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Blood transfusions in colorectal cancer surgery: incidence, outcomes, and predictive factors: an American College of Surgeons National Surgical Quality Improvement Program Analysis

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Abstract

BACKGROUND: Data analyzing the short-term outcomes and predictors of blood transfusions (BTs) in colorectal cancer (CRC) surgery are limited.

METHODS: The American College of Surgeons National Surgical Quality Improvement Program (2005 to 2010) was retrospectively reviewed for CRC cases performed with or without BT. Patient demographics, comorbidities, and operative variables were analyzed. Multivariate regression analysis was performed examining the effect of BT on outcomes. The LASSO algorithm for logistic regression was used to build a predictive model for BT taking into account preoperative and operative variables.

RESULTS: A total of 27,120 patients underwent CRC, and 3,815 (14.07%) had BTs. Transfusions were associated with increased mortality (odds ratio [OR], 1.78), morbidity (OR, 2.38), length of stay (mean difference, 3.52 days), pneumonia (OR, 2.70), and surgical-site infection (OR, 1.45). This effect was ‘‘dose dependent,’’ as patients receiving $\geq$ 3 U of blood had increased morbidity (OR, 1.53), lengths of stay (mean difference, 1.82 days), pneumonia (OR, 2.52), and surgical-site infections (OR, 1.60) compared with those receiving 1 to 2 U. Predictors of BT were hematocrit < 38%, open surgery, proctectomy, low platelet count, American Society of Anesthesiologists class IV or V, total colectomy, metastatic cancer, emergency, ascites, and infection. All P values were < .05.

CONCLUSIONS: BTs are associated with worse short-term outcomes after CRC surgery. Knowledge of predictive factors will help in risk stratification and counseling.

According to the *National Blood Collection and Utilization Survey Report*, > 15 million units of blood were transfused in the United States in 2008, 11.1% of which were

during general surgical procedures.1 Colorectal cancer resections account for a significant number of general surgical procedures[2] and are well known for their blood transfusions requirements. Earlier series from the 1980s reported blood transfusion rates of 39% to 74%3–5 in colorectal cancer surgery, while more recent studies have reported rates between 20% and 28%.[6–8]

Although there is extensive data regarding the detrimental effects of blood transfusions on disease-free and overall survival after colorectal cancer,[9–13] it is interesting to note that only a few studies have examined the effects of blood transfusions on short-term outcomes after colorectal cancer resections. Most of these studies have shown that blood transfusions were associated with higher infection rates, prolonged ventilator assistance, longer lengths of stay, increased mortality, and increased morbidity.[4,11,14–21] However, most of these reports are older and represent single-institution studies. Therefore they are either limited by small sample sizes or have failed to account for the increased adoption of laparoscopy, which has gained widespread acceptance in colorectal surgery.[22] The other question that previous studies have failed to address is related to preoperative anemia, which was previously regarded as an innocent bystander but has been recently shown to independently increase 30-day mortality and morbidity in surgical patients.[23] Thus, it remains unclear which factor has a more significant effect on outcomes: blood transfusions or anemia.[24] Therefore, it becomes important to analyze the effects of blood transfusions and anemia on short-term outcomes.

Moreover, because blood transfusions affect short-term and long-term outcomes, knowledge of the risk factors for blood transfusions would be a valuable tool for clinicians to identify patients at risk and implement strategies to reduce transfusion requirements. These risk factors have been examined in smaller series with some discrepancies.[7,21,25] To date, there is no predictive model or nomogram evaluating the requirement for perioperative blood transfusions in patients with colorectal cancer.

Using the power of a large, validated database, our aims were to (1) examine recent rates of perioperative blood transfusions in colorectal cancer surgery; (2) assess short-term outcomes associated with perioperative blood and preoperative anemia; and (3) build a predictive model for blood transfusions taking into account all available preoperative and operative variables.

Methods

Patient population

The American College of Surgeons National Surgical Quality Improvement Program (NSQIP) was retrospectively reviewed for all patients with colon and rectal cancer who underwent resection between January 1, 2005, and December 31, 2010. NSQIP is the first nationally validated, risk-adjusted, outcomes-based program to measure and improve the quality of surgical care. Data are collected from > 500 participating hospitals by dedicated surgical clinical nurse reviewers using a variety of methods, including medical chart abstraction. A full description of the NSQIP is available on its Web site.[26] Approval for the use of the NSQIP database for this study was obtained

from the institutional review board of the University of California, Irvine, and from NSQIP.

Case selection

Case selection was based on a combination of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic codes and Current Procedural Terminology (CPT) codes. All patients with ICD-9-CM codes for colon cancer (codes 153.0 to 153.9) who underwent elective or emergent, open or laparoscopic, partial or total colon resections (CPT codes 44204–44208, 44210–44212, 44141–44147, 44150, 44151, 44155–44158, and 44160) were included in the analysis. Similarly, patients with rectal cancer (ICD-9-CM codes 154.1, 154.2, and 154.8) who underwent open or laparoscopic proctectomy (CPT codes 45110–45114, 45119–45121, 45123, 45395, and 45397) were included in the analysis. Patients who underwent perioperative blood transfusions were identified using the following variables provided by NSQIP: (1) preoperative transfusion of packed red blood cells during the 72 hours before surgery, including any blood transfused in the emergency room; (2) intraoperative blood transfusion as it appears on the anesthesia record; and (3) postoperative transfusion of packed red blood cells given from the time the patient leaves the operating room up to and including 72 hours postoperatively. Patients were divided into 2 groups: the no-transfusion group and the transfusion group.

Study variables

The independent variables used in our study are provided by the NSQIP database and include patient demographics, American Society of Anesthesiologists (ASA) class, comorbid conditions, preoperative laboratory tests, and operative variables such as emergency designation of the procedure, tumor location (colon vs rectal), surgery type (partial vs total colectomy vs proctectomy), procedure type (laparoscopic vs open), resident involvement in the case categorized into postgraduate year, wound classification, anesthesia time, and operation time.

Study end points

The primary end points of our study were chosen a priori and include 30-day mortality, 30-daymorbidity, length of stay, any surgical-site infections (SSIs), and pneumonia. These end points were studied on multivariate regression analysis. Prediction model Using preoperative and operative variables provided by NSQIP as well as ICD-9-CM and CPT codes for colon and rectal cancer, we built a predictive model for perioperative blood transfusion.

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Statistical analysis

Data extraction and statistical analyses were performed using SAS version 9.3 (SAS Institute Inc, Cary, NC) and the R statistical environment (R Foundation for Statistical Computing, Vienna, Austria). Chi-square and *t* tests were used for univariate analysis as appropriate. Multivariate logistic and linear regression analyses were performed to examine the following: (1) the effect of any blood transfusion on outcomes (transfusion group vs no-transfusion group [the reference group]); (2) the effect of anemia (defined by preoperative hematocrit , 38%) on outcomes in patients who were not transfused; (3) the effect of blood transfusions on outcomes in patients with hematocrit ,38%; and (4) the effect of transfusions of $\geq$ 3 U of packed red blood cells compared with 1 to 2 U.

The following variables were adjusted for all the end points analyzed: age, gender, ASA class, preoperative hematocrit ,38%, cancer location (colon vs rectum), surgery type (partial colectomy vs total colectomy vs proctectomy), procedure type (laparoscopic vs open), and admission type (elective vs emergent). For the pneumonia analysis, in addition to the variables accounted for, we added ventilator dependence before surgery, chronic obstructive pulmonary disease, smoking, and the presence of pneumonia before surgery. For the SSI analysis, we also adjusted for wound classification, diabetes, smoking, obesity, preoperative chemotherapy, and radiotherapy. All of our results were adjusted for the effect of multiple comparisons using Holm's method. Statistical significance was declared for $P < .05$.

In the second part of the analysis, the LASSO algorithm for logistic regression[27] was used to identify predictive variables for perioperative blood transfusion. Variables with .7% of missing data were excluded. This led to the exclusion of the following variables: race, aspartate aminotransferase level, bilirubin, alkaline phosphatase, albumin, prothrombin time, partial thromboplastin time, and international normalized ratios. Exclusion of these variables led to a complete case analysis of 84% of cases. Included cases were split into 2 sets: a training data set (75%) and a validation data set (25%). The LASSO algorithm was used to select variables from the training data set, and 10-fold cross-validation along with the 1-SE rule was used on the validation set to select model size and control for overfitting. [28] Receiver operating characteristic curve analysis with calculation of the area under the curve was used on the validation set to summarize how well the model predicted perioperative transfusion. In contrast to the classic multivariate logistic regression, in which odds ratios are independent of each other and cannot be added together to predict perioperative transfusions, the LASSO assigns a coefficient to each variable. If the coefficient is positive, it is predictive of the end point analyzed. Factors with negative coefficients are protective. The degree of positivity or negativity is proportional to the effect the variable has on the end point under question. The LASSO algorithm also provides odds ratios that are statistically significant. Variables not selected by the LASSO algorithm are unlikely to predict the analyzed end point.

Results

A total of 27,120 patients underwent surgery for colorectal cancer over the study period. Perioperative blood transfusions were required in 3,815 patients (14.07%).

Patients in the transfusion group had a mean age of 69 years, compared with 67 years in the nontransfused group (P < .01). Patients' comorbidities and use of other therapies (steroids, chemotherapy, and radiotherapy) are listed in Table 1. Patients in the transfused group were more likely to have an ASA class of III or IV (P < .01). The incidences of most comorbidities and other therapies were higher in the transfused group, with minor exceptions such as cerebrovascular accident without neurologic deficit, quadriplegia, smoking history, rest pain or gangrene, and obesity.

Table 1 Comparison of patients' characteristics and comorbid conditions in patients who were transfused and those who were not

Age (y)	67 (57–78)	69 (60–80)	<.01
Women	49.08	50.25	.18
ASA class			
I	2.45%	.76%	<.01
II	45.12%	22.49%	<.01
III	47.31%	63.25%	<.01
IV	5.01%	12.92%	<.01
V	.04%	.50%	<.01
TIA	3.37%	3.93%	.09
CVA with neurologic deficit	2.68%	4.74%	<.01
CVA without neurologic deficit	2.58%	3.20%	.03
Hemiplegia	1.07%	1.94%	<.01
Paraplegia	.29%	.58%	<.01
Quadriplegia	.05%	.13%	.14
Current smoker	15.16%	14.02%	.07
Dyspnea	12.87%	20.21%	<.01
COPD	5.72%	7.60%	<.01
Pneumonia	.28%	.68%	<.01
Ventilator dependent	.10%	.60%	<.01
Hypertension	54.84%	62.02	<.01
Angina (past 30 d)	.77%	1.31%	<.01
Myocardial infarction (past 6 mo)	.76%	1.68%	<.01
Previous PCI	6.46%	8.83%	<.01
Previous cardiac surgery	6.37%	9.72%	<.01
CHF (past 30 d)	1.09%	3.01%	<.01
Peripheral vascular disease	1.29%	2.39%	<.01
Rest pain/gangrene	.14%	.10%	.74
Acute renal failure	.15%	.73%	<.01
ESRD on dialysis	.49%	.87%	<.01
Obesity	30.11%	29.67%	.93
Diabetes	16.60%	22.91%	<.01
Weight loss (past 6 mo)	6.08%	12.90%	<.01
Ascites	1.24%	3.46%	<.01
Bleeding disorder	3.85%	8.31%	<.01
Steroid use	2.32%	3.17%	<.01
Metastatic cancer	6.93%	12.90%	<.01
Chemotherapy (past 30 d)	2.36%	4.40%	<.01
Radiotherapy (past 90 d)	9.50%	11.48%	<.01
SIRS	3.03%	7.18%	<.01
Sepsis	.57%	2.67%	<.01
Septic shock	.15%	.92%	<.01
Prior operation (past 30 d)	1.11%	2.41%	<.01

Continuous variables are expressed as mean (interquartile range) and categorical variables as proportions.

ASA = American Society of Anesthesiologists; CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; CVA = cerebrovascular accident; ESRD = end-stage renal disease; PCI = percutaneous coronary intervention; SIRS = systemic inflammatory response syndrome; TIA = transient ischemic attack.

Table 2 lists the preoperative laboratory tests in each group. Percentages are based on available data for each test. Abnormal test results were found at higher percentages in the transfused group. Of special interest is that 52% of patients who were not transfused were anemic (hematocrit ,38%), compared with 85% in the transfused group ($P < .01$).

Table 2 Comparison of preoperative laboratory variables between patients who were transfused and those who were not

Variable	No transfusion	Transfusion	*P*
Sodium > 145 mEg/L	1.33%	1.79%	.03
Sodium < 135 mEg/L	6.38%	10.93%	<.01
BUN > 40 mg/dL	1.28%	3.20%	<.01
Creatinine > 1.2 mg/dL	13.62%	19.25%	<.01
Albumin < 3.5 g/dL	25.32%	50.87%	<.01
Bilirubin > 1.1 mg/dL	6.20%	8.35%	<.01
Serum AST > 40 U/L	6.92%	10.24%	<.01
Alkaline phosphatase > 125 mg/dL	8.40%	13.71%	<.01
WBC count > 11,000/mm^3	8.22%	14.04%	<.01
WBC count < 4,000/mm^3	5.46%	7.25%	<.01
Hematocrit < 38%	52.47%	85.86%	<.01
Platelet count < 150,000/mm^3	4.56%	8.74%	<.01
PT > 13 s	43.24%	53.20%	<.01
PTT > 35 s	8.69%	15.02%	<.01
INR > 1.5	1.92%	3.76%	<.01

Percentages were calculated from available data.
AST = aspartate aminotransferase; BUN = blood urea nitrogen; INR = international normalized ratio; PT = prothrombin time; PTT = partial thromboplastin time; WBC = white blood cell.

Table 3 compares operative variables between transfused and nontransfused patients. Patients in the transfused group were more likely to undergo emergency surgery. There were 20,074 colon cancer operations and 7,046 rectal cancer operations. Blood transfusions were required in 16.18% of patients with rectal cancer and 13.32% of those with colon cancer ($P < .01$). Laparoscopic cases were associated with lower transfusion requirements compared with open cases (7.47% vs 17.22%, $P < .01$). Among olectomies, the requirement for blood transfusion was higher for total compared with partial colectomies (20.36% vs 12.82%, $P < .01$). There was also a higher percentage of 3rd-year, 4th-year, and 5th-year resident involvement in transfused cases compared with nontransfused cases. Both anesthesia and operative times were longer in the transfused group ($P < .01$).

Table 3 Comparison of operative variables between patients who were transfused and those who were not

Variable	No transfusion (n = 23,305)	Transfusion (n = 3,815)	*P*
Emergency case	4.03%	8.81%	<.01
Disease			
Colon cancer	74.66%	70.12%	<.01
Rectal cancer	25.34%	29.88%	<.01
Procedure			
Partial colectomy, open	52.21%	60.87%	<.01
Partial colectomy, laparoscopic	32.39%	15.10%	<.01
Total colectomy, open	2.72%	5.06%	<.01
Total colectomy, laparoscopic	.88%	.55%	.05
Proctectomy, open	10.21%	16.88%	<.01
Proctectomy, laparoscopic	1.60%	1.55%	.86
Resident involvement			
No residents	33.13%	27.92%	<.01
PGY 1 or 2	5.00%	4.88%	.77
PGY 3–5	49.38%	53.45%	<.01
PGY ≥ 6	11.09%	12.58%	<.01
Wound classification			
Clean	.05%	.26%	<.01
Clean/contaminated	91.87%	82.04%	<.01
Contaminated	5.72%	10.35%	<.01
Dirty/infected	2.36%	7.34%	<.01
Anesthesia time (min)	224 (159–270)	293 (190–359)	<.01
Operation time (min)	163 (105–203)	221 (127–278)	<.01

Continuous variables are reported as mean (interquartile range) and categorical variables as percentages.
PGY = postgraduate year.

Table 4 lists the unadjusted outcomes in the 2 groups. All outcomes were significantly worse in transfused patients.

Table 5 lists risk-adjusted analysis for the selected end points. We found that blood transfusions increased the odds of mortality, morbidity, pneumonia, and SSI. Length of stay was also increased by 2.70 days. Analyzing the effect of additional blood units received (≥ 3 vs 1–2 U), we found that transfusion of ≥ 3 U was associated with increased morbidity, length of stay, pneumonia, and SSI. No association was found with mortality. To examine the independent effect of anemia on outcomes (in patients who were not transfused), we performed a risk-adjusted subgroup analysis on patients with hematocrit < 38%. We found that preoperative anemia was independently associated with increased mortality, morbidity, length of stay, and pneumonia. However, no association was found between anemia and SSI. In another subgroup analysis, we analyzed the effect of blood transfusions on outcomes in patients with preoperative anemia. The odds of morbidity were reduced by 30%, but no association was found for mortality, length of stay, pneumonia, or SSI.

Table 5 Multivariate regression analysis of the effects of anemia and perioperative blood transfusions on selected postoperative
outcomes

Variable	Adjusted OR/MD (95% CI)	*P*
Effect of blood transfusions on outcomes in all patients		
Mortality	1.78 (1.01, 3.15)	.05
Morbidity	2.38 (1.98, 2.87)	<.001
Length of stay	3.52 (2.68, 4.35)	<.001
Pneumonia	2.70 (1.84, 3.97)	<.001
SSI	1.45 (1.16, 1.81)	.004
Effect of additional blood transfusions (≥3 vs 1–2 U)		
Mortality	1.79 (.61, 5.28)	.29
Morbidity	1.53 (1.08, 2.18)	.03
Length of stay	1.82 (.19, 3.45)	.03
Pneumonia	2.52 (1.19, 5.37)	.02
SSI	1.60 (1.04, 2.47)	.03
Effect of anemia on outcomes in patients who were not transfused		
Mortality	1.56 (1.25, 1.95)	<.001
Morbidity	1.11 (1.03, 1.18)	<.01
Length of stay	1.55 (1.20, 1.90)	<.001
Pneumonia	1.25 (1.06, 1.49)	<.01
SSI	.96 (.88, 1.05)	1
Effect of blood transfusions in patients with hematocrit <38%		
Mortality	.99 (.54, 1.88)	1
Morbidity	.70 (.57, .85)	<.001
Length of stay	−.83 (−1.81, .16)	1
Pneumonia	1.66 (.66, 4.20)	.25
SSI	1.08 (.98, 1.19)	.20

CI = confidence interval; MD = mean difference; OR = odds ratio; SSI = surgical-site infection.

The LASSO algorithm for logistic regression found the following predictors of blood transfusion, listed in Table 6. The coefficients can be added together to calculate the predicted outcome for each individual. For a coefficient total of x, the risk for perioperative blood transfusion can be predicted using the following formula: $e^x/(1 + e^x)$. The discriminative power of our predictive model was good, with an area under the receiver operating characteristic curve of .79. Of note is that age, gender, smoking, and any of the heart disease variables did not appear to predict requirement for transfusion. Applying the formula to 2 hypothetical clinical scenarios, we found the following: (1) In the high-risk scenario (coefficients are listed in parentheses), a patient with anemia (1.29), dyspnea, metastatic (.18) rectal cancer (.21), and an ASA class of IV (.32) undergoes an emergent (.15), open (.62) proctectomy (.44) for rectal cancer (.21), and the case is considered dirty or infected (.08); this patient's coefficient is 3.5. The intercept (23.12) is added to 3.5, and the x coefficient is now .38. Using the above formula, the risk for requiring a blood transfusion is calculated as 59.39%. (2) In the low-risk scenario, an elective (0), clean-contaminated (2.45), laparoscopic (0), partial (0) colon resection (0) in a patient in ASA class II (2.46) without anemia (0) has a blood transfusion risk of 1.75%.

Table 6 Prediction model for perioperative blood transfusion based on the LASSO algorithm for logistic regression

Variable	Coefficient	LASSO OR
Intercept	−3.12	.04
Predictive factors		
Hematocrit < 38%	1.29	3.64
ASA class V	.83	2.28
Open surgery	.62	1.85
Proctectomy	.44	1.56
ASA class IV	.32	1.38
Weight loss	.22	1.25
Ascites	.21	1.23
Rectal cancer	.21	1.23
Total colectomy	.20	1.22
SIRS	.19	1.21
Metastatic cancer	.18	1.20
Platelet count < 150,000/mm^3	.18	1.20
Sepsis	.16	1.18
Emergency	.15	1.16
Bleeding disorder	.14	1.15
Dirty/infected case	.08	1.09
Surgery day 2 or 3	.08	1.09
Surgery day 4 or 5	.02	1.02
PGY 3–5 resident participation	.02	1.02
Diabetes	.01	1.01
Protective factors		
No dyspnea	−.08	.92
Clean-contaminated case	−.45	.64
ASA class II	−.46	.63

ASA = American Society of Anesthesiologists; OR = odds ratio; PGY = postgraduate year; SIRS = systemic inflammatory response syndrome.

Comments

Perioperative blood transfusions in colorectal cancer surgery occurred in 14% of cases in NSQIP hospitals. This rate appears lower than in previous series and could possibly be explained by the higher use of laparoscopy in more recent years. Our data show that the use of laparoscopy accounted for 32.38% of all procedures and that open cases have 1.85 increased odds of requiring blood transfusions. The other possible explanation could be related to the growing evidence about the negative effect of blood transfusions on cancer-free and overall survival after colorectal cancer surgery.[12] This may lead some surgeons to have a higher threshold for blood transfusions. These explanations remain tentative, however.

Consistent with previous studies demonstrating higher rates of postoperative infections,[4,14–17,27] longer lengths of stay,[21] and higher overall morbidity[6,11] and mortality,[21] our study provides additional evidence that blood transfusions may have detrimental short-term effects. The effect of blood transfusions on SSI appears to be related to the state of immunosuppression it induces, an effect recognized since the

early 1970s.[28] Blood transfusions may lead to increased levels of interleukin-2 and interleukin-6, an enhanced immunosuppressive acidic protein response, and a decrease in lymphocyte proliferation.[14,29] In addition to its short-term implications, immunosuppression caused by blood transfusions carries negative long-term consequences, such as reduced cancer-free and overall survival.[11,12] In an attempt to reduce infectious complications, some investigators have found that the use of leukocyte-reduced or autologous blood may be beneficial.[14,16,30] Of note is that although the effects of blood transfusions on SSI have been previously demonstrated, to our knowledge, our study is the first to report an increased rate of pneumonia in transfused patients undergoing colorectal cancer surgery. The higher rate of pneumonia is due not only to the state of immunosuppression induced by blood transfusions but also could be related to the activation of inflammatory mediators specific to lung compartments, an effect that may be dose dependent.[31] The difference between our study and previous reports is that we accounted for the presence of low preoperative hematocrit (,38%), and our results held true after this adjustment was made.

The other interesting finding in our study is that blood transfusions appear to have a dose-dependent effect on outcomes. This effect was seen for all end points except mortality, which may be explained by the relatively small numbers in this subgroup and the power-reducing effect of multiple adjustments. The adverse outcomes associated with increasing amounts of blood transfusions were demonstrated in a retrospective review of 741 cardiac surgery cases, which showed that transfusion of $\geq$ 5 U was seen as the inflection point beyond which infectious complications, organ dysfunction, and mortality increased substantially.[32] The majority of massive transfusions usually occur intraoperatively.[33] In this setting, it has been shown that massive blood transfusion along with surgical stress may work synergistically, leading to an exaggerated immunosuppressive response, more than what is seen in blood transfusion for anemic patients.[30,34]

Although it appears that blood transfusions have negative effects on short-term outcomes, preoperative anemia without subsequent blood transfusions also appears to negatively affect outcomes. Our findings clearly show that preoperative hematocrit ,38% without subsequent blood transfusions was associated with increased mortality, morbidity, length of stay, and pneumonia. Some of these results (mortality and morbidity) are in line with the finding of Musallam et al,[23] but the independent association of preoperative anemia with postoperative pneumonia and length of stay has not been previously demonstrated. After undertaking this analysis, it became interesting to examine how preoperative anemia and subsequent blood transfusion interact together. We found that in patients with preoperative anemia, subsequent blood transfusions reduced overall morbidity without affecting other outcomes. The positive effect of blood transfusions in this situation could be attributed to a reduction in noninfectious complications such as cardiac and neurologic complications, although this is not shown in our results.

Of note is that the results of our multivariate analyses should be interpreted with caution. Although it appears that blood transfusions are associated with worse outcomes, this effect was not seen in patients with preoperative anemia. Thus, it appears that the negative effects of perioperative transfusions appear to occur in patients with hematocrit

<38% and in those transfused with ≥3 U of blood. Taken together, our findings yield to the conclusion that blood transfusions may be beneficial in highly selected patients when needed, but they should be used judiciously. Similar findings were observed in a review of 239,286 patients undergoing major surgical procedures.[33] This study found that blood transfusions actually lowered mortality rates in patients with low preoperative hematocrit (<36%) who had major intraoperative blood losses, but mortality rates increased by 29% in patients who had higher preoperative hematocrit levels and low operative blood loss.

Our findings call for measures to restrict blood transfusions, because a significant percentage of blood transfusions are given unnecessarily. In a series of 476 patients undergoing colon cancer surgery, it was shown that 30% of patients were transfused unnecessarily, as documented by a predischarge hemoglobin level of 12 g/dL.[35] Recently, the implementation of an integrated transfusion reduction initiative in patients undergoing colorectal cancer surgery has led to a reduction in the transfusion rate from 28% to 15%, without affecting overall morbidity or mortality.[8] Implementing strategies to limit blood transfusion is important in view of the fact that the search for alternatives for blood transfusions has been met with limited success so far.[36,37] Future research should focus on identifying a ‘‘hemoglobin trigger point’’ for transfusion on the basis of patients’ associated comorbidities.

Another strategy aiming at reducing blood transfusions is to identify patients at risk. Knowledge of the predictive factors for blood requirement may be useful to modify certain factors or for counseling purposes. Our predictive model found several preoperative and operative variables that either predicted or lowered the risk for blood transfusions. Surprisingly, older age appeared to be associated with transfusion requirements only on univariate analysis but was not a predictor in the logistic regression model, in contrast to the studies by Nilsson et al[21] and Kim el al.[7] Also in contrast to Nilsson et al’s study, we did not find gender, chronic kidney disease, and chronic obstructive pulmonary disease to be independent predictors of blood transfusions. This may be explained by the fact that our model took into account more variables, and the stronger effects of some variables on blood transfusion requirement may have concealed the effects of less predictive variables. The unique feature of our model is that the coefficients can be added together to predict the requirement for blood transfusions. To our knowledge, this represents the first validated model for predicting blood transfusions in colorectal cancer surgery. The 10-fold cross-validation and the relatively high discriminative power make our model more applicable in day-to-day practice.

Our study had several limitations related to its retrospective design and its inherent biases. It is important to note that some blood transfusions are a marker or surrogate for more extensive and hence bloodier operations. This may affect the results, as demonstrated in a study by Miki et al[34] who demonstrated that excessive intraoperative blood loss in complex colorectal cases may act synergistically with blood transfusions to cause an exaggerated surge of proinflammatory mediators. Because data on blood transfusion are provided up until 72 hours postoperatively, details on blood transfusions after that cutoff period are unavailable, which could mitigate some of the results. Details on whether blood transfusions were autologous or allogeneic are unavailable in NSQIP. Autologous transfusions have been shown to be associated with lower rates of postoperative infections,[27] but they are rarely used in the United States, accounting for

only 1.68% of all transfused blood.[1] Variables such as surgeon's experience, presence of extensive adhesions, estimated blood loss, and vascular injuries in the operating room, which may predict requirement for blood transfusions, are unavailable in NSQIP. Race, which was previously found to be a predictor of blood transfusions,[21] was excluded from our predictive model because it had a high percentage of missing data. Furthermore, the personal or religious beliefs of certain patients may prevent them from receiving blood transfusions. Hospital related policies on blood transfusion and other hospital factors have been found to be predictors of blood transfusions[21,38] and again were not available in the database. All these factors may have lowered the predictive power of our model.

Conclusions

Although blood transfusions may be beneficial in patients with preoperative anemia, they are associated with worse outcomes in other groups of patients. Their detrimental effects appear to be dose related. Therefore, it is important to identify patients at risk and implement strategies to reduce transfusions. Future research should focus on identifying a ''trigger'' hemoglobin level for blood transfusions, taking into account patients' comorbidities.

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Discussion

Michael Corneille, M.D. (Phoenix, AZ): I'd like to congratulate the authors on a very well presented, very well written paper and thank the Southwest Surgical Congress for the opportunity to discuss it. This paper attempts to update the surgical literature with regard to practice patterns of red blood cell transfusion in colorectal surgery as well as examine short-term outcomes associated with perioperative transfusion and perioperative anemia and attempt to answer the question at what point does blood

transfusion counteract the effects of anemia. So my comments and questions are: appropriate transfusion occurs either for anemia or hemorrhage. In other words, preop transfusion for anemia may be different than intraoperative transfusion for hemorrhage. So, first of all, in that database were you able to identify any of the indications and were you able to identify any differences in outcomes based on those indications. A second question: if I were to transfuse patients with a hematocrit of 38, I, as most of you, would get a letter from your blood utilization committee saying that that was not necessarily an appropriate indication, so given that conventional triggers for transfusion are either 7 and 21 or 10 and 30, do you have any data to guide use of transfusion not <38, but at some other more conventional trigger points. And thirdly, the anemia group, as mentioned hematocrit less than 38 defined your anemia group, do you have some data on different cut points for anemia. In other words, a hematocrit 37 is different than 27 is different than 7; however, they were all grouped together in this study. Can you comment on the impact of the severity of anemia as it relates to your outcomes?

Again, very well written paper, very well presented. Thank you.

Wissam J. Halabi, M.D. (Orange, CA): Thank you Dr Corneille. In answer to your first question, the selection criteria we used were: preoperative transfusion in the 72 hours preceding surgery, intraoperative transfusions, and postoperative transfusions 72 hours postop. The intraoperative variable which accounted for 40% of blood transfusions gives you the exact number of units transfused. We did not examine to see if intraoperative transfusions were a marker of increased mortality or morbidity as we combined all transfusions together to increase the power of the analysis. If the data were split otherwise, we would have lost some power bearing in mind the large number of confounding variables we adjusted for. As far as a hematocrit of <38 being a trigger point for transfusion, there is a paper that was published in the Annals of Surgery that looked at that. If I recall well, they had 250,000 surgical patients undergoing noncardiac surgery and they stratified hematocrit from 20 to 24, 24 to 28, and so on and so forth. This paper found that in patients with very low hematocrit and those who sustained major intraoperative blood loss, transfusions were actually beneficial. However, transfusions were harmful in patients with a hematocrit of 30 who had minimal operative blood loss. They did not identify a trigger point as they used large ranges of hematocrit levels. As for the last question concerning the cut point, unfortunately, we would need a larger sample and hence more power to examine this question.

Tom Russell, M.D. (San Francisco, CA): I enjoyed this paper. As you all know, the College began the NSQIP program in 2001, patterned after the success in the VA hospitals in the ’80s and ’90s to improve surgical care. A lot of surgeons have mimed these databases in that 12 or 13 years, the College has been doing this in the private sector. My question to you is, could you make a comment about the ease of dealing with the College in collecting this data? And secondly, you mentioned the limitations of this data. Do you have any ability to put your input back to the College to improve some of the deficiencies of the database? I see more and more surgeons using this which makes us very pleased because it is going to be necessary as we move into more regulated health care in the future. Thank you very much.

Dr Halabi: Thank you for this question. Regarding the ease of the data, the hospital should be part of the NSQIP program in order to have access to the data and use it for

research. Work is under way to include more variables in the database. I believe that Dr Clifford Ko from UCLA is playing an active role in this campaign.
Randall Smith, M.D. (Temple, TX): Can you clarify 1 thing for me? The average hematocrit of the patients that were transfused: was it 38 or <38? What were these people contributing the data to NSQIP? What were they transfusing at?
Dr Halabi: Unfortunately we did not look at the average hematocrit level.
Dr Smith: All right. Thank you very much. I'm just going to make 1 comment for the audience. Just to credit Dr Russell, a lot of the development of NSQIP was under his guidance and leadership and I want to thank him for that. I know he is being humble not even mentioning it, but it was Dr Russell who really helped develop this.

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