CARDIAC ARREST IN CHILDREN PRECEDING PICU ADMISSION: AETIOLOGY AND OUTCOME IN A DEVELOPING COUNTRY

by

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APPJOH002

SUBMITTED TO THE UNIVERSITY OF CAPE TOWN in fulfillment of the requirements for the degree of Master of Philosophy (MPhil) in CRITICAL CARE PAEDIATRICS

Faculty of Health Sciences

UNIVERSITY OF CAPE TOWN
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Date:  13th September 2015
I will like to extend my sincere gratitude to Professor Andrew Argent, Pediatric Intensive Care (PICU) Director whose encouragement and guidance contributed to the completion of this work. I appreciate the work done by Dr Shamiel Salie as my supervisor in taking pains to ensure that deadlines are met and also resources needed were made available to me. Associate Professor Brenda Morrow deserves to be acknowledged for her patience and availing herself and time with the data analysis.

I will also like to thank all PICU consultants, senior registrars and all clinicians and nurses who were part of care of patients with cardiac arrest, staff of medical records and neuro-developmental clinic for the role in documentation and data collection.

Special thanks you to my wife Dr Larko Domeryo Owusu and my three children, John, Alan and Eli who sacrificed their comfort during the period of study.
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CPR: Cardiopulmonary resuscitation
HREC: Human Research Ethics Committee
IHCA: In-hospital cardiac arrest
IQR: Interquartile range
OHCA: Out-of-Hospital cardiac arrest
OR: Odds ratio
VF: Ventricular fibrillation
VT: Ventricular tachycardia
PEA: Pulseless electrical activity
PICU: Pediatric Intensive Care Unit
PIM2: Pediatric index of mortality 2
POPC: Pediatric overall performance category score
CARDIAC ARREST IN CHILDREN PRECEDING PICU ADMISSION: AETIOLOGY AND OUTCOME IN A DEVELOPING COUNTRY

Abstract

Objective: To describe the characteristics and outcomes of children admitted to PICU following cardiac arrest between January 2010 and December 2011.

Methods: Retrospective descriptive study of routinely collected data.

Results: Of 2501 PICU admissions, 110 (4.4%; 58.7% male) had preceding cardiac arrest, 80.6% of which occurred in hospital. Median (IQR) age was 7.2 (2.5 – 21.6) months; 30.8% had chronic underlying disease. Children presented most commonly with respiratory (n=28, 27.2%), cardiovascular (n= 22, 21.4%), and gastrointestinal disease (n= 20, 19.4%). Twenty-eight (27.2%) arrested while undergoing a procedure.

Cardiopulmonary resuscitation (CPR) was given for median (IQR) 10 (5 – 20) minutes. Thirty-five (34%) patients received no adrenaline, 44 (42.7%) received up to 3 doses of adrenaline, and 24 (23.3%) received more than 3 doses of adrenaline during resuscitation. Duration of CPR and number of adrenaline doses did not significantly influence patient outcome.

Survival to PICU discharge was 63 (61.2%), 57 (55.3%) survived to hospital discharge with half the deaths in PICU occurred within 24 hours of PICU admission. Out of 51 survivors whose neurological status were assessed 32 were normal, 6 had mild disability, 7 had moderate disability and 6 had severe disability.

Standardized mortality ratio (actual/mean predicted) was 0.7. The median (IQR) length of stay in PICU and hospital were 3 (1 – 8) and 27 (9 -52) days respectively.

Pediatric risk of mortality (PIM2) score was the only variable independently associated with mortality on multiple logistic regression (adjusted OR 1.05; 95% CI 1.02 – 1.07; p=0.0009).

Conclusion: Mortality was lower than predicted in children admitted to PICU following cardiac arrest. Most survivors had normal neurological function on hospital discharge.
CHAPTER ONE

Introduction

1.1 Context

Cardiac arrest is the cessation of the functional mechanical activity of the heart determined by absent central pulses, unresponsiveness and apnea.\(^1\) Paediatric cardiac arrest is not an uncommon\(^2\) event and it is associated with death but in certain circumstances it is possible to re-establish cardiac output and survivors may have associated morbidity\(^3-5\).

Recognition of life threatening illness and appropriate intervention may prevent cardiac arrest. Sometimes early recognition of cardiac arrest will make it possible to resuscitate the patient and return them to full health. There is limited data on factors affecting cardiac arrest in the developing world. Most information used is extrapolated from studies from the developed countries.

Consequences of cardiac arrest in pediatrics include death or neurological sequelae with poor quality of life. It may be useful to identify the group within a cohort of sick children at risk of cardiac arrest where appropriate intervention may prevent cardiac arrest or in cases of arrest could result in favourable outcome.

Even though cardiopulmonary resuscitation following paediatric cardiac arrest is not futile and many children are successfully resuscitated annually many gaps still exist in what is known about post arrest in children. This study is expected to elucidate some factors associated with outcome in the Sub-Saharan region with specific emphasis on the situation in South African context. It is important to know how this centre is doing as compared to the rest of the world in terms of aetiology and outcome.

Literature Search Strategy

We searched the following databases up to September 2014: Pubmed (from 1960), Embase/Ovid (from 1974), Google scholar (1960), Medline (1990). We used the Medical Subject Headings (MeSH) terms “arrest”, “heart arrest” OR “cardiac arrest”, “epidemiology” “causes”, “management”, “neurological outcome”, “children”, “developing countries” OR ‘Africa”, OR “South America” OR “Asia”. References from identified studies of relevant review studies were searched for further eligible citations. We limited the search to English publications and conducted it in accordance with International Liaison Committee on Resuscitation (ILCOR). We also searched the web to identify online books for citation and reference.

Epidemiology of Paediatric Cardiac Arrest – Incidence, aetiology and outcome

There is no consistent data on global pediatric cardiac arrest incidence owing to the different ways in which it has been reported but Young and Seidel\(^6\) reported that in the United States, 16000 children
suffer cardiac arrest annually. Some epidemiological studies based on the Utstein-style reporting as recommended by the International Liaison Committee on Resuscitation (ILCOR) are shown in table 1.

<table>
<thead>
<tr>
<th>Citation</th>
<th>Population</th>
<th>Sample size</th>
<th>Study type</th>
<th>Entry criteria</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Brazil</td>
<td>129 (83 with ROSC)</td>
<td>Prospective study, Single center</td>
<td>More than 28 days to 14 years Cardiac arrest with CPR initiated in the hospital</td>
<td>1. Respiratory failure is the most common cause of cardiac arrest 2. Preexisting chronic disease were prevalent 3. CPR effective 4. Survival progressively decreased over time 5. One year survival 15%; no demonstrable gross neurological deficit</td>
</tr>
<tr>
<td>7</td>
<td>Finland</td>
<td>118 (74 with ROSC)</td>
<td>Single center, retrospective</td>
<td>Less than age 16 years All patients who received external cardiac compressions or open chest-CPR with sustained ROSC</td>
<td>1. Incidence 0.7% of hospital, admission 2. Etiology cardiovascular (71%), respiratory (10%) 3. 15 of 23 discharge no to mild disability (POPC)</td>
</tr>
<tr>
<td>8</td>
<td>Pakistan</td>
<td>106 (58 with ROSC)</td>
<td>Single center, retrospective</td>
<td>One month to 14 years All IHCA</td>
<td>1. Incidence 0.4% of hospital admissions 2. Duration of CPR (&gt;20 min) best predictor of mortality</td>
</tr>
<tr>
<td>9</td>
<td>Spain</td>
<td>95 (68 with ROSC)</td>
<td>Prospective, multi-center</td>
<td>7 days to 16 years CA and received CPR out-of-hospital</td>
<td>1. Drowning (24), respiratory disease (14) and neurological (13) were top 3 etiology CPR effective in 47.3%</td>
</tr>
</tbody>
</table>
3. Duration of CPR (>20 min) best predictor of mortality
4. One year survival 26.4%; no demonstrable gross neurological deficit

Conclusion: Respiratory diseases and cardiovascular conditions are the most frequent causes of cardiac arrest in the pediatric population.

Questions have been asked about the impact of vasopressor use during resuscitation on patient outcome. Epinephrine has been part of CPR since 1960s when it was recommended in the initial guidelines and continues to be an integral part of advanced life support though there have been very few studies looking at the efficacy and safety of its use following cardiac arrest. The dosage has undergone review but is still part of current ILCOR recommendations, although some studies including those listed in table 2 have raised concerns about its long-term benefit. These show that although it may improve the rate of ROSC, it may decrease chances of survival. Olasveengen et al\textsuperscript{10} found that the long term functional outcome of patients without any intravenous medication such as epinephrine and vasopressin was not significantly different from those with epinephrine administration., Jacobs et al\textsuperscript{11} showed significant improvement in ROSC. Although the studies were underpowered but reported that epinephrine may have improved the numbers surviving to discharge.

Larabee et al\textsuperscript{12} reviewed vasopressor use in pediatric cardiac arrest and concluded that five studies found no differences between high dose epinephrine and low dose epinephrine in ROSC, survival data and neurological outcomes.

<table>
<thead>
<tr>
<th>Citation</th>
<th>Population</th>
<th>Sample size</th>
<th>Study type</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>\textsuperscript{11}</td>
<td>Australia, 18 years and older OHCA Epinephrine vrs Placebo (normal saline)</td>
<td>534</td>
<td>Single center, Double blinded random controlled trial (RCT)</td>
<td>1. ROSC: significantly improved in Epinephrine arm versus placebo { epinephrine (22 [8.4%] placebo vs. 64 [23.5%] epinephrine; OR 3.4; 95% CI 2.5–5.6)} 2. Survival to discharge: No statistical significance between the two groups. {survival to hospital discharge (5 [1.9%] placebo vs. 11 [4%])}</td>
</tr>
<tr>
<td>Study</td>
<td>Country</td>
<td>Setting</td>
<td>Number</td>
<td>Design</td>
</tr>
<tr>
<td>-------</td>
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<td>--------</td>
<td>--------</td>
</tr>
<tr>
<td>13</td>
<td>Japan, 18 years and older</td>
<td>Epinephrine use prehospital arrival and short- and long-term mortality OHCA</td>
<td>417188</td>
<td>Prospective RCT</td>
</tr>
<tr>
<td>10</td>
<td>Norway, Adults Intravenous vrs no intravenous medication</td>
<td>851</td>
<td>Prospective RCT</td>
<td>Intravenous access and drug administration had higher rates of short-term survival with no statistically significant improvement in survival to hospital discharge, quality of CPR, or long-term survival.</td>
</tr>
<tr>
<td>14</td>
<td>Less than 18 yrs of age Cardio arrest requiring chest compressions and Epinephrine (0.01 mg/kg)</td>
<td>29</td>
<td>Prospective, pilot, matched RCT (with vasopressin rescue)</td>
<td>Provide support for a larger randomized controlled trial of arginine vasopressin therapy</td>
</tr>
<tr>
<td>15</td>
<td>Austria, Germany, Switzerland Adults Comparing epinephrine Vs vasopressin</td>
<td>1186</td>
<td>Double-blind, prospective, multicenter RCT</td>
<td>Effects of vasopressin were similar to those of epinephrine in the management of ventricular fibrillation and pulseless electrical activity, Vasopressin was superior to epinephrine in patients with asystole, Vasopressin followed by epinephrine may be more effective than epinephrine alone in the treatment of refractory cardiac arrest.</td>
</tr>
<tr>
<td>12</td>
<td>Adult</td>
<td>Systemic review</td>
<td>4078</td>
<td>3 randomized trials, One retrospective study One prospective</td>
</tr>
</tbody>
</table>
Conclusion: Most of the studies on vasopressor use are in adults over eighteen years and in spite of some adverse effects reported by some studies there is not enough evidence to discontinue vasopressors use during advanced pediatric life support.

**Post cardiac arrest management**

There is high mortality following ROSC which is believed to be due to post arrest syndrome, a pathophysiological process occurring in multiple organs resulting after global tissue hypoxia. Management of the post arrest includes monitoring of parameters such as arterial pressure, peripheral oxygen saturation, central venous pressure and urine output and others may allow for the early detection of complications for early intervention. General measures alongside organ specific therapies are targeted at brain injury, myocardial dysfunction, systemic ischemia and persistent precipitating pathology. Post-ROSC patients require general and advanced intensive care monitoring though this has not been validated.

Optimization of oxygen delivery through manipulation of preload, contractility, afterload and blood oxygen content have been used in similar systemic conditions such as sepsis. It is important to reduce hypoxaemic related brain damage. Use of intravenous fluids, inotropes and blood transfusions and early goal directed therapy (EGDT) in sepsis have been recommended in the last ILCOR guidelines but there is little data to support specific goals of blood pressure, plus oxygen delivery following cardiac arrest.

There is increasing evidence that therapeutic hypothermia may improve brain function after resuscitation from cardiac arrest in adults. After successful cardio-pulmonary resuscitation and establishment of return of spontaneous circulation, reperfusion of the affected tissues may lead to
complex brain derangements and secondary brain injury. The cascade of events including oxygen depletion, calcium metabolism abnormalities, and re-oxygenation induced chemical injuries that may impair consciousness and outcome\textsuperscript{2021}. Distinct regions of the brain (hippocampus, neocortex and cerebellum are more vulnerable to time dependent ischemic injury leading to long term and permanent changes (Kumar et al. 2003).

<table>
<thead>
<tr>
<th>Citation</th>
<th>Population</th>
<th>Sample size</th>
<th>Intervention</th>
<th>Study type</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>22</td>
<td>Taiwan, 2 month to 18 years Cardiac arrest</td>
<td>43</td>
<td>Therapeutic hypothermia (TH)</td>
<td>Retrospective Single center</td>
<td>1. Survival rate was significantly higher ($P = 0.047$) in the therapeutic hypothermia group (11/14, 78.6%) 2. No statistical significance in pediatric cerebral functional category score. (Therapeutic hypothermia group (9/11, 81.8%) than in the normothermia group (6/13, 46.1%) with no statistical significance)</td>
</tr>
<tr>
<td>23</td>
<td>United States, 1 week to 21 years Cardiac arrest</td>
<td>181 cardiac arrest (40 TH)</td>
<td>TH</td>
<td>Single center</td>
<td>1. Therapeutic cooling was feasible 2. No difference in hospital mortality (55.0% therapeutic hypothermia vs. 55.3% standard therapy; $p = 1.0$) 3. Prospective study is urgently needed to determine the efficacy of therapeutic hypothermia in pediatric patients after cardiac arrest.</td>
</tr>
<tr>
<td>24</td>
<td>Taiwan Less than 18 years</td>
<td>54</td>
<td>Extra corporeal cardiopulmonary (ECPR)</td>
<td>Retrospective</td>
<td>1. Cardiac arrest in patients with isolated cardiac diseases is an appropriate indication for ECPR</td>
</tr>
</tbody>
</table>
Therapeutic hypothermia (TH) is a multifactorial neuro-protective process which includes mitigation of oxygen free radicals, modulation of blood-brain barrier damage, preservation of ATP stores and improvement in post-ischemia microcirculation\textsuperscript{25,26,27}.

TH is not without complications, Fink et al (Table 3) showed that TH in paediatric cardiac arrest was feasible and noted that cooling below 32°C was rather detrimental with poor outcome as those in the TH arm received more frequent electrolyte supplementation. It must be noted that the control arm were patients with traumatic brain injury and not cardiac arrest. This study also demonstrated that the risk of infection was no different from control group. Unresolved issues relating to TH include randomized controlled trials to determine ideal temperature, duration of hypothermia and how quickly rewarming take should place.

**Extra-Corporal Cardio-Pulmonary Resuscitation**

Extra-corporal cardio-pulmonary resuscitation (ECPR) is another intervention which has been used to augment conventional CPR with increasing favorable outcome even in patients who had longer duration of CPR (>20 min), as reported by Huang et al \textsuperscript{24}.

Outcome is significantly better in those who received it earlier.

From the perspective of Africa ECPR is not available for resuscitation following cardiac arrest in children and will not be available for the foreseeable future, and as a result we will not review the limited available data.

**1.2 Ethical consideration**

The research protocol was submitted to the School of Child and Adolescent Health Departmental Research Committee who approved it and was subsequently submitted to the Faculty of Health Sciences Human Research Ethics Committee. Faculty of Health sciences Human Research Ethics Committee of the University of Cape Town approval was obtain, HREC REF: 344/2012, (Appendix I) prior to data collection began. Management of Red Cross War Memorial Children’s Hospital approval was obtained (Appendix II). Informed consent was not obtained because no additional procedure was done.
1.3 Author guidelines of Paediatric Critical Care Medicine

The reason for selecting Pediatric Critical Care Medicine journal is because of the specialty it covers and that the subject being researched involves pediatric critical care. Secondly, this journal reaches the pediatric critical care practitioner population which is the expected target audience. Appended (Appendix IV) is the detailed instructions for authors.

1.3 Reference


Cardiac arrest is a potentially devastating event, which is associated with death or severe neurological complication in survivors. This may occur in previously healthy children as well as in children with underlying diseases or abnormalities. The last fifteen years have seen an improvement in epidemiological data collection of cardiac arrest,(1)(2) whilst the publication of guidelines has contributed to improvement in outcome (3–5). There is, however, still little published data on pediatric cardiac arrest from countries outside the highly industrialized countries.

The true incidence of pediatric cardiac arrest is unknown but for out-of-hospital-cardiac arrest (OHCA), it is estimated to be 9 per 100,000 person years whilst arrest within intensive care units is thought to occur 0.94 times per 100 admissions(6)(7)(8). In children, respiratory and cardiovascular failure are the major causes of cardiac arrest, but cardiac arrhythmias may not be as uncommon as was previously thought (9).

The understanding of factors influencing and the sequence of events leading to cardiac arrest is thought to have contributed to improvement in survival (10). Early recognition of patients at risk for arrest (with intervention and institution of effective cardiopulmonary resuscitation following arrest) will potentially improve survival.(11,12)

Cardiopulmonary resuscitation involving ventilation, chest compression and pharmacological agents are the mainstay of management during cardiac arrest (13). Ongoing monitoring and management following return of spontaneous circulation (ROSC) may also have a significant impact on outcomes. Moreover, measures directed at monitoring and maintaining circulation after return of spontaneous circulation could have significant effect on outcome. Moreover, measures directed at monitoring and maintaining circulation after return of spontaneous circulation could have significant effect on outcome.

Cardiac arrest is defined as the cessation of functional mechanical activity of the heart determined clinically by absent central pulses, unresponsiveness and apnea(14–16). Absence of blood flow leads to non-perfusion of vital organs including the brain, kidneys and the heart muscle (17,18). Prolonged ischemia ultimately leads to cell death and abnormal function of these organs.

Though the process of cardiac arrest and resuscitation is a continuum, it may be seen to consist of four phases and usually begins with pre-arrest, no-flow, low flow and return of spontaneous circulation(19)(20). The pre-arrest phase may be associated with respiratory failure or shock states, and it is associated with asphyxia and/or ischemia resulting in inadequate delivery of substrate for cellular metabolism. This phase, if untreated, leads to established cardiac arrest.
involving no-flow, the cessation of mechanical activity of the heart and absent pulses. Low-flow phase ensues when intervention is instituted. The main goal of intervention at this stage is to optimize cerebral, coronary and other vital organ perfusion. Providing effective uninterrupted chest compression is key to a successful outcome at this stage. (21) Abnormalities in oxygenation and ventilation are also common during the initial hours after pediatric cardiac arrest. (22) It makes clinical sense to optimize oxygenation and hemodynamic stability (23)(24) with ventilator support, fluids and inotropic support as required, to ensure improved survival of cardiac arrest patients. (25)

Advances in therapeutic hypothermia (TH) have allowed its use in the management of post anoxic brain injury (26) in adults following cardiac arrest from ventricular fibrillation. Therapeutic hypothermia has been shown to be the one of the interventions that reduces mortality in cardiac arrest. (26,27) TH has also been used in newborns with hypoxic ischemic encephalopathy, which has similar mechanisms of injury as post cardiac arrest syndrome in most age groups but probably different in adults: mainly ischemia, global hypoxia, reperfusion injury, with generation of highly toxic oxygen radicals and excitotoxic molecules coupled with cerebral auto-regulation abnormalities. (28–30). Current evidence for TH use in children does not refute or support its use and more randomized controlled studies are needed to evaluate its use since no differences in hypothermia-related adverse events were found between groups. (31) In addition TH requires significant resource allocation and its use should be based on strong evidence of its utility.

Forty to fifty five percent of out-of-hospital-cardiac-arrest in children occur in infants compared with other age categories (7,32–34). The main objectives of this study are to describe the characteristics and outcomes of PICU patients admitted following a cardiac arrest, and review factors associated with outcome, based on the Utstein-Style reporting of cardiac arrest (35)

**Key words**

Pediatric, cardiac arrest, cardiopulmonary resuscitation (CPR), pediatric overall performance category score (POPC), pulseless electrical activity (PEA), Ventricular tachycardia (VT) pediatric intensive care unit (PICU), in-hospital cardiac arrest (IHCA), out-of-hospital cardiac arrest (OHCA)

**Methods**

**Study Setting and Population**

This retrospective study was conducted at the Pediatric Intensive Care Unit (PICU) of the Red Cross War Memorial Children’s Hospital in Cape Town, South Africa. This children’s hospital is a university teaching hospital with 290 pediatric beds. The multi-disciplinary PICU consists of twenty two
functional beds and accepts patients aged from 0 to 13 years from general pediatric wards, the Emergency and Trauma Department, surgical wards and operating theatres within the hospital and also serves as a referral center for patients in the Western Cape Province of South Africa.

Although there is no dedicated response team in the event of cardiac arrest or potential collapse within the hospital, an intercom system is used to alert doctors (lead by the most senior being a consultant, paediatric registrars or anaesthesia registrars) to the site of the event assisted by nurses on the ward. In cases of out-of-hospital cardiac arrests the patient may be resuscitated a by-bystander or if available by a trained emergency medical technician. There is no clear protocolised guide to termination of CPR, this decision is taken by the resuscitation team when they think treatment is futile after 20 to 30 minutes.

The study population consisted of all children less than 14 years who were admitted to the PICU following a cardiac arrest between 1st January 2010 and 31st December 2011. The patients were identified through review of the PICU electronic database; the records were then extracted from the patient hospital record and entered into case record form. The information was then entered into a 2010 Microsoft excel database.

Data Collection

The questionnaire (Appendix II) was designed to describe patient characteristics, severity of illness, treatment, and outcome characteristics of the cardiac arrest(35). We defined a case as any child who was admitted to the PICU following a documented cardiac arrest outside of the PICU. Records were reviewed to determine the likely cause of the arrest. Only confirmed cases of cardiac arrest who received cardiopulmonary resuscitation (CPR) (36) were included in the study. In patients who had multiple arrests, the data from the first arrest was used.

Patient demographics (age, weight and sex), pediatric index of mortality 2 (PIM2) score,(37) event location (in-hospital or out of hospital), circumstances (expected, deterioration, unexpected or during a procedure) and underlying or primary condition were recorded. Other variables are defined in table 4.

<table>
<thead>
<tr>
<th>Table 4: Definitions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case definition</td>
</tr>
<tr>
<td>Cardiac arrest</td>
</tr>
<tr>
<td>Apnea</td>
</tr>
<tr>
<td>Primary diagnosis</td>
</tr>
<tr>
<td>Bradycardia</td>
</tr>
<tr>
<td>Tachycardia</td>
</tr>
<tr>
<td>Hyperthermia</td>
</tr>
<tr>
<td>Hypothermia</td>
</tr>
</tbody>
</table>
Shock  
A combination of any of the following: abnormal mental status, weak thready pulses, prolonged capillary refill time and cold extremities (39) and low blood pressure

Acute kidney injury  
Documented urine output and creatinine level post arrest episode then with specific p-rifle criteria to categorize the injury(40)

Post-arrest biochemical data (blood sugar, pH, sodium, potassium, chloride, calcium, creatinine and lactate), post arrest treatment (41) (inotrope support, mechanical ventilation, fluid and electrolyte management and treatment of primary cause), level of consciousness at PICU discharge (alert, verbal, pain and unresponsive)(42), event outcome on PICU (survive to discharge from PICU, PICU mortality, ward survival and ward mortality), length of stay in the PICU and length of hospital stay were also recorded. As a general policy the management of post arrest syndrome(25) and its complications are based on targeting normal temperature or mild hypothermia, blood glucose up to 8-10mmol/l (43), ventilation support and early goal-directed hemodynamic stabilization. The ventilation strategy was to achieve normal oxygenation with the use of minimal supplemental oxygen and ventilation using lung protective strategies such as tidal volume target of 6-8 ml/kg.(20, 38)

Neuro-cognitive assessment was done during the course of the patients’ admission on the ward by the neuro-developmental team, occupational therapist or ward doctors assessment using Pediatric Overall performance Category Score.(45)

Faculty of Health sciences Human Research Ethics Committee of the University of Cape Town approval was obtained prior to data collection. Informed consent was waived owing to the retrospective nature of the study.

Data collected by the principal investigator was entered into a case record form modified for in-hospital cardiac arrest from the Utstein-Style guidelines (35).
Data were captured in Epi Info™ 7.0.9.7 software and exported onto 2010 Microsoft Excel software. Statistica version 11 (Statsoft Inc. USA) was used to analyze the data. The Shapiro-Wilk test was applied to examine whether the numerical variables data followed a normal distribution so that the appropriate parametric or non-parametric test could be applied. Numerical variables were presented as medians and inter-quartile ranges. Mann-Whitney-U test was used as test of significance of survivors and non-survivors of cardiac arrest event with significant p-value of <0.05. For categorical variables, the test for associations included Pearson’s chi-squared test with 95% confidence intervals. A stepwise logistic model was used to identify variables independently associated with outcome. Factors significantly associated with outcome on univariate analysis (p < 0.05) were entered into a backward logistic regression analysis model, adjusted for patient age, gender and pediatric risk of mortality (PIM 2) score.

RESULTS
A total of 45417 patients were admitted to the hospital over the period of the study, 2501 (5.5%) of them required PICU admission. One hundred and ten (Fig. 1) patients who had cardiac arrest preceding PICU were identified during the study period, representing a hospital incidence of 2.2 per 1000 hospital admissions.
The patient characteristics are shown in Table 1. The median risk of mortality as assessed using PIM2 was 0.535; IQR0.284-0.845. Most of the patients, 71 (68.9%), were previously well and 32 (30.1%) had underlying chronic disease.
Table 5: Patient demographic, anthropometric and circumstances at admission.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male: female)</td>
<td>60:43 (58.7:41.3)</td>
</tr>
<tr>
<td>Age (months)</td>
<td>7.2 (2.5 – 21.6)</td>
</tr>
<tr>
<td>Age category (%)</td>
<td></td>
</tr>
<tr>
<td>&lt;1 month</td>
<td>12 (11.5)</td>
</tr>
<tr>
<td>1 – 12 months</td>
<td>52 (50.0)</td>
</tr>
<tr>
<td>&gt;12 - 36 months</td>
<td>22 (21.2)</td>
</tr>
<tr>
<td>&gt;36 – 72 months</td>
<td>10 (9.6)</td>
</tr>
<tr>
<td>&gt;72 months</td>
<td>7 (6.7)</td>
</tr>
<tr>
<td>Weight (kg) (IQR)</td>
<td>5.8 (3.7 – 10.0)</td>
</tr>
<tr>
<td>PIM2 score</td>
<td>0.535 (0.284 – 0.845)</td>
</tr>
<tr>
<td>Reason for admission</td>
<td></td>
</tr>
<tr>
<td>Neurological</td>
<td>9 (8.7%)</td>
</tr>
<tr>
<td>Respiratory</td>
<td>30 (29.1%)</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>22 (21.4%)</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>22 (21.4%)</td>
</tr>
<tr>
<td>Trauma</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>Other</td>
<td>17 (16.5%)</td>
</tr>
</tbody>
</table>

Data are presented as median (interquartile range) or n (percentage).

There were 83 (80.6%) patients who had in-hospital cardiac arrest (IHCA) and 20 (19.4%) who had OHCA (Tab 5). Fifty two (62.7%) of the IHCA patients survived to hospital discharge while 11 patients (55.0%) with OHCA survived to hospital discharge (p = 0.7). Sixteen (19.3%) of the IHCA were grouped as others (5 in other hospital location, 6 during inter-facility transport whilst 2 occurred during cardiac catheterization and 1 undocumented). Fifteen (18.1%) of IHCA occurred in facilities outside the index hospital and 6 (7.2%) during inter-hospital transfer in the ambulance.

Table 6 shows the primary underlying condition for which the subjects were treated. Thirty seven (35.9%) cardiac arrests were unexpected, 29 (28.2%) resulted from progressive deterioration in patients with an existing medical condition, 28 (27.2%) arrested while undergoing a procedure, 4 patients (3.9%) arrests were expected and 9 (8.7%) the underlying conditions were not documented. Of the 28 who
arrested during a procedure 24 (85.7%) occurred while undergoing endotracheal intubation and anesthesia, 2 occurred intra-operatively, 1 occurred during cardiac catheterization and the other one during central venous line insertion. Sixteen (66%) of the 24 that occurred during endotracheal intubation and anesthesia occurred in the medical emergency department, other hospitals and the wards whilst the other third occurred in theatre. Only 2 (12.5%) out of 16 patients who arrested whilst undergoing a procedure had senior medical staff supervision during the procedure. Four out of five patients who were in shock were on inotropes prior to arresting during endotracheal intubation. Only in one of the eight who arrested in the theatre occurred during endotracheal intubation.
Table 6: Underlying condition at arrest

<table>
<thead>
<tr>
<th>RESPIRATORY</th>
<th>30 (29.1%)</th>
<th>GASTRO-INTESTINAL</th>
<th>22 (22.4%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute lower respiratory tract infection</td>
<td>21</td>
<td>Acute diarrhoeal disease</td>
<td>14</td>
</tr>
<tr>
<td>- Tuberculosis</td>
<td>1</td>
<td>- Necrotizing enterocolitis</td>
<td>3</td>
</tr>
<tr>
<td>- Foreign body aspiration</td>
<td>2</td>
<td>- Intestinal perforation</td>
<td>2</td>
</tr>
<tr>
<td>- Acute lower respiratory tract infection</td>
<td>21</td>
<td>- Bowel obstruction</td>
<td>1</td>
</tr>
<tr>
<td>- Tension pneumothorax</td>
<td>1</td>
<td>- Gastric haemorrhage</td>
<td>1</td>
</tr>
<tr>
<td>- Pulmonary haemorrhage</td>
<td>1</td>
<td>- Protein energy malnutrition</td>
<td>1</td>
</tr>
</tbody>
</table>

**CARDIOVASCULAR** 22 (22.4%) **OTHERS** 17 (16.5%)

<table>
<thead>
<tr>
<th>Cardiovascular</th>
<th>16</th>
<th>Drowning</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital Heart Disease</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dilated cardiomyopathy and myocarditis</td>
<td>6</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>- Congenital Heart Disease</td>
<td>16</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Draying</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Dilated cardiomyopathy and myocarditis</td>
<td>6</td>
<td></td>
<td>5</td>
</tr>
<tr>
<td>- Sepsis</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Disseminated tuberculosis</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Burns</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NEUROLOGICAL** 9 (8.7%)

<table>
<thead>
<tr>
<th>Neurological</th>
<th>1</th>
<th>Trauma</th>
<th>3 (2.90%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Tumour</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Hydrocephalus</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Meningitis</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Subdural haemorrhage</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Cerebral abscess</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Encephalitis</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Tuberculous meningitis</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Trauma</th>
<th>3 (2.90%)</th>
<th></th>
<th>1</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Abdominal</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Non-accidental injury</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Pedestrian motor-vehicle-accident</td>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Physiological and laboratory:**

Nineteen (18.4%) patients had a documented cardiac rhythm at arrest, 4 had pulseless electrical activity, 10 asystole and 5 had ventricular tachycardia or fibrillation (Tab 7). Seventeen had their temperature at arrest documented with 14 being hypothermic, 1 normothermic while 2 had hyperthermia. Median blood sugar was 6.3 mmol/l (IQR 4.3-13.5 mmol/l) at the time of cardiac arrest. Median pH following ROSC was 7.16 (IQR 6.99 -7.30). Median lactate level after arrest episode was 5.35 (IQR 2.35-11.55).
Table 7: Temperature, electrocardiogram and laboratory characteristics documented at arrest

<table>
<thead>
<tr>
<th>Temperature at arrest</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>- Hypothermic</td>
<td>14</td>
</tr>
<tr>
<td>- Normothermic</td>
<td>1</td>
</tr>
<tr>
<td>- Hyperthermic</td>
<td>2</td>
</tr>
<tr>
<td>- Missing data</td>
<td>86</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>First documented rhythm</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>- PEA</td>
<td>4</td>
</tr>
<tr>
<td>- Asystole</td>
<td>10</td>
</tr>
<tr>
<td>- VT/VF</td>
<td>5</td>
</tr>
<tr>
<td>- Missing</td>
<td>84</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Blood sugar (mmol/l) at arrest</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>6.3(4.3 – 13.5)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>First pH at PICU admission (mmol/l)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>7.16 (6.99 – 7.3)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sodium (mmol/l)</th>
<th>138.0 (134.0 – 142.0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potassium (mmol/l)</td>
<td>4.1 (3.6 – 5.1)</td>
</tr>
<tr>
<td>Chloride (mmol/l)</td>
<td>106.0 (101.0 – 110.0)</td>
</tr>
<tr>
<td>Ionized calcium (mmol/l)</td>
<td>1.26 (1.12 – 1.60)</td>
</tr>
<tr>
<td>Creatinine (µmol/l)</td>
<td>60.0 (36.5- 88.0)</td>
</tr>
<tr>
<td>Lactate (mmol/l)</td>
<td>5.35 (2.35 – 11.55)</td>
</tr>
</tbody>
</table>

Management of Arrest:

The median duration of resuscitation was 10 minutes (IQR 5 – 20). Thirty-five (34%) did not receive any adrenaline during the resuscitation, 44 (42.7%) received up to 3 doses of adrenaline, 24 (23.3%) received more than 3 doses of adrenaline. Thirteen (12.7 %) of the patients received at least one defibrillation. One (1%) patient was cardioverted for supra-ventricular tachycardia following CPR. The duration of CPR, number of adrenaline doses or other pharmacological treatment had no statistically significant effect outcome of arrest.

Post-arrest management:

Ninety eight (99%) received mechanical ventilation after return of spontaneous circulation. One patient received non-invasive continuous positive airway pressure. The median duration of mechanical ventilation was 2 days (IQR 0-5). Seventy four (71.82%) received inotropes during their PICU admission.

Post-arrest organ complication:

Circulatory failure was the most common complication following cardiac arrest with 71 (68.9%) being shocked following the arrest. Twenty five (24.3%) had neurological and 25 (24.3%) had acute kidney injury. Table 4 demonstrate laboratory values, they were mostly normal with the exception of pH, lactate and serum creatinine.

Arrest outcome:

Sixty three (61.2 %) of the study population survived to PICU discharge (Tab 8). Twenty of those patients who died occurred within 24 hours of arrest. Fifty seven (55.3%) survived to hospital discharge. Forty nine were discharged from the ward, 8 were transferred to other hospitals, 4 died on the ward (2
of the deaths were unrelated to the cardiac arrest and the other 2 were undocumented). Fifty two (62.7%) of IHCA and 11(55%) of OHCA survived to PICU discharge. Forty nine (47.6%) of those patients who were discharged from hospital were assessed at 3 to 6 month on follow-up visit neurologically and developmentally. The median length of stay in PICU was 3 (IQR 1 – 8) days and the median hospital stay was 27 days (IQR 9 –52).

Neurological assessment by level of consciousness, 54 of the 63 survivors were discharged from PICU alert, 1 was responsive to voice, 4 to pain and 1 was unresponsive. Characteristics of Pediatric Overall Performance (POPS) Score is shown in table 5.

<table>
<thead>
<tr>
<th>Table 8 Hospital and neurological outcome:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to six month follow-up neurological assessment (POPS) results based on 51 out of the 57 patients discharged home</td>
</tr>
<tr>
<td><strong>Outcome</strong></td>
</tr>
<tr>
<td>PICU length of stay(days)</td>
</tr>
<tr>
<td>PICU Survival</td>
</tr>
<tr>
<td>Hospital length of stay(days)</td>
</tr>
<tr>
<td>Ward outcome</td>
</tr>
<tr>
<td>Discharge from hospital</td>
</tr>
<tr>
<td>Died</td>
</tr>
<tr>
<td>Missing</td>
</tr>
<tr>
<td>Death on ward (n=4)</td>
</tr>
<tr>
<td>- Cardiac arrest related</td>
</tr>
<tr>
<td>- Unrelated to cardiac arrest</td>
</tr>
<tr>
<td>- Missing</td>
</tr>
<tr>
<td>POPS assessed at ward discharge (n)</td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Mild disability</td>
</tr>
<tr>
<td>Moderate disability</td>
</tr>
<tr>
<td>Severe disability</td>
</tr>
<tr>
<td>Coma/vegetative state</td>
</tr>
</tbody>
</table>
Table 9. factors associated with non-survival

<table>
<thead>
<tr>
<th>Variable</th>
<th>Non-survivors (n)</th>
<th>Survivors (n)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Median (interquartile range)</td>
<td>Median (interquartile range)</td>
<td></td>
</tr>
<tr>
<td>PI-Median (interquartile range)</td>
<td>0.833 (0.515 - 0.967)</td>
<td>0.41 (0.230 - 0.677)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of resuscitation (min)</td>
<td>17.5 (10 - 30)</td>
<td>10 (5 - 15)</td>
<td>0.006</td>
</tr>
<tr>
<td>Duration of intubation</td>
<td>0 (0 - 2)</td>
<td>3 (1 - 7)</td>
<td>0.002</td>
</tr>
<tr>
<td>pH</td>
<td>7.07 (6.88 - 7.20)</td>
<td>7.22 (7.09 - 7.36)</td>
<td>0.001</td>
</tr>
<tr>
<td>Chloride (mmol/l)</td>
<td>109 (103 - 118)</td>
<td>104 (101 - 129)</td>
<td>0.027</td>
</tr>
<tr>
<td>Creatinine (mmol/l)</td>
<td>79 (45 - 118.5)</td>
<td>54 (34 - 72)</td>
<td>0.014</td>
</tr>
<tr>
<td>Lactate (mmol/l)</td>
<td>11.5 (5.2 - 15.7)</td>
<td>3.2 (1.4 - 6.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of adrenaline doses (0.1ml/kg of 1:10000)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>13</td>
<td>23</td>
<td>0.6</td>
</tr>
<tr>
<td>1</td>
<td>7</td>
<td>14</td>
<td>0.7</td>
</tr>
<tr>
<td>2</td>
<td>7</td>
<td>6</td>
<td>0.2</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>4</td>
<td>0.6</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>3</td>
<td>0.9</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td>9</td>
<td>0.7</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td>4</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Ten variables found to be associated with non-survival were included after adjusting for age and gender in stepwise backward logistic regression (Tab 9). None of the variable we were interested in were associated with outcome.

DISCUSSION

Incidence

This retrospective study of PICU admissions following cardiac arrest in a single tertiary center in South Africa showed an incidence of 2.2 per 1000 hospital admissions over the period under review. This figure is underestimation of the true incidence of all cardiac arrest in the hospital. We were unable to comment further on other cardiac arrest episodes or attempted CPR within the hospital wards that didn’t survive to PICU admission since there are no source documentation or registry for such events.

Our study found male to female ratio of 1.49 to 1 but this had no impact on mortality outcome. Arrest episodes occurred predominantly in children under a year of age but not in the neonatal period, similar to other studies(46,47).

Aetiology of cardiac arrest

Most of the patients in this study (69.8%) presented with no known underlying condition or co-morbidity. Respiratory, cardiac and gastro-intestinal disorders were the most common primary conditions related to cardiac arrest. We were unable to classify the precipitating cause of arrest into
hypoxia/asphyxia or circulatory shock(20,48). Our data showed respiratory diseases and gastro-intestinal diseases were more likely to be of an acute event whilst cardiac was more related to a chronic underlying condition. In our findings acute respiratory tract infections and other respiratory related causes were associated with hypoxia whilst gastro-intestinal diseases mostly acute diarrheal diseases probably resulted in circulatory failure or hypovolemic shock. (49,50).

Two studies looked at in-hospital cardiac arrest, one prospective in Brazil, Reis et al (48) and the other retrospective in Finland, Suominen et al (35) though limited to in-hospital cardiac arrest they included both arrest in all the wards and had similar data based on the Utstein style reporting. Whilst the latter might have had more resources and also with high literacy rate the former is a middle-income country with comparable characteristic to our study population the latter has comparable economic status as our population. In both studies the model of care and personnel managing patients with cardiac arrest were similar. As at the time of data collection in our study not all patients with cardiac arrest were on continuous monitoring device. We compared and contrasted outcomes of cardiopulmonary resuscitation of sustained return of spontaneous circulation. The Brazilian study reported hospital discharge outcome of 25.3%, the Finish study reported 63% whilst our study showed 55.3% survival to hospital discharge. Most common precipitating cause of cardiac arrest was cardiac (71% and 61% for the Finish and Brazilian studies respectively), whilst in our study hypoxia/asphyxia (26.9%) and circulatory and congenital cardiac condition accounted for 22.1% of arrests. Though cardiac arrhythmias, ventricular tachycardia and fibrillation were documented in 4.8%, we were unable to ascertain if they were the primary causes of cardiac arrest.

The study found that significant numbers of cardiac arrest episodes occurred during emergency endotracheal intubation and anesthetic procedures. Morray et al in their study looking at peri-operative cardiac arrest in children, found a significant proportion (69%) resulted from cardiovascular disease, the severity of underlying disease and drugs related to anesthesia. Review of our cases showed that there was a low level of senior staff supervision during arrest episode related to endotracheal intubation. However it must be noted that most of these patients were probably in peri-arrest status rather than technical incompetence of the personnel involved with intubation. The retrospective nature of this study means we are unable to interrogate this finding any further than noting that the circumstances involved severely ill children with compromised cardiovascular and respiratory conditions which increases the risk of cardiac arrest during endotracheal intubation and anesthesia. Even though from our data we were unable to determine if these arrests were due to pre-arrest states, it must be noted that endotracheal intubation particularly in very young sick children can be a high risk procedure and should not be left in the hands of junior staff.
Duration of cardiopulmonary resuscitation

Cardiopulmonary resuscitation is the main treatment for cardiac arrest. Effective CPR with adequate depth of chest compression and rate alternating with ventilation and oxygen has significantly improved outcome of pediatric cardiac arrest.(51) There is not enough evidence to recommend when to terminate CPR and recent studies by Matos et al (n=3419 children) (52) and Goldberg et al (n=64339 adults) suggested that more patients may survive with longer duration of CPR than previously thought. It has been suggested that prolonged CPR may lead to poor neurological outcome in survivors. Five (5%) of the patients in our study had prolonged CPR, showing that in some cases providers are prepared to continue beyond the “usual” time frame to terminate CPR by convention. The reasons for prolonged resuscitation were not indicated in the patient hospital records. Our study did not find any association between duration of CPR and poor outcome. The data for unsuccessful cardiopulmonary resuscitation is not available for an overall look association of duration of resuscitation and poor outcome.

Impact of cardiac arrest on neurological and other organ function

This study has shown that a large proportion of patients who had successful CPR with ROSC survived to discharge from hospital with reasonable neurological outcome as compared to about decade ago.(52, 53) The nature of this study did not allow for estimation of change in neurological status. Thirty eight (77.6%) had mild to normal POPC score, 5 (10 %) had severe disability. This is comparable to Meert et al in the PECARN study, a multi-cohort study reported (n=353) 76.7% of patients who survived to discharge had documented good neurological outcome (POPC score of 1, 2 or no change).

As with other studies(55) we found that shock was the most prevalent complication following an arrest, with acute kidney impairment and neurological impairment present in equal proportions.

Limitations

This data is limited in that they were collected retrospectively with inherent inadequate documentation and capture resulting in missing data. As a result capture of some variables such as temperature and cardiac rhythm at cardiac arrest may not represent the true predictors of mortality but other variables were mostly well captured and the adopted analytical methodology addressed the concerns of missing data. As at the time of data collection not all the wards had patient monitors to monitor patients early.

Population based studies are necessary to determine incidence of out of hospital cardiac arrest. Our data was limited to the capture of only those participants who arrived at Red Cross War Memorial Children’s Hospital and admitted to PICU. We were therefore unable to determine the true incidence of OHCA.

Notwithstanding the limitations, this study gives insight into cardiac arrest in this population and the significance lies in its ability to elucidate epidemiology and outcome. It is only the first step in the process of finding out ways to prevent and treat pediatric cardiac arrest. Findings from studies such as ours may be used as a baseline or comparison for other studies, inform policy and implement targeted management of pediatric cardiac arrest.
Conclusions

In this retrospective study we found the incidence of cardiac arrest preceding PICU admission with return of spontaneous circulation to be 2.2 per 1000 hospital admissions and almost two thirds were less than one year old. Acute respiratory failure, and circulatory failure from gastrointestinal and cardiac conditions were the most common underlying cause of cardiac arrest. Children undergoing emergency endotracheal intubation and anesthesia are at increased risk of cardiac arrest. Mortality was lower than predicted in children admitted to PICU following cardiac arrest. Most survivors had normal neurological function on hospital discharge.

Recommendations

It is clear that an essential starting point for future research is the establishment of appropriate and comprehensive documentation of cardiac arrest episodes. Development of a cardiac arrest event registry with feedback to medical and nursing personnel would help to sensitize staff to the issues related to cardiorespiratory arrest episodes in children, and would help with documentation.

Patients on the wards who could potentially be at risk of cardiac arrest must be flagged and brought to the attention of staff on duty. Such patients could be nursed at the high dependency units or rooms on the wards.

We recommend that high risk patients should be identified and monitored in the appropriate setting with equipment, staffing and expertise to respond appropriately to any deterioration in clinical condition.

There is the need to strengthen supervision of junior staff who care for all at risk patients within the hospital especially those requiring procedures like intubation.

These interventions could potentially improve data collection, regular auditing and shaping of care of patients with the goal of identifying patients at risk early and institution of appropriate interventions to reduce its incidence.

Acknowledgement

We thank all clinicians who were part of care of patients with cardiac arrest, staff of medical records and neuro-developmental clinic for the role in data collection and documentation and all the other members of the Pediatric Intensive Care Unit of the Red Cross War Memorial Children’s Hospital, Cape Town.
Authorship
Appiah JA, Salie MS, Morrow BM, Argent AC

References


APPENDICES
APPENDIX I: CASE RECORD FORM (CRF)

Hosp ID:........................................... Study ID:.................................

Date of hospital admission: __/__/____ Time of admission: ___h____
Date of birth: __/__/____ Gender: M [ ] / F [ ]
Weight: _____.___kg

Date of PICU admission: __/__/____ Time of PICU admission: ___h____
Reason for hospital admission:
Diagnosis:..........................................................................................................................
PIM Score:.....................................

CARDIAC ARREST
Where did it occur?
Out of hospital [ ], state where...............................................
Time of health worker contact: __/__/____ Time arrival in hospital: __/__/____

In-hospital [ ] State where: Med Reg [ ] Wards [ ] Others[ ] State.................
Date of cardiac arrest: __/__/____ Time of arrest: __/__/____

Vital Signs at Cardiac Arrest

<table>
<thead>
<tr>
<th>Sign</th>
<th>HR</th>
<th>RR</th>
<th>BP</th>
<th>Temp</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOC</td>
<td>A</td>
<td>V</td>
<td>P</td>
<td>U</td>
</tr>
</tbody>
</table>

ECG:    PEA [ ] Asystole [ ] VT/VF [ ] Unknown [ ]

Circumstances Surrounding Arrest:
1. Was it an expected arrest? Yes [ ] No [ ]
2. Continued clinical deterioration Yes [ ] No [ ]
3. During a procedure (intubation) Yes [ ] No [ ]
RESUSCITATION

CPR: Y / N if Y state where? ..............................................................

Medication:

<table>
<thead>
<tr>
<th>Drug</th>
<th>Date (dd/mm/yyyy)</th>
<th>Time given (hh:mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Date resuscitation ended: ___/___/____  Time resuscitation ended: ___h___

Intubated: Yes [ ]  No [ ]  Date of intubation: ___/___/____

Physiological and Laboratory Status on admission to PICU

<table>
<thead>
<tr>
<th></th>
<th>Temp</th>
<th>HGT</th>
<th>pH</th>
<th>K</th>
<th>Na</th>
<th>Cl</th>
<th>Mg</th>
<th>Ca</th>
<th>Urea</th>
<th>Creat</th>
<th>Lactate</th>
</tr>
</thead>
</table>

Date

Time

Post Arrest complication:

1. Brain: Seizures [ ]  persistent altered consciousness [ ]  Focal signs [ ]

CT Brain: Yes [ ]  No [ ]  if Yes Date: ___/___/____

2. Renal failure  Yes [ ]  No [ ]

3. Acidosis  Yes [ ]  No [ ]

4. Shock  Yes [ ]  No [ ]
Post Arrest Treatment:

<table>
<thead>
<tr>
<th>Inotrope support:</th>
<th>Y</th>
<th>N</th>
<th>Ventilation support</th>
<th>Y</th>
<th>N</th>
<th>Date extubation</th>
</tr>
</thead>
</table>

ICU DISCHARGE STATUS

Outcome: 1. Discharged to [Ward] [Home] [Rehab Facility] 2. Died [ ] Date: ___/__/____
Condition at discharge:

<table>
<thead>
<tr>
<th>LOC</th>
<th>A</th>
<th>V</th>
<th>P</th>
<th>U</th>
</tr>
</thead>
</table>

Other impairment (state): .................................................................
.................................................................
.................................................................

WARD DISCHARGE STATUS

Outcome: 1. Discharge [Home] [Rehab Facility] 2. Died [ ] Date: ___/__/____
Causes of death .................................................................
Condition at discharge:

Paediatric Overall Performance Category

<table>
<thead>
<tr>
<th>Score</th>
<th>Category (neuro function)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Normal</td>
<td>Healthy, alert, regular class</td>
</tr>
<tr>
<td>2</td>
<td>Mild disability</td>
<td>Age appropriate interactions, but possible neurologic deficit, grade not appropriate</td>
</tr>
<tr>
<td>3</td>
<td>Moderate disability</td>
<td>Independent ADL but special education or learning deficit</td>
</tr>
<tr>
<td>4</td>
<td>Severe disability</td>
<td>Conscious but dependent on others because of neurologic deficit</td>
</tr>
<tr>
<td>5</td>
<td>Coma/vegetative state</td>
<td>Any degree of coma; unconscious; unaware</td>
</tr>
<tr>
<td>6</td>
<td>Dead</td>
<td></td>
</tr>
</tbody>
</table>

FOLLOW UP STATUS

Date: ___/__/____

Paediatric Overall Performance Category

<table>
<thead>
<tr>
<th>Score</th>
<th>Category (neuro function)</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
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</tr>
<tr>
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</tr>
<tr>
<td>6</td>
<td>Dead</td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX II

UNIVERSITY OF CAPE TOWN

Faculty of Health Sciences
Human Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
Ms S Ariefdien - Tel: [021]4066492 • Fax: [021]4066411
email: sumayah.ariefdien@uct.ac.za

03 July 2012

HREC REF: 344/2012

Dr JA Appiah,
Paediatric Intensive Care unit
Red Cross War Memorial Children’s Hospital
Klipfontein Road
Rondebosch
7700

CC. Prof AC Argent
Paediatric Intensive Care Unit
Red Cross War Memorial Children’s Hospital

Dear Dr Appiah,

PROJECT TITLE: CARDIAC ARREST IN CHILDREN PRECEDING PICU ADMISSION: AETIOLOGY AND OUTCOME IN A DEVELOPING COUNTRY

Thank you for submitting your new study to the Faculty of Health Sciences Human Research Ethics Committee.

It is a pleasure to inform you that the Ethics Committee has formally approved the above-mentioned study.

Approval is granted until 28 July 2013

Please submit an annual progress report (FHS016) if the research continues beyond the expiry date. Please submit a brief summary of findings if you complete the study within the approval period so that we can close our file (FHS010).

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the HREC. REF in all your correspondence.

Yours sincerely

PROFESSOR MARC BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB000001938

This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC)-SA, Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.

The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E8: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.
APPENDIX III: RXH MPhil Approval

Dr John Appiah
PICU
RCWMCH

Dear Dr Appiah,

RE: RESEARCH

Your request to do research in the PICU (CARDIAC ARREST IN CHILDREN PRECEDING PICU ADMISSION: AETIOLOGY AND OUTCOME IN A DEVELOPING COUNTRY) has been approved.

Kindly note that should you request folders from the Medical Records Department, that not more than five (5) folders may be removed at any one time. If they are removed, they must be returned before 16h00 on the same day.

Regards

Dr T A Blake
Manager Medical Services
Red Cross War Memorial Children’s Hospital
Rondebosch, 7700

021 658 5788 (T)
021 658 5166 (F)
thomas.blake@westerncape.gov.za

www.westerncape.gov.za
APPENDIX IV: Instructions for Authors

Instructions for Authors

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Conflicts of Interest and Source of Funding: “Author A has received honoraria from ‘Company 1.’ Author B is currently receiving a grant (#12345) from ‘Organization X,’ and is on the speaker’s bureau for ‘Organization Y’ – the CME organizers for Company 1. For the remaining authors none were declared.

Human and Animal Subjects. All studies of human subjects must contain a statement within the Materials and Methods section indicating approval of the study by the Institutional Review Board (or institutional review body) that subjects have signed written informed consent, or that the Institutional Review Board waived the need for informed consent. Before your submission can be sent out for peer review, it is necessary that you address this issue of institutional review approval. This is in accordance with the International Committee of Journal Editors uniform requirements for manuscripts submitted to biomedical journals. Please see http://www. icmje.org/for more details. All studies must contain a statement within the Materials and Methods section confirming approval by the Institutional Animal Care and Use Committee and that the care and handling of the animals were in accord with National Institutes of Health guidelines or other internationally recognized guidelines for ethical animal treatment.

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Text Material. The text should be organized into the following sections: Introduction, Materials and Methods, Results, Discussion, and Conclusions followed by Acknowledgments, References, Figure Legends, and Tables. Searcultural and editorial assistance are not acknowledged. Results may be presented in the text, in the figures, or in the tables. The Discussion section should interpret the results without unnecessary repetition. References to related studies should be included in the text section.

In addition, the following should be observed:

- The full term for which an abbreviation stands should be used at its first occurrence in the text unless it is a standard unit of measure. The abbreviation should appear in parentheses after the full term. Abbreviations should not be in the title, figure legends or table titles.
- For standard American units, do not use values that are more significant than your analysis is capable of accurately measuring (e.g., PaO2, 84 torr [11.2 kPa], not 83.7 torr).
- Hemodynamic measurements for pressure (e.g., MAP) should appear in mm Hg and gas tension measurements (e.g., PaO2) should appear in torr with SI units in parentheses. The units of vascular resistance are dynes cm-5.
- Please provide r² values for parametric data.

References. All references should be cited in sequential order in the text and typed on a separate sheet of paper. References should be identified in text, tables, and legends by full-size Arabic numerals on the line and in parentheses. Do not use wordprocessing footnote, endnote, or paragraph numbering functions to make a list of references. Titles of journals should be set in italics and abbreviated according to the style used in Index Medicus. If journal titles are not listed in Index Medicus they should be spelled out. Unpublished data or personal communications should be noted parenthetically within the text but not in the References section. Inclusive page numbers (e.g., 1-10) should be used for all references. Listed below are samples of standard references; however, a complete listing of references can be found on the International Committee of Medical Journal Editors Web site, www.icmje.org.


Equations. Equations should be created as normal text or as images. The use of equation editors or utilities may not convert correctly during the manuscript submission process and their use is discouraged.

Tables and Figures. The number of figures and tables should be appropriate for the length of the manuscript; do not use superfluous illustrations. Materials reproduced from another published source must be labeled “Reproduced with permission from...” In addition, a letter granting permission to reproduce the materials from the copyright holder must be received by SCCM when the manuscript is submitted for review. If the manuscript is accepted for publication, it will not be able to be printed unless this permission letter has been submitted. Adapted figure or table materials must be labeled “Adapted with permission from...” Letters of permission are also required for adapted materials. A sample of a permission request can be found on Editorial Manager® in the instruction section.

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1. Learn about the publication requirements for Digital Artwork: http://inksnow.com/ES/A2
2. Create, scan, and save your artwork and compare your final figure to the Digital Artwork Guideline Checklist (below).
3. Upload each figure to Editorial Manager® in combination with your manuscript text and tables.

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- Artwork should be saved as .tif or .eps files.
- Artwork is created as the actual size (or slightly larger) it will appear in the journal. (To get an idea of the size images should be when they print, study a copy of the journal to which you wish to submit. Measure the artwork typically shown and scale your image to match.)
- Crop out any white or black space surrounding the image.
- Diagrams, drawings, graphs, and other line art must be vector or saved at a resolution of at least 1200 dpi.
- Photographs, radiographs, and other halftone images must be saved at a resolution of at least 300 dpi.
- Photographs and radiographs with text must be saved as postscript or at a resolution of at least 600 dpi.
• Each figure must be saved and submitted as a separate file. Figures should not be embedded in the manuscript text file.

Remember:
• Cite figures consecutively in your manuscript.
• Number figures in the figure legend in the order in which they are discussed.
• Upload figures consecutively to the Editorial Manager® Web site and number figures consecutively in the Description box during upload.

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Laboratory Investigations. These include laboratory and animal research. This category of manuscript has a word limit of 2000 to 4000 words (8-16 typed double-spaced pages) which includes an abstract of no more than 300 words; the Discussion section of the manuscript should be limited to no more than 1500 words; a maximum of 40 references; and no more than 7 figures and/or tables.

Review Articles. These consist of critical assessment of literature and data pertaining to clinical topics. In review articles, emphasis should be placed on cause, diagnosis, therapy, prognosis, and prevention. Information concerning the type of study or analysis, population, intervention, and outcome should be included for all data used. The selection process used for all data should be described. Meta-analyses will be considered as review papers. The recommended length of review articles is 2000 to 3000 words (8-12 typed double-spaced pages) which includes an abstract of no more than 300 words; a maximum of 100 references; and no more than 10 figures and/or tables.

Brief Reports. These should be short reports of original studies or evaluations. The recommended length of brief reports is no more than 1500 words (6 typed double-spaced pages) which includes an abstract of no more than 300 words; a maximum of 25 references; and no more than 4 figures and/or tables.

PCCM Perspectives. These include articles that may fall outside the realm of formal clinical or basic science research, such as social policy, professional education, ethical dilemmas, and delivery of compassionate care. The recommended length is no more than 1500 words (6 typed double-spaced pages) which includes an abstract of no more than 300 words; a maximum of 25 references; and no more than 4 figures and/or tables.

Evidence-Based Journal Club. These articles provide an evidence-based critique of a recent important paper in the field of pediatric critical care medicine. The recommended length is no more than 1500 words (6 typed double-spaced pages) which includes an abstract of no more than 300 words; a maximum of 25 references; and no more than 4 figures and/or tables.

Letters to the Editor. Letters to the Editor are encouraged. Letters must specifically address a recent article published in Pediatric Critical Care Medicine. They should be no more than 500 words (2 typed double-spaced pages) with a maximum of 5 references.

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All manuscripts will be reviewed by Editorial Board members or consultants selected by the editor-in-chief. Initial editorial reviews usually are completed within 8-10 weeks of manuscript submission. The time required for review of revised manuscripts is variable.

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Correspondence can also be sent to: Patrick M. Kochanek, MD, MCCM Editor, Pediatric Critical Care Medicine Society of Critical Care Medicine 500 Midway Drive Mt. Prospect, IL 60056