VF) is more common.

Given heightened prevalence of arrythmias in ACHD populations, patients may be on cardiac holters, various antiarrhythmic or antithrombotic medication, ICDs or pacemakers and should be evaluated vigilantly. Patients may also be indicated for cardiac resynchronization therapy (CRT), where an increased risk further supports CRT indication.

9.2.4 – Infective Endocarditis

Risk of Infective Endocarditis (IE) is increased in ACHD patients, with marked variation in differing lesions. Despite this, guidelines only recommend prophylaxis in high risk individuals (outlined in the 2015 ESC guidelines)(39). Physicians should be weary of IE in these patients if poor oral hygiene, piercings/ tattoos, lack of awareness/education on IE is established.

9.2.5 – Antithrombotic treatment

ACHD patients are at increased risk of thromboembolic events. Phycisians involved in ACHD care management are encouraged to evaluate individual CHA2DS2-VASc and HAS-BLED scores as they have proven beneficial(40). Depending on the type of lesion or CHD, thromboembolic therapy may be recommended however, this must be weighed against the thrombogenic risk (especially in cyanotic patients)(41).

9.2.6 – Summary of Medical Management in Cyanotic Patients

Cyanotic patients can be on an extensive range of medical therapies and experience a range of interventions owing to the pathophysiology of their CHD. Therefore, their medical histories are often extensive. It's important to be aware of this to best tailor CHD treatment in noncardiac surgery. This includes PH treatment, antiarrhythmic therapy, serial therapeutic phlebotomies, blood transfusions, iron supplementation, routine anticoagulation/aspirin, hyperuricemia, and gout treatment - see table 3.

Table 3 - Main long term chronic effects of cyanotic CHD with descriptions. VKA, Vitamin K Antagonists; NOACs, Novel Anticoagulants.

Complications	**Description**	**Ref**
PH	PH is progressive and has poor prognosis. Regular assessment is required in those with shunt lesions post defect closure. Proactive treatment is required in all patients with PH. Women with CHD and confirmed pre-capillary PH are to be counselled against pregnancy owing to mortality risk. Anticoagulation data doesn't exits yet (for both VKA and NOACs).	(8,42,43)
Arrythmia	Aim for maintenance of sinus rhythm in ACHD patients. Refer to an MDT for expert ACHD-related arrythmia treatment. Those at high risk for arrythmias should have percutaneous/ surgical intervention discussed prior to procedure. Only initiate medical therapy within a hospital / expert CHD centre.	(8,14)
Hyperviscosity	Signs and symptoms include: headache, faintness, dizziness, fatigue, blurred vision, paresthesia's, muscle pain and weakness. Diagnostics must focus on blood work: CBC, MCV, serum ferritin, creatinine, uric acid, clotting profile, BNP/NT-pro-BNP, folic acid, vit B12. Therapeutic phlebotomy performed in presence of moderate/severe hyperviscosity (in absence of dehydration/iron deficiency). Isovolumetric fluid replacement should be done (750-1000mL per 400-500 mL of blood).	(8,44)
Anemia	Blood transfusions in the presence of iron depleting anemia. Iron replacement in the presence of iron deficiency (MCV <80 fL and low iron stores). Carefully follow in case of rebound effect.	(8,45)
Thromboembolic events	Routine anticoagulation/ aspirin does not show benefit in cyanotic patients – there is increased risk in bleeding. Indicated for atrial flutter/ atrial fibrillation – INR target 2-2.5 (with higher target for high risk factors)	(8,39)
Haemoptysis	CXR and Chest CT required. Therapy includes: discontinuation of aspirin, NSAIDs, oral anticoagulants, treatment of hypovolaemia and anemia, suppression of productive cough. Tranexamic acid and other antifibrinolytics are under investigation and could be a novel approach to treating hemoptysis.	(8,46,47)
Hyperuricaemia	Asymptomatic disease requires no treatment.	(8,45)
Acute Gouty Arthritis	Oral/ IV colchicine, probenecid, anti-inflammatory drugs. Patients with renal failure/ bleeding risk must be evaluated accordingly. Uricosuric (probenecid) and uricostatic (allopurinol) drugs avoid recurrence.	(8,45)

10.0 – Noncardiac Surgery Considerations

Factors associated with increase morbidity and mortality are related to the therapeutic considerations outlined previously. This includes presence, severity or degree of cyanosis, CHF, poor general health, younger age, PH, operations on respiratory and nervous systems, complexity of CHD and/ or urgency of the non-cardiac procedure. Issues to consider for ACHD are outlined in table 1.4.

10.1 - Perioperative Diagnostic tools

Perioperative diagnostics tools include: ECG, Echocardiography, CMR (cardiac magnetic resonance), CCT (cardiac CT), cardiac catheterization and cardiopulmonary testing.

ECGs serially assess cardiac function in conjunction with signs and symptoms. Ambulatory ECG can be used in ACHD at risk of tachyarrhythmias, bradyarrhythmia, heart block or when symptomatic. Sinus node dysfunction is common in patients with TGA while complete heart block is seen in patients with congenitally corrected TGA or late after AV septal defect repair(14). Often, ACHD patients exhibit post-operative heart block and should be managed accordingly. Atrial tachyarrhythmias are common following atrial switch repairs of TGA, Fontan repairs and Ebstein anomaly and should be screened regularly.

Echocardiography identifies valvular abnormalities, ventricular dysfunction, and pulmonary pressures. It is recommended throughout the perioperative period to assess the CHD, residual defect, or post-repair anatomy and function of the heart(7).

CMR imaging best evaluates RV size, although 3D echocardiography may show superiority when focused on ventricular volumes(ref). CMR offers unrestricted access to the heart and great vessels noninvasively, as well as serial measurements. It provides excellent anatomical details and physiological information for many CHDs. CMR requires standard protocols and sequences and therefore requires specialized skills for interpretation. Finally, many previous contraindications to its use are being reduced owing to CMR-compatible pacemakers, leads and other devices.

CCT is useful when information cannot be obtained from primary imaging modalities. It's main disadvantage is the ionizing radiation exposure, especially as ACHD patients accumulate exposure over their lifetime. Therefore, it's use is often restricted unless justification can be sought.

Cardiac catheterization remains the main diagnostic and prognostic tool for when more precise information is required i.e anatomical queries for low flow lesions or regions shielded in other imaging techniques. Information obtained includes direct pressure readings in vessels or chambers, determination of PA pressures and resistance and optimal imaging of vessels where flow is compromised.

Finally, cardiopulmonary exercise testing (CPET) is important to assess baseline functional capacity Specifically, the 6 minute walk test (6MWT) can be used to assess symptom severity, functional capacity and response to therapy (ref).

10.2 - Anaesthetic Management

Previous sections have described the anatomy, physiology, and main complications affecting ACHD patients. This section will now discuss the ways in which ACHD patient's anaesthesia is managed during non-cardiac surgery. As 90% of children with CHD reach adulthood, more literature is available for the management of ACHD in noncardiac surgery(28). Much of the data comes from observational studies, but there have been some larger studies which are discussed.

Each ACHD patient is very different owing to differing anatomy, ventricular dysfunction, dysrhythmia, residual disease, extent of chronic complications and biochemical equilibriums. The specific management of each patient subsequently varies. Additionally, recent European and American guidelines on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery may apply in a general concept, however not directly to ACHD patients(7,8,18). The AHA/ACC 2018 guidelines for the management of ACHD patients suggested a checklist of issues to consider for ACHD patients in the perioperative period and is presented below (table 4)(7).

When it comes to differing cardiac lesions, anesthetic goals must be set. See table 5 for the most common types of problems faced in anesthetic management of CHD patients. Furthermore, univentricular patients undergo varying stages of repair. Therefore, patients requiring non-cardiac surgery can present with differing anatomy. Table 6 displays the different stages and the main anesthetic considerations(48).

ACHD patients present with unusual physiological challenges. Fluid balance shifts in univentricular patients (i.e HLHS or fontan circulations), cyanotic changes in response to fluctuating vascular resistances, and the presence of intra/extracardiac shunting all predispose ACHD patients to excess morbidity and mortality during anesthesia. Even minor complications in non-cardiac surgery can develop into dire situations. Therefore, ACHD patients, especially those with ACHD AP II/III (moderate/ severe disease), should receive intricate perioperative evaluation.

Table 4 - ACHD Noncardiac Surgical Management Checklist

Clarify CHD Diagnosis
Clarify prior procedures, residua, sequelae, and current status, including ACHD AP classification
Be aware that history obtained from only the patient and family may be faulty or incomplete
Obtain and review old records to ensure accurate understanding of past procedures and clinical course Complete additional investigations required to define ACHD AP classification
Develop management strategies to minimize risk and optimize outcome
Factors associated with increased risk of perioperative morbidity and mortality
Cyanosis Congestive HF
Poor general health
Younger age
Pulmonary hypertension
Operations on the respiratory and nervous systems
Complex CHD
Urgent/emergency procedures
Issues to consider
Endocarditis prophylaxis
Complications related to underlying hemodynamics
Abnormal venous and/or arterial anatomy affecting venous and arterial access
Persistent shunts
Valvular disease
Arrhythmias: including bradyarrhythmias
Erythrocytosis
Pulmonary vascular disease
Meticulous line care (also consider air filters for intravenous lines) to reduce risk of paradoxic embolus in patients who are cyanotic because of right-to-left shunts
Adjustment of anticoagulant volume in tubes for some blood work in cyanotic patients
Prevention of venous thrombosis
Monitoring of renal and liver function
Periprocedure anticoagulation
Possible need for nonconventional drug dosing
Increased prevalence of hepatitis C infection because of prior procedures and remote blood transfusions
Developmental disability

Table 5 - Cardiac lesions conferring greatest mortality and morbidity risk with anesthesia

Cardiac lesion	Pathophysiological consideration	Anesthetic Goals	Ref
Suprasystemic pulmonary artery hypertension	Catecholamine release from light anesthesia, hypercarbia, hypoxemia, acidosis, systemic hypotension leads to elevated pulmonary artery pressure, right ventricular failure, low cardiac output, hypoxemia	Maintain oxygenation, ventilation, adequate depth of anesthesia, administer pulmonary vasodilators including nitric oxide	(48–50)
LVOTO, sub, valvar or supravalvar aortic stenosis	Tachycardia, hypovolemia, systemic hypotension, excessive myocardial depression or hypercontractility reduce stroke volume, lead to coronary ischaemia, low cardiac output	Maintain ventricular filling, systemic vascular resistance, normal to slow heart rate, normal myocardial contractility	
Infant with single functional ventricle and systemic to pulmonary artery shunt	Systemic and pulmonary output both ejected by single functional ventricle; pulmonary to systemic vascular resistance ratio determines systemic cardiac output	Maintain ventricular filling, systemic vascular resistance, normal to slow heart rate, normal myocardial contractility	
Dilated cardiomyopathy	Systemic and pulmonary output both ejected by single functional ventricle; pulmonary to systemic vascular resistance ratio determines systemic cardiac output	Avoid any decrease in myocardial contractility; maintain preload, and systemic vascular resistance	

Table 6 - Stages of single ventricle palliation and anesthetic considerations

Stage of palliation	Cardiac lesion	Surgical palliation	Pathophysiological considerations	Anesthetic considerations post palliation
Neonatal	Hypoplastic left heart syndrome	Norwood stage I	Systemic and pulmonary output both ejected by single functional ventricle; pulmonary to systemic vascular resistance ratio determines systemic cardiac output	Avoid hyperoxygenation and hyperventilation; maintain ventricular function; maintain systemic oxygen saturation 80–90%
Neonatal	Tricuspid atresia (hypoplastic right heart) with varying PS	Pulmonary Artery banding, systemic to pulmonary artery shunt	For shunted patients, see above; management of pulmonary to systemic vascular resistance ratio not as critical in banded patients	Maintain ventricular function; maintain systemic oxygen saturation 80–90%
Infant: Cavopulmonary connection (3-6 months)	Any univentricular lesion: left or right heart	Superior cavopulmonary connection (Glenn)	Cerebral-pulmonary-cardiac circulation is predominant in youngest infants	Avoid hyperventilation; most stable stage for elective noncardiac surgery
Fontan completion (2-4 years)	Any single ventricle lesion: hypoplastic right/left heart	Total cavopulmonary connection	Positive pressure ventilation decreases venous return and cardiac output; intolerant of hypovolemia or nonsinus rhythm	Minimize positive pressure ventilation; maintain ventricular volume, sinus rhythm, myocardial contractility; perform elective noncardiac surgery before this stage when possible

This should be conducted in an MDT setting, within a timely manner to allow expert knowledge and relevant consultations can be shared and conducted effectively.

Shunts and cyanosis in CHD are managed through SVR and PVR ratio, most shunts in CHD are R-L, L-R must be considered with echocardiography, as well as the degree of cyanosis. Decreases in PBF can occur primarily due to PH, or secondarily from RVOTO (TOF patients) or reduced systemic resistance (following anesthesia or sepsis). An acceleration in R-L shunting leads to cyanosis, acidosis, and decreased SVR - a vicious cycle (figure 8). Management must prioritize SVR and acute rises in PVR and is effectively controlled by alpha sympathomimetics Phenylephrine and ephedrine while preventing infundibular spasm with B-blockers(51).

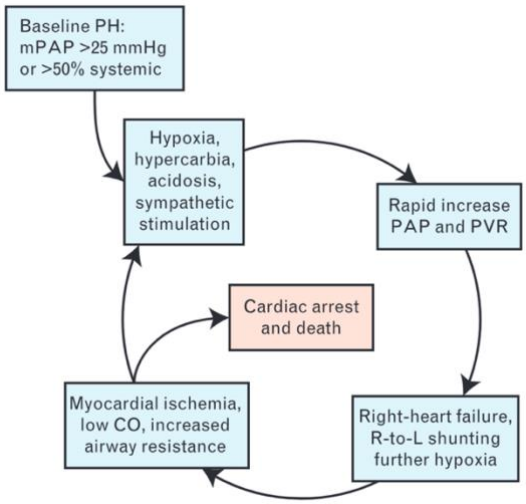

Figure 8 – Pathophysiology of pulmonary hypertensive crisis. If not interrupted, this crisis can lead to cardiac arrest. CO, cardiac output; mPAP, mean pulmonary artery pressure; PH, pulmonary hypertension; PVR, pulmonary vascular resistance.

Dwivedi et al describe an 8 year-old boy with uncorrected TOF presenting with cerebral abscesses – a known complication in CHD patients. Anesthetic management was aimed at maintaining normovolemia, preventing hypoxemia, and avoiding decreases in SVR and increases in PVR(26).

Any decreases in SVR were treated with phenylephrine or norepinephrine and IV fluids, while tachycardia and infundibular spasms were corrected propranolol or esmolol. Ketamine and dexmedetomidine were used for induction where ketamine increases SVR, decreasing R-L

shunting(52,53). This combination has recently been shown to be superior to midazolam-ketamine combination(54). A combination of Ketamine and Fentanyl induction improved oxygenation and saturation. Maintenance included dexmedetomidine owing to its sedative, analgesic and central sympatholytic property, this was balanced with ketamine's cardiostimulatory effects which resulted in physiological haemodynamics. Low doses of dexmedetomidine were used as higher concentrations can cause hypotension, bradycardia and neuroapoptosis (though not in clinical doses)(26,55). This is of great interest from a neurodevelopmental point of view as cumulative exposure can cause neuroapoptosis and potential long-term sequalae in CHD patients who undergo many surgeries from a young brain age. Furthermore, Dexmedetomidine effectively maintains hemodynamic stability, reduces junctional ectopic tachycardia (JET) and diminishes organ injuries in CHD children(56,57).

Low concentrations of volatile anesthetics were also used as this relaxed muscle spasms of the RVOT, increasing arterial oxygenation. Hypovolemia and hypothermia increase blood viscosity and R-L shunting, therefore the patient was given IV fluids and CVP monitoring accordingly.

As per the anesthetic checklist, IV lines were interrogated meticulously to avoid paradoxical emboli. All factors that increase PVR (hypoxia, hypercarbia, acidosis, hypothermia and increased sympathetic tone) were avoided to maintain lower PVR. ABGs were done prior to intubation and post intubation as pulse oximetry is not a reliable indicator of central cyanosis(58). Finally, as pain induces sympathetic activity, fentanyl bolus intraoperatively and paracetamol infusions postoperatively were administered.

Mathew et al (2013) also describe the anesthetic management in a 14 year-old child with AS anatomy undergoing orthopedic surgery following trauma of the right foot. Perioperative evaluation included extensive medical history, pre-anesthetic checkup, laboratory investigations, ECG and 2D echocardiogram. IV access was obtained, avoiding air bubbles (since 2D echocardiogram revealed ASD). It's important to note if the corrective surgery was definitive or palliative as cardiac physiology returns to near normal following definitive repair. Conversely, palliative repair is often asymptomatic until stress (such as surgery) is induced. Therefore, exercise tolerance testing is the most informative way of testing cardiac reserve and therefore a CHD patients ability to cope with surgical intervention.

Key anesthetic concerns matched those outlined in table 4. Main anesthetic manipulations were PVR: SVR ratios, where in L-R shunts a degree of peripheral vasodilation (mild hypotension) was well tolerated. Other anesthetic goals included optimization of preload, heart rate and contractility(59).

Importantly, propofol was avoided owing to reduced systolic/diastolic pressures. As the patient was already on ACE inhibitors, the decrease in blood pressure was compounded(59).

Muscle relaxant use is beneficial in patients where cardiovascular stability is needed, this patient had atracurium for laryngeal mask airway support, as intubation often leads to sympathomimetic responses(60,61). However, in patients that require transesophageal echocardiography for evaluation during intervention, tracheal intubation is prudent(62). Nitric oxide was avoided owing to potential shunt worsening and presence of peripheral cyanosis. Overall, the use of general anesthesia in complex patients seems to be well tolerated. As with previously mentioned cases, perioperative care is essential and management individualized based on comorbidities, type of repair, residual cardiac defects, severity of planned surgery, and experience of the center.

Non parturient patients with Norwood or Fontan procedures circulations are at increased risk of hemodynamic instability during PPV (owing to dependency of transpulmonary pressure gradient). Non-PPV (NPPV) has previously shown enhanced hemodynamic performance in these patients. Fontan hearts also have impaired ventricular systolic function, chronotropic incompetence and pronounced preload dependence. Therefore keeping the patient within their baseline equilibriums is paramount and the anaesthetic goal(63–65).

Neuraxial anesthesia is well established in ACHD patients – specifically epidural analgesia for labor (66,67). Other than typical coagulative contraindications, neuraxial anesthesia can lead to a drop in SVR and is especially more pronounced in patients with left ventricular outflow obstruction or patients with L-R shunting and so vasopressive support is recommended. Therefore, neuraxial anesthesia is preferred in patients with mild-moderate CHD, lower limb surgeries. It is preferred over general anaesthesia (GA) as it (1) attenuated pain (2) decreases release of catecholamines (3) provides adequate surgical anaesthesia and (4) in parturient patients allows for passage of stage 2 of labour (68,69).

Peripheral regional anesthesia is also preferred in ACHD as it offers high hemodynamic stability. But there are several drawbacks including: impaired coagulation and allergy, methemoglobinemia in a patient with low oxygen delivery following local anesthesia with prilocaine in cyanotic patients.

An increasing number of ACHD patients also means an increasing number of CHD women at childbearing age and subsequently labor. Importantly these women should be counselled prior to pregnancy owing to the substantial risks with pregnancy related physiology alone. Importantly, the leading cause of maternal mortality is of cardiac origin and in advanced society, is attributed mainly to CHD(70,71). Jooste et al (2013) looked at patients with univentricular systems. As with other Glenn and Fontan circulations, a normal to low PVR is required to maintain adequate SpO2 by encouraging passive PBF into the lungs. Supplemental oxygen reduces PVR keeping PCO2 levels normal to low, avoiding respiratory acidosis. Furthermore, spontaneous ventilation was beneficial over PPV as it encourages PBF. However, they note that PPV may be beneficial in patients on spontaneous ventilation who are hypoventilating owing to oversedation, enlarged abdomen, supine positioning, and obstruction of upper airways (72). These factors can lead to hypercarbia, acidosis and subsequent increased PVR.

As previously discussed, SVR also effects these patients and is important to keep normal to low. Importantly, if SVR is low owing to low CO, further increasing SVR with vasopressors (especially Phenylephedrine) can worsen CO. The main pressors in labour are still phenylephedrine and ephedrine where ephedrine mediated B-1 stimulation is controlled by b-blockers. Milrinone (positive ionotropic and lusitropic vasodilator) increases CO while reducing PVR and is ideal for cyanotic patients with low baseline CO(73). Studies are lacking in humans however, the benefits seen in univentricular pregnant woman warrant their use during pregnancy, labor, and delivery.

In general, anesthetic goals are to maintain CO by balancing PBF and systemic BF through preservation of ventricular function, minimizing cardiac depression, lowering PVR and maintaining sinus rhythm. Univentricular patients are particularly prone to dysrhythmias and therefore should be maintained with B-blockers, CCBs and digoxin. Electrical cardioversion can be considered in those that become or are at risk of hemodynamic instability.

The second stage of labour should be shortened, as prolonged Valsalva reduces venous return while increasing afterload leading to decreased CO. Type of delivery is dictated by obstetric indications. Vaginal delivery is associated with less blood loss, reduced risk of infection and thromboembolic events. Asfour et al (2013) recommend vaginal deliveries to be conducted in institutes with significant expertise in neuraxial blockade and forceps-assisted vaginal deliveries. Conversely, C-section deliveries remove the hemodynamic manipulation of Valsalva maneuver and the increased intrathoracic pressures(74).

Neuraxial anesthesia in these patients is beneficial as lower body sympathectomy reduces the large fluctuations in blood volume seen during delivery. Sympathectomy should be done gradually with a combination of epidural-spinal block to avoid abrupt changes in SVR and reversal of shunts that lead to maternal hypoxia. Bupivacaine with fentanyl via epidural catheter is recommended pain medication, targeting T10-L1 dermatomes during first stage of labor. Spinal anesthesia can lead to rapid changes in SVR, therefore, subarachnoid medication should be limited to opioids alone or in combination with local anesthetics at a lowered dose. C-section deliveries should utilize existing epidural catheters and bolus lidocaine titrated to a T4 dermatome prior to incision.

Neuraxial anesthesia has additional benefits including: avoidance of negative ionotropic effects. If patients require conversion to GA, hemodynamically stable patients are induced with ketamine and etomidate. Although there are conflicts regarding adrenal suppression following etomidate use and increased mortality as a result. It is suggested to keep etomidate use to one bolus on induction. Importantly, left uterine placement is essential for univentricular patients.

Perioperative monitoring during labour and other non-cardiac surgery is dictated by complexity of CHD and should include ECG, large-bore IV access, arterial catheter for constant BP evaluation, central arterial lines for relevant vasoactive medications. Pulmonary artery catheters are avoided owing to risk of inducing dysrhythmias, thromboembolic events and complexity of anatomy in these patients. Echocardiogram is always indicated as it assesses ventricular function throughout surgery and guides cardiac management. Importantly laboratory analysis prior to surgery includes coagulation status and

chronic hypoxemia assessment. Chronic venous congestion of the liver can lead to chronic disseminated coagulopathy (DIC), reduced vitamin K-dependent clotting factors and abnormal platelets. Finally, infective endocarditis antibiotics are indicated post-delivery owing to prosthetic materials used in surgery and general risk from CHD.

11.0 - Conclusions

In conclusion, due enhanced childhood survivals of CHD patients the number of ACHD patients are increasing. Clinicians should be aware of this and refer CHD patients to specialist centers when appropriate. Perioperative assessment should be conducted prior to non-cardiac surgery to ascertain the complexity of CHD, cardiopulmonary capacity and/or reserve, anatomy of current disease with any residual lesions i.e shunts. The AHA/ACC 2018 guidelines can help guide anesthesiologists when deciding perioperative monitoring and assessment. Importantly, the clinical process should be MDT oriented included specialists with knowledge of CHD patients. All of which should be conducted in a timely manner for provision of excellent care.

The goal of anaesthetic management in these patients is to maintain oxygenation of systemic circulation through careful manipulation of existing shunts via PVR and SVR. Importantly, CHD patients exist in a physiology that is unique to them, therefore understanding their individual equilibrium is key to providing adequate anesthesia. Labour in CHD patients, although contraindicated, is a possibility and therefore a meticulous assessment and perioperative monitoring is required.

Despite their once considered rarity, ACHD patients are now far more prevalent in society and therefore it is wise for clinicians to be aware of the complex and holistic approach that is required to treat these patients effectively.

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