Journal of Pediatric Surgery 53 (2018) 1105–1110

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

# Relationship between perioperative blood transfusion and surgical site infections in pediatric general and thoracic surgical patients

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ARTICLE INFO

*Article history:*
Received 17 February 2018
Accepted 27 February 2018

*Key words:*
Transfusion
Pediatric
NSQIP
Surgical site infections

ABSTRACT

*Background:* Recently, perioperative transfusions were demonstrated to be associated with higher rate of surgical site infections (SSIs) in neonates. We sought to examine whether a similar relationship exists between perioperative blood transfusions and SSI among non-neonatal pediatric general surgical patients.
*Methods:* We conducted an IRB-approved retrospective study reviewing non-neonatal patients (age greater than 28 days and less than 18 years) who underwent a general or thoracic surgical procedure in 2012, 2013, 2014, in the American College of Surgeons National Safety and Quality Improvement Project-Pediatric (ACS-NSQIP-P) Participant User Files. We used Chi-square analyses to perform a bivariate analysis comparing proportions of SSI's between patients who received blood transfusion to those who did not. Multiple logistic regression analyses compared the odds of SSIs in transfused versus nontransfused patients controlling for organ failure, steroid use, nutritional status, current infection, American Society of Anesthesiologists (ASA) Physical Status classification, and wound classification.
*Results:* There were 55,133 patients with 1779 patients who received blood transfusion (≥25 ml/kg body weight) during or within 72 h of surgery. Bivariate analysis showed at least twice the rate of infection in transfused patients compared to nontransfused patients ($p < 0.01$): superficial SSI 3.5% vs 1.5%; deep SSI 0.8% vs 0.2%, organ space SSI 3.8% vs 1.6%; deep dehiscence 2% vs 0.3%. Total wound infections and dehiscence for transfused patients were 10.5% vs 3.8% in nontransfused patients ($p < 0.01$). Multiple regression analysis showed that nutritional issue, current infection, and wounds not classified as "clean" have statistically significant correlation with SSI. Although there was significant interaction between ASA and transfusion ($p < 0.0001$), we found statistically significant associations between transfusions and SSI for ASA class 1–2 (OR = 5.51, 95% CI 3.47–7.52), ASA class 3 (OR = 2.06, 95% CI 1.63–2.61), and ASA class 4–5 (OR = 1.67, 95% CI 1.15–2.42).
*Conclusion:* In non-newborn pediatric general and thoracic surgery patients, transfusions were associated with higher risk of SSI or wound dehiscence. Although there was a significant interaction between ASA and transfusion, OR for SSI was stronger for lower ASA classes.
*Type of Study:* Retrospective Review.
*Level of Evidence:* II



Despite their many benefits, blood transfusions have associated risks. Contemporary blood banking practices have reduced the risk of transfusion-related transmission of infections such as Hepatitis B, Hepatitis C and HIV. [1] Classic immunologic reactions include acute and delayed immune hemolytic reactions. In addition, there are transfusion related effects on immunomodulation [2], lung injury [3], and acute circulatory overload [4] that may significantly complicate patient care.

In surgical patients, transfusion-related morbidities can manifest in many ways. In adults, some postoperative outcomes associated with perioperative transfusions include pulmonary complications, thromboembolic complications, wound complications, and sepsis. [5] In pediatrics, some surgical subspecialties also found possible association between transfusions and postoperative morbidities. In craniofacial [6] and orthopedic [7,8] surgery, perioperative transfusions were associated with higher postoperative complications. In pediatric patients who have sustained greater than 60% total body surface area burns, higher rates of sepsis were seen in those with higher red blood cell (RBC) transfusions. [9] In pediatric cardiac surgery, blood product transfusions were associated with postoperative pulmonary complications

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https://doi.org/10.1016/j.jpedsurg.2018.02.062
0022-3468/

and length of stay. [10] Historically, these particular subspecialties had not been tentative about transfusing their patients in the perioperative period, but the impetus to have better outcomes may be slowly steering physicians to a more deliberate transfusion practice.

Using the American College of Surgeons (ACS) National Safety and Quality Improvement Project-Pediatric (ACS-NSQIP-P), we have found an association between perioperative blood transfusions and surgical site infections in surgical neonates in all surgical subspecialties included in NSQIP. [11] These subspecialties include general and thoracic surgery, urology, otolaryngology, neurosurgery, plastic surgery, and orthopedic surgery. In this study, we focused only on pediatric general and thoracic surgery patients, hypothesizing that there may be an association between perioperative blood transfusions and SSI and other wound complications in non-newborn children.

## 1. Methods

### 1.1. Data source

We queried the American College of Surgeons (ACS) National Safety and Quality Improvement Project-Pediatric (NSQIP-P) Participant User Files (PUF) for the calendar years 2012, 2013, and 2014. ACS-NSQIP-P is a voluntary reporting system designed to provide risk-adjusted outcomes to medical institutions to improve the quality of surgical care on a national level. Clinical data were based on standardized and validated definitions collected on a subset of general and thoracic surgery, urology, otolaryngology, neurosurgery, plastic surgery, and orthopedic surgery patients. Transplant, trauma, and cardiac surgery patients were not included, as outcomes for these patients are already collected in specific national databases. Thirty-day outcomes were recorded by abstractors who have received standardized training, supervision and testing to ensure uniformity in collection of data. Since preoperative comorbidities were known, risk-adjusted outcomes can be calculated allowing individual institutions to compare benchmarks against other centers.

The PUF are Health Insurance Portability and Accountability Act (HIPAA) compliant data files that contain cases submitted to ACS-NSQIP-P, a resource provided to participating institutions for investigation purposes to further advance surgical quality and outcomes. Patient-level and hospital-level data were deidentified.

### 1.2. Study population

We included all patients in the NSQIP-P dataset who underwent general and thoracic operations in 2012, 2013, 2014 excluding neonates. NSQIP-P defined a “neonate” as a term newborn less than 29 days old at the time of surgery or a premature newborn with a gestational age less than 51 weeks at time of surgery.

### 1.3. Exposure variable

The exposure variable that we used was the transfusion of packed red blood cells (RBCs), whole blood, or autologous blood administered during the operation and within 72 h postoperatively. In NSQIP-P, peri- and postoperative transfusions were recorded if the total volume reached 25 ml/kg weight. Transfusion of other blood products such as fresh frozen plasma, platelets, cryoprecipitate or albumin was not abstracted by ACS-NSQIP.

### 1.4. Outcome measures

Our primary outcome measure was the occurrence of a surgical site infection (SSI) or wound dehiscence within 30 days of surgery. SSIs were categorized as follows: 1) superficial = involves only skin or subcutaneous tissue of the incision; 2) deep incisional = involves the deep soft tissue, e.g. fascial and muscle layers of the incision; 3) organ space-involves any part of the anatomy other than the incision, which was opened or manipulated during an operation; or 4) deep dehiscence = separation or disruption of the internal/deep layers of the surgical wound. Superficial dehiscence, defined as separation or disruption of the superficial/external layers of the surgical wound, was a category in the 2013 and 2014 datasets, but not in 2012.

### 1.5. Statistical analysis

Bivariate analyses using Chi-squared analysis compared patient characteristics as well as operative characteristics and transfusion status. For the variable “age”, Student's T-test was used. SSI type with transfused and nontransfused patients was compared using a Pearson's Chi-squared test. Chi-squared analysis was also used to perform bivariate analysis of SSI and potential predictor variables. A multiple logistic regression analysis compared the odds of SSIs in transfused patients versus nontransfused patients controlling for prior operations, organ failure, steroid use, nutritional status, current infection, American Society of Anesthesiologists (ASA) Physical Status classification, and wound classification. For the multiple logistic regression analysis, we collapsed ASA classification into three groupings because of the relatively small number of transfused patients in some classes (1 and 5). We felt that combining ASA 1 and 2 as well as 4 and 5 made sense physiologically and clinically. All tests were conducted as two-tailed tests and p values $<0.05$ were considered statistically significant. All analyses were conducted using SAS 9.4 software (Copyright, SAS Institute Inc., Cary, NC, USA).

### 1.6. Institutional review board

This study was approved by the Institutional Review Board (IRB) at the Children's Hospital of Wisconsin (CHW).

## 2. Results

### 2.1. Patient characteristics (Table 1)

A total of 55,133 patients were captured in the 2012, 2013, and 2014 PUF. There were 1779 patients (3.2%) who received transfusions either intraoperatively or within 72 hours postoperatively. There were slightly more than half male patients in the entire cohort, but equivalent percentages of male and females in both the transfused and nontransfused groups. There was an equal distribution of ethnicities across the cohort. Those who received transfusions were younger ($3.6 \pm 5.4$ years) compared to those who did not ($8.2 \pm 5.9$; $p < 0.0001$).

**Table 1**
Demographic characteristics of non-neonatal pediatric general and thoracic patients in ACS-NSQIP-Pediatric comparing transfused and nontransfused patients. Chi-square statistics were used for the analyses except for age, where we used Student's T test.

| Characteristic | Transfused N = 1779 | Not Transfused N = 53,447 | p-value |
|---|---|---|---|
| Gender, n (%) | | | 0.0269 |
| Male | 964 (54.2) | 30,374 (56.8) | |
| Female | 815 (45.8) | 23,073 (43.2) | |
| Race/Ethnicity, n (%) | | | <0.0001 |
| White, non-Hispanic | 1011 (56.8) | 32,242 (60.3) | |
| African American, non-Hispanic | 298 (16.8) | 6131 (11.5) | |
| Asian, non-Hispanic | 39 (2.2) | 1273 (2.4) | |
| Hispanic | 214 (12.0) | 9519 (17.8) | |
| Other/Unknown | 217 (12.2) | 4282 (8.0) | |
| Age in years, mean (SD) | 3.6 (5.4) | 8.2 (5.9) | <0.0001 |
| Patients with hematology condition n (%) | 550 (30.9) | 2478 (4.6) | <0.0001 |
| Patients with concomitant chemotherapy, n (%) | 57 (3.2) | 120 (0.2) | <0.0001 |
| Patient with malignancy, n (%) | 91 (5.1) | 190 (0.4) | <0.0001 |