Comparison of Perioperative Anesthetic Concerns in Simple and Complex Craniosynostosis Cases: A Retrospective Study

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J Neuroanaesthesiol Crit Care 2022;9:29–34.

Abstract

Background We compared intraoperative and postoperative anesthetic parameters between simple (S-single suture) and complex (C-more than one suture) craniosynostosis cases.

Materials and Methods Data was collected from a retrospective review of anesthetic and postoperative records of patients who underwent craniosynostosis correction surgery between April 2014 and August 2019. Pearson's chi-square and independent sample *t*-tests were used for analysis.

Results We analyzed data of 98 patients (S-simple craniosynostosis: 40 and C-complex craniosynostosis: 58). Statistically significant differences between simple and complex cases were seen only in the incidence of difficult airway, failed extubation, and requirement of postoperative ventilation. Massive blood loss (S: 23.21 mL/kg; C: 22.71 mL/kg) and difficult airway (S: 2.04%; C: 19.39%) were the most common intraoperative adverse events encountered. Metabolic abnormalities, hemodynamic instability, and hypothermia occurred in few patients. The most common postoperative issue was pyrexia (S: 15.31%; C: 17.35%). Anemia and coagulopathy needing transfusion of blood products and vitamin K injection were seen in a significant number of cases. Three nonsyndromic patients developed seizures.

Conclusion The incidence of difficult airway and failed extubation with postoperative ventilation is more frequent following surgery for complex craniosynostosis than simple craniosynostosis. Complications secondary to blood loss and airway issues were the primary cause of morbidity and mortality. A staged approach to surgical management resulted in decreased surgical blood loss among the children with complex craniosynostosis.

Keywords
- anesthesia
- craniosynostosis
- coagulopathy
- syndrome
- simple
- complex
- complications

published online
February 22, 2022

DOI https://doi.org/10.1055/s-0041-1740203
ISSN 2348-0548

Thieme Medical and Scientific Publishers Pvt. Ltd. A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

Introduction

Craniosynostosis is the premature closure of the cranial sutures causing abnormal growth of the skull which affects an estimated 1 in 2,000 to 2,500 live births worldwide.[1] This results in abnormal brain growth, increased intracranial pressure, seizures, and neurodevelopmental impairment. Studies describe an increase of intracranial pressure in 15 to 20% children with single suture craniosynostosis.[2] Many of these children have psychological problems due to their physical appearance.

Craniosynostosis may be classified as simple or complex. In simple craniosynostosis there is involvement of only a single suture whereas in complex cases multiple sutures are involved. Syndromic synostoses include Crouzon, Apert, Muenke, Carpenter, Saethre-Chotzen, craniofrontonasal dysplasia, Antley-Bixler, and Pfeiffer.

Depending on the involvement of sutures, craniosynostosis may present as scaphocephaly, plagiocephaly, trigonocephaly, and brachycephaly.[3]

An early surgical correction is required for the development of the brain and better cosmesis. However, this has to be balanced with implications of subjecting younger infants to major surgery and sometimes prolonged anesthesia. Since there may be reduced ability of the skull to ossify in older children, craniosynostosis surgeries are often performed around 6 to 12 months of age. Endoscopic techniques may be considered to reduce morbidity.

Preoperative airway assessment and cardiac evaluation are important, particularly in syndromic patients. Obstructive sleep apnea and respiratory complications are frequent in syndromic synostoses.

Anesthetic concerns in craniosynostosis surgery include any ongoing respiratory infection, presence of congenital heart disease, difficult intravenous access, difficult ventilation and intubation, positioning of the patient, raised intracranial pressure, and massive blood loss.[4]

Surgical outcome is influenced by surgical techniques, perioperative events, and postoperative complications. In the perioperative period, predictive complicating factors should be monitored. Early intervention prevents serious complications and improves outcome.

Literature is scarce about perioperative complications and the factors leading to it. The objective of this retrospective study was to compare the incidence of perioperative complications between simple and complex craniosynostosis cases and to describe these complications.

Materials and Methods

This study was a retrospective analysis of craniosynostosis corrections done in our institute during the period from April 2014 to August 2019. The data collected include the name, age, gender, diagnosis, date and type of surgery, redo surgeries, intraoperative blood loss and transfusion of blood products, use of tranexamic acid, and intraoperative and postoperative adverse events.

We included all craniosynostosis patients who underwent definitive surgical procedures at our craniofacial unit from January 2014 to December 2019.

For the study purpose we have used the term simple craniosynostosis, which included all patients who had a diagnosis of single suture craniosynostosis, and complex craniosynostosis which included multisutural and syndromic craniosynostosis. The multisutural synostoses include patients whose genetic workup did not identify known syndromes or was not available but had multisutural involvement of the sutures.

Sample Size

Based on the proportion of intraoperative and postoperative complications like venous air embolism (4.2%), blood loss (5.5%), fever (33.7%), and respiratory infection (9.5%) observed in an earlier publication and with 95% confidence and 10% allowable error, the minimum sample size calculated was 86.[5]

The statistical analysis was done using the IBM SPSS version 20.0 software (IBM SPSS, United States). The intraoperative and postoperative categorical complications were computed with 95% confidence interval and measurable complications were estimated according to mean standard deviation. To test the statistical significance of the difference in the proportion between the categorical variables of simple and complex craniosynostosis, Pearson's chi-square test was applied. The statistical significance of the difference in the mean of continuous variables between simple and complex craniosynostosis was assessed using independent sample *t*-test for normal data and Mann–Whitney *U* test was used for skewed data.

Results

This retrospective analysis included 98 patients who underwent craniosynostosis correction between April 2014 and August 2019. Age varied from 3 months to 23 years. The median age of our study population was 2 years, of which 39 were infants and 8 were older than 12 years. The median weight was 10 kg. Fifty-two patients were female while 46 were male.

During the study period 58 complex and 40 simple craniosynostosis patients underwent definitive procedures. Data of 16 patients was inadequate and were excluded from the study. The most common diagnoses among the complex cases were Crouzon syndrome (19; 19.4%), multisutural synostosis (16; 16.3%), and craniofrontonasal dysplasia (12; 12.2%). Among the simple craniosynostosis cases plagiocephaly and brachycephaly were the most common (►**Fig. 1**).

Fronto-orbital advancement (45%) was the most common procedure performed followed by midface correction and hypertelorism correction (►**Fig. 2**). Thirty-two patients underwent a second surgery, 10 patients had three surgeries, and 3 patients had four surgeries.

Assessment of blood loss during craniosynostosis repair is fraught with pitfalls due to patient size and surgical

technique, frequently resulting in underestimation. Blood loss in our cases varied from 50 to 1,300 mL (6.10 to 72.22 mL/kg). The average blood loss was 21.93 mL/kg. Intraoperative transfusion of blood products or isotonic saline was decided by the anesthesiologist based on assessment of hemoglobin concentration, blood loss, central venous pressure, and blood pressure measurements. Except for a few cases in 2014 all our patients received tranexamic acid (loading dose of 10 mg/kg over 10 minutes followed by maintenance of 5 mg/kg/h). Though the blood loss in complex cases was less (22.71 mL/kg) compared with simple craniosynostosis (23.21 mL/kg), this difference was not statistically significant (p = 0.1). Majority (87; 88.78%) of the patients needed packed red blood cell (PRBC) transfusion (17.69 mL/kg). Intraoperatively, fresh frozen plasma (FFP) was given depending on volume of PRBCs transfused and intraoperative international normalized ratio (INR) values (transfusion if INR > 1.4). Forty-four patients received FFP (average of 5 mL/kg).

A total of 21 (21.43%) patients had difficult airway (either difficult ventilation or intubation) out of which 19 were complex and 2 were simple craniosynostosis and the difference was statistically significant (p = 0.004) (►**Table 1**). Twelve of these patients were Crouzon syndrome, 3 were Apert, and 2 were craniofrontonasal dysplasia and 1 each of Saethre–Chotzen and multisutural synostosis. Among the simple craniosynostosis patients, difficult airway was encountered in one trigonocephaly and one brachycephaly case. Seven children had preoperative history of obstructive sleep apnea.

Intraoperative severe hypotension was seen in 3 patients (2 simple and 1 complex) (p = 0.70). All these patients had severe blood loss during surgery and required PRBC transfusion and noradrenaline infusion of more than 0.1 µg/kg/min. One of these children had blood loss complicated by air embolism and cardiac arrest intraoperatively from which the child was resuscitated successfully.

Three patients failed to maintain airway after extubation (4.08%) and needed reintubation. A 26-year-old patient with craniofrontonasal dysplasia and 2 children with Crouzon syndrome desaturated after on-table extubation and needed

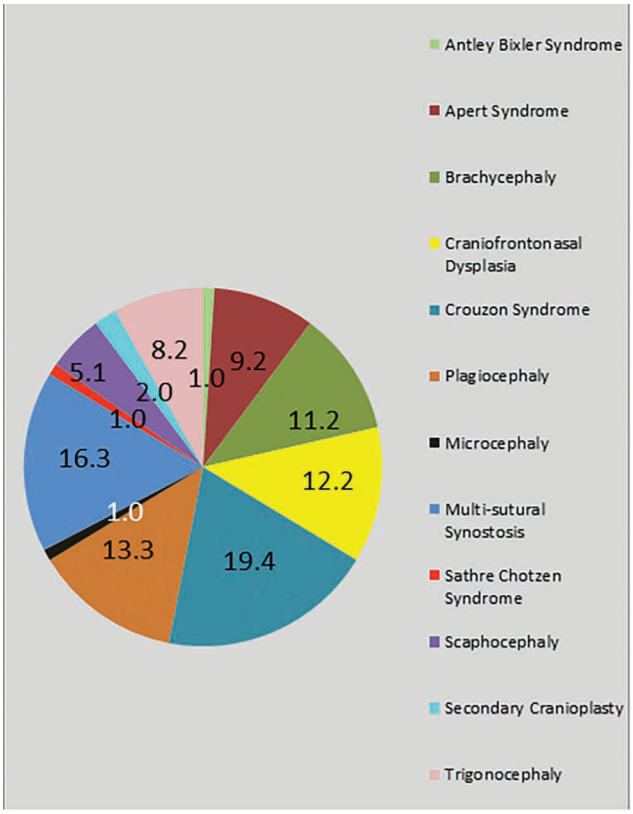

Fig. 1 Distribution of diagnosis.

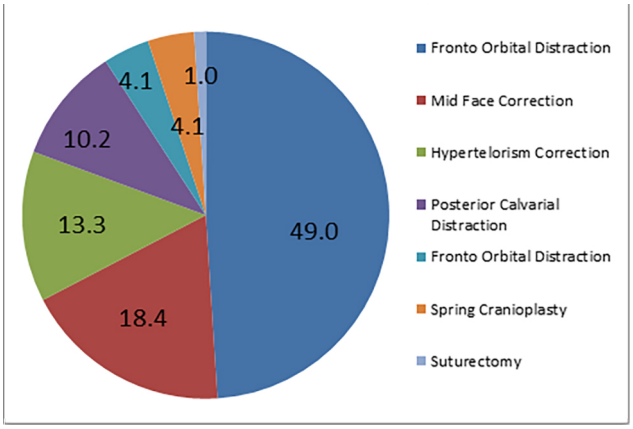

Fig. 2 Distribution of type of surgeries.

Table 1 Comparison of intraoperative concerns/events between simple and complex craniosynostosis

	Number of cases				
Intraoperative concerns	**Simple**		**Complex**		***P*-Value**
	Number	**Percentage (%)**	**Number**	**Percentage (%)**	
Bleeding	38	38.8	49	50	0.133
Difficult airway	2	2.0	19	19.4	0.004
Metabolic abnormalities	1	1.0	5	5.1	0.416
Failed extubation	0	0	3	3.0	0.047
Hypotension	2	2.0	1	1.0	0.742
Hypothermia	0	0	2	2.0	0.646
Air embolism and cardiac arrest	1	1.0	0	0	0.851

Table 2 Comparison of postoperative adverse events/concerns between simple and complex craniosynostosis cases

	Number of cases				
Postoperative concerns	**Simple**		**Complex**		***P*-Value**
	Number	**Percentage (%)**	**Number**	**Percentage (%)**	
Coagulopathy	18	18.4	28	28.6	0.910
Fever	15	15.3	17	17.4	0.612
Anemia	9	9.2	19	19.4	0.269
Ventilation	2	2.0	14	14.3	0.025
Respiratory infection	3	3.1	4	4.1	1.000
Stridor	0	0	3	3.1	0.387
Seizures	3	3.1	0	0	0.128
Epistaxis	1	1.0	0	0	0.851
Sepsis	0	0	1	1.0	1.000

reintubation. All 3 patients were complex cases ($p = 0.046$). An incident of inadvertent intraoperative extubation occurred in a child with Apert syndrome during a maxillary advancement. The child was reintubated without any complications ensuing.

In spite of all the precautions we took, two complex cases (craniofrontonasal dysplasia and multisutural synostosis) developed hypothermia (core body temperature < 35°C) intraoperatively ($p = 0.046$). Both the children received massive blood transfusion.

Metabolic abnormalities were found in five complex cases and one simple case ($p = 0.40$). Two children who received massive blood transfusion developed hyperkalemia. Other metabolic abnormalities seen were hypocalcemia, hypokalemia, hyponatremia, hypoglycemia, hyperglycemia, and metabolic acidosis.

Postoperative assessment of complications was done from the time of admission in intensive care unit (ICU) to shift from ICU (►**Table 2**). All our patients were managed in neurosurgical ICU in the postoperative period. Laboratory assessment of patients included complete blood count, serum electrolytes, biochemical, and coagulation parameters. Following surgery, 28 patients became anemic (19 complex and 9 simple cases) and required PRBC transfusion ($p = 0.3$). Twenty-eight complex and 18 simple cases ($p = 0.9$) developed coagulopathy (measured as raised prothrombin time/INR). They were treated with FFP (36), cryoprecipitate, and vitamin K injection (17).

During the postoperative period, 32 patients (17 complex and 15 simple cases) ($p = 0.6$) developed fever (►**Table 2**). Evaluation of the cause revealed no infective cause in 17 patients, who were labeled as pyrexia of unknown origin. Of the remaining 15, lower respiratory infection and bloodstream infection were the most common causes of fever.

There was a statistically significant difference ($p = 0.025$) in respiratory failure requiring postoperative ventilation between simple and complex cases (14 complex and 2 simple). A Crouzon syndrome child failed multiple weaning attempts and required tracheostomy.

Three cases (Crouzon [1], microcephaly [1], and craniofrontonasal dysplasia [1]) developed stridor after extubation. The first two needed reintubation and the third case responded to medical management. Three of our patients (three simple cases) developed seizures ($p = 0.10$); all responded to medical management.

A 5-month-old child with Crouzon syndrome failed in multiple weaning attempts, developed pneumonia, sepsis, and eventually had cardiac arrest. The child could not be revived.

Discussion

Major morbidity and mortality rates for pediatric complex cranial vault reconstruction surgery has been reported to be less than 0.3% for intracranial and subcranial procedures.[6] A recent report of 225 children undergoing open craniosynostosis surgery identified incidence of postoperative cardiorespiratory events at 14.7%, and 29.7% for hematological events.[7] Independent predictors of morbidity included six multivariate risk factors (body weight < 10 kg, American Society of Anesthesiologists Physical Status > 3, PRBC transfusion > 60 mL/kg, blood product administration, not administering tranexamic acid, and intraoperative complications).[7] A study by Goobie et al found that patients receiving tranexamic acid had a significantly lower perioperative mean blood loss (65 vs. 119 mL/kg) and blood transfusion (33 vs. 56 mL/kg).[8] Tranexamic acid administration was associated with significantly fewer postoperative complications.[9]

Craniofacial reconstruction procedures involve wide scalp dissections with multiple osteotomies leading to significant blood loss. Current literature suggests that longer operative time, younger age (less than 12 months), and lower weight are prone for significant blood loss leading to a high frequency of blood transfusion with adverse effects.[10] Sudden and extensive blood loss can occur during tearing of venous sinuses or major cortical veins.[11]

Studies have shown that the average transfusion in craniosynostosis surgery was 50 to 100 mL/kg.[12] The average blood loss (22.71 mL/kg) and intraoperative PRBC transfusion (17.69 mL/kg) in our study was lower than in many other centers. This may be due to the routine use of tranexamic acid, intraoperative hemodilution, or because of the meticulous surgery. Fenger-Eriksen et al used bolus dose of 10 mg/kg of tranexamic acid followed by an infusion of 3 mg/kg/h and

found reduced perioperative blood loss and transfusion requirements.[13] We used a higher infusion dose of tranexamic acid of 5 mg/kg/h. Unlike other centers, in our study complex cases had slightly less blood loss (22.71 mL/kg) than simple craniosynostosis cases (23.21 mL/kg) which was not statistically significant.

Recently the implementation of a ROTEM-assisted patient blood management found a reduction in intraoperative transfusion requirements and thereby a decrease in transfusion-related complications and costs.[14] A study by Haas et al found that administering fibrinogen concentrates improves the clot strength and reduced platelet and FFP transfusion.[15]

Most of the difficult airway cases (19 cases) were encountered in complex craniosynostosis. All difficult cases were managed with pediatric C-MAC video laryngoscope (Karl Storz). None of our patients required flexible fiberoptic guidance for intubation. The causes for difficult airway in complex craniosynostosis were midface abnormality (hypoplasia or retrusion), maxillary hypoplasia, deficient mandible, prognathism, micrognathism, and acute angulation between forehead and root of nose.

Pediatric patients undergoing craniosynostosis surgery are vulnerable to the development of hypothermia. Patients with Apert syndrome are known to lose heat due to excessive sweating. Hypothermia can lead to increased blood loss, acidosis, and myocardial depression. We took meticulous care in maintaining the temperature of the patients by covering the extremities, raising operating room temperature, using forced air warming blankets, and fluid warmer. Hypothermia significantly amplifies intraoperative blood loss when compared with normothermic patients.[16]

The majority of episodes of vascular air embolism during craniosynostosis repair are without hemodynamic consequences. Using a precordial Doppler, the incidence of air embolism in craniosynostosis surgery was found to be as high as 82.6%.[17] Precordial Doppler and the use of transesophageal echocardiography have been recommended to increase the chance of early diagnosis; however, most centers use waveform capnography for detection. We do not routinely use either echocardiography or precordial Doppler during craniosynostosis surgery.

The perioperative metabolic derangements are primarily due to blood loss and subsequent resuscitation. A study by Choi et al documented the degree of perioperative metabolic disturbance during major craniofacial surgery in children.[18] The incidence of hyperkalemia in patients receiving stored packed cells of more than 2 weeks' duration is as high as 45%.[19]

Postoperative anemia was diagnosed in 28.57% of our patients. Studies suggest that hypervolemic hemodilution may contribute to the postoperative anemia in craniosynostosis surgery. Correction of the volume status with furosemide administration may reduce postoperative transfusion requirement.[20]

The main cause for coagulopathy can be attributed to blood loss and subsequent transfusion of blood products. Postoperatively, 44 patients received FFP (5 mL/kg). Exclusively breastfed infants may benefit from injection vitamin K.[21]

A cautious extubation of syndromic/complex patients is warranted and is should be always in the presence of an experienced anesthetist as the surgery itself may alter airway anatomy and predispose the children both to airway obstruction and desaturation. We found that patients with complex craniosynostosis have a statistically significant risk of postoperative respiratory failure leading to ventilation (p = 0.025). The probable factors predisposing these children to failed extubation include a prolonged duration of surgery, marked fluid shifts and blood transfusions, effects of prolonged prone positioning, and patient factors such as abnormal upper airway anatomy.

In 59.38% of patients, the cause of postoperative fever could not be identified. This may be attributed to prophylactic use of antibiotics, or as sequelae of blood transfusion. Field et al noted that fever of unknown origin is common after craniosynostosis repair and was associated with the duration of hospital stay.[22] We found no statistical difference in postoperative fever between simple and complex cases.

Studies showed the incidence of seizures in nonsyndromic craniosynostosis cases at around 0.7 to 0.8%.[1] In our study, three children with simple craniosynostosis had seizures. Lin et al showed the incidence of sepsis of around 1% in nonsyndromic craniosynostosis.[1] In our series, one child developed pneumonia and sepsis.

Conclusion

Statistically significant differences between simple and complex craniosynostosis cases were seen only in the incidence of difficult airway, failed on-table extubation, and requirement of postoperative ventilation. We therefore conclude that due caution needs to be exercised when managing patients with complex craniosynostosis especially during induction and emergence from anesthesia. Complications secondary to blood loss and airway issues were the primary cause of morbidity and mortality, but this is common to all classes of craniosynostosis. Modalities to reduce transfusion requirements and anticipation of airway-related issues are important in ensuring the best outcomes for children coming for craniosynostosis surgery.

Conflict of Interest
None declared.

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