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Perioperative use of blood products is associated with risk of morbidity and mortality after surgery

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ABSTRACT

Background: Administration of blood products may be associated with increased morbidity and perioperative mortality in surgical patients.
Methods: Patients aged 18 + who underwent gastrointestinal surgery at the Ohio State University Wexner Medical Center 9/10/2015-5/9/2018 were identified. Multivariable logistic regression models were used to evaluate impact of blood product use on survival and complications, as well as to identify factors associated with receipt of transfusions.
Results: Among 10,756 patients, 35,517 units of blood products were transfused. Preoperative nadir hemoglobin was associated with receipt of blood product transfusion (OR 0.55, 95% CI 0.53, 0.68). After adjusting for patient and procedural characteristics, patients undergoing transfusion of blood products had an increased risk of perioperative mortality (OR 7.80, 95% CI 6.02, 10.10).
Conclusions: The use of blood products was associated with increased risk of complication and death. Patient blood management programs should be implemented to provide rational criteria and guidance for the transfusion of blood products.

Summary

The objective of the current study was to examine the use of blood products among patients undergoing gastrointestinal surgery at a large academic tertiary care center and to evaluate the impact of blood product use – including packed red blood cells, fresh frozen plasma, pooled platelets and cryoprecipitate - on perioperative morbidity and mortality. Among 10,756 patients included in the study, the most commonly performed procedures were exploratory laparotomy, cholecystectomy, colectomy and hernia repair. Patients who received blood products more commonly experienced a perioperative complication versus patients who did not receive blood products. After adjusting for patient and procedure factors, receipt of a transfusion also remained associated with an increased risk of perioperative mortality.

Introduction

Blood transfusions can be lifesaving and are recommended for patients with acute hemorrhage, hemodynamic instability, or inadequate oxygen delivery.[1] However, the administration of blood products may be associated with increased morbidity and mortality in some surgical patients.[2–9] In addition, excessive blood product utilization has potential detrimental consequences for the healthcare system including overburdening of the blood bank staff, depletion of blood bank resources, and increased costs.[10,11] While the median price paid per unit in 2015 was $211 for leukocyte-reduced red blood cells, $524 for apheresed platelets, and $54 for

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fresh frozen plasma, the total overall cost including the retrieval, transport, and preparation of blood products may be significantly underestimated.[12] As such, there has been much effort in recent years to reduce the unnecessary administration of blood products in hospitalized patients. As a result, The National Blood Collection and Utilization Survey reported an overall reduction in blood product collection, distribution and transfusion in recent years.[12]

Current guidelines regarding transfusion of packed red blood cells and other blood products recommend restrictive transfusion strategies – limiting the transfusion of packed red blood cells to patients with a nadir hemoglobin of less than 7 or 8 mg/dl.[13,14] In addition, center-specific patient blood management programs often implement alternative strategies to address anemia such as the use of erythropoietin and iron supplementation with beneficial effects.[11,15–18] However, despite evidence that the transfusion of blood products has a negative impact on clinical outcomes, perioperative transfusion practices remain varied in patients undergoing both cardiac and major non-cardiac surgery.[19–23]

Given the variation seen in the use of blood products, the objective of the current study was to examine the use of blood products among patients undergoing gastrointestinal surgery at a large academic tertiary care center. In addition, we aimed to evaluate the impact of blood product use – including packed red blood cells, fresh frozen plasma, pooled platelets and cryoprecipitate - on perioperative morbidity and mortality. Furthermore, we sought to identify patient and procedural characteristics that were associated with increased risk of receiving a blood product transfusion.

Methods

Cohort selection

All patients aged 18 years and older who underwent gastrointestinal surgery at the Ohio State University Wexner Medical Center between 9/10/2015 and 5/9/2018 were identified. Patients who underwent an operation of the liver, pancreas, bile duct, esophagus, stomach, small bowel, colon, rectum, appendix, and spleen were included. Additionally, patients who underwent exploratory laparotomy and miscellaneous procedures, inguinal and ventral herniorrhaphy, cholecystectomy, fundoplication and paraesophageal herniorrhaphy, weight loss surgery, and transplants of the kidney, pancreas and liver were included. Patients with both malignant and benign diagnoses were included.

Patient demographics including age, race, body mass index (BMI), smoking and alcohol use status were obtained. Comorbidities known to be associated with short-term and long-term patient outcomes after surgery were collected and included chronic obstructive pulmonary disease (COPD), myocardial infarction (MI), congestive heart failure (CHF), peripheral vascular disease (PVD), dementia, cerebrovascular accident (CVA), chronic lung disease, rheumatic disease, chronic liver disease, diabetes mellitus with and without end organ damage, hemiplegia, renal disease, and malignancy. The indication for surgery, operative time, emergency status, and American Society of Anesthesiology (ASA) class were also collected.

Blood product transfusion data included the receipt and total units of packed red blood cells (PRBC), cryoprecipitate, platelets, and fresh frozen plasma (FFP) transfused. Additionally, the utilization of massive transfusion protocol (MTP) was recorded. Preoperative, intraoperative and postoperative hemoglobin, hematocrit, platelets and international normalized ratio (INR) were also collected. Common perioperative morbidities examined included surgical site infection (SSI), deep venous thrombosis (DVT), pulmonary embolism (PE), pneumonia, acute myocardial infarction (MI), urinary tract infection (UTI), acute renal failure (ARF), stroke, and sepsis that occurred during the index hospital stay. Perioperative mortality was defined as death that occurred within 90 days from the date of surgery. The study was approved by the Institutional Review Board of the Ohio State University Wexner Medical Center with a waiver of patient consent.

Statistical analysis

Non-normally distributed continuous variables were summarized using median and interquartile ranges. Normally distributed continuous variables were summarized using median and interquartile range. Categorical variables were reported as frequencies and percentages. Chi-squared or Fisher's exact test were used to perform univariate comparisons. In order to provide appropriately adjusted models, all variables were also included in the multivariate comparisons. Secondary analyses were performed to assess non-transplant patients only, as well as to assess outcomes among patients who were transfused 1–3 versus >3 units of blood products. All analysis was completed using Stata/MP 14.2.

Results

Baseline characteristics

There were 10,756 patients who met the inclusion criteria (Table 1). The majority of patients were female (N = 5,828, 54%) and white (N = 8,874, 83%). Median age was 55 years old (Interquartile range [IQR] 41, 65) and median BMI was 30 (IQR 26, 37). Comorbidities were common and included COPD (N = 2,163, 20%), malignancy (N = 2,058, 19%), diabetes mellitus (N = 1,966, 18%) and renal disease (N = 1,304, 12%). The most commonly performed procedures were exploratory laparotomy (N = 2,794, 26%), cholecystectomy (N = 1,796, 17%), colectomy (N = 1,336, 12%) and hernia repair (N = 1,071, 10%). Median operative time for all procedures was 153 min (IQR 119–207); 15% of patients underwent emergency surgery (N = 1,638, 15%). The majority of patients were ASA class 2 (N = 2,938, 27%), 3 (N = 5,513, 51%), or 4 (N = 1,488, 14%). The median preoperative nadir hemoglobin was 10.6 mg/dL (95% CI 8.2, 12.9).

Blood product utilization

Overall, 2,182 (20%) patients received a blood product transfusion with a median of 8 (IQR 2, 34) units of blood products transfused per patient undergoing transfusion; of these 737 (34%) patients received ≤ 3 units. Among transfused patients, 95% of patients received packed red blood cells (N = 2,076, median 6 units, IQR 2, 20). In addition, 56% of patients received fresh frozen plasma (N = 1,213, median 8 units, IQR 3, 21), 37% of patients received platelets (N = 798, median 6 units, IQR 2–20), and 24% received cryoprecipitate (N = 529, median 5 units, IQR 3–12). Of note, 207 (10%) patients were transfused on the MTP. Interestingly, most blood products were ordered (Table 2) by anesthesiologists (N = 15,451, 44%) or other non-surgeon physicians (12,461, 35%); a smaller sub-set of blood product orders were made by allied health providers (N = 7,052, 20%). The majority of blood products were ordered individually through manage orders (N = 24,700, 70%), rather than through an order set.

Several patient characteristics were associated with receipt of blood products (Table 1). Patients who received blood products were less commonly female (No blood: N = 4,843, 56% vs. Blood N = 985, 45%, $p < 0.001$) and more commonly white (No blood: N = 7,050, 82% vs. Blood: N = 1,824, 84%, $p < 0.001$). Patients who received blood products were older (No blood: median age 53 years, IQR 39, 64 vs. Blood: median age 60 years, IQR 49, 68,

Table 1
Patient and procedure characteristics (N = 10,756).

Variable	Entire Cohort (N = 10,756)	No Blood (N = 8,574)	Blood (N = 2,182)	P-value
Age	55 (41–65)	53 (39–64)	60 (49–68)	<0.001
Sex - Female	5828 (54%)	4843 (56%)	985 (45%)	<0.001
Race				
White	8874 (83%)	7050 (82%)	1824 (84%)	<0.001
Black	1278 (12%)	1055 (12%)	223 (10%)	
Other	674 (5%)	469 (6%)	135 (6%)	
Body Mass Index	30 (26–37)	30 (26–37)	30 (25–35)	<0.001
COPD	2163 (20%)	1550 (18%)	614 (28%)	<0.001
Malignancy	2058 (19%)	1481 (17%)	577 (26%)	<0.001
DM	1966 (18%)	1414 (17%)	552 (25%)	<0.001
Renal Disease	1304 (12%)	606 (7%)	698 (31%)	<0.001
Chronic Liver Disease	827 (8%)	446 (5%)	381 (17%)	<0.001
CHF	815 (8%)	388 (5%)	427 (20%)	<0.001
PVD	693 (6%)	308 (4%)	385 (18%)	<0.001
MI	689 (6%)	421 (5%)	268 (12%)	<0.001
Hypertension	504 (5%)	389 (5%)	115 (5%)	<0.001
CVA	272 (3%)	129 (2%)	143 (7%)	<0.001
Rheumatic Disease	233 (2%)	164 (2%)	69 (3%)	<0.001
Hemiplegia	153 (1%)	64 (1%)	89 (4%)	<0.001
Dementia	97 (1%)	54 (1%)	43 (2%)	<0.001
Current Smoker	2568 (24%)	2045 (24%)	523 (24%)	<0.001
Current Alcohol Use	5095 (47%)	4359 (51%)	736 (34%)	<0.001
Procedure Category				
Laparotomy	2794 (26%)	1384 (16%)	1410 (65%)	<0.001
Cholecystectomy	1796 (17%)	1728 (20%)	68 (3%)	
Colon	1336 (12%)	1126 (13%)	210 (10%)	
Hernia	1071 (10%)	1057 (12%)	14 (0.6%)	
Gastric Bypass	929 (9%)	920 (11%)	9 (0.4%)	
Appendectomy	702 (7%)	689 (8%)	13 (0.6%)	
Fundoplication	603 (6%)	588 (7%)	15 (0.7%)	
Pancreas	365 (3%)	313 (4%)	52 (2%)	
Colostomy	287 (3%)	209 (2%)	78 (4%)	
Liver Transplant	231 (2%)	9 (1%)	222 (10%)	
Liver	225 (2%)	195 (2%)	30 (1%)	
Small Bowel	143 (1%)	117 (1%)	26 (1%)	
Esophagus	118 (1%)	102 (1%)	16 (0.7%)	
Gastrectomy	66 (0.6%)	61 (0.7%)	5 (0.2%)	
Bile Duct	31 (0.3%)	30 (0.37%)	1 (0.004%)	
Renal	9 (0.1%)	5 (0.005%)	4 (0.2%)	
Oncologic Indication - Yes	2688 (25%)	2059 (24%)	629 (28%)	<0.001
Operative Time (Minutes)	153 (119–207)	146 (112–200)	175 (140–240)	<0.001
Emergency Case (Yes)	1638 (15%)	732 (9%)	906 (42%)	<0.001
ASA Class				
ASA Class I	391 (4%)	389 (5%)	2 (0.009%)	<0.001
ASA Class 2	2938 (27%)	2856 (33%)	82 (4%)	
ASA Class 3	5513 (51%)	4718 (55%)	795 (36%)	
ASA Class 4	1488 (14%)	440 (5%)	1048 (48%)	
ASA Class 5	223 (2%)	19 (2%)	204 (9%)	
Preoperative Nadir Hemoglobin – Median (IQR)	10.6 (8.2,12.9)	12.1 (10.4, 13.7)	7.9 (6.8, 9.6)	<0.001
Intraoperative Nadir Hemoglobin – Median (IQR)	8.7 (7.3, 10.6)	11 (9.7, 12.4)	7.9 (7, 9.1)	<0.001
Postoperative Nadir Hemoglobin – Median (IQR)	9.9 (8, 11.7)	10.8 (9.2, 12.1)	7.1 (6.6, 8.3)	<0.001

*COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; CHF, congestive heart failure; MI, myocardial infarction; PVD, peripheral vascular disease; CVA, cerebrovascular accident; ASA = American Society of Anesthesiologists.

$p < 0.001$) and more often had comorbidities including COPD (No Blood: N = 1,550, 18% vs. Blood: N = 614, 28%, $p < 0.001$), malignancy (No Blood: N = 1,481, 17% vs. Blood: N = 577, 26%, $p < 0.001$), diabetes mellitus (No Blood: N = 1,414, 17% vs. Blood: N = 552, 25%, $p < 0.001$) and renal disease (No Blood: N = 606, 7% vs. Blood: N = 698, 31%, $p < 0.001$). Patients who received blood products were also more commonly classified as ASA Class 4 (No Blood: N = 440, 5% vs. Blood: N = 1,048, 48%) and ASA Class 5 (No Blood: N = 19, 2% vs. Blood: N = 204, 9%) ($p < 0.001$).

Utilization of blood products also varied by operation type. Patients who underwent laparotomy (Fig. 1) (No Blood: N = 1,384, 16% vs. Blood: N = 1,410, 65%) and liver transplant (No Blood: N = 9, 1% vs. Blood: N = 222, 10%) more commonly received blood products versus patients who underwent cholecystectomy (No Blood: N = 1,728, 20% vs. Blood: N = 68, 3%) and hernia repair (No Blood: N = 1,057, 12% vs. Blood: N = 14, 0.6%) ($p < 0.001$). Patients who underwent a transfusion of blood products were more likely to have had an oncologic indication for their operation (No Blood: N = 2,059, 24% vs. Blood: N = 629, 28%, $p < 0.001$). Median operative time was higher in the group that received a blood transfusion (No Blood: 146 min, IQR 112, 200 vs. Blood: 175 min, IQR 140, 240, $p < 0.001$). Perhaps not surprisingly, a larger proportion of patients who received blood underwent emergency surgery (No Blood: N = 732, 9% vs. Blood: N = 906, 42%, $p < 0.001$).

Factors associated with receipt of red blood cell transfusion

On univariate logistic regression, receipt of blood product transfusion (Table 3) was associated with a low preoperative nadir hemoglobin (OR 0.53, 95% CI 0.51–0.55, $p < 0.001$). Other preoperative factors associated with receipt of blood transfusion included increasing age (OR 1.03, 95% CI 1.03–1.03, $p < 0.001$), female sex

Table 2
Transfusion and ordering data.

Variable		N (%)
Product Type	Red Blood Cells	18,959 (53%)
	Plasma	9639 (27%)
	Platelets	4735 (13%)
	Cryoprecipitate	2184 (6%)
Order Source	Manage Orders	24,700 (70%)
	Anesthesia Intra-Op	9451 (27%)
	Other	1366 (3%)
Order Creator Type	Registered Nurse	21,909 (62%)
	Resident	5912 (17%)
	Anesthesiologist	3773 (11%)
	Nurse Anesthetist	2701 (8%)
	Fellow	536 (2%)
	Anesthesiologist Assistant	392 (1%)
	Nurse Practitioner	277 (1%)
Provider Type	Anesthesiologist	15,451 (44%)
	Physician	12,461 (35%)
	Nurse Practitioner	7052 (20%)
	Fellow	48 (1%)
	Resident	128 (0.36%)
	Nurse Anesthetist	108 (0.30%)
	Physician Assistant	58 (0.16%)
	Registered Nurse	6 (0.02%)

(OR 1.57, 95% CI 1.04–1.73, $p < 0.001$), COPD (OR 1.78, 95% CI 1.60–1.98, $p < 0.001$), malignancy (OR 1.72, 95% CI 1.54–1.92, $p < 0.001$), DM (OR 1.72, 95% CI 1.53–1.92, $p < 0.001$), renal disease (OR 6.18, 95% CI 5.47, 6.98, $p < 0.001$), chronic liver disease (OR 3.86, 95% CI 3.33–4.47, $p < 0.001$), CHF (OR 5.13, 95% CI 4.43–5.94, $p < 0.001$), and PVD (OR 5.75, 95% CI 4.91–6.74, $p < 0.001$). Procedure types associated with increased risk of receiving blood product transfusions included esophagectomy (OR 8.31, 95% CI 3.88–17.77, $p < 0.001$), gastrectomy (OR 4.34, 95% CI 1.50–12.60, $p = 0.007$), laparotomy (OR 54.00, 95% CI 31.04–93.93, $p < 0.001$), liver resection (OR 8.15, 95% CI 4.17–15.93, $p < 0.001$), liver transplant (OR 1307, 95% CI 551–3099, $p < 0.001$), pancreas resection (OR 8.81, 95% CI 4.73–16.40, $p < 0.001$), as well as splenectomy (OR 11.63, 95% CI 4.70–28.80, $p < 0.001$). Other associated factors included oncologic indication (OR 1.28, 95% CI 1.16–1.43, $p < 0.001$) and emergency case status (OR 7.76, 95% CI 6.92–8.70, $p < 0.001$).

On multivariate analysis, low preoperative nadir hemoglobin (OR 0.55, 95% CI 0.53–0.68, $p < 0.001$), as well as history of CHF (OR 1.71, 95% CI 1.28–2.28, $p < 0.001$) and CVA (OR 1.82, 95% CI 1.11–2.98, $p = 0.017$) were associated with increased risk of blood transfusion. Procedures such as laparotomy (OR 3.62, 95% CI 1.70–7.72, $p = 0.001$), liver resection (OR 7.21, 95% CI 2.04–25.48, $p = 0.002$), liver transplant (OR 57.05, 95% CI 17.76–183.34, $p < 0.001$), and pancreas resection (OR 3.71, 95% CI 1.35–10.19, $p = 0.011$). Emergency case status (OR 2.21, 95% 1.76–2.77, $p < 0.001$) was associated with over a two-fold increased risk of blood product transfusion.

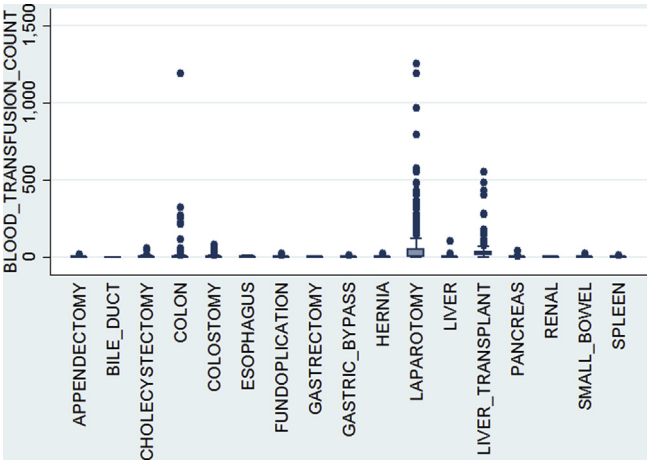

Fig. 1. Distribution of units of blood transfused, by procedure type.

Perioperative morbidity and mortality

The overall incidence of perioperative morbidity was 12% (N = 1295). Patients who received blood products more commonly experienced a perioperative complication versus patients who did not receive blood products (No Blood: N = 447, 5% vs. Blood: N = 848, 40%, $p < 0.001$). The most common complications were acute renal failure (No Blood: N = 122, 1% vs. Blood: N = 513, 24%) and sepsis (No Blood: N = 107, 1% vs. Blood: N = 431, 20%, $p < 0.001$) (Table 4). On multivariable logistic regression, patients who underwent transfusion of blood products (red blood cells, fresh frozen plasma, cryoprecipitate and/or platelets) were three times more likely to experience a perioperative complication (OR 3.78, 95% CI 3.19–4.50, $p < 0.001$) (Table 5).

The overall incidence of perioperative mortality within 90 days from the index operation was 9% (N = 1011). Patients who received a transfusion of blood products were at higher risk of perioperative mortality compared with patients who did not receive blood products (OR 22.14, 95% CI 17.62–27.82, $p < 0.001$) (Table 6). Patient characteristics associated with increased risk of death included older age (OR 1.04, 95% CI 1.04–1.05, $p < 0.001$), female sex (OR 1.76, 95% CI 1.48–2.07, $p < 0.001$), and the presence of several comorbidities including COPD (OR 2.44, 95% CI 2.06–2.90, $p < 0.001$), DM (OR 1.40, 95% CI 1.16, 1.70, $p < 0.001$), renal disease (OR 5.05, 95% CI 4.25–6.02, $p < 0.001$), chronic liver disease (OR 1.93, 95% CI 1.51–2.47, $p < 0.001$), CHF (OR 5.65, 95% CI 4.66–6.86, $p < 0.001$), and CVA (OR 3.94, 95% CI 2.89–5.42, $p < 0.001$). Compared with appendectomy, patients undergoing esophagectomy (OR 6.08, 95% CI 1.21–30.48, $p = 0.028$), emergency laparotomy (OR 49.43, 95% CI 15.84–154.27, $p < 0.001$), small bowel resection (OR 12.00, 95% CI 3.06–46.96, $p < 0.001$) and splenectomy (OR 9.71, 95% CI 1.58–59.50, $p = 0.014$) were at increased risk of perioperative mortality. Additional factors associated with increased risk of perioperative death included oncologic indication (OR 1.46, 95% CI 1.23–1.74, $p < 0.001$) and emergency case status (OR 6.61, 95% CI 5.57–7.83, $p < 0.001$).

In the adjusted logistic regression model of overall survival (Table 6), patient factors associated with increased risk of death on adjusted logistic regression included increasing age (OR 1.02, 95% CI 1.02–1.03, $p < 0.001$), female sex (OR 1.39, 95% CI 1.13–1.71, $p = 0.002$), COPD (OR 1.68, 95% CI 1.35–2.09, $p < 0.001$), renal disease (OR 1.35, 95% CI 1.07–1.70, $p = 0.011$), chronic liver disease (OR 2.17, 95% CI 1.56–3.00, $p < 0.001$), congestive heart failure (OR 1.42, 95% CI 1.08–1.85, $p = 0.011$), and PVD (OR 1.74, 95% CI 1.34–2.26, $p = 0.021$). After adjusting for patient and procedure factors, receipt of a transfusion also remained associated with an increased risk of perioperative mortality (OR 7.79, 95% CI 6.02–10.10, $p < 0.001$).

Secondary analyses

A secondary analysis that excluded patients who underwent liver or renal (N = 240) transplantation was performed. Among these 10,516 patients, 19% (N = 1956) of patients received a blood product transfusion (median 6 units (IQR 2–28) transfused per patient). Overall patient characteristics, as well as the incidence of complications among non-transplant patients was comparable to the overall cohort. Among non-transplant patients, preoperative nadir hemoglobin remained associated with receipt of blood

Table 3
Univariate and multivariate logistic regression for blood product transfusion.

Variable	Univariate OR (95% CI)	P-Value	Multivariate OR (95% CI)	P-Value
Preoperative Nadir Hemoglobin	0.53 (0.51, 0.55)	<0.001	0.55 (0.53, 0.68)	<0.001
Age	1.03 (1.03, 1.03)	<0.001	1.00 (1.00, 1.00)	0.718
Sex - Female	1.57 (1.04, 1.73)	<0.001	1.08 (0.89, 1.29)	0.453
Race				
White	Ref.		Ref.	
Black	0.82 (0.70, 0.96)	0.012	0.70 (0.53, 0.92)	0.011
Other	1.10 (0.90, 1.35)	0.334	1.07 (0.71, 1.62)	0.747
Body Mass Index	0.98 (0.98, 0.99)	<0.001	1.00 (0.99, 1.00)	0.412
COPD	1.78 (1.60, 1.98)	<0.001	1.24 (1.00, 1.54)	0.055
Malignancy	1.72 (1.54, 1.92)	<0.001	1.20 (0.91, 1.54)	0.197
DM	1.72 (1.53, 1.92)	<0.001	1.00 (0.80, 1.25)	0.997
Renal Disease	6.18 (5.47, 6.98)	<0.001	1.02 (0.81, 1.28)	0.871
Chronic Liver Disease	3.86 (3.33, 4.47)	<0.001	1.25 (0.87, `.80)	0.224
CHF	5.13 (4.43, 5.94)	<0.001	1.71 (1.28, 2.28)	<0.001
PVD	5.75 (4.91, 6.74)	<0.001	1.12 (0.83, 1.52)	0.451
MI	2.71 (2.31, 3.19)	<0.001	1.00 (0.73, 1.38)	0.977
CVA	4.59 (3.60, 5.85)	<0.001	1.82 (1.11, 2.98)	0.017
Rheumatic Disease	1.67 (1.26, 2.23)	0.001	0.84 (0.50, 1.41)	0.508
Hemiplegia	5.65 (4.09, 7.82)	<0.001	1.98 (1.16, 3.39)	0.012
Dementia	3.17 (2.11, 4.75)	<0.001	1.07 (0.56, 2.04)	0.837
Current Smoker	1.01 (0.90, 1.12)	0.908	0.86 (0.70, 1.07)	0.179
Current Alcohol Use	0.50 (0.45, 0.55)	<0.001	0.87 (0.71, 1.05)	0.136
Procedure Category				
Appendectomy	Ref.		Ref.	
Bile Duct	1.77 (0.22, 13.85)	0.589	0.84 (0.08, 9.10)	0.884
Cholecystectomy	2.09 (1.15, 3.80)	0.016	0.96 (0.43, 2.16)	0.922
Colon	9.88 (5.60, 17.44)	<0.001	3.15 (1.41, 7.04)	0.005
Colostomy	19.78 (10.77, 36.30)	<0.001	1.18 (0.51, 2.75)	0.696
Esophagus	8.31 (3.88, 17.77)	<0.001	2.37 (0.70, 8.13)	0.169
Fundoplication	1.35 (0.64, 2.87)	0.431	1.00 (0.33, 3.02)	0.991
Gastrectomy	4.34 (1.50, 12.60)	0.007	1.79 (0.38, 8.49)	0.465
Gastric Bypass	0.52 (0.22, 1.22)	0.132	1.76 (0.42, 7.43)	0.442
Hernia	0.70 (0.33, 1.50)	0.373	1.54 (0.47, 5.00)	0.476
Laparotomy	54.00 (31.04, 93.93)	<0.001	3.62 (1.70, 7.72)	0.001
Liver	8.15 (4.17, 15.93)	<0.001	7.21 (2.04, 25.48)	0.002
Liver Transplant	1307 (551.42,3099.50)	<0.001	57.05 (17.76, 183.34)	<0.001
Pancreas	8.81 (4.73, 16.40)	<0.001	3.71 (1.35, 10.19)	0.011
Renal	42.40 (10.20, 176.23)	<0.001	1.42 (0.21, 9.88)	0.719
Small Bowel	11.77 (5.88, 23.58)	<0.001	2.28 (0.87, 6.00)	0.092
Spleen	11.63 (4.70, 28.80)	<0.001	3.31 (0.84, 13.06)	0.086
Oncologic Indication - Yes	1.28 (1.16, 1.43)	<0.001	1.07 (0.82, 1.40)	0.600
Operative Time	1.00 (1.00, 1.00)	<0.001	1.00 (1.00, 1.00)	0.002
Emergency Case (Yes)	7.76 (6.92, 8.70)	<0.001	2.21 (1.76, 2.77)	<0.001
ASA Class				
ASA Class 1	Ref.		Ref.	
ASA Class 2	5.58 (1.37, 22.80)	0.017	3.38 (0.36, 31.83)	0.288
ASA Class 3	32.78 (8.15, 131.78)	<0.001	5.79 (0.62, 54.04)	0.123
ASA Class 4	463.26 (114, 1867)	<0.001	17.62 (1.88, 165.56)	0.012

RBC = red blood cells, FFP = fresh frozen plasma, COPD = chronic obstructive pulmonary disease, DM = diabetes mellitus, CHF = congestive heart failure, PVD = peripheral vascular disease, MI = myocardial infarction, CVA = cerebrovascular accident, ASA = American Society of Anesthesiologists.

product transfusion (OR 0.56, 95% CI 0.53–0.59; $p < 0.001$). Similarly, after adjusting for patient and procedural characteristics, transfusion of blood products remained associated with an increased risk of perioperative mortality (OR 7.80, 95% CI 6.02–10.11, $p < 0.001$).

Among patients who received a blood product transfusion (N = 2182), complications among patients who received 1–3 (N = 737, 34%) versus > 3 units (N = 1,445, 66.2%) were compared. Perhaps not surprisingly, patients who received >3 units of blood products were at a higher risk for overall complications (1–3, 20.6% vs. >3, 48.9%, $p = 0.001$), including sepsis (1–3, 6.9% vs. >3, 16.9%; $p < 0.001$), pneumonia (1–3, 3.4% vs. >3, 6.2%; $p = 0.005$), and surgical site infections (1–3, 1.5% vs. > 3, 5.5%; $p < 0.001$). In contrast, patients who received >3 units were not a higher risk of acute renal failure (1–3, 7.9% vs. > 3, 11.0%; $p = 0.221$), DVT (1–3, 5.8% vs. > 3, 8.0%; $p = 0.062$), or PE (1–3, 3.8% vs. > 3, 2.5%; $p = 0.087$). On multivariable analysis, receipt of >3 units was associated with increased risk of overall complications (>3 OR 6.01, 95% CI 4.89–7.37) and perioperative mortality (>3 OR 9.06, 95% CI 6.92–11.87) compared with patients who did not receive a transfusion (both $p < 0.001$).

Discussion

Though the use of blood products can be life-saving in the surgical patient, inappropriate and over-utilization of these products remain a challenge. Several previous studies have demonstrated marked variation in the utilization of blood products among surgical patients.[2–9] While the use of blood products may have a detrimental effect on perioperative and long-term outcomes, few studies have examined a large cohort of patients undergoing a wide range of gastrointestinal procedures.[2–9] The current study was important because we examined the use of blood products among a large cohort of patients undergoing gastrointestinal surgery at a tertiary care institution. Of note, 1 in 5 patients received a transfusion with some type of blood bank product with the

Table 4
Complications (N = 10,756).

Variable	Entire Cohort (N = 10,756)	No Blood (N = 8574)	Blood (N = 2182)	P-value
Overall Non-Death Complications	1295 (12%)	447 (5%)	848 (40%)	<0.001
Acute Renal Failure	635 (6%)	122 (1%)	513 (24%)	<0.001
Sepsis	538 (5%)	107 (1%)	431 (20%)	<0.001
DVT	264 (2%)	105 (1%)	159 (7%)	<0.001
Pneumonia	172 (2%)	57 (0.7%)	115 (5%)	<0.001
SSI	128 (1%)	37 (0.4%)	91 (4%)	<0.001
PE	138 (1%)	74 (0.9%)	64 (3%)	<0.001
UTI	112 (1%)	64 (1%)	48 (2%)	<0.001
Perioperative Death	1011 (9%)	318 (4%)	693 (32%)	<0.001
Discharge				
Home or Self Care	7472 (70%)	6965 (81%)	507 (23%)	<0.001
Home Health Care Services	1316 (12%)	939 (11%)	377 (17%)	
Skilled Nursing Facility	901 (8%)	496 (6%)	405 (19%)	
Expired (In-Hospital Mortality)	494 (5%)	38 (0.4%)	456 (21%)	
Other	573 (5%)	136 (2%)	437 (20%)	

*SSI, surgical site infection; DVT, deep venous thromboembolism; PE, pulmonary embolism; MI, myocardial infarction; UTI, urinary tract infection.

Table 5
Univariate and multivariate logistic regression for overall complications.

Variable	Univariate OR (95% CI)	P-Value	Multivariate OR (95% CI)	P-Value
Blood Product Transfusion (RBC, Platelet, FFP and/or Cryoprecipitate)	11.77 (10.35, 13.39)	<0.001	3.78 (3.19, 4.50)	<0.001
Age	1.02 (1.02, 1.03)	<0.001	1.00 (1.00, 1.00)	0.093
Sex - Female	1.55 (1.38, 1.75)	<0.001	1.08 (0.94, 1.25)	0.267
Race				
White	Ref.		Ref.	
African American/Black	0.81 (0.67, 0.98)	0.029	0.80 (0.63, 1.00)	0.050
Other	0.94 (0.73, 1.21)	0.630	0.92 (0.67, 1.26)	0.605
Body Mass Index	1.00 (0.99, 1.00)	0.018	1.00 (1.00, 1.00)	0.509
COPD	2.01 (1.77, 2.28)	<0.001	1.37 (1.17, 1.61)	<0.001
Malignancy	1.34 (1.17, 1.54)	<0.001	0.90 (0.72, 1.10)	0.296
DM	1.70 (1.48, 1.94)	<0.001	1.06 (0.89, 1.25)	0.513
Renal Disease	5.52 (4.82, 6.32)	<0.001	1.86 (1.57, 2.21)	<0.001
Chronic Liver Disease	1.67 (1.38, 2.02)	<0.001	0.89 (0.69, 1.16)	0.394
CHF	4.23 (3.61, 4.97)	<0.001	1.26 (1.02, 1.56)	0.030
PVD	5.13 (4.33, 6.06)	<0.001	1.37 (1.10, 1.71)	0.004
MI	2.27 (1.88, 2.75)	<0.001	0.86 (0.68, 1.16)	0.394
Hypertension	1.57 (1.24, 2.00)	<0.001	1.26 (0.94, 1.68)	0.115
CVA	3.00 (2.28, 3.92)	<0.001	0.83 (0.59, 1.16)	0.266
Rheumatic Disease	1.52 (1.07, 2.14)	0.018	0.98 (0.64, 1.48)	0.908
Hemiplegia	6.45 (4.66, 8.92)	<0.001	2.06 (1.40, 3.05)	<0.001
Dementia	2.16 (1.34, 3.50)	0.002	0.88 (0.50, 1.54)	0.648
Current Smoker	1.05 (0.92, 1.20)	0.500	0.98 (0.83, 1.16)	0.826
Current Alcohol Use	0.65 (0.58.0.73)	<0.001	1.02 (0.89, 1.18)	0.745
Procedure Category				
Appendectomy	Ref.		Ref.	
Bile Duct	3.36 (0.73, 15.50)	0.120	2.17 (0.45, 10.57)	0.337
Cholecystectomy	2.54 (1.44, 4.50)	0.001	1.62 (0.86, 3.06)	0.135
Colon	4.09 (2.32, 7.20)	<0.001	1.43 (0.75, 2.72)	0.28
Colostomy	20.39 (11.33, 36.68)	<0.001	5.35 (2.75, 10.42)	<0.001
Esophagus	3.08 (1.22, 7.80)	0.018	0.96 (0.35, 2.66)	0.937
Fundoplication	1.51 (0.75, 3.07)	0.250	0.96 (0.45, 2.06)	0.914
Gastrectomy	1.52 (0.34, 6.86)	0.583	0.66 (0.14, 3.12)	0.600
Gastric Bypass	1.08 (0.54, 2.15)	0.828	0.61 (0.29, 1.28)	0.192
Hernia	1.72 (0.92, 3.22)	0.088	1.21 (0.61, 2.42)	0.584
Laparotomy	20.29 (11.88, 34.66)	<0.001	2.66 (1.44, 4.90)	0.002
Liver	2.27 (1.00, 5/18)	0.052	0.83 (0.34, 2.02)	0.674
Liver Transplant	14.97 (8.13, 27.57)	<0.001	1.03 (0.47, 2.26)	0.931
Pancreas	3.28 (1.67, 6.46)	0.001	1.11 (0.51, 2.39)	0.793
Small Bowel	11.88 (6.07, 23.24)	<0.001	3.95 (1.87, 8.31)	<0.001
Spleen	6.65 (2.44, 18.15)	<0.001	2.28 (0.76, 6.88)	0.143
Oncologic Indication - Yes	1.31 (1.15, 1.49)	<0.001	1.36 (1.10, 1.68)	0.004
Operative Time	1.00 (1.00, 1.00)	0.012	1.00 (1.00, 1.00)	0.924
Emergency Case (Yes)	3.76 (3.31, 4.28)	<0.001	0.97 (0.81, 1.17)	0.071
ASA Class				
ASA Class I	Ref.		Ref.	
ASA Class 2	9.24 (1.28, 66.74)	0.028	6.54 (0.85, 50.14)	0.007
ASA Class 3	41.22 (5.78, 293.97)	<0.001	16.38 (2.15, 124.84)	0.001
ASA Class 4	238.05 (33.36, 1698.93)	<0.001	33.37 (4.35, 255.99)	<0.001

RBC = red blood cells, FFP = fresh frozen plasma, COPD = chronic obstructive pulmonary disease, DM = diabetes mellitus, CHF = congestive heart failure, PVD = peripheral vascular disease, MI = myocardial infarction, CVA = cerebrovascular accident, ASA = American Society of Anesthesiologists.

Table 6
Univariate and Multivariate Logistic Regression for Perioperative Death (within 90 days).

Variable	Univariate OR (95% CI)	P-Value	Multivariate OR (95% CI)	P-Value
Blood Product Transfusion (RBC, Platelet, FFP and/or Cryoprecipitate)	22.14 (17.62, 27.82)	<0.001	7.79 (6.02, 10.10)	<0.001
Age	1.04 (1.04, 1.05)	<0.001	1.02 (1.02, 1.03)	<0.001
Sex - Female	1.76 (1.48, 2.07)	<0.001	1.39 (1.13, 1.71)	0.002
Race				
White	Ref.		Ref.	
Black	0.94 (0.73, 1.22)	0.661	1.26 (0.91, 1.74)	0.164
Other	1.24 (0.90, 1.71)	0.203	1.29 (0.86, 1.96)	0.217
Body Mass Index	1.00 (1.00, 1.00)	0.862	1.00 (1.00, 1.00)	0.053
COPD	2.44 (2.06, 2.90)	<0.001	1.68 (1.35, 2.09)	<0.001
Malignancy	1.87 (1.57, 2.24)	<0.001	1.28 (0.95, 1.74)	0.104
DM	1.40 (1.16, 1.70)	<0.001	0.78 (0.61, 1.00)	0.042
Renal Disease	5.05 (4.25, 6.02)	<0.001	1.35 (1.07, 1.70)	0.011
Chronic Liver Disease	1.93 (1.51, 2.47)	<0.001	2.17 (1.56, 3.00)	<0.001
CHF	5.65 (4.66, 6.86)	<0.001	1.42 (1.08, 1.85)	<0.001
PVD	7.35 (6.04, 8.95)	<0.001	1.74 (1.34, 2.26)	<0.001
MI	3.67 (2.95, 4.59)	<0.001	1.41 (1.05, 1.89(	0.021
CVA	3.94 (2.87, 5.41)	<0.001	1.15 (0.77, 1.72)	0.502
Rheumatic Disease	1.83 (1.18, 2.84)	0.007	1.30 (0.75, 2.23)	0.346
Hemiplegia	2.67 (1.67, 4.26)	<0.001	0.71 (0.40, 1.22)	0.217
Dementia	4.67 (2.86, 7.62)	<0.001	1.13 (0.59, 2.166)	0.723
Current Smoker	0.73 (0.60, 0.90)	0.003	0.62 (0.48, 0.80)	<0.001
Current Alcohol Use	0.43 (0.36, 0.51)	<0.001	0.66 (0.53, 0.82)	<0.001
Procedure Category				
Appendectomy	Ref.		Ref.	
Cholecystectomy	1.83 (0.52, 6.39)	0.343	1.16 (0.32, 4.18)	0.825
Colon	8.12 (2.51, 26.22)	<0.001	2.38 (0.70, 8.11)	0.165
Colostomy	26.19 (7.91, 86.71)	<0.001	7.33 (2.10, 25.57)	0.002
Esophagus	6.08 (1.21, 30.48)	0.028	2.29 (0.41, 12.72)	0.345
Fundoplication	2.74 (0.70, 10.63)	0.146	1.89 (0.47, 7.63)	0.372
Gastrectomy	3.58 (0.37, 34.95)	0.272	2.16 (0.21, 21,82)	0.515
Hernia	0.87 (0.19, 2.91)	0.860	0.75 (0.16, 3.49)	0.718
Laparotomy	49.43 (15.83, 154.27)	<0.001	5.65 (1.74, 18.35)	0.004
Liver	3.15 (0.63, 15.71)	0.162	1.17 (0.22, 6.13)	0.849
Liver Transplant	4.11 (0.91, 18.48)	0.066	0.23 (0.05, 1.17)	0.076
Pancreas	3.89 (0.97, 15.66)	0.056	1.56 (0.36, 6.73)	0.551
Small Bowel	11.99 (3.06, 46.95)	<0.001	4.33 (1.04, 18.03)	0.044
Spleen	9.71 (1.58, 59.49)	0.014	3.42 (0.52, 22.45)	0.551
Oncologic Indication - Yes	1.46 (1.23, 1.74)	<0.001	1.24 (0.92, 1.68)	0.156
Operative Time (Minutes)	1.00 (1.00, 1.00)	0.044	1.00 (1.00, 1.00)	0.082
Emergency Case (Yes)	6.61 (5.57, 7.83)	<0.001	1.71 (1.37, 2.14)	<0.001

RBC = red blood cells, FFP = fresh frozen plasma, COPD = chronic obstructive pulmonary disease, DM = diabetes mellitus, CHF = congestive heart failure, PVD = peripheral vascular disease, MI = myocardial infarction, CVA = cerebrovascular accident, ASA = American Society of Anesthesiologists.

overwhelming majority of patients receiving PRBC. Surprisingly, the median number of units transfused was 8 among patients who underwent transfusion (including any blood product such as PRBC, FFP or platelet) – although the range of units transfused was wide and 30% of all patients who had a transfusion received only 1 or 2 units. Not surprisingly, patients who underwent an emergency operation, as well as patients who underwent more major intra-abdominal procedures (e.g. liver transplantation) were at higher risk of receiving a transfusion, as well as more units of blood when transfused. Furthermore, receipt of blood products was independently associated with an increased risk of perioperative morbidity and mortality.

In a study of patients undergoing cardiothoracic-vascular or gastrointestinal surgery at Johns Hopkins Hospital, Kim et al. noted that 43.3% of patients received packed red blood cells. In the current study, among patients undergoing only gastrointestinal surgery, 20% of patients had a transfusion of blood products – with 95% of patients receiving transfusion of packed red blood cells. Interestingly, several patient and operative characteristics were associated with an increased risk of receiving a transfusion of blood products. Specifically, older patients and individuals with more comorbidities were at markedly higher risk of receiving a transfusion. Kim et al. similarly reported that Charlson Score $\geq$3 and transfusion of packed red blood cells were associated with overall complications.[24] In separate studies involving patients who underwent only pancreatic, hepatic or colorectal resection, patients who received an intraoperative transfusion were also at a higher risk of complication.[25,26] In the current study, we similarly noted that transfusion receipt was associated with both morbidity and mortality. The reasons for this association were likely multifactorial. Undoubtedly, sicker patients with more complicated operative courses were more likely to have received transfusions. As such, whether transfusions were a surrogate for patient illness severity or procedural complexity versus transfusion having mediated the effects on survival more directly would be hard to determine. There is evidence, however, that blood transfusions in and of themselves can be detrimental to patient outcomes. An increasing body of evidence suggests that blood transfusion is not as benign an intervention as was previously considered.[27–29] Although undoubtedly multifactorial, several mechanisms have been proposed to explain the negative prognostic effects of blood transfusion most of which relate to the immunosuppressive effect of PBT via transfusion-related immune modulation (TRIM).[9] Of note, in the current study, patients who received a transfusion were not only at an increased risk of short-term perioperative morbidity, but also long-term worse overall survival.

Another interesting finding of the current study was the high utilization of blood transfusion at our institution among patients undergoing general surgery procedures. Specifically, 1 in 5 patients received a transfusion; in addition, many patients received more

than 1 unit of some type of blood product. These data highlight the need for more proactive and systematic blood management programs. Patient blood management programs take a proactive, patient-centered, and multidisciplinary approach to anemia management. Blood management programs generally adopt a more comprehensive bundled, evidence-based approach to the management of anemia.[11,15–17,30,31] Blood management programs have been implemented to varying degrees across cardiac, orthopedic and gastrointestinal surgery.[17,32,33] Kotze and colleagues reported that implementation of a PBM program resulted in an improvement in transfusion practices, as well as postoperative LOS and 90-day readmission following knee and hip replacement surgery.[33] Furthermore, Gross et al. reported that implementation of a PBM program for patients undergoing cardiac surgery reduced the incidence of acute renal failure, hospital LOS and total direct costs for patients.[32] In a separate study, Gani et al. noted that implementation of a blood management program was associated with fewer patients receiving PRBC transfusion and fewer patients being "over-transfused."[17] Collectively, data from the current study suggest that use of blood product transfusion was extremely common among patients undergoing intra-abdominal procedures. In turn, implementation of a blood management program may provide a means to help reduce the overall utilization of blood products.

There are several limitations of the current study that should be considered when interpreting the data. Data in this study was derived from a single institution and transfusion practices have been noted to be variable among institutions.[19–23] Thus, the Results may not be generalizable to other institutions. Non-academic medical centers and non-tertiary care centers may have especially disparate practice regarding transfusion of blood products. Another limitation was that hemoglobin and vital signs immediately prior to (transfusion trigger) and after red blood cell transfusion (transfusion target) were not available. Additionally, indications for laparotomy and indications for placement on a massive transfusion protocol were also not available. Given that our center is a major level 1 trauma center, it was likely that the indication for laparotomy was trauma related in many instances given the high number of units associated with this procedure. Despite these limitations, this large single center study serves to emphasize the impact of perioperative transfusion of blood products on surgical outcomes.

In conclusion, data from the current study demonstrated that the use of blood product transfusion in patients undergoing gastrointestinal surgery was very common as 1 in 5 patients received a transfusion. Several patient- and procedure-specific factors were associated with increased risk of receiving transfusion of blood products. Of note, receipt of blood products was associated with worse patient outcomes including morbidity and perioperative mortality. These data support the development of institution specific guidelines for transfusion practices, as well as the use of a comprehensive patient blood management program for patients undergoing major abdominal surgery.

Author contribution

EWB, FB, EA, SS, TMP conceived of and designed the work. EWB, FB, AP, OA, KM, SC, MED, CRS, EA, SS, AE, and TMP participated in the acquisition and interpretation of the data. EWB performed the analysis. EWB and AE drafted the manuscript. EWB, FB, AP, OA, KM, SC, MED, CRS, EA, SS, AE, and TMP critically revised the manuscript, provided approval of the final version and agree to be accountable for all aspects of the work.

Conflicts of interest

All authors declare that they have no disclosures to report.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amjsurg.2018.11.015.

References

1. Napolitano LM, Kurek S, Luchette FA, et al. Clinical practice guideline: red blood cell transfusion in adult trauma and critical care. *J Trauma*. 2009;67(6):1439–1442. https://doi.org/10.1097/TA.0b013e3181ba7074.
2. Ferraris VA, Davenport DL, Saha SP, Austin PC, Zwischenberger JB. Surgical outcomes and transfusion of minimal amounts of blood in the operating room. *Arch Surg*. 2012;147(1):49–55. https://doi.org/10.1001/archsurg.2011.790.
3. Kim Y, Amini N, Gani F, et al. Age of transfused blood impacts perioperative outcomes among patients who undergo major gastrointestinal surgery. *Ann Surg*. 2017;265(1):103–110. https://doi.org/10.1097/SLA.0000000000001647.
4. Mavros MN, Xu L, Maqsood H, et al. Perioperative blood transfusion and the prognosis of pancreatic cancer surgery: systematic review and meta-analysis. *Ann Surg Oncol*. 2015;22(13):4382–4391. https://doi.org/10.1245/s10434-015-4823-6.
5. Xiao H, Quan H, Pan S, et al. Impact of peri-operative blood transfusion on post-operative infections after radical gastrectomy for gastric cancer: a propensity score matching analysis focusing on the timing, amount of transfusion and role of leukocyte depletion. *J Canc Res Clin Oncol*. 2018;144(6):1143–1154. https://doi.org/10.1007/s00432-018-2630-8.
6. Glance LG, Dick AW, Mukamel DB, et al. Association between intraoperative blood transfusion and mortality and morbidity in patients undergoing noncardiac surgery. *Anesthesiology*. 2011;114(2):283–292. https://doi.org/10.1097/ALN.0b013e3182054d06.
7. Bernard AC, Davenport DL, Chang PK, Vaughan TB, Zwischenberger JB. Intraoperative transfusion of 1 U to 2 U packed red blood cells is associated with increased 30-day mortality, surgical-site infection, pneumonia, and sepsis in general surgery patients. *J Am Coll Surg*. 2009;208(5):931–937. https://doi.org/10.1016/j.jamcollsurg.2008.11.019, 7.e1-2; discussion 8-9.
8. Frank SM, Ejaz A, Pawlik TM. Optimal transfusion trigger in surgical patients with coronary artery disease. *JAMA Surg*. 2016;151(2):146. https://doi.org/10.1001/jamasurg.2015.3399.
9. Ejaz A, Spolverato G, Kim Y, et al. Impact of blood transfusions and transfusion practices on long-term outcome following hepatopancreaticobiliary surgery. *J Gastrointest Surg*. 2015;19(5):887–896. https://doi.org/10.1007/s11605-015-2776-5.
10. Ganz ML, Wu N, Rawn J, Pashos CL, Strandberg-Larsen M. Clinical and economic outcomes associated with blood transfusions among elderly Americans following coronary artery bypass graft surgery requiring cardiopulmonary bypass. *Blood Transfus*. 2014;12(Suppl 1):s90–s99. https://doi.org/10.2450/2013.0170-12.
11. Shander A, Hofmann A, Isbister J, Van Aken H. Patient blood management–the new frontier. *Best Pract Res Clin Anaesthesiol*. 2013;27(1):5–10. https://doi.org/10.1016/j.bpa.2013.01.001.
12. Ellingson KD, Sapiano MRP, Haass KA, et al. Continued decline in blood collection and transfusion in the United States-2015. *Transfusion*. 2017;57(Suppl 2):1588–1598. https://doi.org/10.1111/trf.14165.
13. Tobian AA, Heddle NM, Wiegmann TL, Carson JL. Red blood cell transfusion: 2016 clinical practice guidelines from AABB. *Transfusion*. 2016;56(10):2627–2630. https://doi.org/10.1111/trf.13735.
14. Excellence NIfHaC. *Blood Transfusion*. 2015.
15. Meybohm P, Richards T, Isbister J, et al. Patient blood management bundles to facilitate implementation. *Transfus Med Rev*. 2017;31(1):62–71. https://doi.org/10.1016/j.tmrv.2016.05.012.
16. Spahn DR, Goodnough LT. Alternatives to blood transfusion. *Lancet*. 2013;381(9880):1855–1865. https://doi.org/10.1016/S0140-6736(13)60808-9.
17. Gani F, Cerullo M, Ejaz A, et al. Implementation of a blood management program at a tertiary care hospital: effect on transfusion practices and clinical outcomes among patients undergoing surgery. *Ann Surg*. 2017. https://doi.org/10.1097/SLA.0000000000002585.
18. Carson JL, Grossman BJ, Kleinman S, et al. Red blood cell transfusion: a clinical practice guideline from the AABB*. *Ann Intern Med*. 2012;157(1):49–58. https://doi.org/10.7326/0003-4819-157-1-201206190-00429.
19. Corwin HL, Gettinger A, Pearl RG, et al. The CRIT Study: anemia and blood transfusion in the critically ill–current clinical practice in the United States. *Crit Care Med*. 2004;32(1):39–52. https://doi.org/10.1097/01.CCM.0000104112.34142.79.
20. Stover EP, Siegel LC, Parks R, et al. Variability in transfusion practice for coronary artery bypass surgery persists despite national consensus guidelines: a 24-institution study. Institutions of the Multicenter Study of Perioperative Ischemia Research Group. *Anesthesiology*. 1998;88(2):327–333.
21. Snyder-Ramos SA, Möhnle P, Weng YS, et al. The ongoing variability in blood transfusion practices in cardiac surgery. *Transfusion*. 2008;48(7):1284–1299. https://doi.org/10.1111/j.1537-2995.2008.01666.x.
22. Ozier Y, Pessione F, Samain E, Courtois F, Transplantation FSGoBTiL. Institutional variability in transfusion practice for liver transplantation. *Anesth Analg*. 2003;97(3):671–679.

23. Qian F, Osler TM, Eaton MP, et al. Variation of blood transfusion in patients undergoing major noncardiac surgery. *Ann Surg*. 2013;257(2):266–278. https://doi.org/10.1097/SLA.0b013e31825ffc37.
24. Kim Y, Spolverato G, Lucas DJ, et al. Red cell transfusion triggers and post-operative outcomes after major surgery. *J Gastrointest Surg*. 2015;19(11): 2062–2073. https://doi.org/10.1007/s11605-015-2926-9.
25. Ejaz A, Spolverato G, Kim Y, Frank SM, Pawlik TM. Variation in triggers and use of perioperative blood transfusion in major gastrointestinal surgery. *Br J Surg*. 2014;101(11):1424–1433. https://doi.org/10.1002/bjs.9617.
26. Postlewait LM, Squires MH, Kooby DA, et al. The relationship of blood transfusion with peri-operative and long-term outcomes after major hepatectomy for metastatic colorectal cancer: a multi-institutional study of 456 patients. *HPB (Oxford)*. 2016;18(2):192–199. https://doi.org/10.1016/j.hpb.2015.08.003.
27. Acheson AG, Brookes MJ, Spahn DR. Effects of allogeneic red blood cell transfusions on clinical outcomes in patients undergoing colorectal cancer surgery: a systematic review and meta-analysis. *Ann Surg*. 2012;256(2):235–244. https://doi.org/10.1097/SLA.0b013e31825b35d5.
28. Amato A, Pescatori M. Perioperative blood transfusions for the recurrence of colorectal cancer. *Cochrane Database Syst Rev*. 2006;(1), CD005033. https://doi.org/10.1002/14651858.CD005033.pub2.
29. Sun C, Wang Y, Yao HS, Hu ZQ. Allogeneic blood transfusion and the prognosis of gastric cancer patients: systematic review and meta-analysis. *Int J Surg*. 2015;13:102–110. https://doi.org/10.1016/j.ijsu.2014.11.044.
30. Leahy MF, Hofmann A, Towler S, et al. Improved outcomes and reduced costs associated with a health-system-wide patient blood management program: a retrospective observational study in four major adult tertiary-care hospitals. *Transfusion*. 2017;57(6):1347–1358. https://doi.org/10.1111/trf.14006.
31. Meybohm P, Froessler B, Goodnough LT, et al. Simplified international recommendations for the implementation of patient blood management" (SIR4PBM). *Perioperat Med*. 2017;6:5. https://doi.org/10.1186/s13741-017-0061-8.
32. Gross I, Seifert B, Hofmann A, Spahn DR. Patient blood management in cardiac surgery Results in fewer transfusions and better outcome. *Transfusion*. 2015;55(5):1075–1081. https://doi.org/10.1111/trf.12946.
33. Kotzé A, Carter LA, Scally AJ. Effect of a patient blood management programme on preoperative anaemia, transfusion rate, and outcome after primary hip or knee arthroplasty: a quality improvement cycle. *Br J Anaesth*. 2012;108(6): 943–952. https://doi.org/10.1093/bja/aes135.