

## Characteristics and Risk Factors for Mortality in Paediatric In-Hospital Cardiac Events in Singapore: Retrospective Single Centre Experience

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### Abstract

**Introduction:** There is limited data on paediatric resuscitation outcomes in Asia. We aimed to describe outcomes of paediatric in-hospital cardiac arrests (IHCA) and peri-resuscitation factors associated with mortality in our institution. **Materials and Methods:** Using data from our hospital's code registry from 2009 to 2014, we analysed all patients younger than 18 years of age with IHCA who required cardiopulmonary resuscitation (CPR). Exposure variables were obtained from clinical demographics, CPR and post-resuscitation data. Outcomes measured were: survival after initial CPR event and survival to hospital discharge. We analysed categorical and continuous variables with Fisher's exact and Wilcoxon rank-sum tests respectively. Statistical significance was taken as  $P < 0.05$ . **Results:** We identified 51 patients in the study period. Median age of patients was 1.9 (interquartile range [IQR]: 0.3, 5.5) years. Twenty-six (51%) patients had bradycardia as the first-recorded rhythm. The most common pre-existing medical condition was respiratory-related ( $n = 25$ , 48%). Thirty-eight (75%) achieved sustained return of spontaneous circulation, 24 (47%) survived to paediatric intensive care unit (PICU) discharge and 23 (45%) survived to hospital discharge. Risk factors for hospital mortality included: age, duration of CPR, adrenaline, calcium or bicarbonate administration during CPR, Paediatric Index of Mortality (PIM)-II scores, first recorded post-resuscitation pH and hyperglycaemia within 24 hours of resuscitation. **Conclusion:** We demonstrated an association between clinical demographics (age, PIM-II scores), CPR variables (duration of CPR and administration of adrenaline, calcium or bicarbonate) and post-resuscitation laboratory results (first recorded pH and hyperglycaemia within 24 hours) with PICU survival. The availability and quality of post-resuscitation care may have implications on survival after paediatric IHCA.

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**Key words:** Cardiopulmonary resuscitation, Child, Infant

### Introduction

Despite advances in resuscitation, survival from paediatric in-hospital cardiac arrests (IHCA) remains poor. Reported peri-resuscitative factors associated with mortality include pre-existing haematological, oncological, immunologic, genetic or metabolic disorders; presence of endotracheal tube or use of vasoactive infusions before arrest; use of adrenaline, calcium or sodium bicarbonate during arrest; and duration of cardiopulmonary resuscitation (CPR).<sup>1-3</sup> Post-resuscitation factors associated with mortality include hypotension, hyperoxia or hypoxia, serum lactate levels,

hypo- or hyperglycaemia, and partial pressure of carbon dioxide ( $\text{PaCO}_2$ ) levels.<sup>4-8</sup> Recent data from large North American cardiac arrest databases suggest a survival-to-discharge rate of between 34.8% to 48.7%.<sup>1,9</sup> There is, however, limited paediatric data available from Asia.<sup>10-12</sup>

We aimed to describe the outcomes of IHCA and study peri-resuscitation factors associated with mortality in our institution. We hypothesised that both resuscitation and post-resuscitation factors were associated with survival. In addition, we aimed to compare our data with other published reports from Asia.

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## Materials and Methods

KK Women's and Children's Hospital is a tertiary paediatric centre with 364 beds, an average of 170,000 paediatric emergency visits and 20,870 admissions per year. Our paediatric intensive care unit (PICU) and high dependency unit (HD) comprises 45 multidisciplinary beds. A specialised code team, established since 1997, provides 24-hour coverage for paediatric cardio-pulmonary arrests. A formal rapid response system comprising early warning scores and a rapid response team was not yet established during the study period.

Post-resuscitation care was at the discretion of managing intensivists. General principles included keeping oxygen saturation ( $\text{SpO}_2$ ) targets at  $>95\%$ , maintaining haemodynamic stability, avoiding hyperthermia and ensuring adequate sedation and analgesia. There was no established protocol for active cooling. Measures to control hyper-pyrexia (defined as  $>38^\circ\text{C}$ ) include the use of anti-pyretics and external cooling measures.

Since 2007, details of all paediatric codes were prospectively collected according to Utstein-style reporting guidelines.<sup>13</sup> For this study, we analysed data from January 2009 to December 2014. The study was approved by the Local Centralised Institutional Review Board. All patients aged 1 day to 18 years who required activation of the code team for an event requiring CPR were included. CPR was defined as any event that required initiation of chest

compression for: 1) inability to palpate a pulse, unresponsive and apnoeic; 2) bradycardia  $<60$  beats per minute with haemodynamic compromise; or 3) ventricular fibrillation or pulseless ventricular tachycardia.<sup>3,13</sup> Sustained return of spontaneous circulation (ROSC) was defined as persistence of palpable pulse or blood pressure for 20 consecutive minutes without the need for CPR. "Office hours" was defined as between the hours of 8.00 am and 5.30 pm on weekdays, while "after office hours" was defined as the hours from 5.31 pm to 7.59 am on weekdays and weekends. Events occurring in the emergency room, non-clinical area or neonatal unit were excluded. We also excluded patients who had a prior "do not resuscitate" order. In the event of multiple arrests, only data from the index event was used.

The dose and route of adrenaline for CPR was standardised according to our national resuscitation council's advanced paediatric life support guidelines.<sup>14</sup> Doses of calcium and sodium bicarbonate were standardised to our institutional guidelines for resuscitation (calcium chloride 0.14 mmol/kg and sodium bicarbonate 1 mmol/kg).

Outcomes measured were immediate survival (i.e. achieved ROSC) and survival to hospital discharge. Data collected included: 1) patient's baseline characteristics; 2) characteristics of CPR events; 3) PICU data (e.g. PIM-II scores, temperature, first recorded serum lactate levels, partial pressure of carbon dioxide [ $\text{PaCO}_2$ ] and partial pressure of arterial oxygen [ $\text{PaO}_2$ ]) in the first 6 hours, and

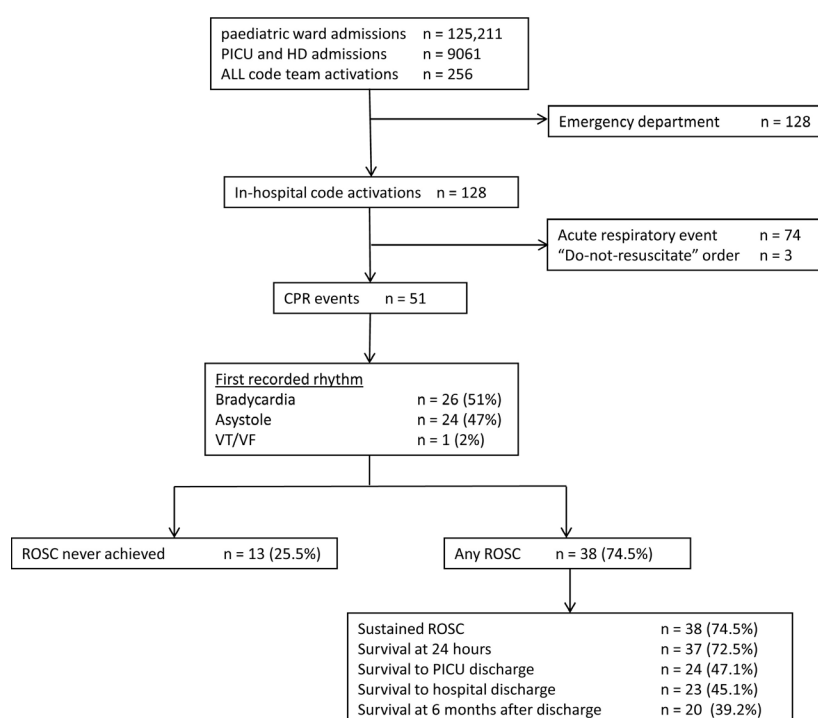


Fig. 1. Outcomes for in-hospital CPR events ( $n = 51$ ). CPR: Cardio-pulmonary resuscitation; HD: High dependency; PICU: Paediatric intensive care unit; ROSC: Return of spontaneous circulation; VF: Ventricular fibrillation; VT: Ventricular tachycardia

highest recorded glucose concentrations in the first 24 hours post-event; and 4) survival to PICU and hospital discharge.

Statistical analysis was performed only for patients with complete data for the studied variables. Categorical variables were described using counts and percentages. We summarised continuous variables with medians and interquartile ranges (IQR). We analysed categorical and continuous variables with Fisher's exact and Wilcoxon rank-sum tests respectively. Statistical significance was taken as  $P < 0.05$  for all tests. Analysis was performed with Stata v12 (College Station, Texas, USA).

## Results

Over the study period, there were 125,211 admissions with 51 CPR events (Fig. 1). Thirty-eight patients (74.5%) achieved ROSC, 24 (47%) survived to PICU discharge and 23 (45%) survived to hospital discharge. Bradycardia ( $n = 26$ , 51%) was the most common first-recorded rhythm. The median age of patients was 1.9 (0.3, 5.5) years. The majority of events occurred after office hours ( $n = 39$ , 76.5%) and in PICU/HD ( $n = 33$ , 67.4%). Respiratory-related disease was the most common pre-existing medical condition [pneumonia,  $n = 17$  (33.3%) and chronic respiratory disease,  $n = 14$  (27.4%)]. Pre-existing oncological conditions were present in 4 patients (7.8%).

Peri-event factors associated with poorer immediate survival included a longer duration of CPR; any use of adrenaline (epinephrine), calcium or bicarbonate; and higher median doses of adrenaline and bicarbonate (Table 1).

Location and timing of the CPR event were not associated with survival to hospital discharge. Variables available pre- and during the arrest that were associated with survival to hospital discharge included: age (0.6 [0.3, 3.5] vs 2.9 [1.0, 8.7] years,  $P = 0.02$ ); CPR duration (2.5 [2, 6] vs 30 [12, 45] minutes,  $P < 0.01$ ); any use of adrenaline, calcium or sodium bicarbonate; median doses of adrenaline administered (0 [0, 1] vs 5 [2.5, 8] doses,  $P < 0.01$ ); and median doses of sodium bicarbonate administered (0 [0] vs 2 [0.5, 3],  $P < 0.01$ ) in survivors and non-survivors, respectively (Table 2).

Among the 38 patients with ROSC, post-resuscitation factors that were associated with survival to hospital discharge were: median PIM-II scores (15.9 [6.7, 24.2] vs 34.0 [11, 87.6],  $P = 0.03$ ), first measured pH (7.3 [7.2, 7.35] vs 7.08 [6.97, 7.27],  $P = 0.01$ ), and median peak serum glucose levels (first 24 hours) (8.45 [7.0, 13.9] vs 15.2 [12.5, 23.5] mmol/L,  $P = 0.01$ ) in survivors and non-survivors, respectively (Table 3).

Arterial blood gas data was available in 24 patients. There was no statistically significant difference in first recorded median lactates between survivors and non-survivors (1.6 [1.15, 3.73] mmol/L vs 7.29 [3.88, 10.19] mmol/L,  $P =$

Table 1. Characteristics of Patients in Relation to Immediate Survival ( $n = 51$ )

|                                                                  | Any ROSC Achieved<br>$n = 38$ | ROSC Never Achieved<br>$n = 13$ | <i>P</i> Value |
|------------------------------------------------------------------|-------------------------------|---------------------------------|----------------|
| <b>Demographics</b>                                              |                               |                                 |                |
| Age (years)                                                      | 1.07<br>(0.29, 5.52)          | 2.34<br>(1.58, 4.19)            | 0.46           |
| Male gender                                                      | 20 (52.6%)                    | 8 (61.5%)                       | 0.41           |
| Race                                                             |                               |                                 | 0.27           |
| Chinese                                                          | 25 (65.8%)                    | 6 (46.1%)                       |                |
| Malay                                                            | 8 (21.1%)                     | 3 (23.1%)                       |                |
| Indian                                                           | 1 (2.6%)                      | 2 (15.4%)                       |                |
| Others                                                           | 4 (10.5%)                     | 2 (15.4%)                       |                |
| Time of event                                                    |                               |                                 | 0.35           |
| Office hours                                                     | 9 (23.7%)                     | 2 (15.4%)                       |                |
| After office hours/<br>weekends                                  | 29 (76.3%)                    | 11 (84.6%)                      |                |
| Location of event                                                |                               |                                 | 0.33           |
| General ward                                                     | 11 (28.9%)                    | 5 (38.5%)                       |                |
| PICU or high<br>dependency                                       | 26 (68.4%)                    | 7 (53.8%)                       |                |
| Others                                                           | 2 (5.3%)                      | 0 (0)                           |                |
| Illness category                                                 |                               |                                 | 0.9            |
| Medical non-cardiac                                              | 30 (78.9%)                    | 11 (84.6%)                      |                |
| Medical cardiac                                                  | 2 (5.3%)                      | 1 (7.7%)                        |                |
| Surgical cardiac                                                 | 3 (7.9%)                      | 0 (0)                           |                |
| Surgical non-cardiac                                             | 3 (7.9%)                      | 1 (7.7%)                        |                |
| <b>Pre-existing medical conditions</b>                           |                               |                                 |                |
| Pneumonia                                                        | 13 (34.2%)                    | 4 (3.1%)                        | 0.55           |
| Chronic respiratory<br>disease                                   | 13 (34.2%)                    | 1 (7.7%)                        | 0.06           |
| Baseline depression in<br>central nervous system<br>(non-stroke) | 12 (31.6%)                    | 3 (23.1%)                       | 0.42           |
| Congenital heart<br>disease                                      | 10 (26.3%)                    | 2 (15.4%)                       | 0.35           |
| Malignancy                                                       | 2 (5.3%)                      | 2 (15.4%)                       | 0.27           |
| Renal impairment                                                 | 2 (5.3%)                      | 1 (7.7%)                        | 0.6            |
| Hepatic impairment                                               | 0 (0)                         | 3 (23.1%)                       | 0.01           |
| <b>Interventions/monitoring present prior to event</b>           |                               |                                 |                |
| Non-invasive<br>ventilation                                      | 13 (34.2%)                    | 4 (30.8%)                       | 0.55           |
| Invasive ventilation                                             | 7 (18.4%)                     | 1 (7.7%)                        | 0.33           |
| Invasive arterial blood<br>pressure monitoring                   | 7 (18.4%)                     | 2 (15.4%)                       | 0.59           |
| Vasoactive infusions                                             | 3 (7.9%)                      | 2 (15.4%)                       | 0.29           |

CPR: Cardiopulmonary resuscitation; PICU: Paediatric intensive care unit; ROSC: Return of spontaneous circulation

Note: Values expressed as absolute counts (percentage) for categorical variables and median interquartile ranges (IQR) for continuous variables.

Table 1. Characteristics of Patients in Relation to Immediate Survival (n = 51) (Cont'd)

|                                                            | Any ROSC Achieved (n = 38) | ROSC Never Achieved (n = 13) | P Value |
|------------------------------------------------------------|----------------------------|------------------------------|---------|
| First recorded rhythm                                      |                            |                              | 0.5     |
| Bradycardia                                                | 21 (55.3%)                 | 5 (38.5%)                    |         |
| Asystole                                                   | 16 (42.1%)                 | 8 (61.5%)                    |         |
| Ventricular fibrillation/pulseless ventricular tachycardia | 1 (2.6%)                   | 0 (0)                        |         |
| CPR characteristics and interventions                      |                            |                              |         |
| Duration of CPR (minutes)                                  | 4.5 (2, 15)                | 45 (45, 50)                  | <0.01   |
| Adrenaline administered during CPR                         | 23 (60.5%)                 | 13 (100%)                    | <0.01   |
| Doses of adrenaline administered during CPR                | 1 (0, 3)                   | 8 (7, 9)                     | <0.01   |
| Calcium administered during CPR                            | 5 (13.2%)                  | 11 (84.6%)                   | <0.01   |
| Bicarbonate administered during CPR                        | 10 (26.3%)                 | 13 (100%)                    | <0.01   |
| Doses of bicarbonate during CPR                            | 0 (0, 1)                   | 3 (2, 4)                     | <0.01   |

CPR: Cardiopulmonary resuscitation; PICU: Paediatric intensive care unit; ROSC: Return of spontaneous circulation

Note: Values expressed as absolute counts (percentage) for categorical variables and median interquartile ranges (IQR) for continuous variables.

0.14). The highest median PaCO<sub>2</sub> recorded within 6 hours post-ROSC was 64.1 (49.9, 91.3) mmHg and 61.5 (38, 78.4) mmHg in survivors and non-survivors respectively ( $P=0.5$ ). The highest median PaO<sub>2</sub> recorded within 6 hours post-ROSC was 83 (66.9, 129.7) mmHg and 165.7 (94.3, 211.1) mmHg in survivors and non-survivors respectively ( $P=0.08$ ). Neither was significantly associated with survival to discharge.

## Discussion

Our findings describe the incidence, clinical characteristics and outcomes of a cohort of paediatric patients who experienced an in-hospital CPR event requiring chest compressions.

Our survival-to-discharge rate for IHCA of 45% is comparable with published rates from North American<sup>9</sup> and European studies,<sup>2</sup> but there is significant heterogeneity of

Table 2. Characteristics of Survivors and Non-Survivors in Relation to Hospital Discharge (n = 51)

|                                                            | Survivors (n = 23) | Non-Survivors (n = 28) | P Value |
|------------------------------------------------------------|--------------------|------------------------|---------|
| Demographics                                               |                    |                        |         |
| Age (years)                                                | 0.6 (0.3, 3.5)     | 2.9 (1.0, 8.7)         | 0.02    |
| Male                                                       | 12 (52%)           | 16 (57%)               | 0.47    |
| Location of event                                          |                    |                        | 0.5     |
| General ward                                               | 7 (30.4%)          | 9 (32.1%)              |         |
| PICU or high dependency                                    | 16 (69.6%)         | 17 (60.7%)             |         |
| Others                                                     | 0 (0)              | 2 (7.1%)               |         |
| Illness category                                           |                    |                        | 0.6     |
| Medical non-cardiac                                        | 18 (78.3%)         | 23 (82.1%)             |         |
| Medical cardiac                                            | 2 (8.7%)           | 1 (3.6%)               |         |
| Surgical cardiac                                           | 2 (8.7%)           | 1 (3.6%)               |         |
| Surgical non-cardiac                                       | 1 (4.3%)           | 3 (10.7%)              |         |
| Pre-existing medical conditions                            |                    |                        |         |
| Pneumonia                                                  | 8 (34.8%)          | 9 (32.1%)              | 0.5     |
| Chronic lung disease                                       | 8 (34.8%)          | 6 (24.1%)              | 0.2     |
| Baseline depression in central nervous system (non-stroke) | 6 (26.1%)          | 9 (32.1%)              | 0.4     |
| Congenital heart disease                                   | 9 (39.1%)          | 3 (10.7%)              | 0.02    |
| Sepsis                                                     | 2 (8.7%)           | 7 (25%)                | 0.12    |
| Malignancy                                                 | 1 (4.3%)           | 3 (10.7%)              | 0.4     |
| Inborn errors of metabolism                                | 2 (8.7%)           | 0 (0%)                 | 0.2     |
| Interventions present prior to event                       |                    |                        |         |
| Non-invasive ventilation                                   | 9 (39.1%)          | 8 (28.6%)              | 0.3     |
| Invasive ventilation                                       | 3 (13%)            | 5 (17.9%)              | 0.5     |
| Vasoactive infusions                                       | 2 (8.7%)           | 2 (7.1%)               | 0.5     |
| First documented rhythm                                    |                    |                        | 0.16    |
| Asystole                                                   | 8 (34.8%)          | 16 (57.1%)             |         |
| Bradycardia                                                | 14 (60.9%)         | 12 (42.9%)             |         |
| Ventricular fibrillation/pulseless ventricular tachycardia | 1 (4.3%)           | 0 (0%)                 |         |
| CPR characteristics and interventions                      |                    |                        |         |
| Duration of CPR (minutes)                                  | 2.5 (2, 6)         | 30 (12, 45)            | <0.01   |
| Adrenaline administered during CPR                         | 11 (47.8%)         | 25 (89.3%)             | 0.02    |
| Doses of adrenaline administered during CPR                | 0 (0, 1)           | 5 (2.5, 8)             | <0.01   |
| Calcium administered during CPR                            | 1 (4.3%)           | 15 (53.4%)             | <0.01   |
| Bicarbonate administered during CPR                        | 2 (8.7%)           | 21 (75%)               | <0.01   |
| Doses of bicarbonate during CPR                            | 0 (0)              | 2 (0.5, 3)             | <0.01   |

CPR: Cardiopulmonary resuscitation; PICU: Paediatric intensive care unit

Note: Values expressed as absolute counts (percentage) for categorical variables and median interquartile ranges (IQR) for continuous variables.

Table 3. Characteristics of Patients with Return of Spontaneous Circulation (n = 38) in Relation to Survival to Hospital Discharge

|                                                             | Survivors<br>(n = 23) | Non-Survivors<br>(n = 15) | P Value |
|-------------------------------------------------------------|-----------------------|---------------------------|---------|
| PIM II scores (%)                                           | 15.9 (6.7, 24.2)      | 34 (11, 87.6)             | 0.03    |
| Use of ECMO within 24 hours after CPR                       | 1 (4.3%)              | 1 (3.6%)                  | 0.6     |
| Peak glucose recorded within 24 hours post-ROSC (mmol/L)    | 8.45 (7, 13.9)        | 15.2 (12.5, 23.5)         | 0.01    |
| Lowest temperature recorded within 24 hours post-ROSC (°C)  | 36 (35.1, 36.2)       | 35.3 (34.0, 36.0)         | 0.3     |
| Highest temperature recorded within 24 hours post-ROSC (°C) | 37.6 (37.2, 38.2)     | 37.4 (36.4, 38.0)         | 0.67    |
| First measured pH after ROSC                                | 7.3 (7.2, 7.35)       | 7.08 (6.97, 7.27)         | 0.01    |

CPR: Cardiopulmonary resuscitation; ECMO: Extra-corporeal membrane oxygenation; PICU: Paediatric intensive care unit; PIM: Paediatric Index of Mortality; ROSC: Return of spontaneous circulation

Note: Values expressed as absolute counts (percentage) for categorical variables and median (IQR) for continuous variables.

survival outcomes from paediatric IHCA across Asia (Table 4). We postulate that this may be secondary to differences in institutional responses and systems of care across Asia. The first report on our institution's IHCA outcomes was in 2001, with 10 CPR events out of 51,241 admissions (0.2 per 1000 admissions).<sup>15</sup> None of these patients survived to hospital discharge. This study provides an updated account of resuscitation outcomes in our institution demonstrating significant improvement over a decade despite a twice-fold increase in CPR events. We postulate that this improvement is related to institutional educational initiatives, regular deliberate practice to maintain competencies in paediatric basic and advanced life support, development of the paediatric intensive care service and standardised reporting of cardiac arrests for auditing purposes.

The majority of events in our cohort occurred after office hours. While adult and paediatric studies have reported lower survival rates at night and during weekends,<sup>16,17</sup> we observed no such differences. This may be related to the observation that the majority of our events occurred in the PICU and HD, which is a resource-rich environment, with less variability in staffing and a high level of monitoring. Berg et al analysed 5870 paediatric CPR events over a 10-year period, and demonstrated an increasing trend towards paediatric cardiopulmonary events occurring in the ICU

compared to in-patient wards, with concomitant increases in ROSC.<sup>9</sup> The authors postulated that the improvement could be due to ICU environments being resource-intense, with higher staff-to-patient ratios, and more recent CPR training, experience and expertise in ICU personnel.

We also found that younger age was associated with improved survival from IHCA. This finding is in keeping with current literature,<sup>10,18</sup> and may be related to the increased chest wall compliance in younger patients, resulting in more effective blood flow during chest compressions.

Symptomatic bradycardia in children is associated with a low cardiac output, and can occur as a physiological consequence to hypoxia and acidosis in neonates. It is also typically a rhythm seen prior to the onset of asystole. There is evidence that paediatric patients requiring chest compressions for haemodynamically significant bradycardia are more likely to survive than those with asystole or pulseless electrical activity,<sup>19,20</sup> but this was not observed in our cohort. We postulate this may be due to inaccuracies in the reporting of the first observed rhythm. While the arrival of the code team is often preceded by resuscitative efforts of the primary in-patient care team, the first recorded rhythm is based on the rhythm present on arrival of the code team, and patients presenting with bradycardia may already have progressed to asystole by the time of the team's arrival.

We noted that longer durations of CPR; any use of adrenaline, calcium and bicarbonate and higher number of doses of adrenaline and bicarbonate were associated with inferior survival outcomes in our cohort. This is not surprising and may be a reflection of the prolonged resuscitation attempt in a sicker cohort of patients with higher PIM-II scores (PIM-II scores: 15.9% [6.7, 24.2] vs 34% [11, 87.6],  $P = 0.03$ , in survivors and non-survivors, respectively).

Patients who regain spontaneous circulation after cardiac arrest undergo a distinct pathophysiological process characterised by brain injury, myocardial dysfunction and a systemic ischaemia/reperfusion response.<sup>21</sup> The focus of post-resuscitation research in recent years has included the role of glucose control, therapeutic hypothermia, and optimal oxygenation and ventilation targets.

Hyperglycaemia has been associated with poorer outcomes in critically ill children.<sup>22-25</sup> Dysregulation in glucose homeostasis is not uncommon after cardiac arrest, and hyperglycaemia post-arrest may also be a reflection of the degree of stress response as well as the cumulative amount of adrenaline required during resuscitation. In a retrospective trial on therapeutic hypothermia in 181 infants and children after cardiac arrest, initial hypo- or hyperglycaemia was independently associated with mortality.<sup>26</sup> Twenty-four (63.2%) of our patients had

Table 4. Summary of Studies on Paediatric In-Hospital Cardiac Arrest in Asia

| Author/Country/<br>Year                       | Type of Institution                           | Incidence                                                                               | Most Common<br>First-Recorded<br>Rhythm | Study<br>Population    | Sustained<br>ROSC                   | Survival to Hospital<br>Discharge                                           | Risk Factors for Mortality/Comments                                                                                                                                                                                                                                                         |
|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------------------------------------------------|-----------------------------------------|------------------------|-------------------------------------|-----------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Mok YH et al; Singapore;<br>2016 <sup>#</sup> | Single centre: 20,870<br>admissions per annum | 0.4 per 1000<br>admissions<br>(n = 51)                                                  | Bradycardia                             | 1 day to 18 years      | 37 (72.5%)                          | 23 (45%)                                                                    | Older age; longer CPR duration; any use of<br>adrenaline, calcium or bicarbonate during CPR;<br>increasing doses of adrenaline during CPR;<br>higher PIM II scores on admission to ICU;<br>hyperglycaemia in the first 24 hours post-<br>ROSC; lower pH recorded immediately after<br>ROSC. |
| Wu E et al; Taiwan;<br>2009 <sup>*</sup>      | Single centre: 8874<br>admissions per annum   | 8.9 per 1000<br>admissions (n = 316).<br>Conventional CPR:<br>252/316. ECPR:<br>64/316. | Bradycardia or<br>asystole              | 7 days to 18<br>years  | Conventional<br>CPR: 153<br>(60.7%) | Overall: 66 (20.9%).<br>Conventional CPR:<br>50 (19.8%). ECPR:<br>16 (25%). | Vasoactive infusions prior to CPR; haematologic<br>or oncologic diseases and longer CPR durations.<br>High percentage of patients who underwent<br>ECPR (20.2%).                                                                                                                            |
| Zeng J et al; China;<br>2013 <sup>†</sup>     | Multicentre                                   | 1.6 per 1000<br>admissions<br>(n = 174)                                                 | Bradycardia                             | 1 month to 18<br>years | 108 (62.1%)                         | 49 (28.2%)                                                                  | Older age, longer CPR duration, and presence of<br>endotracheal tube before arrest.                                                                                                                                                                                                         |
| Haque A; Pakistan;<br>2011 <sup>‡</sup>       | Single centre: 4424<br>admissions per annum   | 4 per 1000 admissions<br>(n = 106)                                                      | Bradycardia                             | 1 month to 14<br>years | 58 (54.7%)                          | 12 (11.3%)                                                                  | Prolonged CPR duration (>20 minutes), ≥<br>doses of adrenaline during CPR and any<br>bicarbonate use during CPR.                                                                                                                                                                            |
| Singh SK et al; India;<br>2013 <sup>§</sup>   | Single centre                                 | 427 patients. Number<br>of admissions not<br>defined.                                   | Not described                           | 1 month to 14<br>years | 26%                                 | 1.9%                                                                        | CPR during night hours, prolonged CPR<br>duration (>10 minutes) and older age (>1 year).                                                                                                                                                                                                    |

CPR: Cardiopulmonary resuscitation; ECPR: Initiation of ECMO during active chest compressions; ICU: Intensive care unit; PIM: Paediatric Index of Mortality; ROSC: Return of spontaneous circulation

<sup>#</sup>Mok YH, Loke APT, Loh TF, Lee JH. Characteristics and risk factors for mortality in paediatric in-hospital cardiac events in Singapore: A retrospective single centre experience. *Annals Acad Med Singapore* 2016;45:534-41.<sup>\*</sup>Wu ET, Li MJ, Huang SC, Wang CC, Liu YP, Lu FL, et al. Survey of outcome of CPR in pediatric in-hospital cardiac arrest in a medical center in Taiwan. *Resuscitation* 2009;80:443-8.<sup>†</sup>Zeng J, Qian S, Zheng M, Wang Y, Zhou G, Wang H. The epidemiology and resuscitation effects of cardiopulmonary arrest among hospitalized children and adolescents in Beijing: an observational study. *Resuscitation* 2013;84:1685-90.<sup>‡</sup>Haque A, Rizvi A, Bano S. Outcome of in-hospital pediatric cardiopulmonary arrest from a single center in Pakistan. *Indian J Pediatr* 2011;78:1356-60.<sup>§</sup>Singh SK, Kumar R, Koonwar S. Epidemiology and outcome of pediatric in-hospital cardiopulmonary resuscitation in Northern India. *J Pediatr Intensive Care* 2013;2:55-61.

hyperglycaemia (glucose levels  $>8.3$  mmol/L) within the first 24 hours after ROSC, and we found that peak blood sugar levels within the first 24 hours post-event was associated with overall mortality. Despite the association between hyperglycaemia and poor outcomes, paediatric intensivists continue to maintain clinical equipoise on glycaemic control.<sup>27</sup> This is understandable, given the risks of hypoglycaemia associated with tight glycaemic control, the lack of randomised studies of glycaemic control in paediatric IHCA survivors, as well as the recent multicentre trial on tight glycaemic control which demonstrated lack of effect on clinical outcomes in critically ill children.<sup>28</sup>

Current guidelines recommend using the minimum fraction of inspired oxygen ( $\text{FiO}_2$ ) concentration to maintain  $\text{SpO}_2 \geq 94\%$ , in an attempt to ensure adequate oxygen delivery while preventing oxidative injury.<sup>29</sup> However, the ideal therapeutic range of oxygenation and  $\text{FiO}_2$  concentrations after paediatric cardiac arrest remains unclear. In a cohort of 1875 patients, Ferguson et al reported an association between both hyperoxia and hypoxia at 1 hour post-ROSC and PICU mortality.<sup>5</sup> However, other studies have not demonstrated such associations. In a prospective multicentre study of 223 children after IHCA, neither hyperoxia nor hypoxia immediately or at 24 hours post-ROSC was associated with hospital mortality.<sup>8</sup> Bennett et al similarly found no association between hyperoxia within 6 hours post-ROSC and hospital survival with good neurological outcomes.<sup>30</sup> Given the differences in  $\text{PaO}_2$  thresholds, time periods and outcomes measured, it is difficult to analyse these studies collectively. In our study, there was no difference in the proportion of survivors in PICU patients with  $\text{PaO}_2 >200$  and  $<200$  mmHg (14/22 vs 1/4,  $P = 0.19$ ). Because of the uncertainty surrounding ideal oxygenation targets in paediatric resuscitation and risks associated with hyperoxia, future studies are needed to examine the impact of low  $\text{FiO}_2$  concentrations for paediatric resuscitation.

Post-arrest serum lactate levels, a global biomarker of tissue hypoxia, has been explored as a means of stratifying injury severity and outcome prognostication to better titrate therapeutic interventions to improve survival. A retrospective cohort study of 264 patients (1 day to 18 years old) post-cardiac arrest demonstrated that elevated lactate levels in the first 12 hours after successful resuscitation from cardiac arrest was associated with increased hospital mortality (maximum serum lactate at 0–6 hours: 5.3 mmol/L [2.2, 10] vs 11.9 mmol/L [6.4, 18.1],  $P < 0.001$ ; maximum serum lactate at 7 to 12 hours: 2.7 mmol/L [1.6, 5.70] vs 8.8 mmol/L [3.8, 15.9],  $P < 0.001$ , in survivors and non-survivors, respectively), and lactate levels in the first 6 hours post-arrest were significantly higher in patients who received more doses of adrenaline.<sup>6</sup> While the serum lactate levels

between survivors and non-survivors in our cohort were clearly different (first recorded median lactate 1.6 mmol/L vs 7.29 mmol/L), this was not statistically significant. This likely arises from our small sample size, which may be inadequately powered to demonstrate statistical significance.

We acknowledge certain limitations in our study. The small sample size precluded multivariate analysis to determine independent factors for mortality in our cohort. Not all PICU and HD patients who require CPR had a code activation; this may have contributed to the low incidence of IHCA in our study. It would have been ideal to report functional outcomes of our survivors, however, not all patients had documented paediatric cerebral performance category scores prior to and after cardiac arrest. Given the low incidence of paediatric IHCA, and the current lack of adequate assessment of neurologic outcomes in our survivors, the authors propose establishment of a regional paediatric cardiac arrest registry, as well as proper attention to functional outcome assessment in paediatric IHCA survivors at our centre.

## Conclusion

We found an association between age, duration of CPR, use of adrenaline, calcium or bicarbonate during CPR, PIM-II scores, first recorded post-resuscitation pH and hyperglycaemia within 24 hours post-resuscitation and hospital survival. There is a marked difference in resuscitation outcomes for paediatric IHCA across Asia. Future regional collaboration and development of a paediatric cardiac arrest registry will be helpful to identify factors that can potentially improve outcomes of paediatric cardiac arrest within Asia.

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