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Is there a need for fresh frozen plasma and platelet transfusion in trauma patients receiving submassive transfusion?

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ABSTRACT

Background Blood transfusions have become a vital intervention in trauma care. There are limited data on the safety and effectiveness of submassive transfusion (SMT), that is defined as receiving less than 10 units packed red blood cells (PRBCs) in the first 24 hours. This study aimed to evaluate the efficacy and safety of fresh frozen plasma (FFP) and platelet transfusions in patients undergoing SMT.

Methods This is a retrospective cohort, reviewing the Trauma Quality Improvement Program database spanning 3 years (2016 to 2018). Adult patients aged 18 years and older who had received at least 1 unit of PRBC within 24 hours were included in the study. We used a multivariate regression model to analyze the cut-off units of combined resuscitation (CR) (which included PRBCs along with at least one unit of FFP and/or platelets) that leads to survival improvement. Patients were then stratified into two groups: those who received PRBC alone and those who received CR. Propensity score matching was performed in a 1:1 ratio.

Results The study included 85 234 patients. Based on the multivariate regression model, transfusion of more than 3 units of PRBC with at least 1 unit of FFP and/or platelets demonstrated improved mortality compared with PRBC alone. Among 66 319 patients requiring SMT and >3 units of PRBCs, 25 978 received PRBC alone, and 40 341 received CR. After propensity matching, 4215 patients were included in each group. Patients administered CR had a lower rate of complications (15% vs 26%), acute respiratory distress syndrome (3% vs 5%) and acute kidney injury (8% vs 11%). Rates of sepsis and venous thromboembolism were similar between the two groups. Multivariate regression analysis indicated that patients receiving 4 to 7 units of PRBC alone had significantly higher ORs for mortality than those receiving CR.

Conclusion Trauma patients requiring more than 3 units of PRBCs who received CR with FFP and platelets experienced improved survival and reduced complications.

Level of evidence Level III retrospective study.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Submassive transfusion (SMT) is vital in trauma care.

⇒ Maintaining a balanced resuscitation improved survival in patients undergoing blood product transfusion.

WHAT THIS STUDY ADDS

⇒ This study aimed to evaluate the efficacy and safety of fresh frozen plasma (FFP) and platelet transfusions in patients undergoing SMT.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study assessed the effects of adding FFP and platelets to the transfused PRBC.

⇒ The results could influence the patient's outcomes that could, in turn, be used in the improvement of the patient's healthcare.

INTRODUCTION

Trauma-related injuries remain one of the significant causes of mortality, especially in the younger population. According to the National Vital Statistics Reports, 6.1% of deaths are due to trauma injuries (unintentional trauma injuries) in the USA.[1] Hypovolemia and decreased tissue perfusion due to hemorrhage are regarded as the most preventable causes of death in patients suffering from trauma-related injuries.[2–6] As a result, transfusion of appropriate blood products is regarded as the gold standard for managing trauma-related injuries.

Massive transfusion protocols (MTPs) are established guidelines for the rapid and aggressive administration of blood products to critically injured patients who are experiencing massive blood loss. These protocols are designed to improve patient outcomes by providing timely and appropriate transfusion therapy, which is critical for preventing or reversing shock and ensuring adequate tissue perfusion. MTPs are typically activated in trauma centers, emergency departments (EDs) or other settings where patients with life-threatening bleeding require urgent resuscitation. The use of MTPs has become increasingly common in recent years, and they are effective in reducing mortality rates and improving patient outcomes in a variety of clinical settings.[7 8]

However, massive transfusion (MT) occurs in about 3% of civilian and 8% of military trauma patients.[9] The rest of the patients only receive less than 10 units PRBCs in the first 24 hours that is referred to as submassive transfusion (SMT). The combined resuscitation (CR), that is defined as transfusion of fresh frozen plasma (FFP) and platelet along with PRBCs, has been the standard of care in patients requiring MT.[8 9] Nevertheless, no

studies have investigated the impact of CR in trauma patients needing SMT and its effects on patient's survival.

Therefore, the overall goal of our study was to evaluate if CR with PRBC, along with FFP and/or platelets is associated with improved outcomes compared with the PRBC alone group in trauma patients requiring SMT and also to evaluate the cut-off of PRBC transfusion above which patients should receive CR and not PRBC alone. The primary outcome was to analyze the cut-off of number of PRBC transfusion above which co-administration of FFP/platelets is associated with improved in-hospital mortality. Our secondary outcome was to evaluate the overall complications as well as the risk of thromboembolic complications in patients receiving CR when compared with those receiving PRBC alone. We hypothesized that CR with PRBC, along with FFP and/or platelets is associated with improved outcomes compared with the PRBC alone group in trauma patients requiring SMT.

METHODS

Study design and population

We conducted a retrospective cohort study analysis acquired from the American College of Surgeons Trauma Quality Improvement Program (ACS-TQIP), targeting a 3-year (2016 to 2018) database. We scrutinized all trauma patients in ACS-TQIP during this 3-year study period. The TQIP is a robust data set administered by the ACS that can be used to compare risk-adjusted outcomes in trauma centers across the USA—more than 700 trauma centers across the USA report data to the TQIP. Specialized data abstractors collect this data set at each institution, and they record more than 100 variables, including patient demographics; prehospital Emergency Medical Services vitals and prehospital interventions; ED vitals; ED disposition; injury parameters (mechanism and mode of injury); objective injury scores (Injury Severity Score (ISS) and Abbreviated Injury Scale (AIS)); in-hospital interventions (blood transfusion), and outcomes (complications, in-hospital mortality and discharge disposition).

Consent

All the data in TQIP are de-identified, and this is a retrospective study and non-obligatory to patient consent.

Inclusion and exclusion criteria

We included all adult trauma patients (age 18 years and above) who received SMT within the first 24 hours from ACS-TQIP during the 3-year study period. SMT is defined as receiving less than 10 units PRBC in the first 24 hours. We excluded all patients transferred from other hospitals or dead within the first 24 hours of arrival. The flow diagram of this study is shown in figure 1.

Operational definitions

Submassive transfusion (SMT): SMT was the transfusion of fewer than 10 units of packed red blood cells (PRBCs) with/without FFP and/or platelets in the first 24 hours post-trauma.

Combined resuscitation (CR): Transfusion of PRBCs combined with at least 1 unit of FFP and/or platelets.

Data points

We extracted the following data points from the TQIP data set: patients' demographic characteristics, including age, gender, and race; prehospital and ED vital parameters, including systolic blood pressure (SBP), heart rate (HR), temperature, and

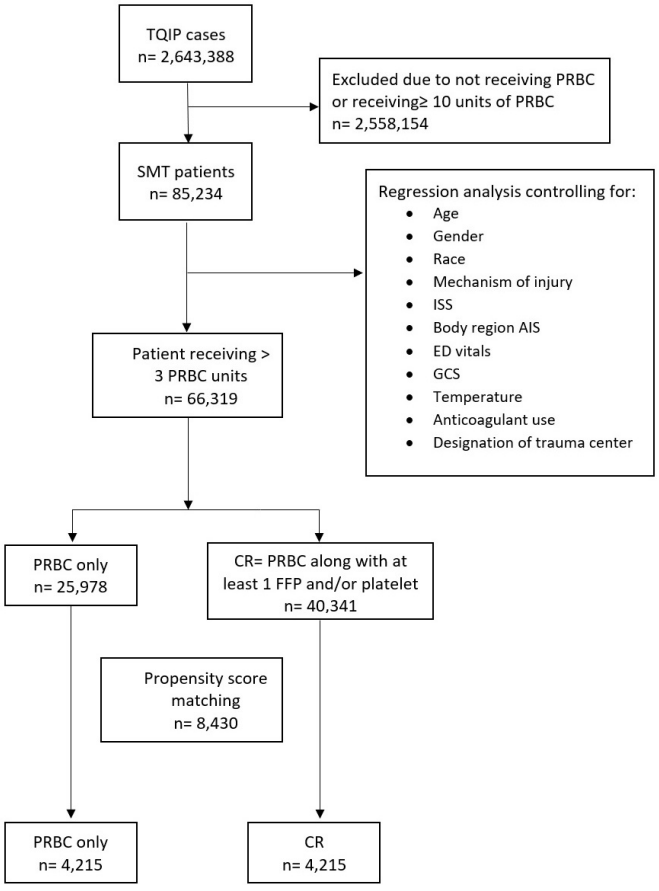

Figure 1 Flow diagram of all patients. AIS, Abbreviated Injury Scale; CR, combined resuscitation; ED, emergency department; GCS, Glasgow Coma Scale; ISS, Injury Severity Score; PRBC, packed red blood cell; SMT, submassive transfusion; TQIP, Trauma Quality Improvement Program.

Glasgow Coma Scale (GCS); injury parameters, including mechanism of injury, ISS and body region-specific AIS; complications, including, acute respiratory distress syndrome (ARDS), acute kidney injury (AKI), sepsis, venous thromboembolism (VTE), and mortality.

Patient stratification

We first performed backward logistic stepwise multivariate regression analysis and evaluated the mortality between the PRBC alone group and CR group for each patient group (PRBC 1 to PRBC 9) to identify the cut-off after which CR improves survival. The regression models are further explained in detail. Based on that cut-off those patients were than stratified into the PRBC alone group and CR group to evaluate the complications.

Outcomes

The primary outcome was the rate of mortality. Secondary outcomes were considered complications, including AKI, ARDS, sepsis, and VTE.

Data reporting and statistical analysis

For continuous variables, we reported data as a mean±SD. Categorical variables were presented as frequencies and percentages. For continuous non-parametric data, median with IQR was used. We performed a χ^2 test to explore the differences in categorical variables between the two groups. In addition, we used the independent Student's t-test for continuous parametric data

and the Mann-Whitney U test for constant non-parametric data. We considered $p<0.05$ as statistically significant for our study.

We performed backward logistic stepwise multivariate regression analysis controlling for age, gender, race, mechanism of injury, ISS, body region-specific AIS, ED vitals, GCS, temperature, anticoagulant use and designation of trauma center, and evaluated the mortality between the PRBC alone group and the CR group for each patients group (PRBC 1 to PRBC 9) to identify the cut-off after which CR improves survival. An individual regression analysis model was run for each PRBC level 1 to 9 between the PRBC alone and CR group and each model fit was assessed by the Hosmer-Lemeshow test. In the multivariable regression model, the Hosmer-Lemeshow test exceeded 0.05, and the tolerance was more significant than 0.1 for all independent variables with a variance inflation factor of less than 10.0.

We determined the cut-off of >3 PRBC, group obtained from the multivariate variate regression analysis, for performing the propensity score matching (PSM). Patients who received >3 PRBCs alone or along with FFP and/or platelets (CR group) were propensity score matched. Propensity score matching is a statistical technique used to balance covariates between treatment groups by matching individuals with similar propensity scores. It estimates the probability of assignment to a particular treatment based on observed characteristics. This method is useful in observational studies to reduce selection bias and mimic the random assignment of participants in experimental designs, thereby improving the validity of causal inference. The technique is described in detail by Brookhart and colleagues.[10] Patients who received >3 PRBCs alone were matched in a 1:1 ratio to a similar cohort of patients receiving >3 PRBCs along with FFP and/or platelets. PSM was used to match both groups for demographics (age, gender, race, body mass index), vital signs (SBP, HR, GCS), mechanism of injury, ISS, body region specific-AIS, comorbidities, preinjury anticoagulant use, and level of trauma center. In our PSM, the dependent variable was the receipt of CR. Using a logistic regression model, a propensity score was generated for each patient based on confounding factors. We used the standardized mean difference to assess for balance after matching, using a maximum of 0.1 as a strong threshold. The standardized mean differences for all variables used in our propensity score matching model were below this threshold, suggesting that groups were balanced. The two groups were matched using the nearest neighbor method without replacement. Owing to unavailability of hospital-specific data, we could not account for intrahospital cluster effects. However, to decrease the interhospital variation of management strategies, both groups were matched for the level of trauma centers. All statistical analyses were performed using the Statistical Package for Social Sciences (SPSS, V.24; IBM, Armonk, New York, USA) with a significance threshold of 0.05.

RESULTS

A total of 85 234 patients received SMT and were included in the study. The demographic details of the study participants are provided in table 1. We performed backward logistic stepwise multivariate regression analysis and evaluated the mortality between the PRBC alone group and CR group for each patients group (PRBC 1 to PRBC 9) to identify the cut-off after which CR improves survival. This is demonstrated in figure 2. Adjusted analysis based on the multivariate regression model demonstrated that CR with administration of PRBC along with FFP and/or platelets in patients only receiving 1 unit to 3 units of PRBC is not associated with improved mortality when compared with patients who did not receive any FFP and platelets and received PRBC only. However, in patients receiving more than 3 units of PRBC, the CR group had improved mortality when compared with the PRBC alone group (4 PRBC group OR: 0.8, 5 PRBC group OR: 0.7, 6 PRBC group OR: 0.8, 7 PRBC group OR: 0.7). Even though the OR for the 8 PRBC group and 9 PRBC group was also below 1, however, due to the decreased sample size of patients receiving the 8 or 9 PRBC but no platelet group, CR in patients who received 8 or 9 PRBC did not achieve statistical significance. The results of univariate and multivariate regression models are summarized in table 2. The number of patients in each group is shown in table 3. These findings are demonstrated in figure 2.

Table 1 Demographic details of the study participants

Parameters		Values
Age (years) (mean±SD)		53±21
Gender (male) (%)		68.5%
Race (white) (%)		74.4%
Mechanism of injury (%)	Penetrating	16%
	Blunt	84%
Injuries	Severe TBI AIS≥3	8%
	Severe chest AIS ≥3	15%
	Severe abdomen AIS >3	25%
Extremity AIS >3		28%
ISS (median (IQR))		11 (9 to 17)
ED vitals	SBP, mean±SD	87±52
	HR, mean±SD	101±48
	Temperature mean±SD	37±5
	GCS, median (IQR)	13 (5 to 15)
Blood products transfused, (median (IQR))		
PRBC		4 (3 to 7)
FFP		2 (1 to 5)
Platelets		2(1 to 4)

AIS, Abbreviated Injury Scale; ED, emergency department; FFP, fresh frozen plasma; GCS, Glasgow Coma Scale; HR, heart rate; ISS, Injury Severity Score; PRBC, packed red blood cell; SBP, systolic blood pressure; TBI, traumatic brain injury.

Based on the cut-off of survival, benefit of CR in patients receiving >3 PRBC units was further analyzed. A total of 65 321 patients received SMT with >3 units of PRBC which were subclassified into two groups: 25 978 received PRBC alone and 40 341 received CR. After propensity matching, 4215 patients were placed into the group that received PRBC; on the collateral side, 4215 received CR. This is demonstrated in figure 1. Patients had no significant difference in age (p=0.85), gender (p=0.66), race (p=0.51), median ISS IQR (p=0.46), mean SBP (p=0.45), mean HR (p=0.85), mean temperature (p=0.99), and median GCS (IQR) (p=0.99). Patients suffering from AIS >3 are likelier to have been administered CR (24% vs 21%) (p=0.23) (table 4). Patients administered CR had a lower rate of any complications developed (15% vs 26%) (p=0.01), ARDS (3% vs 5%) (p=0.03), and AKI (8% vs 11%) (p=0.02). Overall, there was a similar rate of development of sepsis (p=0.45) and VTE (p=0.67). The secondary outcomes are shown in table 5.

DISCUSSION

CR of PRBC along with FFP and platelets has been the standard of care in severely injured patients requiring MT and multiple big studies and randomized controlled trials including the The Prospective, Observational, Multicenter, Major Trauma Transfusion (PROMMTT) and Pragmatic Randomized Optimal Platelet

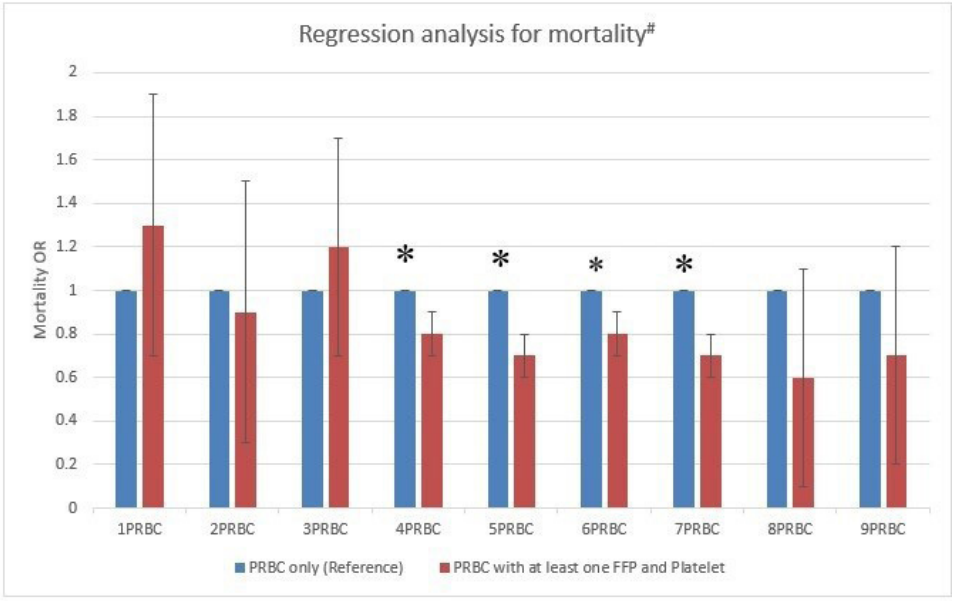

Figure 2 A depiction of significant ORs in patients receiving submassive transfusions. AIS, Abbreviated Injury Scale; ED, emergency department; FFP, fresh frozen plasma; GCS, Glasgow Coma Scale; ISS, Injury Severity Score; PRBC, packed red blood cell.

and Plasma Ratios (PROPPR) Trials have shown similar results. However, it is important to note that only about 3% of civilian and 8% of military trauma patients require MT. The majority of the rest of the patients are more likely to receive SMT, defined as less than 10 units of PRBC within the first 24 hours after trauma. Even though SMT constitutes most of the patients requiring transfusion, the literature on the adjunct administration of FFP and platelet along with PRBC or the optimal ratios has not been explored.[11] In our study we sought to answer the question in trauma patients requiring SMT; is there a need for FFP and/or platelets along with PRBC? The second question was to find the cut-off number of PRBC transfusions above which we should add FFP and/or platelets. To our knowledge this is the first study from a large nationwide database that has sought to answer these two important questions.

The results of our study suggest that administration of FFP and/or platelets along with PRBC in patients receiving more than 3 units of PRBC is associated with improved survival when compared with patients who only received PRBC without any adjunct products. It is mportant to note that FFP and/or platelets administration in patients receiving 1 unit to 3 units of PRBC was not associated with any improved survival. Interestingly enough, in patients who received 8 units or 9 units of PRBC, almost all patients received at least one or more FFP and/or platelets and the sample size in the PRBC alone group was so low that even though the mortality OR was low for patients with CR, it did not achieve statistical significance demonstrating the likely effect of type B error.

When we performed propensity matched analysis of patients on the cut-off of >3 PRBCs obtained from the regression analysis, we demonstrated that patients who received CR not only have a lower mortality, but CR was also associated with decreased ARDS and AKI when compared with the PRBC alone group. This association may be explained by multiple reasons including the decreased use of crystalloids in patients receiving FFP, as injudicious use of crystalloids has been associated with increased ARDS and AKI in literature. Another reason may be the early achievement of hemostasis in patients receiving CR and thus less hypotension and kidney injury.[12 13] Furthermore, this administration of FFP and/or platelets in patients receiving SMT was not associated with any increased risk of VTE or septic complications.

We found limited literature on the safety and efficacy of SMT in the form of CR used within the first 24 hours of a trauma injury. A randomized controlled trial comparing the transfusion of plasma, platelets, and red blood cells in a ratio of 1:1:1 vs 1:1:2, which involved a total of 680 patients (338 transfused with 1:1:1 vs 342 transfused with 1:1:2), indicated lower mortality rates in the patients receiving equal amounts of FFP, PRBCs, and platelets, compared with patients transfused with double the amount of PRBCs. Our study shows similar results regarding mortality; patients who received a higher number of PRBC transfusions had higher odds of mortality than patients who received CR. In the same trial, no statistically significant differences were found for complications, including ARDS, sepsis, anaphylaxis, and VTE.[14 15]

As indicated in a prospective cohort study, decreased mortality was associated with higher plasma and platelet ratios in patients who received at least 3 units of blood products during the first 24 hours after admission. Analysis of the PROMMTT data suggested that the transfusion of FFP and platelets could lead to an improved survival rate, which aligns with the primary outcome of our study, as indicated in figure 2.[6 16] In a secondary analysis of PROMMTT data, Hynes and colleagues evaluated data of 524 patients receiving >3 units of PRBCs during any 1-hour period in the first 6 hours. They reported that maintaining a high ratio of plasma/PRBC during damage-control resuscitationis independently associated with improved survival.[17] Our findings are in line with these data, supporting the use of CR in trauma patients.

In our study, a total of 85 234 patients who received SMT were evaluated. Our findings indicated that in patients receiving 1 unit to 3 units of PRBC, combined transfusion with FFP and/or platelets did not improve survival. However, for patients

Table 2 Univariate and multivariate analysis for mortality

Variable		Univariate		Multivariate	
		OR (95% CI)	P value	OR (95% CI)	P value
Age (every 10-year increment)		1.5 (1.4 to 2.4)	0.02	1.2 (1.1 to 3.5)	0.04
Gender	Male	Reference			
	Female	0.9 (0.6 to 3.1)	0.68	--	--
Race	White	Reference			
	Non-white	1.3 (1.0 to 2.4)	0.15	1.2 (0.6 to 2.9)	0.51
Mechanism of injury	Blunt	Reference			
	Penetrating	2.3 (1.8 to 3.1)	0.01	2.2 (1.6 to 3.5)	0.02
ISS (increase every 5 points)		1.7 (1.3 to 2.9)	0.02	1.3 (1.2 to 3.5)	0.03
Body region AIS	AIS <3	Reference			
	AIS >3	2.9 (1.9 to 3.5)	0.01	2.5 (2.0 to 3.6)	0.01
ED Vitals	No shock	Reference			
	Shock	2.5 (1.5 to 3.1)	0.01	2.1 (1.8 to 3.5)	0.01
Anticoagulant use		1.9 (1.0 to 2.6)	0.16	1.6 (0.9 to 3.2)	0.56
Designation of trauma center	Level III	Reference			
	Level II	0.8 (0.7 to 1.9)	0.21	--	--
	Level I	0.7 (0.6 to 0.9)	0.01	0.8 (0.6 to 0.9)	0.04
1 PRBC	PRBC alone	Reference			
	PRBC alone + FFP/platelet	--	--	1.3 (0.7 to 1.9)	0.56
2 PRBC	PRBC alone	Reference			
	PRBC alone + FFP/platelet	--	--	0.9 (0.3 to 1.5)	0.61
3 PRBC	PRBC alone	Reference			
	PRBC alone + FFP/platelet	--	--	1.2 (0.7 to 1.7)	0.59
4 PRBC	PRBC alone	Reference			
	PRBC alone + FFP/platelet	--	--	0.8 (0.7 to 0.9)	0.03
5 PRBC	PRBC alone	Reference			
	PRBC alone + FFP/platelet	--	--	0.7 (0.6 to 0.8)	0.2
6 PRBC	PRBC alone	Reference			
	PRBC alone + FFP/platelet	--	--	0.8 (0.7 to 0.9)	0.04
7 PRBC	PRBC alone	Reference			
	PRBC alone + FFP/platelet	--	--	0.7 (0.6 to 0.8)	0.03
8 PRBC	PRBC alone	Reference			
	PRBC alone + FFP/platelet	--	--	0.6 (0.1 to 1.1)	0.82
9 PRBC	PRBC alone	Reference			
	PRBC alone + FFP/platelet	--	--	0.7 (0.2 to 1.2)	0.79

AIS, Abbreviated Injury Scale; ED, emergency department; FFP, fresh frozen plasma; ISS, Injury Severity Score; PRBC, packed red blood cell.

receiving more than 3 units of PRBC, combined transfusion resulted in significantly reduced mortality rates. Propensity score matching further validated these results in a subgroup of 66 319 patients, demonstrating that those who received combined transfusion had fewer complications, including ARDS and AKI. In 2011, Holcomb and colleagues retrospectively evaluated data of 22 level I trauma centers during 12 months in 2005 to 2006. They examined low (>1:20), medium (1:2), and high (1:1) platelet:RBC ratios, and observed that higher platelet ratios were associated with increased survival rates at 24 hours and 30 days (p<0.001 for both). They also observed decreased rates of truncal hemorrhage in patients with higher platelet ratios (low: 67%, medium: 60%, high: 47%, p=0.04).[18] These data are consistent with our findings, showing improved survival with combined transfusion of PRBCs, FFP, and/or platelets in patients receiving >3 PRBC units.

Table 3 Frequency of patients based on the number of received products in the regression model

Number of PRBC units	Total (n (%))	Group (n (%))	
		PRBC alone	CR
1	6819 (8%)	6320 (93%)	499 (7%)
2	6815 (8%)	5945 (87%)	870 (13%)
3	5970 (7%)	4356 (73%)	1614 (27%)
4	14 490 (17%)	6945 (48%)	7545 (52%)
5	11 933 (14%)	7004 (59%)	4929 (41%)
6	13 637 (16%)	8956 (66%)	4681 (34%)
7	9376 (11%)	7856 (84%)	1520 (16%)
8	8523 (10%)	8459 (99.7%)	28 (0.3%)
9	7671 (9%)	7625 (99%)	46 (1%)

CR, combined resuscitation; PRBC, packed red blood cell.

The results of our study would add to the body of literature that even in the non-severely injured patients requiring SMT, administration of balanced resuscitation is associated with improved outcomes. This is especially important if patients require at least more than 3 units of PRBC pointing towards the role of FFP and platelets in achieving definite control of bleeding and maintaining hemodynamic stability. The next step

Table 4 A tabulation of demographics of matched data

Matched data		PRBC alone	CR	P value
Age (years) (mean±SD)		52±1	55±19	0.85
Gender (male) (%)		80%	79%	0.66†
Race (white) (%)		62%	60%	0.51†
Mechanism of injury (%)	Penetrating	22%	23%	0.73†
	Blunt	78%	77%	
Injuries (%)	Severe TBI AIS ≥3	11%	12%	0.81†
	Severe chest AIS ≥3	17%	17%	0.99†
	Severe abdomen AIS >3	21%	24%	0.23†
	Extremity AIS >3, %	22%	19%	0.23†
ISS (median (IQR))		14 (9 to 19)	14 (9 to 21)	0.46
ED vitals and parameters (mean±SD)	SBP	90±45	89±39	0.45
	HR	105±48	106±43	0.85
Temperature (degree Celsius) (mean±SD)		37±2	36±3	0.99
GCS (median (IQR))		13 (9 to 15)	13 (9 to 15)	0.99
Blood products transfused, (median (IQR))				
PRBC		5 (4 to 7)	5 (4 to 7)	
FFP		n/a	2 (1 to 5)	
Platelet		n/a	2 (1 to 4)	

*Independent T-test.
†χ^2 test.
AIS, Abbreviated Injury Scale; CR, combined resuscitation; ED, emergency department; FFP, Fresh frozen plasma; GCS, Glasgow Coma Scale; HR, heart rate; ISS, Injury Severity Score; PRBC, packed red blood cell; SBP, systolic blood pressure; TBI, traumatic brain injury.

will be to evaluate the optimal ratio of blood products in patients requiring SMT. These results will also pave the wave for further research investigating the role of whole blood resuscitation in the injured trauma patients as it is essentially a combination of PRBC, FFP, and platelets. At our institution, we are currently making a protocol to prospectively study the role of FFP and platelets as an adjunct to PRBC to develop an SMT protocol for the non-severely injured trauma patients.

Even though our study is the first in the literature to demonstrate the use of CR with PRBC along with FFP and platelets in patients requiring SMT from a large database, our study has certain limitations, and the results should be interpreted appropriately.

Table 5 An elucidation of secondary outcomes of our matched data

Outcomes	PRBCs alone	CR	P value*
ARDS	5%	3%	0.03
AKI	11%	8%	0.02
Sepsis	5%	4%	0.45
VTE	2%	3%	0.67
Overall complications	26%	15%	0.01
In-hospital mortality	9%	6%	0.01
24-hour mortality	7%	4%	0.01

*χ^2 test.
AKI, acute kidney injury; ARDS, acute respiratory distress syndrome; CR, combined resuscitation; PRBC, packed red blood cell; VTE, venous thromboembolism.

RESULTS

First and foremost, this a retrospective study of a large database and has the inherent limitations of a retrospective design and cannot demonstrate causality. However, this study will serve as a hypothesis generator for future studies. Second, the patients were not randomized into two groups, and this may impart an inherent bias. We also could not capture the individual institutional protocols in deciding one treatment over the other. As the TQIP database does not capture the coagulation indices including the prothrombin time, partial thromboplastin time, and International Normalized Ratio (INR), we could not control for these parameters. Furthermore, although the type and timing of hemorrhage control procedures are presented in the TQIP database, our analysis focused more on other aspects of traumatic patient management, and we did not include these variables in our analysis. To limit the survival bias that may affect our study, patients who were severely injured and were dead on initial presentation were excluded in our analysis. In our study, we reported the in-hospital mortality as well as the 24-hour mortality, however, due to the retrospective nature of the database we could not report the 6-hour mortality, which in some studies is now considered the more appropriate endpoint for studies involving acutely bleeding patients. Another important limitation of our study is that we did not examine the effect of whole blood in resuscitation which is recently becoming an important tool in the resuscitation of injured patients. In addition, we could not determine if some institutions used thromboelastography or rotational thromboelastometry-based products replacement. Only a randomized controlled trial can overcome these limitations.

CONCLUSION

In trauma patients requiring more than 3 units of PRBCs, administration of FFP, and/or platelets is associated with improved survival when compared with those patients who received PRBC only. Patients requiring SMT who receive CR within the first 24 hours of trauma have a lower risk of AKI and ARDS without an increase in VTE complications. However, further studies, including randomized controlled trials and prospective cohorts, are needed to analyze the optimal ratio of blood products required for SMT.

Contributors FJ: Substantial contributions to the conception and design of the work, drafting the work, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. BZ: Substantial contributions to the design of the work, analysis, or interpretation of data for the work, revising the article critically for important intellectual content, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. AR: Substantial contributions to the conception and design of the work, drafting the work, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. IS: Substantial contributions to the conception and design of the work, drafting the work, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. JK: Substantial contributions to the conception and design of the work, drafting the work, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. JC: Substantial contributions to the design of the work, analysis, or interpretation of data for the work, revising the article critically for important intellectual content, final approval of the version to be published, agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and

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