Occurrence of significant post-operative arrhythmias in paediatric cardiac surgery patients at an academic hospital

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg in partial fulfilment of the requirements for the degree of Master of Medicine in the branch of Anaesthesiology.

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Declaration

I, Merusha Lindy declare that this research report is my own unaided work. It is being submitted for the Degree of Master of Medicine in the branch of Anaesthesiology at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at any other University.

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For my friend Dyuti who was one of the finest doctors and humans I had the privilege of knowing in this lifetime- you continue to be my daily compass.

Abstract

Background: The immediate post-operative period constitutes a vulnerable time for paediatric patients who have undergone cardiac surgery as they are at risk of developing haemodynamically significant arrhythmias which, could lead to morbidity and mortality. The occurrence of haemodynamically significant arrhythmias in the immediate post-operative period in these patients at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) was previously unknown.

Objectives: To ascertain the occurrence of significant post-operative arrhythmias in paediatric cardiac surgery patients at CMJAH, and secondly to describe these arrhythmias and identify predisposing risk factors.

Methods: This was a retrospective study that looked at clinical records over a 3 year period of patients 18 years and younger. The study was conducted in the cardiothoracic unit at CMJAH. The age, weight, cardiac defect, cardiopulmonary bypass time, aortic cross clamp time as well as magnesium, potassium and calcium levels were documented.

Results: Of the 459 patients who had cardiac surgery, 17 were excluded due to incomplete records. Fifty-three (12%) developed post-operative arrhythmias, of which, 40 (75.5%) occurred within 24 hours of surgery. Supraventricular tachycardia (SVT) 14 (26.4%), junctional ectopic tachycardia (JET) 6 (11.3%) and atrioventricular block (AVB) 7 (13.2%) occurred most frequently. Ventricular septal defect, Tetralogy of Fallot, mitral valve regurgitation, atrioventricular septal defect and coarctation of the aorta, were more common in the arrhythmia patient group. Arrhythmias were more likely to occur in patients with the presence of 2 (p=0.0170) or 3 (p=0.0420) defects.

Conclusion: The occurrence of haemodynamically significant post-operative arrhythmias in paediatric cardiac surgery patients at CMJAH was 12% which is comparable to other studies.

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Abbreviations

AF	Atrial Fibrillation
ASD	Atrial Septal Defect
AV	Atrio-ventricular
AVNRT	Atrio-ventricular nodal re-entrant tachycardia
AVRT	Atrioventricular re-entry tachycardia
VSD	Ventricular septal defect
AVB	Atrioventricular block
BBB	Bundle branch block
ECG	Electrocardiogram
CPB	Cardiopulmonary bypass
ACC	Aortic cross clamp
CTU	Cardiothoracic unit
ICU	Intensive care unit
JET	Junctional ectopic tachycardia
MR	Mitral regurgitation
COA	Coarctation of the aorta
AVSD	Atrioventricular septal defect
ASD	Atrial septal defect
PAC	Premature atrial contraction
PDA	Patent ductus arteriosus
PVC	Premature ventricular contraction

SVT	Supraventricular tachycardia
TOF	Tetralogy of Fallot
VF	Ventricular fibrillation
VT	Ventricular tachycardia

Statement

The Research Report consist of a literature review, draft article, study proposal and appendices. The study proposal is included for background reference and is not for examination.

The formatting of this Research Report complies with the University of the Witwatersrand's Style Guide for Theses, Dissertations and Research Reports. The formatting of the draft article may differ from the rest of the Research Report in order to comply with the author guidelines of the Southern African Journal of Critical Care , the journal to which it is intended to be submitted.

Section 1: Review of the literature

1.1 Introduction

This section will provide insight into significant arrhythmias occurring in the post-operative period following paediatric cardiac surgery as described in the literature. A brief overview of the history of paediatric cardiac surgery will be given followed by the definition and classification of various arrhythmias. Following this, the various methods by which these arrhythmias are diagnosed will be explored and thereafter an overview of the occurrence of post-operative arrhythmias will be provided. Finally, the various risk factors which predispose patients to these arrhythmias will be highlighted.

1.2 A brief history of paediatric cardiac surgery

The forerunners in the field of paediatric cardiac surgery unfortunately did not have the equipment or technology available in the present age to investigate and diagnose the underlying cardiac defect affecting the paediatric cardiac patient or to conduct the actual surgery or anaesthetic. Over time advances in medical science and technology has seen the immense evolution in the fields of paediatric cardiology, cardiac surgery, anaesthesiology and intensive care (1).

Surgical ligation of the patent ductus arteriosus (PDA) was first suggested in 1907 after it was demonstrated on a cadaver by the chief surgeon at the Boston City Hospital (2). It was some years later when Robert Gross performed a surgical ligation of the PDA on a seven and a half -year-old girl. He later devised a technique for ductal division in 1944 using a special ductus clamp to minimise massive haemorrhage (2). However, the first surgical procedure heralding the era of the emergence of paediatric cardiac surgery, was considered to be the Blalock-Taussig shunt first performed in 1944 (2).

Helen Taussig, a paediatric cardiologist at the Johns Hopkins University, initially noted that infants with a tetralogy of Fallot (TOF) defect and a PDA, only developed cyanosis following closure of the PDA. She therefore reasoned that, should the equivalent of a PDA or shunt be created, the cyanosis would be resolved in patients with TOF. She approached the chief of surgery at Johns Hopkins, Alfred Blalock, who with the help of his laboratory assistant devised an appropriate procedure on dogs. The first Blalock-Taussig shunt was performed on a 15-month old, 4.5 kg girl. The thoracotomy was performed with open drop ether anaesthetic technique as the hospital did not have appropriate sized paediatric

endotracheal tubes and a failed attempt at intubation had occurred with a urethral catheter (2). This procedure has been modified and refined over a past few decades and is now known as the modified Blalock-Taussig shunt (2).

The initial Blalock-Taussig shunt, although successful, could not be performed with small calibre arteries of infants, therefore, in 1946, Willis Potts, a paediatric surgeon at the Children's Memorial Hospital in Chicago, developed the Potts shunt as a means of supplementing pulmonary blood flow (2). His partial occluding clamp allowed distal flow to avoid spinal cord ischaemia from aortic cross-clamping. The actual procedure had many drawbacks and is therefore no longer used but the concept of the partial occluding clamp was first introduced through Pott's shunt (2).

These, along with various other early, classic paediatric cardiac surgical operations were named after the surgeons who developed these techniques (2). Many procedures were developed after prior attempts were carried out in laboratories on animal subjects and cadavers. Along with the advances in surgery came an evolution in paediatric anaesthesiology and paediatric intensive care to what it is in the present era (2). The complexities that have accompanied these advances have also meant that these patients may be at risk for other post-operative complications such as cardiac arrhythmias which requires a high degree of suspicion to treat effectively and improve the surgical outcome.

1.3 Definition and classification of arrhythmias

A cardiac arrhythmia is the manifestation of a disturbance of electric impulse formation and /or conduction (3). Arrhythmias regarded as significant causing haemodynamic instability, in the context of the cardiothoracic unit (CTU) will be discussed. Significant arrhythmias in this study are broadly classified as tachyarrhythmias and bradyarrhythmias (4). They include, but are not limited to:

- Sinus tachycardia
- Premature atrial contractions (PACs)
- Atrial flutter
- Atrial fibrillation (AF)
- Supraventricular tachycardia (SVT)
- Junctional rhythm

- Junctional ectopic tachycardia (JET) / atrio-ventricular nodal re-entrant tachycardia (AVNRT), atrioventricular re-entry tachycardia (AVRT)
- Premature junctional contractions
- Premature ventricular contractions (PVC)
- Monomorphic ventricular tachycardia
- Polymorphic ventricular tachycardia
- Ventricular fibrillation (VF)
- Sinus bradycardia
- First-degree heart block
- Second-degree heart block (Type 1 and 2)
- Third-degree heart block.

1.4 Significant tachyarrhythmias

A heart rate that is higher than normal for age and causing haemodynamic compromise, is considered a significant tachyarrhythmia (4). Various methods are used to classify the spectrum of tachyarrhythmias encountered, however, classifying them according to QRS duration is commonly used. A tachyarrhythmia with a normal PR interval for age is usually considered to arise from above the atrioventricular (AV) node. Those with a prolonged PR interval are considered to arise from below the AV node (5).

1.4.1 Sinus tachyarrhythmia

Sinus tachyarrhythmia or tachycardia is characterised by a P wave preceding every QRS complex. The P wave has a normal axis. The rates are age dependent and the ranges are provided below:

- newborn – 3 months > 205 beats per minute (bpm)
- 3 months – 2 years > 190 bpm
- 2 years – 10 years > 140 bpm
- > 10 years > 100 bpm. (4, 5).

Sinus tachycardia can occur as an appropriate physiological response to anxiety and exercise due to an increased sympathetic tone. Nicotine, caffeine, alcohol and some medications may also evoke a sinus tachycardia (6). Further it can also occur in response to

fever, hypotension, anaemia, thyrotoxicosis, hypovolemia, pulmonary emboli, myocardial ischemia and shock as well as in myocarditis or severe congestive cardiac failure (5).

1.4.2 Supraventricular tachycardias

Supraventricular tachycardias (SVT) is one of the most common arrhythmias encountered in the paediatric population. It refers to any tachyarrhythmia arising from above the level of the Bundle of His. In neonates and infants, the heart rate is >220 bpm. In older children the heart rate is >180 bpm. They are initiated and propagated either by the atria or AV node. SVTs are typically narrow-complex tachycardias having a short QRS duration (3, 5-7).

Two common SVTs, involving re-entry mechanisms, exist in children. These are the AVNRT, involving the AV node, or AVRT involving any accessory pathway near the AV node. The heart rates range between 140–250 bpm, have narrow QRS complexes and exhibit no P waves. Treatment includes the implementation of vagal manoeuvres, failing which adenosine, beta-blockers or calcium channel blockers may be used. Catheter ablation may be considered in recurrent episodes not amenable to medical therapy (3, 5-8).

1.4.3 Ventricular pre-excitation syndromes

Ventricular pre-excitation syndromes occur when there is normal conduction of impulses from the sino-atrial node to AV node through to the Bundle of His and Purkinje fibres as well as the accessory pathway, namely, the Bundle of Kent (7). Early depolarisation of the ventricle occurs prior to any conduction through the AV node. The most common condition in which this is seen is in Wolf Parkinson White syndrome (6), which is characterised by a short PR interval, widened QRS complex and an upward inflection in the upstroke of the QRS complex which is known as the delta wave (7).

1.4.4 Junctional ectopic tachycardia

JET is commonly seen post-operatively following the correction of congenital heart defects (5, 9-12). It is characterised by narrow QRS complexes, usually with AV dissociation, and an atrial rate that is slower than the ventricular rate (5, 13). 'It is driven by a focus with abnormal automaticity within or immediately adjacent to the AV junction of the cardiac conduction system (i.e., AV node–His bundle complex)' (10).The precise mechanism is unclear (10, 13), however, it is thought to be caused by mechanical trauma (oedema), to the proximal conduction tissue in the surgical setting (13). It is most commonly seen in procedures involving closure of a ventricular septal defect (VSD) (9). These arrhythmias are usually malignant and, if left untreated, may eventuate into haemodynamic instability and features of congestive cardiac failure. They can even result in the sudden onset of VF, which can then progress to paroxysmal complete AV block (10). Post-operative JET is usually transient in nature and commences as the patient is rewarmed at the end of CPB. This is an extremely vulnerable, when nodal inflammation and ischaemia contributes to ventricular dysfunction and is responsible for its related morbidity and mortality (10). Treatment is initially supportive and includes cooling the patient and addressing the underlying electrolyte abnormalities. These patients are often sedated and ventilated to reduce the catecholamine induced stress response. Atrial pacing is often used to achieve atrial synchrony (9, 13). Amiodarone is often administered as a loading dose followed by a continuous infusion to address the ventricular rate (9, 10, 13). Propafenone has been used to control and prevent JET in some neonates (10) Mildh et al (13) suggests the use of milrinone as a first line ionotropic agent in the presence of low cardiac contractility.

1.4.5 Premature ventricular contractions.

A PVC is a premature beat arising from an ectopic focus within the ventricles. It is characterised by a broad QRS complex, ST segment and T wave changes and is followed by a compensatory pause (5, 14). PVCs are usually benign. The causes include anxiety, sympathomimetics, beta-agonists, hypokalaemia, hypomagnesaemia, digoxin toxicity and myocardial ischemia. Three or more PVC at a regular rate of 120-180 bpm is classified as a VT and this may progress to VF if not treated promptly (5, 14).

1.5 Significant bradyarrhythmias

Bradyarrhythmia is defined as a heart rate slower than the lower limit of normal for the patient's age (7). The following limits are applied to the different age groups:

- 3 years or younger <100 bpm
- 3 – 9 years <60 bpm
- 9 – 16 years <50 bpm
- >16 years old/adolescents <40 bpm (5).

A sinus bradyarrhythmia or bradycardia must have a P wave preceding every ORS complex. A junctional bradycardia on the other hand has either no P waves preceding every ORS complex or the P waves may be inverted (7). The causes for bradyarrhythmias include vagal stimulation, hypoxaemia, acidosis, hyperkalaemia, hypercalcaemia, hypothermia, hypothyroidism, medications such as B-blockers or an acute elevation of intracranial pressure (7). Hypoxemia constitutes the most common cause of bradycardia in the paediatric population. Treatment is usually directed at the underlying cause and this may include correcting hypoxemia. Pharmacological therapeutic measures include the use of atropine or adrenaline when initial management is unsuccessful. Cardiopulmonary resuscitation requiring assisted ventilation and chest compressions is usually necessary when the heart rate is < 60 bpm together with haemodynamic compromise (7).

1.5.1 Atrioventricular blocks

An atrioventricular block (AVB) is regarded as a disturbance in the conduction of an impulse from the atria to the ventricle. The type of AVB is determined by the anatomic location of the problem within the conduction pathway (4, 5).

1.5.2 First- degree AVB

First-degree AVB occurs due to a conduction defect between the sinus impulse and its ventricular response. It is characterised by a PR interval that is longer than the normal limit for a given age. Every P wave is followed by a QRS complex. It is usually asymptomatic and may be seen in in the sleeping state and in athletes (5). It may also be a surrogate marker of of coronary artery disease, acute rheumatic fever, Lyme disease, digoxin toxicity or electrolyte disturbances (7, 15). Although this form of heart block is usually symptomless it has the potential to progress to second or third-degree heart block. Whilst

no treatment is usually required, the underlying diseases must be investigated and treated if detected (7).

1.5.3 Second-degree AVB

Second-degree AVB occurs when there is intermittent failure of an impulse to pass through the AV node or the Bundle of His (15). Variations of these include Type 1 ABV and Type 2 AVB.

Type 1 AVB/Wenckebach: Progressive lengthening of the PR interval until a beat is dropped due to an increased refractory period at the level of the AV node. The entire cycle is repeated after the last dropped beat. This can occur in healthy athletes, myocarditis, myocardial infarctions, cardiomyopathies, congenital heart disease and digoxin toxicity, but it is also common after repair of structural congenital heart defects (5).

Type 2 AVB/Mobitz: There is either normal AV conduction with a normal PR interval or a complete block in conduction (7), resulting in a P wave without a subsequent QRS complex. The conduction failure occurs at the Bundle of His level whereas the refractory period is prolonged in the Purkinje system. The same underlying causes of Type 1 second-degree block can also be responsible for Type 2 second-degree block. Type 2 second-degree block however has the potential to progress to the more ominous third-degree heart block. The presence of any symptomatic second-degree AVB necessitates temporary pacing, and is often followed by permanent pacing in most patients (6).

1.5.4 Third-degree heart block.

Third-degree heart block is also known as complete heart block. There is an absence of conduction between the atria and ventricles (5) resulting in complete dissociation of the P waves and QRS complexes. The ventricular escape complexes are usually wide and occur at around 30 – 40 bpm (6). The P waves are regularly spaced and not related to the ventricular escape rhythm. This rhythm may be congenital, occurring in infants born to mothers with anti-Ro and anti-La antibodies (5), or babies having associated cardiac structural lesions e.g. transposition of the great arteries (7). The acquired form may be attributed to surgery for congenital heart disease (5). Symptomatic presentation may include dizziness, syncope, fatigue, confusion and even sudden death. Infants typically display features of congestive cardiac failure whilst older children often manifest with

syncopal attacks known as Stokes-Adams attacks. Atropine or isoproterenol administration, to temporarily increase the heart rate is often utilised whilst awaiting the insertion of a pacemaker (7).

1.5.5 Bundle branch blocks

Prolonged conduction through either of the branches of the Bundle of His can cause either a right or left bundle branch block (BBB). This typically manifests as a prolonged QRS complex. These blocks may be classified as either complete or incomplete. The right BBB with a QRS of normal duration may be observed in healthy people whereas the left BBB is usually a marker of underlying heart disease, especially if it is related to cardiac symptoms such as acute chest pain, which may be suggestive of a myocardial infarction (6).

1.6 Diagnosis of arrhythmias in the CTU

Monitoring modalities and the incidence of arrhythmias thereof varies in the literature (16-22). Various forms of electrocardiographic (ECG) monitoring have been used pre and post-operatively in various studies to detect the presence of arrhythmias. These ECG traces have been useful in detecting sustained and haemodynamically significant arrhythmias (16). One lead overhead bedside monitoring represents a modality that is frequently used. The overhead monitors have sometimes been connected to a central monitoring station with a memory function in order to save the heart rate trends (17, 23, 24).

Continuous Holter monitoring has also been employed pre-operatively and post-operatively by Grosse-Wortmann et al (16) whereas this form of sensitive monitoring has only been used by Pfammatter et al (18) in patients with relevant post-operative arrhythmias. Whilst this form of monitoring reflects both benign and non-benign arrhythmias, the authors believe that it had the benefit of detecting shorter or more subtle rhythm disorders. This may reflect electrical instability of the myocytes, which have the potential of developing into haemodynamically significant arrhythmias (16).

Standard 12-lead ECG monitoring was used at various points during the patients stay in the hospital both pre and post-operatively, as seen in the study by Makhoul et al (12). Patients had a baseline 12-lead ECG performed upon admission to the medical unit and thereafter at various intervals throughout their stay (12). Valsangiacomo et al (19) occasionally performed a12-lead ECG only when suspicious rhythms were detected on the overhead bedside monitor which had no memory function, allowing for review of the rhythm

disturbance (19). Similarly, the study conducted by Talwar et al (20), retrospectively reviewed information from 12 lead ECG's as well as 6 lead (limb lead) ECG's when standard ECG monitoring was not possible (due bandages affecting chest lead placement). Atrial pacing leads placed intraoperatively have been used in some of these studies as a modality to further assess the underlying rhythm, when it was difficult to appreciate the distinct diagnostic features of the arrhythmia on the bedside monitors and 12-lead ECGs (16, 21).

Haemodynamic assessment has included identifying physiological signs of a reduced cardiac output leading to hypotension, oliguria, metabolic acidosis or poor peripheral perfusion (22). Doppler studies have been used to assess significant left to right shunting and residual pulmonary stenosis. Pulmonary artery catheters placed intraoperatively have been used to monitor persistent pulmonary hypertension (18). The method of surveillance of these post-operative arrhythmias and the incidences detected have varied in all these studies (16-22, 24). A summary of the relevant findings from these studies follows.

1.7 Incidence of arrhythmias in the CTU

The overall incidence of arrhythmias ranged from between 6.7% (11) to 79.1% (16). This wide range can be attributed to several reasons when the various studies are looked at individually.

The study by Grosse-Wortmann et al (16) used a highly sensitive continuous Holter monitoring and accounted for all arrhythmias both benign and non-benign. When arrhythmias causing haemodynamic instability were highlighted, this range decreased to between 29.6%-38.9%.

This is far more comparable to the various other studies reflecting an overall incidence of haemodynamically significant arrhythmias to be between 27-29% (18, 24, 25). Whilst the comparator studies did not employ as sensitive a method as 24-hour Holter monitoring, the comparative incidences highlight that clinically significant arrhythmias rarely remain undetected even with forms of monitoring (12 lead ECG, 6 lead ECG /limb lead ECG, overhead/bedside monitoring telemetry strips) other than 24-hour Holter monitoring (12). A few studies have recorded incidences as low as 8%-9% (17, 25). This may be attributed to the patient profile, surgical procedure and the method of evaluating the arrhythmias (25).

The incidence of specific arrhythmias varied as follows:

- SVT 2.6% – 41.2% (24)
- JET 1.4% – 36.4% (12)
- VT 2.1% – 33% (23)
- PVC 11% – 20% (16)
- CAVB 3.7% – 19.6% (23)
- AF 2.5% – 9.8% (16).

The above vary according to the types of surgery, methods of monitoring and risk factors as will be discussed below.

1.8 Risk factors that contribute to arrhythmias in the CTU

Various authors have tried to predict possible risk factors to the occurrence of the arrhythmias encountered in the post-operative period in an effort to improve surveillance, prophylactic measures and treatment. These include but are not limited to age, weight sex, surgical technique, cardiopulmonary bypass times (CPB) and Aortic cross clamp times (ACC), electrolyte disturbances, post-operative inotrope use and troponin levels.

1.8.1 Age and weight

Many studies have revealed a higher incidence of arrhythmias in younger patients, in particular neonates (17, 18, 21, 23, 25). Hoffman et al (22) demonstrated that JET had a tendency to occur more frequently in neonates. Rekawek et al (26) demonstrated that younger children with lower body weight were at a higher risk of developing significant post-operative arrhythmias. It has been hypothesised that younger patients are usually sicker and undergo more complex procedures and the cumulative effect of the various other risk factors in this younger age group is believed to result in a higher incidence of particular types of arrhythmias such as JET (17).

1.8.2 Sex

Grosse-Wortmann et al (16) demonstrated that the incidence of arrhythmia occurrence was higher in male neonates as compared to females and this might be explained by the pathogenesis of the arrhythmia. It is proposed that cytokines have a role in the development of arrhythmias (11, 20). An inflammatory cascade triggered by events (contact between blood, foreign surfaces of the extra-corporeal circulation circuit and the reperfusion of tissue) is believed to result in cell damage and cell death, which is attributed to cytokines (27). Increased levels of IL-10 (anti-inflammatory cytokine) and progesterone have been noted after CPB in both male and female infants however ILl-10 was higher in female infants compared with males (28). Furthermore, cytokine production is modulated by steroid and sex hormones (27, 28).

1.8.3 Surgical technique

Many mechanisms have been put forward linking surgical procedures to arrhythmia development post-operatively. The variable complexities and direct trauma to the conducting pathways is one such mechanism highlighted in various studies (16-19, 21-23, 25, 29).

Yildirim et al (25), showed that there was a lower risk of arrhythmias with close heart surgery as the myocardium was effectively untouched and the negative effects of CPB were not a consideration. They also highlighted that the first 24 hrs post-surgery is an important period for the development of arrhythmias hence surveillance is paramount during this period. Specific types of surgery were also associated with specific types of rhythm disturbances This has been largely attributed to the different complexities of the surgery and the anatomical defect as described by Rekawek et al (26). AVSD repair and arterial switch procedures together with a VSD closure accounted for an arrhythmia incidence of 72% and 62.5% respectively (23). Sahu et al (11) also demonstrated that patients with VSD (with or without TOF), and transposition of the great vessels, were at higher risk for developing post-operative arrhythmias (11).

An increased incidence of JET has been noted in arterial switch procedures, AV canal repair (due to its proximity to the AV node) and the Norwood procedure (17, 22, 23). Grosse-Wortmann et al (16) demonstrated that JET incidence was not linked to AVSD

repair. The occurrence of arrhythmias is reported to be 26% – 30% with atriotomy procedures (21, 29) and 28% in ventriculotomy procedures (29).

1.8.4 Cardiopulmonary bypass times and Aortic cross clamp times

An increase in CPB time was associated with a higher incidence of arrhythmias in the many of the studies (18, 19, 22, 23, 25, 26, 29). Pfammatter et al (18) demonstrated a 28% arrhythmia incidence when the CPB time ranged between 50 – 100 minutes with a further increase to 33% when the CPB time exceeded 100 minutes (29). The same trend was observed with ACC times. Ischaemic reperfusion injury is implicated in both instances (19). Interestingly, the study by Grosse-Wortmann et al (16) demonstrated an increased incidence of arrhythmias with a shorter CPB time in neonates. They attribute this finding to a more rapid rewarming and a shorter recirculation time allowing for greater myocardial injury in neonate (16).

1.8.5 Electrolyte disturbances

Serum electrolyte aberrations are also regarded as important precursors in the development of arrhythmias. This is believed to be due to the associated cardiac instability that accompanies certain electrolyte abnormalities (30).

Magnesium plays a pivotal role in the maintenance of the resting membrane potential of myocytes and attenuates the electrophysiological effects of hyperkalaemia (31). Its prophylactic administration has been known to be protective against the development of arrhythmias in adults (31). In the paediatric population undergoing surgery for congenital heart disease, electrolyte abnormalities have been shown to demonstrate a variable predisposition to arrhythmias (22, 23, 31). Whilst the study by Dorman et al (31) demonstrated a link between the development of JET with a low magnesium level, other studies have shown no relationship with the development of arrhythmias in the presence of low magnesium levels (22, 23).

Potassium serves as the primary ion mediating cardiac repolarisation therefore both hypokalaemic and hyperkalaemic states can be highly arrhythmogenic. Elevated and subnormal levels exhibit characteristic changes noted on the ECG. If abnormal levels are not identified and treated, they can lead to fatal outcomes in cardiac patients (32).

A regular cardiac rhythm requires the coordinated movement of calcium within the cardiac myocyte to drive excitation contraction coupling (33). Abnormal calcium levels may also lead to a disruption of this coordinated electrical activity resulting in both fatal ventricular rhythm VF and VT as well as an abnormal atrial rhythms, AF and atrial flutter (34).

1.8.6 Post-operative medication

Hoffman et al (22) implicated dopamine use in the first 72 hours to being associated with a higher incidence of post-operative arrhythmias, highlighting its catecholamine releasing properties as a possible cause (22). Dopamine and milrinone have been described to be associated with an increase in incidence of JET when used post-operatively by Hofman et al (22).

1.8.7 Increasing troponin levels

In light of myocardial ischaemia being a pathogenic mechanism, serum troponin levels as a marker of myocardial injury and ischaemia have been used as a predictor of post-operative arrhythmias (16, 29). The incidence of immediate post-operative arrhythmias was shown to correlate with the maximum post-operative serum levels of cardiac troponin (29). A troponin level between 10 – 50 ug/L was associated with a 46% incidence of post-operative arrhythmias whereas levels greater than 50 ug/L were associated with a 69% incidence (17, 29).

1.9 Summary

The aforementioned clearly suggests that the paediatric surgery patient may be predisposed to significant cardiac arrhythmias. It is therefore imperative to determine the incidence in one's own population. Ascertaining the incidence would help gauge one's own performance and set the scene for seeking out population specific risk factors so that it may be used to improve patient outcomes.

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- Acts: South Africa. National Health Act No. 61 of 2003. Regulations to an Act: South Africa. National Health Act of 2003.
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Section 3: Draft article

Occurrence of significant post-operative arrhythmias in paediatric cardiac surgery patients at an academic hospital

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Key words: paediatric cardiac surgery, post-operative arrhythmias, haemodynamically unstable

Abstract

Background: The immediate post-operative period constitutes a vulnerable time for paediatric patients who have undergone cardiac surgery as they are at risk of developing haemodynamically significant arrhythmias which, could lead to morbidity and mortality. The occurrence of haemodynamically significant arrhythmias in the immediate post-operative period in these patients at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) was previously unknown.

Objectives: To ascertain the occurrence of significant post-operative arrhythmias in paediatric cardiac surgery patients at CMJAH, and secondly to describe these arrhythmias and identify predisposing risk factors.

Methods: This was a retrospective study that looked at clinical records over a 3 year period of patients 18 years and younger. The study was conducted in the cardiothoracic unit at CMJAH. The age, weight, cardiac defect, cardiopulmonary bypass time, aortic cross clamp time as well as magnesium, potassium and calcium levels were documented.

Results: Of the 459 patients who had cardiac surgery, 17 were excluded due to incomplete records. Fifty-three (12%) developed post-operative arrhythmias, of which, 40 (75.5%) occurred within 24 hours of surgery. Supraventricular tachycardia (SVT) 14 (26.4%), junctional ectopic tachycardia (JET) 6 (11.3%) and atrioventricular block (AVB) 7 (13.2%) occurred most frequently. Ventricular septal defect, Tetralogy of Fallot, mitral valve regurgitation, atrioventricular septal defect and coarctation of the aorta, were more common in the arrhythmia patient group. Arrhythmias were more likely to occur in patients with the presence of 2 (p=0.0170) or 3 (p=0.0420) defects.

Conclusion: The occurrence of haemodynamically significant post-operative arrhythmias in paediatric cardiac surgery patients at CMJAH was 12% which is comparable to other studies.

Introduction

Paediatric cardiac surgery has evolved significantly over the last half century, along with advances in paediatric anaesthesia and post-operative intensive care. [1-4] This in turn has led to a decline in mortality [5, 6] such that it currently resides at 2 – 7%. [3, 5, 7]

Arrhythmias remain a cause for concern in the immediate post-operative period. [8] Arrhythmias occurring during this vulnerable phase following a major stressful event, such as cardiac surgery, may culminate into significant haemodynamic instability. [9, 10] This compromises recovery, impacting on morbidity and mortality. [9, 11] The incidence of all arrhythmias in the post-operative period is highly variable and has been reported as ranging from 6.7 – 79.1%. [7, 8, 11-18] Haemodynamically significant arrhythmias occurring in the post-operative period range from 6.7 – 38.9%. [7, 12-15, 18, 19]

It has been suggested that patient profile and various factors and processes during the surgical procedure, predispose to arrhythmia development post-operatively. Several studies report that, younger patients, the specific cardiac defect, specific surgical procedures, abnormal electrolyte levels, prolonged cardiopulmonary bypass (CPB) and aortic cross clamp (ACC) times, are some of these factors that contribute to arrhythmia occurrence. [8, 14, 20-22] An interdependence exists between various risk factors, which contributes to a high incidence of arrhythmias in this group. [17]

If not anticipated and not treated, the arrhythmias encountered in the immediate post-operative period may contribute to an increase in morbidity and mortality, as well as contribute to a prolonged duration of intensive care unit and hospital stay. This also impacts on the financial burden. [3, 23]

Therefore, institutional knowledge of the occurrence and risk factors of significant arrhythmias is important. The aim and primary objective of this study was to describe the occurrence of significant arrhythmias in the immediate post-operative period in paediatric cardiac surgery patients at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) as this was previously unknown. The secondary objectives were to identify the haemodynamically significant arrhythmias encountered and to ascertain the existing risk factors, which predisposed these patients to significant arrhythmias.

Methods

Approval to conduct the study was obtained from the University of the Witwaterstrand Human Research Ethics Committee (Medical) and other relevant authorities. A retrospective, contextual, descriptive research design was used.

The CTU at Charlotte Maxeke Johannesburg Academic Hospital consists of wards (where stable patients are admitted prior to surgery or stepped down from high care after surgery), as well as a cardiothoracic intensive care unit and high-care facility. The CTU in this study refers to the intensive care unit and high care portions of the facility. There was on average capacity for 4 paediatric ICU and 4 paediatric high care beds during the study period.

The study population was the paediatric cardiac patients in the cardiothoracic unit (CTU) at CMJAH. The sample size was determined by the number of clinical records available during a 3-year period (July 2010 – June 2013) and consecutive convenience sampling was used. The records included were those of paediatric patients 18 years and younger with significant arrhythmias that occurred within the first week post-operatively. Significant arrhythmias were defined as arrhythmias that cause haemodynamic instability requiring an intervention. Records not containing any of the information required in this study, or illegible and incomplete records, as well as records of patients taking anti-arrhythmic drugs pre-operatively were excluded from the study. The records, which were reviewed by the author (ML), included the CTU data base, CTU charts as well as anaesthetic and the perfusionists' recorded charts. The in-patient records of all paediatric patients admitted to the CTU requiring surgery during the study period were reviewed in order to calculate the occurrence. The CTU employs overhead bedside monitoring of cardiac rhythms and occasionally when circumstances permit, formal 12-lead ECG monitoring is used to further assess the underlying arrhythmia. Patients with haemodynamically significant arrhythmias are herefrom referred to as 'arrhythmia patients'.

A data collection sheet containing key elements highlighted from the literature review was drawn up in consultation with an intensivist working in the CTU.The following patient parameters were included: age, weight, cardiac lesion, surgical procedures, CPB in minutes, ACC in minutes, arrhythmia causing haemodynamic instability, time of occurrence, magnesium, calcium and potassium level at time of arrhythmia.

A Microsoft Excel 2010 (Microsoft® , USA) spreadsheet was used to capture data. Data were analysed in consultation with a biostatistician using the statistical program XLStat 2018.7 (Addinsoft, USA). Categorical data were summarised using frequencies and percentages. Medians and interquartile ranges were used to report continuous data, as data were not normally distributed. The Mann-Whitney test was used to compare the significance of age, weight, electrolyte levels, and CPB and ACC times, between the arrythmia patients versus non-arrythmia patients. Logistic regression tests were used to assess the likelihood of arrhythmia occurrence against age, weight, electrolyte levels, CPB and ACC times, as well as cardiac defects, across the two groups of patients (arrhythmia patients vs non-arrhythmia patients). A p-value of 0.05 or less was considered as statistically significant.

Results

During the study period, 459 patients underwent cardiac surgery. Of these 17 patients were excluded as records were missing or incomplete. Fifty-three (12%) of the remaining 442 patients developed significant arrhythmias post-operatively. Of these 53 arrhythmia patients, 6 (11.3%) developed repeat episodes. The arrhythmias occurred anywhere from immediately post surgery up to day 5 thereafter. The majority, 40 (75.5%), however occurred within the first 24 hours. The patients' ages and weights are depicted in Table 1 and the cardiac defect and arrhythmias are shown in Table 2. There was no statistically significant difference, in terms of age or weight in patients who developed arrhythmias compared to those who did not do so.

Among the 442 patients, 131 (29.6%) exhibited multiple cardiac defects. When these 131 patients with multiple cardiac defects were further assessed, 23 were from the arrhythmia group and 108 were from the non-arrhythmia group. This translates into 43.3% (23/53) of patients with multiple defects exhibiting arrhythmias, whilst 27.8% (108/389) of patients with multiple defects having no significant arrhythmias.
The overall occurrence of arrhythmias in the 442 patients was 12%; but the occurrence of arrhythmias in patients with multiple cardiac defects is 17.6%, (23/131). This is significantly higher than the occurrence of arrhythmias in the group with single cardiac defects which was 9.6% (30/442-131).

Furthermore, logistic regression analysis demonstrated that arrhythmias are more likely to occur in patients with the presence of 2 (p=0.0170) or 3 (p=0.0420) defects.

Table 1: Patient demographics and comparisons between groups 1

Demographics	Median (IQR)			p-value
	All patients 442	Non-arrhythmia 389	Arrythmia 53	
Age (month)	24.0 (10.0 - 79.0)	24.0 (10.0 - 83.0)	16.0 (11.0 - 38.0)	0.1292
Weight (kg)	10.0 (6.1 - 19.0)	10.0 (6.5-20.0)	8.7 (5.6-11.6)	0.0616

The seven most commonly occurring defects in the combined groups of patients were analysed. Among these, ventricular septal defect (VSD), Tetralogy of Fallot (TOF), mitral regurgitation (MR), atrioventricular septal defect (AVSD) and coarctation of the aorta (COA), occurred more commonly in the arrhythmia patient group when compared to the non-arrhythmia group, as shown in Table 2 below. Some patients had more than one cardiac defect resulting in the number of defects being greater than the overall number of patients.

Table 2: Cardiac defects and occurrences of arrhythmias in patients

Defect	All patients n (%)	Non-arrhythmia n (%)	Arrythmia n (%)	p-value
VSD*	120 (27.1)	100 (25.7%)	20 (37.7%)	0.0003
PDA	115 (26.0%)	108 (27.8%)	7 (13.2%)	0.4397
TOF*	56 (12.7%)	44 (11.3%)	12 (22.6%)	0.0002
ASD	34 (7.7%)	32 (8.2%)	2 (3.8%)	0.4787
MR*	34 (7.7%)	26 (6.7%)	8 (15.1%)	0.0007
AVSD*	24 (5.4%)	18 (4.6%)	6 (11.3%)	0.0005
COA*	21 (4.8%)	17 (4.4%)	4 (7.5%)	0.0128
Other	196 (44.3%)	173 (44.5%)	23 (43.4%)	0.2327

*occurred more commonly in arrhythmia patient;

VSD -ventricular septal defect, PDA- patent ductus arteriosus, TOF- Tetralogy of Fallot, ASD- atrial septal defect, MR- mitral regurgitation, AVSD- atrioventricular septal defect, COA- coarctation of the aorta

Table 3 depicts the arrhythmias in the 53 patients who developed bradyarrhythmia and tachyarrhythmias in terms of the anatomical location along the conducting pathway.

Table 3: Classification of arrhythmias

Bradyarrhythmia		Tachyarrhythmia	
	n (%)		n (%)
Sinus bradycardia	16 (30.2)	SVT	14 (26.4)
AV block	7 (13.2)	JET	6 (11.3)
Junctional rhythm	6 (11.3)	Ventricular fibrillation	2 (3.8)
		Atrial flutter	1 (1.9)
		Ventricular tachycardia	1 (1.9)
Total	**29 (54.7)**	**Total**	**24 (45.3)**

Table 4 denotes the specific type of cardiac defect and the surgical procedures in the bradyarrhythmia and tachyarrhythmia patients. Some patients (11.3%) exhibited repeat episodes of the same arrythmias. Patients with multiple defects were sometimes subject to more than one corrective procedure at the time of surgery whilst others did not have all defects corrected in one surgery, as they would return when older for surgical repair of the defects in stages. Therefore, the number of defects and number of procedures are greater than the actual number of patients.

Table 4: Arrhythmias, cardiac defect, surgical procedure

	Arrythmia n (%)	Defect (n)	Surgical procedure (n)
Bradyarrhythmia 29 (54.7%)	**Sinus bradycardia** **16 (30.2)**	6 = VSD 5 = TOF 3 = COA 2 = AVSD, PDA, PA, TA 1 = AVC, I. IVC, MR, O.Ao, PR, PA DEFECT, TA	3 = CoA R 2 =AVSD R, PDA LIG, RVOT R, TOF R, VSD R 1 = DORV R, GLEN SHUNT, MV R, PA BAND, PFO R, PA R, PV R, WATERSON SHUNT
	AV block 7 (13.2)	2 = MR, PDA, VSD 1 = AVC, DEXTRO, I. AA, LVOT, PFO, TAPVC, TOF,	2 = VSD 1 = AVC R, DSAS, I AA R, MV R, PDA LIG, PM INSERTION, TAP, TAPVC TOF R
	Junctional rhythm **6 (11.3)**	3 = VSD, TOF 1 = MR, PA, PFO	3 = VSD R, TOF R 1 = AVC R, PDA LIG, TAP
Tachyarrhythmia 24 (45.3%)	**SVT 14 (26.4)**	5 = VSD 3 = MR, PDA, TGV 2 = ASD, AVSD 1 = AVC, CoA, DEXTRO, DORV, PS, TOF	3 = PDA LIG, VSD 2 = ART SWITCH, AVC R, AVSD, 1 = CoA R, FM BAND EXCISION, GLEN SHUNT, MVR, PFO R, RVOT R, TOF R
	JET 6 (11.3)	4 = VSD 2 = AVSD 1 = DORV	4= VSD R 2 = AVSD R, PFO R
	VF2 (3.8)	2 = PS 1 = TOF	1 = TOF R 1 = TAP
	AF 1 (1.9)	1 = TOF	1 = TOF R, PFO R
	VT 1(1.9%)	1 = MR	1 = MV R

PDA: Patent ductus arteriosus, PA- pulmonary atresia, TA- tricuspid atresia;), AVC- Atrioventricular canal, I. IVC- interrupted inferior vena cava, MR mitral regurgitation, O.Ao- overriding aorta, PR pulmonary valve regurgitation, PA DEFECT- pulmonary artery defect, TA – tricuspid atresia, DEXTRO - dextrocardia, I. AA- interrupted aortic arch, LVOT- left ventricular outflow tract, TAPVC- total anomalous pulmonary venous return, DORV- double outlet right ventricle, PS- pulmonary stenosis COA R – coarctation repair, PDA LIG- patent ductus arteriosus ligation, TAP- trans annular patch, ART SWITCH- arterial switch

Table 5 shows the CBP and ACC times as well as the electrolyte levels across all groups of patients over the study period. No statistically significant difference for CPB time, ACC time, and any of the electrolyte levels was demonstrated between the patients who developed to arrhythmia compared to those who did not.

Table 5: Risk factors for arrhythmias in the surgical population

Potential risk factors	Median (IQR)			p-value
	All Patients	Non- arrhythmia	Arrhythmia	
CBP time (minutes)	122.0 (88.0 - 162.0)	141.0 (107.5-177.5)	120.0 (86.0-157.6)	0.0509
ACC time (minutes)	71.0 (45.0-104.5)	76.0 (51.5-111.0)	70.5 (42.0-104.0)	0.3578
Mg level (mmol)	1.0 (0.9-1.7)	1.1 (0.8-1.8)	1.0 (0.9-1.7)	0.2044
Ca level (mmol)	2.3 (2.2-2.4)	2.2 (2.0-2.3)	2.3 (2.2-2.4)	0.0540
K level (mmol)	4.5 (4.1-4.9)	4.2 (3.8-4.7)	4.5 (4.2-4.9)	0.7634

Discussion

The occurrence of haemodynamically significant arrhythmias in this study, conducted at an academic hospital in Johannesburg, was 12%. This is in keeping with the described incidence of haemodynamically significant arrhythmias which is in the range of 6.7 – 38.9%. [7, 12-15, 18, 19] The study by Yildirim et al, [13] which showed an arrhythmia occurrence of 8.8%, used a similar method to monitor cardiac rhythms as the CTU at CMJAH. When using the more sensitive monitoring method, Holter monitoring, Grosse-Wortmann et al [18] displayed a similar occurrence in arrhythmias post-operatively as studies employing less sensitive methods. [13, 15, 19] The similar occurrence noted in the study conducted at CMJAH suggests that haemodynamically significant arrhythmias are rarely missed in the CTU.

In this study 75.5% of these arrhythmias occurred in the first 24 hours after surgery. This finding is similar to the 69.4% found by Yildirm et al. [13] The studies highlight that the immediate post-operative period is indeed when the patient is most vulnerable and when extra vigilance must be applied.

No significant difference between the ages and weights of the arrhythmia and non-arrhythmia patients were found at CMJAH It is suggested that younger age and lower weight predispose paediatric patients to significant arrhythmias after cardiac surgery. [14, 17,

[21] This may be as a result of more complex surgeries being performed on younger patients. [17] The finding in this study may be as a result of patients being operated on at a later stage due to the long waiting lists in public hospitals which service a large population under resource constraints.

Our observation was that VSD, TOF MR, AVSD and COA occurred more commonly in the arrhythmia population. In the study by Rekawek et al, [8] VSD (13%), TOF (20.6%) and AVSD (47.1%) were associated with a higher arrhythmia occurrence.

We also found that 43.3% of the patients who developed a significant arrhythmia post-operatively, exhibited more than one cardiac defect. This is significantly greater than the 27.8% of non-arrhythmia patients who exhibited multiple cardiac defects. This finding therefore suggests that more complex surgery was required when more than one defect was present. Valsangiacomo et al [17] and Rekawek et al [8] found a similar trend when investigating the association of arrhythmia occurrence and surgical complexity. Rekawek et al [8] found that a higher Aristotle score (complexity scoring system for the surgical procedure) was a risk factor for post-operative arrhythmia occurrence as did Valsangiacomo et al [17] who looked at categories of surgical complexity. Direct trauma to the underlying conducting system was the mechanism implicated in arrhythmogenesis in these and other studies. [8, 9, 12, 17]

This study noted that SVT (26.4%), and JET (11.3%) were the most frequent occurring tachyarrhythmias whilst AVB (13.2%) was the most frequently occurring bradyarrhythmia. Furthermore, in this study, patients exhibiting JET, SVT and AVB had more than one cardiac defect. Delaney et al [14] noted an 8.5% and 3.7% incidence of JET and AVB respectively, but a lower incidence of SVT (1%). The higher incidences of these arrhythmias in our study may be due to the greater number of defects requiring repair and the potential for injury to the myocardium and conducting system in the process.

Whilst we did not show any significant difference in CPB and ACC times between the arrhythmia and non-arrhythmia patients, prolonged CPB and ACC have been identified as risk factors for post-operative arrhythmias by Pfammatter et al [24] and Delaney et al [14] as the myocardium is at risk of ischaemic injury following reperfusion.

A statistical relationship implicating electrolyte abnormalities as a risk factor for arrhythmogenesis was not demonstrated in this study. Yildirim et al [13] and Delaney et al

[14] did not find any significant difference in electrolyte levels between the arrhythmia and non-arrhythmia patients. The similar findings in this study may reflect the current practice to ensure that all electrolytes are replaced following CPB in theatre, and continued monitoring and supplementation into the post-operative period by both anaesthetic and CTU staff. This may account for why these electrolyte abnormalities are rarely found in this subset of patient.

Possible limitations of this study include poor record keeping. We recommend a larger sample size for future studies which might unmask other risk factors not revealed in this study. Despite the limitations, the study helps with risk assessment in this setting to curtail morbidity and mortality arising from such events.

Conclusion

The occurrence of post-operative arrhythmias in the CTU at CMJAH is 12% which is similar to other units in the post-operative period. The first 24 hours is the most vulnerable period during which most arrhythmias occur. Patients with more than one cardiac defect are at higher risk of developing significant arrythmias due to the greater complexity of surgery and potential to injure the conducting pathways. SVT, JET, AVB occurred most frequently in this study and these arrythmias were associated with more than one cardiac defect, further highlighting the increased potential for injury to the myocardium and conducting pathways in more complex surgeries.

Conflict of interest

The authors declare that we have no financial or personal relationships which may have inappropriately influenced us in writing this paper.

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Section 4: Proposal

Occurrence of significant post-operative arrhythmias in paediatric cardiac surgery patients at an academic hospital

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4.1 Introduction

Paediatric cardiac surgery has evolved significantly over the last half century, along with advances in paediatric anaesthesia and post-operative intensive care. This in turn has led to a decline in mortality following paediatric cardiac surgery to as low as 2 – 7% in the 21st century (1-3).

Despite advances in paediatric cardiac surgery and post-operative healthcare, arrhythmias remain a cause for concern in the post-operative period. Arrhythmias occurring during this vulnerable phase following a major stressful event such as cardiac surgery, can lead to significant haemodynamic instability, compromising recovery and impacting on both morbidity and mortality (3-5).

The incidence of all arrhythmias in the post-operative period is highly variable and may range from 8 – 79.1% (3, 4, 6-9). Haemodynamically significant arrhythmias during the post-operative period range from 8 – 38.9% (6, 9, 10) when non-benign arrhythmias are discounted. Other studies note a lower incidence of between 8 – 9% (4, 6, 11). One explanation for this variability may be the differences in the sensitivity of the monitoring methods used in various studies. This is illustrated in the study by Grosse-Wortmann et al (9) in which a prevalence as high as 79.1% is noted when a more sensitive method, namely continuous Holter monitoring is employed. Furthermore, this study reveals that haemodynamically significant arrhythmias vary from 29.6 – 38.9% when the benign arrhythmias are discounted(9). This figure is similar to other studies in which the occurrence of significant arrhythmias ranges from 27 – 29%(6-8). These findings reflect that all clinically significant arrhythmias rarely remain undetected when other less sensitive means of monitoring are used (9).

Various factors predisposing to the development of arrhythmias have been identified in this patient population in an attempt to improve surveillance, monitoring and treatment of these events. Many studies note that younger patients, most often neonates, have a tendency to develop arrhythmias in the early post-operative period (6, 8, 10-12). This is thought to be due to being more ill pre-operatively and/or due to them requiring more complex surgeries. There is, therefore, an interdependence between various other risk factors which contributes to a higher incidence of arrhythmias in this group (11).

The early post-operative period is associated with a surge of pro-inflammatory mediators which in turn causes irritability of the myocyte membrane, hence predisposing to arrhythmias (9, 13). It is hypothesised that the mediation of inflammatory cytokines, by female hormones namely oestradiol, may have an anti-arrhythmogenic effect on the myocardium therefore accounting for a lower incidence of post-operative arrhythmias is females (9, 13, 14).

It has been suggested that certain processes during surgical procedures predispose to the development of arrhythmias post-operatively. The increased complexities of the surgical procedures and direct trauma to the conducting pathways may explain the mechanism underlying the development of arrhythmias (6, 8-12, 15-17). A lower risk of arrhythmias has been observed with closed heart surgery as noted by Yildirim et al (6), as the myocardium remains untouched and the negative effects of cardio-pulmonary bypass (CPB) are eliminated. The incidence of arrhythmias also varies with different procedures. Atrioventricular septal defect (AVSD) repair and arterial switch procedures with ventricular septal defect (VSD) closure, account for an arrhythmia incidence of 72% and 62.5% respectively (10). Furthermore, an increased incidence of junctional ectopic tachycardia (JET) has been observed in arterial switch procedures, atrioventricular (AV) canal repair (due to its proximity to the AV node) and the Norwood procedure (10, 11, 16).

The prevalence of arrhythmias also increases as the CPB time and aortic cross clamp (ACC) time increases (10, 15). Pfammatter et al(17), demonstrates a 28% arrhythmia incidence when CPB times range between 50 - 100 minutes and increases to 33% when CPB times exceed 100 minutes . The same trend is seen with increasing ACC times (17). It is suggested that the mechanism by which prolonged CPB and ACC times predispose to arrhythmias is due to myocardial ischaemia and as a result of reperfusion (9, 10, 17).

In light of myocardial ischaemia being a pathogenic mechanism, serum troponin levels as a marker of myocardial injury and ischaemia is used as a predictor of post-operative arrhythmias (9, 17). The incidence of immediate post-operative arrhythmias is shown to correlate with the maximum post-operative serum levels of cardiac troponin (17). A troponin level between 10 – 50 ug/L is associated with a 46% incidence of post-operative arrhythmias whereas levels greater than 50 ug/L are associated with a 69% incidence (11, 17).

Serum electrolyte aberrations are also regarded as important precursors in the development of arrhythmias. This is believed to be due to the associated cardiac instability that accompanies certain electrolyte abnormalities (4, 18).

Magnesium (Mg) plays a pivotal role in the maintenance of the resting membrane potential of myocytes and attenuates the electrophysiological effects of hyperkalaemia (19). Its prophylactic administration is known to be protective against the development of arrhythmias in adults (19). In the paediatric population undergoing surgery for congenital heart disease electrolyte abnormalities demonstrate a variable predisposition to arrhythmias (10, 16, 19). Whilst the study by Dorman et al (19), demonstrate a link between the development of JET with a low Mg level, other studies show no statistical relationship to the development of arrhythmias in the presence of a low Mg level in either group, i.e. patients who developed an arrhythmia and those who did not (10, 16).

Potassium serves as the primary ion mediating cardiac repolarisation therefore both hypokalaemic and hyperkalaemic states can be highly arrhythmogenic. Each state has defining changes noted on ECG. Such changes, if not immediately recognised and treated, can lead to fatal outcomes in these cardiac patients (20).

The above literature suggests that the paediatric surgery patient may be predisposed to significant cardiac arrhythmias. It is therefore imperative to identify predisposing risk factors in order to implement appropriate preventative strategies. This may prove to be beneficial in terms of reducing the risk of significant arrhythmias and may translate into improved patient outcomes.

4.2 Problem statement

The immediate post-operative period is a vulnerable time for paediatric patients who have undergone cardiac surgery. The incidence of post-operative arrhythmias in the international literature varies from 8 – 79.1% (6-12, 15, 17).

Arrhythmias encountered in the immediate post-operative period may contribute to an increase in morbidity and mortality, intensive care unit (ICU) and hospital stay, resulting in financial burden (6-8, 15). A wide variety of risk factors such as patient demographics, the underlying cardiac defects, as well as surgical techniques and procedures have been

identified as contributing to the incidence of arrhythmias in this period (6, 7, 9, 10, 16, 17, 21).

Institutional knowledge of the occurrence and risk factors of significant arrhythmias has the potential to reduce the morbidity and mortality of paediatric patients who undergo cardiac surgery. The occurrence of these significant post-operative arrhythmias in the paediatric cardiothoracic population at Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) is not known. It is not known if the risk factors identified from other institutions, are also applicable to this patient population.

4.3 Aim and objectives

4.3.1 Aim

The aim of this study is to describe the occurrence of significant arrhythmias in the immediate post-operative period in paediatric cardiac surgery patients at CMJAH.

4.3.2 Objectives

The objectives of this study are to:

- describe the occurrence of significant arrhythmias in paediatric patients 18 years or younger
- describe the different significant arrhythmias recorded
- identify and describe the existing risk factors, if any, which predispose these patients to significant arrhythmias.

4.4 Research assumptions

The following definitions will be used in the study.

Paediatric patient: is a paediatric patient 18 years of age and younger. However, will further categorised patients into the following groups for more clarity:

- 5 years and younger
- 6 to 18 years.

Immediate post-operative period: this will be the first seven days following surgery.

Significant arrhythmias: any arrhythmias that cause haemodynamic instability requiring an intervention. In this study it will include the following:

- Premature atrial contractions (PACs)
- Atrial flutter
- Atrial fibrillation (AF)
- Supraventricular tachycardia (SVT)
- Junctional rhythm
- Junctional ectopic tachycardia (JET) / AV nodal re-entrant tachycardia
- Premature junctional contraction
- Premature ventricular contractions (PVC)
- Monomorphic ventricular tachycardia
- Polymorphic ventricular tachycardia
- Ventricular fibrillation (VF)
- First degree heart block
- Second degree heart block (type 1 and 2)
- Third degree heart block.

Clinical records: In this study these will include:

- ICU charts
- patient hospital files
- anaesthetic records
- perfusionist's records
- cardiothoracic surgeon patient summaries.

4.5 Demarcation of study field

This study will be done in the cardiothoracic unit (CTU) at CMJAH. The hospital is a central academic hospital offering a range of secondary, tertiary and highly specialised services to patients across Gauteng as well as neighbouring provinces and countries through a strict referral system (22).

The CTU is a specialised unit, with an ICU and high care facility admitting adult and paediatric patients for pre-operative and post-operative care. On average 150 paediatric patients are admitted annually.

4.6 Ethical considerations

Approval to conduct this study will be obtained from the Graduate Studies Committee and the Human Research Ethics Committee (Medical) of the University of the Witwatersrand. In addition, approval will be obtained from the CEO of CMJAH (Appendix 1). Approval to access the clinical records will be obtained from the CTU Director (Appendix 2) and the Consultant Paediatric Cardiac Surgeon (Appendix 3).

Confidentiality of the data will be maintained as only the researcher and the supervisor will have access to the data. Each patient will be given a study number. The study numbers and respective patient hospital numbers will be entered on a sheet that will be kept separate from the collected data (Appendix 4). Only study numbers will be used during data analysis.

The collected data will be stored securely for six years following completion of study on a password protected database.

This study does not involve the administration of any drug or therapeutic management, therefore no patient consent was required. It will be conducted by adhering to good clinical research practice as set out in the South African Good Clinical Practice Guideline (23) and the Declaration of Helsinki (24).

4.7 Research methodology

4.7.1 Research design

The research or study design is the overall plan for addressing a research question (25). It defines the method used to collect data so that valid answers to research questions can be obtained (26, 27).

This is a retrospective, contextual, descriptive study.

Retrospective studies investigate phenomena, situations, problems or issues that have occurred in the past and are conducted on the basis that data is available for that period (28). The data in this study will be obtained from ICU clinical records from July 2010 - June 2013.

Context is described by De Vos et al (29), as a "small-scale world" of, amongst others, clinics, hospital wards or critical care units. This study is contextual as it aggregates information within the domain of the CTU at CMJAH.

A descriptive study provides an account of the characteristics of a particular individual, event or group in real- life situations for the purpose of discovering new meaning, describing what exists, determining the frequency with which something occurs and categorising information (27). This study describes the occurrence of significant arrhythmias occurring in the post-operative period in paediatric patients undergoing cardiac surgery in the CTU at CMJAH.

4.7.2 Study population

The study population will be the clinical records of paediatric patients in the CTU at CMJAH.

4.7.3 Study sample

Sample size

The sample size will be determined by the number of clinical records available over a 3-year period (July 2010 - June 2013).

Sampling method

Consecutive convenience sampling will be used over the three-year period. Convenience sampling assesses the most readily available participants or objects for the study (25, 26) whereas consecutive implies that all the units from an accessible population that meet the eligibility criteria over the specific time interval will be included in the sample (25). The records used are filed chronologically and therefore allow for consecutive sampling.

4.7.4 Inclusion and exclusion criteria

Inclusion criteria for this study will be

- clinical records of patients 18 years and younger
- significant arrhythmias that occurred within the first week of the post-operative period.

Exclusion criteria for this study will be:

- incomplete (records not containing any of the information explored by this study) or illegible records
- patients taking anti-arrhythmic drugs at the time of surgery

4.7.5 Data collection

All paediatric cardiac surgery patients are admitted either pre- or- post-operatively to the CTU. The ICU chart is filled in by the receiving ICU doctor who documents information about the patient's underlying condition and the procedure from the handover report given by the anaesthetist, surgeon and perfusionist accompanying the patient. A management plan for the ICU stay is then outlined. The patient's vital signs, ventilation settings, biochemical investigations, fluid intake and output, as well as medication is documented on the chart and updated hourly on these charts in the immediate post-operative period by the ICU nurse caring for the patient. The ICU doctor documents his/her clinical assessment on the chart on a daily basis as well as any important events or changes in the patient's clinical condition. Input from ICU consultants' ward-rounds as well as other attending clinicians who are consulted to manage any other problem the patient may have, is also documented on these charts. All this information serves to provide an overall picture of the patient's condition at any given time and also charts the course of the patient's ICU stay.

Upon discharge, a discharge form is filled out and the ICU charts are filed and stored chronologically in a storage facility within the department. The paediatric cardiothoracic surgical consultant generates a pre-, intra- and- post-operative comprehensive summary for each patient. This summary includes information regarding significant arrhythmias causing haemodynamic instability.

The patient's files containing information from the time of workup for the cardiac lesion to the time of discharge from ICU are also filed in alphabetical order and stored within the department. The perfusionist's chart and the anaesthetic record for each patient is stored in a similar manner.

The relevant records from the above list will be sourced when identifying data related to the patient parameters highlighted below. Patients' ICU records will first be sourced. Outstanding data will then be sourced from the other records when required.

A data collection sheet containing key elements highlighted from the literature review was drawn up in consultation with an expert in the field. The following patient parameters will be recorded:

- age of patient
- weight
- cardiac lesion
- surgical procedure
- cardio-pulmonary bypass time (in minutes) (CPB)
- aortic cross clamp time (in minutes) (ACC).
- arrhythmia causing haemodynamic instability
- time of occurrence
- magnesium level at time of arrhythmia
- calcium level at time of arrhythmia
- potassium level at time of arrhythmia
- intervention.

Any additional risk factors which may be discovered in the course of collecting the data will be added consecutively to the data analysis.

Each patient will be given a study number. The study numbers and respective patient hospital numbers will be entered on a sheet that will be kept separate from the collected data (Appendix 4). Only study numbers will be used during data analysis.

All paediatric patients admitted to the CTU requiring surgery during the study period will be noted. Those having significant arrhythmias causing haemodynamic instability will be further highlighted in order to calculate the occurrence.

The data will be captured on a Microsoft Excel spreadsheet. A biostatistician will be consulted to assist with the analysis of the data. Data will be analysed using XLStat 2018.7. Descriptive statistics will be used to analyse the data. Categorical data will be summarised using frequencies and percentages. Continuous variables will be analysed using means and standard deviations if normally distributed and medians and interquartile ranges will be used for variables that are not normally distributed.

4.7.6 Data analysis

A Microsoft Excel spreadsheet will be used to capture data. Data will be analysed in consultation with a biostatistician using the statistical program XLStat 2018.7.

The data will be captured on a Microsoft Excel spreadsheet. A biostatistician will be consulted to assist with the analysis of the data. Data will be analysed using XLStat 2018.7. Descriptive statistics will be used to analyse the data. Categorical data will be summarised using frequencies and percentages. Continuous variables will be analysed using means and standard deviations if normally distributed and medians and interquartile ranges will be used for variables that are not normally distributed.

A p-value of 0.05 or less will be considered statistically significant.

4.8 Significance of the study

The immediate post-operative period following cardiac surgery is crucial in the course of a patient's recovery, more so in this already vulnerable group of paediatric cardiac patients. Arrhythmias in this period can significantly impact on the morbidity and mortality of these patients. It is therefore important to identify which of these patients are most at risk of developing an arrhythmia, particularly those arrhythmias which have a tendency to cause haemodynamic instability.

The occurrence of these significant arrhythmias in the paediatric cardiothoracic population at CMJAH is unknown. It is also not known if the risk factors identified from other institutions are relevant to this patient population. The results from this study may provide insight into the occurrence of significant arrhythmias and into their predisposing risk factors. Such insights may help to reduce the morbidity and mortality of paediatric patients who undergo cardiac surgery at CMJAH

4.9 Validity and reliability of the study

Validity refers to the degree to which the variables of the study are accurately reflected. Reliability refers to the consistency and repeatability of the study (26, 30).

The validity and reliability of this study will be ensured by the following:

- using an appropriate study design after conducting an extensive literature review
- data collection sheets were developed in consultation with an expert in the field
- all outlined patient records over an extended, i.e. three-year period will be reviewed
- checking every 10^{th} entry for accuracy
- data being collected by a single researcher

analysing data in consultation with a bio statistician.

4.10 Potential limitations

Limitations are theoretical and methodological restrictions or weaknesses in a study that may decrease the generalisability of the findings (27).

This study is contextual as it is limited to the CTU of one hospital, CMJAH. The result may not necessarily be reflective of other similar units with their unique surgical approaches and ICU protocols.

The daily ICU chart is completed by registrars. Registrars rotate to the CTU for a one to two-month period. This might influence the accuracy and quality of the data recorded.

Overhead bedside monitoring is used in this study and a 12 lead ECG is only used when a clinically significant arrhythmia occurs. The lack of more sensitive 24 hour monitoring as used by Grosse-Wortmann et al (9), may exclude the detection of arrhythmias that are not of clinical significance and could portray the overall occurrence of arrhythmias to be less than it really is. Whilst their study found an overall higher incidence in these post-operative arrhythmias, it also illustrated that the number was comparable to figures found in other studies that did not use such sensitive monitoring methods, when benign arrhythmias were excluded. This showed that clinically significant arrhythmias are appropriately detected despite the lack of more sensitive continuous monitoring (1).

4.11 Project outline

4.11.1 Time frame

Activity	Jan-Feb 2014	Mar 2014	Mar 2014	Sep-Dec 2014	Jan-Mar 2015	Jan-Mar 2015	Apr 2015	May 2015	Jun 2015	Feb 2019
Proposal preparation										
Literature review										
Proposal submission										
Ethics approval										
Postgraduate approval										
Data collection										
Data analysis										
Draft article										
Submission										

4.11.2 Budget

Item	Price per page	Number of pages	Copies	Total
Proposal	1	15	10	R 150
Ethics	1	10	25	R 250
Post graduate form	1	2	6	R 12
Complete report	1	100	4	R 400
Grand total				**R 812**

The Wits Department of Anaesthesiology will incur the costs of paper and printing.

4.12 References

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2010.

Section 4 Appendices

Appendix 1 Request to the CEO of Charlotte Maxeke Johannesburg Academic Hospital

Dr Merusha Lindy

Department of Anaesthesiology

University of the Witwatersrand

January 2014

Dear Ms. Bogoshi

I am a registrar in the Department of Anaesthesiology currently doing research for my Master of Medicine in Anaesthesiology degree. My research entitled **Occurrence of significant post-operative arrhythmias in paediatric cardiac surgery patients at an academic hospital**, will involve auditing the ICU records of paediatric patients who underwent surgery for congenital heart defects from June 2010 to June 2013.

The study involves a retrospective review of the charts of these patients. The names of the patients and respective clinicians involved in the patients' management will be kept anonymous.

There will be no financial implication for CMJAH or Gauteng Provincial Department of Health. A copy of the final report will be made available to you. I hereby request permission to conduct this study.

Attached please find copies of my research proposal and Graduate Studies Committee approval. HREC approval is pending as it is subject to the approval by the CEO.

Yours sincerely

Dr Merusha Lindy

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL

Enquiries:
Mr. J. Maepa
Office of the Clinical Director
Tell: (011): 488-3385
Email:Johannes.maepa@gauteng.gov.za
25 February 2016

Dear Dr. M. Lindy

STUDY TITLE: Occurrence of significant post-operative arrhythmias in Paediatric Cardiac Surgery patients at an academic hospital.

Permission is granted for you to conduct the above recruitment activities as described in your request provided:

1. Charlotte Maxeke Johannesburg Academic Hospital will not anyway incur or inherit costs as result of the said study.
2. Your study shall not disrupt services at the study sites.
3. Strict confidentiality shall be observed at all times.
4. Informed consent shall be solicited from patients participating in your study.

Please liaise with the HOD and Unit Manager or sister in charge to agree on the dates and time that would suit all parties.

Kindly forward this office with the results of your study on completion of the research.

Supported/not supported

Dr.M.T. Mofokeng
Clinical Director
DATE: 2/3/2016

Approved/not approved

Ms G. Beghshi
Chief Executive Officer
DATE: 08.03.2016

Appendix 2 Letter to Prof Richards (Head of ICU CMJAH)

Dr Merusha Lindy

Department of Anaesthesiology

University of the Witwatersrand

January 2014

Dear Prof Richards

I am a registrar in the Department of Anaesthesiology currently doing research for my Master of Medicine in Anaesthesiology degree. My research entitled **Occurrence of significant post-operative arrhythmias in paediatric cardiac surgery patients at an academic hospital,** will involve auditing the ICU records of paediatric patients who underwent surgery for congenital heart defects from June 2010 to June 2013.

The study involves a retrospective review of the charts of these patients. Kindly allow me access to the ICU charts of the patients admitted to the ICU during this period. The names of the patients and respective clinicians involved in the patients' management will be kept anonymous.

Yours sincerely

Dr. M. Lindy

January 2014

Professor Richards

CMJAH

27/02/14

To whom it may concern

I hereby grant permission to Dr. Merusha Lindy to access the ICU records for the purpose of conducting the study entitled **Occurrence of significant arrhythmias in paediatric cardiac surgery patients at an academic hospital.**

Yours sincerely

Professor Richards

ICU (CMJAH)

27/02/14

Appendix 3: Letter to Dr Van Den Donck (consultant paediatric cardiothoracic surgeon CMJAH)

Dr Merusha Lindy

Department of Anaesthesiology

University of the Witwatersrand

January 2014

Dear Dr Van Den Donck

I am a registrar in the Department of Anaesthesiology currently doing research for my Master of Medicine in Anaesthesiology degree. My research entitled **Occurrence of significant post-operative arrhythmias in paediatric cardiac surgery patients at an academic hospital,** will involve auditing the ICU records of paediatric patients who underwent surgery for congenital heart defects from June 2010 to June 2013.

The study involves a retrospective review of the charts of these patients. Kindly allow me access to the ICU charts, perfusionists charts and patient summaries of the patients admitted to the ICU during this period. The names of the patients and respective clinicians involved in the patients' management will be kept anonymous.

Yours sincerely

Dr. M. Lindy

Appendix 4: Data collection sheet

Study number		01	02	03	04	05	06	07	08	09
Age	(years)									
Weight	(kg)									
Cardiac lesion:	(defect)									
Previous surgery	(procedure)									
Surgical procedure										
CPB time	(min)									
ACC time	(min)									
Arrhythmia										
Initial episode	Time of occurrence (hrs)									
	Intervention (type)									
	Mg level									
	Ca level									
	K level									
Additional episode 1	Time of occurrence (hrs)									
	Intervention (type)									
	Mg level									
	Ca level									
	K level									

Section 5: Annexures

5.1 Ethics approval

R14/49 Dr Merusha Lindy and Prof Paruk

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M140352

NAME: (Principal Investigator)	Dr Merusha Lindy and Prof Paruk
DEPARTMENT:	Anaesthesiology Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	Occurence of Significant Post-operative Arrhythmias in Paediatric Cardiac Surgery Patients at an Academic Hospital
DATE CONSIDERED:	28/03/2014
DECISION:	Approved unconditionally
CONDITIONS:	Title change(01/04/2016)
SUPERVISOR:	Helen Perrie
APPROVED BY:	Professor P Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	31/03/2014

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Secretary in Room 10004, 10th floor, Senate House, University.
I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report.**

Principal Investigator Signature _____ Date _____

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

5.2 Graduate studies approval

5.2.1 Approval of title of research

UNIVERSITY OF THE
WITWATERSRAND
JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172078

Reference: Ms Thokozile Nhlapo
E-mail: thokozile.nhlapo@wits.ac.za

25 January 2016
Person No: 0101384J
PAG

Dr M Lindy
72 Aquila
10 Lynton Place
Oakdene
JHB
2190
South Africa

Dear Dr Lindy

Master of Medicine: Approval of Title

We have pleasure in advising that your proposal entitled *Occurrence of post-operative arrhythmias in paediatric cardiac patients at an academic hospital* has been approved. Please note that any amendments to this title have to be endorsed by the Faculty's higher degrees committee and formally approved.

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

5.2.2 Approval of change of title of research

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

Private Bag 3 Wits, 2050
Fax: 027117172119
Tel: 02711 7172076

Reference: Ms Thokozile Nhlapo
E-mail: thokozile.nhlapo@wits.ac.za

23 February 2016
Person No: 0101384J
TAA

Dr M Lindy
72 Aquila
10 Lynton Place
Oakdene
JHB
2190
South Africa

Dear Dr Lindy

Master of Medicine: Change of title of research

I am pleased to inform you that the following change in the title of your Research Report for the degree of **Master of Medicine** has been approved:

From:	**Occurrence of post-operative arrhythmias in paediatric cardiac patients at an academic hospital**
To:	**Occurrence of significant post-operative arrhythmias in paediatric cardiac surgery patients at an academic hospital**

Yours sincerely

Mrs Sandra Benn
Faculty Registrar
Faculty of Health Sciences

5.3 Turnitin report

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG | FACULTY OF HEALTH SCIENCES

25th March, 2019

The Chairperson
Graduate Studies Committee
Faculty of Health Sciences
University of the Witwatersrand

Dear Madam,

Re: M Med: **Occurrence of significant post-operative arrhythmias in paediatric cardiac surgery patients at an academic hospital.**

Dr Merusha Lindy, student number: 0101384J, has submitted her research report to Turnitin which revealed a similarity index of 14%. These similarities appear not to be plagiarism but, mainly the use of common terminology and phrases specific to the topic of the research.

Yours sincerely,

H C Perrie

Helen Perrie
Supervisor

0101384j:turn_it_in_2.docx

ORIGINALITY REPORT

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