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Original Contribution

Transfusion targets and adverse events in pediatric perioperative acute Anemia

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HIGHLIGHTS

- Many pediatric patients had anemia before surgery.
- Patients may receive transfusions because of preexisting anemia or blood loss.
- Limited evidence guides hemoglobin targets for intraoperative transfusions.
- Limited adverse event data exist on perioperative pediatric transfusions.
- We found no evidence of a transfusion hemoglobin target that changed outcomes in children.

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ABSTRACT

Study objective: To evaluate the association between pretransfusion and posttransfusion hemoglobin concentrations and the outcomes of children undergoing noncardiac surgery.

Design: Retrospective review of patient records. We focused on initial postoperative hemoglobin concentrations, which may provide a more useful representation of transfusion adequacy than pretransfusion hemoglobin triggers (the latter often cannot be obtained during acute surgical hemorrhage).

Setting: Single-center, observational cohort study.

Patients: We evaluated all pediatric patients undergoing noncardiac surgery who received intraoperative red blood cell transfusions from January 1, 2008, through December 31, 2018.

Interventions: None.

Measurements: Associations between pre- and posttransfusion hemoglobin concentrations (g/dL), hospital-free days, intensive care unit admission, postoperative mechanical ventilation, and infectious complications were evaluated with multivariable regression modeling.

Main results: In total, 113,713 unique noncardiac surgical procedures in pediatric patients were evaluated, and 741 procedures met inclusion criteria (median [range] age, 7 [1–14] years). Four hundred ninety-eight patients (68%) with a known preoperative hemoglobin level had anemia; of these, 14% had a preexisting diagnosis of anemia in their health record. Median (IQR) pretransfusion hemoglobin concentration was 8.1 (7.4–9.2) g/dL and median (IQR) initial postoperative hemoglobin concentration was 10.4 (9.3–11.6) g/dL. Each decrease of 1 g/dL in the initial postoperative hemoglobin concentration was associated with increased odds of transfusion within the first 24 postoperative hours (odds ratio [95% CI], 1.62 [1.37–1.93]; $P < .001$). No significant relationships were observed between postoperative hemoglobin concentrations and hospital-free days ($P = .56$), intensive care unit admission ($P = .71$), postoperative mechanical ventilation ($P = .63$), or infectious complications ($P = .74$).

Abbreviations: ASA, American Society of Anesthesiologists; EBL, estimated blood loss; EHR, electronic health record; ICU, intensive care unit; LOS, length of stay; NEC, necrotizing enterocolitis; OR, operating room; RBC, red blood cell.

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Conclusions: In transfused patients, there was no association between postoperative hemoglobin values and clinical outcomes, except the need for subsequent transfusion. Most transfused patients presented to the operating room with anemia, which suggests a potential opportunity for perioperative optimization of health before surgery.

1. Introduction

Allogeneic red blood cells (RBCs) are the most commonly transfused blood products in children [1]. RBCs are transfused to replenish intraoperative blood loss to optimize oxygen-carrying capacity and tissue oxygenation [2]. In children undergoing noncardiac surgery, factors influencing the decision to transfuse include the degree and rapidity of hemorrhage, the presence of comorbidities, and, if known, the hemoglobin value.

All transfusion decisions in children involve balancing the benefits of transfusion with risks that are numerous and well described [3]. Several studies evaluating outcomes for children undergoing transfusions have been published. These studies often focus on defining optimal transfusion triggers for patients in nonoperative settings [4,5]. While such studies provide important information to guide transfusion decisions outside of the operating room (OR), extending such data to surgical hemorrhage is problematic. Obtaining an immediate pretransfusion hemoglobin may be impractical due to the rapidity of hemorrhage relative to blood volume and potential difficulty in obtaining and analyzing a blood sample. As such, comparatively few studies have evaluated transfusion practices during operative hemorrhage [6–8]. Posttransfusion targets have been suggested as an appropriate alternative to traditional pretransfusion triggers. A posttransfusion target for acute hemorrhage would aim to not “overtransfuse” a patient (eg, to values >9–11 g/dL) to prevent negative outcomes such as longer hospitalization, postoperative mechanical ventilation, infection, death, reoperation, and intensive care unit (ICU) admission [2]. Among adult noncardiac surgical patients, those with hemoglobin levels that were too high (>11.5 g/dL) or too low (<7.5 g/dL) had greater risk of negative clinical outcomes [9]; however, we do not know whether the same holds true among pediatric surgical patients. We hypothesized that an ideal posttransfusion hemoglobin range would exist for children and therefore evaluated the associations between pretransfusion and posttransfusion hemoglobin concentrations and the outcomes of children undergoing noncardiac surgery.

2. Methods

The Strengthening the Reporting of Observational Studies in Epidemiology guidelines were followed in the conduct of this study and in the reporting of its results [10].

This retrospective cohort study analyzed children undergoing noncardiac surgery who received intraoperative RBC transfusion (10 mL/kg or greater) over a 10-year period. We analyzed data only from those patients whose parents had provided consent for use of the child’s electronic health record (EHR) for research. Before study commencement, the study analysis plan was created and deemed exempt by the Mayo Clinic Institutional Review Board. Pediatric patients (age < 18 years) were eligible for study inclusion if they underwent noncardiac surgery and received 10 mL/kg or more of intraoperative allogeneic RBCs at Mayo Clinic in Rochester, Minnesota, from January 1, 2008, through December 31, 2018. We excluded all cardiac surgery patients because transfusion practices for children undergoing surgical interventions for congenital heart disease may not be comparable with children in other operative settings.

Study-eligible patients were identified with the Multidisciplinary Epidemiology and Translational Research Intensive Care group’s existing electronic database, the OR data mart [11]. This database houses a near real-time feed of EHR data that rapidly recalls all potentially

eligible patients from our study period. When an eligible patient’s EHR number was identified, it was entered into 3 existing EHR databases: the OR data mart, the Advanced Cohort Explorer, and the Peri-Operative Information Tool. These institutional databases permit aid-scale extraction of all pertinent perioperative data points. Data that could not be extracted were manually reviewed and entered by 2 researchers (L.L.W. and L.R.H.G.).

Exclusion criteria included parents’ denial of research authorization for the child’s EHR, cyanotic congenital heart disease, American Society of Anesthesiologists (ASA) class VI (because of already high risk of non – transfusion-related morbidity and mortality), and age >18 years. If a patient underwent multiple procedures during the study dates, all procedures associated with intraoperative transfusion were included in the analysis. Hemoglobin concentrations included, in chronologic order:

- Immediate preoperative (the last one available, up to 90 days before OR start time and date)
- Pretransfusion (intraoperative hemoglobin concentration nearest to the first RBC transfusion)
- Lowest (nadir) intraoperative
- Initial postoperative, defined as the first hemoglobin level measured after surgery, if measured within the first 6 h after surgical completion.

Anemia was defined by a hemoglobin concentration that was >2 standard deviations below age- and sex-specific means [12].

Medications that may increase bleeding risk were evaluated if prescribed within 90 days of the operation and then were included if the medication had not passed an anticipated washout period (eg, 7 days since aspirin administration, 5 days since warfarin, 24 h since low-molecular-weight heparin). Infusion of cell saver units was not considered a transfusion. Infectious complications were defined as growth in blood cultures that was not present at admission. Growth in urine cultures or positive chest radiography findings were excluded because each was confounded by many factors with limited specificity for widespread infection.

Our primary outcome was hospital-free days (28 minus the post-procedure hospital length of stay [LOS] in days). Hospital-free days were used instead of LOS because this calculation considers death as a negative outcome, rather than as a potentially short LOS. In addition, hospital-free days have less skewed data for uncharacteristically long stays. Secondary outcomes were 1) postoperative mechanical ventilation (any invasive mechanical ventilation that extended beyond the OR time), 2) infectious complications (positive blood culture), 3) hospital death, 4) reoperation within 24 h of surgery completion, 5) ICU admission within 24 h of surgery completion, and 6) postoperative allogeneic transfusions within the first 24 h of surgery completion, inclusive of RBCs, fresh frozen plasma, platelets, and cryoprecipitate. Reoperation was purposefully limited to 24 h to incorporate only complications that were most likely to be associated with transfusion, rather than with wounds or comorbid conditions.

2.1. Statistical methods

Demographic characteristics, including medical history, medications, procedure information, laboratory values, and outcomes, were summarized according to age group by using median (IQR) for continuous variables and frequency (percentage) for categorical variables. Missing values for ASA physical status, emergency status, and

hemoglobin values were imputed with use of 50 multiply imputed data sets. Use of continuous variables was justified because we evaluated the functional form of the relationship between postoperative hemoglobin and outcomes, and there was no evidence of nonlinearity, with the exception of the secondary outcome of transfusion within 24 h.

Models for categorical and continuous outcomes were fit with logistic regression and linear regression, respectively. All models were adjusted for ASA physical status (grouped as 1 and 2; 3 and 4; and 5), emergent status, preoperative hemoglobin, preoperative platelet count, current anticoagulant medication (warfarin, enoxaparin, or heparin), type of surgery (abdominal, neurologic, orthopedic, spine, and other), age (as a restricted cubic spline), and length of surgery. Postoperative hospital LOS was modeled on the natural log scale, to ensure distributional assumptions. Estimates from the 50 multiply imputed data sets were combined with use of Rubin's rules. The interaction between age and postoperative hemoglobin concentration was assessed. In the absence of a statistically significant interaction effect, the model was reported with main effects only. Effect estimates associated with a decrease of 1 g/dL in postoperative hemoglobin, with 95% CIs and *P* values, are presented. *P* < .05 was considered statistically significant. No a priori power analysis was done to justify the size of this convenience sample. However, in general, when assessing the association between hemoglobin and postoperative hospital-free days, a sample size of 741 provides >90% power to detect a correlation coefficient of 0.12, which corresponds to an R^2 value of 0.014.

The imputation model included preoperative hospital LOS; age (as a restricted cubic spline with 3 knots); procedure type; past medical history indicators for anemia, cancer, thrombocytopenia, chronic kidney disease (EHR search), and liver disease (EHR search); current aspirin, heparin, enoxaparin, and warfarin use; intraoperative hemoglobin values; surgery duration; transfusion count; and outcomes, including

postoperative hospital LOS, mechanical ventilation, infectious complication, hospital death, ICU admission, reoperation within 24 h, and transfusions within 24 h. The functional form of the relationship between postoperative hemoglobin level and outcomes was evaluated, and generalized linear models with robust empirical variance estimates (generalized estimating equations) were used to assess the association between postoperative hemoglobin values and outcomes. All models were adjusted for the same covariables. These variables were chosen a priori as potential confounders for the postoperative outcomes of interest.

All analyses were done with the use of statistical software (SAS version 9.4; SAS Institute Inc).

3. Results

A total of 113,713 unique noncardiac surgical procedures in pediatric patients were evaluated, from which 741 patients met all study inclusion criteria (Fig. 1). Their median (IQR) age was 7 (1–14) years and female patients were nearly one-half of the population ($n = 362$, 49%) (Table 1). The most common procedural types were neurologic ($n = 245$, 33%), spinal ($n = 153$, 21%), orthopedic ($n = 98$, 13%), and abdominal ($n = 88$, 12%).

3.1. Preoperative hemoglobin values

Baseline hemoglobin values (defined as within 90 days before surgery) were available for all but 3 patients. Approximately two-thirds of patients were anemic preoperatively (69%, age < 1 month; 66%, 1–11 months; 71%, 1–3 years; 67%, 4–10 years; and 67%, 11–17 years).

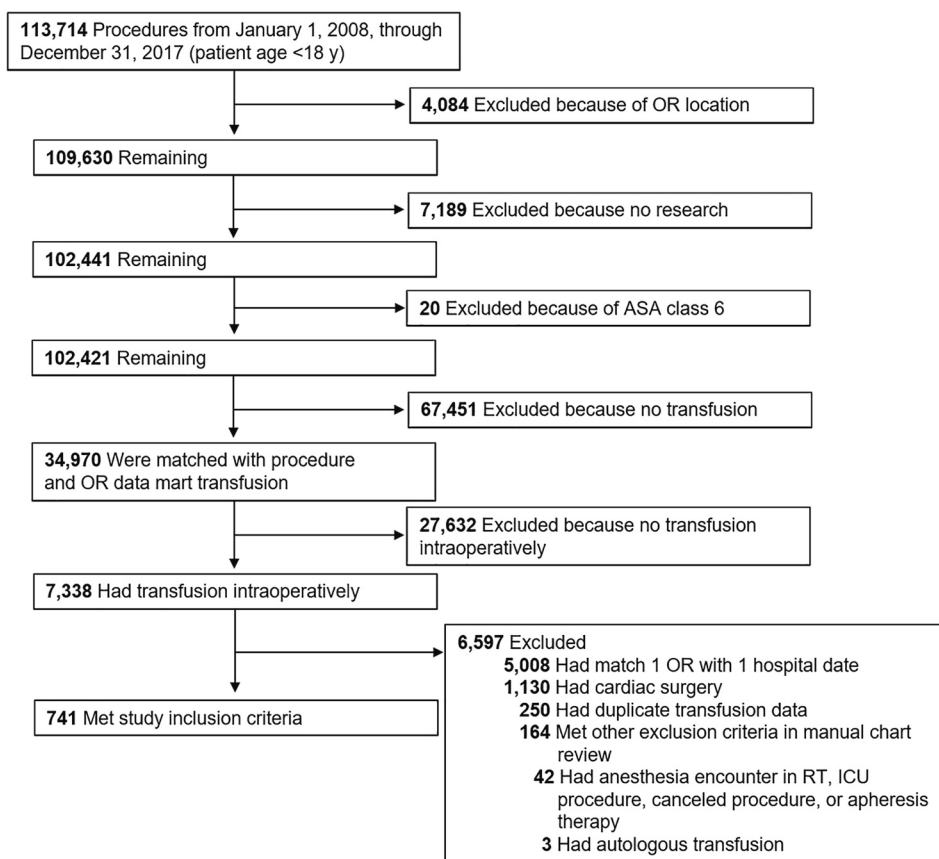


Fig. 1. Pediatric transfusion study inclusion criteria. ASA indicates American Society of Anesthesiologists; ICU, intensive care unit; OR, operating room; RT, radiation therapy.

Table 1
Patient, procedural, laboratory, and medication characteristics overall and according to age.

Characteristic ^a	Patient age ^a					
	Overall (n = 741)	<1 mo (n = 13)	1–11 mo (n = 150)	1–3 y (n = 117)	4–10 y (n = 169)	11–17 y (n = 292)
Patient and procedural						
Female sex	362 (49)	9 (69)	55 (37)	51 (44)	78 (46)	169 (58)
ASA PS score (n = 727)						
≥3 ^b	267 (37)	10 (77)	44 (31)	41 (36)	77 (46)	95 (33)
Preop hospital LOS, days						
0	551 (74)	3 (23)	119 (79)	83 (71)	131 (78)	215 (74)
1–3	100 (14)	4 (31)	9 (6)	17 (15)	21 (12)	49 (17)
≥4	90 (12)	6 (46)	22 (15)	17 (15)	17 (10)	28 (10)
Emergent status (n = 727)	64 (9)	1 (8)	8 (5)	9 (8)	22 (13)	24 (8)
Procedure type						
Neurologic	245 (33)	3 (23)	104 (69)	66 (56)	47 (28)	25 (9)
Spinal	153 (21)	0 (0)	2 (1)	5 (4)	35 (21)	111 (38)
Abdominal	88 (12)	7 (54)	21 (14)	11 (9)	16 (9)	33 (11)
Orthopedic	98 (13)	0 (0)	3 (2)	7 (6)	26 (15)	62 (21)
Transplant	39 (5)	0 (0)	7 (5)	7 (6)	12 (7)	13 (4)
HEENT	27 (4)	1 (8)	3 (2)	5 (4)	8 (5)	10 (3)
Other	91 (12)	2 (15)	10 (7)	16 (14)	25 (15)	38 (13)
Anesthesia duration, min		236 (143–270)	265 (207–377)	437 (322–536)	432 (277–599)	509 (297–684)
No. of transfusions in OR		2 (1–2)	1 (1–2)	1 (1–2)	1 (1–2)	2 (1–3)
Laboratory value ^c						
Preop Hb, g/dL (n = 738)		10.7 (9.3–14.6)	9.8 (8.7–11.3)	10.2 (9.1–11.2)	10.8 (8.8–12.2)	11.2 (9.6–13.1)
Preop platelets, ×10 ⁹ /μL (n = 553)		214 (201–306)	372 (250–466)	296 (178–370)	263 (152–351)	235 (168–300)
Initial transfusion Hb, g/dL (n = 605)		10.0 (8.1–12.8)	8.1 (7.0–9.4)	8.1 (7.2–9.3)	8.0 (7.4–8.7)	8.3 (7.6–9.2)
Lowest Hb, g/dL (n = 670)		9.5 (7.2–10.2)	7.8 (7.0–8.9)	7.6 (6.9–8.4)	7.7 (7.1–8.3)	7.9 (7.4–8.6)
Postop Hb, g/dL (n = 479)		11.1 (8.6–13.4)	10.8 (9.4–12.3)	11.0 (9.7–12.0)	10.4 (9.3–11.3)	10.1 (9.0–11.0)
Past medical history						
Anemia	161 (22)	2 (15)	24 (16)	25 (21)	45 (27)	65 (22)
Cancer	115 (16)	0 (0)	9 (6)	20 (17)	27 (16)	59 (20)
Thrombocytopenia	89 (12)	0 (0)	12 (8)	17 (15)	24 (14)	36 (12)
Chronic kidney disease	20 (3)	0 (0)	0 (0)	5 (4)	4 (2)	11 (4)
Liver disease	16 (2)	0 (0)	6 (4)	2 (2)	3 (2)	5 (2)
Antiplatelet or anticoagulant medication ^d	159 (21)	1 (8)	16 (11)	21 (18)	27 (16)	94 (32)

Abbreviations: ASA PS, American Society of Anesthesiologists Physical Status Classification System; Hb, hemoglobin; HEENT, head, eyes, ears, nose, and throat; LOS, length of stay; OR, operating room; postop, postoperative; preop, preoperative.

^a Values are presented as number (percentage) for categorical variables; median (IQR) for continuous variables. When some data were not available, numbers of patients with complete data are presented.

^b Seven patients were classified as ASA PS score 5.

^c Preop laboratory values were obtained anytime within 90 days before the procedure time. Initial transfusion hemoglobin level was obtained before transfusion in the OR. Lowest hemoglobin was obtained in the OR. Postop hemoglobin was obtained within 6 h of the transfusion or after exiting the OR.

^d Four patients were taking warfarin; they were in the 11-to-17-year age group.

3.2. Pretransfusion hemoglobin values

Pretransfusion hemoglobin values were available for 605 procedures (82%), measured at a median (IQR) of 28 (15–44) minutes before transfusion. When infants required a transfusion, those younger than 1 month had a median of 2 RBC transfusions, whereas patients aged 1 to 10 years had a median of 1 RBC transfusion.

3.3. Lowest intraoperative posttransfusion hemoglobin values

Hemoglobin values within 6 h after transfusion were available for 65% of patients. The Supplemental Table summarizes patient and procedural characteristics, stratified by the presence or absence of a postoperative hemoglobin measurement within 6 h.

Posttransfusion hemoglobin level was not associated with postoperative hospital LOS ($P = .66$), hospital-free days ($P = .56$), ICU admission ($P = .71$), postoperative mechanical ventilation ($P = .63$), or infectious complications ($P = .74$) (Table 2). Each decrease of 1 g/dL in the initial postoperative hemoglobin concentration was associated with increased odds of RBC transfusion within the first 24 postoperative hours (odds ratio [95% CI], 1.62 [1.37–1.93]; $P < .001$). Hemoglobin nadirs were lower for patients older than 1 month.

Postoperative patient outcomes were generally similar according to age for patients older than 1 month (Table 3). Patients younger than 1 month had longer hospital LOS and higher rates of postoperative

mechanical ventilation, ICU admission, transfusion, and complications. The interaction between age and first postoperative hemoglobin value was not statistically significant in any outcome model.

4. Discussion

Pediatric surgery patients may undergo transfusion if they have preoperative anemia, in anticipation of expected blood loss, or in the context of acute surgical hemorrhage. Because of the paucity of studies reporting operative transfusion practices in children relative to nonsurgical patients, we sought to evaluate the relationship of pretransfusion and posttransfusion hemoglobin on numerous clinical outcomes. We found no evidence of a pretransfusion or posttransfusion hemoglobin level that was associated with either improved or worsened outcomes. Specifically, these variables showed no association with our primary outcome of hospital-free days, nor in our secondary outcomes of hospital LOS, ICU admission, infectious complications, or need for postoperative mechanical ventilation. However, a decreased postoperative hemoglobin value was associated with the need for subsequent transfusion within 24 h, and much of our patient population presented to the OR with anemia.

The study of operative transfusion practices is particularly challenging. The rapidity and severity of intraoperative hemorrhage can make acquisition of traditional transfusion triggers difficult, if not impossible, before a transfusion decision needs to be made. Therefore,

Table 2

Association between postoperative hemoglobin values and outcomes estimated from multivariable analyses.^a

Outcome	Estimated OR (95% CI)	P value
Postop hospital LOS ^b	1.01 (0.96 to 1.07)	0.66
28-d hospital free ^c	-0.13 (-0.55 to 0.30)	0.56
ICU admission	0.97 (0.83 to 1.14)	0.71
Postop mechanical ventilation	0.97 (0.84 to 1.11)	0.63
Infectious complication	0.98 (0.86 to 1.11)	0.74
Transfusion within 24 h ^d	1.62 (1.37 to 1.93)	<0.001

Abbreviations: ICU, intensive care unit; LOS, length of stay; OR, odds ratio; postop, postoperative.

^a Estimates are from multivariable linear regression analysis of multiply imputed data. Generalized estimating equations were used to account for the repeated observations for some patients. For outcomes other than transfusion, estimates reflect estimated multiplicative increase in odds of the given event associated with a 1 g/dL-decrease in postop hemoglobin. All models were adjusted for American Society of Anesthesiologists physical status (grouped as 1 and 2; 3 and 4; and 5), emergent status, preoperative hemoglobin, preoperative platelet count, current anticoagulant medication (warfarin, enoxaparin, or heparin), type of surgery (abdominal, neurologic, orthopedic/spine, and other), age (as a restricted cubic spline), and length of surgery.

^b For postop LOS, the log-transformed values are modeled. The estimate corresponds to the multiplicative increase in geometric mean associated with a 1 g/dL-decrease in postop hemoglobin.

^c Estimate for increase in number of days alive and out of hospital in the 28 days following transfusion.

^d Estimates correspond to the multiplicative increase in odds of transfusion for each 1 g/dL-decrease in postop hemoglobin.

children should not undergo transfusion based solely on a hemoglobin value. Relative to adult patients, these difficulties may be even more challenging among children with a lower total blood volume, thereby enhancing the need for a more rapid transfusion decision. Given that many of our patients had pretransfusion targets above 7 g/dL, clinical circumstances may have warranted the transfusion.

Anemia is prevalent in pediatric medicine, occurring in up to 20% of children at some point before age 18 years [13]. A similar percentage (14%) of our patient cohort had anemia listed in their health history. However, our study group had a substantial number of patients with preoperative anemia. Although healthy children can present for elective surgery, the surgical procedure often is necessary because of a coexisting illness. For critically ill children, causes of anemia include acute or chronic blood loss, underlying disease, or treatment that suppresses the bone marrow, or a combination of these factors [14]. Iron deficiency anemia is also common, accounting for 10% of anemia in US children [15,16].

Although children presenting for emergency operations may be

unable to achieve a full correction of anemia, >90% of operations for this cohort were elective, which implies sufficient time for preoperative optimization. If pediatric patients could be preoperatively treated with iron [17], darbepoetin alfa, or erythropoietin, RBC transfusion rates possibly could be decreased [18–20]. Our data highlight an important opportunity to optimize the health of pediatric patients before surgery.

RBC transfusion has been studied in congenital heart disease, pediatric hematology and oncology, pediatric intensive care, intrauterine transfusion, scoliosis surgery [21], and neonatology [22,23]. Perioperative transfusions occur with limited guidance on the posttransfusion hemoglobin target and postoperative adverse events [24]. Pediatric operations most likely to require transfusion are cardiac, craniofacial, and scoliosis procedures [25], and this outcome was consistent with our data. We excluded cardiac surgery patients because the hemoglobin targets of children with congenital heart disease may not be comparable with children who have normal cardiac anatomy. Our study findings were consistent with those of the Transfusion Requirements in the Pediatric Intensive Care Unit study, which compared restrictive (7 g/dL) with liberal (9.5 g/dL) hemoglobin transfusion thresholds and found no statistically significant increase in adverse outcomes. We similarly showed that there was no statistically significant increase in adverse outcomes for any postoperative hemoglobin threshold.

In adult patients, first postoperative hemoglobin values are associated with important clinical outcomes. Postoperative hemoglobin values between 7.5 and 11.5 g/dL are associated with increased risk of mortality, postoperative mechanical ventilation, acute kidney injury, cerebral ischemia, and decreased hospital-free days relative to adult patients with more extreme values. Although we could not define postoperative target hemoglobin values associated with clinical outcomes in children, it is noteworthy that the IQR of our data set was largely within the optimal adult postoperative hemoglobin range described above. We are cautious about extending the specifics of such literature to children; however, these data do suggest that the optimal postoperative hemoglobin ranges may be similar and that a much larger data set would be necessary to define a specific range. We also note that there are diagnoses specific to pediatrics for which transfusion targets have been described. For example, in infants with very low birth weights, a hemoglobin level <8 g/dL was associated with an increased risk of necrotizing enterocolitis, but transfusion itself was not found to be a risk factor [22]. Thus, although considerable overlap likely exists between adults and children regarding general postoperative hemoglobin targets, we caution against such a literal translation across the spectrum of pediatric ages and disease states [22].

Patients who received a transfusion were more likely to receive an additional transfusion within the following 24 h. This characteristic held true despite the median postoperative hemoglobin values being higher than transfusion thresholds. Estimated blood loss (EBL) is known for

Table 3

Summary of postop patient outcomes overall and according to age group.

Outcome ^a	Overall (n = 741)	Patient age				
		<1 mo (n = 13)	1–11 mo (n = 150)	1–3 y (n = 117)	4–10 y (n = 169)	11–17 y (n = 292)
Hospital LOS, d	6 (4–11)	48 (32–97)	4 (3–7)	6 (4–12)	7 (4–13)	6 (5–10)
Postop mechanical ventilation	245 (33)	12 (92)	42 (28)	34 (29)	59 (35)	98 (34)
Infectious complication	161 (22)	8 (62)	24 (16)	28 (24)	45 (27)	56 (19)
Hospital death	12 (2)	1 (8)	4 (3)	3 (3)	1 (1)	3 (1)
24-h outcomes						
Reoperation	45 (6)	1 (8)	8 (5)	12 (10)	13 (8)	11 (4)
ICU admission	570 (77)	12 (92)	119 (79)	92 (79)	128 (76)	219 (75)
Any transfusion	134 (18)	4 (31)	22 (15)	16 (14)	37 (22)	55 (19)
RBCs	111 (15)	3 (23)	19 (13)	15 (13)	31 (18)	43 (15)
FFP	35 (5)	1 (8)	7 (5)	5 (4)	11 (7)	11 (4)
Platelets	29 (4)	1 (8)	6 (4)	4 (3)	6 (4)	12 (4)
Cryoprecipitate	12 (2)	0 (0)	4 (3)	0 (0)	4 (2)	4 (1)

Abbreviations: FFP, fresh frozen plasma; ICU, intensive care unit; LOS, length of stay; postop, postoperative; RBC, red blood cell.

^a Values are number (percentage) for categorical outcomes; median (IQR) for continuous outcomes.

being unreliable but is particularly challenging in smaller patients, in whom much of the blood loss is not quantifiable in surgical sponges or appears minimal. Ideally, EBL is quantified before transfusion; however, our records do not have reliable chart EBL values at regular time intervals.

This work has limitations. First, despite the use of a large cohort of pediatric surgical patients, the number of transfused patients continues to be small. Second, certain outcomes, such as death, were rare, which limited our ability to assess potentially important exposure-outcome relationships. Third, the single-center design may limit generalizability. Fourth, certain patient groups were excluded, including those with congenital heart disease. As such, the findings above may not be generalizable to specific patients with unique disease states. Finally, the decision to transfuse was subject to variabilities over a 12-year time frame that could not be accounted for in this retrospective analysis. For example, the elapsed time varied between when hemoglobin was measured and when the transfusion was administered, and all clinical parameters (anemia vs hemodynamic instability vs bleeding) necessitating a transfusion could not be individually quantified. Patients generally received few units (ie, 1 10-mL/kg unit, rather than 10); therefore, the dose exposure may have been too low to detect an association. Although administration of more units would probably influence recovery because of fluid shifts, TRALI or TACO, or surgical complexity, our findings likely still hold true for most pediatric patients. Laboratory values such as pH, lactate, and base deficit were not routinely obtained often enough to draw reasonable conclusions.

The present study took a comprehensive look at our transfusion practice in a large population of pediatric surgical patients. Among patients receiving transfusions, postoperative hemoglobin values were not associated with clinical outcomes, and the postoperative hemoglobin range was largely within optimal ranges defined for adult patient populations. However, for some secondary outcomes, the 95% confidence interval for the effect estimate does include potentially meaningful effects; therefore, further study is warranted. Most patients receiving transfusions presented to the operating room with anemia, which suggests a potential opportunity for optimization of health before elective surgery.

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Author statement

All authors have seen and approved the final version of the manuscript being submitted. We warrant that the article is our original work, hasn't received prior publication and isn't under consideration for publication elsewhere.

CRediT authorship contribution statement

Lindsay L. Warner: Conceptualization, Data curation, Formal analysis, Funding acquisition, Methodology, Writing – original draft, Writing – review & editing. **Leanne Thalji:** Conceptualization, Formal analysis, Methodology, Writing – original draft, Writing – review & editing. **Lindsay R. Hunter Guevara:** Data curation, Formal analysis, Writing – original draft, Writing – review & editing. **Matthew A. Warner:** Conceptualization, Formal analysis, Writing – review &

editing. **Daryl J. Kor:** Conceptualization, Formal analysis, Writing – review & editing. **David O. Warner:** Conceptualization, Formal analysis, Writing – review & editing. **Andrew C. Hanson:** Conceptualization, Formal analysis, Writing – review & editing. **Michael E. Nemerugut:** Conceptualization, Formal analysis, Funding acquisition, Methodology, Writing – original draft, Writing – review & editing.

Declaration of competing interest

No conflicts of interest declared.

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jclinane.2024.111405>.

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