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Perioperative Management and Outcomes of Pediatric Craniosynostosis Patients Undergoing Cranioplasty: A Retrospective Analysis

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Abstract: Cranioplasty is a major surgical procedure typically performed in children under 1 year of age, often associated with significant complications. The scientific literature on perioperative management for children with craniosynostosis undergoing cranioplasty is limited. The authors' objective was to retrospectively evaluate the management, complication rates, and outcomes among children undergoing cranioplasty at our institution. The authors conducted a single-center retrospective analysis of craniosynostosis children who underwent cranioplasty at Fondazione IRCCS San Gerardo dei Tintori between 2009 and 2023. 102 children were studied. Median admission age was 307 days, 30.4% of patients had syndromic disease; 28.4% underwent multi-suture cranioplasty. Median blood loss was 225 ml, and 85% of patients required red blood cell transfusion. There was a significant difference neither in indexed blood loss between the single and the multi-suture groups nor in perioperative transfusion requirement. 93.2% of patients in the single-suture group were extubated upon completion of the procedure against 65.5% of multi-suture group. No deaths were recorded. All patients were admitted to the intensive care unit after surgery. 8.8% patients suffered at least one complication. Airway management was the most common (7.8% of patients), intraoperative blood loss > 90% of estimated blood volume occurred in 4 (3.9%) patients, whereas 3 children (2.9%) developed intracranial hypertension. Syndromic patients exhibited a significantly higher incidence of perioperative complications. Managing children's cranioplasty perioperative care is challenging, especially in multi-suture and syndromic cases. These findings stress the importance of multidisciplinary collaboration, precise intraoperative management, and comprehensive postoperative monitoring.

Key Words: Blood loss, children, complications, cranioplasty, perioperative management

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Craniosynostosis is a congenital anomaly characterized by the premature fusion of one or more cranial sutures. This abnormality restricts normal skull growth, resulting in cranial deformities. It can be associated with various complications, including intracranial hypertension, Chiari malformation, hydrocephalus, ventriculomegaly, visual deficits, and neuropsychiatric disorders.[1,2] The prevalence of craniosynostosis is estimated to be ~1 in 2100 to 2500 births.[2]

This condition can be classified as isolated (non-syndromic), accounting for 60% of cases, or syndromic, constituting the remaining 40% of cases and often presenting with more severe manifestation. The syndromes associated with this condition number about 180, with the most common ones being Muenke, Crouzon, Pfeiffer, and Apert syndrome.[3] Syndromic forms generally involve more than one suture and are accompanied by other congenital abnormalities, including hearing loss, facial morphologic abnormalities, cardiac complications, musculoskeletal, and genitourinary abnormalities.[4]

Craniosynostosis requires surgical correction aimed at preventing compensatory growth of the calvarium and mitigating associated complications. Surgical correction is usually performed between the ages of 9 and 12 months. The complications associated with surgical treatment comprise postoperative hyperthermia, infection, hematoma formation, rupture of the dura mater, cerebrospinal fluid (CSF) leakage, and blood loss.[2] The reported mortality and morbidity rate for intracranial procedures is 0.1%, with severe hemorrhage being one of the most important contributor to mortality.[5]

Current guidelines[1] recommend that surgery should be performed in specialized centers where a multidisciplinary team is

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available. Patients with syndromic forms are more likely to require multiple surgeries[6] and face an increased risk of surgical complications due to a higher rate of reoperation and the comorbidities associated with these conditions.[1] Postoperative intensive care unit admission is recommended.

The aim of this study is to retrospectively describe the perioperative management, the rate of complications and the outcomes of craniosynostosis patients undergoing cranioplasty at our institution.

MATERIALS AND METHODS

We conducted a retrospective analysis of records from craniosynostosis children that underwent cranioplasty between 2009 and January 2023 at Fondazione IRCCS San Gerardo dei Tintori.

According to the local regulations, no ethics committee approval is required for retrospective epidemiological studies using health care administrative databases for research purposes and with individuals identified by an anonymous patient code.

This study was conducted and reported based on the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.

Patient Management

Our institution is a referral center for craniosynostosis in Italy. Preoperative planning is conducted by a multidisciplinary team involving neurosurgeons, maxillofacial surgeons, a dedicated pediatric anesthesia team, intensivists, pediatricians, child neuropsychiatrists, ear, nose, and throat (ENT) physicians, pediatric cardiologists, and ophthalmologists.

In the operating room (OR), the pre-induction procedure involves the positioning of at least two peripheral venous accesses, one of which in a large caliber vein (e.g., external saphenous vein). If cannulation is not feasible, inhalation induction is used. Airway management prioritizes direct laryngoscopy as the primary choice for intubation. Additional devices, such as fiberscopes and video laryngoscopes, are available for managing predicted and unpredicted difficult airways. Armored endotracheal tubes are used to ensure the maintenance of airway patency, regardless of patient positioning during surgery. Anesthesia is maintained through halogenated gas and a continuous infusion of remifentanil. Finally, an arterial catheter and a central venous catheter are positioned. Intraoperative monitoring includes peripheral oxygen saturation, electrocardiography, precordial Doppler ultrasound, end-tidal CO_2, invasive blood pressure, central venous pressure, temperature, and urinary output.

Tranexamic acid is administered intraoperatively as a bolus (10–20 mg/kg) followed by continuous infusion (5 mg/kg/h) throughout the surgical procedure to reduce blood loss and the need for transfusion.[7] Repeated blood sampling is conducted to monitor gas exchange, hemoglobin levels, platelets, and coagulation tests (prothrombin time, activated partial thromboplastin time, fibrinogen). Thromboelastography is used in cases of severe bleeding to promptly detect specific coagulation abnormalities.

Fluid balance is meticulously monitored, with maintenance fluid calculated using the Holiday and Segar 4/2/1 rule.[8] Replacement fluid is estimated considering preoperative fasting (20 mL/kg), insensible perspiration (5–8 mL/kg/h) and estimated blood losses. Isotonic balanced crystalloid solutions are utilized.

Packed red blood cells (PRBC) are administered based on clinical indications. Common triggers for transfusions include, for instance, estimated blood losses exceeding 15% of circulating blood volume, hemoglobin level below 8 g/dL, or hemodynamic instability. An early pre-emptive transfusion strategy[9] was eventually adopted at our center, so that most patients are now transfused before clinical signs of significant blood loss present. Fresh frozen plasma (FFP) is administered to prevent dilutional coagulopathy. Platelets are transfused if their count falls below 50,000/μL.

Data Collection

We retrospectively collected data from patient records regarding intraoperative management, focusing specifically on pre and postoperative hemoglobin levels, fluid balance, transfused packed red blood cells, plasma and platelets, and the use of tranexamic acid. Furthermore, we gathered information on postoperative management, including intensive care admission and length of stay, time to extubation, post-extubation complications, and volume of blood loss from surgical drainage.

Statistical Analysis

Continuous data are presented as median and 25^{th} to 75^{th} percentile, and categorical data as count and percentage. Patients were stratified based on the type of surgery (i.e., single-suture versus multi-suture) and into syndromic and non-syndromic groups. Groups were compared using the Wilcoxon test for numerical variables and the Pearson χ^2 or Fisher test for categorical variables, as appropriate. A p-value below 0.05 was considered statistically significant. Statistical analysis was performed with JMP 16.0 (SAS).

RESULTS

A total of 102 children underwent neurosurgical treatment for craniosynostosis between 2009 and 2022 and were included in this study. Table 1 shows the characteristics of the study population.

[Supplemental Table 1, Supplemental Digital Content 1, http://links.lww.com/SCS/G883].

Most of the patients had isolated craniosynostosis, whereas 31 (30.4%) were affected by syndromic disease.

All patients underwent cranioplasty surgery, 2 of them with a mini-invasive technique. In 8.8% of cases, it was a revision surgery.

62.7% of patients were younger than 1 year at the time of the surgery. Only 9 patients were over 5 years old.

Median intraoperative indexed blood loss was 23.9 (18.4–30.1) ml/kg. Most patients received a blood component transfusion intraoperatively: 85.3% received at least one unit of packed red blood cells and 67.6% fresh frozen plasma. This was consistent with the institution protocol of pre-emptive intravascular volume loss replacement. Most of the patients (85.3%) were extubated immediately at the end of the surgical procedure and only 3 (3.4%) of them required additional oxygen support (HFNC) after extubation. All patients were admitted to an intensive care unit postoperatively.

Supplemental Table 2, Supplemental Digital Content 1, http://links.lww.com/SCS/G883 present the characteristics of the study population after stratification on the type of surgery (single-suture versus multi-suture).

Patients affected by multi-suture synostosis were more frequently syndromic, underwent surgical intervention at an older age, and exhibited a higher body weight, corresponding to a larger estimated blood volume. Multi-suture surgery took longer and incurred greater blood loss, as compared with single-suture surgery. However, indexed blood loss and requirements for blood product transfusions did not differ between the two groups. Notably, a higher proportion of patients in the single-

suture group were extubated upon completion of the procedure, whereas post-extubation respiratory support was more frequently required for patients with multi-suture synostosis.

The median ICU length-of-stay was 1 day. Patients that were extubated in the ICU had a median duration of intubation of 10 (2.3–16.5) hours, 3 (30%) of them required post-extubation HFNC, and 3 (30%) of them required low-flow oxygen supplementation. Twenty-two (21.6%) patients required inhaled corticosteroids, helium, or nebulized adrenaline after extubation. Median losses from surgical drainage were 50 (5–150) ml.

9 (8.8%) patients suffered at least one complication. Airway management was the most common (8 patients, 7.8%), including reintubation, bronchospasm and laryngospasm. Intraoperative blood loss > 90% of estimated blood volume (EBV) occurred in 4 patients (3.9%). No cases of air embolism were recorded. Four patients (2.9%) developed intracranial hypertension; 2 patients (2%) developed hyponatremia. Postoperative nausea and vomiting (PONV) occurred in 3 patients (2.9%) and anemia requiring blood transfusion occurred in 3 patients (2.9%).

One patient with Pfeiffer syndrome had a particularly complicated postoperative course. He had a 29-day ICU stay during which they required reintubation due to glottic edema and developed intracranial hypertension, necessitating ventriculoperitoneal shunt placement and subsequent peritoneal effusion. In addition, he developed acute respiratory distress syndrome (ARDS), and required tracheostomy for difficult ventilatory weaning.

Supplemental Table 3, Supplemental Digital Content 1, http://links.lww.com/SCS/G883 presents a further stratification into syndromic and non-syndromic patient subgroups.

Airway management was more changeling in syndromic patients. Only 64.5% of syndromic patients were successfully extubated in the operating room, compared with 94.4% of non-syndromic patients, and they necessitated a greater oxygen and pharmacological support (in particular inhaled helium and nebulized adrenaline) when extubated. Moreover, syndromic patients exhibited a higher incidence of airway management complications and a higher incidence of postoperative hyponatremia (0.0% versus 6.4%) as compared with their non-syndromic counterparts.

DISCUSSION

In this retrospective cohort study, we comprehensively described the perioperative management, complications, and outcomes in craniosynostosis patients undergoing cranioplasty at our institution. Our findings contribute valuable insights to the existing body of knowledge on the perioperative challenges and outcomes associated with pediatric cranioplasty, particularly in cases involving syndromic and multi-suture craniosynostosis.

Our study recorded a high level of intraoperative blood loss, corresponding to a 30.7% loss of estimated blood volume (EBV), with 83% of patients requiring PRBC transfusion. Previous studies have documented varying percentages of EBV loss depending on the type of sutures involved. Kearney and Roales[10] reported a mean blood loss of 24% to 65%, influenced by the suture type and surgical techniques used in the 1970s and 1980s. Although surgical and anesthetic techniques have significantly improved since then, accurately estimating blood loss remains challenging due to the variability in methods[11] and reliance on subjective assessments. Unlike previous reports,[11] our study found no significant difference in indexed blood loss between single-suture and multi-suture patients, suggesting that the complexity of the procedure may not always correlate with increased blood loss.

A pre-emptive transfusion and infusion strategy, as advocated by Cortellazzi and Caldiroli, may be associated with better postoperative outcomes. In our cohort, intraoperative fluid balance was managed with a median infusion rate of 0.5 ml/kg/h, lower than that reported in earlier studies. Although preoperative interventions, such as erythropoiesis-stimulating agents (ESA)[12] and autologous transfusions[13], have been proposed to optimize hemoglobin levels and reduce transfusion needs, their use is limited by cost and invasiveness.[1] Similarly, intraoperative blood recollection devices are not recommended due to their limited efficacy in this surgical context. Furthermore, techniques such as local vasoconstrictor infiltration and controlled hypotension have not shown significant benefits in reducing blood loss and transfusion requirements.[1]

Recent reports suggest that preoperative antifibrinolytics like tranexamic acid might reduce blood loss and transfusion requirements.[7] In our study, 43% of patients received tranexamic acid before surgery. Although there is a physiological rationale and growing evidence supporting its use, our data did not allow for a definitive assessment of its impact on minimizing blood loss. Further research is needed to establish standardized protocols for antifibrinolytics in pediatric cranioplasty.

Our study identified an intraoperative complication rate of 4.6%, primarily related to extensive bleeding (> 90% of EBV) and airway management issues, including bronchospasm with desaturation in 2 patients. Postoperative complications occurred in 8.8% of patients, with airway management issues being the most common (7.8%). Significant complications included two cases of laryngospasm after extubation—one leading to cardiac arrest requiring reintubation with the return of spontaneous circulation (ROSC)—and 2 cases of desaturation managed with high-flow nasal cannulas (HFNC). In addition, we observed one case of repeated apnea in a patient with known obstructive sleep apnea syndrome (OSAS) requiring noninvasive ventilation (NIV) and one instance of temporary vocal cord paralysis. Other issues included hyponatremia, postoperative nausea and vomiting (PONV), ARDS and infections.[14] Major neurological complications were relatively rare, including seizures (0.9%), cerebrospinal fluid (CSF) leaks (0.9%), and intracranial hypertension (1.83%).

Despite these complications, the majority of patients had a successful postoperative course, with a median ICU length of stay of 1 day and only one reported case of extubation failure. Importantly, there were no reported deaths in our study group. Notably, major postoperative complications were more common among syndromic patients, consistent with the increased risk of complications in this group. These complications were primarily related to airway management, likely due to anatomical alterations associated with syndromic conditions. This highlights the critical importance of vigilant postoperative monitoring and tailored management for patients with syndromic forms of craniosynostosis.

This study has some limitations that should be considered when interpreting the findings.

First, the retrospective nature of the analysis may introduce selection and recall biases, as data were collected from medical records rather than through prospective methods. This may affect the completeness and accuracy of the data, particularly regarding the documentation of complications and intraoperative management details.

Second, the study was conducted at a single center, which may limit the generalizability of the findings to other institutions with different practices or patient populations. Variations in surgical techniques, anesthetic protocols, and postoperative care practices at other centers could influence outcomes and complicate direct comparisons.

In addition, the relatively small sample size, although substantial, may limit the statistical power to detect differences or

associations that might be present in a larger cohort. The lack of a comparative group or external benchmarks also makes it challenging to contextualize the results within broader practice trends and standards.

Another limitation is the lack of a standardized protocol for the use of antifibrinolytics and other blood conservation strategies in our cohort. Although we administered tranexamic acid to a portion of the patients, the variability in its use prevents a definitive assessment of its impact on blood loss and transfusion requirements.

Finally, as with any study involving complex surgical procedures, the heterogeneity in patient conditions, especially among syndromic cases, introduces variability that may affect outcomes. The specific anatomical and physiological challenges presented by syndromic craniosynostosis may not be fully captured in the aggregate data.

CONCLUSIONS

Our study highlights the importance of individualized perioperative care for pediatric cranioplasty, focusing on blood conservation and meticulous monitoring. Despite significant risks, particularly for syndromic patients, careful planning and multidisciplinary collaboration can lead to successful outcomes. These findings offer valuable insights for improving clinical practices and emphasize the need for further research to refine protocols and enhance patient care in this challenging field.

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