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Transfusion futility thresholds and mortality in geriatric trauma: Does frailty matter?

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ABSTRACT

Background: Data on massive transfusion (MT) in geriatric trauma patients is lacking. This study aims to determine geriatric transfusion futility thresholds (TT) and TT variations based on frailty.**Methods:** Patients from 2013 to 2018 TQIP database receiving MT were stratified by age and frailty. TTs and outcomes were compared between geriatric and younger adults and among geriatric adults based on frailty status.**Results:** The TT was lower for geriatric than younger adults (34 vs 39 units; $p = 0.03$). There was no difference in TT between the non-frail, frail, and severely frail geriatric adults (37, 30 and 25 units, respectively, $p > 0.05$). Geriatric adults had higher mortality than younger adults (63.1% vs 45.8%, $p < 0.01$). Non-frail geriatric adults had the highest mortality (69.4% vs 56.5% vs 56.2%, $p < 0.01$).**Conclusions:** Geriatric patients have a lower TT than younger adults, irrespective of frailty. This may help improve outcomes and optimize MT utilization.

1. Background

Exsanguination is a leading cause of death in trauma patients.¹ Along with hemorrhage control, resuscitation with blood products—in large quantities when necessary—improves survival compared to the use of high-volume crystalloid.² Massive transfusion protocols (MTPs) can facilitate the expeditious transfusion of blood products.³ Despite the life-saving potential of massive transfusion (MT), it can cause significant complications and may not always improve mortality.⁴ Despite extensive research, there is a paucity of data regarding MT in a growing subgroup of adults – the geriatric trauma patients.^{3,5,6}

First, transfusion futility thresholds (TTs) – the amount of transfused blood product after which the odds of mortality do not improve with additional transfusion – for the geriatric population are unknown.^{7–10} Morris et al. demonstrated that both increased age and amount of packed red blood cells (pRBCs) were associated with increased mortality.⁹ In the same study, all patients aged ≥ 80 years who received ≥ 51 units of pRBCs within the first 4 h of admission died, but the point of obvious futility in pRBC transfusion varied widely by decade of life. Schneider et al. examined the number of pRBCs transfused within 4 h of admission at

which point 50% of patients will die by age group: 34 units for patients aged 18–64 years, 18 units for patients aged 65–79 years, and 6 units for patients aged ≥ 80 years.¹⁰ While both studies suggest more judicious use of transfusion in older patients, they stopped short of providing a TT for geriatric trauma patients.

Second, it remains unclear whether frailty affects TTs in geriatric patients. Physiologically, geriatric patients respond to trauma differently than younger adults given their increased comorbidities, polypharmacy, and physiologic differences.^{11,12} However, the geriatric population is not homogenous. One analysis of geriatric patients with blunt abdominal trauma demonstrated that age alone correlates with mortality yet frailty, a state of increased vulnerability to stressors, is an age-independent predictor of mortality.^{13,14} It is well known that frailty drives outcomes in geriatric surgical patients independent of chronological age.^{15,16} An analysis of the American College of Surgeons Trauma Quality Improvement Program (TQIP) data demonstrated that severe frailty was associated with higher short-term mortality.¹⁷ Joseph et al. demonstrated that among geriatric trauma patients at a Level 1 trauma center, frailty independently predicted discharge to a skilled nursing facility or death.¹⁸ Another institutional study found that trauma patients with frailty had

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longer hospitalizations as well as increased complications, more nonhome discharges, and higher mortality.¹⁹ While these studies demonstrate how frailty affects outcomes, the impact of frailty on geriatric patients receiving MT and on geriatric TTs is unknown.

Therefore, we conducted this study by applying bootstrapping and regression modeling to TQIP data in order to: 1) define TTs for geriatric trauma victims as opposed to younger adult patients, and 2) compare geriatric TTs when stratified by frailty. We hypothesized that the TT will be lower for geriatric patients compared to younger adults. Furthermore, the TT for frail and severely frail geriatric patients will be lower than that of non-frail geriatric patients.

2. Methods

2.1. Study design and patient population

The 2013–2018 TQIP database was queried for adult patients (age ≥ 18 years old) who received at least one unit of pRBCs within 24 h of admission. Although additional years of TQIP data are available, collection of transfusion data within 24 h of admission was discontinued in 2019. The TQIP database contains data from over 875 trauma centers in the United States and represents one of the largest databases of trauma patients.²⁰ The TQIP database contains only deidentified, national data; therefore, institutional review board approval was not required for this study. Our independent variables were age and frailty. Patients were categorized by age into younger adults (18–64 years old) and geriatric adults (≥ 65 years old). Geriatric patients were stratified into no frailty, frailty, and severe frailty using the 5-factor modified frailty index (mFI-5). Because of the variables included in the TQIP database, we were limited to this comorbidity-based index, which does have validity evidence for use in large databases including the National Surgical Quality Improvement Program (NSQIP) and TQIP.^{19,21,22} The index is composed of five variables: 1) Chronic obstructive pulmonary disease (COPD); 2) Congestive heart failure (CHF); 3) Diabetes; 4) Hypertension (HTN) requiring medications; and 5) Functionally dependent health status. Patients without these variables are “non-frail,” those positive for one variable are considered “frail,” and those positive for two or more variables are considered “severely frail.”

2.2. Data extraction

A researcher performed the database search and extracted patients meeting inclusion criteria. Variables collected for each patient included admission year, demographics (age, sex, race), mechanism of injury (blunt, penetrating, other), preexisting medical conditions (advanced directive limiting care, alcohol use disorder, anticoagulation use, bleeding disorder, cerebrovascular accident [CVA], COPD, chronic renal failure, cirrhosis, CHF, current smoker, dementia, diabetes, disseminated cancer, functionally dependent health status, HTN, myocardial infarction [MI], peripheral artery disease [PAD], steroid use, and substance use disorder), ED vital signs (systolic blood pressure [SBP], respiratory rate [RR], and heart rate [HR]), and injury parameters (Glasgow coma scale [GCS], injury severity score [ISS], revised trauma score [RTS], brain abbreviated injury score [AIS-brain], thoracic abbreviated injury score [AIS-thorax], abdominal abbreviated injury score [AIS-abdomen], and extremity abbreviated injury score [AIS-extremity]). Transfusion variables collected were number of units of pRBCs transfused within 24 h and number of units of fresh frozen plasma (FFP) transfused within 24 h. We chose to omit platelet transfusion data from our study for two reasons. First, a recent survey of the American Association for the Surgery of Trauma centers found that only 58% of centers have platelets in the first MTP cooler suggesting a wide range of practice patterns between institutions.²³ Second, there may be inconsistencies in reporting platelet data (eg. centers may report one super pack of platelets as one unit or multiple subunits depending on local practice). Outcome variables

collected included 24-h and in-hospital mortality, hospital and ICU length of stay (LOS), and number of days ventilated. Complications (acute kidney injury [AKI], acute respiratory distress syndrome (ARDS), cardiac arrest, catheter-associated urinary tract infection (CAUTI), central line-associated blood stream infection (CLABSI), deep surgical site infection [SSI], deep vein thrombosis [DVT], delirium, MI, pulmonary embolism [PE], pressure ulcer, severe sepsis, stroke/CVA, superficial SSI, unplanned ICU admission, unplanned return to OR, and ventilator-associated pneumonia (VAP), and discharge disposition (short term care, intermediate care, home health, home/self-care, skilled nursing facility, hospice, inpatient rehab, and long term care) were also collected. Data cleaning procedures were conducted on pRBC and FFP values. If the volume of transfusion was coded as “cc's” of product but the amount was < 100 , it was recoded as “units”. If volume of transfusion was coded as “units” but the amount was > 100 , it was removed because the value is either an extreme outlier or a data entry error. Prior literature has similarly excluded patients who were reported to have received > 100 units of pRBCs within a 24-h period.⁷

2.3. Data analysis

Bivariate analyses were conducted to examine differences between younger adults and geriatric adults and between geriatric adults who were non-frail, frail, and severely frail. The bivariate analyses were limited to patients who received MT defined as ≥ 10 units of pRBCs within 24 h of admission. While the number of units of pRBCs transfused each hour may more accurately reflect illness severity, TQIP does not contain transfusion data with this level of granularity.²⁴ Demographics, mechanism of injury, preexisting medical conditions, ED vital signs, injury parameters, hospital parameters, transfusion variables, and outcomes including hospital and ICU LOS (calculated excluding patient mortalities), number of days ventilated, overall mortality, complications, and discharge disposition were compared between groups using chi square testing for categorical data and t-testing or ANOVA for continuous data. The threshold for statistical significance was set at $p < 0.05$ using two-tailed tests.

A multiple logistic regression analyses was conducted to determine the effect of blood product, age, frailty, and ISS on mortality. Using a bootstrapping methodology and accounting for differences by ISS, models were built to examine the change in odds of survival as blood product transfusion increased. Bootstrapping is a robust statistical method that involves repeated random sampling from the original data to estimate population-level statistics such as confidence intervals.²⁵ To estimate the confidence intervals of the TT point directly, we employed bootstrap samples to fit a multiple logistic regression. Similar to previous definitions, each bootstrap sample's TT estimate was defined as the point at which the odds of mortality between the group receiving 10 fewer units of blood product (reference) and the group receiving 10 more units of blood product than the number of blood product itself was equal to 1.⁷ This approach allowed us to perform a *t*-test on the difference of the TTs between groups. Subgroup analyses were performed between geriatric and younger adults by injury mechanism. The threshold for statistical significance was set at $p < 0.05$ using one-tailed tests given our a priori hypotheses that increased age and worsening frailty will decrease the TT. Of note, the multiple logistic regression included all patients who received any pRBCs within 24 h of admission. In order to model an odds ratio beginning at 10 units of pRBCs transfused, mortality data was needed for patients receiving 10 fewer units than this point (ie. Receiving 1–9 units pRBCs). Because these patients did not receive MT, they were only used to for the model to determine TTs and not used for bivariate models or the multivariate model for hazard ratio of death. All analyses were conducting using R (version 4.2.2). The Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines were followed.²⁶

3. Results

A total of 115,158 adult patients from the 2013–2018 TQIP database met inclusion criteria of receiving at least one unit of pRBCs within 24 h of admission. A total of 20,358 patients (17.7%) received MT, of which 17,809 (87.5%) were younger adults and 2,549 (12.5%) were geriatric adults. Of the geriatric adults who received MT, 1,313 (51.5%), 789 (31.0%), and 447 (17.5%) were not frail, frail, and severely frail, respectively.

3.1. Transfusion threshold

3.1.1. Age – geriatric vs younger adults

Fig. 1 shows the multivariate model depicting the odds ratios of survival and their 95% confidence intervals (shaded area) with increased transfusion between geriatric and younger adults for pRBCs transfused (Fig. 1A) and pRBCs + FFP transfused (Fig. 1B) within 24 h. The odds of survival with increased transfusion steadily decrease for both groups but with a faster decline shown in the geriatric adults. The TT in pRBCs, the point at which additional transfusion does not improve survival (OR = 1), is 34 units (95% CI 30–37) for geriatric adults compared to 39 units (95% CI 37–44) for younger adults ($p = 0.0321$, Fig. 1A). The TT in

pRBCs + FFP is 54 units (95% CI 46–61) for geriatric adults and 70 units (95% CI 66–82) for younger adults ($p = 0.0242$, Fig. 1B). Among patients suffering blunt trauma, the TT in pRBCs is 27 units (95% CI 22–31) for geriatric adults compared to 35 units (95% CI 32–38) for younger adults ($p = 0.0167$). Among patients suffering penetrating trauma, the TT in pRBCs is 17 units (95% CI 11–21) for geriatric adults compared to 30 units (95% CI 26–36) for younger adults ($p = 0.0019$).

3.1.2. Frailty status in geriatric adults

Fig. 2 shows the multivariate model depicting the odds ratios of survival and their 95% confidence intervals (shaded area) with increased transfusion between geriatric patients by frailty group for pRBCs transfused (Fig. 2A) and pRBCs + FFP transfused (Fig. 2B) within 24 h. The odds of survival with increased transfusion steadily decrease for all groups. The TT in pRBCs for geriatric adults with no frailty, frailty, and severe frailty is 37 (95% CI 35–59), 30 (95% CI 24–39), and 25 (95% CI 20–32), respectively (Fig. 2A). None of these pairwise differences (no frailty vs frailty, $p = 0.3088$; no frailty vs severe frailty, $p = 0.3612$; and frailty vs severe frailty, $p = 0.2012$) reached statistical significance. The TT in pRBCs + FFP for geriatric adults with no frailty, frailty, and severe frailty is 54 (95% CI 46–66), 54 (95% CI 41–70), and 59 (95% CI 50–92), respectively (Fig. 2B). None of these pairwise differences (no frailty vs

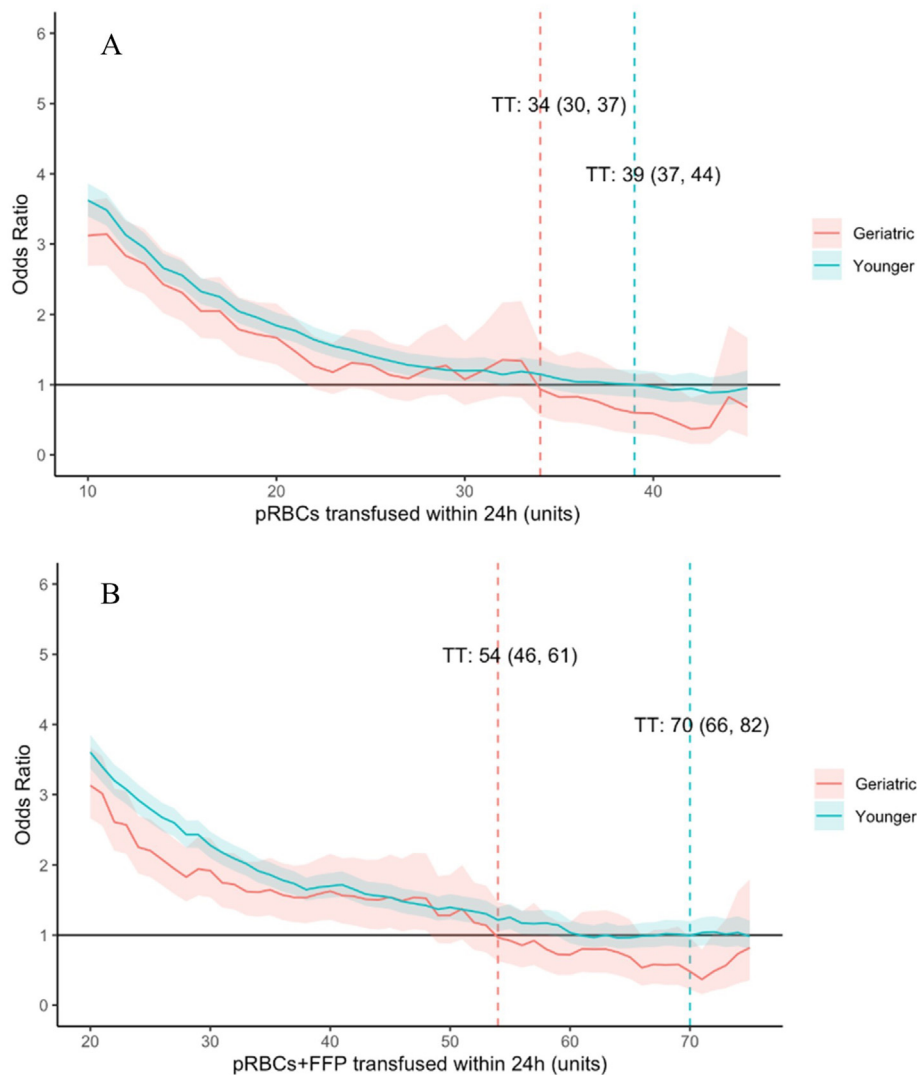


Fig. 1. Odds of survival with increased transfusion by units of pRBCs (A) and pRBCs + FFP (B) transfused within 24 h of admission. Geriatric adults (age ≥ 65 years) are shown in red and younger adults (age < 65 years) are shown in blue. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

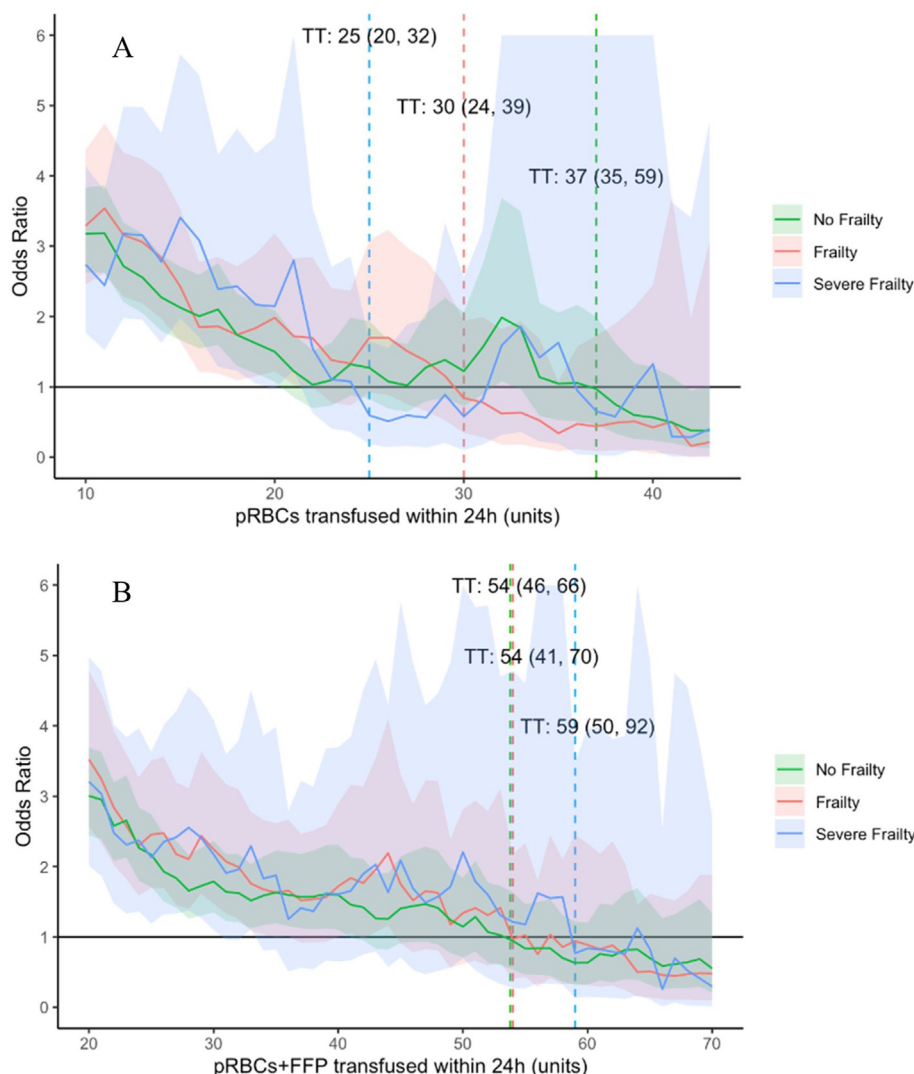


Fig. 2. Odds of survival with increased transfusion by units of pRBCs (A) and pRBCs + FFP (B) transfused within 24 h of admission. Geriatric adults with no frailty (green), frailty (red), and severe frailty (blue) are shown. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

frailty, $p = 0.4845$; no frailty vs severe frailty, $p = 0.3388$; and frailty vs severe frailty, $p = 0.3561$) reached statistical significance.

3.2. Clinical outcomes

3.2.1. Age – geriatric vs younger adults

Baseline characteristics of geriatric vs younger adults are shown in [Table 1](#). Notably, geriatric adults had a lower admission HR (89 vs 105, $p < 0.0001$), higher admission SBP (95 vs 90, $p < 0.0001$), lower ISS (29 [21–38] vs 29 [21–41], $p = 0.0002$), and higher GCS (9 vs 6, $p < 0.0001$) than younger adults. Outcomes by age are shown in [Table 2](#). Geriatric adults had a higher 24-h (28.4% vs 26.1%, $p = 0.0192$) and in-hospital mortality (63.1% vs 45.8%, $p < 0.0001$) than younger adults. Geriatric adults had a shorter hospital LOS than younger adults (12 [3–25] vs 17 [7–31] days, $p < 0.0001$). There was no difference in ICU LOS (9 [3–18] vs 9 [4–18] days, $p = 0.2054$) between groups. Cardiac arrest (29.2% vs 26.9%, $p = 0.0358$), MI (3.3% vs 0.6%, $p < 0.0001$), and pressure ulcers (6.2% vs 4.9%, $p < 0.0001$) were all more common in geriatric adults. Deep SSI (1.4% vs 3.7%, $p < 0.0001$), DVT (6.6% vs 10.1%, $p < 0.0001$), PE (2.5% vs 3.7%, $p = 0.0058$), and superficial SSI (1.2% vs 2.3%, $p = 0.0027$) were all more common in younger adults. Fewer geriatric adults were discharged to home/self-care (5.8% vs 35.0%, $p = 0.0159$) and

inpatient rehab (20.8% vs 21.5%, $p < 0.0001$) than younger adults. More geriatric adults were discharged to long term care (24.2% vs 14.6%, $p < 0.0001$), skilled nursing facility (29.7% vs 10.2%, $p < 0.0001$), or hospice (5.1% vs 0.8%, $p < 0.0001$) than younger adults.

3.2.2. Frailty status in geriatric adults

Baseline characteristics of geriatric adults by frailty group are shown in [Table 3](#). Notably, non-frail geriatric adults had the highest penetrating trauma rate (10.1% vs 6.8% vs 6.8%, $p < 0.0001$), highest admission HR (93 vs 96 vs 88, $p = 0.0086$), highest ISS (30 vs 27 vs 26, $p < 0.0001$), and lowest GCS (6 vs 13 vs 14, $p < 0.0001$). Outcomes among geriatric adults by frailty group are shown in [Table 4](#). Non-frail geriatric adults had the highest 24-h (36.6% vs 21.3% vs 17.4%, $p < 0.0001$) and in-hospital mortality (69.4% vs 56.5% vs 56.2%, $p < 0.0001$). Non-frail geriatric adults had the shortest hospital (10 vs 14 vs 14 days, $p = 0.0207$) and ICU LOS (8 vs 9 vs 9 days, $p = 0.0493$). There were no differences in discharge to home/self-care (6.7% vs 6.5% vs 2.9%, $p = 0.6732$), inpatient rehab (22.1% vs 20.9% vs 17.9%, $p = 0.9937$), long term care (23.0% vs 28.1% vs 19.7%, $p = 0.8806$), skilled nursing facility (27.0% vs 26.5% vs 40.5%, $p = 0.4445$), or hospice (5.8% vs 4.3% vs 5.2%, $p = 0.7957$) between frailty groups.

Table 1
Comparison of characteristics between geriatric and younger adult patients by age among those receiving MT.

Characteristics	Geriatric Adult (n = 2,549)	Younger Adult (n = 17,809)	OR (95% CI)	p-value
Age, median [IQR]	73 [68–79]	34 [25–48]	N/a	<0.0001
Male, n (%)	1,697 (66.6)	14,304 (80.4)	0.49 (0.45–0.53)	<0.0001
Race, n (%)				
White	1,995 (81.0)	9,292 (54.4)	3.71 (1.73–7.96)	<0.0001
Black	219 (8.9)	5,567 (32.6)	0.68 (0.31–1.47)	0.3257
American Indian	7 (0.3)	121 (0.7)	Ref	Ref
Asian	99 (4.0)	327 (1.9)	5.23 (2.36–11.58)	<0.0001
Pacific Islander	3 (0.1)	55 (0.3)	0.94 (0.23–3.78)	0.9338
Other	139 (5.7)	1,720 (10.1)	1.40 (0.64–3.05)	0.3996
Comorbidities, n (%)				
Advanced directive	112 (5.6)	74 (0.7)	9.02 (6.69–12.14)	<0.0001
Alcohol use disorder	95 (4.8)	1,183 (10.4)	0.43 (0.34–0.53)	<0.0001
Bleeding disorder	248 (12.4)	228 (2.0)	6.89 (5.71–8.30)	<0.0001
CVA	169 (8.5)	53 (0.5)	5.79 (3.94–8.49)	<0.0001
COPD	169 (8.5)	351 (3.1)	2.88 (2.39–3.49)	<0.0001
Chronic renal failure	44 (2.2)	61 (0.5)	4.15 (2.81–6.14)	<0.0001
Cirrhosis	91 (4.6)	437 (3.9)	1.19 (0.94–1.50)	0.1450
CHF	110 (5.5)	68 (0.6)	9.63 (7.09–13.08)	<0.0001
Current smoker	158 (7.9)	2736 (24.2)	0.27 (0.23–0.32)	<0.0001
Dementia	65 (3.3)	10 (0.1)	37.99 (19.49–74.06)	<0.0001
Diabetes	413 (20.6)	649 (5.7)	4.28 (3.74–4.89)	<0.0001
Disseminated cancer	30 (1.5)	9 (0.1)	19.14 (9.07–40.37)	<0.0001
Functionally dependent health status	83 (4.2)	68 (0.6)	7.16 (5.18–9.91)	<0.0001
HTN	984 (49.2)	1,460 (12.9)	6.98 (6.30–7.75)	<0.0001
Myocardial infarction	32 (1.6)	45 (0.4)	4.07 (2.58–6.43)	<0.0001
Steroid use	22 (1.1)	31 (0.3)	4.05 (2.34–7.01)	<0.0001
	52 (2.6)	1,643 (14.5)		<0.0001

Table 1 (continued)

Characteristics	Geriatric Adult (n = 2,549)	Younger Adult (n = 17,809)	OR (95% CI)	p-value
Substance use disorder			0.16 (0.12–0.21)	
Mechanism of injury				
Blunt	1,945 (90.9)	8,702 (58.7)	Ref	Ref
Penetrating	181 (8.5)	6,018 (40.6)	0.13 (0.12–0.16)	<0.0001
Other	14 (0.7)	110 (0.7)	0.57 (0.33–1.00)	0.0462
Vitals, median [IQR]				
Systolic BP (mmHg)	95 [70–120]	90 [64–117]	N/a	<0.0001
Respiratory rate (x/min)	18 [13–23]	18 [12–23]	N/a	0.9774
Heart rate (x/min)	89 [69–110]	105 [74–128]	N/a	<0.0001
Injury parameters, median [IQR]				
ISS	29 [21–38]	29 [21–41]	N/a	0.0002
AIS-Brain	3 [2–4]	3 [2–5]	N/a	<0.0001
AIS-Thorax	3 [3–4]	3 [3–4]	N/a	0.0003
AIS-Abd	3 [2–4]	4 [3–4]	N/a	<0.0001
AIS-Upper extremity	2 [1–2]	2 [1–2]	N/a	0.0008
AIS-Lower extremity	3 [2–3]	3 [2–4]	N/a	0.3143
GCS	9 [3–15]	6 [3–14]	N/a	<0.0001
Transfusion Data				
pRBCs, median [IQR]	14 [11–21]	16 [12–24]	N/a	<0.0001
FFP, median [IQR]	10 [6–15]	11 [7–18]	N/a	<0.0001
pRBCs:FFP ratio, mean+/-SD	1.94 ± 1.72	1.88 ± 1.66	N/a	0.1024

3.3. Risk of mortality

The multiple logistic regression model for hazard ratio of mortality is shown in [Table 5](#). The risk of mortality increases with increasing pRBC transfusion amount (≤ 10 units, HR 0.24, $p < 0.0001$; 11–29 units reference; >30 units, HR 1.78, $p < 0.0001$). Age ≥ 65 (HR 1.87, $p < 0.0001$) and increased ISS (HR 1.03, $p < 0.0001$) are independently associated with mortality. Among geriatric adults, no frailty vs frailty was associated with a decreased risk of mortality (HR 0.46, $p < 0.0001$) while there was no association between severe frailty vs frailty on mortality (HR 1.12, $p = 0.0704$).

4. Discussion

Despite the life-saving potential of MT when paired with hemorrhage control, high-volume transfusion does not always improve outcomes. MT and its impacts have been studied in adults, but studies specific to the geriatric population are limited.^{3,5–7} Through extensive analysis on TQIP data, we defined TTs specific to geriatric patients and compared geriatric TTs when stratifying by degree of frailty. Our study demonstrated that geriatric patients have a lower TT than younger adults. However, accounting for frailty did not significantly change TTs within the geriatric population. To the best of our knowledge, this study is the first to define TTs for geriatric trauma victims and examine the impact of frailty on TTs. The findings will help to shed light on care delivery and optimize outcomes for geriatric trauma patients, as the population aged 65 and older will double from 2012 to 2050 in the US.²⁷ Analyses of the National Trauma Data Bank (NTDB) have showed that the percentage of all trauma patients aged 65 and older increased from 18% in 2005 to 30% in 2015.²⁸

In our analysis, we identified 24-h TTs of 34 units of pRBCs or 54 units of pRBCs + FFP for geriatric patients and 39 units of pRBCs or 70 units of pRBCs + FFP for younger adults. Quintana et al. demonstrated the TT for the general population was 39 units of pRBCs + FFP in 4 h but did not

Table 2
Comparison of outcomes between geriatric and younger adult patients by age among those receiving MT.

Outcomes	Geriatric Adult (n = 2,549)	Younger Adult (n = 17,809)	OR (95% CI)	p-value
24-h mortality	680 (28.4)	4,418 (26.1)	1.12 (1.02-1.23)	0.0192
In-hospital mortality	1,570 (63.1)	8,021 (45.8)	2.02 (1.85-2.20)	<0.0001
Hospital LOS, median [IQR]	12 [3–25]	17 [7–31]	N/a	<0.0001
ICU LOS, median [IQR]	9 [3–18]	9 [4–18]	N/a	0.2054
Vent Days, median [IQR]	3 [1–11]	3 [1–10]	N/a	0.2412
Complications, n (%)				
AKI	266 (13.9)	1,590 (12.4)	1.14 (0.99-1.31)	0.0717
Acute respiratory distress syndrome	131 (6.8)	903 (7.1)	0.97 (0.80-1.17)	0.7304
Cardiac Arrest	558 (29.2)	3,436 (26.9)	1.12 (1.01-1.25)	0.0358
CAUTI	88 (4.6)	471 (3.7)	1.27 (1.00-1.60)	0.0504
CLABSI	16 (0.8)	139 (1.1)	0.77 (0.46-1.30)	0.3248
Deep SSI	27 (1.4)	465 (3.7)	0.38 (0.26-0.56)	<0.0001
DVT	126 (6.6)	1,285 (10.1)	0.63 (0.52-0.76)	<0.0001
Myocardial Infarction	63 (3.3)	81 (0.6)	5.34 (3.83-7.45)	<0.0001
PE	47 (2.5)	474 (3.7)	0.65 (0.48-0.89)	0.0058
Pressure ulcer	118 (6.2)	631 (4.9)	1.27 (1.03-1.55)	0.0223
Severe sepsis	112 (5.9)	769 (6.0)	0.97 (0.79-1.19)	0.7821
Stroke/ Cerebrovascular accident	47 (2.5)	298 (2.3)	1.06 (0.77-1.44)	0.7348
Superficial SSI	23 (1.2)	289 (2.3)	0.53 (0.34-0.81)	0.0027
Unplanned ICU Admission	73 (3.8)	585 (4.6)	0.83 (0.65-1.06)	0.1337
Unplanned visit to OR	196 (10.2)	1,456 (11.4)	0.89 (0.76-1.04)	0.1395
VAP	211 (11.0)	1,376 (10.8)	1.03 (0.89-1.21)	0.6743
Discharge Disposition				
Home/self-care	47 (5.8)	2,985 (35.0)	0.56 (0.35-0.90)	0.0159
Home health	28 (3.5)	1,001 (11.7)	Ref	Ref
Short term care	63 (7.8)	423 (5.0)	5.32 (3.36-8.43)	<0.0001
Intermediate care	25 (3.1)	117 (1.4)		<0.0001

Table 2 (continued)

Outcomes	Geriatric Adult (n = 2,549)	Younger Adult (n = 17,809)	OR (95% CI)	p-value
			7.64 (4.31-13.54)	
Long term care	195 (24.2)	1,242 (14.6)	5.61 (3.74-8.41)	<0.0001
Inpatient rehab	167 (20.8)	1,839 (21.5)	3.25 (2.16-4.88)	<0.0001
Skilled nursing facility	239 (29.7)	867 (10.2)	9.86 (6.59-14.73)	<0.0001
Hospice	41 (5.1)	65 (0.8)	22.55 (13.11-38.78)	<0.0001

evaluate 24-h TTs.⁷ While 4-h TTs may inform the initial resuscitation, 24-h TTs may be more useful. The first 4-h of a patient's care may be filled with obtaining IV access, damage control surgery, laboratory testing, imaging, etc. After the first 24-h, however, clinicians may have a moment to consider the bigger picture of the patient's condition. Others have similarly demonstrated that survival declines precipitously with transfusion of 30–50 units within the first 4–24 h without defining a specific TT.^{8,29,30} Only a few studies have examined the impact of additional transfusion in geriatric patients receiving MT—while all have demonstrated that increased transfusion is associated with increased mortality in the elderly, none established TTs.^{9,10,31} These results do, however, support our conclusion that the geriatric TT is lower than the younger adult TT. The reasons for this are unknown, but one prospective study found that elderly trauma patients exhibit an attenuated hyperdynamic and hypermetabolic response to injury as manifested by their decreased ability to mount a febrile response and reduced oxygen consumption.³² A more recent study prospectively compared plasma inflammatory marker concentrations between adults age ≥55 years old to adults <55 years old with traumatic brain injury and found evidence of a chronic inflammatory state in the elderly with decreased wound healing.³³ Other studies have found similar differences in posttraumatic immune response between young and elderly patients following other injuries such as femur fracture.³⁴ These studies highlight the cellular dysfunction associated with aging, which most likely reduces the body's ability to recover from significant trauma.

Previous studies have demonstrated that geriatric patients receiving MT had higher mortality and were more frequently discharged to unfavorable locations. For example, a 2022 study of all patients in the US National Trauma Data Bank utilized propensity score matching to isolate the effect of age on outcomes while controlling for age-related comorbidities including four of the five factors in the frailty index used in our study (CHF, COPD, DM, HTN) as well as additional comorbidities.¹³ They showed that patients age ≥65 years had longer hospital and ICU LOS, more days ventilated, higher complications, and increased mortality – 8% compared to 1.9% in younger adults.¹³ Specific to patients receiving MT, our findings are corroborated by one single-institution study, which found that age ≥65 was independently associated with mortality.³⁵ Furthermore, a multi-center study found that among patients receiving ultramassive transfusion (>20 units in 24 h), age >50 was a significant discriminatory variable in predicting a poor outcome.³⁶ One study of TQIP data found that among patients receiving MT, age was not associated with mortality.³⁷ They chose to include HR and SBP in their multivariate model. Given that vital signs are more variable and less predictive of mortality in geriatric trauma patients, this may have confounded their model.³⁸ One additional single-institution study found no difference in survival between elderly patients and younger adults receiving MT although their sample size was only 66 total patients.³⁹

Table 3
Characteristics by frailty among geriatric adults receiving MT.

Characteristics	No Frailty (n = 1,313)	Frailty (n = 789)	Severe Frailty (n = 447)	p-value
Age, median [IQR]	72 [67–78]	74 [69–80]	74 [69–80]	<0.0001
Male, n (%)	877 (66.8)	521 (66.0)	299 (66.9)	0.9267
Race, n (%)				
White	1,012 (80.1)	650 (84.9)	333 (77.1)	0.1690
Black	108 (8.5)	59 (7.7)	52 (12.0)	0.4438
American Indian	2 (0.2)	2 (0.3)	3 (0.7)	Ref
Asian	58 (4.6)	26 (3.4)	15 (3.5)	0.1347
Pacific Islander	2 (0.2)	1 (0.1)	0 (0.0)	0.3564
Other	82 (6.5)	28 (3.7)	29 (6.7)	0.2499
Comorbidities, n (%)				
Advanced directive	39 (5.1)	42 (5.3)	31 (6.9)	0.3703
Alcohol use disorder	39 (5.1)	36 (4.6)	20 (4.5)	0.8432
Bleeding disorder	75 (9.8)	99 (12.6)	74 (16.6)	0.0026
CVA	11 (1.4)	22 (2.8)	20 (4.5)	0.0061
COPD	0 (0.0)	43 (5.5)	126 (28.2)	<0.0001
Chronic renal failure	6 (0.8)	15 (1.9)	23 (5.2)	0.0023
Cirrhosis	35 (4.6)	33 (4.2)	23 (5.2)	0.7365
CHF	0 (0.0)	21 (2.7)	89 (19.9)	<0.0001
Current smoker	61 (8.0)	57 (7.2)	40 (9.0)	0.5552
Dementia	21 (2.8)	22 (2.8)	22 (4.9)	0.0769
Diabetes	0 (0.0)	97 (12.3)	316 (70.7)	<0.0001
Disseminated cancer	8 (1.1)	18 (2.3)	4 (0.9)	0.0659
Functionally dependent health status	0 (0.0)	30 (3.8)	53 (11.9)	<0.0001
HTN	0 (0.0)	598 (75.8)	419 (93.7)	<0.0001
Myocardial infarction	6 (0.8)	18 (2.3)	8 (1.8)	0.0171
Steroid use	5 (0.7)	7 (0.9)	10 (2.2)	0.0295
Substance use disorder	24 (3.1)	15 (1.9)	13 (2.9)	0.2777
Mechanism of injury				
Blunt	980 (89.5)	608 (92.1)	357 (92.7)	Ref
Penetrating	110 (10.1)	45 (6.8)	26 (6.8)	0.0279
Other	5 (0.5)	7 (1.1)	2 (0.5)	0.3205
Vitals, median [IQR]				
Systolic BP (mmHg)	93 [69–121]	98 [71–118]	98 [76–120]	0.3900
Respiratory rate (x/min)	18 [12–23]	18 [14–23]	18 [15–22]	0.0224
Heart rate (x/min)	93 [70–112]	86 [66–106]	88 [70–106]	0.0086
Injury parameters, median [IQR]				
ISS	30 [22–41]	27 [20–38]	26 [18–36]	<0.0001
AIS-Brain	3 [2–4]	3 [2–4]	3 [2–4]	0.0093
AIS-Thorax	3 [3–4]	3 [3–4]	3 [3–4]	0.0075
AIS-Abd	3 [2–4]	3 [2–4]	3 [2–4]	0.7610
AIS-Upper extremity	2 [1–2]	2 [1–2]	2 [1–2]	0.1420
AIS-Lower extremity	3 [2–3]	3 [2–3]	3 [2–3]	0.7960
GCS	6 [3–14]	13 [5–15]	14 [6–15]	<0.0001
Transfusion Data				
pRBCs, median [IQR]	15 [12–21]	14 [11–20]	14 [11–19]	<0.0001
FFP, median [IQR]	10 [6–16]	10 [6–15]	9 [6–14]	0.0432
pRBCs:FFP ratio, mean±SD	2.02 ± 2.01	1.79 ± 1.16	1.99 ± 1.63	0.0119

Interestingly, although the pRBC TT among geriatric patients decreased with increasing frailty, there was no statistically significant effect of frailty on TT in our study. While frailty is hypothesized to impact the body's response to trauma and transfusion, this was not demonstrated in our study.⁴⁰ To our knowledge, there are no other studies addressing TTs by frailty. Frailty did, however, have an independent impact on mortality. Outcomes following MT were worse for non-frail geriatric adults on bivariate analyses; however, on multivariate analysis, frailty had a significant, independent impact on mortality. The non-frail geriatric adults had worse injury, which likely drove their increased

Table 4
Characteristics by frailty among geriatric adults receiving MT.

Outcomes	No Frailty (n = 1,313)	Frailty (n = 789)	Severe Frailty (n = 447)	p-value
24-h mortality	445 (36.6)	161 (21.3)	74 (17.4)	<0.0001
In-hospital mortality	883 (69.4)	439 (56.5)	248 (56.2)	<0.0001
Hospital LOS, median [IQR]	10 [2–23]	14 [4–26]	14 [5–24]	0.0207
ICU LOS, median [IQR]	8 [3–17]	9 [4–19]	9 [4–19]	0.0493
Vent Days, median [IQR]	2 [1–9]	5 [2–13]	5 [2–13]	<0.0001
Complications, n (%)				
AKI	95 (10.0)	100 (16.5)	71 (19.7)	<0.0001
ARDS	61 (6.4)	38 (6.3)	32 (8.9)	0.2315
Cardiac Arrest	311 (32.8)	163 (26.9)	84 (23.3)	0.0011
CAUTI	35 (3.7)	32 (5.3)	21 (5.8)	0.1500
CLABSI	9 (1.0)	3 (0.5)	4 (1.1)	0.5303
Deep SSI	10 (1.1)	15 (2.5)	2 (0.6)	0.0217
DVT	62 (6.6)	40 (6.6)	24 (6.7)	0.9969
Myocardial Infarction	23 (2.4)	24 (4.0)	16 (4.4)	0.1026
PE	18 (1.9)	20 (3.3)	9 (2.5)	0.2225
Pressure ulcer	47 (5.0)	40 (6.6)	31 (8.6)	0.0433
Severe sepsis	43 (4.5)	39 (6.4)	30 (8.3)	0.0255
Stroke/Cerebrovascular accident	12 (1.3)	22 (3.6)	13 (3.6)	0.0040
Superficial SSI	8 (0.8)	10 (1.7)	5 (1.4)	0.3433
Unplanned ICU Admission	22 (2.3)	33 (5.4)	18 (5.0)	0.0032
Unplanned visit to OR	88 (9.3)	74 (12.2)	34 (9.4)	0.1583
VAP	78 (8.2)	83 (13.7)	50 (13.9)	0.0004
Discharge Disposition				
Home/self-care	22 (6.7)	20 (6.5)	5 (2.9)	0.6732
Home health	12 (3.7)	11 (3.6)	5 (2.9)	Ref
Short term care	29 (8.9)	21 (6.9)	13 (7.5)	0.8546
Intermediate care	9 (2.8)	10 (3.3)	6 (3.5)	0.8193
Long term care	75 (23.0)	86 (28.1)	34 (19.7)	0.8806
Inpatient rehab	72 (22.1)	64 (20.9)	31 (17.9)	0.9937
Skilled nursing facility	88 (27.0)	81 (26.5)	70 (40.5)	0.4445
Hospice	19 (5.8)	13 (4.3)	9 (5.2)	0.7957

Table 5
Logistic regression model showing the hazard ratio of mortality.

Characteristics	HR (95% CI)	p-value
pRBCs transfused (units)		
≤10	0.24 (0.23-0.26)	<0.0001
11-29	Ref	
>30	1.78 (1.63-1.94)	<0.0001
Age ≥65	1.87 (1.75-1.99)	<0.0001
Degree of frailty		
No frailty	0.46 (0.43-0.50)	<0.0001
Frailty	Ref	
Severe frailty	1.12 (0.99-1.26)	0.0704
ISS (1-pt ↑)	1.03 (1.03-1.03)	<0.0001

mortality. When accounting for ISS in the multivariate model, age and frailty (although there was no difference between frailty and severe frailty levels) were both independently associated with mortality. A 2023 meta-analysis of frailty in elderly trauma patients identified 6 studies that reported multivariable regression analyses comparing frailty, ISS, and age.⁴¹ All six studies found an impact of frailty on outcomes while only two of the six found a simultaneous impact of age on outcomes. This current study adds to the evidence for independent effects of age and frailty on outcomes in trauma patients.

Our study was not without limitations. Most importantly, because this study utilized the TQIP database, we were limited to the mFI-5, comorbidity-based frailty assessment. Although the mFI-5 has validity evidence to support its use, other frailty indices include additional variables that

are not captured in large, multi-institutional databases.^{19,21} The mFI-5 is the only frailty index that could be applied to TQIP. Other frailty indices such as the frailty index (FI) or trauma-specific frailty index (TSFI) may provide a more comprehensive measure of frailty. The Frailty Index (FI) includes data points related to daily activities (eg. Do you need help cooking meals?), health attitude (eg. How often do you feel lonely?), and function (eg. Do you get regular exercise?) and correlates to unfavorable discharge disposition in geriatric trauma.⁴² A simpler, 15-item trauma-specific frailty index (TSFI) was developed, which still predicted poor outcomes in the short term and at 3-months following discharge in a prospective, multi-institutional study.⁴³ Nevertheless, performing these complex, time-intensive assessments is challenging in the trauma setting. The 5-item FRAIL scale (fatigue, resistance, ambulation, illnesses, and loss of weight) may serve as a rapid clinical frailty screening tool, but these variables are not captured in TQIP.⁴⁴ The application of a different frailty index to another dataset may produce different results. Furthermore, additional physiologic variables such as lactate or thromboelastography values may convey the clinical status of a patient and influence outcomes but are not included in the TQIP database.⁴⁵ Regarding the age cutoff to define the “geriatric” patient, we utilized the standard Medicare definition of age ≥ 65 years old. Future studies should define the age at which TTs differ between younger and older groups of patients.

5. Conclusion

We demonstrated a lower TT for geriatric patients compared to younger adults. Frailty does not significantly impact TTs among geriatric trauma patients. Both age and frailty impact mortality among patients receiving MT. Overall, geriatric patients who receive MT have worse outcomes than younger adults. These results may help optimize MT utilization. As any patient nears a TT, we recommend a critical review of the plan for achieving hemorrhage control and the utility of ongoing blood product administration by a multidisciplinary team rather than blind cessation of transfusion.

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Statements and declarations

None.

Declaration of competing interest

The authors declare no conflict of interest.

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