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Blood utilization in patients with burn injury and association with clinical outcomes

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Abstract

BACKGROUND—Uncontrolled bleeding is an important cause of increased transfusion in burn victims; however, description of blood utilization patterns in the burn population is lacking.

STUDY DESIGN AND METHODS—We conducted a single-institution, retrospective cohort study to measure blood utilization in 89 consecutive burn patients with 15–65% total body surface area (TBSA) burn within 60 days of injury. We also evaluated the relationship of blood product utilization with clinical variables including anticoagulant usage and mortality.

RESULTS—We determined that: (a) the predictors for increased packed red blood cells (PRBC) and plasma transfusions were high TBSA burn and the use of argatroban anticoagulation (for suspected heparin-induced thrombocytopenia); (b) TBSA burn and patient age were independent predictors of mortality, but not PRBC or plasma transfusion; and (c) the incidence of symptomatic venous thromboembolic events is not uncommon (11.2%), although heparin-induced thrombocytopenia is rare (1.1%).

CONCLUSION—Despite concerns about adverse correlation between increased number of transfusions and mortality in other clinical settings, we did not find this association in our study.

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However, we demonstrated that the type and intensity of anticoagulation carries substantial risk for increased PRBC as well as plasma usage.

Keywords

burn injury; blood transfusion; blood utilization; mortality; anticoagulation; heparin; argatroban; venous thromboembolic events; heparin-induced thrombocytopenia

INTRODUCTION

Severe burn injuries are characterized by activation of inflammation and coagulation leading to coagulation system dysfunction, multi-organ failure, and mortality.[1] Following burn injury, patients experience acute anemia associated with the surgical management of wounds, iatrogenic blood loss, and anemia of critical illness.[2] A variety of therapeutic strategies are used in clinical practice to control peri-operative bleeding including the use of local manual pressure, electrocautery, topical soaked epinephrine pads, tumescence, thrombin and fibrin sealants, tourniquets, and the application of topical hemostatic dressings.[2–4] To date, there is limited literature describing the magnitude of blood utilization in the burn population. [2,4–9]

Given recent heightened concerns that blood transfusion in several clinical settings may be associated with increased morbidity and mortality,[9–18] we measured the number of packed red blood cells (PRBC) and plasma transfusions administered within 60 days of burn injury in our institution, and evaluated these data in relation to clinical variables including burn severity and mortality. We hypothesized that blood utilization might be related to anticoagulant usage for the prophylaxis or treatment of venous thromboembolic events (VTE) in this high-risk population. Therefore, we recorded the incidence of VTE as well as the use and complications of anticoagulant therapy. Furthermore, we hypothesized that the amount of blood transfusion in 60 days is a marker of burn severity and has independent adverse effect on survival.

PATIENTS AND METHODS

Study design and objectives

At a single large volume adult and pediatric American Burn Association (ABA)-verified Burn Center (The Jaycee Burn Center at the University of North Carolina at Chapel Hill), we conducted a retrospective cohort study and evaluated blood utilization in burn patients admitted to the Center between January 1, 2008 and December 31, 2009. Recognizing the heterogeneity of burn severity, we measured the number of PRBC and plasma transfusions in different total body surface area (TBSA) burn categories to compare their actual blood utilization. Patients were grouped arbitrarily according to burn severity as 15–30, 31–50, 51–65, and 66–100% total body surface (TBSA) burn.

The primary study objective was to estimate the total number of blood transfusions administered and to determine its association with TBSA burn, patient age, gender, presence of co-existing inhalation injury, mechanism of burn injury, type and intensity of anticoagulant used, presence of VTE, and overall mortality. The diagnosis of co-existing inhalation injury on admission was suggested by clinical findings of singed nostril hairs and carbonaceous sputum and confirmed by fiberoptic bronchoscopy. The secondary study objective was to determine the 60-day incidence of symptomatic VTE including limb deep vein thrombosis (DVT) and pulmonary embolism (PE) as well as heparin-induced thrombocytopenia (HIT). The diagnosis of DVT was made by duplex ultrasound, while PE was diagnosed by chest CT angiography. However, in cases wherein patients' renal

dysfunction precluded getting a diagnostic CT angiography, those patients were treated on the basis of clinical suspicion of PE alone. Both upper and lower extremity DVTs were included. HIT was defined as a positive heparin-platelet factor 4 antibody test and confirmed by heparin-dependent platelet aggregation test in the context of suspicious clinical criteria such as unexplained acute thrombocytopenia, a platelet count that had fallen 50% or more from baseline, or development of thrombosis associated with new onset thrombocytopenia.[19] Investigation for DVT, PE, and HIT was conducted only if clinically suspected.

Eligibility criteria

Subjects included adult patients (≥ 18 years old) with 15–100% TBSA burn. All mechanisms of burn injury were included except electrical injury. Patients with and without co-existing inhalation injury were included, while patients with associated traumatic injuries who required medical attention, or patients on therapeutic anticoagulation (heparin or warfarin) before injury, or with known bleeding disorders were excluded. Burns exceeding 15% TBSA were selected as the lower limit of burn size because burns of this magnitude are often associated with increased activation of inflammatory and coagulation mediators that may contribute to adverse clinical outcomes.[1] This study was conducted after approval of the Institutional Review Board of the University of North Carolina.

Patients

Patient demographics such as age, gender, medical history, and mechanism/ extent/ timing of burn injury were obtained from electronic medical records. The total number of transfusions of individual blood components— PRBC, plasma, platelets, and cryoprecipitate– was obtained from the records. Information regarding survival status and development of VTE within 60 days after injury, as well as types and doses of anticoagulation used during the 60-day hospitalization period were noted.

As part of routine burn care in our institution, heparin thromboprophylaxis was initiated at the time of admission and was continued throughout the study period, unless there was an absolute contraindication. In patients in whom there was a high clinical suspicion for PE due to acute onset of unexplained hypoxemia in association with severe burn and co-existing inhalation injury, empiric treatment with therapeutic anticoagulation using heparin was used until VTE was ruled out, while patients who developed acute thrombocytopenia suspicious for HIT within the first 2 weeks of hospitalization were treated with a parenteral direct thrombin inhibitor (i.e. argatroban) until HIT was ruled out. Subsequently these patients either stayed on therapeutic anticoagulation if VTE was confirmed or were switched to prophylactic doses of anticoagulation when the suspicion was resolved. Therapeutic anticoagulation with heparin was not transitioned to warfarin until patients were hemodynamically stable and preparing for hospital discharge. Thromboprophylaxis was not routinely held when patients were taken to the operating room for excision and/or grafting procedures, but therapeutic anticoagulation with intravenous unfractionated heparin was held for 6–8 hours prior to surgery and gradually resumed once post-operative hemostasis was established. Ambulation was encouraged throughout the hospital stay, starting from the day of admission until the first operative procedure, with prompt resumption once post-operative dressings were taken down. Typically, our transfusion threshold for PRBC is < 7g/dL in hemodynamically stable patients; however, patients with significant cardiac history and/or bleeding with or without hemodynamic instability are transfused with PRBCs to keep their hemoglobin closer to 10 g/dL. Occasionally, patients with larger burns and/or co-existing cardiac disease are pre-emptively transfused with PRBC to raise their hemoglobin to 9–10 g/dL before surgery, in anticipation of significant intra-operative bleeding. We try to minimize intra-operative bleeding by using electrocautery, topical soaked epinephrine pads,

tumescence, thrombin and fibrin sealants, and the application of topical hemostatic dressings. Our threshold for plasma transfusion is generally the presence of active bleeding from wounds and coagulation laboratory abnormalities such as an international normalized ratio (INR) ≥ 1.5 and prolonged activated partial thromboplastin time (aPTT).

Statistical analysis

We used Kruskal-Wallis tests and chi-square tests, when appropriate, to determine the association between the number of blood transfusions, 60-day survival status, and patent's characteristics, which include TBSA burn, age, gender, mechanism of burn injury, presence of co-existing inhalation injury, type of anticoagulant used, and VTE. The association was further adjusted by including multiple covariates in a linear regression model for the increased number of blood transfusions, and in a logistic regression model for mortality. Descriptive statistics such as median and range were reported due to skewness of the data. *P* values smaller than 0.05 were considered statistically significant. Statistical analyses were implemented using IBM SPSS Statistics 19 (SPSS, Inc., Chicago, IL).

RESULTS

Patient characteristics

A total of 102 patients with 15–100% TBSA burn were identified. Ten of 13 (76.9%) patients with 66–100% TBSA burn expired within 48 hours of admission while receiving comfort care measures. No transfusions were administered to those patients. To eliminate a possible confounding effect of transfusion on mortality in this 66–100% TBSA group, we excluded this group of patients from the analysis. Thus, a total of 89 patients with 15–65% TBSA burn were studied.

The study cohort consisted of 61 males and 28 females. The median age of the cohort was 48.3 years (range: 18.2–90.5 years), while the median TBSA was 22% (range: 15–65% TBSA). The majority (82.0%) of patients were younger than 65 years old. Sixty-three patients (70.8%) had 15–30% TBSA burn, while 26 patients (29.2%) had more severe burns, with 31–65% TBSA burn. The mechanism of burn injury was categorized as flame-related injuries and others. Flame-related injuries included thermal (48 cases), conflagration (10), explosion (11), motor vehicle collision (4), and grease burn (9), while others included scald (3), steam (1), and chemical (3) burns. The majority of patients experienced flame-related injuries, which accounted for 82 (92.1%) cases. Co-existing inhalation injury was present in 24 patients (27.0%) (Table 1).

Anticoagulation usage

On admission, 76 patients were started on DVT prophylaxis using subcutaneous unfractionated heparin 5,000 units three times daily (73 cases), enoxaparin either 40 mg once daily or 30 mg twice daily (2), or fondaparinux 2.5 mg once daily (1), while 11 patients received empiric therapeutic anticoagulation with either intravenous unfractionated heparin monitored by an in-house heparin aPTT nomogram (10 cases) or subcutaneous weight-based enoxaparin at 1 mg/kg twice daily (1). Two patients did not receive pharmacologic thromboprophylaxis. Together, the majority of patients (87 of 89, 97.7%) received either prophylactic or therapeutic doses of anticoagulation on admission. Subsequently during the hospital course, 5 additional patients received therapeutic anticoagulation with either intravenous unfractionated heparin or subcutaneous low molecular weight heparin (for a total of 16 patients on therapeutic heparin) due to a clinical suspicion for or confirmed VTE, while 11 patients were treated with argatroban because of a clinical suspicion for HIT. Argatroban therapy was initially administered at 1–2 mcg/kg/minute as continuous

intravenous infusion and was monitored based on our institution's argatroban protocol by following serial aPTT measurements.

Association of patient characteristics to number of PRBC and plasma transfusions

A total of 1,233 units of blood products (953 PRBC, 238 plasma, 40 doses of apheresed platelets, and 2 pools of cryoprecipitate) were administered within 60 days after injury. Of the 89 patients, 64 (71.9%) received PRBC and 40 (44.9%) received plasma transfusions. The median number of PRBC and plasma transfusions over 60 days was 6 units (range: 0–51 units) and 0 unit (range: 0–29 units), respectively. All patients who received plasma transfusions had also received PRBC transfusions. The patients who received higher numbers of PRBCs also received higher numbers of plasma transfusions. The majority of patients who received PRBC transfusion received more than 10 units of PRBC. Nine patients received at least 1 dose of platelets while a single patient received two pools of cryoprecipitate. Due to the low volume of platelet and cryoprecipitate transfusions, no additional analysis of these two components was performed.

The number of PRBC and plasma transfusions was significantly influenced by TBSA burn, the presence of co-existing inhalation injury, and the type of anticoagulation used. Patients with more extensive burns had a higher likelihood of receiving more PRBC and plasma transfusions. This association between TBSA burn and the number of PRBC and plasma transfusions follows a linear correlation (R^2: 0.45 and 0.33 respectively; $p < 0.001$ for both). The median number of units of PRBC was 3, 20, and 35 in patients with 15–30, 31–50, and 51–65% TBSA burn, respectively. The corresponding number of units of plasma was 0, 3, and 4. In patients with co-existing inhalation injury, the median number of PRBC and plasma units administered was 19 and 3, respectively. In contrast, 3 PRBC and 0 plasma units were transfused in patients without inhalation injury. Importantly, patients who received therapeutic anticoagulation with either heparin or argatroban received as much as 5–8 times more PRBC and 2–4 more units of plasma compared to patients who received only prophylactic anticoagulation. The effects of female gender, flame-related injuries, and the presence of VTE on the number of PRBC transfusions were also significantly substantial. Patients with these characteristics received more PRBC transfusions but they did not influence the number of plasma transfusions. To adjust for confounding variables, a linear regression analysis showed that the predictors for increased PRBC as well as plasma transfusions were high TBSA burn and the use of argatroban for anticoagulation. Patients who were older, female, had flame-related injuries, used heparin for therapeutic anticoagulation, and had longer hospital stays received more PRBC transfusions. The presence of co-existing inhalation injury did not have a significant impact on the number of PRBC or plasma transfusions (Table 2).

Association of patient characteristics to survival

The 60-day overall mortality rate of the cohort was 14.6% (13 of 89 patients). More men died than women (8 *vs.* 6), although the number of men in the study markedly outnumbered the number of women. Survivors were younger than non-survivors [median age of 43 years (range: 18–77 years) *vs.* 73 years (range: 26–90 years)], respectively. All deaths were seen in flame-related injuries. About a third of patients with co-existing inhalation injury died.

The clinical variables that demonstrated significant associations with mortality were TBSA burn, age, the presence of co-existing inhalation injury, and number of plasma transfusions (Table 3). In a multivariate logistic regression analysis, the predictors of mortality were found to be TBSA burn and age [odds ratio: 1.13 (95% CI: 1.03, 1.25) and 1.14 (95% CI: 1.04, 1.24), respectively, both $p < 0.05$]. The relationship between mortality and the numbers of PRBC and plasma transfusions did not reach statistical significance. While the

number of plasma transfusions showed a trend towards mortality (odds ratio: 1.37; 95% CI: 0.99, 1.88; *p*: 0.055), the effect of the number of PRBC transfusions surprisingly showed a trend towards survival rather than mortality (odds ratio: 0.89; 95% CI: 0.76, 1.03; *p*: 0.13). There was no observed effect of co-existing inhalation injury on mortality. The mechanism of burn injury, type of anticoagulant used, and the presence of VTE were not included in the mortality model because of small numbers of patients (Table 4).

Incidence of VTE

Nine patients had radiographically proven DVT, while two patients— one of whom had HIT– developed PE. Overall, the incidence of symptomatic VTE was 11.2% (10 of 89), while the incidence of confirmed HIT was 1.1% (1 of 89). Nine of 16 patients who received therapeutic anticoagulation with heparin ultimately had a confirmed VTE (a 44% false positive rate), while 1 of 11 patients treated with argatroban was confirmed to have HIT (a 91% false positive rate). The median time to diagnosis of VTE was 15.5 days (range: 4–35 days). The median age and TBSA of patients who developed VTE were 50.5 years (range: 20–73 years) and 20.5% (range: 15–52%), respectively (Table 5). The median time to initiation of therapeutic anticoagulation with heparin was 24 hours from the time of injury (range: 1–6 days), while in patients in whom HIT was suspected, the median time to initiation of argatroban was the third day of admission (range: 1–4 days). All patients who developed VTE had previously received thromboprophylaxis with unfractionated heparin and were alive at 60 days after injury.

DISCUSSION

There is limited literature describing blood utilization in burn victims. In 2006, a multi-center retrospective study reported the effect of blood transfusion on adverse outcomes after major burn injury. The outcomes analyzed included number of infections, length of hospital stay, type of anticoagulant used, and mortality. Of the 666 patients with ≥ 20% TBSA burn, 79% survived but received a mean of 14 units of PRBC during hospitalization. Mortality was related to TBSA burn, patient age, inhalation injury, number of units of blood transfused outside the operating room, and the total number of transfusions. The number of infections per patient increased with each unit of blood transfused. The authors hypothesized that the immunomodulatory potential of blood transfusion could compromise the suppressed immune system of burn victims, thereby predisposing patients to infection and increased mortality.[9] The adverse effect of blood transfusion on clinical outcomes has been similarly reported in other patient populations. In trauma, blood transfusion was demonstrated to be an independent predictor of mortality, intensive care unit admission, systemic inflammatory response syndrome, ventilator-associated pneumonia, organ dysfunction, and length of stay.[11–14] Among patients undergoing cardiac surgery, the use of a restrictive peri-operative transfusion strategy compared with a more liberal strategy resulted in non-inferior rates of the combined outcome of 30-day all-cause mortality and severe morbidity,[20] similar to the results in critically ill medical patients.[15]

We have shown that predictors for increased PRBC and plasma transfusions were high TBSA burn and the use of argatroban for therapeutic anticoagulation. While TBSA burn is a known predictor of increased transfusion,[21] the effect of anticoagulation on the number of transfusions in burn patients has not been fully described, and it is probably underestimated in clinical practice. In a previous multi-center study, the 35% of patients who were on anticoagulation during their hospital stay received more PRBC transfusions than those who were not on anticoagulation (16.3 ± 1.5 *vs.* 12.3 ± 1.5 units, $p < 0.001$).[9] However, in that study, patients received different doses of anticoagulation (both prophylactic and therapeutic intents), thereby precluding a meaningful conclusion of the effect of anticoagulation on number of PRBC transfusions. Also there was no analysis of the number of plasma

transfusions. In our study, therapeutic anticoagulation using heparin and argatroban was associated with increased PRBC transfusions, when compared to prophylactic anticoagulation. Furthermore, argatroban use was not only associated with increased PRBC transfusions but also increased plasma transfusions. Although the trauma literature has provided convincing observational studies regarding the clinical benefits of early and aggressive plasma administration during resuscitation,[22–24] there is limited information in the burn population to guide optimal plasma utilization. It is possible that patients on therapeutic anticoagulation received both PRBCs to ameliorate anemia and plasma in an attempt to reverse bleeding. However, this blood utilization practice lacks evidence and requires further study.

In a multivariate logistic regression model including established risk factors for mortality (i.e. TBSA burn, age, and presence of co-existing inhalation injury),[21] we were able to demonstrate that TBSA burn and age are independent predictors of mortality. However, we did not find the number of PRBC or plasma transfusions or the presence of co-existing inhalation injury to be significantly associated with mortality, which differs from a previous report.[9] However, the number of plasma transfusions showed a trend towards statistical significance (odds ratio: 1.37; 95% CI: 0.99, 1.88; p: 0.055) suggesting that increased plasma utilization may be associated with mortality and that our sample size was too small to detect this association. While we did not find the association of co-existing inhalation injury and mortality, studies suggest that the presence of co-existing inhalation injury increases mortality by 20–60%, and burn patients develop a coagulopathy mediated by systemic activation of coagulation and fibrinolysis,[25] which may contribute to their increased transfusion needs.

Burn patients are perceived to be at risk for VTE due to immobilization, vascular injury, systemic hypercoagulability, and the use of central venous lines.[26–34] However, the degree to which this hypothesized risk translates into thrombotic events has not been fully elucidated. While the reported incidence of asymptomatic (radiographically detected) VTE in a limited number of studies is 6–23%,[35–36] the incidence of symptomatic VTE was reported to be as low as 0.25–2.9%.[27–28,33,37–38] This wide variability in incidence may be largely due to uncontrolled study designs, undiagnosed subclinical VTEs, different sample sizes and study duration, and whether routine thromboprophylaxis was utilized or not. One survey showed that about 76% of burn centers in the United States use routine VTE prophylaxis, varying from lower limb sequential compression devices to varying doses and types of heparin products.[39] As VTEs are increasingly recognized in the burn population, the American College of Chest Physicians' guidelines (8th edition, 2008) previously recommended thromboprophylaxis in burn patients who have additional risk factors for VTE including advanced age, morbid obesity, extensive or lower extremity burns or concomitant trauma, use of femoral venous catheter, and/or prolonged immobility (Recommendation Grade 1A).[40] However, in its recent version (9th edition, 2012), this recommendation is not included.[41]

Our observed incidence of symptomatic VTE was 11.2 %, while the single case of HIT in our cohort equated to a frequency of 1.1%. These results indicate that while symptomatic VTE is not uncommon, HIT is rare. A critical assessment of immune-mediated HIT suggests a frequency of 0.2–5.0% in patients exposed to heparin for more than 4 days, with an overall incidence of 2.6% noted in a meta-analysis.[42–44] Burn patients are believed to be at low risk for HIT. Recent studies of burn patients who received heparin thromboprophylaxis found the incidence of HIT to be 0–1.6%.[26,45–46] In comparison, the frequency of HIT in orthopedic and cardiac surgery patients was reported to be 4.9% and 1.0%, respectively. [45–46] While extensive data strongly supports the clinical benefit and cost-effectiveness of routine thromboprophylaxis in trauma, surgical, and medical populations,[41] the adverse association

between increased number of transfusions and possible overzealous use of therapeutic anticoagulation in our study raises the question about the risk-benefit ratio of routine anticoagulation. Because it was sometimes difficult or impossible to obtain satisfactory diagnostic radiology studies on patients with renal dysfunction who were suspected of having a PE, a number of patients were initiated on therapeutic anticoagulation with heparin on the basis of clinical suspicion alone. In fact, only 9 of 16 patients who received therapeutic anticoagulation with heparin ultimately had a confirmed VTE. In addition, because guidelines have previously recommended the use of full intensity anticoagulation with a non-heparin parenteral anticoagulant (such as a direct thrombin inhibitor) when there is moderate to high clinical suspicion of HIT,[40–41] a number of our patients were empirically treated with argatroban while awaiting the results of definitive laboratory studies. In fact, consistent with other studies, [26,45] only 1 out of 11 patients treated with argatroban was ultimately confirmed to have HIT. However, because VTE treatment was sometimes initiated for hypoxemia, which may be seen as part of the natural history of inhalational injury, and because argatroban was in some cases initiated for early onset thrombocytopenia (within 72 hours post burn), which may be due to marrow suppression, wound consumption, and hemodilution from fluid resuscitation,[2,47] we acknowledge that there is a need to enforce more consistent guidelines on the use of therapeutic anticoagulation. In particular, these results suggest that the risk and benefit of therapeutic anticoagulation must be individually assessed especially in patients with large burns requiring multiple operations, who may be at higher risk for both bleeding and thrombosis.

Our study has several limitations. First, this is a single-center study. The second major limitation is that our transfusion protocol is not standardized. Other limitations include the retrospective study design, small sample size, short follow-up, and possibility of selection and referral biases. In addition, information regarding body location(s) of burn injury, admission body weights, number of operations, and presence of infections and/or multi-organ dysfunction were not determined, which may be relevant, since these factors may be considered additional risk factors for VTE and increased transfusion requirements.[2,4,27–28,33,38–40] In patients with a history of cardiovascular disease, we did not evaluate for concurrent anti-platelet therapy usage, which has been demonstrated to predispose to post-operative bleeding and increased blood utilization, albeit in cardiac surgery patients.[48] We were also unable to evaluate the immediate cause of death to determine if bleeding was contributory. Lastly, we measured the total number of blood transfusions administered within 60 days in relation to TBSA burn, age, gender, presence of co-existing inhalation injury, and mortality, but did not provide insight into the time course of blood transfusion in relation to the number of surgical procedures, pre-transfusion laboratory test results, and indication(s) for transfusion.

Although our population may not be representative of patients seen in all Burn Centers, we believe that our results may provide useful estimates of transfusion requirements and anticoagulation prophylaxis practices in burn patients stratified according to TBSA burn. The results can be used to improve resource allocation of blood products, establish a benchmark to guide future transfusion-related studies, and improve clinical practice.

CONCLUSIONS

Blood loss is a serious problem in the management of burn patients. Despite concerns about adverse correlation between quantity of transfusion and mortality in other clinical settings, we did not find such an association in our study. Nonetheless, it is clear that TBSA burn and patient age are major predictors of increased PRBC transfusion. In addition, we also demonstrated that anticoagulation carries substantial risk of iatrogenic bleeding. We recognize that this study may not reflect other institutions' practices including surgical

technique and local transfusion thresholds that may independently contribute to blood utilization patterns. However, this study provides some compelling preliminary observations that indicate the need for further investigation.

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Abbreviations

TBSA	total body surface area
DVT	deep vein thrombosis
PE	pulmonary embolism
VTE	venous thromboembolic events
HIT	heparin-induced thrombocytopenia

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Table 1

Association of patients with 15–65% TBS A burn to number of PRBC and plasma transfusions

Variables	Total# of patients (%)	#of PRBC transfusions		#of Plasma transfusions	
		Median (range)	*P*value	Median (range)	*P*value
Total	**89**	**6 (0–51)**		**0(0–29)**	
# of PREC transfusions (units)			-		<0.001
0	25 (28.1)	-		0 (0)	
1–10	27 (30.3)	-		0 (0–8)	
> 10	37 (41.6)	-		4 (0–29)	
# of plasma transfusions (units)			<0.001		-
0	49 (55.1)	0(0–15)		-	
1–6	31 (34.8)	18 (3–38)		-	
>6	9 (10.1)	32 (8–51)		-	
Total body surface area burn (%)			<0.001		<0.001
15–30	63 (70.8)	3 (0–28)		0 (0–15)	
31–50	19 (21.3)	20 (0–43)		3 (0–23)	
51–65	7 (7.9)	35 (13–51)		4 (4–29)	
Age (years)			0.295		0.115
18–40	36 (40.4)	3 (0–38)		0 (0–14)	
41–65	37 (41.6)	12 (0–43)		0 (0–23)	
>65	16 (18.0)	10 (0–51)		2 (0–29)	
Gender			0.020		0.124
Male	61 (68.5)	3 (0–51)		0 (0–29)	
Female	28 (31.5)	11.5 (0–43)		2 (0–23)	
Mechanism of injury			0.022		0.095
Flame-related	82 (92.1)	7.5(0–51)		0 (0–29)	
Others	7 (9.2)	0 (0–12)		0 (0–3)	
Inhalation injury			<0.001		<0.001
Yes	24 (27.0)	19 (0–51)		3 (0–29)	
No	65 (73.0)	3 (0–38)		0 (0–15)	

Variables	Total# of patients (%)	#of PRBC transfusions		#of Plasma transfusions	
		Median (range)	*P*value	Median (range)	*P*value
Total	**89**	**6 (0–51)**		**0(0–29)**	
Type of anticoagulation			<0.001		<0.001
Prophylactic	60 (67.4)	3(0–38)		0(0–15)	
Heparin therapeutic	16 (18.0)	17(0–38)		2(0–6)	
Argatroban	11 (12.4)	26(12–51)		4(0–29)	
None	2 (2.2)	0 (0)		0 (0)	
Venous thromboembolic events			0.028		0.09
Yes	10 (11.2)	14(2–38)		2 (0–11)	
No	79 (88.8)	4(0–51)		0 (0–29)	

Table 2

Linear regression model for increased number of PRBC and plasma transfusions

Variables	# of PRBC transfusions			# of Plasma transfusions		
	Beta	*p* value	95%CI	Beta	*p* value	95%CI
Total body surface area burn	0.55	<0.001	0.42, 0.67	0.19	<0.001	0.12, 0.26
Age, year	0.09	0.036	0.01, 0.17	0.03	0.28	−0.02, 0.07
Gender, female	3.08	0.047	0.08, 6.08	0.92	0.30	−0.80, 2.63
Mechanism of injury, flame-related	10.3	<0.001	5.02, 15.5	2.43	0.12	−0.57, 5.42
Inhalation injury	−1.86	0.38	−5.97, 2.24	−1.57	0.19	−3.92, 0.77
Type of anticoagulation						
Prophylactic (ref.)	0.00	-	-	0.00	-	-
Heparin therapeutic	6.09	0.008	1.70, 10.5	0.64	0.62	−1.87, 3.14
Argatroban	16.5	<0.001	11.2, 21.8	7.47	<0.001	4.45, 10.5
None	−2.60	0.60	−12.3, 7.03	−1.26	0.66	−6.77, 4.24
Venous thromboembolic events	1.89	0.46	−3.11, 6.90	−0.82	0.59	−3.67, 2.04
Length of hospital stay	0.21	0.001	0.10, 0.33	0.008	0.81	−0.06, 0.08

Table 3

Association of patients with 15–65% TBSA burn to survival

Variables	Total# of patients, n (%)	Survivors, n(%)	Non-survivors, n(%)	*p* value
Total	**89**	**76 (85.4)**	**13 (14.6)**	
#of PRBC transfusion (units)				0.131
0	25 (28.1)	21 (27.6)	4 (30.8)	
1–10	27 (30.3)	26 (34.2)	1 (7.7)	
> 10	37 (41.6)	29 (38.2)	8 (61.5)	
#of plasma transfusion (units)				<0.001
0	49 (55.1)	45 (59.2)	4 (30.8)	
1–6	31 (34.8)	28 (36.8)	3 (23.1)	
>6	9 (10.1)	3 (3.9)	6 (46.2)	
Total body surface area burn (%)				0.012
15–30	63 (70.8)	58 (76.3)	5 (38.5)	
31–50	19 (21.3)	14 (18.4)	5 (38.5)	
51–65	7 (7.9)	4 (5.3)	3 (23.1)	
Age (years)				<0.001
18–40	36 (40.4)	35 (46.1)	1 (7.7)	
41–65	37 (41.6)	34 (44.7)	3 (23.1)	
>65	16 (18.0)	7 (9.2)	9 (69.2)	
Gender				0.556
Male	61 (68.5)	53 (69.7)	8 (61.5)	
Female	28 (31.5)	23 (30.3)	5 (38.5)	
Mechanism of injury				0.254
Flame-related	82 (92.1)	69 (90.8)	13 (100)	
Others	7 (9.2)	7 (9.2)	0 (0)	
Inhalation injury				0.018
Yes	24 (27.0)	17 (22.4)	7 (53.8)	
No	65 (73.0)	59 (77.6)	6 (46.2)	
Type of anticoagulation				0.058
Prophylactic	60 (67.4)	53 (69.7)	7 (53.8)	
Heparin therapeutic	16 (18.0)	15 (19.7)	1 (7.7)	
Argatroban	11 (12.4)	7 (9.2)	4 (30.8)	
None	2 (2.2)	1 (1.3)	1 (7.7)	
Venous thromboembolic events				0.165
Yes	10 (11.2)	10 (13.2)	0 (0)	
No	79 (88.8)	66 (86.8)	13 (100)	

Table 4

Adjusted logistic regression model for 60-day mortality

Variables	Odds Ratio	*p* value	95% CI
Total body surface area burn	1.13	0.012	1.03, 1.25
Age	1.14	0.004	1.04, 1.24
Gender, female	1.21	0.87	0.11, 12.8
Inhalation injury	6.21	0.24	0.30, 127.1
#of PRBC transfusions	0.89	0.13	0.76, 1.03
# of Plasma transfusions	1.37	0.055	0.99, 1.88

Mechanism of injury, type of anticoagulant, and VTE were not included in the mortality model because of non-significance in the bivariate analysis.

Table 5

Characteristics of patients with symptomatic venous thromboembolic events

Patient	TBSA burn	Inhalation injury	Age	Gender	Venous thromboembolic events			Time to event (from day of admission)
					DVT	Pulmonary embolism	HIT	
1	15	None	57	Male	LE	+	-	4
2	16	Yes	36	Female	LE	−	-	35
3	16	None	73	Male	LE	−	-	11
4	19	None	20	Female	UE	−	-	13
5	20	None	65	Male	LE	−	-	6
6	21	None	48	Female	UE	−	-	18
7	24	Yes	53	Male	None detected	+	+	5
8	41	Yes	30	Male	LE	−	-	21
9	45	Yes	56	Male	LE and UE	−	-	27
10	52	None	45	Female	LE	−	-	31

TBSA: total body surface area; DVT: deep vein thrombosis; HIT: heparin-induced thrombocytopenia; LE: lower extremity; UE: upper extremity