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ORIGINAL ARTICLE

Changing Risk of In-Hospital Cardiac Arrest in Children Following Cardiac Surgery in Victoria, Australia, 2007–2016

Misha Dagan, MD [a,d], Warwick Butt, MBBS [a,c,d], Johnny Millar, PhD [a,c,d], Yves d'Udekem, MD, PhD [b,c,d], Jenny Thompson [a,c], Siva P. Namachivayam, MBBS, MEpi [a,c,d*]

[a]Intensive Care Unit, Royal Children's Hospital, Melbourne, Vic, Australia
[b]Cardiac Surgery, Royal Children's Hospital, Melbourne, Vic, Australia
[c]Murdoch Children's Research Institute, Melbourne, Vic, Australia
[d]Department of Paediatrics, University of Melbourne, Vic, Australia

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Background Reported incidence of in hospital cardiac arrest (IHCA) after paediatric cardiac surgery varies between 3–4% in high income countries and this risk may have changed over time. We sought to examine this trend in detail.

Methods A retrospective observational study of 3,781 children who underwent 4,938 cardiac surgeries between 1 January 2007 and 31 December 2016 in a tertiary children's hospital. IHCA was defined as cessation of cardiac mechanical activity requiring cardiac massage for $\geq$1 minute. Surgical complexity was categorised using risk adjusted congenital heart surgery (RACHS-1) category. Poisson regression was used to analyse trends for every two-year period.

Results There were a total of 211 (4.3%) IHCA events after surgery. These patients were younger, more likely to have had a premature birth, have a chromosomal or genetic syndrome association and have a high surgical complexity. Overall, there was a 52% reduction in IHCA rate over 10 years: reducing from 5.4 /100 surgeries in 2007–08 to 2.6/100 surgeries in 2015–16 (p-trend = <0.001). The reduction was mainly seen in low-to-moderate risk categories (RACHS-1 categories 1–4) and not in high risk categories (RACHS-1 category 5–6). Children in high risk categories were 13.6 times more likely to experience an IHCA (compared to low risk categories). Overall hospital mortality for children suffering IHCA decreased from 42.5/100 patients in 2007–08 to 11.1/100 patients in 2015–16 (p-trend = 0.037).

Conclusions The IHCA rate following cardiac surgery has more than halved over the last decade; children who experience IHCA also have lower mortality than in previous years. High risk procedures still have a substantial rate of IHCA and efforts are needed to minimise the burden further in this population.

Keywords Cardiac arrest • In-hospital • Intensive care • Child • Cardiac surgery • Cardiopulmonary resuscitation

*Corresponding author at: Intensive Care Unit, The Royal Children's Hospital, Flemington Rd, Parkville 3052, Victoria, Australia. Tel.: +61 3 93455093; Fax: +61 3 93456960., Email: siva.namachivayam@rch.org.au

Introduction

Recent single centre studies and registry reports suggest that in-hospital cardiac arrest (IHCA) occurs in 3% to 4% of children following cardiac surgery [1–3]. This rate is much higher in high risk groups, such as children undergoing complex operations and those who have had a previous cardiac arrest, with IHCA rates reaching up to 20% in these children [1,3–5]. While the majority of IHCA following cardiac surgery occurs in the highly monitored intensive care setting, outcomes are still poor with hospital mortality approaching 30–50% and poor neurological outcomes in up to 25% of survivors [4,6,7].

Collected reviews from several investigators over the last 15 years suggest that both the incidence of, and survival following, IHCA after cardiac surgery is improving. Incidence has fallen to 3–4% from 6–10% and survival has risen to 70% from 19% [1,3,4,8–11]. These estimates, however, come from different regions, with studies conducted at different time periods and utilising differing definitions of IHCA. Genuine changes in IHCA rates after cardiac surgery over time can only be inferred from such reports. In addition, there has been limited discussion about factors that might have had an impact on changes in IHCA rate. Monitoring IHCA trends and understanding factors that may have influenced these trends is a high priority for quality improvement. In this report, we analyse changes in the rates of IHCA and mortality in children experiencing IHCA following cardiac surgery, and discuss factors which may have influenced these changes over a 10-year period.

Materials and Methods

Study Population and Setting

The study was undertaken at the Royal Children's Hospital, Melbourne (RCH), Australia. The institution is a referral centre for specialised paediatric cardiac services and performs all major paediatric cardiac surgeries for children from the Australian states of Victoria, Tasmania, South Australia, Northern Territory and Western Australia, encompassing a population of approximately eight million. The Paediatric Intensive Care Unit (PICU) is a 30-bed multidisciplinary unit with a dedicated 12-bed cardiac ICU. The study was approved by the Human Research and Ethics Committee at The Royal Children's Hospital (DA004-2016-18). Study participants were children <18 years of age undergoing cardiac surgery between January 2007 and December 2016. Participants were identified from the PICU database and information was collected from this resource and medical records. Study participants were restricted to infants and children for whom a risk adjustment for congenital heart surgery (RACHS-1) category could be assigned (see Appendix A) [12]. Overall, 206 (4%) surgeries could not be assigned a RACHS-1 category and were excluded from the analysis.

Data Collection and Study Definitions

The following variables were collected: sex, age and weight at surgery, prematurity (<37 weeks gestation), presence of underlying chromosomal or genetic syndrome association, requirement for extracorporeal life support (ECLS), duration of mechanical ventilation (MV), length of ICU and hospital stay. ECLS was the postoperative requirement for either ECMO (extracorporeal membrane oxygenation) or VAD (ventricular assist device). Underlying chromosomal or genetic syndrome was defined as defects due to specific identified genes or recognised by constellation of clinical features, eg: Down's syndrome or Velo-cardio facial syndrome [13]. Participants were categorised according to one of the six RACHS-1 categories. RACHS-1 categorises surgeries for congenital heart disease from lowest to highest risk of in-hospital mortality, with 1 being lowest and 6 being highest [12]. High complexity procedures include RACHS-1 categories 5–6, low complexity procedures include RACHS-1 categories 1–2 (Appendix A).

In-hospital cardiac arrest was defined as cessation of effective cardiac mechanical activity requiring internal or external cardiac massage for greater than or equal to one minute, as recommended by the Utstein guidelines [14]. For the IHCA cohort, additional data collected included location of arrest, time to arrest post-surgery (hours) and duration of cardiopulmonary resuscitation (CPR). Information was collected for every cardiac surgery and every IHCA event that followed a cardiac surgery.

Study Criteria and Outcomes

Episodes of IHCA were included if the arrest event occurred within the same hospital admission as the cardiac surgery. The following were exclusions: (1) Children with medical cardiac conditions, such as cardiomyopathy or myocarditis, (2) children who suffered IHCA following procedures such as cardiac catheterisation, (3) IHCA occurring prior to cardiac surgery, (4) and children with do not resuscitate orders.

The main study outcome was rate and changes in rate of IHCA during the 10-year period. The IHCA rate was expressed per 100 surgeries:

$$\text{IHCA rate per hundred surgeries} = (\text{Number of IHCAs following surgery}/\text{total number of surgeries}) \times 100$$

Recurrent IHCA events following the same cardiac surgery were included in the numerator, however the denominator remained the same.

Statistical Analysis

Baseline characteristics were compared between surgeries with IHCA and those without. Continuous variables were compared using the rank-sum test and presented as medians with interquartile range (IQR). Categorical variables were compared using the chi-squared test and presented as number (percentage). The main outcomes of interest were the IHCA rate and changing trends in IHCA rate. The IHCA rate was calculated for every 2-year period (2007–08, 2009–10, 2011–12, 2013–14, 2015–16). Poisson regression was used to estimate the incidence rate ratios (95% confidence intervals) and determine the significance of trends. The dependent variable in the model was IHCA count and the unit of analysis is each 2-year period (2007–08 being reference). A separate stratified analysis (after controlling for effect of study duration) was also performed to study the influence of surgical complexity (RACHS-1 cat1 and 2[reference]; RACHS-1 cat 3 and 4; RACHS-1 cat 5 and 6) on IHCA rate. The IHCA rate is reported using number of surgeries as denominator; this is because the risk of having a cardiac arrest is likely to follow a set of factors which is unique not only to the patient but also to the surgery and its postoperative care. Additionally, the mortality rate in patients who experienced IHCA is reported utilising patients as denominator. A two-sided p-value of less than 0.05 was considered to indicate statistical significance. All analyses were performed using Stata-IC version 15.1 (StataCorp, LP, College Station, TX, USA).

Results

Study Population and Baseline Characteristics

We analysed data from 3,781 children with congenital heart disease who underwent 4,938 surgeries during a 10-year period. A total of 382 episodes of IHCA were identified. After 171 exclusions (Figure 1), there were 211 IHCA events following surgery that met inclusion criteria. Children who had IHCA were younger, more likely to be female, to have had a preterm birth and to have an underlying chromosomal or genetic syndrome association (Table 1). Children who experienced IHCA suffered considerable morbidity, as evidenced by the higher ECLS rate (42% vs. 3%), and prolonged mechanical ventilation, intensive care and hospital length of stay. The median (IQR) duration of CPR was 12 (3–30) minutes. Eighty-two per cent (82%) of the arrests occurred in PICU, 9% in operating theatre after completion of surgery and 9% in the ward after discharge from PICU.

Table 2 compares characteristics of the 211 IHCAs after dividing them into their respective RACHS-1 categories. Children undergoing RACHS-1 category 5–6 procedures experienced more morbidity (requirement for ECLS, longer duration of ventilation and ICU stay).

Overall and RACHS-1 Category Specific IHCA Rates

The overall IHCA rate for the 10-year study period was 4.3 per 100 surgeries (Table 3); this rate declined from 5.4% in 2007–08 to 2.6% in 2015–16 (decreased by 52%) (Figure 2), corresponding to an estimated incidence rate ratio (IRR) for successive 2-year period of 0.84 (95% CI 0.76–0.92, $p < 0.001$).

When stratified by RACHS-1 category, the following results were obtained: for RACHS categories 1 and 2, the IHCA rate was 1.43/100 surgeries with an IRR for every 2-year period of 0.74 (95% CI 0.57–0.95, p = 0.02). The IHCA rate for RACHS categories 3 and 4 was 5.4/100 surgeries, with a successive 2-yearly IRR of 0.86 (95% CI 0.77–0.97, p = 0.02) and RACHS categories 5 and 6 experienced an IHCA rate of 20.9/100 surgeries and there was no change in the incidence rate ratio over the study period: 1.05 (95% CI 0.85–1.31, p = 0.61).

After controlling for the effect of study duration (10 years) and using RACHS categories 1–2 as reference, surgeries in RACHS categories 3 and 4 were 3.71 (95% CI 2.51–5.47, $p < 0.001$) times more likely to result in an IHCA and those in RACHS-1 categories 5 and 6 were 13.6 (95% CI 8.49–21.93, $p < 0.001$) times more likely to result in an IHCA respectively.

Hospital Mortality Post IHCA and for all Children Undergoing Cardiac Surgery

Hospital mortality for the 10-year period in children suffering IHCA was 30.1/100 children (Table 4); this rate dropped from 42.5/100 patients in 2007–08 to 11.1/100 patients in 2015–16, corresponding to an incidence rate ratio of 0.80 (95% CI 0.65–0.98, p = 0.037). When stratified by RACHS-1 category, the mortality rate was highest for RACHS-1 categories 5–6 patients (Table 4). Overall hospital mortality following cardiac surgery was 2.9% during the 10-year study period with an IRR of 0.82 (0.72–0.94, p = 0.004) for successive 2-year period.

IHCA Mortality Relative to All-Cause Mortality Following Cardiac Surgery

The proportion of IHCA mortality relative to all-cause mortality (Figure 3) did not significantly change over the study period (Pearson Chi^2 [4] = 4.67, p = 0.32). This indicates that the falling mortality rate in IHCA patients was in line with the downward trend seen in overall mortality following cardiac surgery. Additionally, an analysis of the proportional changes between IHCA rate and overall cardiac surgery mortality over time also did not show any significant changes over time (Pearson Chi^2 [4] = 3.21, p = 0.52), indicating the fall in IHCA rate is in proportion to fall in cardiac surgery mortality.

Discussion

Major Findings

In this analysis involving 3,781 children who underwent 4,938 cardiac surgeries, we noted a 52% reduction in the rate of IHCA over a 10-year period. The IHCA rate based on the most recent period (2015–16) was 2.6%. However, this decrease was only seen in low to moderate risk surgeries (RACHS-1 categories 1–4), with no change in high risk surgeries. Children undergoing high risk surgeries were 13.6 times more likely to experience IHCA and were less likely to survive to hospital discharge following arrest compared to those undergoing low risk surgeries. Finally, the decrease in IHCA rate and the decrease in

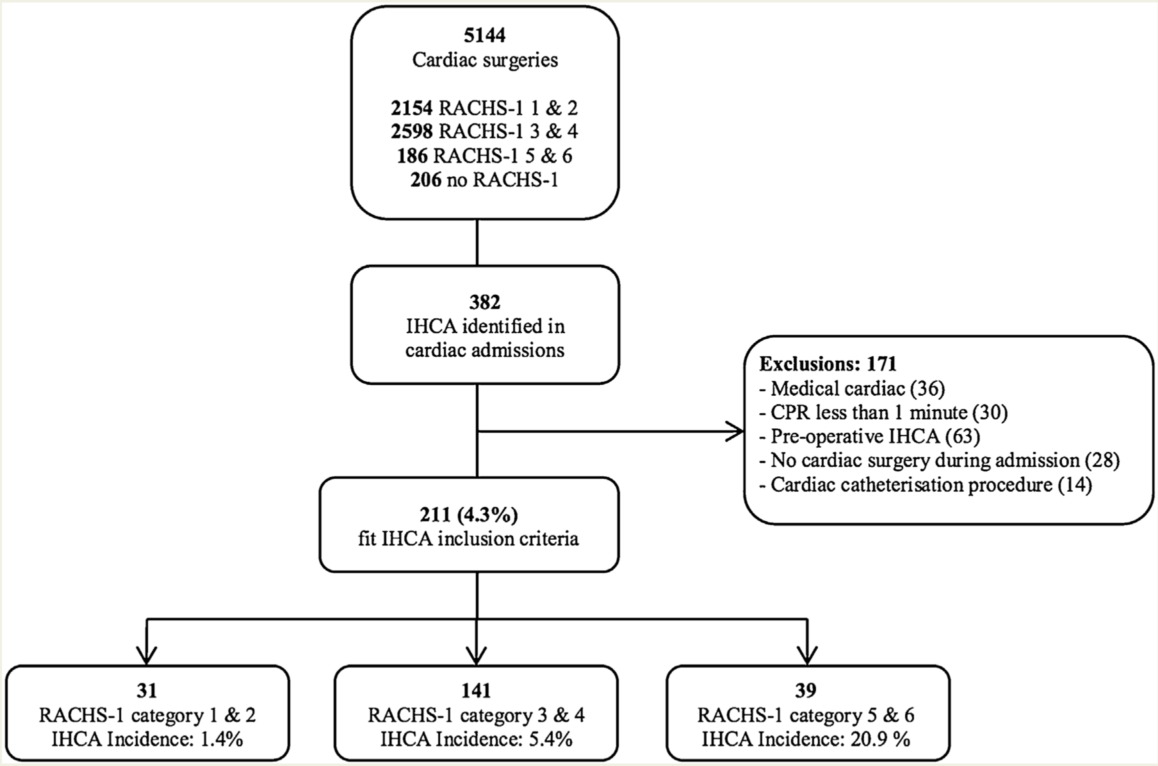

Figure 1 Flow chart of in-hospital cardiac arrest events flowing cardiac surgery by RACHS-1 categories.
Abbreviations: RACHS-1, risk adjusted congenital heart surgery; no RACHS-1, no designated RACHS-1 category; IHCA, in hospital cardiac arrest; Medical cardiac, medical illness that is cardiovascular in origin, eg cardiomyopathy, myocarditis; CPR, cardiopulmonary resuscitation.

mortality following IHCA (along with the downtrend for overall mortality following cardiac surgery) suggests that efforts to control IHCA rate can have a substantial impact on overall mortality after cardiac surgery.

Possible Reasons for Declining IHCA Rates Following Paediatric Cardiac Surgery

In attempting to explain why IHCA has become less common after cardiac surgery, it is reasonable to suggest some plausible contributors. These include incremental experience gained by surgical and medical personnel resulting in improved surgical performance and perioperative management. The development of and adherence to perioperative protocols specific to cardiac surgical patients, increased use of therapies that modulate the post cardiopulmonary-bypass inflammatory response and resultant low cardiac output syndrome [15] may have also contributed to the reduction of IHCA rates. Introduction and use of a hospital-wide medical emergency team and outreach service allowing for rapid response to the deteriorating patient and ongoing strict internal quality review processes may have also helped. It has also been suggested that early placement on ECLS for unstable postoperative patients could play a role in improving outcomes related to prevention or reduction of acidosis, earlier unloading of vulnerable myocardium and reduction in cardiac arrests [16]. It must be emphasised that the above-mentioned factors remain speculative and cannot be inferred from the current study.

As IHCA following cardiac surgery occurs in several locations (operating theatre, PICU and ward), interventions specifically aimed at reducing IHCA in these locations may also have had an impact. More than 80% of IHCA following cardiac surgery occurs in ICU [7,17], and most of these occur within the first 48 hours after surgery [1,2]. These early events are usually associated with the development of the postoperative low cardiac output state (LCOS) [8]. The occurrence and timing of LCOS is predictable [18], and very often associated with early warning signs [11]; as such a targeted approach may play a role in the reduction of cardiac arrest. LCOS protocols were proposed some time ago [19] and centres have reported the effectiveness of these protocols in terms of lives saved and also their utilisation within resource limited settings [20]. They could be effective in modern cardiac ICUs involving multiple health professionals with varying levels of expertise and experience, particularly if protocol adherence can be enhanced. Our institution, like many others, developed and implemented a protocol-based approach to the identification and early management of LCOS (shown in Appendix B), which may

Table 1 Comparison of characteristics between cardiac surgeries with and without subsequent IHCA.

Characteristic	Overall (n = 4957)	No IHCA (n = 4746)	IHCA (n = 211)	P-value
Age, days	178 (34-1536)	192 (42-1592)	20 (5-101)	<0.001
Weight, kg	6.2 (3.7-15.6)	6.5 (3.8-16.0)	3.5 (2.7-4.7)	<0.001
Sex, male	2,859 (58%)	2,761 (58%)	98 (46%)	0.001
Prematurity	640 (13%)	595 (13%)	45 (21%)	<0.001
Chromosomal/genetic syndrome	682 (14%)	646 (13%)	49 (23%)	<0.001
Requirement for ECLS	217 (4%)	129 (3%)	88 (42%)	<0.001
RACHS-1 category				<0.001
1-2	2,157 (44%)	2,126 (45%)	31 (15%)	
3-4	2,612 (53%)	2,471 (52%)	141 (67%)	
5-6	188 (4%)	149 (3%)	39 (18%)	
Mechanical ventilation, hours	22 (10-91)	21 (10-79)	226 (124-451)	<0.001
ICU length of stay, hours	47 (24-119)	46 (23-113)	266 (145-520)	<0.001
Hospital length of stay, hours	224 (131-443)	220 (130-423)	688 (358-1254)	<0.001
Location of IHCA				
PICU		-	173 (82%)	-
Theatre		-	20 (9%)	-
Ward		-	18 (9%)	-
CPR duration, minutes		-	12(3–30)	-

Continuous variables are presented as median (IQR), categorical variables are presented as n (%).
Total number of cardiac surgeries over the 10 years, excluding those without a RACHS-1 category was 4,938. In this table the number of No IHCA plus IHCA is 4,957 because there were recurrent IHCA events following the same cardiac surgery on 19 occasions.
Abbreviations: ECLS, extracorporeal life support; RACHS-1, risk adjustment for congenital heart surgery; PICU, paediatric intensive care unit; CPR, cardiopulmonary resuscitation.

Table 2 Comparison of IHCA following cardiac surgery between RACHS-1 category groupings.

Variable	RACHS-1 categories			P-value
	Category 1 & 2 (n = 31)	Category 3 & 4 (n = 141)	Category 5 & 6 (n = 39)	
Age, days	101 (48-246)	23 (6-104)	3 (2-7)	<0.001
Weight, kg	4.5 (3.1-6.8)	3.5 (2.8-4.7)	3.1 (2.6-3.7)	0.002
Sex, male	17 (55%)	62 (44%)	19 (49%)	0.52
Prematurity	11 (35%)	25 (18%)	9 (23%)	0.09
Chromosomal/genetic syndrome	11 (35%)	31 (22%)	7 (18%)	0.18
Time to arrest, hours	26 (8-96)	24 (4-119)	105 (2-353)	0.23
CPR duration, minutes^	5 (3-20)	12 (3-30)	13 (4-30)	0.57
Requirement for ECLS	9 (29%)	57 (40%)	22 (56%)	0.06
Mechanical ventilation, hours	165 (74-283)	215 (101-416)	372 (216-559)	0.003
ICU length of stay, hours	197 (117-314)	260 (129-475)	416 (262-583)	0.006
Hospital length of stay, hours	651 (203-1254)	672 (380-1249)	871 (463-1560)	0.37

Categorical variables presented as n (%), Continuous variables presented as median (interquartile range).
Abbreviations: RACHS-1, risk adjustment for congenital heart surgery; ICU, intensive care unit; ECLS, extracorporeal life support; CPR, cardiopulmonary resuscitation; ^n = 29, 129 and 39 respectively due to missing data.

have been partly responsible for the decreasing rate of IHCA.

The scientific literature over the last three decades has clearly documented the relationship between case volume and outcomes. Specialised teams, which see and treat a high volume of a cases, provide better outcomes with lower mortality [21,22]. This is particularly true in paediatric cardiac surgery where analysis has shown that the relationship is

Table 3 Overall rates and RACHS-1 category specific rates of IHCA per 100 cardiac surgeries.

Surgical category	IHCA rate per 100 surgeries*	Incidence rate ratio**	95% CI	P-value
Overall	4.3	0.84	0.76, 0.92	<0.001
RACHS-1 categories				
Category 1 & 2	1.4	0.74	0.57, 0.96	0.02
Category 3 & 4	5.4	0.86	0.77, 0.97	0.02
Category 5 & 6	20.9	1.06	0.85, 1.31	0.61

Abbreviations: RACHS-1, risk adjusted congenital heart surgery; IHCA, in-hospital cardiac arrest.
*Rate given for the 10-year study period.
**Incidence rate ratio estimated for successive 2-year study periods using 2007-08 as reference.

mediated by case-complexity and type of surgical procedure performed. High volume units (performing >350 cardiac surgeries per year) have also been shown to have lower mortality after IHCA than low volume units [3]; this is likely related to their ability to rescue patients successfully after an IHCA. Our centre performs approximately 600 such operations per year, and the low contemporary post IHCA mortality rate reported here is in keeping with this.

The use of a hospital-wide medical emergency team (MET) may also have contributed to reduction in post-cardiac surgical IHCA rate on the wards; the introduction of MET in 2002 reduced the incidence of preventable cardiac arrest and mortality at our institution [23].

Factors Associated With IHCA

The rate of IHCA is directly related to factors such as age, prematurity, underlying genetic syndrome association and surgical complexity, all of which have been reported previously [4]. While several of these factors are likely to be present in the same patient (such as young age and surgical complexity), it is likely that each factor has distinct biological reasons for influencing cardiac arrest. For example, younger age and prematurity can be seen as good surrogates for developmental immaturity of the cardiovascular system. The neonatal myocardium is particularly vulnerable to the effects of cardiopulmonary bypass and ischaemia, resulting in myocardial oedema, impaired contractility and diminished response to vasoactive medications [24]. All of these translate into a higher rate of major adverse events such as cardiac arrest, emergency chest reopening and requirement for ECMO. Not only are newborns at greater risk of the sequelae of cardiopulmonary bypass but they may be sicker preoperatively, and also require longer cardiopulmonary bypass times than older, more mature patients [3,4,11]. Further research into specific causes of IHCA following high complexity procedures could allow for more targeted management of these children. Particularly focussing on the first 48 hours following cardiac surgery, when children are at highest risk of suffering IHCA [2,25].

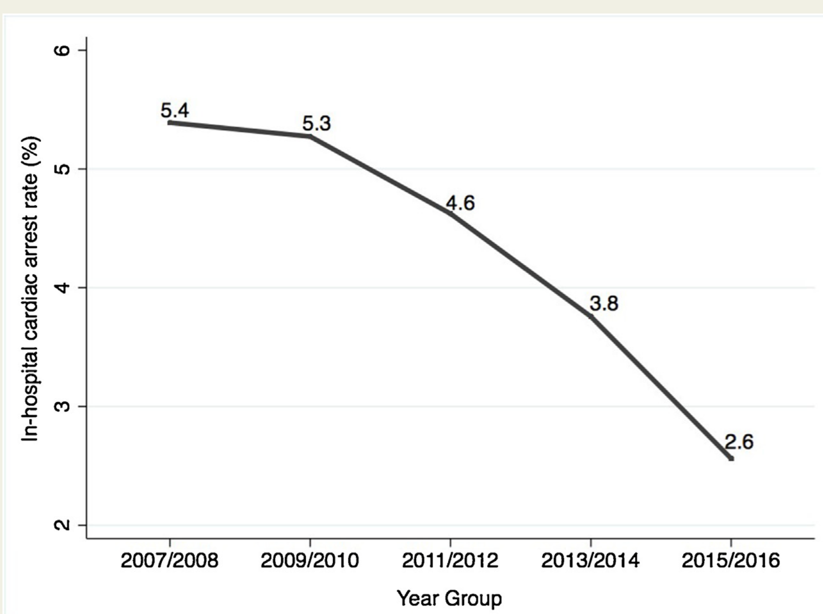

Figure 2 Incidence of in-hospital cardiac arrest in children following cardiac surgery per year group.

Table 4 Hospital mortality for children who experienced an IHCA (IHCA cohort) and for all children who underwent cardiac surgery (overall cardiac surgery cohort).

Surgical category	IHCA cohort			Overall cardiac surgery cohort		
	Mortality rate following IHCA (%)*	Incidence rate ratio (95% CI)**	P-value	Mortality rate following cardiac surgery (%)*	Incidence rate ratio (95% CI)**	P-value
Overall	30.1	0.80 (0.65-0.98)$	0.037	2.9	0.82 (0.72-0.94)$	0.004
RACHS-1 category						
Category 1&2	26.0	0.71 (0.32-1.55)	0.39	0.6	0.71 (0.45 – 1.12)	0.15
Category 3&4	28.5	0.84 (0.65-1.07)	0.16	3.7	0.78 (0.66 – 0.93)	0.007
Category 5&6	37.8	0.74 (0.48-1.13)	0.16	19.5	1.17 (0.93 – 1.47)	0.17

Abbreviations: IHCA, in-hospital cardiac arrest; CI, confidence interval; RACHS-1, risk adjusted congenital heart surgery.
*Rate given for the 10-year study period and expressed per 100 patients.
**Incidence rate ratio estimated for successive 2-year periods of study using 2007–08 as reference.
$Incidence rate ratio not controlled for RACHS-1 categories.

Study Implications

(1) With a high global burden of congenital heart disease and with >90% of children who experience this burden living in low-to-middle income countries, it can be said that IHCA following paediatric cardiac surgery is a substantial global issue [26,27]. Prevention/early treatment of LCOS in the first 24–48 hours after surgery is an important way to reduce IHCA after cardiac surgery. Currently, there are no international consensus guidelines or recommendations for the management of early postoperative LCOS. Development of such LCOS protocols, particularly if tailored to resource-limited settings, could potentially have a major impact in reducing IHCA rates. Such an approach has been shown to lead to reductions in mortality in units with no access to high cost interventions such as ECLS [20].

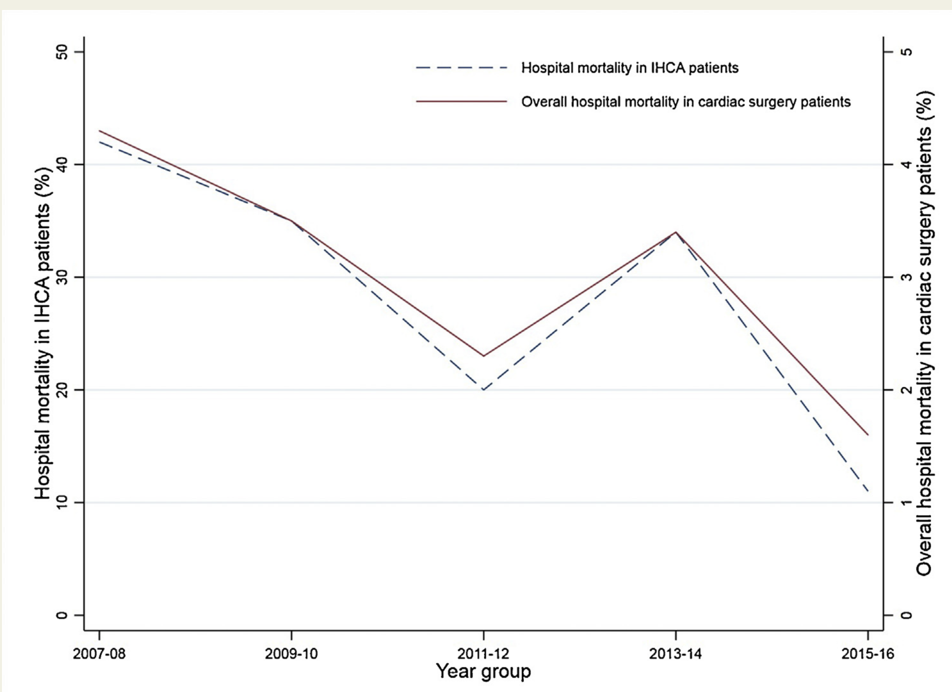

Figure 3 Proportional changes in hospital mortality for children who experienced an in-hospital cardiac arrest (IHCA) and for all children who underwent cardiac surgery.
Rate given for every 2-year study period and expressed per 100 patients.

(2) We found a high IHCA rate and high mortality following RACHS-1 categories 5 and 6 procedures, in keeping with other reports [1]. It is likely children who have an arrest in lower RACHS categories are more likely to be effectively rescued and do not eventually die compared to RACHS 5 and 6. These high risk patients are clearly at greatest risk of arrest, therefore, this should be a clear target for further improvement both in terms of preventing an arrest and also reducing mortality.

(3) The ischaemic reperfusion injury and systemic inflammatory response associated with cardiac surgery are major drivers in the development of LCOS [28]; ongoing research efforts in this area is vital to further minimise complications related to LCOS, such as cardiac arrest.

Limitations

This study has the following limitations: (a) Within the study population, we did not make distinctions between the different causes of IHCA, timing of IHCA, and how these may have changed over the years. The influence of these factors and their relation to IHCA should be addressed in future studies. (b) Another important limitation is the lack of investigation into medical and nursing staffing patterns and their changes over time and how they may have influenced IHCA rates. (c) This report comes from a single institution, albeit one that services a large geographical area and operates on a high volume of complex congenital heart disease.

Conclusions

In conclusion, data from this single, large centre study shows that there was a 52% reduction in the rate of IHCA in children following cardiac surgery over the 10-year study period. This reduction was likely possible for many reasons, including personnel and organisational factors and evolving developments in the care of children requiring cardiac surgery. The fall in IHCA rate, along with a fall in mortality among patients experiencing an IHCA, is likely to have contributed to reductions in all-cause mortality after cardiac surgery. High complexity procedures still have a substantial rate of IHCA, and efforts targeted to this population are needed to further minimise the burden.

Conflicts of Interest

No potential conflicts of interest exist for any of the authors.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.hlc.2018.11.003.

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