Pediatric Perioperative Cardiac Arrest, Death in the Off Hours: A Report From Wake Up Safe, The Pediatric Quality Improvement Initiative

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BACKGROUND: Pediatric perioperative cardiac arrest (CA) is a rare but catastrophic event. This case–control study aims to analyze the causes, incidence, and outcomes of all pediatric CA reported to Wake Up Safe. Factors associated with CA and mortality after arrest are examined and possible strategies for improving outcomes are considered.

METHODS: CA in children was identified from the Wake Up Safe Pediatric Anesthesia Quality Improvement Initiative, a multicenter registry of adverse events in pediatric anesthesia. Incidence, demographics, underlying conditions, causes of CA, and outcomes were extracted. Descriptive statistics and logistic regression were used to study the above factors associated with CA and mortality after CA.

RESULTS: A total of 531 cases of CA occurred during 1,006,685 anesthetics. CA was associated with age (odds ratio [95% confidence interval] comparing ≥6 vs <6 months of 0.26 [0.22–0.32]; $P = .014$), American Society of Anesthesiologists physical status (ASA PS III–V versus I–II, 9.24, 7.23–11.8; $P < .001$), and emergency status (3.55, 2.88–4.37; $P < .001$). Higher ASA PS was associated with increased mortality (ASA PS III–V versus I–II, 3.25, 1.20–8.81; $P = .02$) but anesthesia-related arrests were correlated with lower mortality (0.44, 0.26–0.74; $P = .002$). ASA emergency status (1.83, 1.05–3.19; $P = .03$) and off hours (night and weekend versus weekday, 2.17, 1.22–3.86; $P = .008$) were other factors associated with mortality after CA.

CONCLUSIONS: The Wake Up Safe data validate single-institution studies' findings regarding incidence, factors associated with arrest, and outcomes of pediatric perioperative CA. However, CA occurring during the off hours had significantly worse outcomes, independent of patient physical status or emergency surgery. This suggests an opportunity for improved outcomes. (Anesth Analg 2018;127:472–7)

KEY POINTS

- **Question:** What are the causes, incidence, and outcomes of pediatric perioperative cardiac arrest, and what modifiable factors are associated with outcomes?
- **Findings:** While many single-institution findings were validated, cardiac arrest on nights and weekends was associated with significantly worse outcome, independent of patient status or emergency surgery.
- **Meaning:** Outcomes may be improved through root cause analysis and additional research on off-hours cardiac arrest.

Cardiac arrest (CA) remains one of the most catastrophic complications of pediatric anesthesia. Investigations into causes and factors associated with CA have been conducted for more than 150 years[1,2] but have been limited by low incidence and lack of consistent definitions of such events.

Many single-institution studies[3–9] examining the incidence and risk factors for CA have identified the impact of surgical site (including cardiac surgery),[7] higher American Society of Anesthesiologists physical status (ASA PS), and emergency status.[10] However, single-institution studies have been limited by the heterogeneity of case mix and medical practices among institutions and by the small number of CA in any 1 institution.

Registry studies such as the American Society of Anesthesiologists Closed Claims Database,[11] Pediatric

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This article describes human research. IRB contact information: Institutional Review Boards of the UM Medical School, 2800 Plymouth Rd, Bldg 200, Room 2086, Ann Arbor, MI 48109. E-mail: irbmed@umich.edu.

The requirement for written informed consent was waived by the institutional review board. This article describes an observational clinical study. The author states that the article includes every item in the EQUATOR checklist for case–control observational clinical studies.

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Perioperative Cardiac Arrest Registry,[12–14] and the American Heart Association Get with the Guidelines-Resuscitation (formerly National Registry of Cardiopulmonary Resuscitation)[15] have allowed the capture of a larger number of events from a variety of institutions. These studies examined patterns of CA and outcomes after arrest but were limited by the lack of demographic information (eg, ASA PS, age, and emergency status), thus precluding any meaningful calculation of incidence values or risk factors for CA.

Wake Up Safe is a patient safety organization that maintains a national registry of deidentified, serious adverse events.[16–18] The ultimate goal of Wake Up Safe is to implement changes in processes of care that improve the quality and safety of anesthetic care provided to pediatric patients nationwide. As of December 31, 2015, 29 US children's hospitals had joined Wake Up Safe. Details about each CA, including the cause of arrest, associated factors, and outcome, are reported to a centralized data bank as described in the Methods section. Member institutions must also provide annual demographic information on all cases in which anesthetic care was delivered. Large numbers of CAs from multiple institutions can be analyzed, and incidence figures can be calculated. One previous study analyzed a small subset of these arrests occurring in the pediatric postoperative care unit.[19]

Our study aims to analyze the causes, incidence, and outcomes of all pediatric CA reported to Wake Up Safe. Factors associated with CA and mortality after arrest are examined, and possible strategies for improving outcomes are considered.

METHODS

Wake Up Safe

After obtaining local institutional review board approval, all institutions participating in Wake Up Safe submitted data on a standardized form (Supplemental Digital Content, Appendix 1, http://links.lww.com/AA/C352) to a central data repository (Axio Research, Seattle, WA). No patient or institutional identifiers were included, so institutional review board approval for research on the database and informed consent from individual cases was not required. This article adheres to the applicable Enhancing the QUAlity and Transparency Of health Research (EQUATOR) guidelines. Participating institutions submitted annual data regarding the types and numbers of anesthetics performed (eg, ASA PS categories, age, sex, and emergency status). Before each significant adverse event case submission, 3 anesthesiologists who were not involved in the event analyzed the event using a standardized root cause analysis method to identify the causal or contributing factors.[18] Representatives from each member institution received education on root cause analysis methodology before participation in an effort to standardize significant adverse event case evaluation across sites.

Inclusion Criteria

For the purposes of this study, CA cases within 24 hours of the induction of anesthesia in pediatric patients (<18 years old) reported to Wake Up Safe from January 1, 2010 to December 31, 2015 were included after eliminating duplicate cases and those who did not receive any anesthesia (such as CAs reported from cases when anesthesia providers were called to assist in airway management in the emergency department). Reported caseload data through December 31, 2015 were also obtained from Wake Up Safe. This includes off-site anesthesia, cardiac surgery, and cardiac catheterization cases. All patients with ASA PS VI (organ donors) were excluded. Those CA cases for which the institutional caseload data were incomplete (67) were also excluded.

Definitions

Before data analysis, CA was defined as "cessation of cardiac mechanical activity as confirmed by the absence of signs of circulation requiring the use of cardiac compressions with or without defibrillation." A CA was defined as anesthesia related (ARCA) if the reporting institution indicated that anesthesia was either a primary or secondary factor in the arrest. If anesthesia was reported as not a contributing factor, the case was defined as non-ARCA. When the role of anesthesia was not defined by the reporting institution, 4 authors (R.E.C., A.C.L., J.K.D., J.P.M.) reviewed the narrative description of the case using the Pediatric Perioperative Cardiac Arrest Registry definitions[12] and defined the case as ARCA or non-ARCA by unanimous (4/4) agreement. When unanimity could not be achieved, the causal nature of the case was reported as unknown.

For the CA cases, surgical severity was scored as low, moderate, high, or unclear (low severity surgery = noninvasive diagnostic or superficial surgery with minimal blood loss; moderate = invasive, anticipated moderate blood loss, emergent, or airway procedure; high = major procedure, anticipated excessive blood loss)[20] based on reported current procedural terminology code and narrative description. Night was defined as 7 PM to 7 AM. Weekend was defined as Saturday and Sunday. Root cause and all other data were defined and used as reported to Wake Up Safe (Supplemental Digital Content, Appendix 1, http://links.lww.com/AA/C352). Mortality was reported as whether the CA led to the patient's demise, regardless of time frame or discharge.

Database Preparation

Because the demographic data are submitted to a different database from adverse events, the 4 variable demographic data (ASA PS categories, age, sex, and emergency status) contained both CA cases and nonarrest cases. In preparation for analysis, it was necessary to identify the CA cases from the overall database of all anesthetics to allow comparison between the CA and non-CA cases. Because both databases are deidentified, we took the following steps to separate cases identical on all 4 variables to the CA patients from the nonarrest patients. For every CA case, a case identical on all variables was separated (randomly selecting if more than 1 was identical on all variables) from the billing data. For example, for a CA case in a 2-year-old ASA PS 4E female, a case of a 2-year-old ASA PS 4E female was separated from the database of all anesthetics. Thus, for each CA case, an identical case was separated from the larger database of all anesthetics, allowing comparison between the nonarrest cases and CA cases. Due to deidentification, we could not be certain that we had removed the exact case, but the cases were identical in all analyzed variables.

Statistical Analysis

We used descriptive statistics including frequency and percent to summarize the CA cases and the billing data. Preoperative and intraoperative data and causes of CA between survivors and nonsurvivors were compared among the CA patients. The following independent risk factors associated with CA were included in a logistic regression model: age, sex, ASA PS, and ASA emergency status (all reported data).

We used a penalized logistic regression analysis (using the pentrace() and update() functions in the rms library in the software R; R Core Team, Vienna, Austria) to assess independent factors associated with mortality after CA including age, sex, ASA PS, ASA emergency status (I–II, III–V), surgical severity (low, moderate, high), cardiopulmonary bypass, anesthesia related (yes/no), location (operating room/other), and night/weekend (yes/no). Model overfitting is a phenomenon where the results may be applicable to the current data set but may not be generalizable to an independent data set. Overfitting can occur when there are fewer than 10 events per degree of freedom in a logistic regression model. To overcome this issue, we used a penalized regression model, which shrinks regression coefficients toward zero, thus making the results more generalizable to an independent data set. The variables included in the model were chosen a priori based on previous literature. All tests were 2 sided assuming a significance level of 5%. Results should be considered exploratory and no adjustments were made for multiple testing. All statistical analyses were done using the software R.

RESULTS

A total of 616 pediatric CA cases were reported to Wake Up Safe between January 1, 2010 and December 31, 2015. Eighteen cases were not included because the patients did not receive anesthesia or were duplicates of existing cases. Sixty-seven cases were not included because of incomplete associated caseload data. The remaining 531 cases of CA occurred during 1,006,685 anesthetics at the reporting institutions in the same time period, yielding an overall incidence of 5.3 per 10,000 anesthetics. In the 522 CA in which anesthesia or nonanesthesia relatedness could be determined, 329 (63%) were anesthesia related (3.3 per 10,000 anesthetics). The incidence of anesthesia-related death was 0.36 per 10,000 anesthetics.

Table 1 reports the noncardiac arrest caseload of 1,006,154 compared to the 531 suffering CA. Age >6 months was significantly associated with reduced CA (odds ratio [OR], 0.26; 95% confidence interval [CI], 0.22–0.32; $P < .001$), sex (OR, 0.81 male to female, 95% CI, 0.0.68–0.96; $P = .014$), ASA PS (OR for PS III–V versus I–II, 9.24, 95% CI, 7.23–11.8; $P < .001$), and emergency status (OR, 3.55; 95% CI, 2.88–4.37; $P < .001$).

Table 2 summarizes the results of the multivariable logistic regression analysis of the above. ASA PS ≥III, emergency status, and age <6 months were significantly associated with increased odds of CA. Female sex was also associated with increased odds of CA.

Table 3 reports the comparison between survivors and nonsurvivors of CA, while Table 4 reports the proximate causes of CA. Table 5 summarizes the outcomes of the CAs. The most common cause of arrest was cardiovascular, accounting for 49% (261) of all CA. Respiratory causes accounted for the second most common cause of CA at 35% (186). Medication related (37, 7%), central venous line (15, 3%), and blood products (3, 1%) accounted for most of the remaining causes of CA. Of the cardiovascular causes of CA, arrhythmia was the most common subcategory (87, 33%), followed by primary cardiac failure (50, 19%) and hemorrhage (48, 18%). Of the respiratory causes of CA, airway obstruction (80, 43%) was the most common etiology, followed by inability to intubate or ventilate (20, 11%).

Of note, 285 (54%) of both survivors and nonsurvivors (in equal proportion) had congenital heart disease, while 159 (30%) had some form of pulmonary disease. A total of 210 (40%) were receiving some form of physiologic support before surgery, ranging from oxygen and/or inotropes to extracorporeal membrane oxygenation (7, 1%). A total of 513 (97%) of the patients suffering arrest received general anesthesia, while only 8 (2%) received sedation or monitored anesthetic care. Patient disease and individual provider factors such as judgment or decision making accounted for the majority of primary and secondary causes assessed during root cause analysis.

Table 1. Factors Associated With Cardiac Arrest

Category	Nonarrest Cases N = 1,005,623 N (%)	Cardiac Arrest Cases N = 531 N (%)
Age		
<1 mo	19,351 (2)	90 (17)
1–5 mo	51,204 (5)	103 (19)
6–11 mo	66,130 (7)	76 (14)
1–3 y	268,320 (27)	110 (21)
4–8 y	294,577 (29)	58 (11)
9–12 y	145,264 (14)	30 (6)
13–17 y	161,308 (16)	64 (12)
Sex		
Male	576,703 (57)	272 (51)
Female	429,451 (43)	259 (49)
ASA physical status		
I	258,417 (26)	24 (5)
II	418,162 (42)	54 (10)
III	281,175 (28)	205 (39)
IV	46,982 (5)	220 (41)
V	1418 (0)	28 (5)
ASA emergency status		
No	948,831 (94)	413 (78)
Yes	57,323 (6)	118 (22)

Abbreviation: ASA, American Society of Anesthesiologists.

Table 2. Factors Associated With Cardiac Arrest From a Multivariable Logistic Regression Analysis

Variable	Comparison	Odds Ratio (95% Confidence Interval)	*P* Value
Age	≥6 vs <6 mo	0.26 (0.22–0.32)	<.001
Sex	Male versus female	0.81 (0.68–0.96)	.014
ASA physical status	III–V vs I–II	9.24 (7.23–11.80)	<.001
ASA emergency	Yes versus no	3.55 (2.88–4.37)	<.001

The *C* statistic for the model is 0.64. No adjustments were made for multiple testing. All available variables considered for the model included age, sex, ASA physical status, and ASA emergency status.

Abbreviation: ASA, American Society of Anesthesiologists.

Table 3. Factors for Mortality After Arrest

Variable	N[a]	Nonsurvivors (N = 94) N (%)	Survivors (N = 437) N (%)	Combined (N = 531) N (%)
ASA physical status	531			
I		0 (0)	24 (5)	24 (5)
II		1 (1)	53 (12)	54 (10)
III		22 (23)	183 (42)	205 (39)
IV		51 (54)	169 (39)	220 (41)
V		20 (21)	8 (2)	28 (5)
ASA emergency	531	44 (47)	74 (17)	118 (22)
Age	531			
<1 mo		29 (31)	61 (14)	90 (17)
1–5 mo		13 (14)	90 (21)	103 (19)
6–11 mo		10 (11)	66 (15)	76 (14)
1–3 y		18 (19)	92 (21)	110 (21)
4–8 y		7 (7)	51 (12)	58 (11)
9–12 y		6 (6)	24 (5)	30 (6)
13–17 y		11 (12)	53 (12)	64 (12)
Sex	531			
Male		39 (41)	233 (53)	272 (51)
Female		55 (59)	204 (47)	259 (49)
Weekend (Saturday–Sunday)	518	13 (14)	27 (6)	40 (8)
Night (19:00–7:00)	499	24 (28)	41 (10)	65 (13)
Off hours (night or weekend)	496	30 (34)	59 (14)	89 (18)
Surgical severity	526			
Low		7 (8)	80 (18)	87 (17)
Moderate		31 (33)	201 (46)	232 (44)
High		55 (59)	152 (35)	207 (39)
Cardiopulmonary bypass	531	9 (10)	50 (11)	59 (11)
Location	531			
Computed tomography scan		2 (2)	5 (1)	7 (1)
Cardiac catheterization		13 (14)	77 (18)	90 (17)
Emergency department		1 (1)	1 (0)	2 (0)
Endoscopy suite		1 (1)	1 (0)	2 (0)
Intensive care unit		14 (15)	29 (7)	43 (8)
Induction room		0 (0)	4 (1)	4 (1)
Interventional radiology		0 (0)	10 (2)	10 (2)
Magnetic resonance imaging		1 (1)	9 (2)	10 (2)
Nursing unit/hospital room		0 (0)	5 (1)	5 (1)
Operating room		53 (56)	265 (61)	318 (60)
Postanesthesia care unit		1 (1)	25 (6)	26 (5)
Radiation oncology		0 (0)	1 (0)	1 (0)
Sedation unit		0 (0)	1 (0)	1 (0)
Transport		2 (2)	0 (0)	2 (0)
Treatment room		0 (0)	1 (0)	1 (0)
Other		6 (6)	3 (1)	9 (2)
Anesthesia related	522	36 (40)	293 (68)	329 (63)

Abbreviation: ASA, American Society of Anesthesiologists.
[a]Total number of cases for which data were not missing or unknown.

Table 6 summarizes the simultaneous risk factors associated with mortality after CA from the logistic regression analysis. Higher ASA PS was significantly associated with increased odds of mortality after CA (OR for PS III–V versus I–II, 3.25; 95% CI, 1.20–8.81; $P = .02$). ASA emergency status (OR, 1.83; 95% CI, 1.05–3.19; $P = .03$) and arrests during nights/weekends (OR, 2.17; 95% CI, 1.22–3.86; $P = .008$) were also significantly associated with increased mortality, while anesthesia-related arrests were associated with lower mortality after CA (OR, 0.44; 95% CI, 0.26–0.74; $P = .002$).

DISCUSSION

Validation of Single-Institution Reports

This study represents one of the largest databases of pediatric perioperative CAs to date and validates many previous findings regarding incidence and factors correlated with CA. The incidence of CA (5.3 per 10,000) is consistent with recent single-institution reports.[7,8] The overall mortality rate for all perianesthetic CA of 17.7% is slightly lower than previously reported.[7,12,13] This may be because the majority of arrests were anesthesia related, with the mortality rate for ARCA at 10.9%. This may also reflect recent emphasis nationally on perioperative CA management and early recognition. While the incidence of ARCA (3.3 per 10,000) was slightly higher than reported in previous studies,[8,13] it was significantly more survivable. Age <6 months, ASA PS ≥3, and ASA emergency status were significantly correlated with arrest on multivariate analysis. Six months, rather than 1 year, was chosen as an inflection point because CA increased 3-fold when patients were <6 vs ≥6 months of age, reinforcing recent national guidelines.[21] To a lesser extent, female sex was also significantly associated with

Table 4. Proximate Causes of Arrest (N = 531)

Proximate Cause of Arrest	N (%)
Cardiovascular	261 (49)
Pulmonary hypertension	30
Primary cardiac failure	50
Pulmonary embolus	3
Metabolic	10
Hypovolemia (nonhemorrhage)	16
Hemorrhage	48
Electrolyte abnormality	6
Cardiac tamponade	11
Arrhythmia	87
Air embolus	10
Unclear	5
Arterial line (cardiology wire)	1 (0)
Central venous line	15 (3)
Arrhythmia	6
Cardiac tamponade	4
Sepsis	1
Unclear central venous line	4
Medication related	37 (7)
Inhaled anesthetic	8
Local anesthetic	1
Muscle relaxant	6
Muscle relaxant reversal	2
Narcotic	9
Vasodilator	1
Other/unclear medication event	10
Medication error related	6
Blood products	3 (1)
Respiratory	186 (35)
Respiratory failure	13
Premature extubation	19
Pneumothorax	6
Inability to intubate or ventilate	20
Esophageal intubation	6
Difficult intubation	6
Aspiration	3
Airway obstruction	80
Upper airway obstruction	13
Patient disease related (eg, tumor, secretions)	14
Laryngospasm	43
Foreign body	2
Endotracheal tube–related obstruction	7
Bronchospasm	8
Unclear obstruction	3
Unclear respiratory	10
Could not be determined	36 (14)

Table 5. Outcome of Arrest

Outcome of Arrest	n (%)
No harm	54 (10)
Emotional distress or inconvenience	15 (3)
Additional treatment	196 (37)
Temporary harm	129 (24)
Permanent harm	32 (6)
Death	94 (18)
Unknown	10 (2)

CA. However, there was no clear explanation for this incidental finding. On multivariate analysis of the factors associated with mortality after arrest, ASA PS and emergency status were significant, validating prior studies.[7,12,13,22]

Mortality in the Off Hours

As a new finding, arrests on nights or weekends carried a more than 2-fold OR for mortality. Previous studies, including a single-institution mixed adult and pediatric study[23,24] and a study of pediatric in-hospital arrest,[25] have shown increased survival in day/evening versus night CA, albeit inconsistently. This may be a reflection of the number of cases required to see this effect. For example, the study by Zgleszewski et al[8] did not see an increased incidence of arrest in the off hours but only had 3 off-hours arrests. In like manner, another[23] had an increased incidence but not enough to be statistically significant.

With our large data set, we appear to have captured off hours as an unmeasured factor associated with mortality, independent of patient comorbidity load (as measured by ASA PS), emergency surgery, or surgical severity. While it is not possible to avoid all anesthesia in the off hours, this systemic factor represents an opportunity for improved outcome as root cause analysis and further research may identify modifiable elements driving these outcomes.

Limitations

The voluntary, multicenter nature of the database used in this study poses potential for selection and reporting biases, such as a bias toward more frequent reporting for anesthesia-related arrest. Furthermore, despite centralized training, as well as specific guidelines and definitions, there may be institutional variability in data, particularly preventability and the root cause analysis methodology. Certain factors known to be associated with arrest and outcomes, such as the timing of epinephrine administration,[26] quality of compressions,[27] or anesthesiologist-specific information,[8] were not reported. The influence of individual institution or providers on arrest rate or outcomes could not be analyzed due to deidentification. The demographic data did not include timing information, so we could not assess the incidence of CA during the off hours. Inaccurate data may also have been entered during the manual data entry process, as evidenced by the duplicate entry of cases. These data must therefore be interpreted with caution. Finally, most reporting institutions are tertiary pediatric centers, which may hinder the ability to generalize findings to other practice models where children receive anesthetic care.

SUMMARY

Our examination of the Wake Up Safe data validates many of the previous single-institution studies' findings regarding incidence, associated factors, and outcomes of pediatric perioperative CA. However, our study is the first large-scale pediatric study to show a clear association between the timing of perianesthetic CA and outcome. While we can speculate on factors that make CA on nights and weekends less survivable, such as circadian performance issues or decreased staffing, further research and root cause analysis are needed to examine the incidence of CA in the off hours and identify particular strategies for mitigation.

DISCLOSURES

Name: Robert E. Christensen, MD.
Contribution: This author helped design the study, conduct the study, analyze the data, and write the article.
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Contribution: This author helped design the study, conduct the study, analyze the data, and write the article.

Table 6. Factors Associated With Mortality After Cardiac Arrest From the Penalized Multivariable Logistic Regression Model (n = 483)

Variable	Comparison	Odds Ratio (95% Confidence Interval)	*P* Value
Age	≥6 vs <6 mo	0.77 (0.46–1.28)	.31
Sex	Male versus female	0.67 (0.41–1.09)	.11
ASA physical status	III–V vs I–II	3.25 (1.20–8.81)	.02
ASA emergency	Yes versus no	1.83 (1.05–3.19)	.03
Surgical severity	Moderate versus low	0.90 (0.40–2.03)	.81
	High versus low	1.76 (0.76–4.06)	.19
Cardiopulmonary bypass	Yes versus no	0.56 (0.27–1.17)	.12
Anesthesia related	Yes versus no	0.44 (0.26–0.74)	.002
Location	Operating room versus other	0.93 (0.54–1.58)	.77
Night/weekend	Yes versus no	2.17 (1.22–3.86)	.008

Factors included in the model were selected a priori based on literature. The *C* statistic for the model was 0.76. No adjustments were made for multiple testing.
Abbreviation: ASA, American Society of Anesthesiologists.

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