Original Investigation

Potential Economic Impact of Using a Restrictive Transfusion Trigger Among Patients Undergoing Major Abdominal Surgery

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IMPORTANCE Transfusion practice among surgeons varies despite several evidence-based recommendations supporting the restrictive use of blood products.

OBJECTIVE To define the economic impact of liberal blood transfusions as assessed through an analysis of hemoglobin (Hb) triggers.

DESIGN, SETTING, AND PARTICIPANTS Using a prospective database, data on Hb levels that triggered a transfusion and overall blood product use were obtained for patients undergoing pancreas, liver, or colorectal surgery between January 1, 2010, and August 31, 2013, at Johns Hopkins Hospital. An economic analysis was performed using a range of costs for a single unit of packed red blood cells (PRBCs) based on actual institutional acquisition costs ($220/unit) and an estimated activity-based cost ($760/unit). Guidelines define a liberal Hb trigger as transfusion of PRBCs for an intraoperative Hb level of 10 g/dL or greater or a postoperative Hb level of 8 g/dL or greater (to convert to grams per liter, multiply by 10.0).

MAIN OUTCOMES AND MEASURES Numbers of surgical patients who received PRBC transfusion, estimated cost per transfusion, and estimated cost of excessive blood transfusions.

RESULTS Among 3027 patients, 942 (31.1%) received at least 1 PRBC transfusion, intraoperatively in 264 patients (8.7%), postoperatively in 429 (14.2%), or both in 249 (8.2%). A total of 4000 units of PRBCs (range, 0-167 units/patient) were transfused in the intraoperative (1581 units [39.5%]) and postoperative (2419 units [60.5%]) periods. Estimated total costs of PRBC transfusion ranged from $880 000 to $3 040 000, with marked variation in costs per patient across procedure type and surgeon. Among the 942 patients who received a transfusion, 456 units (11.4%) were transfused using a liberal trigger (intraoperative, 122 patients [13.0%]; postoperative, 79 patients [8.4%]). By adopting a restrictive trigger, total overall PRBC transfusion costs may have been reduced by $100 320 to $346 560 during the 44-month study period or $27 360 to $94 516 per year for patients undergoing a pancreas, liver, or colorectal resection.

CONCLUSIONS AND RELEVANCE More than 1 in 10 units of PRBCs were transfused using a liberal Hb trigger. Patient blood management programs should aim to identify and reduce liberal transfusion practice in the surgical patient.

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The use of blood transfusions in the surgical patient is critical in maintaining hemodynamic stability, oxygen delivery, and organ perfusion. Particularly in patients undergoing major abdominal operations who are at high risk for perioperative hemorrhage and anemia, the transfusion of packed red blood cells (PRBCs) is often necessary. Several studies, however, have shown an association between the receipt of PRBC transfusions and worse perioperative and long-term outcomes among surgical patients.[1-6] Given this association, several well-conducted randomized clinical trials have shown that the restrictive use of blood transfusions results in equivalent or even better outcomes as compared with liberal use of these products.[7-11] Hemoglobin (Hb) triggers (the Hb level that prompts a PRBC transfusion) have commonly been used to assess a clinician's compliance with evidence-based transfusion guidelines and prevent the overuse of these valuable products.[12,13] Despite these data, however, our group and others have shown that transfusion practice remains varied among surgeons.[12-16]

In addition to potentially worse clinical outcomes associated with the overuse of PRBCs, the economic impact of such practice must be considered. The ballooning cost of health care in the United States and worldwide necessitates a comprehensive economic evaluation of clinical treatment decisions in addition to the assessment of standard clinical outcomes. With regard to transfusion practice, Frank et al[17-19] recently published data on the development and implementation of a maximal surgical blood order schedule to reduce unnecessary preoperative blood orders. However, the costs associated with the overuse of PRBC transfusions in the surgical patient undergoing a major abdominal operation based on Hb triggers remain much less studied. As such, we sought to define the clinical and economic impact in the liberal, noncompliant transfusion strategy among patients undergoing a hepatic, pancreatic, or colorectal resection at our institution. Furthermore, we aimed to identify variations in excessive and potentially unnecessary transfusion costs based on patient, clinician, and surgical service levels. We hypothesized that increased compliance with national guidelines regarding use of a restrictive transfusion strategy would result in significant potential cost savings.

Methods

Surgeon and Patient Selection and Data Collection

We queried the Johns Hopkins surgical database for all patients who underwent select pancreatic (pancreaticoduodenectomy, total pancreatectomy, partial pancreatectomy, proximal pancreatectomy, distal pancreatectomy), hepatic or biliary (partial hepatectomy, hepatic lobectomy, extrahepatic biliary duct resection), and colorectal (sigmoidectomy, hemicolectomy, total colectomy, low anterior resection, abdominoperineal resection) resections between January 1, 2010, and August 31, 2013, using the corresponding *International Classification of Diseases, Ninth Revision* procedure codes. Standard patient demographic and clinicopathologic data were collected, including age, sex, race, Charlson comorbidity index scores, American Society of Anesthesiologists (ASA) status, and the primary diagnosis and indication for surgery. The presence of an in-hospital perioperative complication was ascertained through discharge *International Classification of Diseases, Ninth Revision* diagnosis codes as previously described[16] and included minor infections (urinary tract infection, surgical site infection, and *Clostridium difficile* infection), major infections (sepsis, ventilator-associated pneumonia, and drug-resistant infections), transient ischemic attack, cerebrovascular accident, myocardial infarction, deep vein thrombosis, pulmonary embolism, and disseminated intravascular coagulation. This study was approved by the Johns Hopkins Institutional Review Board. A consent waiver was obtained for this retrospective medical record review and patients were not required to provide written informed consent for this study.

Perioperative hospital transfusion data, including Hb triggers that prompted a PRBC transfusion, were obtained through a comprehensive proprietary blood management intelligence portal (IMPACT Online; Haemonetics Corp).[12] Intraoperative transfusion use data were extracted from a prospectively collected automated anesthesia information management system (Metavision; iMDsoft).[13] Postoperative transfusion was defined as any transfusion given during the index hospitalization not in the operating room. All data in both the intraoperative anesthesia management system and perioperative blood management system are collected prospectively and undergo routine quality reviews to verify their accuracy. For this study, only PRBC transfusions were analyzed. Based on the most commonly cited large randomized clinical trials analyzing transfusion triggers, a liberal Hb trigger was defined as patients who received a PRBC transfusion with a nadir Hb level of 8 g/dL or greater (to convert to grams per liter, multiply by 10.0) as previously defined.[16] As no clinical trials exist, to our knowledge, analyzing the restrictive intraoperative use of blood transfusions, a liberal intraoperative Hb trigger was defined as an Hb level of 10 g/dL or greater based on our most recent study and the most recent report from the ASA Task Force on Perioperative Blood Transfusion and Adjuvant Therapies.[15,20]

Cost Analysis

Two figures were used to estimate the total cost of a single unit of PRBCs: actual institutional acquisition costs ($220/unit) and an estimated activity-based cost ($760/unit). The estimated activity-based cost is based on a recent report from the Society for the Advancement of Blood Management.[21] This estimate calculates the cumulative cost of each step involved in delivering 1 unit of PRBCs from a donor to a recipient; technical, administrative, and clinical processes are all included in this estimate. Although the report provides a range of the cost estimate of a single unit of PRBCs ($522-$1183), the mean estimate calculated ($760/unit) was used for our study.

Statistical Analysis

Continuous variables are presented as the median with interquartile range (IQR) or as the mean with standard deviation as appropriate. Categorical variables are displayed as whole numbers and percentages. Univariate comparisons were as-

Table. Clinicopathologic and Operative Characteristics Stratified by Need for PRBC Transfusion

Characteristic	All (N = 3027)	Perioperative PRBC Transfusion (n = 942)	No Perioperative PRBC Transfusion (n = 2085)	*P* Value
Age, median (IQR), y	59 (48-69)	63 (52-72)	58 (46-67)	<.001
Male, No. (%)	1458 (48.2)	471 (50.0)	987 (47.3)	.18
White, No. (%)	2341 (77.3)	698 (74.1)	1643 (78.8)	.04
ASA class 3 or 4, No. (%)	1864 (61.6)	727 (77.2)	1137 (54.5)	<.001
Charlson comorbidity index score, No. (%)				
0-3	1783 (58.9)	444 (47.1)	1339 (64.2)	<.001
≥4	1244 (41.1)	498 (52.9)	746 (35.8)	
Selected diagnosis, No. (%)				
Pancreatic head neoplasm	393 (13.0)	185 (19.6)	207 (9.9)	<.001
Benign pancreatic neoplasm	176 (5.8)	39 (4.1)	137 (6.6)	
Secondary liver metastasis	198 (6.5)	53 (5.6)	145 (7.0)	
Rectal adenocarcinoma	108 (3.6)	31 (3.3)	77 (3.7)	
Procedure type				
Pancreaticoduodenectomy	797 (26.3)	339 (36.0)	458 (22.0)	<.001
Distal pancreatectomy	271 (9.0)	73 (7.7)	198 (9.5)	
Partial hepatectomy	438 (14.5)	116 (12.3)	322 (15.4)	
Right hemicolectomy	413 (13.6)	105 (11.1)	308 (14.8)	
Preoperative Hb level, mean (SD), g/dL	12.7 (2.0)	11.7 (2.2)	13.1 (1.7)	<.001
EBL, median (IQR), mL	300 (150-600)	700 (300-1200)	200 (100-450)	<.001
Crystalloid fluids, median (IQR), mL	5000 (3600-6500)	6000 (4400-8000)	4500 (3350-6000)	<.001
LOS, median (IQR), d	7 (5-12)	11 (7-18)	6 (5-9)	<.001
Complications, No. (%)	537 (17.7)	314 (33.3)	223 (10.7)	<.001
Minor infection	359 (11.9)	186 (19.8)	173 (8.3)	
Major infection	97 (3.2)	83 (8.8)	14 (0.7)	
VTE	66 (2.2)	48 (5.1)	18 (0.9)	
Respiratory	50 (1.7)	25 (2.7)	25 (1.2)	
DIC	55 (1.8)	47 (5.0)	8 (0.4)	
MI	17 (0.6)	15 (1.6)	2 (0.1)	
CVA	6 (0.2)	5 (0.5)	1 (0.1)	

Abbreviations: ASA, American Society of Anesthesiologists; CVA, cerebrovascular accident; DIC, disseminated intravascular coagulation; EBL, estimated blood loss; Hb, hemoglobin; IQR, interquartile range; LOS, length of stay; MI, myocardial infarction; PRBC, packed red blood cell; VTE, venous thromboembolism.

SI conversion factor: To convert Hb to grams per liter, multiply by 10.0.

sessed using the χ^2 test, analysis of variance, or Mann-Whitney *U* test as indicated. Cost estimates were based on total PRBC units administered based on either a restrictive or liberal Hb trigger. For all statistical analysis, $P < .05$ (2-tailed) was deemed significant. All analyses were carried out with Stata version 13.0 statistical software (StataCorp LP).

Results

Description of Cohort

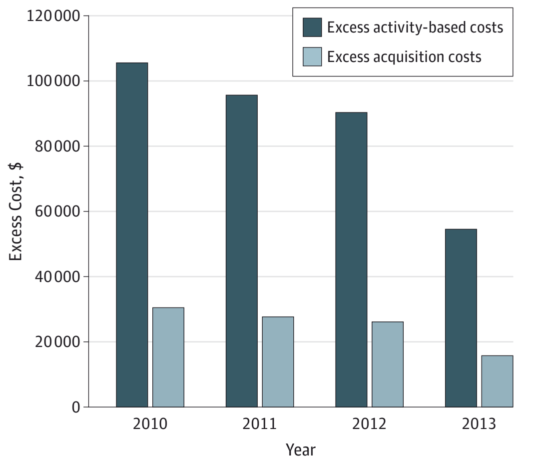
We identified 3027 patients undergoing a colorectal (n = 1266 [41.8%]), pancreatic (n = 1177 [38.9%]), or liver (n = 584 [19.3%]) resection between January 1, 2010, and August 31, 2013, at our institution. There was a slight majority of women (n = 1569 [51.8%]) in the cohort (**Table**). The median age was 59 years (IQR, 48-69 years), and the majority of patients were white (n = 2341 [77.3%]). Comorbidities were common as most patients were classified as ASA class 3 or 4 (n = 1864 [61.6%]) and the median Charlson comorbidity index score was 3 (IQR, 1-6).

The indication for surgery was more often for malignant disease (n = 1678 [55.4%]), with pancreatic head neoplasms (n = 393 [13.0%]), secondary liver metastasis (n = 198 [6.5%]), and rectal adenocarcinoma (n = 108 [3.6%]) being the most common. Of the benign indications (n = 1349 [44.6%]) for surgery, benign pancreatic neoplasms (n = 176 [5.8%]) and diverticulitis (n = 99 [3.3%]) were most common. At the time of surgery, patients underwent a variety of resections that most commonly included pancreaticoduodenectomy (n = 797 [26.3%]), partial hepatectomy (n = 438 [14.5%]), and right hemicolectomy (n = 413 [13.6%]).

Use of PRBCs

A total of 942 patients received at least 1 unit of PRBCs, for an overall transfusion rate of 31.1%. The PRBC transfusions were more common during pancreas resections (n = 457 [48.5%]) than liver (n = 152 [16.1%]) or colorectal (n = 333 [35.4%]) resections ($P < .001$). Transfusion rates also varied among different pancreas resections (pancreaticoduodenectomy, n = 339 [36.0%]; distal pancreatectomy, n = 73 [7.7%]; $P < .001$), liver resections (partial hepatectomy, n = 116 [26.5%]; hepatic lobectomy, n = 19 [33.9%]; $P = .01$), and colorectal resections (laparoscopic right hemicolectomy, n = 9 [6.6%]; total colectomy, n = 19 [32.8%]; $P < .001$). Patients receiving a PRBC transfusion compared with those not receiving a PRBC transfusion were more often older

Figure 1. Excess Transfusion Costs by Year Assuming Use of a Restrictive Transfusion Hemoglobin Trigger



(median [IQR], 63 [52-72] vs 58 [46-67] years; $P < .001$), were more often white (n = 698 [74.1%] vs n = 1643 [78.8%]; $P = .04$), and had higher Charlson comorbidity index scores (median [IQR], 4 [2-6] vs 2 [1-6]; $P < .001$). Patients receiving PRBCs compared with those without a PRBC transfusion also had lower preoperative Hb levels (mean [SD], 11.7 [2.2] vs 13.1 [1.7] g/dL; $P < .001$) and had higher operative blood loss (median [IQR], 700 [300-1200] vs 200 [100-450] mL; $P < .001$).

A total of 4000 units of PRBCs (range, 0-167 units/patient) were transfused during the study period, with the majority of PRBC transfusions outside the operating room during the postoperative period (2419 units [60.5%]) and fewer in the intraoperative period (1581 units [39.5%]). Most patients required only a postoperative transfusion (n = 429 [14.2%]), whereas a smaller portion required only intraoperative transfusion (n = 264 [8.7%]) or received a transfusion in both the intraoperative and postoperative periods (n=249 [8.2%]). The median number of PRBCs transfused was 2 units (IQR, 1-3 units), regardless of the timing of the transfusion (intraoperative vs postoperative). The majority of PRBC units were transfused among patients undergoing pancreas resections (1905 units [47.6%]) as compared with colorectal (1488 units [37.2%]) or liver (607 units [15.2%]) resections.

Perioperative Outcomes Associated With PRBC Transfusion

A perioperative complication occurred in 537 patients, for a morbidity rate of 17.7%. Median length of stay (LOS) among the entire cohort was 7 days (IQR, 5-12 days). The incidence of any perioperative complication was higher among patients undergoing a colorectal resection (n = 261 [20.6%]) than among those undergoing a pancreas (n = 205 [17.4%]) or liver (n = 71 [12.2%]) resection ($P < .001$).

Patients who received PRBCs had a higher incidence of perioperative morbidity (n = 314 [33.3%]) as compared with patients who did not receive PRBCs (n = 223 [10.7%]) ($P < .001$). Not surprisingly, patients who received PRBCs also had a longer LOS (median, 11 days; IQR, 7-18 days) than patients who did not receive PRBCs (median, 6 days; IQR, 5-9 days) ($P < .001$). On multivariate analysis, after adjusting for clinicopathologic factors including age, sex, ASA class, Charlson comorbidity index score, resection type, diagnosis, and baseline Hb level, patients receiving a PRBC transfusion were at an independently higher risk for perioperative morbidity (odds ratio = 3.93; 95% CI, 3.16-4.88; $P < .001$). Among patients with a nadir Hb of 8 to 10 g/dL, perioperative morbidity was significantly higher among patients who received a PRBC transfusion than among those who did not (n = 20 [20.8%] vs n = 152 [12.6%], respectively; $P < .001$). This resulted in a longer median LOS among those who received a transfusion vs those who did not (median [IQR], 11.5 [8-17.5] vs 7 [5-10] days, respectively; $P < .001$).

Variation in Perioperative Hb Triggers and Effect on Transfusion Costs

The mean (SD) intraoperative Hb trigger was 8.8 (1.6) g/dL, whereas the mean postoperative Hb trigger was 7.1 (0.9) g/dL. Among the 942 patients who received a PRBC transfusion, however, 122 (13.0%) received an intraoperative PRBC transfusion with a liberal intraoperative Hb trigger (≥10 g/dL) and 79 (8.4%) received a postoperative PRBC transfusion using a liberal postoperative Hb trigger (≥8 g/dL). This resulted in 456 units (11.4%) of PRBCs potentially unnecessarily transfused. Patients undergoing pancreas resections were more likely to receive a transfusion using a liberal Hb trigger (n = 106 [23.2%]) than those undergoing colorectal (n = 54 [16.2%]) or liver (n = 30 [19.7%]) resections ($P = .05$).

Estimated total costs of PRBC transfusion ranged from $880 000 to $3 040 000. Total PRBC units transfused using a liberal Hb trigger (456 units) varied by resection type (pancreas, 274 units [60.1%]; colorectal, 108 units [23.7%]; and liver, 74 units [16.2%]; $P = .008$). Estimated excess transfusion costs for these patients treated using a liberal transfusion strategy ranged from $100 320 to $346 560 (11.4% of the total transfusion costs) and varied by resection type (pancreas, $60 280-$208 420; colorectal, $23 760-$82 080; and liver, $16 280-$56 240). By avoiding liberal PRBC transfusions, institutional transfusion costs may have been reduced by $27 360 to $94 516 per year for patients undergoing a pancreas, liver, or colorectal resection. Interestingly, excess institutional costs decreased by year during the study period (2010, $30 580-$105 640 [13.3%]; 2011, $27 720-$95 760 [12.7%]; 2012, $26 180-$90 440 [10.9%]; and 2013, $15 840-$54 720 [9.4%]) (**Figure 1**).

Of the 92 surgeons included in the current cohort, 42 (45.6%) gave at least 1 patient a transfusion using a liberal Hb trigger. Based on our institutional guidelines attempting to prevent the use of PRBCs in patients with an Hb trigger of 8 g/dL or greater, the overwhelming majority of patients treated under a liberal transfusion strategy (n = 152 [80.0%]) were treated by only the 9 least compliant (lowest 10th percentile) surgeons. Furthermore, these surgeons were responsible for nearly 80% ($78 980-$272 840) of the total overall excess transfusion costs during the 44-month study period (**Figure 2**).

Discussion

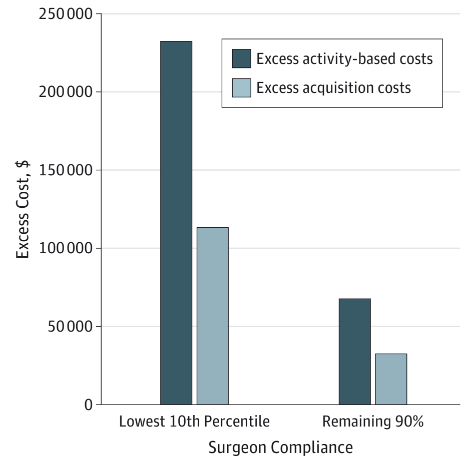
Despite several studies and national transfusion guidelines advocating for the restrictive use of PRBC transfusions,[7-11] trans-

fusion practice remains varied among surgeons.[13] Our group previously showed significant variation in Hb triggers used to guide transfusion practice.[15,16] Furthermore, we showed that the restrictive use of PRBC transfusion resulted in equivalent outcomes as compared with the liberal use of such products.[15,16] Given the current economic health care climate, we aimed to evaluate the economic impact of such clinical decisions. Further expanding on our previous studies, the current study illustrates the financial impact a liberal transfusion practice has on transfusion costs. We found that more than 1 in 10 units of PRBCs and 6.3% of patients at our institution received at least 1 unit of PRBCs using a liberal Hb trigger after undergoing a pancreas, colorectal, or liver resection. We found significant variation in transfusion practice and costs at our institution on both the patient and clinician levels. Perhaps of equal importance, this liberal use of blood products led to excess transfusion costs ranging from $100 320 to $346 560 during the 44-month study period.

Several authors have attempted to elucidate the true comprehensive cost of transfusion. Simply using institutional acquisition costs of PRBCs ($220/unit) does not fully account for other technical, administrative, and clinical processes associated with the acquisition of this valuable resource. In this study, we included these overhead costs as calculated by Shander et al[21] where every step in the process between the donor and the recipient was evaluated from a cost perspective, which they defined as the activity-based cost of blood. In the article by Shander and colleagues, the mean estimate for 1 unit of PRBCs was $760. Based on this estimate, the true cost of 1 unit of PRBCs is nearly 3.5 times our institutional acquisition cost. Furthermore, we did not account for other costs associated with blood transfusions in this study. Frank et al[17,18] showed that unnecessary preoperative blood ordering (ie, type and screen/type and crossmatch) was common among surgical patients and estimated that these preoperative costs resulted in an excess of $43 135 per year or $1.81 per surgical patient at our institution. Moreover, in our cohort, perioperative morbidity and LOS were significantly higher among patients who received at least 1 unit of PRBCs; these excess health care costs were not taken into consideration in our economic analysis. However, Fischer et al[22] estimated that each unit of blood transfusion administered in patients undergoing breast reconstruction was independently associated with an added cost of $1500, mostly due to an increase in medical complications associated with potentially unnecessary transfusions. Taken together, the actual costs of liberal, potentially unnecessary use of blood products far exceed simple institutional acquisition costs and should be taken into consideration.

Hemoglobin triggers have been extensively used to analyze and guide the practice of transfusing PRBCs.[12,13] Our group previously showed significant patient- and surgeon-related variation in the use of Hb triggers.[15,16] In the current study, these variations significantly increased potentially unnecessary excess transfusion costs. For example, patients undergoing a pancreatic resection at our institution accounted for more than 60% of the excess transfusion costs in our cohort. Perhaps more interestingly, surgeon variation and their respective impact on excess transfusion costs seemed to be skewed to a small sample of noncompliant surgeons. That is, surgeons deemed to be in the lowest 10th percentile in terms of compliance with institutional guidelines (deterring the use of PRBCs in patients with an Hb trigger ≥8 g/dL) accounted for nearly 80% of identified excess transfusion costs. By targeting these surgeons, institutional and overall health care costs can potentially be significantly reduced. Politsmakher et al[23] established a successful intervention to ensure compliance with evidence-based institutional transfusion criteria and reduced the costs of all blood products in all patients by more than $2.2 million during a 2-year period. Our data support these findings and show how interventions to reduce the unnecessary use of PRBCs can have a significant impact on costs. For example, a best-practice alert during all electronic orders for PRBCs at our institution was established during the study period. As shown in the data, institutional excess costs decreased each year during the study period. These findings support the premise that patient blood management programs are an effective way to identify, target, and reduce excess and unnecessary transfusion use and costs.

Figure 2. Excess Transfusion Costs Based on Surgeon Compliance With Institutional Evidence-Based Restrictive Transfusion Guidelines



Several limitations need to be considered when interpreting the data. The decision to administer PRBCs often accounts for various shifting patient- and case-specific factors, in particular the presence of perioperative hemorrhage that may not be immediately reflected in laboratory Hb values in the surgical patient. However, previous studies showed the overall incidence of clinically significant perioperative hemorrhage to be relatively rare.[24] As such, the use of Hb triggers can be of significant help to limit the liberal use of PRBCs. Furthermore, as we used the lowest Hb level recorded as our Hb trigger, it is possible that this laboratory value may not have been independently used to guide transfusion practice. However, as a significant number of patients received more than 1 unit of PRBCs, it is possible that additional units of PRBCs were transfused with a higher Hb trigger and thus actually may have led to an underestimation of the overuse of blood products. Although data on other laboratory values (eg, albumin) and intraoperative variables were not available, this should not have affected the analyses given that we analyzed PRBC use relative to Hb trigger.

Conclusions

Overuse of PRBC transfusion in the surgical patient is common. More than 1 in 10 units of PRBCs were transfused using a liberal Hb trigger. By avoiding liberal PRBC transfusions, institutional transfusion costs may have been reduced by $27 360 to $94 516 per year for patients undergoing a pancreas, liver, or colorectal resection. Our data support the use of patient blood management systems to identify and reduce the liberal use of PRBC transfusions in the surgical patient.

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Study concept and design: Ejaz, Frank, Spolverato, Pawlik.
Acquisition, analysis, or interpretation of data: Ejaz, Frank, Spolverato, Kim.
Drafting of the manuscript: Ejaz, Frank, Spolverato, Kim.
Critical revision of the manuscript for important intellectual content: Ejaz, Frank, Spolverato, Pawlik.
Statistical analysis: Ejaz, Kim.
Administrative, technical, or material support: Frank, Spolverato.
Study supervision: Frank, Pawlik.

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