

Intraoperative Cardiopulmonary Arrest in Children Undergoing Spinal Deformity Correction

Causes and Associated Factors

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Study Design. Retrospective review.

Objective. To report the incidence of and risk factors for intraoperative cardiopulmonary arrest (ICA) in children undergoing spinal deformity surgery.

Summary of Background Data. Spinal deformities in children are associated with comorbidities that can pose substantial risks during surgery.

Methods. We reviewed records of patients who underwent surgery at two pediatric tertiary-care hospitals from 2004 through 2014. Fisher exact test and the Student *t* test were used to compare ICA and non-ICA groups by patient diagnosis, estimated blood loss, number of vertebral levels fused, and proportion of blood volume lost (significance, $P < 0.05$). We classified proximate causes of ICA based on hemoglobin, metabolic panel/electrolyte imbalance, electrocardiogram/echocardiography, and vital signs.

Results. ICA occurred in 11 of 2524 (0.4%) patients. Patients with neuromuscular disorders had a 3-fold higher risk of ICA compared with those without neuromuscular disorders. At the time of ICA, hemoglobin levels were 5 g/dL or less in four patients, potassium was higher than 5.5 mEq/L in six patients, and ionized calcium was less than or equal to 1 mmol/L in two patients. There were significant differences between the ICA and non-ICA groups in mean number of vertebral levels fused (15 vs. 12), patient weight (34 vs. 49 kg), estimated blood loss (2623 vs. 959 mL), and proportion of blood volume lost (1.03 vs. 0.33) (all $P < 0.01$). Suspected causes of ICA were cardiovascular causes (eight

patients) and anaphylaxis, primary rhythm disturbance, and respiratory/airway cause (one patient each). The incidence of ICA for patients with idiopathic scoliosis was 0.13%. Ten of the 11 patients were successfully resuscitated, and one patient died.

Conclusion. ICA occurs in approximately 0.4% of children undergoing spinal fusion surgery. Patients with neuromuscular disorders are at greater risk of ICA than those without these disorders.

Key words: blood loss, cardiopulmonary resuscitation, electrolyte imbalance, intraoperative cardiopulmonary arrest, spinal deformity.

Level of Evidence: 3

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Pediatric spinal deformity correction is associated with perioperative complications, including infection, major blood loss, and spinal cord injury.^{1–5} Intraoperative complications are especially common in patients with nonidiopathic scoliosis. Intraoperative cardiopulmonary arrest (ICA), defined as an event requiring cardiopulmonary resuscitation (CPR) while in the operating room, is a potentially fatal complication of surgical spinal deformity correction. To our knowledge, there are no reports on the incidence of and risk factors for ICA in children undergoing spinal deformity correction.

The exact causes of ICA during pediatric spinal deformity surgery remain unknown. Various studies have speculated about potential risk factors for and causes of ICA in general pediatric surgery.^{6–8} Hypovolemia with electrolyte imbalance, anaphylaxis, primary rhythm disturbance, and airway disorder/obstruction might predispose patients to ICA.

The purpose of this study was to report the incidence, timing, and potential causes of ICA in children during spinal deformity correction.

MATERIALS AND METHODS

After institutional review board approval, we performed a retrospective review of clinical records of all children aged 0 to 18 years who underwent spinal deformity correction at

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two pediatric tertiary-care hospitals from January 2004 through June 2014.

Study Participants and Study Variables

For the 2524 children who met the inclusion criteria, the following information was recorded: patient age, sex, weight, diagnosis, the degree of scoliosis curve, surgical approach (anterior/posterior), intraoperative estimated blood loss (EBL), proportion of blood volume (BV) lost (EBL/BV), and number of vertebral levels fused. We analyzed complete blood count for hemoglobin at the time of ICA to serve as proxy for adequate blood volume repletion and resuscitation. We also analyzed the metabolic panel to evaluate for electrolyte imbalance (high potassium [normal range = 3.6–5.2 mEq/L] and low ionized calcium [normal range = 1.1–1.4 mmol/L]), which may predispose patients to cardiac arrhythmias and arrest.

Patient Demographic and Surgical Characteristics

We grouped patients into five diagnostic categories: idiopathic scoliosis ($n = 1594$), neuromuscular scoliosis ($n = 731$), syndromic and skeletal dysplasia ($n = 102$), congenital scoliosis ($n = 54$), and connective tissue disorder ($n = 43$) (Table 1). Eleven patients experienced ICA (Table 2), and 2513 patients did not experience ICA (non-ICA group). Probable causes of ICA were assigned on review by a pediatric anesthesiologist, a consulting cardiologist, and the treating orthopedic surgeon, who reached consensus in all cases. The probable causes were categorized as (1) cardiovascular causes (defined as electrolyte imbalance and/or hypovolemia), (2) allergy/anaphylaxis, (3) primary rhythm disturbance, or (4) respiratory/airway cause.

The ICA group consisted of six girls and five boys with a mean age of 12.7 years (range, 1.5–17 years). The non-ICA group consisted of 1682 girls and 831 boys with a mean age of 14 years (range, 10–16 years).

One patient in the ICA group underwent single-stage combined anterior and posterior spinal fusion, and 10 patients underwent isolated posterior spinal fusion. In the non-ICA group, 2213 patients underwent isolated posterior spinal fusion,

130 underwent isolated anterior spinal fusion, and 170 underwent combined anterior and posterior spinal fusion.

Statistical Analysis

We used the Fisher exact test to analyze associations of patient diagnosis with occurrence of ICA. We used the Student t test to compare the ICA versus non-ICA group with respect to number of levels fused, EBL, body weight, and EBL/BV. Significance was set at $P < 0.05$. Stata, version 12.0 (StataCorp LP, College Station, TX) was used for all analysis.

RESULTS

Incidence and Risk Factors

Eleven of 2524 (0.4%) patients in our study group experienced ICA. Six of these 11 patients had neuromuscular disorders; four had cerebral palsy, and one patient each had paraparesis from spinal cord tumor and congenital myopathy. The remaining five patients had nonneuromuscular diagnoses; two had connective tissue disorders, and one patient each had infantile idiopathic scoliosis, adolescent idiopathic scoliosis, and congenital scoliosis. Patients with neuromuscular disorders had 3-fold higher risk of ICA (0.82%) compared with patients without neuromuscular disorders (0.28%), although this difference was not significant ($P = 0.090$). One patient in the ICA group died, and there were no intraoperative deaths in the non-ICA group.

At the time of ICA, hemoglobin levels were 5 g/dL or less in three patients, potassium levels were greater than 5.5 mEq/L in six patients, and ionized calcium levels were less than or equal to 1 mmol/L in two patients.

The mean number of spinal levels fused differed significantly between the ICA group (mean, 15 levels) and non-ICA group (mean, 12 levels ($P = 0.044$)). The two groups also differed significantly in mean body weight (34 kg for ICA group *vs.* 49 kg for non-ICA group), mean EBL (2623 mL for ICA group *vs.* 959 mL for non-ICA group), and mean EBL/BV (1.03 for ICA group *vs.* 0.33 for non-ICA group (all $P < 0.01$) (Table 3).

TABLE 1. Patient Characteristics by ICA Group in Children Undergoing Spinal Deformity Correction Surgery

Characteristic	ICA Group (n = 11)	Non-ICA Group (n = 2513)
Female sex	6 (54%)	1681 (67%)
Age (yr)	12.7 (range, 1.5–17)	14 (range, 10–16)
Body weight (kg)	34 (range, 14–68)	49 (range, 32–66)
Diagnosis		
Idiopathic scoliosis	2	1594
Neuromuscular disorder	6	725
Syndromic/dysplasia	0	102
Congenital scoliosis	1	53
Connective tissue disorder	2	53

ICA, intraoperative cardiopulmonary arrest.

TABLE 2. Characteristics of Children Who Experienced ICA During Surgical Correction of Spinal Deformity

Patient No. by Time of ICA	Diagnosis	Age (yr)	Sex	Body Weight (kg)	EBL (mL)	EBL/BV	No. of Levels Fused	Curve Magnitude (°)	Suspected Cause of ICA
Intubation									
1	Loeys-Dietz syndrome	11	M	23.6	0	0	0	90 (T), 60 (TL)	Respiratory/airway cause
Positioning [§]									
2	Adolescent IS	16	F	47.2	0	0	0	75 (T), 48 (L)	Primary rhythm disturbance
Instrumentation									
3	Marfan syndrome	17	M	67.6	2200	0.4	14	50 (TL)	Cardiovascular cause*
4	Cerebral palsy	12	F	28.0	600	0.3	14	140 (T), 133 (L)	Cardiovascular cause*
5	Cerebral palsy	17	M	32.0	4600	2.0	0 [†]	155 (TL)	Cardiovascular cause*
6	Infantile IS	9	F	22.0	5	0	0 [†]	76 (TL)	Anaphylaxis
7	Congenital myopathy	12	M	45.8	8000	2.3	15	93 (T), 72 (L)	Cardiovascular cause*
8	Congenital scoliosis [‡]	1.5	F	13.6	600	0.6	0 [†]	43 (T)	Cardiovascular cause*
Wound closure									
9	Cerebral palsy	14	M	28.5	2400	1.1	15	90 (TL)	Cardiovascular cause*
10	Cerebral palsy	15	F	36.3	3000	1.3	15	88 (TL)	Cardiovascular cause*
11	Spinal cord tumor	15	F	26.2	2200	1.3	18	96 (T), 50 (L)	Cardiovascular cause*

BV, blood volume; EBL, estimated blood loss; ICA, intraoperative cardiopulmonary arrest; IS, idiopathic scoliosis; L, lumbar; T, thoracic; TL, thoracolumbar.

*Electrolyte imbalance/hypovolemia.

[†]ICA during instrumentation resulting in wound closure without fusion.

[‡]Hemivertebra and kyphoscoliosis.

[§]Placement in prone position.

Cardiac Arrest Timing

ICA occurred during spinal instrumentation in six of 11 patients in our study cohort. Three patients experienced ICA during wound closure, and two patients experienced ICA at other times.

Causes of Cardiac Arrest

There were various suspected causes of ICA. We determined ICA to be the result of cardiovascular causes in eight patients (73%), anaphylaxis in one patient, respiratory or airway disorder in one patient, and primary cardiac dysrhythmia in one patient. In all six patients with neuromuscular scoliosis and in one patient with Marfan syndrome and one patient with congenital scoliosis, we determined ICA to be the result of cardiovascular causes (electrolyte imbalance and hypovolemia). In one patient with infantile idiopathic scoliosis,

one patient with Loeys-Dietz syndrome, and one patient with adolescent idiopathic scoliosis, we determined anaphylaxis, respiratory/airway cause, and primary rhythm disturbance, respectively, to be the most likely causes of ICA.

DISCUSSION

We determined that cardiovascular factors likely caused 8 of the 11 cases of ICA in our study. We also found that 6 of the 11 patients who experienced ICA had neuromuscular disorders; this represents a 3-fold higher risk of ICA compared with patients without neuromuscular disorders. In studies that have reported on the correlation between patient diagnosis and blood loss, pediatric spinal fusion surgery^{5,6} (and specifically neuromuscular scoliosis surgery^{2,9,10}) was reported to be most commonly associated with high

TABLE 3. Factors Associated With ICA in Children Undergoing Spinal Deformity Correction Surgery

Factor	ICA Group (n = 11)	Non-ICA Group (n = 2513)	P Value
No. of levels fused	15 (range, 14–18)	12 (range, 8–16)	0.044
Body weight (kg)	34 (range, 14–68)	49 (range, 32–66)	<0.01
EBL (mL)	2623 (range, 5–8000)	959 (range, 142–1776)	<0.01
EBL/BV	1.03	0.33	<0.01

BV, blood volume; EBL, estimated blood loss; ICA, intraoperative cardiopulmonary arrest.

intraoperative blood loss in children. These findings are consistent with those of our study, in which cardiovascular reasons were the most likely cause of ICA. EBL and EBL/BV are especially important and must be monitored during surgery to ensure adequate BV repletion. Five of the 11 patients in the ICA group had EBL/BV ratios greater than 1.0 at the time of ICA. Major blood loss (which we defined as EBL/BV ratio of more than 0.4) leading to hypovolemia was observed in 6 of 11 patients who experienced ICA in our study group.

ICA may be caused by various factors, including loss of blood volume, electrolyte imbalance, vascular injury, cardiopulmonary disease, and allergic reaction. Bhananker *et al*⁶ reported on anesthesia-related causes of ICA in children undergoing various types of surgery. In a recent review of the Pediatric Perioperative Cardiac Arrest Registry,⁸ Bhananker *et al* reported that cardiovascular causes are most commonly implicated in anesthesia-related ICA. Cardiovascular cause was defined as blood loss leading to hypovolemia or electrolyte imbalance. Hypovolemia was reported as the most common single identifiable factor, most often occurring during spinal fusion, craniotomy, or craniectomy surgery. Flick *et al*⁷ reported on perioperative cardiac arrest in children undergoing various types of surgery. Children undergoing cardiac surgery were most likely to sustain perioperative cardiac arrest with a reported rate of 127/10,000. In children undergoing noncardiac surgery, the incidence of anesthetic-related cardiac arrest was 2.9/10,000. Hypovolemia with subsequent hyperkalemia secondary to high-volume blood transfusion was reported as the most common likely cause of cardiac arrest in these children. In the four children who underwent spinal surgery in their study, hemorrhage, hypovolemia, and high-volume blood replacement with hyperkalemia were reported as the most likely causes of perioperative cardiac arrest.

Blood loss during spinal deformity surgery has been positively correlated with the number of spinal levels fused.^{2,11,12} In our study, patients in the ICA group had a significantly higher number of levels fused compared with patients in the non-ICA group. Rapid transfusion (defined as transfusion at rates greater than 0.3 mL/kg) and transfusion of old blood (at least 2 weeks old) have been associated with electrolyte imbalance, which may predispose patients to ICA.^{13–15} Brown *et al*¹⁴ reported on hyperkalemia during rapid blood transfusion and hypovolemic cardiac arrest in children. They reported the possible causes of hyperkalemia, including rapid blood transfusion, transfusion of old blood, and transfusion in the setting of depressed cardiac output from excess blood loss and hypovolemia. Hyperkalemia is associated with disturbances in cardiac rhythm, and this is especially important in the setting of an acute rise in potassium. In this setting, a lower potassium level may lead to depressed cardiac output and potential cardiac arrest in contrast with chronic hyperkalemia, which typically requires a higher serum potassium level.¹⁶ Although we were unable to determine the exact amount of blood transfused during ICA, the age of the blood transfused, or the rate

of transfusion, the mean amount of blood transfused was 9 units (range, 1–17 units) for the five patients who experienced ICA as a result of blood loss or hypovolemia. In our study population, hyperkalemia (defined as potassium more than 5.5 mEq/L) was observed in 5 of 11 patients with ICA and in four of five patients with ICA caused by hypovolemia and high-volume blood loss.

Blood transfusion to treat hemorrhage and hypovolemia has also been associated with hypocalcemia, a potential cause of cardiac arrhythmia and ICA. Total body calcium is composed of ionized calcium and protein-bound calcium. Ionized calcium is an important measure for critically ill patients receiving fluid transfusion. Cardiovascular manifestations of low ionized calcium include bradycardia and tachycardia, prolonged QT interval, and dysrhythmias.^{17,18} Normal ionized calcium levels are commonly reported as 1.12 to 1.32 mmol/L.¹⁹ The mean (standard deviation) ionized calcium level in the ICA group was 1.2 ($\pm$ 0.43) mmol/L. Two of the 11 patients who experienced ICA in our study had ionized calcium levels 1.0 mmol/L or less at the time of ICA. We were unable to determine whether low ionized calcium caused ICA, even though it is a potential risk factor.

Respiratory/airway disorder was determined to be the most likely cause of ICA in one patient. Inadequate endotracheal tube placement, endobronchial intubation, aspiration, and mucous plug are all potential complications of endotracheal or nasotracheal intubation. Hypoxia caused by inadequate ventilation and metabolic acidosis may lead to cardiopulmonary arrest. ICA in this patient occurred during a difficult nasotracheal intubation after 9 days of traction for cervicothoracic kyphosis. Difficult intubation in this case was attributed to abnormal nasotracheal anatomy.

Primary rhythm disturbance, defined as a disruption of the normal cardiac electrical signal pathway, may predispose patients to cardiopulmonary arrest. Potential causes of primary rhythm disturbance include sinoatrial node disorder, cardiomyopathy, coronary artery disease, abnormal heart valve, birth defects, and electrolyte abnormalities. Diagnosis of primary rhythm disturbance is typically made with an electrocardiogram. Primary rhythm disturbance can also be potentiated or induced by external factors, including stress, alcohol, and prescription or nonprescription medications. Use of intraoperative methadone to limit perioperative opioid demand has been described.²⁰ Intraoperative use of methadone is associated with prolonged cardiac action potential shown on electrocardiogram as a prolonged QT interval^{21,22} and clinically as cardiopulmonary arrest. Electrocardiography after ICA was also notable for a borderline prolonged QT interval for one of our patients with adolescent idiopathic scoliosis. Prolonged QT syndrome potentiated by the use of methadone during induction of anesthesia was determined to be the most likely cause of ICA in this patient.

Anaphylaxis may also manifest as cardiopulmonary arrest. Anaphylaxis was determined to be the most likely cause of ICA in one patient in our study. Thrombin is a

biologically active agent that is commonly used in spine surgery for hemostasis. Thrombin anaphylaxis has been reported as a cause of rapid decline in blood pressure with decrease in ventilation and oxygen saturation.^{23,24} Thrombin anaphylaxis occurred in a 9-year-old patient with infantile idiopathic scoliosis in our study. Severe hypotension and hypoxia secondary to presumed thrombin anaphylaxis *versus* embolus was noted after use of thrombin gelatin. The patient was successfully resuscitated with CPR, steroids, and diphenhydramine. This potential adverse effect must be considered when evaluating patients with ICA and during preoperative risk evaluation.

There are some limitations to this study. First, this is a retrospective study of data from two tertiary-care centers, and the recording of data by the surgical and anesthesia teams was slightly different. Second, patient medical records omitted certain details regarding blood transfusion, including the rate of transfusion and the age of the blood transfused, which may influence electrolyte imbalance and its cardiovascular effects; however, the rate of transfusion and the age of the blood transfused are not typically documented in the operating room. We were able to obtain electrolyte values recorded before, during, and after ICA. On the basis of these data, the electrolyte imbalance observed during ICA can potentially be attributed to the volume and rate of blood transfused and the patients' hemodynamic status. Further, although we found that ICA occurred more often in patients with neuromuscular disorders, our study was underpowered to detect a statistically significant difference. A *post hoc* power analysis showed that 3092 patients would be required in each group to detect a difference between the 0.08% ICA rate in the neuromuscular group and the 0.03% rate in the nonneuromuscular group with a power of 0.8 and alpha of 0.05.

CONCLUSION

This study reports an incidence of ICA of 0.4% in children undergoing spinal deformity correction surgery. This is the first evaluation of causes of ICA and associated risk factors in children undergoing spinal deformity correction by analyzing the entire at-risk population. The number of vertebral levels fused, patient weight, EBL, and EBL/BV were found to be significant risk factors. Although causes of ICA are multifactorial, cardiovascular causes are the most common. Patients with nonidiopathic scoliosis are at a higher risk of ICA than are patients with idiopathic scoliosis. Awareness of the normalized rate of blood loss and interventions to limit blood loss and replace blood volume during surgery are recommended, especially in patients with neuromuscular disorders.

➤ Key Points

- ❑ ICA occurs in approximately 0.4% of children undergoing spinal deformity correction surgery.
- ❑ Cardiovascular causes (electrolyte imbalance, hypovolemia) appear to be the most common cause of ICA.

- ❑ Greater blood loss, higher ratio of EBL to total BV, lower body weight, and greater number of vertebral levels fused are risk factors for ICA.
- ❑ Children with idiopathic scoliosis are at lower risk of ICA than those with other types of scoliosis.

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