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Explaining the excess morbidity of emergency general surgery: packed red blood cell and fresh frozen plasma transfusion practices are associated with major complications in nonmassively transfused patients

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Emergency general surgery;
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Abstract

BACKGROUND: Intraoperative blood product transfusions carry risk but are often necessary in emergency general surgery (EGS).

METHODS: We queried the American College of Surgery-National Surgical Quality Improvement Program database for EGS patients (2008 to 2012) at 2 tertiary academic hospitals. Outcomes included rates of high packed red blood cell (pRBC) use (estimated blood loss:pRBC $<$ 350:1) and high fresh frozen plasma (FFP) use (FFP:pRBC $>$1:1.5). Patients were then stratified by exposure to high blood product use. Stepwise logistic regression was performed.

RESULTS: Of 992 patients, 33% underwent EGS. Estimated blood loss was similar between EGS and non-EGS (282 vs 250 cc, P = .288). EGS patients were more often exposed to high pRBC use (adjusted odds ratio [OR] = 2.01, 95% confidence interval [CI] = 1.11 to 3.66) and high-FFP use (OR = 2.75, 95% CI: = 1.10 to 6.84). High blood product use was independently associated with major nonbleeding complications (high pRBC: OR = 1.73, 95% CI = 1.04 to 2.91; high FFP: OR = 2.15, 95% CI = 1.15 to 4.02).

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CONCLUSIONS: Despite similar blood loss, EGS patients received higher rates of intraoperative blood product transfusion, which was independently associated with major complication.

Emergency general surgery (EGS) patients are known to be at increased risk for death and complications. EGS patients are 5 to 8 times more likely to die than non-EGS (NEGS) patients receiving the same operations electively,[1–4] and as many as 58% of EGS patients will have postoperative complications.[5] After adjusting for differences in baseline patient characteristics and physiologic acuity that might predispose EGS patients to adverse outcomes, EGS patients are still 39% more likely to die and 31% more likely to experience a major postoperative complication than their NEGS counterparts.[1]

Perioperative blood product transfusions have been associated with adverse outcomes.[6–8] Emergency surgery has been identified as an independent risk factor for perioperative blood product transfusions in vascular surgery patients.[7] In the EGS population, patients who receive blood transfusions are at 5.5 times greater odds of experiencing major complications.[9] Although intraoperative blood product transfusions may not be avoidable because of clinical necessity, the thresholds for packed red blood cell (pRBC) transfusion and ratios of fresh frozen plasma (FFP) to pRBCs are modifiable parameters that may affect outcomes.

Much of the literature surrounding intraoperative transfusion practices focuses on the massively transfused trauma patient.[10–13] These findings cannot be generalized to the nonmassively transfused general surgery patient. Intraoperative transfusion practices in EGS have not been well studied. Prior studies of outcomes in EGS have been limited by the absence of intraoperative variables that may be related to clinical indications for transfusion.[1–5,9,14,15]

The objectives of this study were to (1) identify differences in intraoperative transfusion practices between nonmassively transfused EGS and NEGS patients undergoing the same operations and (2) determine if high-intraoperative transfusion rates contribute to adverse outcomes in nonmassively transfused general surgery patients. We hypothesized that EGS patients receive higher rates of intraoperative blood product transfusion than NEGS patients, which contributes to adverse outcomes.

Methods

Study design

After obtaining Institutional Review Board approval, we performed a retrospective cohort study of adult patients (age $\geq$18) in the American College of Surgeons-National Surgical Quality Improvement Project (ACS-NSQIP) database who underwent 1 of 14 procedures common to both EGS and NEGS from January 1, 2008, to December 31, 2012, at 2 academic medical centers (Brigham and Women's Hospital and Massachusetts General Hospital). These procedures were selected based on a summary of clinical conditions encompassing EGS as defined by the American Association for the Surgery of Trauma (Appendix A).[16]

Exclusion criteria were the use of autologous transfusion with cell saver and massive transfusion. We excluded patients who received autologous transfusions to prevent confounding from the different risks associated with autologous vs nonautologous transfusions. In accordance with previously described methods, massive transfusion was defined as the administration of 10 or more units of pRBCs within any contiguous 24-hour period around the operation.[12]

The preoperative patient characteristics and postoperative complications were obtained from ACS-NSQIP. The preoperative variables obtained are listed in Tables 1 and 2.

A chart review was performed to collect intraoperative data. A single evaluator reviewed the intraoperative anesthesia record, the intraoperative nursing record, the surgeon's operative notes, and any laboratory tests drawn between incision time and surgery end time for all patients. The following intraoperative variables were collected: length of operation, start time classification (day vs night), estimated blood loss (EBL), units of pRBCs transfused, units of FFP transfused, volume of crystalloid administered, volume of albumin administered, number of vasopressor medications administered, vital signs (lowest mean arterial pressure, lowest heart rate [HR], and lowest temperature), and laboratory measurements (lowest pH and highest blood glucose). These intraoperative variables were selected based on their previously demonstrated association with postoperative morbidity and mortality or their clinical relevance to transfusion.[17–20]

For all measurements obtained during chart review, all values were considered true values unless they were incompatible with physiology (eg, temperature of 0 °C) or a specific note was mentioned in the record that the value was falsely captured (eg, "probe fell off" when HR was recorded as abnormally low). For estimated values such as blood loss that could potentially differ among records, the order of precedence was as follows: (1) the surgical resident's operative note, (2) the attending surgeon's operative note, and (3) the intraoperative anesthesia record. For intraoperative hemodynamics, recordings on an invasive arterial line took precedence over noninvasive blood pressure cuff measurements. For the administration of vasopressors (to include ephedrine, phenylephrine,

Table 1 Baseline preoperative characteristics of nonemergency general surgery vs emergency general surgery patients ($n = 992$)

	NEGS ($n = 660$)	EGS ($n = 332$)	*P*	Missing n
Age*, y	58.78 ± 15.56	63.87 ± 15.17	<.0001	0
Male, (%)	42.27	42.77	.881	0
Body mass index*, kg/m^2	27.58 ± 7.44	27.38 ± 7.46	.672	28
Diabetes mellitus, (%)	10.60	15.06	.014	0
Dyspnea at rest, (%)	.45	6.33	<.0001	0
Partially/totally dependent functional status, (%)	8.18	32.53	<.0001	0
Chronic obstructive pulmonary disease, (%)	3.18	11.75	<.0001	0
Hypertension requiring medications, (%)	44.55	52.71	.015	0
Disseminated cancer, (%)	13.94	10.24	.099	0
Open wound, (%)	5.91	11.14	.003	0
Smoking history, (%)	17.73	18.67	.714	0
Alcohol history, (%)	1.05	2.50	.321	625
Patients presenting from home, (%)	88.03	63.86	<.0001	0
Steroid use, (%)	11.06	15.06	.071	0

EGS = emergency general surgery; NEGS = nonemergency general surgery.
*Data are given as mean ± standard deviation.

epinephrine, norepinephrine, vasopressin, dopamine, and dobutamine), the anesthesia record was reviewed for all medications administered and the number of different vasopressors used was noted; the distinction of whether each vasopressor was administered in the form of a drip or a bolus was not made.

Outcome measures

Patients were 1st stratified by EGS status. Outcomes included the rates of high pRBC use and high-FFP use. High pRBC use was defined as intraoperative transfusion of pRBCs at an EBL:pRBC ratio less than 350:1. This ratio

Table 2 Preoperative clinical and physiologic characteristics of nonemergency general surgery vs emergency general surgery patients ($n = 992$)

	NEGS ($n = 660$)	EGS ($n = 332$)	*P*	Missing n
Ascites within 30 d, (%)	2.73	7.53	<.0001	0
Congestive heart failure within 30 d, (%)	.30	5.12	<.0001	0
Weight loss >10% in last 6 mon, (%)	11.97	9.64	.272	0
Ventilator dependence within 48 h, (%)	1.21	16.27	<.0001	0
Acute renal failure within 24 h, (%)	.76	6.63	<.0001	0
Pneumonia, (%)	1.49	8.45	<.0001	308
Currently requiring dialysis within 2 wk, (%)	.76	4.82	<.0001	0
Impaired sensorium, (%)	.64	17.37	<.0001	308
Systemic inflammatory response syndrome, (%)	5.37	14.80	<.0001	9
Septic shock, (%)	1.07	25.98	<.0001	9
Sepsis within 48 h, (%)	5.06	24.47	<.0001	9
Bleeding disorders, (%)	7.42	22.89	<.0001	0
pRBC transfusion within 72 h, (%)	1.97	5.12	.006	0
American Society of Anesthesia class ≥ IV, (%)	2.73	29.82	<.0001	1
Laboratory values (90 d)*				
Hematocrit (%)	36.24 ± 5.65	35.40 ± 6.70	.041	18
Partial thromboplastin time (sec)	30.74 ± 8.62	32.58 ± 12.15	.014	197
International normalized ratio	1.12 ± .19	1.31 ± .37	<.0001	148
Albumin	3.69 ± .72	3.26 ± .86	<.0001	176
Creatinine	.92 ± .51	1.44 ± 1.21	<.0001	26

EGS = emergency general surgery; NEGS = nonemergency general surgery; pRBC = packed red blood cells.
*Data are given as mean ± standard deviation.

was based on studies showing 1 unit of pRBCs contains an average of 350 cc of fluid with a hematocrit averaging 60%.[21,22] High-FFP use was defined as intraoperative transfusion of FFP at an FFP:pRBC ratio greater than 1:1.5. This ratio was based on studies showing mortality reduction among trauma patients transfused at a high (1:1) vs low (1:4) ratio of FFP:pRBC.[11] Patients with EBL less than 350 cc but any pRBC transfusion were included in the high-pRBC use group. Any patient that received FFP but zero units of pRBCs was placed in the high-FFP use group.

Patients were then stratified by exposure to high-blood product use. Outcomes were death within 30 days of the operation (30-day mortality), major complications, major nonbleeding complications, and thromboembolic complications. Major complications included organ/space surgical site infection (SSI), wound disruption, stroke, cerebrovascular accident, progressive renal insufficiency, acute renal failure, myocardial infarction, cardiac arrest requiring cardiopulmonary resuscitation, pneumonia, unplanned intubation, ventilator dependence within 48 hours, pulmonary embolism, bleeding requiring transfusion, sepsis, and septic shock. Major complications excluded superficial SSI, deep SSI, urinary tract infection, deep venous thrombosis, and peripheral nerve injury. Major nonbleeding complications were defined as any major complication except postoperative bleeding requiring transfusion. Thromboembolic complications included deep venous thrombosis and pulmonary embolism. All variables were defined in accordance with ACS-NSQIP definitions for postoperative complications.

Statistical analysis

Patient characteristics were compared using Chi-square test for categorical variables and Wilcoxon rank-sum test for continuous variables. To use all the observations in our statistical model, we imputed missing data using previously described methods.[23–25]

Multivariate logistic regression was performed to determine the relationship between emergency status (EGS vs NEGS) and intraoperative transfusion rates (high-pRBC use and high-FFP use). We then performed a second multivariate logistic regression to determine the relationship between intraoperative transfusion rates (high-pRBC use and high-FFP use) and postoperative outcomes (death, major complications, and thromboembolic complications). To select control variables for each multivariate analysis, we 1st performed a logistic regression stepwise selection algorithm with entry threshold of .3 and stay threshold of .055 to detect all the variables selected within multiple imputations from all preoperative and intraoperative variables listed in Tables 1–3. We then conducted colinearity diagnostics using variance inflation factor and excluded any variable with variance inflation factor greater than 10. Multiple imputation procedure was used to create valid statistical inferences from the multiply imputed data sets reflecting the potential statistical error because of missing values and creating correct probability coverage.

Alpha level was set at .05. All the computations were made with SAS 9.3 by SAS Institute Inc., Cary, NC.

Table 3 Intraoperative characteristics of nonemergency general surgery vs emergency general surgery patients (n = 992)

	NEGS (n = 660)	EGS (n = 332)	P	Missing n
Night-time surgery (start time: 6pm to 6am), (%)	6.06	44.58	<.0001	0
Length of operation (min)*	157.38 ± 102.45	144.30 ± 74.18	.039	0
Length of operation for vascular cases (min)*	326.45 ± 120.48	200.00 ± 131.75	.096	5
Length of op. for nonvascular cases (min)*	149.23 ± 93.76	143.94 ± 73.68	.375	5
Intraoperative blood loss and resuscitation*				
Estimated blood loss	249.85 ± 486.05	281.99 ± 364.80	.288	0
Crystalloid volume (cc)	2,687.30 ± 1,496.83	2,672.96 ± 1,620.50	.890	2
Albumin volume (cc)	116.81 ± 307.20	241.84 ± 502.55	<.0001	2
Transfusion of pRBCs (units)	.23 ± .77	.61 ± 1.19	<.0001	0
Transfusion of FFP (units)	.10 ± .60	.53 ± 1.38	<.0001	0
High pRBC use, (%)	5.76	18.98	<.0001	0
High FFP use, (%)	1.97	15.06	<.0001	0
Intraoperative vital signs and pressors*				
Lowest mean arterial pressure	62.27 ± 9.83	61.22 ± 10.05	.115	8
Lowest heart rate	60.34 ± 13.25	73.93 ± 16.54	<.0001	11
Lowest temperature (degrees C)	35.42 ± 1.70	35.93 ± 1.62	<.0001	62
>2 pressure support medications, (%)	.63	9.85	<.0001	22
Intraoperative laboratory measurements*				
Lowest pH	7.36 ± .07	7.28 ± .12	<.0001	659
Highest blood glucose	152.17 ± 73.16	162.63 ± 60.15	.109	565

EGS = emergency general surgery; FFP = fresh frozen plasma; NEGS = nonemergency general surgery; pRBC = packed red blood cells.
*Data are given as mean ± standard deviation.

Results

Over the 5-year period from 2008 to 2012, a total of 1,072 patients met the inclusion criteria. Six patients were excluded for massive transfusion and 74 patients were excluded for cell-saver use. A total of 992 patients were included in our final analysis. Of these, 33% underwent EGS. Tables 1 and 2 illustrate the demographics and preoperative variable comparisons between EGS and NEGS patients.

Demographics and baseline characteristics

Patients who underwent EGS were notably older (64 years vs 59 years, $P < .001$) and had more chronic illnesses and comorbid conditions (Table 1). A limited number of preoperative variables were not significantly different. These included sex, body mass index, smoking history, alcohol history, history of disseminated cancer, history of steroid use, and history of weight loss.

The clinical and physiologic characteristics suggested that EGS patients were significantly more acutely ill on admission compared with NEGS patients (Table 2). These differences were significant for every variable related to the clinical indications for transfusion, including bleeding disorder (22.9% EGS vs 7.5% NEGS, $P < .001$), pRBC transfusion within 72 hours (5.6% vs 1.9%, $P = .001$), preoperative hematocrit (35.4 ± 6.7 vs 36.5 ± 5.7, $P = .01$) (mean ± standard deviation), preoperative partial thromboplastin time (PTT) (32.0 ± 10.9 vs 31.1 ± 9.0, $P = .002$), and preoperative international normalized ratio (INR) (1.3 ± .4 vs 1.1 ± .2, $P < .001$).

Intraoperative characteristics

Table 3 demonstrates the intraoperative characteristics for EGS vs NEGS. EGS cases were slightly shorter in duration (2 hours 24 minutes ± 1 hour 14 minutes vs 2 hours 37 minutes ± 1 hour 42 minutes, $P = .04$). However, these data regarding length of operation were greatly skewed by lengthy vascular NEGS cases. When only nonvascular cases were analyzed, there was no significant difference in length of operation in EGS vs NEGS (2 hours 24 minutes ± 1 hour 14 minutes vs 2 hours 29 minutes ± 1 hour 34 minutes, $P = .38$).

EBL was not significantly different in EGS vs NEGS (282.0 ± 364.8 cc vs 249.9 ± 486.1 cc, $P = .29$). Although the EBL was similar between EGS and NEGS, the number of blood product units transfused was significantly greater in EGS (.61 ± 1.19 pRBC units; .53 ± 1.38 FFP units) vs NEGS (.23 ± .77 pRBC units, $P < .001$; .10 ± .60 FFP units, $P < .001$).

High-intraoperative pRBC use occurred in a total of 101 patients; the rate of high-pRBC use was 19.0% (63 of 332 patients) for EGS vs 5.8% (38 of 660 patients) for NEGS ($P < .001$).

High-intraoperative FFP use occurred in a total of 63 patients; the rate of high-FFP use was 15.1% (50 of 332 patients) for EGS vs 2.0% (13 of 660 patients) for NEGS ($P < .001$).

The remainder of the differences in intraoperative characteristics between NEGS and EGS is provided in Table 3. Of the intraoperative vital signs and laboratory markers, statistically significant differences were noted in the lowest HR, the lowest temperature, and the lowest pH.

Emergency general surgery and postoperative outcomes

Table 4 shows the postoperative outcomes stratified by EGS status. EGS patients had higher rates of death, major complications, major non-bleeding complications, and thromboembolic complications.

Relationship between emergency general surgery and intraoperative transfusion practices

Table 5 demonstrates the relationship between EGS and intraoperative transfusion practices. On multivariate analysis, EGS patients were more likely than NEGS patients

Table 4 Unadjusted postoperative outcomes of nonemergency general surgery vs emergency general surgery patients ($n = 992$)

	NEGS ($n = 660$)	EGS ($n = 332$)	P	Missing n
Death 30-day mortality, (%)	2.27	17.77	<.0001	0
Major complication*, (%)	23.94	53.92	<.0001	0
Bleeding requiring transfusion, (%)	15.15	34.34	<.0001	0
Major complication excluding bleeding requiring transfusion, (%)	12.73	39.76	<.0001	0
Thromboembolic complication†, (%)	2.58	5.72	.012	0

EGS = emergency general surgery; NEGS = nonemergency general surgery.

*Major complication: organ/space surgical site infection, wound disruption, stroke, cerebrovascular accident, progressive renal insufficiency, acute renal failure, myocardial infarction, cardiac arrest requiring cardiopulmonary resuscitation, pneumonia, unplanned intubation, ventilator dependence within 48 hours, pulmonary embolism, sepsis, septic shock, or bleeding requiring transfusion.

†Thromboembolic complication: deep venous thrombosis requiring therapy or pulmonary embolism.

Table 5 Relationship between emergency general surgery and intraoperative transfusion practices

	Univariate		Multivariate		
Outcome	OR (95% CI)	*P*	OR (95% CI)	*P*	AUROC (95% CI)
High-pRBC use	3.834 (2.501–5.877)	<.0001	2.010 (1.106–3.660)	.0220	.921 (.906–.937)
High-FFP use	8.824 (4.719–16.502)	<.0001	2.745 (1.102–6.835)	.0301	.959 (.946–.971)

High-pRBC use (EBL/pRBC <350).
High-FFP use (FFP/pRBC >1/1.5).
AUROC = area under receiver operating characteristic; CI = confidence interval; FFP = Fresh frozen plasma; OR = odds ratio; pRBC = packed red blood cells.

to be exposed to high-pRBC use (adjusted odds ratio = 2.01, 95% confidence interval = 1.11 to 3.66). The multivariate model included emergency status, hematocrit, INR, PTT, albumin, lowest temperature, history of dialysis, history of pRBC transfusion within 72 hours, and history of bleeding disorder.

EGS patients were also more likely than NEGS patients to be exposed to high-FFP use (odds ratio = 2.75, 95% confidence interval = 1.10 to 6.84). The multivariate model included emergency status, EBL, length of operation, INR, PTT, creatinine, lowest pH, wound class, history of ascites, history of congestive heart failure, history of dialysis, history of pRBC transfusion within 72 hours, and history of bleeding disorder.

Relationship between intraoperative transfusion practices and postoperative outcomes

Appendices B, C, D, and E illustrate the demographics and preoperative variable comparisons between patients stratified by exposure to high-blood product use. Appendices F and G illustrate the intraoperative variable comparisons between patients stratified by exposure to high-blood product use.

Table 6 demonstrates the relationship between high-intraoperative pRBC use, high-FFP use, and postoperative outcomes. In the entire cohort of nonmassively transfused general surgery patients, high-pRBC use and high-FFP use were not independently associated with 30-day mortality or thromboembolic complications. However, high-pRBC use and high-FFP use were both independently associated with major complications. After excluding postoperative bleeding requiring transfusion as a major complication, high-pRBC use and high-FFP use were both independently associated with major nonbleeding complications.

Comments

This multicenter study was designed to identify differences in intraoperative transfusion practices between EGS and NEGS and to determine the relationship between those transfusion practices and adverse outcomes. In our sample of 992 nonmassively transfused, nontrauma patients, we demonstrated that EGS is independently associated with high rates of intraoperative blood product transfusion. EGS patients were 2 times more likely to be exposed to high-intraoperative pRBC use and nearly 3 times more likely to be exposed to high-intraoperative FFP use despite similar

Table 6 Relationship between high-intraoperative blood product use and postoperative outcomes

	High-pRBC use (EBL/pRBC <350)			High-FFP use (FFP/pRBC >1/1.5)		
Outcome	OR (95% CI)	*P*	AUROC (95% CI)	Or (95% CI)	*P*	AUROC (95% CI)
Death (30-day mortality)	.853 (.388–1.872)	.6911	.886 (.863–.909)	.831 (.359–1.923)	.6659	.887 (.864–.910)
Major complication*	42.838 (15.019–122.185)	<.0001	.820 (.803–.837)	3.827 (1.755–8.341)	.0007	.783 (.765–.802)
Bleeding requiring transfusion	34.857 (15.144–80.232)	<.0001	.846 (.827–.866)	3.639 (1.585–8.354)	.0023	.819 (.799–.839)
Major complication excluding bleeding requiring transfusion	1.734 (1.036–2.901)	.0361	.804 (.785–.824)	2.153 (1.154–4.019)	.0160	.801 (.781–.821)
Thromboembolic complication†	.841 (.280–2.523),	.7572	.732 (.688–.776)	.814 (.193–3.425)	.7788	.733 (.689–.777)

AUROC = area under receiver operating characteristic; CI = confidence interval; EGS = emergency general surgery; FFP = fresh frozen plasma; OR = odds ratio; pRBC = packed red blood cells.
*Major complication: organ/space surgical site infection, wound disruption, stroke, cerebrovascular accident, progressive renal insufficiency, acute renal failure, myocardial infarction, cardiac arrest requiring cardiopulmonary resuscitation, pneumonia, unplanned intubation, ventilator dependence within 48 hours, pulmonary embolism, sepsis, septic shock, or bleeding requiring transfusion.
†Thromboembolic complication: deep venous thrombosis requiring therapy or pulmonary embolism.

blood loss when compared with NEGS patients. Those who were exposed to high-pRBC use had a 73% increased risk of major nonbleeding complications, and those who were exposed to high-FFP use had a 2.2-fold increased risk of major nonbleeding complications. These increases were independent of patients' preoperative comorbid, physiologic, and hematologic conditions and were further independent of intraoperative factors known to be associated with poor outcomes.

These findings are consistent with prior reports. Obi et al[7] recently showed that emergency status was independently associated with a 40% increased odds of perioperative blood transfusion in a study of 2,946 vascular surgery patients (25% of whom required blood transfusion). This study and others have demonstrated that perioperative transfusion is independently associated with adverse outcomes (to include 85% to 138% increased odds of morbidity, 2.7 to 7.4-fold increased odds of pneumonia, and 2.4 to 6.9-fold increased odds of mortality).[6–8] These studies were limited by an absence of comparison between blood lost and blood transfused. Furthermore, these studies had no findings concerning FFP transfusion, and were limited in generalizability to vascular, colorectal, and gynecologic cancer patients.

The differences between EGS and NEGS patients in our study were consistent with prior reports. A nationally representative sample of more than 66,000 patients also found that history of disseminated cancer and history of weight loss were not significantly different between EGS and NEGS patients.[1] However, we may have been underpowered to detect differences in select preoperative variables (sex, body mass index, smoking history, alcohol history, and history of steroid use), which were shown to be different between EGS and NEGS in the larger study. Our postoperative outcomes data were also consistent with this prior report, which showed 30-day mortality rates of 12.50% in EGS vs 2.66% in NEGS and major complication rates of 32.8% in EGS vs 12.74% in NEGS. We have expanded on the findings of this report by demonstrating that intraoperative resuscitation variables, vital signs, and laboratory measurements were also significantly different between EGS and NEGS, and that differences in transfusion practices contribute to adverse outcomes in EGS.

Many studies have demonstrated that evidence-based transfusion guidelines reduce blood product overutilization.[26–30] Despite this, evidence-based intraoperative blood product transfusion guidelines for the nonmassively transfused, nontrauma patient do not currently exist. In the absence of guidelines, intra-operative pRBC transfusion is often left to physician judgment and is therefore subject to interphysician variability. By contrast, the recommendation for high-FFP:pRBC ratios was derived from studies showing mortality reduction among trauma patients (26.0% mortality in the high [1:1] transfusion group vs 87.5% in the low [1:4] transfusion group).[11] However, that mortality reduction was not seen in the nonmassively transfused subpopulation. Evidence-based guidelines for blood product transfusion during EGS might reduce blood product overutilization in a nonmassively transfused population in whom transfusion at high rates may not confer a mortality reduction and may even contribute to increased morbidity and mortality.

We have several hypotheses to explain why EGS patients may be at increased risk of exposure to high-intraoperative transfusion rates. First, EGS patients had greater physiologic and hemodynamic derangements than NEGS patients. This may lead to bias toward more aggressive intervention in the context of emergencies. Second, a preponderance of emergency procedures was performed at night. There may be differences in providers and resources between day and night. Finally, the institutions participating in this study have mature acute care surgical services performing most of the EGS procedures at night. These surgeons have advanced training in-trauma management, and may therefore default to trauma literature in the absence of EGS literature. Further research is needed to elucidate causative factors for such aggressive transfusion.

There are several important limitations to this study. First, we had a small sample size. Of 992 patients, only 101 patients (10.2%) were exposed to high-intraoperative pRBC use and 63 patients (6.4%) were exposed to high-intraoperative FFP use. Nonetheless, the effect size was strong enough that a statistically significant impact of these variables could be detected. Second, our study was limited to 2 academic medical centers in the same major metropolitan area. Both of these hospitals are level I trauma centers with dedicated acute care surgical services who are responsible for the vast majority of EGS cases. This limits the generalizability of our results. Third, our study was limited to only 14 procedures. In designing this study, we opted to limit the procedures to those that were representative of procedures performed by an acute care surgeon, and procedures that were common to both EGS and NEGS. Although we believe this constraint improved the rigor of the comparison between EGS and NEGS, this constraint further reduces the generalizability of our results. Finally, the collection of intraoperative variables had some inherent flaws. Blood loss estimates are imprecise, hand-written anesthesia records fail to capture data in between points, which can be as far apart as 5 minutes, and electronic anesthesia records can have artifacts secondary to continuous monitoring.[31,32] We addressed this limitation by using a single reviewer to collect all intraoperative data in the same manner to prevent inter-rater reliability issues.

Our findings have important implications for the field of EGS. These data suggest that a change in transfusion practice during EGS could reduce morbidity. Our group is currently working on a checklist including a preoperative discussion to define appropriate transfusion thresholds at the start of EGS procedures to avoid unnecessary

transfusion and excess morbidity. Prospective studies are needed to define optimal transfusion ratios in nonmassively transfused EGS patients.

Conclusion

We have demonstrated that EGS patients receive higher rates of intraoperative blood product transfusion for the same blood loss as NEGS patients, and that this increased exposure to blood products contributes to the increased morbidity found in EGS. To address these findings, evidence based guidelines for blood product transfusion during EGS should be established.

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.amjsurg.2015.11.031.

References

1. Havens JM, Peetz AB, Do WS, et al. The excess morbidity and mortality of emergency general surgery. J Trauma Acute Care Surg 2015;78:306–11.
2. Ingraham AM, Cohen ME, Bilimoria KY, et al. Comparison of hospital performance in nonemergency versus emergency colorectal operations at 142 hospitals. J Am Coll Surg 2010;210:155–65.
3. Ingraham AM, Cohen ME, Raval MV, et al. Comparison of hospital performance in emergency versus elective general surgery operations at 198 hospitals. J Am Coll Surg 2011;212:20–28.e21.
4. Sorensen LT, Malaki A, Wille-Jorgensen P, et al. Risk factors for mortality and postoperative complications after gastrointestinal surgery. J Gastrointest Surg 2007;11:903–10.
5. Patel SS, Patel MS, Goldfarb M, et al. Elective versus emergency surgery for ulcerative colitis: a National Surgical Quality Improvement Program analysis. Am J Surg 2013;205:333–7; discussion 337–338.
6. Halabi WJ, Jafari MD, Nguyen VQ, et al. Blood transfusions in colorectal cancer surgery: incidence, outcomes, and predictive factors: an American College of Surgeons National Surgical Quality Improvement Program analysis. Am J Surg 2013;206:1024–32.
7. Obi AT, Park YJ, Bove P, et al. The association of perioperative transfusion with 30-day morbidity and mortality in patients undergoing major vascular surgery. J Vasc Surg 2015;61:1000–1009.e1.
8. Prescott LS, Aloia TA, Brown AJ, et al. Perioperative blood transfusion in gynecologic oncology surgery: analysis of the National Surgical Quality Improvement Program database. Gynecol Oncol 2015;136:65–70.
9. Matsuyama T, Iranami H, Fujii K, et al. Risk factors for postoperative mortality and morbidities in emergency surgeries. J Anesth 2013;27:838–43.
10. Borgman MA, Spinella PC, Perkins JG, et al. The ratio of blood products transfused affects mortality in patients receiving massive transfusions at a combat support hospital. J Trauma 2007;63:805–13.
11. Duchesne JC, Hunt JP, Wahl G, et al. Review of current blood transfusions strategies in a mature level I trauma center: were we wrong for the last 60 years? J Trauma 2008;65:272–6; discussion 276–278.
12. Holcomb JB, Tilley BC, Baraniuk S, et al. Transfusion of plasma, platelets, and red blood cells in a 1:1:1 vs a 1:1:2 ratio and mortality in patients with severe trauma: the PROPPR randomized clinical trial. JAMA 2015;313:471–82.
13. Holcomb JB, Wade CE, Michalek JE, et al. Increased plasma and platelet to red blood cell ratios improves outcome in 466 massively transfused civilian trauma patients. Ann Surg 2008;248:447–58.
14. Akinbami F, Askari R, Steinberg J, et al. Factors affecting morbidity in emergency general surgery. Am J Surg 2011;201:456–62.
15. Kwan TL, Lai F, Lam CM, et al. Population-based information on emergency colorectal surgery and evaluation on effect of operative volume on mortality. World J Surg 2008;32:2077–82.
16. Shafi S, Aboutanos MB, Agarwal Jr S, et al. Emergency general surgery: definition and estimated burden of disease. J Trauma Acute Care Surg 2013;74:1092–7.
17. Gawande AA, Kwaan MR, Regenbogen SE, et al. An Apgar score for surgery. J Am Coll Surg 2007;204:201–8.
18. Regenbogen SE, Bordeianou L, Hutter MM, et al. The intraoperative surgical Apgar score predicts postdischarge complications after colon and rectal resection. Surgery 2010;148:559–66.
19. Regenbogen SE, Ehrenfeld JM, Lipsitz SR, et al. Utility of the surgical Apgar score: validation in 4119 patients. Arch Surg 2009;144:30–6; discussion 37.
20. Regenbogen SE, Lancaster RT, Lipsitz SR, et al. Does the surgical Apgar score measure intraoperative performance? Ann Surg 2008;248:320–8.
21. Kauvar DS, Sarfati MR, Kraiss LW. Intraoperative blood product resuscitation and mortality in ruptured abdominal aortic aneurysm. J Vasc Surg 2012;55:688–92.
22. Riley JB, Samolyk KA. On-line autotransfusion waste calculator. J Extra Corpor Technol 2008;40:68–73.
23. Allison PD. Multiple imputation for missing data: a cautionary tale. Sociol Methods Res 2000;28:301–9.
24. Barnard J, Meng XL. Applications of multiple imputation in medical studies: from AIDS to NHANES. Stat Methods Med Res 1999;8:17–36.
25. Horton NJ, Kleinman KP. Much ado about nothing: a comparison of missing data methods and software to fit incomplete data regression models. Am Statistician 2007;61:79–90.
26. Adams ES, Longhurst CA, Pageler N, et al. Computerized physician order entry with decision support decreases blood transfusions in children. Pediatrics 2011;127:e1112–9.
27. Collins RA, Triulzi DJ, Waters JH, et al. Evaluation of real-time clinical decision support systems for platelet and cryoprecipitate orders. Am J Clin Pathol 2014;141:78–84.
28. Goodnough LT, Shieh L, Hadhazy E, et al. Improved blood utilization using real-time clinical decision support. Transfusion 2014;54:1358–65.
29. Rothschild JM, McGurk S, Honour M, et al. Assessment of education and computerized decision support interventions for improving transfusion practice. Transfusion 2007;47:228–39.
30. Yerrabothala S, Desrosiers KP, Szczepiorkowski ZM, et al. Significant reduction in red blood cell transfusions in a general hospital after successful implementation of a restrictive transfusion policy supported by prospective computerized order auditing. Transfusion 2014;54(10 Pt 2):2640–5.
31. Cook RI, McDonald JS, Nunziata E. Differences between handwritten and automatic blood pressure records. Anesthesiology 1989;71:385–90.
32. Reich DL, Wood Jr RK, Mattar R, et al. Arterial blood pressure and heart rate discrepancies between handwritten and computerized anesthesia records. Anesth Analg 2000;91:612–6.

Appendix A Current Procedural Terminology (CPT) codes common to emergency and nonemergency general surgery

Group	CPT	CPT description
A	44,143	Colectomy, partial, with end colostomy and closure of distal segment (Hartmann type procedure)
	44,150	Colectomy, total, abdominal, without proctectomy, with ileostomy or ileoproctostomy
	44,120	Enterectomy, resection of small intestine, single resection, and anastomosis
B	49,561	Repair initial incisional or ventral hernia, incarcerated or strangulated
	49,566	Repair recurrent incisional or ventral hernia, incarcerated or strangulated
C	35,633	Bypass graft, with other than vein; ilio-mesenteric
D	35,537	Bypass graft, with vein; aortoiliac
	35,538	Bypass graft, with vein; aortobi-iliac
	35,539	Bypass graft, with vein; aortofemoral
	35,540	Bypass graft, with vein; aortobifemoral
	35,637	Bypass graft, with other than vein; aortoiliac
	35,638	Bypass graft, with other than vein; aortobi-iliac
	35,646	Bypass graft, with other than vein; aortofemoral
	35,647	Bypass graft, with other than vein; aortobifemoral

Appendix B Baseline preoperative characteristics of patients stratified by high-pRBC use

Variable	Not exposed to high-pRBC use ($n = 891$)	Exposed to high-pRBC use ($n = 101$)	*P*	Missing n
Age*, y	60.16 ± 15.49	63.37 ± 16.38	.0379	0
Male, (%)	41.86	47.52	.2755	0
Body mass index*, kg/m^2	27.68 ± 7.45	26.11 ± 7.27	.0165	28
Diabetes mellitus, (%)	11.90	13.86	.4880	0
Dyspnea at rest, (%)	1.91	6.93	<.0001	0
Partially/totally dependent functional status, (%)	13.02	45.54	<.0001	0
Chronic obstructive pulmonary disease, (%)	5.72	8.91	.2031	0
Hypertension requiring medications, (%)	46.69	52.48	.2699	0
Disseminated cancer, (%)	12.68	12.87	.9569	0
Open wound, (%)	6.51	17.82	.0001	0
Smoking history, (%)	18.52	13.86	.2490	0
Alcohol history, (%)	1.17	3.85	.2577	625
Patients presenting from home, (%)	82.15	60.40	<.0001	0
Steroid use, (%)	11.56	19.80	.0173	0

pRBC = packed red blood cells.
*Data are given as mean ± standard deviation.

Appendix C Baseline preoperative characteristics of patients stratified by high-FFP use

Variable	Not exposed to high-FFP use (n = 929)	Exposed to high-FFP use (n = 63)	P	Missing n
Age*, y	60.10 ± 15.61	66.17 ± 14.61	.0026	0
Male, (%)	42.09	47.62	.3903	0
Body mass index*, kg/m^2	27.67 ± 7.53	25.24 ± 5.43	.0250	28
Diabetes mellitus, (%)	11.52	15.43	.0181	0
Dyspnea at rest, (%)	1.83	11.11	<.0001	0
Partially/totally dependent functional status, (%)	14.21	47.62	<.0001	0
Chronic obstructive pulmonary disease , (%)	5.06	20.63	<.0001	0
Hypertension requiring medications, (%)	46.61	57.14	.1053	0
Disseminated cancer, (%)	12.59	14.29	.6965	0
Open wound, (%)	6.67	22.22	<.0001	0
Smoking history, (%)	18.51	11.11	.1394	0
Alcohol history, (%)	1.43	.00	.6096	625
Patients presenting from home, (%)	81.05	63.49	.0006	0
Steroid use, (%)	11.73	22.22	.0145	0

FFP = fresh frozen plasma.
*Data are given as mean ± standard deviation.

Appendix D Preoperative clinical and physiologic characteristics of patients stratified by high-pRBC use

Variable	Not exposed to high-pRBC use (n = 891)	Exposed to high-pRBC use (n = 101)	P	Missing n
Ascites within 30 d, (%)	3.59	10.89	.0006	0
Congestive heart failure within 30 d, (%)	1.12	8.91	<.0001	0
Weight loss >10% in last 6 mon, (%)	10.44	17.82	.0258	0
Ventilator dependence within 48 h, (%)	4.49	21.78	<.0001	0
Acute renal failure within 24 h, (%)	2.13	7.92	.0007	0
Pneumonia, (%)	2.57	14.52	<.0001	308
Currently requiring dialysis within 2 wk, (%)	1.35	8.91	<.0001	0
Impaired sensorium, (%)	4.82	16.13	.0003	308
Systemic inflammatory response syndrome, (%)	7.94	13.86	<.0001	9
Septic shock, (%)	7.14	29.70	<.0001	9
Sepsis within 48 h, (%)	10.54	20.79	<.0001	9
Bleeding disorders, (%)	10.10	34.65	<.0001	0
pRBC transfusion within 72 h, (%)	1.91	12.87	<.0001	0
American Society of Anesthesia class ≥ IV, (%)	8.65	39.60	<.0001	1
Laboratory values (90 d)*				
Hematocrit (%)	36.79 ± 5.57	28.74 ± 5.07	<.0001	18
Partial thromboplastin time (sec)	30.44 ± 7.13	38.28 ± .28	<.0001	197
International normalized ratio	1.16 ± .26	1.41 ± .40	<.0001	148
Albumin	3.64 ± .73	2.67 ± .75	<.0001	176
Creatinine	1.05 ± .79	1.48 ± 1.20	.0021	26

pRBC = packed red blood cells.
*Data are given as mean ± standard deviation.

Appendix E Preoperative clinical and physiologic characteristics of patients stratified by high-FFP use

Variable	Not exposed to high-FFP use (n = 929)	Exposed to high-FFP use (n = 63)	P	Missing n
Ascites within 30 d, (%)	3.66	14.29	.0001	0
Congestive heart failure within 30 d, (%)	1.18	12.70	<.0001	0
Weight loss >10% in last 6 mon, (%)	10.98	14.29	.4207	0
Ventilator dependence within 48 h, (%)	4.63	30.16	<.0001	0
Acute renal failure within 24 h, (%)	2.05	12.70	<.0001	0
Pneumonia, (%)	3.43	6.98	.2308	331
Currently requiring dialysis within 2 weeks, (%)	1.40	12.70	<.0001	0
Impaired sensorium, (%)	4.52	25.58	<.0001	331
Systemic inflammatory response syndrome, (%)	7.93	17.46	<.0001	9
Septic shock, (%)	7.61	36.51	<.0001	9
Sepsis within 48 h, (%)	11.09	19.05	<.0001	9
Bleeding disorders, (%)	10.55	42.86	<.0001	0
pRBC transfusion within 72 h, (%)	2.80	6.35	.1115	0
American Society of Anesthesia class ≥ IV – (%)	9.49	46.04	<.0001	1
Laboratory values (90 d)*				
Hematocrit (%)	36.22 ± 5.93	32.09 ± 6.35	<.0001	18
Partial thromboplastin time (sec)	30.45 ± 7.34	42.81 ± 23.11	<.0001	200
International normalized ratio	1.14 ± .18	1.80 ± .56	<.0001	150
Albumin	3.57 ± .78	2.89 ± .75	<.0001	193
Creatinine	1.04 ± .78	1.88 ± 1.28	<.0001	28

pRBC = packed red blood cells; FFP = fresh frozen plasma.
*Data are given as mean ± standard deviation.

Appendix F Intraoperative characteristics of patients stratified by high-pRBC use

Variable	Not exposed to high-pRBC use (n = 891)	Exposed to high-pRBC use (n = 101)	P	Missing n
Emergency general surgery, (%)	30.19	62.38	<.0001	0
Night-time surgery (start time: 6pm to 6am), (%)	17.17	34.65	<.0001	0
Length of operation (min)*	150.05 ± 90.58	179.08 ± 118.25	<.0001	0
Intraoperative blood loss and resuscitation*				
Estimated blood loss	249.56 ± 458.08	358.02 ± 348.45	<.0001	0
Crystalloid volume (cc)	2,645.69 ± 1,477.91	3,006.56 ± 1,973.48	.1798	2
Albumin volume (cc)	140.19 ± 371.70	320.79 ± 482.04	<.0001	2
Transfusion of pRBCs (units)	.14 ± .59	2.29 ± 1.31	<.0001	0
Transfusion of FFP (units)	.13 ± .69	1.27 ± 1.93	<.0001	0
High FFP use, (%)	4.04	26.73	<.0001	0
Intraoperative vital signs and pressors*				
Lowest mean arterial pressure	62.36 ± 9.90	58.08 ± 9.17	.0001	8
Lowest heart rate	63.63 ± 15.13	75.95 ± 17.15	<.0001	11
Lowest temperature (degrees C)	35.60 ± 1.69	35.50 ± 1.71	.7510	62
>2 pressure support medications, (%)	2.75	12.12	<.0001	22
Intraoperative laboratory measurements*				
Lowest pH	7.32 ± .10	7.29 ± .14	.1034	659
Highest blood glucose	152.44 ± 65.26	175.24 ± 72.36	.0010	565

FFP = fresh frozen plasma; pRBC = packed red blood cells.
*Data are given as mean ± standard deviation.

Appendix G Intraoperative characteristics of patients stratified by high-FFP use

Variable	Not exposed to high-FFP use (n = 929)	Exposed to high-FFP use (n = 63)	P	Missing n
Emergency general surgery, (%)	30.36	79.37	<.0001	0
Night-time surgery (start time: 6pm to 6am), (%)	17.33	42.86	<.0001	0
Length of operation (min)*	151.02 ± 92.82	182.35 ± 107.97	.0120	0
Intraoperative blood loss and resuscitation*				
Estimated blood loss	234.98 ± 421.64	638.57 ± 639.73	<.0001	0
Crystalloid volume (cc)	2664.08 ± 1481.40	2953.65 ± 2213.46	.9729	2
Albumin volume (cc)	142.05 ± 365.03	402.38 ± 588.84	<.0001	2
Transfusion of pRBCs (units)	.26 ± .78	1.76 ± 1.78	<.0001	0
Transfusion of FFP (units)	.04 ± .27	3.22 ± 2.00	<.0001	0
High pRBC use, (%)	7.97	42.86	<.0001	0
Intraoperative vital signs and pressors*				
Lowest mean arterial pressure	62.07 ± 10.02	59.69 ± 7.85	.0798	9
Lowest heart rate	64.14 ± 15.40	75.94 ± 17.39	<.0001	12
Lowest temperature (degrees C)	35.60 ± 1.64	35.44 ± 2.30	.9300	67
>2 pressure support medications, (%)	3.08	13.12	.0132	23
Intraoperative laboratory measurements*				
Lowest pH	7.32 ± .10	7.26 ± .14	.0017	669
Highest blood glucose	153.98 ± 66.62	177.64 ± 69.00	.0089	565

FFP = fresh frozen plasma; pRBC = packed red blood cells.
*Data are given as mean ± standard deviation.