



Clinical paper

Risk factors and outcomes of in-hospital cardiac arrest following pediatric heart operations of varying complexity[☆]

Punkaj Gupta^{a,*}, Mallikarjuna Rettiganti^b, Howard E. Jeffries^{c,d}, Matthew C. Scanlon^{d,e}, Nancy S. Ghanayem^e, Jennifer Daufeldt^d, Tom B. Rice^{d,e}, Randall C. Wetzel^{d,f}

^a Division of Pediatric Cardiology, Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, AR, United States

^b Section of Biostatistics, Department of Pediatrics, University of Arkansas for Medical Sciences, Little Rock, AR, United States

^c Department of Pediatrics, Seattle Children's Hospital, University of Washington School of Medicine, Seattle, WA, United States

^d Virtual PICU Systems, LLC, Los Angeles, CA, United States

^e Division of Critical Care, Department of Pediatrics, Medical College of Wisconsin, Milwaukee, WI, United States

^f Division of Critical Care Medicine, Department of Pediatrics and Anesthesiology, Children's Hospital Los Angeles, USC Keck School of Medicine, Los Angeles, CA, United States

ARTICLE INFO

Article history:

Received 17 February 2016

Received in revised form 5 April 2016

Accepted 25 April 2016

Keywords:

Cardiac arrest
Cardiac surgery
Complexity
Heart operation
Children

ABSTRACT

Background: Multi center data regarding cardiac arrest in children undergoing heart operations of varying complexity are limited.

Methods: Children <18 years undergoing heart surgery (with or without cardiopulmonary bypass) in the Virtual Pediatric Systems (VPS, LLC) Database (2009–2014) were included. Multivariable mixed logistic regression models were adjusted for patient's characteristics, surgical risk category (STS-EACTS Categories 1, 2, and 3 classified as “low” complexity and Categories 4 and 5 classified as “high” complexity), and hospital characteristics.

Results: Overall, 26,909 patients (62 centers) were included. Of these, 2.7% had cardiac arrest after cardiac surgery with an associated mortality of 31%. The prevalence of cardiac arrest was lower among patients undergoing low complexity operations (low complexity vs. high complexity: 1.7% vs. 5.9%). Unadjusted outcomes after cardiac arrest were significantly better among patients undergoing low complexity operations (mortality: 21.6% vs. 39.1%, good neurological outcomes: 78.7% vs. 71.6%). In adjusted models, odds of cardiac arrest were significantly lower among patients undergoing low complexity operations (OR: 0.55, 95% CI: 0.46–0.66). Adjusted models, however, showed no difference in mortality or neurological outcomes after cardiac arrest regardless of surgical complexity. Further, our results suggest that incidence of cardiac arrest and mortality after cardiac arrest are a function of patient characteristics, surgical risk category, and hospital characteristics. Presence of around the clock in-house attending level pediatric intensivist coverage was associated with lower incidence of post-operative cardiac arrest, and presence of a dedicated cardiac ICU was associated with lower mortality after cardiac arrest.

Conclusions: This study suggests that the patients undergoing high complexity operations are a higher risk group with increased prevalence of post-operative cardiac arrest. These data further suggest that patients undergoing high complexity operations can be rescued after cardiac arrest with a high survival rate.

© 2016 Elsevier Ireland Ltd. All rights reserved.

Introduction

The incidence of post-operative cardiac arrest after pediatric heart surgery ranges from 2% to 6% with an associated mortality of 42–50%.^{1–3} With improving recognition, rapid response systems, and rapid deployment extracorporeal cardiopulmonary resuscitation (ECPR), survival following cardiac arrest appears to be improving.^{4,5} Cardiac surgery in children is now being offered to children with greater comorbidities and increasingly complex heart

[☆] A Spanish translated version of the abstract of this article appears as Appendix in the final online version at <http://dx.doi.org/10.1016/j.resuscitation.2016.04.022>.

* Corresponding author at: Division of Pediatric Cardiology, Department of Pediatrics, University of Arkansas for Medical Sciences, College of Medicine, Arkansas Children's Hospital, 1 Children's Way, Slot 512-3, Little Rock, AR 72223, United States.

E-mail address: pgupta2@uams.edu (P. Gupta).

defects in centers with varying levels of expertise, potentially leading to increased post-operative complications.^{6–8} It is postulated that patient related morbidities, complexity of cardiac surgery, and hospital characteristics are potential risk factors for post-operative cardiac arrest; however, definitive multi-center data regarding cardiac arrest in children undergoing heart operations of varying complexity are limited.

To address these knowledge gaps, this study evaluated the epidemiology and outcomes of cardiac arrest in children undergoing heart operations of varying complexity using the Virtual Pediatric Systems (VPS, LLC) Database. A secondary objective of this study was to identify the risk factors associated with incidence of cardiac arrest and mortality after cardiac arrest in children undergoing cardiac surgery. The outcomes evaluated included odds of cardiac arrest, intensive care unit (ICU) mortality after cardiac arrest, and good neurological outcomes at ICU discharge among patients with cardiac arrest.

Materials and methods

Data source

The VPS, LLC Database is an online pediatric critical care network formed by NACHRI (National Association of Children's Hospitals and Related Institutions) (now part of the Children's Hospital Association) and Children's Hospital Los Angeles to develop a web-based database with prospective data collection using standardized clinical data definitions, data quality control and data analysis. The VPS database is a prospective observational cohort of consecutive PICU admissions from a diverse set of hospitals caring for children in the United States. Data is collected and entered by trained individuals. VPS performs initial and quarterly inter-rater reliability (IRR) testing. The IRR concordance in the VPS database is consistently above 95%. There is extensive quality validation performed by VPS staff prior to release of the data for analysis, and thus the data has better reliability. The University of Arkansas for Medical Sciences Institutional Review Board for the protection of human subjects reviewed the study protocol and determined that querying de-identified patient data does not fall under the jurisdiction of the Institutional Review Board review process.

Patient population

This analysis focused on the most recent six years (2009–2014) of de-identified data available in the VPS Database. Patients <18 years of age who underwent operations (with or without cardiopulmonary bypass) for congenital heart disease at one of the participating PICUs in the VPS database were included. The initial study population included 40,903 ICU admissions from 64 hospitals. ICU readmissions during the same hospital stay were excluded (3658 ICU admissions). ICU admissions with no documented first cardiovascular operation of hospital admission or index operation (1352 ICU admissions), and ICU admissions associated with surgical closure of an isolated patent ductus arteriosus (380 ICU admissions) were also excluded. ICU admissions associated with operations that were not classified into one of the Society of Thoracic Surgeons-European Association for Cardiothoracic Surgery (STS-EACTS) Mortality Categories (category 1, lowest mortality risk; category 5, highest mortality risk) (8603 ICU admissions) were also excluded.⁹ The final study population included 26,909 patients (or ICU admissions) from 62 hospitals. The study exclusions applied in our study were similar to other studies in pediatric cardiac surgical population.^{1,10}

Data collection

Data on demographics, patient diagnoses, cardiac arrest, conventional mechanical ventilation, severity of illness scores, and outcomes were collected. Specific demographic and severity of illness data included age, gender, developmental disorder, failure to thrive, genetic disorder, low birth weight, Pediatric Index of Mortality 2 (PIM-2) score, and Pediatric Risk of Mortality III (PRISM III) score.^{11,12} The severity of illness scores for the purpose of this study were calculated at the time of ICU admission after cardiac surgery. For the purpose of this study, cardiac arrest was defined as any event characterized by either pulselessness or critically compromised perfusion treated with external chest compressions and/or defibrillation.¹³ Patients were grouped into two levels of complexity on the basis of the STS-EACTS Mortality Categories (Categories 1, 2, and 3 are classified as “low” complexity and Categories 4 and 5 classified as “high” complexity).¹ Data were also collected on the use of cardiopulmonary bypass (CPB) pump during the cardiac surgery, use of extracorporeal membrane oxygenation (ECMO) after cardiac surgery, mortality, and good neurological outcomes.

Neurological status was assessed at the time of discharge using the Pediatric Cerebral Performance Category (PCPC) scale which divides outcome into the following six categories: (1) normal, age-appropriate neurodevelopment function, (2) mild disability, (3) moderate disability, (4) severe disability, (5) coma or vegetative state, and (6) brain death.^{14,15} Good neurological status was defined as a score of 1, 2, 3 or no change in score from pre arrest to hospital discharge.^{14,15} Center characteristics were also collected, including average annual ICU discharges per center, average annual number of cardiac surgery cases per center, presence of dedicated Cardiac ICU, around-the-clock presence of in-house attending level cardiac intensivist (24/7 coverage), free-standing children's hospital, university affiliation (includes both university-based and university-affiliated hospitals), and residency and fellowship training programs. The average annual program volume for each particular variable (ICU discharges, cardiac surgery cases) was calculated by dividing the number of patients receiving that particular intervention by the number of months that the program participated in the database during the study period and then multiplying by 12.

Statistical analysis

We summarized and compared demographics, operation details, clinical characteristics, and hospital characteristics between cardiac arrest and no cardiac arrest groups. Descriptive statistics such as mean and standard deviation for continuous variables and median and percent for categorical variables were used to summarize predictors and outcomes. Categorical variables were compared using a Chi-squared test of association, while continuous variables were compared between groups using a two-sample *t*-test.

Multivariate mixed effects logistic regression models with random center effects were used to identify simultaneous risk factors associated with odds of cardiac arrest and mortality among those with cardiac arrest.

The final multivariate model predicting cardiac arrest included the following patient level predictors: age (<28 days, 29 days to <1 year, 1 year to <8 years, and >8 years), gender, weight-for-age Z-score, PIM-2 score, complexity of operation performed, genetic abnormality, development disorder, single ventricle anatomy, use of mechanical ventilation prior to surgery, pulmonary hypertension, sepsis, acute lung injury, renal failure, seizures, arrhythmia, vocal cord paralysis, diaphragm paralysis, chylothorax, brain hemorrhage, presence of arterial line, use of mechanical ventilation, presence of central venous catheter, and use of hemodialysis

catheter. The hospital characteristics included in the multivariable model predicting cardiac arrest included presence of residency or fellowship training, 24/7 coverage, dedicated cardiac ICU, and average annual cardiac surgery cases for each center. In addition to the variables included above, we included deployment of ECMO, and use of ventricular assist device in the model predicting mortality among patients with cardiac arrest. PRISM-3 score, failure to thrive, cardiopulmonary bypass were multi collinear and were not included in the multivariate models. Model fit was evaluated using the generalized Chi-squared statistic. As a sensitivity analysis, we identified predictors of cardiac arrest and mortality after cardiac arrest after including readmissions within the same hospital stay. We analyzed length of stay in the ICU as time to death while censoring patients who did not die in the ICU. We used Kaplan–Meier analysis (log-rank test) to compare survival estimates between the cardiac arrest and no cardiac arrest groups as a function of ICU length of stay. All tests were two-sided assuming a significance level of 5%. All statistical analyses were generated using SAS/STAT software, Version 9.4 of the SAS System for Windows 7, Copyright © 2002–2012 SAS Institute Inc. All plots were generated using the ggplot2 package in R (R Core Team, Vienna, Austria).

Results

Study population characteristics

A total of 26,909 patients from 62 centers were included. Of these, 736 patients (2.7%) had cardiac arrest with an associated mortality of 31% ($n = 229$). The overall mortality was 3.0% ($n = 809$), and the mortality in those without cardiac arrest was 2.2% ($n = 580$). Overall, 6826 patients (25.4%) received high complexity operations (STS-EACTS mortality categories 4 and 5). By univariate analysis, cardiac arrest rate was associated with younger age, lower weight, increased presence of pre-operative morbidities, and higher severity of illness scores. Patients who had a cardiac arrest were more commonly associated with high complexity operations, need for reoperation, and deployment of ECMO. Diagnoses such as single ventricle anatomy, pulmonary hypertension, acute lung injury, seizures, sepsis, and renal failure were more common in patients with cardiac arrest. Complications such as vocal cord paralysis, diaphragm paralysis, chylothorax, and arrhythmias were also more common in the cardiac arrest group (Table 1).

We further stratified the cardiac arrest patients by surgical complexity of heart operation performed during their hospital stay (e-Table 1 of the online supplement). Patients undergoing high complexity operations were younger in age, and had higher severity of illness scores at ICU admission. Patients undergoing high complexity operations more commonly had single ventricle anatomy, need for reoperation, deployment of ECMO, renal failure, arrhythmias, and use of mechanical ventilation.

Variation in rates of cardiac arrest and outcomes after cardiac arrest across operations of varying complexity

Patients undergoing low complexity operations had a lower incidence of cardiac arrest as compared to patients undergoing high complexity operations (low complexity vs. high complexity: 1.7% vs. 5.9%) (Table 2). Outcomes after cardiac arrest were significantly better in patients undergoing low complexity operations (mortality: 21.6% vs. 39.1%, good neurological outcomes: 78.7% vs. 71.6%). After adjusting for patient and center characteristics, odds of cardiac arrest was significantly lower among patients undergoing low complexity operations (Odds Ratio, OR: 0.55, 95% Confidence Interval, CI: 0.46–0.66). Though not statistically significant, there are trends toward lower mortality after cardiac arrest in

children undergoing low complexity operations (OR: 0.79, 95% CI: 0.49–1.28). Regardless of the complexity of operation performed, there was no difference in good neurological outcomes after cardiac arrest (OR: 0.61, 95% CI: 0.15–2.41) (Table 2). Overall mortality in the study population increased with increasing ICU length of stay.

Risk factors associated with incidence of cardiac arrest and mortality after cardiac arrest

In adjusted models, patient factors associated with post-operative cardiac arrest included younger age, lower weight, high complexity operations, use of mechanical ventilation before surgery, higher PIM-2 score, single ventricle anatomy, pulmonary hypertension, acute lung injury, renal failure, presence of chylothorax, arrhythmia, seizures, brain hemorrhage, use of mechanical ventilation after surgery, and presence of hemodialysis catheter. Presence of an in-house attending level pediatric intensivist (24/7 coverage) was independently associated with lower incidence of post-operative cardiac arrest (Table 3). The independent factors associated with mortality after cardiac arrest included younger age, use of ECMO, renal failure, brain hemorrhage, and presence of hemodialysis catheter. Presence of a dedicated cardiac ICU was associated with lower mortality after cardiac arrest (Table 4). Further, we identified predictors of cardiac arrest and mortality after cardiac arrest after including ICU readmissions within the same hospital stay. The predictors from these sensitivity analyses demonstrated fairly similar results as the original analyses (e-Tables 2 and 3 of the online supplement).

Discussion

Data from this large, multi-center study establish that post-operative cardiac arrest occurs in approximately 3% of patients undergoing pediatric heart operations with an associated mortality of 31%. The prevalence of cardiac arrest increases with increasing case complexity. However, the risk of mortality and good neurological outcomes after cardiac arrest remain similar regardless of level of complexity of operation performed. Further, our results suggest that in children undergoing heart surgery, cardiac arrest and mortality after cardiac arrest are a function of patient characteristics, surgical risk category, and hospital characteristics.

To date, few studies have investigated the outcomes of cardiac arrest in children with heart disease.^{1–3} In a recent study from The Society of Thoracic Surgeons Congenital Heart Surgery Database (STS-CHSD), the authors reported a mortality of 50% after post-operative cardiac arrest among children undergoing heart operations.¹ The results from our study are in contrast to this previous study; as we report a mortality of only 31% after cardiac arrest in this select patient population. The relatively high survival rates even among patients undergoing high complexity operations may be partially attributable to the fact that the arrests in our study took place in the highly monitored ICUs, in which rapid and appropriate defibrillation of shockable rhythms, and high quality CPR may be more likely to occur.^{16–19} Another reason for lower mortality in our study could be due to the fact that we reported data only on mortality at ICU discharge. It is possible that patients may have been transferred to wards prior to their death, and our study may have missed the mortality outcome of these patients at hospital discharge.

In our unadjusted analysis, we found that mortality after cardiac arrest was higher in patients undergoing high complexity operations as compared to patients undergoing low complexity operations. On the surface, this finding supports the common anecdotal impression that outcomes among patients undergoing high complexity operations are associated with poor outcomes. In our

Table 1
Patient and center characteristics.

Variable	Overall (N = 26,909)	No cardiac arrest (N = 26,173)	Cardiac arrest (N = 736)	P
Demographics				
Age (months)	37.6 (55.7)	38.0 (55.7)	25.3 (52.6)	<0.001
Weight-for-age Z-score	−0.9 (1.4)	−0.9 (1.4)	−1.1 (1.4)	<0.001
Male gender	14,821 (55.1%)	14,427 (55.1%)	394 (53.5%)	0.39
Genetic disorder	4829 (17.9%)	4679 (17.9%)	150 (20.4%)	0.08
Development disorder	769 (2.9%)	732 (2.8%)	37 (5.0%)	<0.001
Failure to thrive	2369 (8.8%)	2259 (8.6%)	110 (14.9%)	<0.001
Low birth weight	1394 (5.2%)	1330 (5.1%)	64 (8.7%)	<0.001
Altered code status	5959 (22.4%)	5757 (22.2%)	202 (30.2%)	<0.001
Operation details				
CPB case	18,660 (69.3%)	18,378 (70.2%)	282 (38.3%)	<0.001
High complexity operation ^a	6826 (25.4%)	6424 (24.5%)	402 (54.6%)	<0.001
Need for reoperation	4090 (15.2%)	3687 (14.1%)	403 (54.8%)	<0.001
ECMO	985 (3.7%)	678 (2.6%)	307 (41.7%)	<0.001
Ventricular assist device	32 (0.1%)	26 (0.1%)	6 (0.8%)	<0.001
Clinical characteristics				
PIM-2 score	−3.8 (1.3)	−3.9 (1.3)	−2.7 (1.6)	<0.001
PRISM-3 score	7.0 (5.3)	6.9 (5.1)	11.0 (8.1)	<0.001
Common ventricle	4387 (16.3%)	4154 (15.9%)	233 (31.7%)	<0.001
Heart failure	5941 (22.1%)	5294 (20.2%)	647 (87.9%)	<0.001
Pulmonary hypertension	1401 (5.2%)	1290 (4.9%)	111 (15.1%)	<0.001
Use of MV before surgery	2547 (9.5%)	2268 (8.7%)	279 (37.9%)	<0.001
Acute lung injury	7650 (28.4%)	7308 (27.9%)	342 (46.5%)	<0.001
Renal failure	805 (3.0%)	670 (2.6%)	135 (18.3%)	<0.001
Vocal cord paralysis	861 (3.2%)	806 (3.1%)	55 (7.5%)	<0.001
Diaphragm paralysis	563 (2.1%)	527 (2.0%)	36 (4.9%)	<0.001
Chylothorax	365 (1.4%)	329 (1.3%)	36 (4.9%)	<0.001
Arrhythmia	4616 (17.2%)	4301 (16.4%)	315 (42.8%)	<0.001
Seizures	790 (2.9%)	675 (2.6%)	115 (15.6%)	<0.001
Sepsis	325 (1.2%)	290 (1.1%)	35 (4.8%)	<0.001
Brain hemorrhage	132 (0.5%)	105 (0.4%)	27 (3.7%)	<0.001
Arterial line	26,183 (97.3%)	25,467 (97.3%)	716 (97.3%)	0.97
Mechanical ventilation	20,589 (76.5%)	19,894 (76.0%)	695 (94.4%)	<0.001
Central venous catheter	21,930 (81.5%)	21,261 (81.2%)	669 (90.9%)	<0.001
Hemodialysis catheter	99 (0.4%)	75 (0.3%)	24 (3.3%)	<0.001
Hospital characteristics				
Residency training	14,117 (52.5%)	13,782 (52.7%)	335 (45.5%)	<0.001
Fellowship training	20,390 (75.8%)	19,848 (75.8%)	542 (73.6%)	0.17
University affiliated	12,815 (47.6%)	12,526 (47.9%)	289 (39.3%)	<0.001
Freestanding children's	19,110 (71.0%)	18,645 (71.2%)	465 (63.2%)	<0.001
24/7 coverage	16,488 (61.3%)	16,099 (61.5%)	389 (52.9%)	<0.001
Dedicated cardiac ICU	16,457 (61.2%)	15,986 (61.1%)	471 (64.0%)	0.11
Average annual ICU discharges per center	940 (480)	942 (481)	853 (426)	<0.001
Average annual cardiac surgery cases per center	340 (185)	340 (185)	333 (176)	0.35
Outcomes				
ICU Mortality	809 (3.0%)	580 (2.2%)	229 (31.1%)	<0.001
Good neurological outcome	10,401 (98.3%)	10,268 (98.1%)	133 (75.1%)	<0.001
ICU length of stay (d)	9.5 (13.0)	9.0 (12.2)	26.7 (24.0)	<0.001
ICU LOS in died patients (d)	27.5 (24.0)	28.0 (23.4)	26.3 (25.3)	0.40
Duration of MV (d)	6.3 (11.0)	5.8 (10.1)	20.6 (21.1)	<0.001
Duration of MV in died patients (d)	26.0 (23.8)	26.7 (23.8)	24.3 (23.9)	0.23

Continuous variables are summarized as mean (SD). Categorical variables are summarized as N (%).

^a High complexity operations are represented by STS-EACTS Categories 4–5.

Abbreviations: CPB: cardiopulmonary bypass; PIM: Pediatric Index of Mortality; PRISM: pediatric risk of mortality; ECMO: extracorporeal membrane oxygenation; MV: mechanical ventilation; ICU: intensive care unit.

study, the patients undergoing high complexity operations were younger in age and had higher severity of illness scores, increased need for reoperation, increased ECMO deployment, and increased organ dysfunction. Of note, after controlling for important potentially confounding patient's characteristics, surgical risk category, and hospital characteristics, there was no survival disadvantage after cardiac arrest for patients undergoing high complexity operations compared to patients undergoing low complexity operations. These data suggest that the patients undergoing high complexity operations are a higher risk group in general, and that these patients have a higher mortality risk likely related to both their comorbidities as well as to their surgical complexity.

The presence of an in-house attending level pediatric intensivist was independently associated with a lower incidence of cardiac

arrest, and presence of dedicated cardiac ICU was associated with lower mortality after cardiac arrest. Differences across centers with respect to rates of cardiac arrest, and mortality in those with cardiac arrest following heart surgery have been previously evaluated in the pediatric population.^{1,20,21} For example, our previous work has suggested that high performing centers do not necessarily have a lower rate of cardiac arrest or other important post-operative complications following congenital heart surgery, but instead a lower rate of death in those who develop complications (e.g. lower “failure to rescue”).¹ It has been demonstrated that implementation of 24/7 pediatric intensivist coverage was associated with improved outcomes in children with critical illness.²¹ Contrary to the existing literature, our study demonstrated that presence of a dedicated cardiac ICU was associated with lower mortality after cardiac arrest.

Table 2

Patient and center data across operations of varying complexity.

	All patients	Low complexity operations	High complexity operations
Number of patients	26,909	20,083	6826
Number of centers	62	61	57
Range of center-specific sample size	1–1978	1–1444	1–534
Overall mortality	809 (3.0%)	260 (1.3%)	549 (8.0%)
Range of center-specific mortality in all patients	0–100%	0–33%	0–100%
Overall good neurological outcomes ^a	10,401 (97.7%)	7861 (98.9%)	2540 (94.2%)
Range of center-specific good neurological outcomes in all patients	0–100%	95–100%	0–100%
Number of cardiac arrest	736 (2.7%)	334 (1.7%)	402 (5.9%)
Range of center-specific rate of cardiac arrest	0–50%	0–50%	0–17%
Mortality in those with cardiac arrest	229 (31.1%)	72 (21.6%)	157 (39.1%)
Range of center-specific mortality in those with cardiac arrest	0–100%	0–100%	0–100%
Good neurological outcomes in those with cardiac arrest ^a	133 (75.1%)	70 (78.7%)	63 (71.6%)
Range of center-specific good neurological outcomes in those with cardiac arrest	50–100%	0–100%	0–100%
Unadjusted		OR (95% CI)	
Cardiac arrest rate	N/A	0.27 (0.23–0.31)	Reference
Mortality after cardiac arrest	N/A	0.43 (0.31–0.60)	Reference
Good neurological outcomes after cardiac arrest	N/A	1.46 (0.73–2.92)	Reference
Adjusted		OR (95% CI)	
Cardiac arrest rate	N/A	0.55 (0.46–0.66)	Reference
Mortality after cardiac arrest	N/A	0.79 (0.49–1.28)	Reference
Good neurological outcomes after cardiac arrest	N/A	0.61 (0.15–2.41)	Reference

^a Good Neurological Outcomes available in 10,646 patients (among all patients), and 177 patients with cardiac arrest.

In a recent study, Burstein et al. did not detect a difference in post-operative morbidity or mortality associated with the presence of a dedicated cardiac ICU for children undergoing heart surgery.²²

Our study has several potential limitations. This study is subject to the limitations of all observational analyses, including selection bias, residual confounding, and measurement error. Other limitations of the present study are related to the nature of the VPS dataset. Not all US pediatric hospitals participate in the VPS database. Nonetheless, the present report represents the most inclusive evaluation, with data from 64 pediatric heart centers.

We were also limited to consideration of variables collected in the VPS database. As such, we could not evaluate or account for the

potential impact of variables such as hospital structure and process measures (e.g., mock codes, debriefing after codes, rapid response teams, and use of telemetry), training or availability of ICU personnel, or nursing factors, in our evaluation of cardiac arrest rates, for example.

Our data reported an ICU mortality of 2.2% in the No cardiac arrest group. This finding is somewhat counterintuitive. Despite mortality, the patients in this group were not reported to having a cardiac arrest during their ICU stay. It is possible that mortality was an expected outcome in these patients, and the data abstractors did not code them as having a cardiac arrest due to this expected outcome. Being a retrospective, database study, we do not have an

Table 3

Risk factors associated with cardiac arrest after pediatric heart surgery.

Variable	Comparison	Odds Ratio (95% CI)	P
Age	<28 days vs. >8 years	1.16 (0.93, 1.43)	0.19
	28 days to <1 year vs. >8 years	0.73 (0.56, 0.96)	0.03
	<1 year to <8 years vs. >8 years	1.11 (0.82, 1.50)	0.50
Weight-for-age Z-score	1 SD increase	0.93 (0.88, 0.99)	0.03
Gender	Female vs. Male	1.18 (1.01, 1.38)	0.04
Genetic disorder	Yes vs. no	0.99 (0.81, 1.21)	0.89
Development disorder	Yes vs. no	1.71 (1.16, 2.51)	0.01
Low birth weight	Yes vs. no	0.86 (0.64, 1.17)	0.34
High complexity case	Yes vs. no	1.81 (1.51, 2.16)	<0.001
Use of MV before surgery	Yes vs. no	2.79 (2.33, 3.35)	<0.001
PIM-2 score	1 unit increase	1.28 (1.20, 1.36)	<0.001
Common ventricle	Yes vs. no	1.30 (1.08, 1.57)	0.01
Pulmonary hypertension	Yes vs. no	1.80 (1.42, 2.28)	<0.001
Acute lung injury	Yes vs. no	1.50 (1.27, 1.77)	<0.001
Renal failure	Yes vs. no	2.92 (2.29, 3.71)	<0.001
Vocal cord paralysis	Yes vs. no	1.12 (0.77, 1.64)	0.54
Diaphragm paralysis	Yes vs. no	1.12 (0.70, 1.79)	0.64
Chylothorax	Yes vs. no	1.65 (1.11, 2.47)	0.01
Arrhythmia	Yes vs. no	2.69 (2.29, 3.16)	<0.001
Seizures	Yes vs. no	3.60 (2.82, 4.59)	<0.001
Sepsis	Yes vs. no	0.92 (0.61, 1.39)	0.69
Brain hemorrhage	Yes vs. no	2.13 (1.27, 3.57)	<0.001
Arterial line	Yes vs. no	0.58 (0.35, 0.96)	0.04
Mechanical Ventilation	Yes vs. no	1.52 (1.07, 2.16)	0.02
Central venous catheter	Yes vs. no	1.31 (1.00, 1.73)	0.05
Hemodialysis catheter	Yes vs. no	1.98 (1.13, 3.46)	0.02
24/7 coverage	Yes vs. no	0.35 (0.26, 0.47)	<0.001
Cardiac ICU	Yes vs. no	1.04 (0.81, 1.32)	0.78
Residency or fellowship training	Yes vs. no	0.82 (0.60, 1.12)	0.21
Average annual cardiac surgery cases per center	100 case increase	1.00 (0.94, 1.07)	0.96

Table 4
Risk factors associated with mortality after cardiac arrest in children with heart surgery.

Variable	Comparison	OR (95% CI)	P
Age	<28 days vs. >8 years	0.47 (0.28, 0.81)	0.01
	28 days to <1 year vs. >8 years	0.47 (0.22, 1.01)	0.05
	<1 year to <8 years vs. >8 years	0.48 (0.19, 1.22)	0.12
Weight-for-age Z-score	1 SD increase	0.87 (0.74, 1.02)	0.09
Gender	Female vs. Male	1.05 (0.71, 1.56)	0.80
Genetic disorder	Yes vs. no	1.61 (0.99, 2.62)	0.05
Development disorder	Yes vs. no	0.88 (0.30, 2.57)	0.81
Low birth weight	Yes vs. no	1.94 (0.96, 3.92)	0.07
High complexity case	Yes vs. no	1.26 (0.78, 2.03)	0.33
ECMO	Yes vs. no	3.04 (2.02, 4.57)	<0.001
Ventricular assist device	Yes vs. no	9.45 (0.96, 93.16)	0.05
Use of MV before surgery	Yes vs. no	0.81 (0.52, 1.27)	0.35
PIM-2 score	1 unit increase	1.00 (0.88, 1.14)	0.95
Common ventricle	Yes vs. no	1.60 (1.04, 2.46)	0.03
Pulmonary hypertension	Yes vs. no	0.97 (0.55, 1.72)	0.92
Acute lung injury	Yes vs. no	1.04 (0.68, 1.6)	0.85
Renal failure	Yes vs. no	2.78 (1.70, 4.54)	<0.001
Vocal cord paralysis	Yes vs. no	0.54 (0.19, 1.55)	0.25
Diaphragm paralysis	Yes vs. no	1.75 (0.52, 5.87)	0.36
Chylothorax	Yes vs. no	1.33 (0.56, 3.14)	0.51
Arrhythmia	Yes vs. no	1.17 (0.78, 1.76)	0.43
Seizures	Yes vs. no	0.79 (0.46, 1.37)	0.40
Sepsis	Yes vs. no	1.47 (0.61, 3.5)	0.38
Brain hemorrhage	Yes vs. no	3.09 (1.10, 8.62)	0.03
Arterial line	Yes vs. no	0.51 (0.13, 1.98)	0.32
Mechanical ventilation	Yes vs. no	1.65 (0.53, 5.1)	0.38
Central venous catheter	Yes vs. no	0.58 (0.27, 1.21)	0.14
Hemodialysis catheter	Yes vs. no	3.42 (1.05, 11.15)	0.04
24/7 coverage	Yes vs. no	1.22 (0.58, 2.58)	0.59
Cardiac ICU	Yes vs. no	0.48 (0.25, 0.92)	0.03
Residency or fellowship training	Yes vs. no	0.79 (0.36, 1.71)	0.54
Average annual cardiac surgery cases per center	100 case increase	1.10 (0.93, 1.32)	0.26

explanation for the event leading to death in the No cardiac arrest group. The definition of cardiac arrest used in our study differs in some respects from international Utstein guidelines definition of cardiac arrest used in other pediatric studies. According to the most commonly used definition, pediatric cardiac arrest is defined as any event characterized by either pulselessness or critically compromised perfusion treated with either chest compressions, and/or defibrillation for more than or equal to 1 min.^{23,24} Elements such as duration of cardiopulmonary resuscitation, and precipitating events leading to cardiac arrest were not available in our study. It is, therefore, possible that our study included a group of patients with a brief arrest and rapid return of spontaneous circulation that would not be included in other studies of cardiac arrest. In addition, pre-arrest and post-arrest characteristics are also not collected currently in our study. Our study also lacked data on other Utstein's outcomes such as return of spontaneous circulation >20 min, and 24-h survival.

Conclusions

The multi-center study demonstrates that prevalence of post-operative cardiac arrest increases with increasing case complexity. However, the risk of mortality and good neurological outcomes after cardiac arrest remain similar regardless of the level of complexity of operation performed. These data further suggest that both odds of cardiac arrest, and mortality after cardiac arrest in children undergoing heart surgery are a function of patient's characteristics, surgical risk category, and hospital characteristics. These analyses represent an initial step in evaluating the risk factors and outcomes associated with post-operative cardiac arrest after heart operations of varying complexity. Further analyses are needed to evaluate if the mortality in children undergoing operations of varying complexity is related to cardiac arrest or complexity of operation performed. Using databases such as the

Virtual Pediatric Systems (VPS, LLC) for clinical outcomes research may in the future decrease the cost of discovery and guide us in improving outcomes for critically ill patients.

Conflict of interest statement

None.

Funding source

No authors received any honorarium, grant, or other form of payment to produce the manuscript.

Other disclosures

VPS data was provided by the VPS, LLC. No endorsement or editorial restriction of the interpretation of these data or opinions of the authors has been implied or stated.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.resuscitation.2016.04.022>.

References

- Gupta P, Jacobs JP, Pasquali SK, et al. Epidemiology and outcomes following in-hospital cardiac arrest after pediatric cardiac surgery. *Ann Thorac Surg* 2014;98:2138–44.
- Rhodes JF, Blaufox AD, Seiden HS, et al. Cardiac arrest in infants after congenital heart surgery. *Circulation* 1999;100:194–9.
- Ortmann L, Prodan P, Gossett J, et al., American Heart Association's Get With The Guidelines – Resuscitation Investigators. Outcomes after in-hospital cardiac arrest in children with cardiac disease: a report from Get With The Guidelines – Resuscitation. *Circulation* 2011;124:2329–37.

4. Kane DA, Thiagarajan RR, Wypij D, et al. Rapid-response extracorporeal membrane oxygenation to support cardiopulmonary resuscitation in children with cardiac disease. *Circulation* 2010;14:122.
5. Prodhon P, Fiser RT, Dyamenahalli U, et al. Outcomes after extracorporeal cardiopulmonary resuscitation (ECPR) following refractory pediatric cardiac arrest in the intensive care unit. *Resuscitation* 2009;80:1124–9.
6. Kalfa D, Krishnamurthy G, Duchon J, et al. Outcomes of cardiac surgery in patients weighing <2.5 kg: affect of patient-dependent and -independent variables. *J Thorac Cardiovasc Surg* 2014;148:2499–506.
7. Cheng HH, Almodovar MC, Laussen PC, et al. Outcomes and risk factors for mortality in premature neonates with critical congenital heart disease. *Pediatr Cardiol* 2011;32:1139–46.
8. Fudge Jr JC, Li S, Jaggars J, et al. Congenital heart surgery outcomes in Down syndrome: analysis of a national clinical database. *Pediatrics* 2010;126:315–22.
9. O'Brien SM, Clarke DR, Jacobs JP, et al. An empirically based tool for analyzing mortality associated with congenital heart surgery. *J Thorac Cardiovasc Surg* 2009;138:1139–53.
10. Welke KF, O'Brien SM, Peterson ED, Ungerleider RM, Jacobs ML, Jacobs JP. The complex relationship between pediatric cardiac surgical case volumes and mortality rates in a national clinical database. *J Thorac Cardiovasc Surg* 2009;137:1133–40.
11. Slater A, Shann F, Pearson G, for the PIM Study Group. PIM2: a revised version of the paediatric index of mortality. *Intensive Care Med* 2003;29:278–85.
12. Pollack MM, Patel KM, Ruttimann UE. PRISM III: an updated pediatric risk of mortality score. *Crit Care Med* 1996;24:743–52.
13. Gupta P, Tang X, Gall CM, Lauer C, Rice TB, Wetzel RC. Epidemiology and outcomes of in-hospital cardiac arrest in critically ill children across hospitals of varied center volume: a multi-center analysis. *Resuscitation* 2014;85:1473–9.
14. Fiser DH. Assessing the outcome of pediatric intensive care. *J Pediatr* 1992;121:68–74.
15. Fiser DH, Long N, Roberson PK, et al. Relationship of pediatric overall performance category and pediatric cerebral performance category scores at pediatric intensive care unit discharge with outcome measures collected at hospital discharge and 1- and 6-month follow-up assessments. *Crit Care Med* 2000;28:2616–20.
16. Gupta P, Yan K, Chow V, et al. Variability of characteristics and outcomes following CPR events in diverse ICU settings in a single, tertiary care children's hospital. *Pediatr Crit Care Med* 2014;15:e128–41.
17. Sutton RM, Niles D, French B, et al. First quantitative analysis of cardiopulmonary resuscitation quality during in-hospital cardiac arrests of young children. *Resuscitation* 2014;85:70–4.
18. Nadkarni VM, Larkin GL, Peberdy MA, et al., National Registry of Cardiopulmonary Resuscitation Investigators. First documented rhythm and clinical outcome from in-hospital cardiac arrest among children and adults. *JAMA* 2006;295:50–7.
19. Samson RA, Nadkarni VM, Meaney PA, et al., American Heart Association National Registry of CPR Investigators. Outcomes of in-hospital ventricular fibrillation in children. *N Engl J Med* 2006;354:2328–39.
20. Gupta P, Beam BW, Noel TR, et al. Impact of pre-operative location on outcomes in congenital heart surgery. *Ann Thorac Surg* 2014;98:896–903.
21. Nishisaki A, Pines JM, Lin R, et al. The impact of 24-h, in-hospital pediatric critical care attending physician presence on process of care and patient outcomes. *Crit Care Med* 2012;40:2190–5.
22. Burstein DS, Jacobs JP, Li JS, et al. Care models and associated outcomes in congenital heart surgery. *Pediatrics* 2011;127:e1482–9.
23. Suominen P, Olkkola KT, Voipio V, Korpela R, Palo R, Rasanen J. Utstein style reporting of in-hospital paediatric cardiopulmonary resuscitation. *Resuscitation* 2000;45:17–25.
24. Recommended guidelines for uniform reporting of pediatric advanced life support: the pediatric Utstein, style. A statement for healthcare professionals from a task force of the American Academy of Pediatrics, the American Heart Association, and the European Resuscitation Council. *Pediatrics* 1995;96:765–79.