

Beware of Blood Transfusion in Colectomy for Diverticular Disease

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Abstract

Introduction: Diverticular disease is one of the most frequent causes of severe lower gastrointestinal bleeding and about 15% of patients admitted for acute diverticulitis will require emergent surgical treatment. Previously, studies have focused on effects of blood transfusion in colorectal cancer resection but there is a lack of data concerning transfusion in benign colon surgery. Our objective was to analyze the effect of blood transfusion on the outcomes of emergent colectomy for diverticular disease.

Methods: Patients with diverticulosis or diverticulitis of the colon who underwent emergent colectomy from 2005-2010 were selected from the ACS NSQIP and separated based on blood transfusion status. Patients with a preoperative hematocrit less than 30% were identified. Multivariate logistic and linear regression was performed to determine the effect of blood transfusion on 30-day mortality, morbidity, and length of hospital stay.

Results: A total of 3,385 patients were included and 1,285 (37.9%) patients received blood transfusions. Overall, blood transfusions were associated with increased mortality (odds ratio [OR] 2.15), morbidity (OR 1.66), infectious outcomes (OR 1.36), respiratory outcomes (OR 1.77), vascular outcomes (OR 1.53) and length of stay (mean difference 2.22 days). In patients with hematocrit <30%, blood transfusion was associated with increased mortality (OR 2.90), morbidity (OR 1.77), infectious (OR 1.53) and respiratory (OR 1.75) outcomes.

Conclusion: Blood transfusion in patients with acute diverticular disease following emergent colectomy is associated with increased 30-day mortality, morbidity, and length of stay. In patients with hematocrit <30%, blood transfusion is associated with increased mortality and morbidity.

Keywords: Blood transfusion; Colorectal surgery; Diverticulosis; Diverticulitis; ACS NSQIP

Introduction

Diverticular disease is a common affliction of patients in the Western world with prevalence correlating with age. By age 60, approximately 30% of the population is affected and up to 25% of these patients will go on to develop diverticulitis. About 15% of patients will develop sequelae, such as perforation or bleeding, requiring acute surgical intervention. Furthermore, it has been well established that emergent surgery in the setting of uncontrolled bleeding carries a postoperative mortality rate of 10 to 20%[1-5].

Severe hematochezias are one of the manifestations of diverticular disease [6, 7]. In 2011, almost 14 million units of red blood cells were transfused in the United States, with 20% of these related to surgical procedures[8]. It has been widely demonstrated that blood transfusions are associated with poor outcomes in colorectal cancer surgery [9-11]. There is, however, virtually no data regarding blood transfusion in benign colectomy, such as diverticular disease, the most common cause of significant lower gastrointestinal bleeding[12].

Our objective was to analyze a large, national database to determine the effect of perioperative blood transfusion on 30-day outcomes following colectomy for acute diverticular disease.

Methods

Data Collection

Data was obtained from the American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP), which uses a systematic sampling process to collect 240 variables for randomly selected patients in several categories, which include: surgical profile, preoperative risk factors, preoperative laboratory data, operative data, and 30-day postoperative outcomes. A trained surgical clinical reviewer collects data through both the medical record and direct communication with the patient or patient's family. After collection, all data within the database is then deidentified.

Patient Selection

Patients that underwent resection for acute sequelae of colonic diverticular disease from 2005-2010 were selected based on the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic codes and Current Procedure Terminology (CPT) codes. All patients with a diagnosis of diverticulosis or diverticulitis of the colon (ICD-9: 562.10, 562.11, 562.12, 562.13) who underwent an emergent open or laparoscopic, partial or total colectomy were included in the analysis (CPT: 44025, 44140, 44141, 44143, 44144, 44145, 44146, 44147, 44150, 44151, 44155, 44156, 44157, 44158, 44160, 44204, 44205, 44206, 44207, 44208, 44210, 44211, 44212, 44213, 45110, 45111, 45112, 45113, 45114, 45116, 45119, 45120, 45121, 45123, 45395, 45397).

Patients who received perioperative blood transfusions were identified based on variables provided by the ACS NSQIP. Definitions included: (1) preoperative transfusion of >4 units 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 >4 units of packed red blood cells given from the time the patient leaves the operating room up to and including 72 hours postoperatively. Cohorts were created based on transfusion status: transfusion and no transfusion. Patients with a preoperative hematocrit less than 30% were also identified as this is a common threshold for blood transfusion[13].

Study Outcomes

The primary outcomes of our study include 30-day mortality, morbidity, and length of stay. Morbidity included one or more of the following postoperative complications: surgical site infection (SSI), wound dehiscence, pneumonia, unplanned intubation, ventilator dependence, cardiac arrest, myocardial infarction, cerebrovascular accident (CVA), deep venous thrombosis (DVT), pulmonary embolism, renal insufficiency, acute renal failure, urinary tract infection (UTI), sepsis, septic shock, and return to the operating room. The following composite outcomes were also created and analyzed: infectious (SSI, pneumonia, UTI, sepsis, and septic shock), respiratory (unplanned intubation, ventilator dependence), and vascular (cardiac arrest, myocardial infarction, CVA, DVT, pulmonary embolism).

Statistical Analysis

Perioperative variables were analyzed by univariate analysis using chi-square and t-tests as appropriate with significance set at $p < 0.05$. Multivariate logistic and linear regressions were used to analyze primary outcomes in the following scenarios: (1) the effect of blood transfusion in all patients, (2) the effect of preoperative hematocrit $< 30\%$ in patients who were not transfused and (3) the effect of blood transfusion in patients with a preoperative hematocrit $< 30\%$. Preoperative variables with a $p < 0.05$ on univariate analysis were included in the regression model with the exception of ASA class which is a subjective categorization with little inter-rater reliability [14, 15]. All statistical analysis was

performed using SPSS software (SPSS 20; IBM Corporation, Armonk, NY, USA).

Results

Patient demographics, preoperative status, and surgical profiles are shown in Table 1. Overall, 3,385 patients underwent emergent colectomy for diverticular disease with 1,285 patients receiving blood transfusion. The mean age of the transfused group was 72 years compared to 61 years in the nontransfused group ($p < 0.001$). Patients that received a blood transfusion were more likely to have multiple comorbidities and a higher ASA score. There was a higher incidence of total colectomy and a longer operation time in the transfused group.

Table 1: Comparison of patient demographics and risk factors in patients that received blood transfusions and those who did not

	No transfusion (n = 2,100)	Transfusion (n = 1,285)	p
Demographic			
Age (y)	61 (50 – 73)	72 (63 – 80)	<0.001
Women	49.2%	51.8%	0.237
Preoperative Status			
Current smoker	23.5%	18.2%	0.003
BMI	28.1 (24.5 – 32.5)	27.8 (24.2 – 32.3)	0.482
Diabetes	11.5%	23.4%	<0.001
Dyspnea	12.1%	23.1%	<0.001
Ventilator Dependent	1.9%	6.7%	<0.001
Pneumonia	1.2%	3.4%	<0.001
CHF (past 30 d)	1.9%	5.1%	<0.001
Hypertension	51.7%	75.0%	<0.001
Coronary artery disease*	11.2%	21.2%	<0.001
Peripheral vascular disease†	1.2%	2.9%	0.001
Acute renal failure	1.3%	5.4%	<0.001
ESRD on dialysis	2.3%	5.7%	<0.001
Ascites	3.4%	6.7%	<0.001
TIA	3.1%	5.7%	0.001
CVA with neurologic deficit	2.6%	5.0%	0.001
CVA without neurologic deficit	2.5%	4.8%	<0.001
Steroid use	12.2%	16.4%	0.003
Bleeding disorder	9.8%	26.5%	<0.001
SIRS/Sepsis	61.7%	57.1%	0.039
Prior operation (past 30 d)	3.1%	5.4%	0.002
Preoperative HCT			
HCT < 24%	1.0%	17.3%	<0.001
HCT < 30%	8.8%	63.3%	<0.001

Surgical profile

ASA classification			<0.001
1-No disturbance	3.1%	0.0%	
2-Mild disturbance	36.6%	8.3%	
3-Severe disturbance	43.3%	46.3%	
4-Life threatening	16.0%	42.8%	
5-Moribund	0.8%	2.2%	
Procedure type			
Partial colectomy	98.2%	86.5%	<0.001
Total colectomy	1.5%	13.3%	<0.001
Laparoscopic	8.4%	6.1%	0.049
Total operation time (min)	116 (88 – 153)	139 (105 – 180)	<0.001

* History of angina 1 month before surgery, history of myocardial infarction 6 months before surgery, previous percutaneous cardiac intervention, or previous cardiac surgery.

†History of revascularization or amputation for peripheral vascular disease and rest pain or gangrene.

COPD = chronic obstructive pulmonary disease; ESRD = end-stage renal disease; TIA = transient ischemic attack; CVA = cerebrovascular accident; SIRS = systemic inflammatory response syndrome; HCT = hematocrit; ASA = American Society of Anesthesiologists.

Table 2 lists the unadjusted outcomes compared between the two groups. Transfused patients had a higher incidence of mortality within 30 days (11.7% vs 4.8%, $p < 0.001$). The outcomes in the transfused group were significantly worse. Of the transfused group, 11.7% patients died within 30 days

compared to 4.8% in the nontransfused group. Transfused patients suffered a higher rate of morbidity (46.1% vs 35.8%, $p < 0.0001$), with most complications of infectious or respiratory origin.

Table 2: Unadjusted analysis of postoperative outcomes in patients who were transfused compared to those who were not

	No transfusion (n = 2,100)	Transfusion (n = 1,285)	p
Mortality	100 (4.8%)	150 (11.7%)	<0.001
Morbidity	752 (35.8%)	593 (46.1%)	<0.001
Infectious	516 (24.6%)	352 (27.4%)	0.068
Respiratory	300 (14.3%)	316 (24.6%)	<0.001
Vascular	101 (4.8%)	137 (10.7%)	<0.001
Length of Stay	8.0 (6.0 – 12.0)	9.0 (7.0 – 15.0)	<0.001
SSI			
Superficial	196 (9.3%)	104 (8.1%)	0.218
Deep incisional	57 (2.7%)	29 (2.3%)	0.412
Organ/space	93 (4.4%)	68 (5.3%)	0.252
Wound dehiscence	85 (4.0%)	43 (3.3%)	0.299
Pneumonia	126 (6.0%)	125 (9.7%)	<0.001
Unplanned intubation	99 (4.7%)	121 (9.4%)	<0.001
On ventilator >48 h	219 (10.4%)	238 (18.5%)	<0.001
Cardiac arrest	15 (0.7%)	41 (3.2%)	<0.001

Myocardial infarction	13 (0.6%)	31 (2.4%)	<0.001
CVA	14 (0.7%)	11 (0.9%)	0.532
DVT	45 (2.1%)	49 (3.8%)	0.004
Pulmonary embolism	24 (1.1%)	23 (1.8%)	0.118
Renal insufficiency	26 (1.2%)	25 (1.9%)	0.101
Acute renal failure	27 (1.3%)	35 (2.7%)	0.002
UTI	50 (2.4%)	66 (5.1%)	<0.001
Sepsis	123 (5.9%)	97 (7.5%)	0.053
Septic Shock	131 (6.2%)	123 (9.6%)	<0.001
Return to OR in 30 d	182 (8.7%)	155 (12.1%)	0.001

SSI = surgical site infection; CVA = cerebrovascular accident; DVT = deep vein thrombosis; UTI = urinary tract infection; OR = operating room

Primary outcomes following risk-adjusted analysis are shown in table 3. Blood transfusion increased the mortality, morbidity, and length of stay in all patients. The risk of morbidity was increased in all categories: infectious, respiratory, and cardiovascular. After analyzing the independent effect of a preoperative hematocrit less than 30% (these patients received no blood transfusions), there

was no significant risk associated with a low preoperative hematocrit, with the exception of an extended length of stay. In patients with a hematocrit less 30%, however, blood transfusion was associated with increased mortality, infectious and respiratory complications, but not vascular complications or length of stay.

Table 3: Multivariate regression analysis of the effects of perioperative blood transfusions and low preoperative hematocrit on postoperative outcomes

	Adjusted OR/MD (95% CI)	p
All patients with blood transfusion		
Mortality	2.15 (1.52 – 3.03)	<0.001
Morbidity	1.66 (1.34 – 2.06)	<0.001
Infectious	1.36 (1.08 – 1.70)	0.008
Respiratory	1.77 (1.38 – 2.27)	<0.001
Vascular	1.53 (1.09 – 2.15)	0.014
LOS	2.22 (1.24 – 3.20)	<0.001
HCT<30 with no transfusion		
Mortality	0.87 (0.459 – 1.63)	0.657
Morbidity	1.07 (0.791 – 1.45)	0.657
Infectious	0.90 (0.645 – 1.26)	0.541
Respiratory	1.13 (0.757 – 1.68)	0.553
Vascular	1.18 (0.690 – 2.00)	0.551
LOS	1.42 (0.221 – 2.62)	0.020
HCT<30 with transfusion		
Mortality	2.90 (1.51 – 5.55)	0.001
Morbidity	1.77 (1.22 – 2.56)	0.002
Infectious	1.53 (1.04 – 2.27)	0.032

Respiratory	1.75 (1.13 – 2.70)	0.012
Vascular	1.43 (0.805 – 2.55)	0.221
LOS	1.27 (0.842 – 3.38)	0.238

OR = odds ratio, MD = mean difference

Discussion

To our knowledge, this is the first analysis of a large, nationwide database on the effects of perioperative blood transfusion on the outcomes of surgery for diverticular disease. Our findings are consistent with previous studies, which demonstrate that blood transfusions are associated with higher rates of overall postoperative morbidity and mortality, as well as length of stay [10, 16, 17]. The majority of this pre-existing data, however, has been obtained in the context of colorectal malignancy; very little has been established about these effects in benign disease. Despite the fact that indications for emergency surgical therapy in the setting of severe diverticular hemorrhage includes large transfusion requirements [18], data is lacking concerning the effect of blood transfusions on the postoperative outcomes.

We report a 30-day mortality rate of 11.7% in patients that received blood transfusions compared to 4.8% in those that did not. Emergency surgery for diverticular disease itself carries a high postoperative mortality [18], and this is not unexpected given its acute nature. Multiple cohort studies have suggested that there is no postoperative mortality benefit of blood transfusion in patients with preoperative hematocrit levels of 24-33%, and that blood transfusion may increase the risk of mortality [19, 20]. We account for the presence of low preoperative hematocrit (<30%) and found that blood transfusion increased the risk of postoperative mortality whereas anemia alone did not. Causes of higher mortality in the transfused group are likely multifactorial, however the significantly higher rates of infectious and respiratory complications in transfused patients suggests a correlation between blood transfusion and postoperative mortality.

Blood transfusion carries many potential risks, including transmission of blood-borne pathogens [21], hemolytic reactions, acute lung injury, volume overload, and immunosuppression [22]. Our findings are consistent with multiple previous studies that have described blood transfusion as a major risk factor for postoperative infectious complications [11, 23]. Transfusion-induced immunosuppression is thought to be mediated by an enhanced response to IL-6, an increase in acute phase reactants, and decreased lymphocyte proliferation [24, 25]. An increased incidence of postoperative pneumonia may be due to both immunosuppression and the activation of inflammatory mediators specific to the lung [26]. It has been

suggested that the use of leukocyte-reduced blood products may reduce infection rates following colorectal surgery; this, however, remains controversial [25].

Our data demonstrates that blood transfusion is associated with an increased risk of respiratory complications, which include unplanned intubation and ventilator dependence. This is in concordance with current literature, which suggests that transfusion-related lung injury (TRALI) may play more of a role than initially thought in postoperative respiratory failure [22].

This data does not indicate that a low preoperative hematocrit has any independent effect on postoperative morbidity and mortality. Furthermore, blood transfusion in patients with a low preoperative hematocrit has a higher risk of postoperative mortality and morbidity. A study by Musallam et al. demonstrated that moderate and severe preoperative anemia was associated with an increased risk of 30-day mortality and morbidity major following non-cardiac surgery [27]. Wu et al. found a 1.6% increase in 30-day postoperative risk of death for every preoperative hematocrit point below 39% in elderly veteran patients undergoing major non-cardiac surgery [28]. Previous studies focused on a wide breadth of procedures in specific high-risk populations, which may have contributed to higher postoperative morbidity and mortality.

Our findings call for a more judicious use of blood transfusion in benign emergent and urgent colectomy, as it has already been well established that a significant number of blood transfusions are given unnecessarily despite the associated risks. Various studies have discussed a common threshold for blood transfusion, with a general consensus that a hemoglobin of 7 to 8 g/dL is appropriate in surgical patients with no ischemic risk factors, whereas a threshold of 10 g/dL can be justified for patients considered at risk, leaving an area of uncertainty between hemoglobin values of 7 to 10 g/dL [13, 22]. In this study, 63.3% of patients that received a blood transfusion had a preoperative hematocrit of less than 30%. Wu et al. found mortality risk reductions in transfused patients undergoing major noncardiac surgery with a preoperative hematocrit < 24% and in patients with mild or no preoperative anemia (hematocrit >30%) when there is substantial operative blood loss (500-999 mL) [19]. In addition to the associated risks of blood transfusion, red blood cell transfusions carry a significant financial burden to healthcare [29]. Further prospective studies are needed to determine a threshold for transfusion based on the patient's associated comorbidities and the nature of the procedure.

Our study has several limitations. The retrospective nature of this study makes it difficult to discern the clinical picture that lead to the decision to utilize blood transfusions. The ACS NSQIP does not provide data concerning hemodynamic stability, which most likely lowered the threshold for transfusion in patients that had hematocrit <30%. The decision not to transfuse patients with a hematocrit <30% was likely based on the patient's clinical status at the time. Additionally, it is inherent that some operations experience more blood loss than others. Hospital policies on blood transfusions and other factors have been shown to be predictors for blood transfusion[31], however the ACS NSQIP is a multi-institutional, national database and information regarding individual hospital practices is not available. It is likely that patients in this study with severely low preoperative hematocrit experienced worse outcomes, however due to the number of patients in this study we were unable to examine the effect of anemia in patients with various ranges of preoperative hematocrit. The ACS NSQIP database provides data 72 hours leading up to the operation and 72 hours following the operation; details

before and after those periods are unavailable. Information on whether blood transfusions are autologous or allogenic is unavailable. Autologous blood transfusions have been shown to be associated with lower rates of postoperative infections; however they are rarely used in the United States[8, 30]. All of these factors could have influenced the outcomes of our study.

Conclusion

We conclude that following emergent colectomy for acute diverticular disease, perioperative blood transfusion is associated with an increased risk of postoperative mortality and morbidity. Preoperative anemia was not independently associated with worse outcomes, although blood transfusion in anemic patients is significant for increased mortality and morbidity. More research is required to determine a threshold for blood transfusion in patients undergoing surgery for diverticular disease.

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