Perioperative Outcomes and Management in Pediatric Complex Cranial Vault Reconstruction

A Multicenter Study from the Pediatric Craniofacial Collaborative Group

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ABSTRACT

Background: The Pediatric Craniofacial Collaborative Group established the Pediatric Craniofacial Surgery Perioperative Registry to elucidate practices and outcomes in children with craniosynostosis undergoing complex cranial vault reconstruction and inform quality improvement efforts. The aim of this study is to determine perioperative management, outcomes, and complications in children undergoing complex cranial vault reconstruction across North America and to delineate salient features of current practices.

Methods: Thirty-one institutions contributed data from June 2012 to September 2015. Data extracted included demographics, perioperative management, length of stay, laboratory results, and blood management techniques employed. Complications and outlier events were described. Outcomes analyzed included total blood donor exposures, intraoperative and perioperative transfusion volumes, and length of stay outcomes.

Results: One thousand two hundred twenty-three cases were analyzed: 935 children aged less than or equal to 24 months and 288 children aged more than 24 months. Ninety-five percent of children aged less than or equal to 24 months and 79% of children aged more than 24 months received at least one transfusion. There were no deaths. Notable complications included cardiac arrest, postoperative seizures, unplanned postoperative mechanical ventilation, large-volume transfusion, and unplanned second surgeries. Utilization of blood conservation techniques was highly variable.

Conclusions: The authors present a comprehensive description of perioperative management, outcomes, and complications from a large group of North American children undergoing complex cranial vault reconstruction. Transfusion remains the rule for the vast majority of patients. The occurrence of numerous significant complications together with large variability in perioperative management and outcomes suggest targets for improvement. **(Anesthesiology 2017; 126:276-87)**

SINCE the inception of the discipline of pediatric craniofacial surgery with the pioneering work of Dr. Paul Tessier in the late 1960s, morbidity and mortality have steadily declined but remain relevant with recent reports of massive blood loss and life-threatening events.[1–6] Cranial vault reconstruction is performed in infants and children with craniosynostosis to improve appearance and prevent or treat neurologic impairment. Despite improvements in surgical technique and anesthetic management, many of which focused on limiting blood loss and transfusion, today, these patients may still experience massive blood loss and transfusion and are at risk of significant complications. There are currently no large-scale comprehensive analyses of both multicenter practices and outcomes for pediatric complex cranial vault reconstruction surgery (CCVR).

The Pediatric Craniofacial Collaborative Group was formed under the auspices of the Society for Pediatric Anesthesia in 2011. This group met and determined data elements to be collected and established the Pediatric Craniofacial Surgery Perioperative Registry (PCSPR) to elucidate current practices and outcomes in this population, with the ultimate goal of informing improvement efforts and optimizing care. The aim of this study is to determine perioperative management, outcomes,

What We Already Know about This Topic

- Cranial vault reconstruction for craniosynostosis is attendant with significant complications. A database of the rates of complications and modes of practice for complex cranial vault reconstruction is not available.
- In a multicenter assessment, the Pediatric Craniofacial Surgery Perioperative Registry was queried and anesthetic management and complications were evaluated.

What This Article Tells Us That Is New

- The majority of patients received blood transfusion and were admitted to the intensive care unit postsurgery.
- Notable complications included cardiac arrest, hypotension, seizures, coagulopathy, and large-volume blood transfusion.
- There were significant variations in perioperative management practices and in-hospital outcomes. These results serve as a platform for future comparisons of management practice.

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and complications in children undergoing CCVR and to delineate salient features of current practices. Specifically, this study aims to describe current North American trends in perioperative management of infants and children undergoing CCVR by reporting hospital outcomes including length of stay (LOS), major perioperative complications, anesthetic management techniques, fluid and transfusion practices, and the application of patient blood management strategies.

Materials and Methods

We queried the PCSPR for subjects undergoing CCVR. CCVR was defined as frontoorbital advancement/anterior cranial vault reconstruction, middle/posterior cranial vault reconstruction, or total cranial vault reconstruction. All procedures involved a craniotomy. Procedures identified as neuroendoscopic procedures, spring-mediated cranioplasties, and modified π procedures or variants thereof were excluded. Data extracted included demographic and surgical data, fluid and transfusion data, intensive care unit (ICU) and hospital LOS, perioperative management, and complications.

PCSPR

Participating institutions began entering data after local institutional review board or equivalent approval. Study data were collected and managed using research electronic data capture tools hosted at the Children's Hospital of Philadelphia, Philadelphia, Pennsylvania.[7] Data entry began on June 25, 2012. A deidentified dataset with data through September 30, 2015, was analyzed. Individual institutions were represented using an institution code and were not identifiable.

Data Collection, Entry, and Validation

Thirty-one institutions contributed data during the study time period (appendix 1). Sites were required to provide quarterly reports quantifying case capture rates to ensure the absence of reporting bias. The aggregate capture rate across all institutions was 96%. The median (25th to 75th interquartile range) case capture rate was 100% (97 to 100%) at the 25 institutions where informed consent was not required and 99% (68 to 100%) at the six institutions where informed consent was required. All participating institutions were required to report data collection and auditing processes to ensure accuracy. At 29 institutions, the principal investigator or designee reviewed more than 50% of cases before registry entry. At two institutions, 10 to 25% of cases were reviewed before registry entry.

In addition to the above, the study principal investigator at the Data Coordinating Center (P.A.S.) audited data before analysis. This included scrutinizing cases for omissions of critical data (*e.g.*, age and weight) and identification of outlier data. Cross-validation of data within individual records was performed to optimize data accuracy. Queries based on omissions, outliers, and discrepancies identified through this process were aggregated and sent to site investigators for rectification.

Outcomes and Analysis

Demographic data were analyzed using descriptive statistics. We divided the population into two age subgroups for the majority of the analyses: age less than or equal to 24 months (subsequently referred herein as the infant group and infants) and age more than 24 months (older group). The groups reflect the two principal demographics of children undergoing these procedures: those undergoing usually primary procedures in the first 2 yr of life (the majority of cases) and those presenting for surgery later in childhood (late presentations, redo procedures, and syndromic patients).

Outcomes analyzed included the following: total perioperative blood donor exposures, volume of erythrocyte-containing blood products (ECBPs) transfused intraoperatively, total volume of blood products transfused perioperatively (intraoperatively and in the first postoperative 48 h), hospital LOS, and ICU LOS. ECBPs include packed erythrocytes, whole blood, and reconstituted blood composed of packed erythrocytes and fresh frozen plasma (FFP).[8] Perioperative blood products included packed erythrocytes, reconstituted blood, whole blood, FFP, platelets, and cryoprecipitate. Owing to profound inaccuracies/biases of blood loss estimates in these infants and children, the collaborative group decided not to include estimated blood loss in the PCSPR. Transfusion volumes were used as surrogates for blood loss since they are systematically and accurately recorded. Anesthetic and surgical management, fluid and transfusion management, complications, and the application of blood conservation strategies are also described. Data measured on a continuous scale are presented as mean ± SD or median (25th to 75th interquartile range); frequencies and percentages are presented for categorical variables. Differences in selected outcomes by age group were compared using the independent sample Student's t test (two tailed) and the Wilcoxon–Mann–Whitney test. A $P < 0.05$ was considered statistically significant. Statistical analysis was done with the statistical package SAS (SAS Institute Inc., USA).

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*Members of the Pediatric Craniofacial Collaborative Group are listed in appendix 2.

Results

Demographics

The registry query yielded a total of 1,223 subjects from 31 institutions, with 935 aged less than or equal to 24 months and 288 aged more than 24 months. Demographic data are presented in table 1. In the infant group, the most common diagnoses were metopic, sagittal, and unicoronal synostosis. In the older group, the most common diagnoses were syndromic, sagittal, and multiple suture synostosis. Seventy-one percent of subjects in the older group and 23% of subjects in the younger group underwent redo operations or had either syndromic or multiple-suture (more than or equal to three sutures) synostosis. Compared to the infant group, older subjects had higher rates of total vault reconstruction ($P < 0.0001$), distractor placement ($P = 0.0003$), previous craniofacial surgery ($P < 0.0001$), syndromic craniosynostosis ($P < 0.0001$), preoperative elevated intracranial pressure ($P < 0.0001$), higher preoperative hemoglobin ($P < 0.0001$), and higher American Society of Anesthesiologists physical status ($P < 0.0001$; table 1). Among patients of all ages, preoperative evidence of increased intracranial pressure was more frequent in children with syndromic craniosynostosis than in those without (34% *vs.* 10%, respectively; $P < 0.001$).

Perioperative Outcomes

Selected perioperative outcomes are presented in table 2. The majority of patients were transfused perioperatively in both groups; only 5% of infants were not transfused. Transfusion volumes (ml/kg) were greater in the infant group. In terms of blood donor exposures, the most striking difference was the percentage of patients having at least one blood donor exposure (95% infant group *vs.* 79% older group).

Postoperative ICU admission was routine practice for the majority of patients at 90% (28/31) of institutions in the infant group and at 92% (22/26) of institutions in the older group. ICU LOS data were available for 872 (93%) and 279 (97%) patients in these groups, respectively; the median ICU LOS was 2 days for both groups. Only 4% (39/872) of infants and 3% (7/279) of older children were not admitted to the ICU.

Hospital LOS data were available for 887 (95%) infant group cases and 281 (98%) older group cases. The median hospital LOS was 4 days in infants: 97% stayed more than or equal to 3 days and 80% stayed more than or equal to 4 days. Findings were similar in older children, for whom median hospital LOS was 5 days: 96% stayed more than or equal to 3 days, and 79% stayed more than or equal to 4 days.

Perioperative Complications and Outlier Events

Selected perioperative complications and outlier events for all age patients are presented in table 3. There were no deaths. Notable events included cardiac arrest, hypotension, unplanned postoperative mechanical ventilation, seizures, coagulopathy (table 3), and large-volume transfusion (more than 40 ml/kg).

Anesthetic and Intraoperative Management

Data describing the anesthetic and intraoperative management of patients in each group are presented in table 4. Nearly all patients were managed with an inhaled anesthetic-opioid technique, at least two peripheral intravenous catheters, and invasive arterial blood pressure monitoring. A central venous catheter was placed in 13% of infants and 14% of older children. Thromboelastography was utilized in a minority of patients; TEG® (Haemonetics Corporation, USA) was the modality in all but one of these cases.

Perioperative Fluids and Transfusion

There was wide variability in perioperative transfusion volumes across institutions, as shown in figure 1; intraoperative fluid and transfusion data are shown in table 5. Nearly all patients (91%) in the infant group were transfused intraoperatively.

In the infant group, 24% of patients were transfused FFP and 3% were transfused platelets intraoperatively. In this group, the volume of intraoperative ECBPs was 46.7 ± 29.3 ml/kg in patients transfused FFP (excluding FFP in reconstituted blood), while the volume of ECBPs was 96.1 ± 51.4 ml/kg in those who received transfused platelets.

The majority of patients in both groups were not transfused postoperatively. In those who were transfused, packed erythrocytes were the predominant product: only 6% of infants and 3% of older patients were transfused FFP, platelets, or cryoprecipitate.

Blood Conservation Techniques and Transfusion-free Hospital Course

Data describing the utilization of various blood conservation strategies are presented in table 6. Specific transfusion protocols to guide transfusion were employed in a minority of cases. There were 82 infants (9%) and 69 older children (24%) who were not transfused intraoperatively. Of these, 37 (45%) and 7 (10%), respectively, received a postoperative transfusion; thus, a total of 45 infants and 62 older children experienced a transfusion-free hospital course. Among those patients with a transfusion-free hospital course, no specific conservation strategies were utilized in 9 of 45 (20%) in the infant group and 19 of 62 (31%) in the older group.

Discussion

In this study, we present a comprehensive description of perioperative management and outcomes from 1,223 children undergoing CCVR in North America during a 3-yr period. This report is from a prospective registry specifically designed for this population, with contributions from 29 institutions in the United States and two in Canada.

Patient Characteristics

Consistent with known epidemiology of craniosynostosis, males predominated in our dataset. In the infant group, metopic synostosis was the most prevalent diagnosis, followed by sagittal and unicoronal synostosis. Syndromic and multiple-suture

Table 1. Patient Demographic Data

Variable*	≤ 24 mo	> 24 mo
No. of subjects	935	288
No. of institutions represented	31	26
No. of cases per institution	24 (9–38)	5.5 (3–16.5)
Age, mo	10.5 ± 4.9	66.6 ± 41.7
Weight, kg	8.8 ± 1.9	22.2 ± 13.8
Sex, male/female	557/378	162/126
Race, n (%)		
White/Caucasian	707 (76)	191 (67)
Black/African American	85 (9)	52 (18)
Asian	31 (3)	8 (3)
Other	104 (11)	35 (12)
Not recorded	8 (0.9)	2 (0.7)
Diagnosis, n (%)		
Metopic	240 (26)	17 (6)
Sagittal	203 (22)	63 (22)
Unicoronal	156 (17)	25 (9)
Syndromic	118 (13)	83 (29)
Multiple (≥ 3 sutures)	70 (7)	54 (19)
Bicoronal	52 (6)	13 (5)
Lambdoid	26 (3)	1 (0.3)
Sagittal plus metopic	26 (3)	7 (2)
Metopic plus unicoronal	5 (0.5)	0 (0)
Sagittal plus unicoronal	5 (0.5)	7 (2)
Sagittal plus lambdoid	4 (0.4)	2 (0.7)
Unicoronal plus lambdoid	2 (0.2)	1 (0.3)
Other/not recorded	12 (1)	13 (5)
Procedure category, n (%)		
Anterior cranial vault/frontoorbital advancement	608 (65)	152 (53)
Mid/posterior cranial vault	254 (27)	81 (28)
Total cranial vault	73 (8)	55 (19)
Distractor placement, n (%)	93 (10)	52 (18)
Previous craniofacial surgery, n (%)	90 (10)	152 (53)
Craniosynostosis syndrome,† n (%)	118 (13)	83 (29)
Other named syndrome/disorder (excluding craniosynostosis syndromes), n (%)	33 (4)	18 (6)
Tracheostomy present, n (%)	22 (2)	12 (4)
Preoperative evidence of elevated intracranial pressure, n (%)	56 (6)	117 (41)
Preoperative hemoglobin, g/dl,‡ n (%)	11.9 ± 1.2	12.5 ± 1.2
ASA physical status	2 (2–2)	2 (2–3)
Plastic surgeon operated, n (%)	891 (95)	285 (99)
Neurosurgeon operated, n (%)	930 (99)	284 (99)
Dedicated craniofacial team anesthesiologist, n (%)	455 (53)	169 (59)
Other discipline procedures performed, n (%)	42 (5)	21 (7)

*Data are presented as median (interquartile range) for the number of cases per center, ASA physical status. Data are presented as mean ± SD for age, weight, and preoperative hemoglobin. All other variables are reported as n or n (%). †Craniosynostosis syndromes include Apert syndrome, Crouzon, Pfieffer, Saethre–Chotzen, Muenke syndrome, Antley Bixler syndrome, and Carpenter syndrome. ‡Preoperative hemoglobin measurement available in 872 patients less than or equal to 24 months old and 276 patients more than 24 months old.

ASA = American Society of Anesthesiologists.

craniosynostosis were among the most prevalent diagnoses in the older group, and more than 50% of patients in this group underwent repeat procedures. Total cranial vault reconstruction and placement of distractor hardware were more frequent in this group, reflecting the surgical complexity of these patients.

Blood Loss, Transfusion, and Blood Conservation Strategies in CCVR

We found wide variability in perioperative transfusion volumes, both between institutions and within individual institutions (fig. 1). The intraoperative transfusion volumes we report are consistent with previous studies, with 30% of patients in the infant group receiving more than 40 ml/kg intraoperative ECBPs.[9–14] Despite high transfusion volumes, the median number of blood donor exposures was just one for both groups (table 2), a finding attributable to the fact that a single unit of packed erythrocytes with a volume of 320 ml represents 40 ml/kg in an 8-kg infant.

Antifibrinolytics. Two randomized placebo-controlled prospective trials have shown that tranexamic acid decreases blood loss and transfusion in CCVR.[10,15] In less rigorous observational studies, aminocaproic acid was associated with decreased blood loss and transfusion in CCVR.[16,17] In our population, antifibrinolytic administration was used in 63% of children despite evidence of efficacy. Our finding that antifibrinolytics were not administered to 37% of children suggests that broadening antifibrinolytic administration is a potential improvement intervention.

Cell Saver. Cell saver was the second most common blood conservation technique used in CCVR in our dataset. No controlled study has evaluated cell saver as a stand-alone modality in CCVR. Overall, cell saver utilization was relatively low, perhaps due to costs and availability of equipment and personnel.

Erythropoietin. Synthetic erythropoietin has been studied as a means to increase the amount of blood loss that can be safely tolerated in infants undergoing craniofacial surgery.[18–20] Despite potential benefits, only three patients in our dataset received preoperative erythropoietin. It appears that cost, inconvenience, and concerns for complications have all but eliminated the use of erythropoietin in CCVR.

Acute Preoperative Normovolemic Hemodilution. Acute preoperative normovolemic hemodilution has been applied to pediatric craniofacial surgery patients.[21,22] Mathematical modeling predicts blood savings to be modest at best with this technique.[23] Moreover, it is difficult to obtain sufficient blood from patients under 30 kg.[24] Acute preoperative normovolemic hemodilution was only applied in two patients in our dataset, indicating that this technique has been abandoned in CCVR.

Deliberate Hypotension. Four percent of infants and 9% of older children had deliberate hypotension despite a lack of high-level evidence to support the efficacy or safety of this technique in CCVR. Upon closer review, the degree to which the children in our dataset were rendered hypotensive is unclear. Recent publications have argued there is no indication for deliberate hypotension in these infants.[25,26]

Transfusion Thresholds/Protocols. There is evidence in pediatric ICU patients and pediatric postsurgical patients

Table 2. Selected Perioperative Outcomes*

Outcome	≤ 24 mo (n = 935)	> 24 mo (n = 288)	*P* Value†
Intraoperative erythrocyte-containing blood products,‡ ml/kg	33.9 ± 27.2	21.9 ± 19.4	< 0.0001
> 40	30%	16%	< 0.0001
> 60	11%	3.5%	< 0.0001
> 80	5%	1.0%	0.003
Total perioperative blood products,§ ml/kg	45.3 ± 41.6	26.7 ± 27.1	< 0.0001
Total perioperative blood donor exposures	1 (1–2)	1 (1–2)	0.01
≥ 1	95%	79%	< 0.0001
≥ 2	46%	43%	0.54
≥ 3	20%	19%	0.90
Duration of surgery, min	227 ± 85	268 ± 118	< 0.0001
Initial postoperative hemoglobin,‖ g/dl	11.3 ± 2.3	10.9 ± 1.9	0.002
Δ hemoglobin,‖ g/dl	0.5 ± 2.4	1.5 ± 1.9	< 0.0001
Last hemoglobin before discharge, g/dl	10.7 ± 1.8	10.4 ± 1.5	0.01
ICU LOS, d	2 (1–3)	2 (2–3)	0.03
Hospital LOS, d	4 (4–5)	5 (4–6)	0.20

*Data presented as mean ± SD for transfusion volumes and duration of surgery. Data are presented as median (25th to 75th interquartile range) for the LOS and total blood perioperative donor exposures. †Student's *t* test for comparisons of transfusion volumes, duration of surgery, and last hemoglobin before discharge, Wilcoxon rank sum test for overall blood donor exposure and LOS comparisons, and chi-square test for comparisons of percentages in transfusion volume and percentages of patients having specified blood donor exposures. ‡Intraoperative erythrocyte-containing products include packed red blood cells, whole blood, and reconstituted blood. §Total perioperative blood products include erythrocyte-containing products, fresh frozen plasma, platelets, and cryoprecipitate. ‖Initial postoperative hemoglobin measurement (day of surgery) available in 855 patients less than or equal to 24 months old and 266 patients more than 24 months old. Preoperative and initial postoperative hemoglobin measurements available in 798 patients less than or equal to 24 months old and 253 patients more than 24 months old.

ICU = intensive care unit; LOS = length of stay.

that employing restrictive transfusion thresholds is safe and effective.[27,28] There is evidence that accepting lower hemoglobin values[29] and implementing postoperative transfusion protocols[30] are effective in CCVR. We found formal transfusion protocols were not used in approximately two thirds of patients. The adoption of restrictive transfusion practices, and in particular the implementation of postoperative transfusion thresholds, is a potential low-cost improvement intervention to reduce transfusion in CCVR.

Bloodless Craniosynostosis Surgery. Despite numerous publications during the past 20 yr describing methods to reduce and avoid transfusion in CCVR, a transfusion-free hospital course was achieved in only a small minority of infants, and the majority of institutions had no infants with a transfusion-free course. Interestingly, 20% of infants and 31% of older children with a transfusion-free hospital course had no specific blood conservation technique employed, including the use of transfusion protocols (infant group). Two things are suggested by this finding. First, perhaps the greatest determinant of blood loss and the need for transfusion is a variable not captured in this or other studies: surgical technique. Second, institutions with some transfusion-free patients without using these techniques might increase the number of transfusion-free patients by adopting multimodal blood management practices (*e.g.*, antifibrinolytics and transfusion thresholds).

ICU and Hospital LOS

We observed a relatively consistent hospital LOS of 4 to 5 days. ICU admission after CCVR is a standard practice at most institutions inasmuch as only a minority of children were not admitted to the ICU postoperatively. In one study, preexisting medical conditions and higher blood loss were identified as predictors for the need of ICU admission.[31] In another study, the authors proposed an algorithm for predicting an event requiring ICU admission based on risk factors.[11] It remains to be determined whether these findings can be applied at different institutions and whether patients can be safely selected for ward *versus* ICU admission. Efforts to judiciously limit ICU LOS may be a strategy to minimize costs as many centers had ICU stays of 1 day, while at others, multiple-day stays were the rule.

Perioperative Complications and Events

Mortality rates in pediatric craniofacial surgery have steadily declined, from 1.6% in 1979[1] to 0.1% more recently.[4] The absence of deaths in our study is consistent with a continuation of this trend; based on the rule of three, we can conclude from our dataset with 95% confidence that the mortality rate is less than 0.2%.

Although there were no deaths, there were major events indicative of severe clinical problems. Cardiovascular complications, respiratory complications, and sequelae of large-volume blood loss replacement predominated. Notable events included cardiac arrest, intravenous epinephrine bolus administration, inadvertent intraoperative extubation, unplanned postoperative intubation, postoperative seizures, coagulopathy, respiratory failure, unplanned second surgery, and massive transfusion.

Hematologic derangements were more frequent in the infant group, which likely relates to higher ECBP transfusion volumes in this group. The incidence of hyponatremia

Table 3. Reported Adverse Events, Complications, and Outlier Outcomes (All Ages)

	n	%
Cardiovascular		
Intraoperative vasopressor infusion	89	7.3
Intraoperative hypotension*	65	5.3
Intravenous epinephrine bolus	39	3.2
Bradycardia requiring treatment†	19	1.6
Postoperative vasopressor infusion	7	0.6
Suspected venous air embolism (VAE)	7	0.6
Suspected VAE with $ETCO_2$ plus blood pressure changes	6	0.5
Suspected VAE with cardiovascular collapse	1	0.1
Postoperative hypovolemic shock or hypotension	6	0.5
Intraoperative cardiac arrest‡	3	0.2
Postoperative cardiac arrest, code, or rapid response call	2	0.2
Respiratory		
Unplanned postoperative intubation/mechanical ventilation	29	2.4
Difficult airway§	27	2.2
Postoperative respiratory failure	16	1.3
Unintentional intraoperative extubation	13	1.1
Intraoperative bronchospasm	11	0.9
Reintubation (failed extubation in OR)	10	0.8
Postoperative reintubation	4	0.3
Postoperative pneumonia	3	0.2
Postoperative pulmonary edema	2	0.2
Neurologic		
Postoperative seizures	9	0.7
Seizures attributed to hyponatremia	2	0.2
Transfusion		
Intraoperative erythrocyte-containing blood product transfusion, ml/kg		
> 40	328	26.8
> 60	115	9.4
> 80	50	4.1
Total blood perioperative blood donor exposures, ≥ 6	46	3.8
Suspected transfusion reaction	2	0.2
Hematologic		
Initial postoperative INR > 1.5, PTT > 45 s, or fibrinogen < 100 mg/dl	59	4.8
Initial postoperative platelet count, < 100,000/μl	41	3.4
Initial postoperative hemoglobin, < 6.5 mg/dl	7	0.6
Electrolyte		
Hyponatremia: $[Na^+]$ < 135 mEq/l	251	20.5
Hyperkalemia: $[K^+]$ > 5.5 mEq/l	3	0.2
Other		
Intraoperative hypothermia (temperature, < 35°C)	35	2.9
Unplanned second surgical procedure	8	0.7
Cerebrospinal fluid leak	7	0.6
Surgical-site infection	5	0.4
Diabetes insipidus	1	0.1
Central catheter–associated bloodstream infection	1	0.1
Deep venous thrombosis	1	0.1
Sepsis	1	0.1
LOS, d		
ICU length of stay, ≥ 6	39	3.2
Hospital length of stay ≥ 9	46	3.8

*Hypotension defined as low blood pressure requiring active treatment as identified by the clinician or noted in the record. †Bradycardia requiring treatment defined as intraoperative bradycardia requiring treatment or identified as significant by the clinician. ‡Intraoperative cardiac arrest was defined as any case in which chest compressions were initiated. §Difficult airway defined as difficulty with facemask ventilation (requires two providers or unstable/inadequate ventilation with a facemask, unable to ventilate by facemask) or with tracheal intubation by conventional direct laryngoscopy.

$ETCO_2$ = end-tidal carbon dioxide; ICU = intensive care unit; INR = international normalized ratio; LOS = length of stay; PTT = partial thromboplastin time; OR = operating room; VAE = venous air embolism.

Table 4. Anesthetic/Intraoperative Management

Variable*	≤ 24 mo, n = 935	> 24 mo, n = 288
Anesthetic technique, n (%)		
Inhalational	920 (98)	287 (100)
Propofol infusion	10 (1)	8 (3)
Dexmedetomidine infusion	25 (3)	8 (3)
Ketamine infusion	0 (0)	4 (1)
Intermittent opioid bolus	813 (87)	245 (85)
Sufentanil infusion	76 (8)	30 (10)
Remifentanil infusion	71 (8)	39 (14)
Fentanyl infusion	41 (4)	13 (5)
Vascular access/monitoring		
No. of peripheral IVs	2 (2–2)	2 (2–2)
Arterial catheter, n (%)		
Radial/ulnar	863 (92)	275 (95)
Femoral	18 (2)	0 (0)
Other	37 (4)	7 (2)
None	14 (1)	6 (2)
Not documented	3 (0.3)	0 (0)
Central venous catheter, n (%)		
Internal jugular	97 (10)	26 (9)
Femoral	22 (2)	6 (2)
Subclavian	3 (0.3)	8 (3)
None	806 (86)	245 (85)
Not documented	7 (0.7)	3 (1)
Additional monitoring, n (%)		
Automated arterial waveform analysis	307 (33)	86 (31)
Precordial Doppler	194 (21)	36 (13)
Thromboelastography		
TEG® (Haemonetics Corporation, USA)	70 (7)	15 (5)
ROTEM® (Basel, Switzerland)	1 (0.1)	0 (0)
Vasoactive drug infusion, n (%)		
Dopamine infusion	29 (3)	12 (4)
Epinephrine infusion	7 (0.7)	0 (0)
Norepinephrine infusion	3 (0.3)	10 (3)
Phenylephrine infusion	23 (2)	10 (3)
Nitrogylcerine infusion	0 (0)	0 (0)
Nitroprusside infusion	0 (0)	0 (0)
Nicardipine infusion	0 (0)	1 (0.3)
Local anesthetic infiltration, n (%)		
Periincisional infiltration	670 (72)	178 (62)
Scalp nerve blocks	29 (3)	6 (2)
Scalp epinephrine infiltration (for vasoconstriction)	809 (87)	263 (91)
Needle tip electrocautery	673 (72)	194 (67)
Raney scalp hemostasis clips	165 (18)	80 (28)
Elevation of head of bed	264 (28)	120 (42)
Postoperative tracheal intubation and mechanical ventilation†	131 (14)	23 (8)

*Data are presented as median (25th to 75th interquartile range) for number of peripheral intravenous cathethers (IVs). All other variables are reported as n (%). †Excludes patients with tracheostomies.

we observed is similar to that in a previous report[32] in which there were no serious events although one patient had a serum sodium concentration of 121 mEq/l. Seizures from hyponatremia after CCVR have not previously been reported; the two occurrences in our population illustrate the potential severe sequelae of hyponatremia in CCVR.

Anesthetic and Intraoperative Management

Our dataset defines national perioperative management of children undergoing CCVR. Some elements of management are nearly universal: most patients were managed with general anesthesia maintained with a combined inhalation-opioid technique, at least two peripheral intravenous catheters placed, and invasive arterial blood pressure monitoring. A central venous catheter was placed in 13 to 14% of children. A practice survey in 2011 revealed that 65% of institutions place central catheters in less than 10% of patients; inadequate peripheral venous access was the most common rationale.[33] A subsequent study in CCVR demonstrated no improvement in the frequency or duration of hypotension with central venous pressure monitoring.[34] Central venous pressure has been consistently shown to be a poor predictor of fluid responsiveness in children.[35] Central catheter insertion is associated with significant complications in children, including cardiac arrest.[36] Based on the above, we suggest these catheters are not generally required for CCVR and their use be reserved for cases with inadequate peripheral venous access or other specific circumstances.

Venous air embolism occurs frequently in children undergoing open craniofacial surgical procedures, and routine use of precordial Doppler has been suggested.[37,38] Doppler monitoring is sensitive but nonspecific, with the vast majority of episodes being clinically insignificant. The lack of widespread adoption of precordial Doppler in CCVR underscores its primary limitation: a subjective monitor with a signal-to-noise ratio too low to justify routine use.

Automated analysis of the invasive arterial waveform was used in approximately one third of patients. This is interesting given that parameters derived from the arterial waveform (such as systolic pressure and pulse pressure variation with respiration) remain unproven as reliable indicators of volume responsiveness in children.[35,39,40]

Standard laboratory tests of coagulation have a limited ability to predict clinical bleeding.[25] Thromboelastography has been purported to be a means to assess specific components of coagulation function and guide hemostatic therapy,[41,42] and its use has demonstrated efficacy in CCVR.[43] In our dataset, thromboelastography was utilized in only a minority of patients; this may represent an area for improvement.

Limitations

The limitations of this study include those inherent to a large multicenter clinical database analysis including inaccurate or missing data.[44] For example, some complications may not have been reported, and the incidence rates presented may underestimate the true incidence for some of the variables presented. Another limitation is that, as with any observational dataset, cause and effect relationships cannot be established. Our primary intent was to assess current practices, outcomes, and complications in CCVR rather than delineate cause and effect relationships.

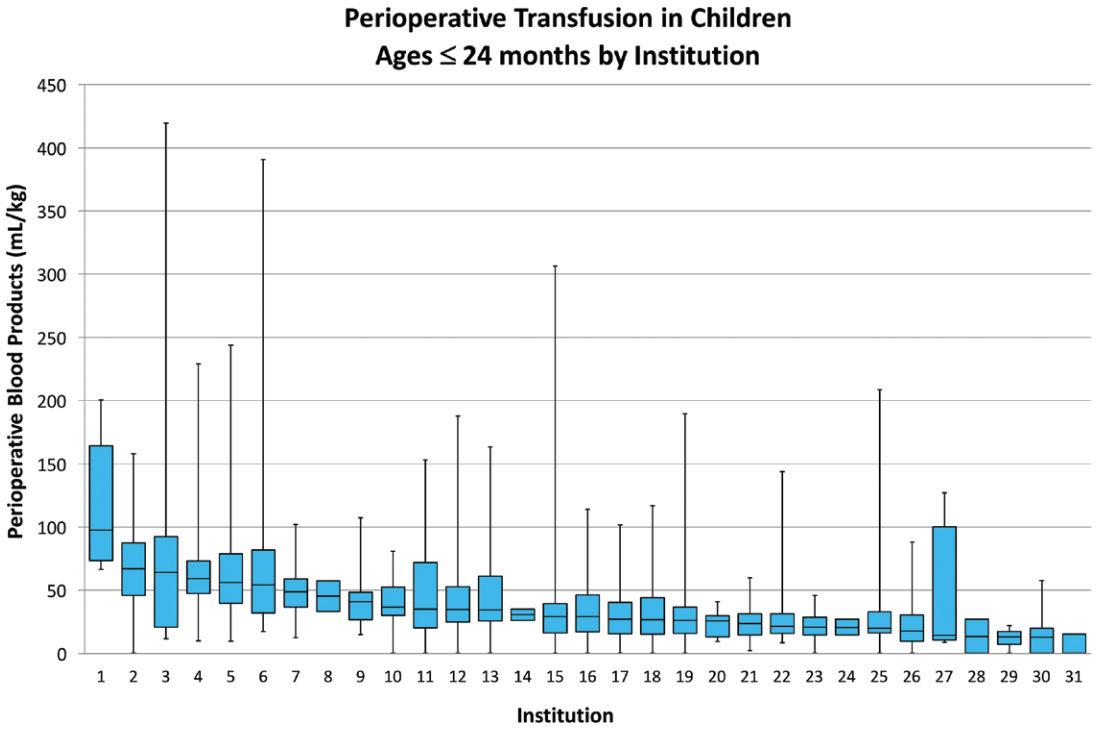

Fig. 1. Box plots showing perioperative blood product transfusion (ml/kg) in the infant group (age less than or equal to 24 months) by institution. Perioperative blood products include packed red erythrocytes, whole blood, reconstituted blood, fresh frozen plasma, platelets, and cryoprecipitate administered intraoperatively and in the first postoperative 48 h. Institutions except 10, 22, 23, 24, 27, and 30 had at least six cases.

Table 5. Perioperative Fluids and Transfusion*

	≤ 24 mo		> 24 mo	
	Receiving, n (%)	Volume, ml/kg	Receiving, n (%)	Volume, ml/kg
Intraoperative period				
Erythrocyte-containing blood products	849 (91)	37.3 ± 26.2	225 (78)	28.0 ± 17.6
Packed erythrocytes†	736 (79)	32.7 ± 20.5	171 (59)	24.8 ± 15.3
Reconstituted blood†	52 (6)	75.5 ± 36.1	19 (7)	40.7 ± 19.9
Whole blood	69 (7)	53.7 ± 30.9	38 (13)	30.4 ± 16.3
FFP†	229 (24)	27.9 ± 18.2	49 (17)	21.0 ± 14.9
Platelets	27 (3)	19.7 ± 12.9	5 (2)	12.6 ± 2.8
Cryoprecipitate	17 (2)	7.8 ± 9.1	7 (2)	1.2 ± 0.5
Cell saver	116 (12)	9.2 ± 17.4	31 (11)	4.7 ± 4.1
Autologous blood	2 (0.2)	27.7 (n = 2)	1 (0.3)	11.6 (n = 1)
Crystalloid	935 (100)	59.7 ± 37.5	288 (100)	60.2 ± 73.1
5% albumin	300 (32)	19.4 ± 14.8	95 (33)	16.8 ± 10.6
Hetastarch	13 (1.4)	17.8 ± 11.7	6 (2)	16.2 ± 5.0
Postoperative period				
Packed erythrocytes	162 (17)	16.7 ± 9.3	21 (7)	14.3 ± 4.2
FFP	38 (4)	17.6 ± 12.8	6 (2)	13.7 ± 6.7
Platelets	23 (4)	9.7 ± 5.9	4 (1)	7.2 ± 5.6
Cryoprecipitate	7 (0.7)	6.0 ± 5.4	1 (0.3)	2.1 (n = 1)

*Volume data are presented as mean ± SD. Volume data are reported for those patients who received the fluid/blood product. †Number of patients and volumes administered of packed erythrocytes and FFP does not reflect packed erythrocyte or FFP component of Reconstituted Blood. Similarly, data reported for Reconstituted Blood includes packed erythrocytes and FFP that are not included in the data for these individual components.

FFP = fresh frozen plasma.

Future Directions

In our analysis, we identified areas of practice variability, as well as gaps between evidence-based practices and implementation of these practices. Some of these represent targets for improvement interventions within the PCCG. Specifically, we have identified the routine administration of

Table 6. Blood Conservation Technique and Transfusion-free Patient Data

	≤ 24 mo, n = 935	> 24 mo, n = 288
Blood conservation technique, n (%)		
Antifibrinolytic	608 (65)	165 (57)
Aminocaproic acid	238 (25)	85 (30)
Tranexamic acid	370 (40)	80 (28)
None	311 (33)	121 (42)
Not recorded	16 (2)	2 (1)
Cell saver	129 (14)	34 (12)
Deliberate hypotension	45 (5)	29 (10)
Preoperative erythropoietin	2 (0.2)	1 (0.3)
Acute preoperative normovolemic hemodilution	1 (0.1)	1 (0.3)
Transfusion thresholds/protocols		
Intraoperative erythrocyte	278 (30)	94 (33)
Intraoperative hemostatic blood product*	257 (27)	89 (31)
Postoperative erythrocyte	226 (24)	101 (35)
Postoperative hemostatic blood product	180 (19)	93 (32)
Blood conservation techniques in transfusion-free patients, n (%)		
No. of patients with transfusion-free perioperative course	45/935 (5)	62/288 (22)
No. of institutions with ≥ 1 patient with transfusion-free perioperative course	15/31 (48)	19/26 (73)
Intraoperative blood conservation techniques utilized in transfusion-free patients		
Antifibrinolytic	26/45 (58)	25/62 (40)
Cell saver	14/45 (31)	22/62 (35)
Preoperative erythropoietin	2/45 (4)	1/62 (2)
Acute preoperative normovolemic hemodilution	2/45 (4)	2/62 (3)
Deliberate hypotension	4/45 (9)	4/62 (6)
Any of above conservation techniques	36/45 (80)	43/62 (69)
Transfusion protocols in transfusion-free patients		
Intraoperative erythrocyte protocol	2/45 (4)	9 (15)
Intraoperative hemostatic blood product protocol	2/45 (4)	9 (15)
Postoperative erythrocyte protocol	12 (27)	24 (39)
Postoperative hemostatic blood product protocol	12 (27)	21 (34)

*Hemostatic blood products include fresh frozen plasma, platelets, and cryoprecipitate

antifibrinolytics to CCVR patients as one such intervention. As we move to expand antifibrinolytic administration, we will use the PCSPR to track administration and monitor for improved outcomes and adverse events.

Although there is robust evidence supporting transfusion thresholds in children, they were applied in just one third of our patients. We plan to pursue implementation of postoperative transfusion thresholds at PCCG institutions to improve transfusion practices, using the PCSPR to evaluate implementation and effects on transfusion outcomes.

We identified significant variability in the duration of postoperative ICU admission, a costly component of hospital care, with some centers having overnight stays and others having 3- to 4-day stays. Individual PCCG institutions may use these data to critically reevaluate whether the duration of ICU admission can be safely reduced and use the PCSPR to monitor local outcomes.

Other investigators have evaluated the relationships between craniosynostosis, corrective surgery, and neurocognitive outcomes.[45,46] In the future, collaborators from the PCCG could use data from the PCSPR in conjunction with neurocognitive assessments to explore the relationships between perioperative variables, complications, and longer term outcomes in this population.

Conclusions

In this comprehensive evaluation of pediatric CCVR in North America, we identified significant variability for both perioperative management and in-hospital outcomes. In CCVR, transfusion remains the rule, especially in the youngest patients. A transfusion-free course was achieved in some cases without the use of specific blood conservation techniques, suggesting that surgical technique may be a significant determinant of blood loss. Although there were no deaths, there were numerous adverse events representing severe clinical problems. The results presented serve as a platform for future comparisons of surgical approaches and perioperative interventions. Moving forward, our goal is to leverage collaborative relationships together with the PCSPR as a tool to select, implement, and assess improvement efforts in this vulnerable pediatric population.

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Competing Interests

The authors declare no competing interests.

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Appendix 1: List of Participating Institutions

- American Family Children's Hospital, University of Wisconsin-Madison, Madison, Wisconsin
- Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, Illinois
- Arkansas Children's Hospital, Little Rock, Arkansas
- Boston Children's Hospital and Harvard Medical School, Boston, Massachusetts
- Charlotte R. Bloomberg Johns Hopkins Children's Center, Baltimore, Maryland
- Children's Healthcare of Atlanta at Egleston, Atlanta, Georgia
- Children's Hospital and Medical Center, Omaha, Nebraska
- Children's Hospital Colorado, Denver, Colorado
- Children's Hospital of Philadelphia, Philadelphia, Pennsylvania
- Children's Hospital of Wisconsin, Milwaukee, Wisconsin
- Children's National Health System, Washington, DC
- CHU Sainte-Justine, Montreal, Quebec, Canada
- Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio
- Cleveland Clinic Children's, Cleveland, Ohio
- Driscoll Children's Hospital, Corpus Christi, Texas
- Duke Children's Hospital and Health Center, Durham, North Carolina
- Johns Hopkins All Children's Hospital, St. Petersburg, Florida
- Monroe Carell Jr. Children's Hospital at Vanderbilt, Vanderbilt University Medical Center, Nashville, Tennessee
- Montreal Children's Hospital, Montreal, Quebec, Canada
- New York Presbyterian Hospital – Weill Cornell Medical College, New York, New York
- Oregon Health & Science University, Doernbecher Children's Hospital, Portland, Oregon
- Seattle Children's Hospital, Seattle, Washington, DC
- Texas Children's Hospital, Baylor College of Medicine, Houston, Texas
- The Children's Hospital of Pittsburgh of UPMC, Pittsburgh, Pennsylvania
- The University of Chicago Medicine Comer Children's Hospital, Chicago, Illinois
- UNC Children's, Chapel Hill, North Carolina
- University of California, San Diego, Rady Children's Hospital, San Diego, California
- University of Kansas Medical Center, Kansas City, Kansas
- University of New Mexico, Albuquerque, New Mexico
- University of Texas Southwestern and Children's Medical Center, Dallas, Texas
- UT Health-University of Texas Medical School at Houston, Houston, Texas

Appendix 2: Pediatric Craniofacial Collaborative Group (June 2012 to September 2015)

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ANESTHESIOLOGY REFLECTIONS FROM THE WOOD LIBRARY-MUSEUM

The Crawford W. Long Museum: Sharing the History of Anesthesia

The Liaison Committee of the Wood Library-Museum of Anesthesiology has maintained its longest continuous "sister" relationship with the Crawford W. Long Museum in Jefferson, Georgia. To reach Jefferson, visitors can fly into the world's busiest airport, Hartsfield-Jackson Atlanta International Airport. From there, they can travel 65 miles northeast on I-85 North, then 5 miles southeast on U.S. 129 South toward Jefferson's Historic Square. Located at 28 College Street, the Crawford W. Long Museum (*above*) celebrates both local history and a local hero, Crawford Williamson Long, M.D. (1815 to 1878), who etherized James Venable for minor surgery in Jefferson on March 30, 1842. Reflecting the broad interests of physician-pharmacist Crawford Long, the museum complex includes an 1840s apothecary and physician's office housed in the 1858 Pendergrass Store building. To their mutual benefit, the Crawford W. Long Museum and the Wood Library-Museum of Anesthesiology have shared the history of anesthesia with each other, with professionals, and with the public.

George S. Bause, M.D., M.P.H., Honorary Curator and Laureate of the History of Anesthesia, Wood Library-Museum of Anesthesiology, Schaumburg, Illinois, and Clinical Associate Professor, Case Western Reserve University, Cleveland, Ohio. UJYC@aol.com.