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Title: Massive Blood Transfusion Following Older Adult Trauma: The Effect of Blood Ratios on Mortality

Brief Title: Older Adult Trauma Blood Transfusion Ratios

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Abstract

Background: Massive blood transfusion (MBT) following older adult trauma poses unique challenges. Despite extensive evidence on optimal resuscitative strategies in the younger adult patients, there is limited research in the older adult population.

Methods: We used the Trauma Quality Improvement Program (TQIP) database from 2013 to 2017 to identify all patients over 65 years old who received a massive blood transfusion. We stratified our population into 6 FFP:pRBC ratio cohorts (1:1, 1:2, 1:3, 1:4, 1:5, 1:6+). Our primary outcomes were 24-hour and 30-day mortality. We constructed multivariable regression models with 1:1 group as the baseline and adjusted for confounders to estimate the independent effect of blood ratios on mortality.

Results: A total of 3,134 patients met our inclusion criteria (median age 73±7.6 years, male = 65%). On risk-adjusted multivariable analysis, 1:1 FFP:pRBC ratio was independently associated with lowest 24-hour mortality (1:2 OR=1.60, CI=1.25-2.06, p<0.001) and 30-day mortality (1:2 OR=1.44, CI=1.15-1.80, p=0.002).

Conclusions: Compared to all other ratios, the 1:1 FFP:pRBC ratio had the lowest 24-hour and 30-day mortality following older adult trauma consistent with findings in the younger adult population.

Introduction

Massive blood transfusion (MBT) is a life-saving tool used for severe, acute blood loss, particularly in the setting of trauma often initiated in the emergency department.[1] MBT replenishes intravascular volume, restores oxygen carrying capacity, and corrects coagulopathies through the transfusion of red blood cells (pRBC), fresh frozen plasma (FFP), and platelets (PLT).[2] While the benefit of massive transfusion in the setting of severe blood loss has been demonstrated,[1,3] there remains debate about which ratio of blood products confers the highest survival among trauma patients.[4,5]

In the 1970s, the use of blood components rather than whole blood became widespread. As a result, many patients received higher amount of pRBCs and crystalloids in comparison to FFP and PLTs.[6,7] Although these changes were not supported by evidence, it was thought that patients take time to develop coagulopathy and therefore the benefits did not merit the logistical challenges and cost of preparing additional units of FFP.[8,9] In recent years, however, numerous studies have suggested that this practice is detrimental because many patients have a coagulopathy at the time of presentation, which is then worsened by the dilutional effect of excess RBCs and fluids on platelets and plasma.[8,10–12] This led to the evaluation of the effect of higher blood to plasma ratios on survival.[4] However, a large randomized control trial (PROPPR) ultimately showed no difference in 24-hour or 30-day mortality in 1:1:1 vs 1:1:2 ratios of FFP:PLT:pRBC.[5] This has caused further debate on the ideal ratio.

While many studies have examined the effect of different ratios of FFP:PLT:pRBC in MBT, few focus on special populations such as older adults patients. These patients are more likely to have decreased cardiac output, increased systemic vascular resistance, and impaired renal function, which makes it harder for them to compensate for physiologic aberrations.[13]

Additionally, older adults are more likely to have multiple comorbidities and increased polypharmacy which further alters their hemodynamics and response to trauma.[13] In the PROPPR trial, the mean age of participants was 34.5 years with the oldest participant being 51 years, limiting the generalizability of their results to the older adult population.[5]

The older adult population is growing rapidly in the United States in part due to increased life expectancy.[14] As a result, the frequency of older adult trauma will also likely continue to rise. Therefore, it is paramount to identify how to best manage this population with the goal of maximizing survival and minimizing morbidity. Identifying which ratio confers the highest survival in this group is an important step in improving outcomes. In this study, we use a national trauma database to compare survival in older adult patients who received different ratios of FFP:pRBC during massive transfusion for trauma.

Methods

Data source

We performed a multicenter, retrospective, cohort analysis of all patients with trauma from 2013-2017 using the American College of Surgeons (ACS) Trauma Quality Improvement Program (TQIP) National Trauma Data Bank (NTDB). ACS TQIP is a national program that gathers data from over 850 trauma centers in the United States. The data were collected by a trained clinical reviewer through chart review and is submitted voluntarily on a regular basis from individual centers and standardized before being entered into the NTDB. Variables include patient demographics, comorbidities, emergency department presentation, injury characteristics, injury severity score (ISS), procedures performed within 24 hours of admission, and disposition at discharge. Our study was exempt from the institutional review board as it used a de-identified data set. Exact definitions of each variable are available on the TQIP website.

Inclusion and exclusion criteria

We included all patients who were 65 years or older who received a MBT (Figure 1). We defined MBTs as receiving ≥10 units (3000 mLs) of pRBCs within 24 hours or ≥5 units (1,500 mLs) of pRBCs within 4 hours of admission to the emergency department for trauma.[15] We calculated standardized FFP:pRBC ratios at 24 hours and stratified our population into 6 cohorts (1:1, 1:2, 1:3, 1:4, 1:5, 1:6+). We rounded patient ratios to the nearest integer.

Outliers were removed if they were lesser or greater than 1.5 times interquartile range and treated as if they were missing. This was done for ISS, total Glasgow Coma Scale (GCS), systolic blood pressure, pulse rate, respiratory rate, and length of stay in days. We excluded patients who were transferred from another facility to enable consistent ratio reporting for each patient because all necessary blood transfusions were from a single hospital. We excluded all patients who were dead on arrival to the emergency department to remove patients who would not respond to treatment irrespective of transfusion ratios. We also excluded patients who had discordant and implausible blood ratios, such as patients who received more FFP than pRBC and were not able to be rounded to 1:1 group, and patients who received more than 300 units of pRBC. Patients who did not receive any plasma were excluded. We excluded platelet data from our analysis due to a high proportion of missing and inconsistent data.

Outcomes of interest

Our primary outcomes of interest were 24-hour and 30-day all-cause mortality. Secondary outcomes included hospital and ICU length of stay, ventilator days, presence of complications, and need for emergency surgery for hemorrhage control. To better characterize injuries, we used ICD-9 or ICD-10 codes provided by TQIP to identify injury types and body locations. We specifically analyzed femur fractures, gastrointestinal injuries, lung injuries, pelvic fractures, rib fractures, and traumatic brain injuries due to their strong effect on hospital outcomes in the older adults.

Missing Data

The percent of missing data for each variable was calculated and then compared between the different cohorts. On missing variable analysis 7 variables were noted to have missing data (Supplemental Table 1). Of this, temperature was noted to have the highest proportion of missingness (43.28%). As a result, we chose to exclude this variable from all models. The other 6 variables had a relatively lower proportion of missingness and for all models that included these variables, we utilized a multivariate imputation chained equations scheme to impute all missing data.[16] The data were collected across multiple hospitals from over a thousand patients, but we also manually inspected and visualized imputed data to verify our missing at random assumptions.[17]

Statistical and machine learning analysis

On baseline, we evaluated over 60 variables including ISS, vitals, injury type, comorbidities, and hospital trauma level certification. To evaluate for confounding variables, we performed a univariate exploratory analysis after stratifying our patients based on their blood ratio cohorts. Continuous parametric data were analyzed using a one-way analysis of variance (ANOVA) test, and continuous nonparametric data were analyzed with a Kruskal-Wallis test.[18]

To determine the association between blood ratios and our primary outcomes, i.e., 24-hour and 30-day all-cause mortality, we constructed multivariable, least absolute shrinkage and selection operator (LASSO) logistic regression models. LASSO is a regression analysis method that was created to help overcome overfitting of a regression model.[19] This method uses both regularization and shrinkage in order to select the fewest number of model covariates, or inputs.

This included patient demographics, comorbidities, injury characteristics, units of transfused FFP in 24 hours, vitals recorded at presentation in the emergency department, and ACS trauma center level. We used the 1:1 cohort as our reference group for each LASSO regression.

To test the goodness of fit of our model, we divided the data into 80% training and 20% testing datasets and evaluated for receiver operating characteristic area under the curve (ROC AUC) on the testing dataset. Missing values were imputed before division into training and testing datasets with the outcome variables removed. In a LASSO model, the parameter alpha balances the tradeoff between model accuracy, in our case ROC AUC, and model complexity, in our case the number of covariates that have non-zero coefficients, and must be set by the user. To optimize for alpha, we utilized the procedure described by least angle regression (LAR) optimized for the Bayesian information criterion (BIC) on the training dataset.[20,21] The alpha selected from the LAR procedure were used as the input for the LASSO model trained on the entire training dataset. We report the models' ROC AUC on the testing dataset. For each covariate with a statistically significant association with outcome (p-value < 0.05), we report the coefficient, odds ratios, and their respective 95% confidence intervals.

All statistical analysis was performed using scientific Python libraries including scikit-learn, SciPy, and statsmodels and the code is available upon request.[22–24]

Results

Baseline Characteristics

Of the 3,087,735 patients in the TQIP NTDB database from 2013-2017, 3,134 met our inclusion criteria. Our study population was 65% male with a median age was 73. Most patients (66.34%) had at least 1 comorbidity, with the three most common comorbidities being bleeding disorder (10.72%), diabetes mellitus (15.95%), and hypertension (38.54%). Other baseline population characteristics including demographics, comorbidities, injury descriptions, transfused blood products, vitals, and hospital characteristics are shown in Table 1. The largest groups where the 1:1 and 1:2 cohorts, accounting for 30.7% and 39.9% of the study population, respectively. The median units of pRBC given to the 1:1 FFP:pRBC cohort and 1:2 cohort were 11 units and 12 units, respectively. The median units of FFP given to the 1:1 cohort and 1:2 cohort were 9 units and 6 units, respectively. The 1:1 FFP:pRBC and 1:2 FFP:pRBC cohorts had the same mean ISS of 29 ($p < 0.001$). We observed significant variation at baseline in the types of injuries in the study population with 1:1 FFP:pRBC having the highest proportion of gastrointestinal injuries when compared to the other groups (56.28%, $p < 0.001$).

Primary Outcomes

The odds ratios (ORs), 95% confidence intervals, and p-values for each blood ratio cohort for both of our primary outcomes are shown in Table 2, which was generated after adjusting for all confounders related to patient demographics, comorbidities, injury characteristics, vitals, and hospital level variables. Only significantly associated covariates are in Table 2, while a list of all covariates included in the model can be found in Supplementary Table 2. For our primary outcome of 24-hour all-cause mortality, we observed that the 1:1 ratio has significantly decreased odds of mortality when compared to 1:2, 1:3, and 1:6+ (1:2 OR = 1.60, 1.25-2.06, $p < 0.001$, 1:3 OR = 1.62, 1.14-2.31, $p = 0.007$, 1:6+ OR = 2.69, 1.71-4.24, $p <0.001$) . With 30-day-all-cause mortality, we observed that the cohorts greater than 1:1 FFP:pRBC are associated with increased odds of mortality (1:2 OR = 1.44, 1.15-1.80, $p = 0.002$). The covariates that were independently associated with 24-hour and 30-day mortality are shown in Supplemental Table 2 (ROC AUC 24-hour mortality = 0.72; 30-day mortality = 0.75). Additionally, we cross-validated our models to the younger adult population, patients ages 18-

64, to establish generalizability of our findings and observed a similar effect in blood ratios (Supplemental Table 3).

Secondary Outcomes

Unadjusted secondary outcomes including inpatient morbidity and length of stay are noted in Table 3. Overall, 57.31% of the patients had at least one hospital complication with the three most common being cardiac arrest (18.89%), acute kidney injury (7.91%), and intubation (5.78%). Patients in the 1:1 cohort had a higher proportion of acute respiratory distress syndrome and myocardial infarction (5.92%, $p = 0.022$ and 3.53%, $p = 0.028$, respectively). The 1:1 FFP:pRBC cohort had the longest median total length of stay (7, $p = 0.004$). Patients in the 1:1 FFP:pRBC and 1:2 cohorts had higher incidence of laparotomy for hemorrhage control (44.13% and 40.54% respectively, $p = 0.001$) while patients in the 1:3, 1:4, 1:5, and 1:6+ cohorts had higher incidence of having no surgery for hemorrhage control (42.92%, 46.06%, 43.64%, and 44.39%, respectively, $p < 0.001$).

Discussion

In this multicenter, retrospective, cohort analysis of older adult trauma patients (≥65), risk-adjusted the 1 FFP: 1pRBC ratio was associated with the lowest mortality at both 24-hours and 30-days. We observed similar associations with FFP:pRBC ratio and mortality in the younger adult population (18-64) in our supplementary analysis, indicating that these populations are similar in their response to massive blood transfusions.

Our results of 1:1 ratio agree with previous large studies on MTP. The PROPPR trial randomized 680 participants who were 15 years or older to either a 1:1:1 FFP:PLT:pRBC or a 1:1:2 ratio to treat major bleeding and found no significant difference in mortality at 24-hours or 30-days. A 1:1:1 ratio was associated with improved hemostasis and fewer deaths due to exsanguination at 24 hours, findings that cannot be directly compared to our study due to being unadjusted. Although they did not show a significant association between a 1:1 ratio and decreased mortality, this study has been interpreted by clinicians as support for using a 1:1 ratio in massive transfusions due to the secondary findings.[5] Our study reinforces these findings in the older adult population, with lower mortality in patients receiving a 1:1 FFP to pRBC ratio.

Our findings are relevant and timely because the older adult population is growing rapidly[14], and is uniquely vulnerable to high rates of mortality due to trauma.[25] We found that increasing age was associated with higher mortality among older adult trauma patients receiving MBT. Currently, there are few studies examining outcomes of older adult patients receiving MBT. Importantly, age has been independently associated with mortality in patients who receive MBT.[26] However, other studies have found no significant difference in mortality.[27] Conflicting results from these reports may indicate the presence of confounding variables such as patient-level and institutional-level factors like comorbidities and triage. Our study attempts to control for these confounders by including patient demographics, comorbidities, injury characteristics, interventions, and hospital level.

In our study, patients in the 1:1 FFP:pRBC cohort had overall higher rates of complications such as increased rates of acute respiratory distress syndrome (ARDS). However, we were unable to perform a risk-adjusted analysis for all of our secondary outcomes. When compared to the 1:2 cohort, the 1:1 FFP:pRBC cohort had longer hospital length of stay and increased incidence of myocardial infarctions. It is likely these results are confounded by survival bias, where patients in the 1:1 FFP:pRBC observed decreased mortality were, therefore, more likely to remain in the hospital for a longer duration.

We acknowledge that our findings have limitations. First, this was a retrospective cohort study from a large trauma database, and as such we were unable to balance all population characteristics across cohorts. To circumvent unbalanced populations, we risk-adjusted for all possible patient- and institutional-level confounders. However, we were only able to adjust for confounders that were recorded in the TQIP database, and it is therefore possible that there may be unreported confounders. For example, ACS TQIP does not record the cause of death which may be an important outcome to analyze. Second, while ACS has multiple checks to ensure the quality of data, there is always a possibility for erroneous values. To counteract this, we created additional criteria to detect erroneous and improbable values that included a visual evaluation of data with dot plots and interquartile ranges and subsequently masked outliers. Third, we were not powered to perform an adjusted analysis of secondary outcomes. Therefore, our interpretation of them is limited. Fourth, the term "older adult" is broadly encompassing, and there are no well-defined clinical criteria to ascertain such a label. Biological and chronological aging may be two separate entities. We predetermined an acceptable cutoff to aid analysis, but these cutoffs may not capture the continuous relationship of age with mortality.[28] Fifth, we could not divide patients into exact blood cohort ratios; most patients were rounded to their nearest whole integer cohort. While this may weaken our association to clinical outcomes, this may be more reflective of the clinical administration of MBTs. Sixth, we were unable to account for other fluid or medication administration that may have affected patient outcomes. Seventh, we excluded patients who were transferred or dead on arrival to the emergency department which may introduce some survivorship bias into our results, as patients with significant injuries that required relocation or passed quickly are disproportionally excluded. However, within this excluded cohort of patients we could not guarantee that they received consistent ratios between hospitals or that any transfusion ratio influenced outcome. Finally, we excluded platelet data from our analysis due to a high proportion of missing and inconsistent data. This precludes us from drawing conclusions about the role of platelet ratio in the outcomes of these patients.

Conclusions

We demonstrate that the 1:1 FFP:pRBC ratio is associated with increased survival at both 24-hours and 30-days for both the older adult and younger adult populations. Many factors, including physiologic differences, comorbidities, and polypharmacy may affect how older adults respond to trauma and massive blood transfusion. Further clinical trials may be able to better quantify and identify how all these factors interact to affect outcomes.

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Table 1. Patient demographics, comorbidities, injury characteristics, units of FFP, and vitals at presentation and hospital level of the blood cohorts.

Variable	**1:1** (n = 963)	**1:2** (n = 1253)	**1:3** (n =438)	**1:4** (n =165)	**1:5** (n =110)	**1:6** + (n =196)	**P-value**

Population Demographics							
Age, year[a]	73(68-81)	73 (68-80)	74 (68-82)	71 (67-79)	74 (68-79)	75 (68-82)	0. 126
Male sex[c]	641 (66.63)	820 (65.44)	291 (66.44)	98 (59.39)	69 (62.73)	121 (61.73)	0. 704
Race[c]							
American Indian or Alaska Native	3 (0.31)	4 (0.32)	1 (0.23)	1 (0.61)	1 (0.91)	1 (0.51)	0. 890
Asian	41 (4.26)	66 (5.27)	14 (3.2)	2 (1.21)	7 (6.36)	13 (6.63)	0. 063
Black or African American	86 (8.93)	110 (8.78)	43 (9.82)	8 (4.85)	8 (7.27)	14 (7.14)	0. 449
Native Hawaiian or Other Pacific Islander	1 (0.1)	5 (0.4)	1 (0.23)	0 (0)	0 (0)	0 (0)	0. 639
White	740 (76.84)	949 (75.74)	337 (76.94)	137 (83.03)	87 (79.09)	144 (73.47)	0. 322
Comorbidities[c]							
Bleeding Disorder	113 (11.73)	136 (10.85)	41 (9.36)	21 (12.73)	8 (7.27)	17 (8.67)	0. 440
Cerebrovascular Accident	24 (2.49)	30 (2.39)	6 (1.37)	3 (1.82)	1 (0.91)	4 (2.04)	0. 698
COPD	74 (7.68)	70 (5.59)	29 (6.62)	11 (6.67)	6 (5.45)	16 (8.16)	0. 423
Congestive Heart Failure	48 (4.98)	45 (3.59)	19 (4.34)	10 (6.06)	5 (4.55)	7 (3.57)	0. 528
Chronic Renal Failure	13 (1.35)	21 (1.68)	10 (2.28)	3 (1.82)	0 (0)	2 (1.02)	0. 543
Cirrhosis	24 (2.49)	32 (2.55)	10 (2.28)	5 (3.03)	0 (0)	2 (1.02)	0. 436
Current Smoker	67 (6.96)	76 (6.07)	25 (5.71)	12 (7.27)	3 (2.73)	12 (6.12)	0. 586
Dementia	26 (2.70)	31 (2.47)	9 (2.05)	5 (3.03)	4 (3.64)	9 (4.59)	0. 541
Diabetes	159 (16.51)	190 (15.16)	74 (16.89)	27 (16.36)	17 (15.45)	33 (16.84)	0. 941
Disseminated Cancer	8 (0.83)	13 (1.04)	4 (0.91)	1 (0.61)	3 (2.73)	3 (1.53)	0. 502
Functionally Dependent Health Status	25 (2.60)	23 (1.84)	15 (3.42)	4 (2.42)	4 (3.64)	11 (5.61)	0. 043
Hypertension	377 (39.15)	480 (38.31)	169 (38.58)	62 (37.58)	46 (41.82)	74 (37.76)	0. 979

Mental/Personality Disorder	58 (6.02)	73 (5.83)	31 (7.08)	17 (10.30)	10 (9.09)	21 (10.71)	0.038
Myocardial Infarction	13 (1.35)	13 (1.04)	4 (0.91)	2 (1.21)	3 (2.73)	2 (1.02)	0.698
Peripheral Arterial Disease	12 (1.25)	12 (0.96)	4 (0.91)	1 (0.61)	0 (0)	0 (0)	0.532
Steroid Use	3 (0.31)	11 (0.88)	6 (1.37)	1 (0.61)	0 (0)	0 (0)	0.159
Advanced Directive Limiting Care	43 (4.47)	67 (5.35)	25 (5.71)	6 (3.64)	10 (9.09)	11 (5.61)	0.345
Injury Characteristics[c]							
Blunt Trauma	673 (69.89)	844 (67.36)	311 (71.00)	100 (60.61)	74 (67.27)	139 (70.92)	0.142
Penetrating Trauma	355 (36.86)	500 (39.90)	151 (34.47)	70 (42.42)	36 (32.73)	57 (29.08)	0.306
Femur Fracture	221 (22.95)	281 (22.43)	92 (21.00)	40 (24.24)	19 (17.27)	49 (25.00)	0.640
Gastrointestinal Injury	542 (56.28)	652 (52.04)	201 (45.89)	75 (45.45)	58 (52.73)	75 (38.27)	< 0.001
Lung Injury	585 (60.75)	753 (60.10)	253 (57.76)	84 (50.91)	64 (58.18)	106 (54.08)	0.127
Pelvic Fracture	511 (53.06)	664 (52.99)	228 (52.05)	78 (47.27)	55 (50.00)	89 (45.41)	0.306
Rib Fracture	642 (66.67)	824 (65.76)	277 (63.24)	106 (64.24)	77 (70.00)	113 (57.65)	0.160
Traumatic Brain Injury	429 (44.55)	514 (41.02)	196 (44.75)	82 (49.70)	57 (51.59)	58 (29.59)	< 0.001
Injury Severity Score[b]	29 (13)	29 (12)	28 (13)	27 (12)	29 (13)	25 (13)	< 0.001
Management[a]							
Units FFP in 24 hours	9 (7-15)	6 (4-10)	4 (2-5)	3 (2-3)	2 (2-3)	1 (1-2)	< 0.001
Vitals							
Glasgow Coma Score[a]	13 (3-15)	13 (3-15)	13 (3-15)	13 (3-15)	14 (3-15)	14 (3-15)	0.701
Pulse Oximetry[a]	98 (94-100)	97 (93-100)	97 (93-100)	98 (94-100)	97 (93-99)	97 (93-100)	0.190
Pulse Rate[b]	97 (26)	96 (25)	96 (26)	95 (23)	96 (26)	94 (26)	0.663
Respiratory Rate[b]	21 (6)	20 (6)	21 (6)	20 (6)	21 (7)	21 (6)	0.664
Systolic Blood Pressure[b]	106 (32)	104 (31)	107 (32)	107 (34)	108 (30)	103 (31)	0.266
ACS Trauma							

Center Level[c]							
Level I	454 (75.67)	602 (71.07)	201 (68.14)	74 (67.27)	52 (68.42)	110 (74.83)	0.295
Level II	145 (24.17)	241 (28.45)	92 (31.19)	35 (31.82)	23 (30.26)	37 (25.17)	0.295
Level III	1 (0.17)	4 (0.47)	2 (0.68)	1 (0.91)	1 (1.32)	0 (0)	0.295

[a] = median (IQR)
[b] = mean (SD)
[c] = number (%)
Abbreviations: FFP=fresh frozen plasma, COPD=chronic obstructive pulmonary disease, SD=standard deviation, IQR=interquartile range

Table 2. Results from multivariable regression model for covariates independently associated with 24-hour and 30-day mortality for the older adult population. Only significantly associated variables after adjustment are listed here. For a list of all covariates that were used in the LASSO regression, please see Supplementary Table 2.

Variable	**24-Hour Mortality Odds Ratio (95% CI, p-value)**	**30-Day Mortality Odds Ratio (95% CI, p-value)**
ACS Trauma Center Level I*	-	1.23 (1.00-1.51, 0.045)
Advanced Directive Limiting Care	-	2.42 (1.56-3.75, <0.001)
Age	1.03 (1.02-1.05, <0.001)	1.06 (1.04-1.07, <0.001)
Cirrhosis	-	4.16 (2.18-7.94, <0.001)
Current Smoker	0.59 (0.34-0.99, 0.048)	-
Diabetes Mellitus	0.71 (0.51-0.98, 0.040)	-
Gastrointestinal Injury	-	1.22 (1.01-1.47, 0.038)
Glasgow Coma Score	0.91 (0.89-0.93, <0.001)	0.90 (0.89-0.92, <0.001)
Hypertension	0.62 (0.49-0.79, <0.001)	0.77 (0.63-0.94, 0.011)
Injury Severity Score	1.03 (1.02-1.04, <0.001)	1.03 (1.02-1.04, <0.001)
Lung Injury	1.32 (1.03-1.69, 0.027)	-
Mental/Personality Disorder	0.37 (0.21-0.65, 0.001)	0.53 (0.36-0.78, 0.001)
Pelvic Fracture	0.74 (0.59-0.92, 0.006)	-

Pulse Oximetry	0.97 (0.95-0.99, <0.001)	0.98 (0.96-1.00, 0.010)
Traumatic Brain Injury	0.53 (0.42-0.67, <0.001)	-
Units FFP in 24 hours	1.05 (1.04-1.07, <0.001)	1.11 (1.09-1.13, <0.001)
Blood Ratios**		
1:2	1.60 (1.25-2.06, <0.001)	1.44 (1.15-1.80, 0.001)
1:3	1.62 (1.14-2.31, 0.007)	1.60 (1.17-2.19, 0.003)
1:4	1.60 (0.96-2.68, 0.072)	1.57 (1.01-2.45, 0.044)
1:5	1.74 (0.94-3.21, 0.077)	2.13 (1.26-3.60, 0.005)
1:6+	2.70 (1.72-4.25, <0.001)	2.00 (1.31-3.04, 0.001)

*ACS Trauma Center Level III was used as reference category
**1:1 group was used as reference category
Risk-adjusted using all variables from Table 1

Abbreviations: CI=confidence interval, FFP=fresh frozen plasma

Table 3. Unadjusted secondary outcomes for each of the blood cohorts for the older adult population.

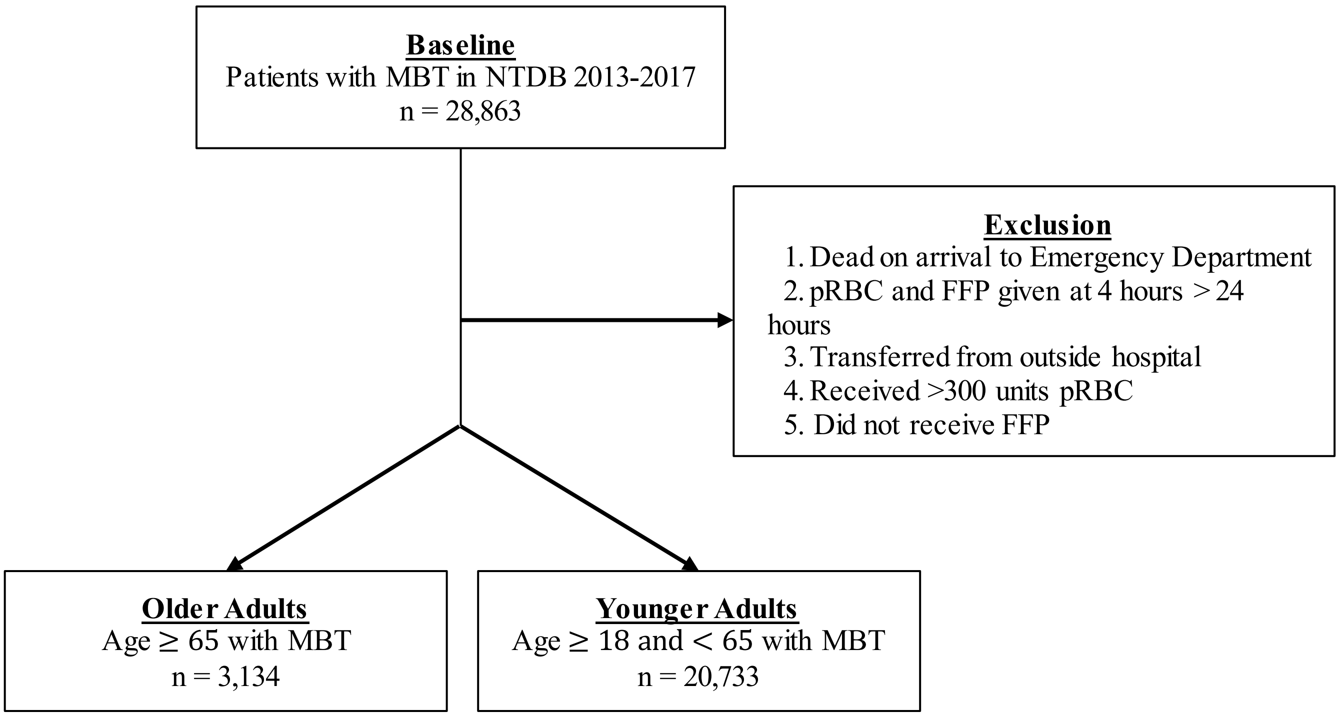
Secondary Outcomes	**1:1** (n = 963)	**1:2** (n = 1253)	**1:3** (n =438)	**1:4** (n =165)	**1:5** (n =110)	**1:6+** (n =196)	**P-value**
Hospital Complications[c]							
Acute Kidney Injury	91 (9.45)	89 (7.10)	35 (7.99)	12 (7.27)	10 (9.09)	11 (5.61)	0.310
Acute Respiratory Distress Syndrome	57 (5.92)	41 (3.27)	16 (3.65)	7 (4.24)	2 (1.82)	5 (2.55)	0.022
Cardiac Arrest with CPR	196 (20.35)	245 (19.55)	73 (16.67)	18 (10.91)	23 (20.91)	37 (18.88)	0.069
Pressure Ulcer	41 (4.26)	45 (3.59)	17 (3.88)	8 (4.85)	3 (2.73)	5 (2.55)	0.794
Deep Surgical Site Infection	8 (0.83)	17 (1.36)	3 (0.68)	5 (3.03)	0 (0)	2 (1.02)	0.117
Deep Vein Thrombosis	47 (4.88)	69 (5.51)	22 (5.02)	9 (5.45)	1 (0.91)	10 (5.10)	0.468
Extremity Compartment Syndrome	9 (0.93)	6 (0.48)	4 (0.91)	2 (1.21)	0 (0)	1 (0.51)	0.637
Myocardial Infarction	34 (3.53)	28 (2.23)	7 (1.60)	5 (3.03)	0 (0)	1 (0.51)	0.028

Organ Space Surgical Site Infection	10 (1.04)	15 (1.20)	4 (0.91)	1 (0.61)	1 (0.91)	0 (0)	0.730
Pulmonary Embolism	19 (1.97)	32 (2.55)	7 (1.60)	2 (1.21)	0 (0)	3 (1.53)	0.384
Stroke	23 (2.39)	22 (1.76)	7 (1.60)	4 (2.42)	1 (0.91)	3 (1.53)	0.774
Superficial Incisional Surgical Site Infection	9 (0.93)	17 (1.36)	4 (0.91)	2 (1.21)	2 (1.82)	2 (1.02)	0.908
Unplanned Intubation	65 (6.75)	64 (5.11)	22 (5.02)	15 (9.09)	7 (6.36)	8 (4.08)	0.181
Osteomyelitis	1 (0.10)	3 (0.24)	0 (0)	0 (0)	0 (0)	0 (0)	0.788
Unplanned Return to the OR	53 (5.50)	83 (6.62)	20 (4.57)	12 (7.27)	1 (0.91)	4 (2.04)	0.018
Unplanned Admission to the ICU	33 (3.43)	30 (2.39)	14 (3.20)	8 (4.85)	2 (1.82)	3 (1.53)	0.283
Severe Sepsis	40 (4.15)	47 (3.75)	11 (2.51)	11 (6.67)	5 (4.55)	3 (1.53)	0.106
Catheter Associated Urinary Tract Infection	12 (1.25)	5 (0.40)	2 (0.46)	0 (0)	0 (0)	2 (1.02)	0.123
Central Line Associated Bloodstream Infection	4 (0.42)	5 (0.40)	1 (0.23)	1 (0.61)	0 (0)	0 (0)	0.881
Ventilator Associated Pneumonia	26 (2.70)	30 (2.39)	6 (1.37)	4 (2.42)	1 (0.91)	0 (0)	0.146
Surgery for Hemorrhage Control[c]							
Amputation	26 (2.70)	38 (3.03)	17 (3.88)	4 (2.42)	1 (0.91)	4 (2.04)	0.560
Extremity	40 (4.15)	60 (4.79)	20 (4.57)	8 (4.85)	6 (5.45)	9 (4.59)	0.980
Neck	5 (0.52)	9 (0.72)	4 (0.91)	1 (0.61)	2 (1.82)	2 (1.02)	0.726
Laparotomy	425 (44.13)	508 (40.54)	152 (34.70)	58 (35.15)	37 (33.64)	64 (32.65)	0.001
Other Soft Tissue	11 (1.14)	8 (0.64)	5 (1.14)	1 (0.61)	0 (0)	4 (2.04)	0.337
Sternotomy	6 (0.62)	8 (0.64)	2 (0.46)	1 (0.61)	0 (0)	3 (1.53)	0.640
Thoracotomy	69 (7.17)	126 (10.06)	23 (5.25)	7 (4.24)	10 (9.09)	16 (8.16)	0.007
None	326 (33.85)	441 (35.20)	188 (42.92)	76 (46.06)	48 (43.64)	87 (44.39)	<0.001

Disposition at Discharge[c]							
Deceased	526 (55.25)	681 (55.82)	229 (54.27)	68 (41.72)	61 (57.01)	87 (45.79)	0.020
Home	4 (0.42)	5 (0.41)	0 (0)	0 (0)	0 (0)	1 (0.53)	0.020
Hospice	13 (1.37)	20 (1.64)	5 (1.18)	4 (2.45)	5 (4.67)	4 (2.11)	0.020
Transitional Care/Skilled Nursing Facility	374 (39.29)	468 (38.36)	167 (39.57)	78 (47.85)	34 (31.78)	87 (45.79)	0.020
Other	35 (3.68)	46 (3.77)	21 (4.98)	13 (7.98)	7 (6.54)	11 (5.79)	0.020
Time in Hospital[a]							
Total Length of Stay	7 (1-20)	6 (1-18)	6 (1-16)	8 (1-22)	3 (1-14)	5 (1-17)	0.004
ICU Length of Stay	5 (1-14)	5 (1-13)	5 (1-12)	7 (2-15)	3 (1-10)	3 (1-10)	0.001
Ventilator Days	3 (1-11)	3 (1-10)	3 (1-9)	4 (1-10)	2 (1-8)	2 (1-7)	<0.001

[a] = median (IQR)
[b] = mean (SD)
[c] = number (%)
Abbreviations: CPR=cardiopulmonary resuscitation, OR=operating room, ICU=intensive care unit

Figure 1. Exclusion criteria.



Abbreviation: MBT=massive blood transfusion, NTDB=National Trauma Database, pRBC=packed red blood cells, FFP=fresh frozen plasma