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Clinical Study

Effect of liberal blood transfusion on clinical outcomes and cost in spine surgery patients

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Abstract

BACKGROUND CONTEXT: Blood transfusions in spine surgery are shown to be associated with increased patient morbidity. The association between transfusion performed using a liberal hemoglobin (Hb) trigger—defined as an intraoperative Hb level of ≥10 g/dL, a postoperative level of ≥8 g/dL, or a whole hospital nadir between 8 and 10 g/dL—and perioperative morbidity and cost in spine surgery patients is unknown and thus was investigated in this study.
PURPOSE: This study aimed to describe the perioperative outcomes and economic cost associated with liberal Hb trigger transfusion among spine surgery patients.
STUDY DESIGN/SETTING: This is a retrospective study.
PATIENT SAMPLE: The surgical billing database at our institution was queried for inpatients discharged between 2008 and 2015 after the following procedures: atlantoaxial fusion, anterior cervical fusion, posterior cervical fusion, anterior lumbar fusion, posterior lumbar fusion, lateral lumbar fusion, other procedures, and tumor-related surgeries. In total, 6,931 patients were included for analysis.
OUTCOME MEASURES: The primary outcome was composite morbidity, which was composed of (1) infection (sepsis, surgical-site infection, *Clostridium difficile* infection, or drug-resistant infection); (2) thrombotic event (pulmonary embolus, deep venous thrombosis, or disseminated intravascular coagulation); (3) kidney injury; (4) respiratory event; and (5) ischemic event (transient ischemic attack, myocardial infarction, or cerebrovascular accident).
MATERIALS AND METHODS: Data on intraoperative transfusion were obtained from an automated, prospectively collected anesthesia data management system. Data on postoperative hospital transfusion were obtained through a Web-based intelligence portal. Based on previous research, we analyzed the data using three definitions of a liberal transfusion trigger in patients who underwent

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red blood cell transfusion: a liberal intraoperative Hb trigger as a nadir Hb level of 10 g/dL or greater, a liberal postoperative Hb trigger as a nadir Hb level of 8 g/dL or greater, or a whole hospital nadir Hb level of 8–10 g/dL. Variables analyzed included in-hospital morbidity, mortality, length of stay, and total costs associated with a liberal transfusion strategy.

RESULTS: Among patients with a whole hospital stay nadir Hb between 8 and 10 g/dL, transfused patients demonstrated a longer in-hospital stay (median [interquartile range], 6 [5–9] vs. 4 [3–6] days; p<.0001) and a higher perioperative morbidity (n=145 [11.5%] vs. n=74 [6.1%], p<.0001) than those not transfused. Even after adjusting for age, gender, race, American Society of Anesthesiologists class, Charlson Comorbidity Index score, estimated blood loss, baseline Hb value, and surgery type, logistic regression analysis revealed that patients with a nadir Hb of 8–10 g/dL who were transfused had an independently higher risk of perioperative morbidity (odds ratio=2.11, 95% confidence interval, 1.44-3.09; p<.0001). Estimated additional costs associated with liberal trigger use, defined as a transfusion occurring in patients with a whole hospital stay nadir Hb of 8–10 g/dL, ranged from $202,675 to $700,151 annually.

CONCLUSIONS: Transfusion using a liberal trigger is associated with increased morbidity, even after controlling for possible confounders. Our results suggest that modification of transfusion practice may be a potential area for improving patient outcomes and reducing costs. © 2017 Elsevier Inc. All rights reserved.

Keywords: Cost saving; Economic; Outcomes; Red blood cells; Surgery; Transfusion

Introduction

Blood loss is a major concern in spine surgery, with an estimated 8%–36% of patients requiring perioperative blood transfusions [1–5]. Blood transfusion promotes oxygen delivery and tissue perfusion during long, complex surgeries, yet carries with it rare but notable risks. Among these risks are acute lung injury, febrile reactions, allergic episodes, infection, and impaired immune response [6–18]. The hemoglobin (Hb) trigger—the Hb value that initiates clinician administration of packed red blood cells (PRBCs)—is frequently used to evaluate physician compliance with existing transfusion guidelines [19,20]. Randomized clinical trials have demonstrated similar or improved outcomes among patients undergoing blood transfusions using a restrictive Hb trigger—defined as an intraoperative Hb level of <10 g/dL, a postoperative Hb level of <8 g/dL, or a whole hospital stay nadir Hb of 8–10 g/dL—versus a liberal Hb trigger (≥10 g/dL intraoperatively or ≥8 g/dL postoperatively) in cardiac and hip surgery [21–24]. However, the association between transfusion performed using a liberal Hb trigger and perioperative morbidity in patients undergoing spine surgery is not known. In addition, estimation of the costs associated with different Hb triggers has not been previously investigated in patients undergoing spine surgery.

In terms of other non-spine surgical procedures, Ejaz et al. found that more than 1 in 10 patients undergoing hepatic, pancreatic, or colorectal resection were transfused under a liberal trigger, which was associated with worse patient outcomes and increased institutional cost compared with the restrictive trigger group [25]. To the authors' knowledge, no study has examined the associated morbidity and financial impact of liberal transfusions within spinal surgery. We thus aimed to determine the perioperative clinical outcomes and costs associated with liberal versus restrictive transfusion triggers among spine surgery patients.

Materials and methods

Collected data

The surgical billing database at our institution was queried for inpatients discharged following spinal surgery between 2008 and 2015, yielding 33,043 patients. Patients were stratified into eight groups according to the surgical procedure performed: atlantoaxial fusion, anterior cervical fusion, posterior cervical fusion, anterior lumbar fusion, posterior lumbar fusion, lateral lumbar fusion, other procedures, and tumor-related surgeries (Table 1). Following the exclusion of patients who underwent surgeries other than the abovementioned eight major groupings, 6,931 patients were included for analysis. The present study was approved by our Institutional Review Board (IRB# 00078426).

The surgical database provided data on basic patient characteristics, including the American Society of Anesthesiologists (ASA) status, the Charlson Comorbidity Index (CCI) score, and the total red blood cell (RBC) units given during the hospitalization. Procedure codes and perioperative morbidity data were identified using discharge *International Classification of Diseases, Ninth Revision* (ICD-9) codes. The primary outcome was composite morbidity, which was composed of (1) infection (sepsis, surgical-site infection, *Clostridium difficile* infection, or drug-resistant infection); (2) thrombotic event (pulmonary embolus, deep venous thrombosis, or disseminated intravascular coagulation); (3) kidney injury; (4) respiratory event; and (5) ischemic event (transient ischemic attack, myocardial infarction, or cerebrovascular accident) [26].

We considered only PRBC transfusion for the purposes of the present study. Data on intraoperative transfusion were

EVIDENCE & METHODS

Context

In this retrospective study, the authors assessed whether transfusions used "liberally" (for hemoglobins in the 8 to 10 range) were associated with increased morbidity following spine surgery.

Contribution

They found that morbidity rates were doubled when liberal transfusions were given while statistically controlling for other factors. They also found increased costs (the blood and transfusion process itself and, potentially more, if costs could be directly tied to complications of transfusion).

Implications

The findings suggest that careful consideration of potential risks and benefits should be given when giving transfusions to those without absolute indications.

obtained from an automated, prospectively collected anesthesia data management system (MetaVision; iMDsoft, Needham, MA, USA) [20]. Data on postoperative hospital transfusion were obtained through a Web-based intelligence portal (IMPACT Online; Haemonetics Corp., Braintree, MA, USA) [19]. We considered postoperative transfusions as those occurring during the hospitalization outside of the operating room.

Based on previous research, we analyzed the data using three definitions of a liberal transfusion trigger in patients who underwent an RBC transfusion:

1. a liberal intraoperative Hb trigger as a nadir Hb level of 10 g/dL or greater,
2. a liberal postoperative Hb trigger as a nadir Hb level of 8 g/dL or greater,
3. or a whole hospital nadir Hb level of 8–10 g/dL.

A restrictive Hb trigger was defined as follows:

1. a restrictive intraoperative Hb trigger as a nadir Hb level of less than 10 g/dL
2. or a restrictive postoperative Hb trigger as a nadir Hb level of less than 8 g/dL.

As shown in previous research [25], transfusions in patients with a whole hospital nadir Hb level of 8–10 g/dL can be considered liberal because this level of nadir Hb is in the intermediate zone where transfusions have been deemed to be unnecessary for some patients [25,27–29].

Cost analyses

We estimated the total cost of a unit of PRBCs using two figures from our previous work [25]. The values used were the reported institutional acquisition cost ($220/unit) and a mean estimated activity-based cost ($760/unit) based on a Society for the Advancement of Blood Management (SABM)

Table 1
List of surgical procedure groups included and corresponding subgroups identified by ICD-9 codes

Group number	Group name	Procedure name (ICD-9 code)
1	Atlantoaxial fusion	Atlas-axis spinal fusion (81.01)
		Refusion of atlas-axis spine (81.31)
2	Anterior cervical fusion	Other cervical fusion, anterior technique (81.02)
		Refusion of other cervical spine, anterior technique (81.32)
3	Posterior cervical fusion	Other cervical fusion, posterior technique (81.03)
		Refusion of other cervical spine, posterior technique (81.33)
4	Anterior lumbar fusion	Dorsal and dorsolumbar fusion, anterior technique (81.04)
		Refusion of dorsal and dorsolumbar spine, anterior technique (81.34)
		Refusion of lumbar and lumbosacral spine, anterior technique (81.36)
5	Posterior lumbar fusion	Dorsal and dorsolumbar fusion, posterior technique (81.05)
		Lumbar and lumbosacral fusion, anterior technique (81.06)
		Lumbar and lumbosacral fusion, lateral transverse process technique (81.07)
		Refusion of dorsal and dorsolumbar spine, posterior technique (81.35)
		Refusion of lumbar and lumbosacral spine, posterior technique (81.38)
6	Lateral lumbar fusion	Refusion of lumbar and lumbosacral spine, lateral transverse process technique (81.37)
7	Other procedures	Excision, destruction, and other repair of intervertebral disc (80.5)
		Division of intraspinal nerve root (03.1)
		Excision of intervertebral disc (80.51)
		Other partial ostectomy, other bones (77.89)
		Reopen laminectomy site (3.02)
		Lysis of adhesions of spinal cord and nerve roots (03.6)
		Spinal fusion, not otherwise specified (81.00)
8	Tumor-related surgeries	Excision of spinal cord lesion (3.4)
		Spinal cord or meninges biopsy (3.32)

ICD-9, *International Classification of Diseases, Ninth Revision*.

report [30]. The estimated activity-based cost incorporates all overhead costs associated with bringing one RBC unit from the donor to the recipient.

Statistical analyses

The statistical association of transfusion with age, preoperative Hb level, estimated blood loss (EBL), total crystalloid fluid use, CCI, ASA class, and length of stay (LOS) was tested using the Mann-Whitney *U* test, independent samples *t*-test, or the Kruskal-Wallis test. The association of transfusion with gender, race, surgery group, morbidity, and mortality was tested using the chi-square test. Logistic regression was used to test the effect of transfusion strategy on morbidity while controlling for the following potential confounding factors: age, gender, ASA class, surgery group, EBL, and baseline Hb level. Variables with a p value less than .1 in the univariate analyses were included in the multivariate logistic regression model. Results of the logistic regression analysis were presented as odds ratios (ORs) with 95% confidence intervals (CIs). All data were analyzed using SPSS 24 (IBM; SPSS Inc., Chicago, IL, USA). A p value of less than .05 was considered to be statistically significant.

Results

Patient characteristics

A total of 6,931 patients met the inclusion criteria. Between December 4, 2008, and June 26, 2015, these patients underwent atlantoaxial fusion (112 [1.6%]), anterior cervical fusion (1,264 [18.2%]), posterior cervical fusion (571 [8.2%]), anterior lumbar fusion (198 [2.9%]), posterior lumbar fusion (3,096 [44.7%]), lateral lumbar fusion (226 [3.3%]), other procedures (901 [13.0%]), and tumor-related surgeries (563 [8.1%]) (Table 2). Of our sample, 3,132 were men (45.2%) and the median age was 53 (interquartile range [IQR], 32–64 years). The majority of our patient population self-identified as white (n=5,111 [73.8%]). The median CCI score was 0 (IQR, 0–1) and 45.8% of patients were classified as ASA class 3 or 4 (n=2,583).

PRBC usage

A total of 2,374 patients underwent a PRBC transfusion (at least 1 unit of PRBCs), yielding an overall transfusion rate of 34.3%. Patients undergoing a PRBC transfusion were

Table 2
Demographic and surgical groupings for patients with or without transfusion

Patient characteristics	All (N=6,931)	No PRBC transfusion (N=4,557, 65.75%)	PRBC transfusion (N=2,374, 34.25%	p Value
Age (y), median (IQR)	53 (32–64)	50 (33–62)	57 (31–68)	<.0001
Male, n (%)	3,132 (45.2)	2,197 (48.2)	935 (39.4)	<.0001
White, n (%)	5,111 (73.8)	3,374 (74.1)	1,737 (73.2)	.44
ASA score, median (IQR)	2 (2–3)	2 (2–3)	3 (2–3)	<.0001
ASA class 3 or 4, n (%)	2,583 (45.8)	1,322 (35.7)	1,261 (65.1)	<.0001
ASA class 1, n (%)	268 (4.8)			
ASA class 2, n (%)	2,789 (49.5)			
ASA class 3, n (%)	2,463 (43.7)			
ASA class 4, n (%)	120 (2.1)			
CCI score, median (IQR)	0 (0–1)	0 (0–1)	1 (0–2)	<.0001
0–3, n (%)	6,434 (92.8)	4,386 (96.2)	2,048 (86.3)	<.0001
≥4, n (%)	497 (7.2)	171 (3.8)	326 (13.7)	
Procedure type				
Atlantoaxial	112 (1.6)	72 (1.6)	40 (1.7)	<.0001
Cervical spine (anterior technique)	1,264 (18.2)	1,215 (26.7)	49 (2.1)	
Cervical spine (posterior technique)	571 (8.2)	455 (10.0)	116 (4.9)	
Lumbar spine (anterior technique)	198 (2.9)	85 (1.9)	113 (4.8)	
Lumbar spine (posterior technique)	3,096 (44.7)	1,355 (29.7)	1,741 (73.3)	
Lumbar spine (lateral technique)	226 (3.3)	72 (1.6)	154 (6.5)	
Other	901 (13.0)	835 (18.3)	66 (2.8)	
Tumor	563 (8.1)	468 (10.3)	95 (4.0)	
Preoperative Hb level (g/dL), mean (SD)	12.760 (1.835)	12.993 (1.734)	12.324 (1.938)	<.0001
EBL (mL), median (IQR)	350 (100–800)	200 (100–400)	1,000 (600–1,700)	<.0001
Crystalloid fluids (mL), median (IQR)	3,700 (2,000–5,000)	3,000 (2,000–4,000)	5,000 (3,000–6,628.33)	<.0001
LOS (d), median (IQR)	4 (3–7)	3 (2–5)	7 (5–10)	<.0001
Complications, n (%)	478 (6.9)	154 (3.4)	324 (13.6)	<.0001
Infection	146 (2.1)	41 (0.9)	105 (4.4)	<.0001
Thrombotic event	176 (2.5)	50 (1.1)	126 (5.3)	<.0001
Kidney injury	117 (1.7)	49 (1.1)	68 (2.9)	<.0001
Respiratory event	78 (1.1)	22 (0.5)	56 (2.4)	<.0001
Ischemic event	34 (0.5)	4 (0.1)	30 (1.3)	<.0001
Death	16 (0.2)	2 (0.04)	14 (0.59)	<.0001

Hb, hemoglobin; PRBC, packed red blood cell; ASA, American Society of Anesthesiologists; CCI, Charlson Comorbidity Index; LOS, length of stay; IQR, interquartile range; SD, standard deviation; EBL, estimated blood loss.

generally older (median [IQR], 57 [31–68]) than those who did not undergo a transfusion (median [IQR], 50 [33–62] years; p<.0001). Transfused patients versus non-transfused patients had higher estimated operative blood loss (median [IQR], 1,000 [600–1,700] vs. 200 [100–400] mL; p<.0001), higher CCI scores (median [IQR], 1 [0–2] vs. 0 [0–1]; p<.0001), lower preoperative Hb levels (mean [SD], 12.3 [1.9] vs. 13.0 [1.7]; p<.0001), and increased volume of intraoperative crystalloid fluids (median [IQR], 5,000 [3,000–6,628] vs. 3,000 [2,000–4,000]; p<.0001).

During the study period, 10,309 total units of PRBCs were used (range, 1–56 units/patient). Most of the transfusions were postoperative (5,955 units total [57.76%]) with the remainder intraoperative (4,355 units total [42.2%]). For patients who underwent transfusions, most underwent PRBCs only during the postoperative period (n=1,009, 42.5%) or during both the intraoperative and postoperative periods (n=863, 36.4%). Fewer patients were given only intraoperative transfusions (n=502, 21.2%). The median number of PRBC units transfused during the intraoperative period was significantly higher (median [IQR], 3 [2–5]) than that during the postoperative period (median [IQR], 2 [1–3]; p<.0001). Compared with the other surgical groups, most PRBC use occurred within procedure Group 5 (Table 1; posterior lumbar fusion, ICD-9 codes 81.05, 81.06, 81.07, 81.35, and 81.38) (8,115 units [78.7%]).

At least one complication occurred in 478 patients, yielding an overall morbidity rate of 6.9% (Table 2). A total of 567 complications were reported. Transfused patients also demonstrated higher rates of morbidity (n=324 [13.6%]) versus non-transfused patients (n=154 [3.4%], p<.0001). Patients in procedure Group 5 had the highest incidence of perioperative complications (n=274, [57.3%]) among all eight surgery types (p<.0001). Within this procedure group, transfused patients demonstrated higher rates of morbidity (n=225 [12.9%]) versus non-transfused patients (n=49 [3.6%], p<.0001). The median LOS among all patients was 4 days (IQR, 3–7 days). Patients in procedure Group 4 (Table 1; anterior lumbar fusion, ICD-9 codes 81.04, 81.34, and 81.36) had the longest LOS (median [IQR], 6 [4–10] days; p<.0001).

Patients undergoing PRBC transfusion had a higher incidence of perioperative mortality (n=14 [0.59%]) compared with patients who were not transfused (n=2 [0.04%], p<.0001). There were significantly higher rates of perioperative morbidity for transfused patients in each of the five morbidity categories (p<.0001 for each category). Transfused patients had a longer LOS (median [IQR], 7 [5–10] days) than those who were not transfused (median [IQR], 3 [2–5] days; p<.0001). After adjusting for age, gender, ASA class, CCI score, EBL, baseline Hb value, and surgery type, logistic regression analysis revealed that patients transfused with PRBC had an independently higher risk of any perioperative morbidity (OR=2.54; 95% CI, 1.84-3.50; p<.0001), infection (OR=4.59; 95% CI, 2.58-8.19; p<.0001), thrombotic event (OR=2.03; 95% CI, 1.21-3.40; p=.007), and ischemic event (OR=14.53; 95% CI, 2.81-75.25; p=.001).

PRBC transfusions with a liberal trigger

The mean intraoperative Hb trigger was 10.1 (standard deviation [SD]=1.7) g/dL and the mean postoperative Hb trigger was 10.1 (SD=2.1) g/dL. For the 2,374 patients who were transfused with PRBCs, 1,420 (59.8%) underwent a postoperative PRBC transfusion with a liberal postoperative Hb trigger (≥8 g/dL), whereas 529 (22.3%) underwent an intraoperative PRBC transfusion with a liberal intraoperative Hb trigger (≥10 g/dL). In total, potentially 6,047 units of PRBCs were given using a liberal Hb trigger (defined here as Hb≥10 g/dL intraoperatively or ≥8 g/dL postoperatively) (58.7% of all PRBCs given). Patients in procedure Group 5 had the highest likelihood of being transfused with a liberal Hb trigger among all surgical groups (n=1,105 [53.7%]; p<.0001).

Patients with a whole hospital stay nadir Hb between 8 and 10 g/dL were then considered separately (Table 3). A total of 1,258 patients with a nadir whole hospital Hb between 8 and 10 g/dL underwent a PRBC transfusion (at least 1 unit of PRBCs), yielding an overall transfusion rate of 50.9%. Patients undergoing a PRBC transfusion were generally older (median [IQR], 60 [47–69]) than those who did not undergo a transfusion (median [IQR], 51 [16–64] years; p<.0001). Transfused patients versus non-transfused patients also had higher estimated operative blood loss (median [IQR], 1,000 [600–1,500] vs. 350 [200–600] mL; p<.0001), higher CCI scores (median [IQR], 1 [0–2] vs. 0 [0–1]; p<.0001), higher preoperative Hb levels (mean [SD], 12.303 [1.879] vs. 12.046 [1.754]; p<.0001), and increased use of intraoperative crystalloid fluids (median [IQR], 5,000 [3,000–6,500] vs. 3,570 [2,011–4,900]; p<.0001).

For patients with a whole hospital stay nadir Hb between 8 and 10 g/dL (n=2,470), at least one complication occurred in 219 patients, yielding an overall morbidity rate of 8.9% (Table 3). Of these patients, 50.9% (n=1,258) were transfused. Transfused patients had a significantly higher occurrence of at least one complication (n=145 [11.5% or 145/1,258]) than those not transfused (n=74 [6.1% or 74/1,212]; p<.0001). The median LOS among all patients with a nadir Hb between 8 and 10 g/dL was 5 days (IQR, 4–8 days). Moreover, patients who had a transfusion were noted to have had a longer median LOS (median [IQR], 6 [5–9] days) versus patients who did not have a transfusion (median [IQR], 4 [3–6]; p<.0001). After adjusting for age, gender, race (white versus non-white), ASA class, CCI score, EBL, baseline Hb value, and surgery type, logistic regression analysis revealed that patients with a nadir Hb of 8–10 g/dL transfused with PRBC had an independently higher risk of perioperative morbidity (OR=2.11; 95% CI, 1.44-3.09; p<.0001).

Economic outcomes

Using the hospital's reported PRBC acquisition costs ($220/unit) and the mean estimated activity-based cost ($760/unit) described previously [30], we can estimate the total costs of PRBC transfusion during this time period of approximately 6.6

Table 3
Demographic and surgical groupings for patients with a whole hospital nadir Hb between 8 and 10 g/dL with or without transfusion

Patient characteristics	All (N=2470)	No PRBC transfusion (N=1,212, 49.1%)	PRBC transfusion (N=1,258, 50.9%)	p Value
Age (y), median (IQR)	56 (32–67)	51 (16–64)	60 (47–69)	<.0001
Male, n (%)	874 (35.4)	372 (30.7)	502 (39.9)	<.0001
White, n (%)	1781 (72.1)	852 (70.3)	329 (73.8)	.049
ASA score, median (IQR)	3 (2–3)	2 (2–3)	3 (2–3)	<.0001
ASA class 3 or 4, n (%)	1,066 (52.8)	405 (41.3)	661 (63.6)	<.0001
ASA class 1, n (%)	73 (3.6)			
ASA class 2, n (%)	880 (43.6)			
ASA class 3, n (%)	1,007 (49.9)			
ASA class 4, n (%)	59 (2.9)			
CCI score, median (IQR)	1 (0–2)	0 (0–1)	1 (0–2)	<.0001
0–3, n (%)	2,215 (89.7)	1,137 (93.8)	1,078 (85.7)	<.0001
≥4, n (%)	255 (10.3)	75 (6.2)	180 (14.3)	
Procedure type, n (%)				
Atlantoaxial	54 (2.2)	33 (2.7)	21 (1.7)	<.0001
Cervical spine (anterior technique)	125 (5.1)	93 (7.7)	32 (2.5)	
Cervical spine (posterior technique)	189 (7.7)	127 (10.5)	62 (4.9)	
Lumbar spine (anterior technique)	129 (5.2)	45 (3.7)	84 (6.7)	
Lumbar spine (posterior technique)	1,574 (63.7)	681 (56.2)	893 (71.0)	
Lumbar spine (lateral technique)	131 (5.3)	41 (3.4)	90 (7.2)	
Other	127 (5.1)	99 (8.2)	28 (2.2)	
Tumor	141 (5.7)	93 (7.7)	48 (3.8)	
Preoperative Hb level (g/dL), mean (SD)	12.177 (1.823)	12.046 (1.754)	12.303 (1.879)	<.0001
EBL (mL), median (IQR)	600 (300–1100)	350 (200–600)	1,000 (600–1500)	<.0001
Crystalloid fluids (mL), median (IQR)	4,000 (2,500–5,700)	3,570 (2,011.29–4,900)	5,000 (3,000–6,500)	<.0001
LOS (d), median (IQR)	5 (4–8)	4 (3–6)	6 (5–9)	<.0001
Complications, n (%)	219 (8.9)	74 (6.1)	145 (11.5)	<.0001
Infection	59 (2.4)	24 (2.0)	35 (2.8)	.192
Thrombotic event	85 (3.4)	23 (1.9)	62 (4.9)	<.0001
Kidney injury	54 (2.2)	20 (1.7)	34 (2.7)	.074
Respiratory event	41 (1.7)	12 (1.0)	29 (2.3)	.011
Ischemic event	14 (0.6)	2 (0.2)	12 (1.0)	.009
Death	5 (0.2)	0 (0.0)	5 (0.4)	

Hb, hemoglobin; PRBC, packed red blood cells; ASA, American Society of Anesthesiologists; CCI, Charlson Comorbidity Index; EBL, estimated blood loss; LOS, length of stay; IQR, interquartile range; SD, standard deviation.

Transfusions that occurred in patients with a whole hospital nadir Hb of 8–10 g/dL were considered liberal.

years as between $2,268,079 and $7,835,182 (calculated from the total number of units given in both the restrictive and liberal transfusion groups). A liberal transfusion is defined here as occurring in transfused patients with a whole hospital stay nadir Hb of 8–10 g/dL. PRBC units transfused under a liberal transfusion strategy (6,047 units over all years) varied by surgery type (Table 4). Over all 6.6 years, the total cost associated with liberal transfusion was between $1,330,439 and $4,596,062, with the cost varying by surgery type (Figure, Top). This estimates to $202,675–$700,151 in institutional costs incurred

Table 4
Total PRBC units transfused using a liberal Hb trigger and estimated additional institutional cost by surgery group

Group number	Units of PRBC using liberal Hb trigger (total=6,047), n (%)	Low estimated excess cost (US$220/unit)	High estimated excess cost (US$760/unit)	p Value
1. Atlantoaxial	71 (1.2)	15,620	53,960	<.0001
2. Cervical spine (anterior technique)	77 (1.3)	16,940	58,520	
3. Cervical spine (posterior technique)	169 (2.79)	37,180	128,440	
4. Lumbar spine (anterior technique)	389 (6.43)	85,580	295,640	
5. Lumbar spine (posterior technique)	4,578.45 (75.71)	1,007,259	3,479,622	
6. Lumbar spine (lateral technique)	388 (6.42)	85,360	294,880	
7. Other	160 (2.65)	35,200	121,600	
8. Tumor	215 (3.56)	47,300	163,400	
Total		1,330,439	4,596,062	

PRBC, packed red blood cells; Hb, hemoglobin.

Transfusions that occurred in patients with a whole hospital nadir Hb of 8–10 g/dL were considered liberal.

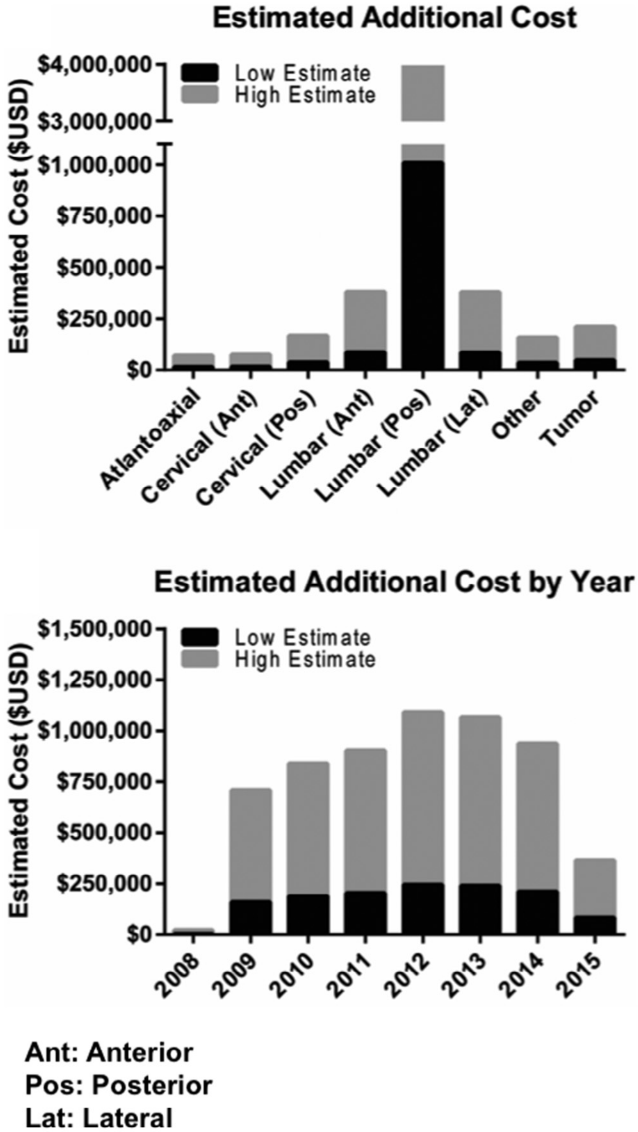

Figure. Estimated additional cost associated with liberal transfusion trigger use (transfusions occurring in patients with a whole hospital nadir hemoglobin of 8–10 g/dL) varies by surgery group (Top) and by year (Bottom).

per year among patients undergoing spine surgery (Table 5) with no consistent trend in costs by year (Figure, Bottom).

Discussion

Our analysis revealed that a majority of spine surgery patients were transfused under a liberal transfusion strategy. Patients with a nadir Hb of 8–10 g/dL who were transfused had higher perioperative morbidity, even after adjusting for potential confounders. The estimated annual cost incurred from liberal transfusion trigger reliance ranged from an estimated $202,675 to $700,151 annually.

Our findings of worse perioperative outcomes associated with PRBC use in patients with a nadir Hb of 8–10 g/dL reflect similar findings in other surgical fields [21–24]. Ejaz et al. found that patients with a nadir Hb of 8–10 g/dL undergoing colorectal, pancreatic, or liver resection who underwent a PRBC transfusion had a significantly higher LOS and overall in-hospital morbidity than those patients who were not transfused [25]. Other spine studies raised awareness about the potential negative postoperative outcomes associated with transfusion in general but did not consider liberal versus restrictive trigger outcomes separately [31–33]. As Frank et al. proposed, consideration of transfusion Hb triggers and targets may prove to be the most reliable method to evaluate the morbidity associated with perioperative transfusions [19].

Our estimated range of the costs associated with liberal trigger transfusion relied on the reported institutional acquisition cost ($220/unit) and an approximate activity-based cost ($760/unit) proposed by the SABM [30]. Unlike the simple acquisition cost, the $760/unit estimate includes all overhead costs associated with bringing one RBC unit from the donor to the recipient. Blanchette et al. used similar estimates when calculating the cost of transfusion associated with spinal fusion. Blanchette et al.'s database relied on total cost—defined as the sum of direct costs and overhead costs—for which a per-unit figure is unfortunately unavailable [34]. However, as Ejaz et al. have described, even the upper SABM value we cited may underestimate the total costs associated

Table 5
Estimated additional costs caused by liberal PRBC transfusion, by year

Year	Units of PRBC using liberal Hb trigger (total=6,047), n (%)	Low estimated excess cost (US$220/unit)	High estimated excess cost (US$760/unit)
2008 (December 4 to year end)	22.0 (0.36)	4,840	16,720
2009	722.0 (11.94)	158,840	548,720
2010	855.0 (14.14)	188,100	649,800
2011	921.0 (15.23)	202,620	699,960
2012	1113.0 (18.40)	244,860	845,880
2013	1088.5 (18.00)	239,459	827,222
2014	955.0 (15.79)	210,100	725,800
2015 (until June 26)	371.0 (6.13)	81,620	281,960

PRBC, packed red blood cells; Hb, hemoglobin.
Transfusions that occurred in patients with a whole hospital nadir Hb of 8–10 g/dL were considered liberal.

with transfusing a unit of PRBCs [25]. Consider, for example, the medical costs incurred with increased complications following transfusion. Fischer et al. estimated an added cost of $1,500 per unit of blood transfused during breast reconstruction, most likely because of these associated morbidities [35]. We recognize that the true cost of transfusions using a liberal trigger may be higher than the estimates provided here.

The limitations of the present study should be considered when interpreting our findings. Although our study was strengthened by a large sample size, we were limited to a convenience sample of patients presenting to an isolated tertiary care center. Future multicenter studies are necessary to obtain more nationally representative data on spine surgery patients. We recognize that transfusion in patients with a most recent Hb between 8 and 10 g/dL is often appropriate for patients who are actively bleeding. However, to account for active bleeding as a potential confounder, we included the EBL and the type of surgery in the multivariable analysis, and liberal transfusion remained independently associated with increased morbidity. Furthermore, the databases used relied on appropriate and consistent coding of diagnoses, procedures, and complications developed among patients. One additional limitation is that the morbidities patients developed in the hospital could have happened at any point during their stay, such that we were unable to confirm if the transfusion occurred before the complication [26]. This brings us to a larger point of caution, which is that our findings only demonstrate correlation that is not sufficient to prove causation. Prospective studies are needed to more adequately test the relationships among PRBC transfusion, liberal Hb triggers, and clinical outcomes within spine surgery patients.

In conclusion, although transfusion is common within spinal surgery, little data exist that investigate the clinical and economic outcomes associated with a liberal transfusion strategy. Patients undergoing spine surgery with a whole hospital nadir Hb between 8 and 10 g/dL who underwent PRBC transfusions had higher overall morbidity and a longer LOS versus patients who were not transfused. The cost associated with liberal transfusion was substantial. These findings point to a potential area for clinicians and institutions to improve patient outcomes and reduce costs.

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