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Resuscitate early with plasma and platelets or balance blood products gradually: Findings from the Prospective, Observational, Multicenter, Major Trauma Transfusion (PROMMTT) Study

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Abstract

Background—The trauma transfusion literature has yet to resolve which is more important for hemorrhaging patients: transfusing plasma and platelets along with red blood cells (RBCs) early in resuscitation or gradually balancing blood product ratios. In a previous report of PROMMTT results, we found 1) plasma and platelet:RBC ratios increased gradually over the 6 hours following admission, and 2) patients achieving ratios >1:2 (relative to ratios <1:2) had significantly decreased 6–24 hour mortality adjusting for baseline and time-varying covariates. To differentiate the association of in-hospital mortality with early plasma or platelet transfusion from that with delayed but gradually balanced ratios, we developed a separate analytic approach.

Methods—Using PROMMTT data and multi-level logistic regression to adjust for center effects, we related in-hospital mortality to the early receipt of plasma or platelets within the first 3–6 transfusion units (including RBCs) and 2.5 hours of admission. We adjusted for the same covariates as in our previous report: injury severity score, age, time and total number of blood product transfusions upon entry to the analysis cohort, and bleeding from the head, chest or limb.

Results—Of 1245 PROMMTT patients, 619 were eligible for this analysis. Early plasma was associated with decreased 24 hour and 30 day mortality (adjusted odds ratios, ORs=0.47, p=0.009; 0.44, p=0.002 respectively). Too few patients (24) received platelets early for meaningful assessment. In the subgroup of 222 patients receiving no early plasma but continuing transfusions beyond hour 2.5, achieving gradually balanced plasma and platelet:RBC ratios ≥1:2 by hour 4 was not associated with 30 day mortality (adjusted ORs=0.9 and 1.1 respectively). There were no significant center effects.

Conclusion—Plasma transfusion early in resuscitation had a protective association with mortality whereas delayed but gradually balanced transfusion ratios did not. Further research will require considerably larger numbers of patients receiving platelets early.

Level of Evidence—Prospective, Level II

Keywords

PROMMTT; Massive transfusion; trauma; plasma; platelets

INTRODUCTION

In the trauma transfusion literature it is unclear which is more important, early transfusion of plasma and platelets or gradually balancing their ratios relative to red blood cells (RBCs) after a consecutive series of RBC units have been transfused.[1–8] The Prospective Observational Multicenter Major Trauma Transfusion (PROMMTT) study reported that 1) plasma and platelet:RBC transfusion ratios increased gradually over the 6 hours following admission to the Emergency Department (ED), and 2) among patients receiving at least 3 blood product transfusions within 24 hours of admission, transfusion ratios approaching 1:1 (as in fresh whole donor blood) were associated with decreased 6–24 hour mortality relative to ratios of 1:2 or less.[9] Left unanswered, however, was the key question of whether early initiation or just gradually balanced transfusion ratios are important.[10]

Several systematic reviews and meta-analyses have summarized the findings from observational studies associating reduced in-hospital mortality with the establishment of massive transfusion protocols in Level I trauma centers (7 studies)[11, 12] and with increased plasma and platelet:RBC ratios closer to 1:1 (16 studies).[13–16] In addition, clinical practice guidelines regarding the use of plasma[17] and platelet[18] transfusion for massively hemorrhaging patients have been published recently. The studies evaluating the initiation of massive transfusion protocols have consistently reported significant associations with decreased mortality. Implementing the protocols is believed to accelerate and better coordinate the availability of blood products. In contrast, the reviews detected significant and unexplained heterogeneity among the findings reported from studies of blood component transfusion ratios, fueling concerns for selection and survival bias.[14] The recent clinical practice guidelines are circumspect and recommend a tailored approach to therapy over a single uniform massive transfusion protocol.[17, 18]

For the current study based on PROMMTT data, we hypothesized that early transfusion of plasma and platelets (within the first 3–6 units of blood products transfused by hour 2.5 post admission) would be associated with decreased in-hospital mortality. We also hypothesized that gradually balanced plasma:RBC and platelet:RBC ratios would be associated with decreased mortality in PROMMTT patients, independently of the association between mortality and early transfusion of plasma and platelets. Because deaths among severely bleeding trauma patients occur within a few hours of admission if hemostasis is not achieved,[19] the endpoints for efficacy decisions among varying massive transfusion protocols are typically early mortality at 6 and 24 hours and later mortality reflecting complications at 30 days.[9, 20]

METHODS

PROMMTT enrolled 1,245 adult trauma patients requiring the highest level of trauma activation across 10 US Level 1 trauma centers during July 2009–October 2010. Severely injured patients were eligible if they were age 16 years or older and received at least one unit of red blood cells (RBCs) within the first 6 hours after admission. Exclusions included transfers, received < 5 minutes of CPR prior to or within 30 minutes after admission, pregnancy, inhalation injury, >20% burn injury, prisoners, or death within 30 minutes of admission. Real-time data collection on timed infusions and other treatments and their indications was initiated on consecutive patients until active resuscitation ended or patients were identified to be ineligible for the study at which point they were withdrawn and their data were destroyed. Information on in-hospital mortality, complications, and later treatment were recorded daily from the medical record until death or discharge. Additional details regarding the design and main results of PROMMTT have been previously published.[9, 21] PROMMTT was approved by all local Institutional Review Boards at the 10 clinical sites

and the Data Coordinating Center as well as the US Army Human Research Protections Office.

Statistical Analysis

The primary outcome was in-hospital mortality at 6 and 24 hours and 30 days post admission. PROMMTT patients were eligible for the analysis if they had received 3–6 blood product transfusions including at least one unit of RBCs within 2.5 hours of admission. The 2.5 hour time window was considered sufficient time for blood banks to deliver and trauma teams to transfuse multiple consecutive transfusions for patients with the most severe blood loss or coagulopathy upon admission across all 10 PROMMTT sites. To reduce the potential for survival bias[9, 22–24] and enable a reasonable classification of whether early plasma or platelets had been transfused, the initial 2.5 hour study entry period was subdivided into smaller time intervals. Since patients who expired in the first 30 minutes were ineligible and excluded from PROMMTT regardless of prior transfusions, patients could not enter the PROMMTT analysis cohort (to be considered "at risk of death") until after minute 30. Because the peak mortality rate for seriously injured trauma patients occurs in the first hour after admission[9, 20], the first two entry time intervals, from >30 minutes to hour 1, were limited to 15 minutes. Three consecutive 30-minute intervals were established for the entry period, >hour 1 to hour 2.5. Patients' entry time interval (1–5) was included as a covariate in multi-level logistic regression that adjusted for center differences in random intercept models[25]. The primary independent variables were binary indicators of whether at least one unit of plasma and one unit of platelet concentrate (containing on average, the amount of platelets in approximately 6 units of fresh whole donor blood) had been transfused by mid-point of the patients' entry time interval. The cumulative sum of the total units of blood products transfused (RBCs, plasma and platelet concentrate) by mid-point of the entry time interval was computed and used as a covariate. Other covariates were injury severity score, age, and bleeding sites (head, chest or limb).[9]

The rationale for setting a minimum of three blood product transfusions as an eligibility criterion for the analysis was that only after the third transfusion would PROMMTT patients have had the chance to receive plasma and platelets in addition to RBCs. The rationale for setting a maximum of six unit transfusions arose from the need to tailor the analysis strategy to both the research questions and the PROMMTT eligibility criteria. Most of the patients receiving more than six units of blood products upon entry (67/85 or 80%) had received these multiple transfusions by minute 30 and were thus at the highest risk for early mortality.[3, 20] However, PROMMTT's exclusion of patients dying within the first 30 minutes precluded a valid assessment of the association between early mortality and the earliest possible transfusion of plasma or platelets. In addition, of the 85 patients exceeding 6 transfusions at cohort entry, 81 (>95%) received plasma among the 7–18 units they were given by midpoint of the entry time interval rendering the data for this subgroup relatively non-informative.

To assess whether gradually balanced ratios of plasma:RBCs and platelets:RBCs were associated with mortality independently of early plasma and platelet transfusion, we used multi-level logistic regression[25] stratified by patients' early plasma transfusion status. Too few patients had received early platelets (24) to warrant any further stratification. We selected the subgroup of 493 patients (of the 619 in our analysis cohort) who received additional transfusions after cohort entry at hour 2.5 and survived to at least to hour 4. These subgroup selection criteria enabled a reasonable stratification by early vs delayed (> hour 2.5) plasma transfusion status and an assessment of the association between mortality and the cumulative hour 4 transfusion ratios relatively free of survival bias[9, 16, 24] (patients had to survive at least to hour 4). Identifying patients in the delayed plasma transfusion subgroup enabled us to assess the association of mortality with gradually balanced transfusion ratios

independent of early plasma transfusion. Plasma:RBC ratios were computed as the hour 4 cumulative total plasma units divided by the hour 4 cumulative total RBC units. Platelet:RBC ratios were computed by multiplying the hour 4 cumulative total units of platelet concentrate times 6 and dividing the product by the hour 4 cumulative total RBC units. Plasma and platelet ratios were then classified as balanced by hour 4 (≥1:2) or not (<1:2). Substituting the cumulative sum of total blood product transfusions by hour 4 for the cumulative sum of transfusions at cohort entry (hour 2.5), we adjusted for the other covariates in the same manner described above. Further assessment of gradually balanced ratios beyond hour 4 was precluded by the small number of cohort patients still receiving transfusions after having received neither early plasma/platelet transfusions nor balanced ratios at hour 4 (N=29 receiving additional transfusions by hour 6).

In an ancillary analysis of 24 hour survivors, we evaluated the association between early plasma and platelet transfusion and the early end of RBC transfusion if it occurred before the sixth hour with no additional RBC transfusions up to hour 24. Of the 493 patients receiving additional transfusions after cohort entry, 462 survived to at least hour 24. Time to early end of RBC transfusion was computed by subtracting the time of cohort entry (having received ≥ 3 transfusions) from the time of the last RBC transfusion before the 6^{th} hour if there were no further RBC transfusions up to hour 24. Patients surviving to hour 24 with no further RBC transfusions after entry (19) were assigned 0.1 hours for their time to final RBC transfusion. Patients receiving additional RBC transfusions after hour 6 and up to hour 24 were classified as censored at hour 6 without achieving an early end of RBC transfusion. We used Cox proportional hazards models incorporating the same set of covariates described above for the logistic models of early plasma and platelet transfusion. To adjust for center differences, we included site indicator variables with the largest-volume site serving as the referent category.

In another ancillary analysis among 24-hour survivors, we used mixed linear regression to examine the association between early plasma and platelet transfusions with the cumulative count of total RBC transfusions and cumulative sum of all blood product transfusions at 24 hours. Patients included in these analyses were the 462 who survived at least 24 hours and the subset of 230 patients who also achieved an early end of RBC transfusion within 6 hours as defined above. We adjusted for the same set of covariates described above and used a random intercept term to account for center differences.[25]

RESULTS

For this study, a total of 619 severely injured and hemorrhaging PROMMTT patients were followed for in-hospital mortality after receiving at least 3 blood product transfusions within 2 hours of admission. Upon entry to the analysis cohort, 295 patients (48%) had received 3 units of blood products, 191 (31%) had received 4 units, 76 (12%) had received 5 units and 57 (9%) had received 6 units. A total 44% of the 619 study patients entered the analysis cohort at time interval 1 (>30–45 minutes after admission), 14% at time interval 2 (>45–60 minutes), 13% at time interval 3 (>60–90 minutes), 17% at time interval 4 (minute >1.5–2 hours) and 12% at time interval 5 (>2–2.5 hours).

Compared with the entire PROMMTT cohort (N=1245) and the “original PROMMTT analysis cohort” (OPAC, N=905)[9] (Table 1), the subset of 619 patients eligible for this study was similar overall with relatively modest differences in systolic blood pressure (4% lower than OPAC), base deficit (13% higher than OPAC), bleeding sites (12% fewer head than OPAC, 10% more chest than OPAC), and damage control surgery (6% more than OPAC).

In our study sample of 619 trauma patients selected for comparable transfusion indications using prospective data and time-dependent, multi-level analysis strategies to minimize survival and other sources of bias, early plasma transfusions were consistently and significantly associated with 6 hour, 24 hour and 30 day in-hospital mortality suggesting less than half the risk relative to transfusions of RBCs without early plasma (Table 2). In contrast, the observed non-significant associations for early platelet transfusions varied in magnitude and direction reflecting the small number of patients receiving platelets early.

In the subset of 493 patients who received additional transfusions after cohort entry, neither plasma:RBC nor platelet:RBC ratios balanced to ≥1:2 by hour 4 were significantly associated with 6-hour, 24-hour or 30-day mortality, regardless of early plasma transfusion status (Table 3). However, most of the odds ratios were in the protective direction and some approached significance, especially in the subgroup of patients that had received early plasma at cohort entry (Stratum II, Table 3).

In the subset of 462 patients surviving at least 24 hours, early plasma and platelets were not associated with an early end of RBC transfusion (Table 4). On the other hand, early plasma was associated with a significant reduction in the total units of RBCs transfused by hour 24, and the same magnitude and degree of significant correlation was evident in the subgroup of 230 patients achieving an early end of RBC transfusion (Table 5). Although of lower magnitude and non-significant statistically, the association between early plasma and total units of blood products transfused by hour 24 was in the same direction.

DISCUSSION

Early plasma transfusion was significantly associated with reduced in-hospital mortality. Too few patients had received early platelet transfusion to assess fairly the potential for survival benefit. Our null findings for early platelets were not surprising given that platelets are most often transfused in trauma patients only after 3 or more hours post admission.[9] Studies focused specifically on the association of mortality with early plasma transfusion (as opposed to cumulative plasma:RBC ratios 6–24 hours after admission[5, 26, 27]) are relatively scarce in the trauma transfusion literature.[1, 8, 28] The findings among these studies are conflicting and difficult to interpret due to the use of retrospective study designs with different patient selection criteria and research methods. Findings from observational studies using time-dependent analyses and relating plasma and platelet transfusions to mortality in the earliest time intervals of an hour or less[1, 22, 29] (including PROMMTT)[9] are also conflicting, with differences in approach to analysis (e.g., defined time intervals and adjustment for potential confounders) as well as estimated strength of association.

In our stratified analyses to assess whether plasma:RBC and platelet:RBC ratios balanced to ≥1:2 by hour 4 were associated with mortality, independently of early plasma transfusions (Table 3), the null and non-significant adjusted odds ratios for 30 day mortality in stratum I without early plasma (0.9 and 1.1 for plasma and platelet ratios respectively) suggest that gradually balanced ratios may not be as beneficial as early plasma transfusion. The other adjusted odds ratios for stratum I in Table 3 were generally protective but non-significant. The magnitude of association was consistent with that observed for early plasma and platelet transfusions, suggesting a lack of statistical power due to the smaller sample sizes. We interpret the data as suggestive but inconclusive for an independent protective association between 6 and 24-hour mortality and gradually balanced plasma and platelet transfusion ratios. The odds ratios in the subgroup of patients receiving early plasma (stratum II, Table 3) warrant further research to confirm or refute the potential benefit of a transfusion protocol that initiates plasma and platelets early and sustains balanced ratios. To our knowledge,

mortality associated with gradually balanced ratios has not previously been differentiated from mortality associated with early plasma transfusion.

Early plasma and platelets were not associated with the early end of RBC transfusion as defined. On the other hand, early plasma was associated with fewer total units of RBCs transfused by hour 24 in all survivors and in the subgroup achieving an early end of RBC transfusion by hour 6 (Table 5). To our knowledge, there are no previous reports of early plasma and platelets associated with an early end of RBC transfusion or with total blood product transfusions in trauma survivors receiving repeat transfusions.

Strengths of this study include its prospective design and availability of transfusion timing data enabling stratified analyses to tease apart associations of mortality with early plasma and platelets and with gradually balanced ratios. All statistical models were adjusted for potential confounding from the sum total of transfusions received upon entry to the analysis cohort and for the cohort entry time. Total RBC transfusions has only recently been recognized as a potential confounder in studies evaluating plasma and platelet ratios.[30] Because units of blood products take time to transfuse (whether administered individually or from a rapid infuser), we adjusted for the sum total of all blood product units transfused upon cohort entry (including RBCs, plasma and platelets). We reasoned that patients within the same class of total units transfused at cohort entry (whether all RBCs, or some combination) would be more similar in bleeding severity than patients within the same class of total RBC units. To be in the same total RBC class at cohort entry (say 5 RBCs), a patient receiving a 1:1 protocol of alternating RBCs and plasma would have received 10 total units of blood products (possibly indicating greater bleeding severity) while his counterpart receiving a 0:5 protocol without plasma at cohort entry would have received only five.

Future studies will benefit from larger samples with many more patients receiving early platelet transfusions, and from including the experience of all clinically eligible patients, even those dying early after admission, especially if they have received transfusions. Although several steps were taken in this study to address indication and survival bias[9, 16, 24], they remain major challenges in observational trauma research. Data elements that sufficiently characterize injury and bleeding severity at the time when transfusion protocols are first ordered and initiated are typically not available for analysis.[12] The operational definitions used for patient subgroups and outcomes (e.g., early end of transfusion) in this study may have limited generalizability. Only a well-designed, conducted and analyzed randomized trial could possibly overcome the many threats to validity in the trauma setting. The need to manage dynamic treatment regimes for heterogeneous, high risk patient populations makes trauma resuscitation research an ideal proving ground for the development of innovative and robust comparative effectiveness research methods. Several promising design and analysis approaches (e.g., adaptive trial design, artificial censoring and inverse probability weighting, sequential Cox analysis), motivated by conceptually similar challenges in other clinical research contexts, could be extended to the trauma setting toward a better integrated system of research and clinical practice.[31–34]

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Table 1

Admission and treatment characteristics and unadjusted survival in PROMMTT patients

		All enrolled patients (N=1245)		Subcohort ≥3 units/24 hrs (N=905)		Subcohort 3–6 units/2hrs (N=620)	
Admission characteristics		**Median (IQR)**	**complete**	**Median (IQR)**	**complete**	**Median (IQR)**	**complete**
Age, y		38 (24–54)	1244	37 (24–53)	904	38 (24–54)	619
Male, No. (%)		923 (74.2)	1245	687 (75.9)	905	469 (75.7)	620
Blunt injury, No. (%)		796 (64.5)	1235	579 (64.4)	899	387 (62.4)	620
Systolic blood pressure, mm Hg		106 (86–128)	1213	102 (82–124)	876	98 (80–120)	604
Heart rate, bpm		105 (86–124)	1218	109 (88–128)	887	110 (88–129)	608
Temperature, C		36.1 (35.6–36.6)	630	36.1 (35.6–36.6)	440	36.1 (35.6–36.6)	290
Glasgow Coma Score		14 (3–15)	1135	13 (3–15)	826	12 (3–15)	566
Base deficit		6 (3–10)	960	7 (4–11)	716	7.9 (4–11)	501
pH		7.3 (7.2–7.3)	975	7.3 (7.2–7.3)	730	7.2 (7.1–7.3)	511
International Normalized Ratio (INR)		1.2 (1.1–1.4)	1081	1.3 (1.1–1.5)	792	1.3 (1.1–1.5)	542
Partial thromboplastin time (PTT), seconds		27 (24–33)	1045	29 (25–35)	762	29 (25–35)	522
Prothrombin time (PT), seconds		15 (13–17)	902	15 (14–17)	662	16 (14–18)	458
Hemoglobin, g/dL		11.7 (10.1–13.3)	1198	11.5 (9.9–13.1)	869	11.4 (9.8–12.8)	597
Injury Severity Score (ISS)		25 (16–34)	1243	26 (17–36)	905	26 (17–38)	620
Bleeding sites[a]							
	Head, No. (%)	181 (14.5)	1245	128 (14.1)	905	78 (12.6)	620
	Face, No. (%)	340 (27.3)	1245	246 (27.2)	905	163 (26.3)	620
	Neck, No. (%)	57 (4.6)	1245	41 (4.5)	905	31 (5.0)	620
	Chest, No. (%)	299 (24.0)	1245	237 (26.2)	905	179 (28.9)	620
	Abdomen, No. (%)	396 (31.8)	1245	320 (35.4)	905	221 (35.6)	620
	Pelvis, No. (%)	164 (13.2)	1245	143 (15.8)	905	94 (15.2)	620
	Limb, No. (%)	441 (35.4)	1245	334 (36.9)	905	225 (36.3)	620
	Unknown, No. (%)	121 (9.7)	1245	79 (8.7)	905	56 (9.0)	620
Treatment characteristics							
Damage control surgery performed, No. (%)		239 (19.3)	1241	222 (24.6)	904	162 (26.1)	620

	All enrolled patients		Subcohort ≥3 units/24 hrs		Subcohort 3–6 units/2hrs	
	(N=1245)		(N=905)		(N=620)	
Admission characteristics	**Median (IQR)**	**complete**	**Median (IQR)**	**complete**	**Median (IQR)**	**complete**
6-hour RBC unit total	4 (2–7)	1224	5 (3–9)	905	5 (3–9)	620
6-hour plasma unit total	2 (0–5)	1224	4 (2–7)	905	3 (1–7)	620
6-hour platelet unit total	0 (0–6)	1224	0 (0–6)	905	0 (0–6)	620
24-hour RBC unit total	5 (2–9)	1244	6 (4–11)	905	6 (4–11)	620
24-hour plasma unit total	4 (0–8)	1245	5 (2–9)	905	4 (2–8)	620
24-hour platelet unit total	0 (0–6)	1245	0 (0–6)	905	0 (0–6)	620
Unadjusted in-hospital mortality						
24-hour mortality, No. (%)	148 (12.2)	1245	132 (15.1)	905	91 (14.7)	620
30-day mortality, No. (%)	260 (22.4)	1097	220 (26.5)	905	147 (23.7)	620

Abbreviations: IQR, Interquartile Range

[a]Bleeding site categories are not mutually exclusive and patients were counted in multiple categories if appropriate.

Table 2

Adjusted Odds Ratios (95% Confidence Intervals) Associating In-hospital Mortality with Early Plasma and Platelet Transfusion Status at Entry to the Analysis Cohort *

Plasma & Platelets at Entry	6 Hour Mortality	24 Hour Mortality	30 Day Mortality
At least one unit plasma	0.37 (0.19 – 0.73) p=0.004	0.47 (0.27 – 0.84) p=0.01	0.44 (0.27 – 0.73) p=0.002
At least one unit platelets	0.49 (0.09 – 2.60) p=0.402	1.37 (0.44 – 4.24) p=0.582	1.26 (0.42 – 3.74) p=0.678

* A total of 619 patients entered this analysis cohort having received 3–6 units of blood products (including RBCs) within 2.5 hours of admission. Odds ratios are adjusted for the cumulative sum of unit blood products transfused at entry, injury severity score, entry time interval, age, bleeding sites (head, chest and limb) and center differences as a random intercept in the multi-level logistic models[25].

Table 3

Adjusted Odds Ratios (95% Confidence Intervals) Associating In-hospital Mortality with Blood Component Ratios Balanced by Hour 4, Stratified by Early Plasma Transfusion Status*

Plasma & Platelets Received	6 Hour Mortality	24 Hour Mortality	30 Day Mortality
Stratum I: None at Entry (N=222)			
≥ 1:2 plasma ratio at 4 hours	0.10 (0.002 – 4.60) p=0.238	0.50 (0.10 – 2.55) p=0.403	0.90 (0.35 – 2.31) p=0.830
≥ 1:2 platelet ratio at 4 hours	0.42 (0.01 – 15.34) p=0.634	0.32 (0.05 – 2.13) p=0.240	1.10 (0.43 – 2.85) p=0.839
Stratum II: Plasma at Entry (N=271)			
≥ 1:2 plasma ratio at 4 hours	0.42 (0.027 – 6.38) p=0.531	0.12 (0.01 – 1.43) p=0.094	0.44 (0.76 – 2.51) p=0.353
≥ 1:2 platelet ratio at 4 hours	0.89 (0.144 – 5.52) p=0.904	0.35 (0.07 – 1.68) p=0.191	0.48 (0.18 – 1.30) p=0.150

*A total of 493 patients entered this analysis cohort having received 3–6 units of blood products (including RBCs) within 2.5 hours of admission and surviving to receive additional transfusions by hour 4. Odds ratios are adjusted for the cumulative sum of unit blood products transfused by hour 4, entry time interval, injury severity score, age, bleeding sites (head, chest and limb) and center differences as a random intercept in the multi-level logistic models[25].

Table 4

Adjusted Hazard Ratios Associating Early End of RBC Transfusion by Hour 6 with Plasma and Platelet Transfusion Status at Entry*

Plasma & Platelets at Entry	Early End of RBC Transfusion
At least one unit of plasma	0.93 (0.67 – 1.30) p=0.602
At least one unit of platelets	0.83 (0.41 – 1.67) p=0.602

*A total of 462 patients entered this analysis cohort having received 3–6 units of blood products (including RBCs) within 2.5 hours of admission and surviving to receive additional RBC transfusions by hour 4 with the potential for subsequent RBC transfusions by their 24th hour of survival. A total of 230 patients achieved an early end of RBC transfusion by hour 6. Hazard ratios are adjusted for the cumulative sum of unit blood products transfused at entry, injury severity score, entry time interval, age, bleeding sites (head, chest and limb) and center differences.

Table 5

Adjusted Regression Coefficients Associating the Sum of Blood Components Transfused by Hour 24 with Plasma and Platelet Transfusion Status at Entry*

Plasma & Platelets at Entry	Sum of RBCs by Hour 24	Total Units** by Hour 24
For All 462 Patients Receiving Additional Transfusions and Surviving 24 hours		
At least one unit of plasma	−2.79 p=0.001	−1.99 p=0.244
At least one unit of platelets	0.69 p=0.758	2.00 p=0.652
For the Subset of 230 Patients Achieving Early End of RBC Transfusion by Hour 6		
At least one unit of plasma	−2.06 p<0.0005	−0.96 p=0.369
At least one unit of platelets	0.46 p=0.696	1.47 p=0.553

*The 462 patients in this analysis received 3–6 units of blood products within 2.5 hours of admission and survived to receive additional blood component transfusions by hour 4 with the potential for subsequent transfusions by their 24th hour of survival. A separate analysis focused on 24 hour blood product consumption in the subset of 230 patients achieving an early end of RBC transfusion by hour 6. Coefficients for plasma and platelets are adjusted using mixed linear regression. Covariates include the cumulative sum of unit blood products transfused at entry, injury severity score, entry time interval, age, bleeding sites (head, chest and limb) and center differences (by inclusion of a random intercept term).

**Includes all units of RBCs, plasma and platelets transfused.