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Assessing Factor V Antigen and Degradation Products in Burn and Trauma Patients

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ABSTRACT

Introduction: Proposed mechanisms of acute traumatic coagulopathy (ATC) include decreased clotting potential due to factor consumption and proteolytic inactivation of factor V (FV) and activated factor V (FVa) by activated protein C (aPC). The role of FV/FVa depletion or inactivation in burn-induced coagulopathy is not well characterized. This study evaluates FV dynamics following burn and nonburn trauma.

Methods: Burn and trauma patients were prospectively enrolled. Western blotting was performed on admission plasma to quantitate levels of FV antigen and to assess for aPC or other proteolytically derived FV/FVa degradation products. Statistical analysis was performed with Spearman's, Chi-square, Mann–Whitney *U* test, and logistic regression.

Results: Burn ($n = 60$) and trauma ($n = 136$) cohorts showed similar degrees of FV consumption with median FV levels of 76% *versus* 73% ($P = 0.65$) of normal, respectively. Percent total body surface area (TBSA) was not correlated with FV, nor were significant differences in median FV levels observed between low and high TBSA groups. The injury severity score (ISS) in trauma patients was inversely correlated with FV ($\rho = -0.26$; $P = 0.01$) and ISS ≥ 25 was associated with a lower FV antigen level (64% *versus*. 93%; $P = 0.009$). The

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proportion of samples showing proteolysis-derived FV was greater in trauma than burn patients (42% *versus*. 16%; $P = 0.0006$).

Conclusions: Increasing traumatic injury severity is associated with decreased FV antigen levels, and a greater proportion of trauma patient samples exhibit proteolytically degraded FV fragments. These associations are not present in burns, suggesting that mechanisms underlying FV depletion in burn and nonburn trauma are not identical.

Introduction

Acute traumatic coagulopathy (ATC) is present in approximately 25% of trauma patients on admission and is associated with worse outcomes and increased mortality.[1,2] ATC is present early after traumatic injury and can be exacerbated by resuscitative measures.[2] The 'lethal triad' of hypothermia, acidosis, and coagulopathy is a vicious cycle developing after hemorrhage and is responsible for most in-hospital deaths following traumatic injury.[2-4] Understanding of the pathophysiology of ATC led to the concepts of 'damage control' resuscitation and surgery, aimed at abating life-threatening hemorrhage while mitigating the development and/or introduction of further imbalances to coagulation homeostasis.[2,3,5-7] Burns are often considered a subset of trauma and like traumatic injury, burns induce a systemic hyperinflammatory response leading to dysregulated homeostasis and shock states.[8,9] Like trauma patients, burn patients develop coagulopathy, acidosis, and hypothermia as a result of their injuries.[10] However, burn induced coagulopathy (BIC) likely differs mechanistically from ATC, as ATC is primarily driven by hemorrhage. Proposed mechanisms of ATC include decreased clotting potential due to overall factor consumption, dilution, and/or dysregulation of the protein C pathway.[1,11-13] The endogenous anticoagulant activated Protein C (aPC) is a serine protease that inactivates several factors in the coagulation cascade, including factor V (FV).[14] aPC has been implicated in the pathogenesis of ATC,[11] and traumatic injury is associated with decreased FV activity.[15,16] Protein C activity has been shown to be normal or decrease in the early phase after burn injury, depending on the severity.[17] Limited investigation in burn patients suggests that FV activity is normal following injury.[18,19] The hypothesis of this study was that mechanisms behind ATC and BIC differ and that this difference could be elucidated by studying the presence of degradation products of factor V, which are created by activated protein C that has been implicated as an important mediator of ATC.

Methods

Study population

This study was approved by the Medstar Health Research Institute and the University of Vermont and State Agricultural College Institutional Review Boards. A second-level review and approval were completed by the Human Research Protections Office of the US Army Medical Research and Development Command. Patients presenting within 4 h of thermal injury to a regional burn center in Washington, DC, and nonburn patients with blunt or penetrating trauma presenting to a regional trauma center in Burlington, VT, were screened for enrollment. Patients with a preexisting history of coagulopathy, those taking anticoagulants, pregnant women, and those less than 18 y of age were excluded at both sites. Chemically injured patients were also excluded from the burn population. Patients were enrolled prospectively into this observational study between 2012 and 2017. Detailed sampling procedures have been described elsewhere.[20] All patients or their legally authorized representatives provided written consent to participate in the study.

Clinical data

A total of 196 patients, including 60 burn patients (30.6%) and 136 nonburn trauma patients (69.3%), were included in the analysis. Patient demographics, injury characteristics, vital signs, laboratory data, and treatment information were collected from the medical record.

Sample collection

Admission blood samples were collected from patients into SCAT-144 tubes (500 μM of AEBSF, 20 μM of elastin, 10 μM of GGACK, 4.5 mM of EDTA, 5 μM of E64, 1 μM of pepstatin A, 300 KIU/mL of aprotinin; Hematologic Technologies, Essex Junction, Vermont). This inhibitor cocktail is designed to reduce the likelihood of proteolysis post phlebotomy.[20] Tubes were spun at 400 g for 10 min after which platelet-rich plasma was isolated and respun at 3,000 g for 17 min. Platelet-poor plasma aliquots were flash frozen and stored at −80°C.

Western blot analysis of factor V and degradation products

Patient plasmas were diluted 1 to 8 in a solution containing 62.5 mM Tris, 2% SDS, 10% glycerol, 2% β-mercaptoethanol pH 6.8. Four standards to be used for the quantitation of intact FV in patient samples were generated by successive dilutions of a healthy donor plasma pool ($n = 10$) into the same solution. Proteins in each patient sample or standard were separated using SDS-PAGE (4%-15% linear gradient gels), transferred to a nitrocellulose membrane (Bio-Rad) as previously described,[21] and probed with an in house mouse monoclonal antibody (αFVa_{HC} 17: 5 μg/mL) in concert with a horseradish peroxidase-conjugated goat anti-mouse polyclonal (Biorad). αFVa_{HC} is directed at an epitope located on the heavy chain of FV/FVa between residues 307 and 506.[14,22] It is useful for detecting intact FV (MW 330 kD), a thrombin/FXa-derived FV activation intermediate (160 kD fragment: residues 1-1018), the heavy chain of FVa (104 kD: residues 1-709), a thrombin-derived

inactivation product (97 kD: residues 1-643)[23,24] and aPC-derived fragments of the FVa heavy chain (75 kD: residues 1-506; 30 kD, residues 307-506) (Fig. S1). FV was purified as described previously[25] and used as a mobility standard to identify intact FV in the patient and standard plasma samples and as a source for FVa heavy chain and aPC-derived 30 kD fragment mobility standards.[26]

Blots were imaged using a chemiluminescence imager LAS4000 (Fujifilm, Tokyo, Japan) (Fig. S2). Quantitative densitometry was performed using the Multigauge imaging software from Fujifilm (ver. 3.1). In general, signal intensity values from an intact FV band (absorbance units) were measured, as was the area from which the signal was acquired, and then the signal intensity expressed relative to the area of its band (signal density). Given variable FV band dimensions, a correction for nonspecific background contributions to each FV signal density, standard or patient sample, was made by measuring the signal density in a lane of the gel in which an FV deficient plasma[25] was loaded. This measurement was made over a sample specific area in the region of the gel where FV would have migrated had it not been immuno-depleted. These background corrections generally ranged from 5% to 15% but were more pronounced in samples with weaker FV signals. FV levels in patient samples were estimated from a standard curve in which the corrected signal density values from the intact FV band in each plasma standard were plotted *versus* their corresponding % plasma values (Fig. S3). Given the 8-fold dilution of all patient samples, dilutions of 4, 8, 16, and 32-fold were used to produce a range of FV concentrations from 200% to 25% mean physiologic.

Immunoreactive species other than intact FV were identified by visual inspection. The criterion applied was that the signal intensity of these species in the patient plasmas must be greater than that observed in a region of identical mobility in the 200% plasma standard; that is more than twice any background signal seen in the lane representing 100% MDP.

Statistical analysis

Descriptive statistics characterized the demographics and injuries of patients categorized as burn or nonburn trauma. Categorical variables were presented as frequencies and percentages and tested using the Chi-square (χ^2) or Fisher's exact test. Continuous variables were expressed as median and interquartile ranges (IQR) and tested for differences between groups using the Mann–Whitney *U* test. The Akaike Information Criteria (AIC) was used for model fit. FV antigen levels in patient samples were expressed relative to % physiologic FV antigen levels defined by pooled healthy plasma and compared between burn and nonburn trauma subgroups. Associations between FV antigen levels and both injury severity in burn measured by the percentage of total body surface area burned (%TBSA) and nonburn trauma measured by Injury severity score (ISS) and systolic blood pressure (SBP) at time of blood draw were investigated using Spearman's rank correlation coefficients and simple linear regression. Factor V antigen levels were compared within each injury subgroup (burn or nonburn trauma) categorized by low (TBSA $<$ 30%, ISS $<$ 25) and high (TBSA $\geq$ 30%, ISS $\geq$ 25) injury severity. Samples were categorized by the presence or absence of FV fragments and compared between subgroups using Fisher's exact test. Within the nonburn trauma group, FV antigen levels and fragments were compared between patients with or without shock defined by both SBP $\leq$ 90 mmHg and heart rate (HR) $\geq$ 108 beats per minute (BPM).[27] Likelihood of FV fragments (odds ratio [OR]) was calculated using logistic regression for the presence of FV fragments between burn or nonburn trauma and while adjusting for possible confounding factors. Statistical significance was determined at the 2-sided $P < 0.05$ level. All data were analyzed using Graphpad Prism version 8 for Windows (Graphpad Software, San Diego, CA).

Results

Demographics

Patients were mostly male (72.4%) with a median age of 43 y (IQR, 27-58 y) and a median BMI of 26 (IQR, 23.7-30). A greater proportion of trauma patients were Caucasian, and trauma patients had longer elapsed times from the point of injury to blood draw (188 min *versus* 96 min; $P < 0.0001$) (Table 1). Within the burn group, median burn TBSA was 17.3% (IQR, 4-41.8%), 38.3% of patients suffered severe burns (TBSA $\geq$ 30%), and 26.7% of patients had concomitant inhalation injury. Within the trauma group, median ISS was 17 (IQR, 11-25), 26% of patients suffered critical injury (ISS $>$25), and 43% had concomitant traumatic brain injury diagnosed with GCS and clinical exam (TBI) (Table 1). There was no difference between groups in admission Glasgow Coma Scale (GCS) score, hospital length of stay (LOS), admission to the intensive care unit (ICU), prehospital crystalloid administration and volumes, ventilator requirement, or mortality. However, burn patients were more likely to be intubated prior to arrival or on admission, had longer ICU LOS, and more ventilator days. Furthermore, trauma patients had significantly lower Hemoglobin (Hgb) levels on admission labs (Table 1).

Admission factor V antigen levels and relationship to injury severity

Burn and nonburn trauma patients had similar plasma levels of FV antigen on admission (76%; IQR, 43%-118% *versus* 73%, 43%-107%, $P = 0.65$) (Table 1). There was no significant correlation between burn %TBSA and admission FV antigen (Fig. 1A). Increasing trauma ISS was negatively correlated admission FV antigen ($\rho = -0.26$, $P = 0.002$; Fig. 1B). There was no significant correlation between burn patient SBP at time of blood draw and FV antigen ($\rho = 0.04$, $P = 0.73$; Fig. 1C). Increasing trauma patient SBP at blood draw was positively correlated with FV antigen ($\rho = 0.27$, $P = 0.001$; Fig. 1D). Injury severity was categorized into low and high severity subgroups for burn defined as $<$30% or $\geq$30% TBSA and for nonburn trauma defined as ISS $<$25 or $\geq$25. There was no significant difference in admission FV antigen levels between %TBSA categories (Fig. 2A; $P = 0.92$). Among nonburn trauma patients, median admission FV antigen levels were significantly lower within the high ISS group (58%, 36%-81% *versus* 82%, IQR, 49%-113%, $P = 0.009$; Fig. 2B).

Table 1 – Demographics and injury characteristics.

Characteristic	All	Trauma	Burn	P value
No. of patients, no. (%)	196 (100.0)	136 (69.3)	60 (30.6)	–
Male, no. (%)	142 (72.4)	98 (72)	44 (73)	0.85
Age, y, median (IQR)	43 (27-58)	46 (26-58)	39 (28-56)	0.57
BMI, median (IQR)	26.0 (23.7-30)	25.8 (23.4-30)	26.5 (24-30.4)	0.48
Ethnicity, no. (%)				**<0.0001**
Caucasian	148 (75.5)	125 (91.9)	23 (38.3)	
African American	25 (12.7)	2 (1.4)	23 (38.3)	
Other	21 (11.6)	9 (6.5)	14 (23.3)	
Time POI to blood draw, min	141 (80-242)	188 (88.5-297)	96 (71-150)	**<0.0001**
Injury Etiology				
Blunt	-	126 (92.6)	-	
Penetrating	-	10 (7.35)	-	
Flame	-	-	34 (56.67)	
Scald (hot liquid, not grease)	-	-	11 (18.33)	
Flash	-	-	11 (18.33)	
Contact	-	-	2 (3.33)	
Scald (grease)	-	-	2 (3.33)	
Total %TBSA burned, %	-	-	17.3 (4.0-41.8)	
% Full thickness burn			0.5 (0-18.75)	
TBSA ≤30%, no. (%)	-	-	37 (61.7)	
≥30%	-	-	23 (38.3)	
Inhalation injury, no. (%)	-	-	16 (26.7)	
Injury severity score, median (IQR)	-	17 (10.5-25)	-	
ISS ≤24, no. (%)	-	101 (74)	-	
≥25	-	35 (26)	-	
TBI, no. (%)	-	59 (43)	-	
Prehospital crystalloid, no. (%)	100 (51)	73 (53.6)	27 (45)	0.26
Volume, Liters, median (IQR)	1 (0.5-2)	1 (1-2)	0.6 (0.3-2)	0.07
Hgb at ADM, median (IQR)	13.6 (12.1-14.9)	13.4 (12.0-14.5)	14.7 (13.2-15.8)	**<0.01**
GCS at ADM,	15 (11-15)	15 (13-15)	15 (7-15)	0.37
Emergent Intubation, no. (%)	52 (27)	22 (16)	23 (20.2)	**<0.0001**
Hgb at ADM			14.7 (13.25-15.75)	
LOS, days, median (IQR)	5 (2-12)	5 (2-9)	6 (1-24)	0.45
ICU ADM, no. (%)	111 (57)	79 (58)	32 (53)	0.54
ICU LOS, median (IQR)	3 (1-10)	3 (1-5)	13 (2-37)	**0.0002**
Ventilated, no. (%)	73 (37)	47 (36)	26 (43)	0.24
Ventilator days, median (IQR)	4 (1-13)	3 (1-6)	14 (2-28)	**0.0007**
Mortality, no. (%)	29 (15)	16 (12)	13 (22)	0.07
ADM FV antigen, % physiologic, median (IQR)	74 (43-107)	73 (43-102)	76 (43-118)	0.65

Significant P-values ($P < 0.05$) are bolded.
BMI = body mass index; POI = point of injury; ADM = admission; TBSA = total body surface area; ISS = injury severity score; TBI = traumatic brain injury; Hgb = hemoglobin; PTA = prior to arrival; GCS = Glasgow Coma Scale; LOS = length of stay; ICU = intensive care unit; FVa = factor V antigen.

Factor V degradation products in burn and nonburn trauma

Samples were categorized based on the presence or absence of FV fragments, as well as the presence or absence of the specific FV fragment (30 kD) produced after proteolytic cleavage by activated protein C. The percentage of samples that exhibited any proteolytically derived FV fragments was significantly higher in the nonburn trauma population when compared to the burn population (42% *versus* 17%, $P = 0.0006$) (Fig. 3A). The likelihood of FV fragments (OR) was computed to further investigate associations between the presence of FV fragments among burn and nonburn trauma (Table 2). On univariate analysis, each year's increase in age was associated with a higher likelihood of FV fragments (OR 1.02, $P = 0.01$).

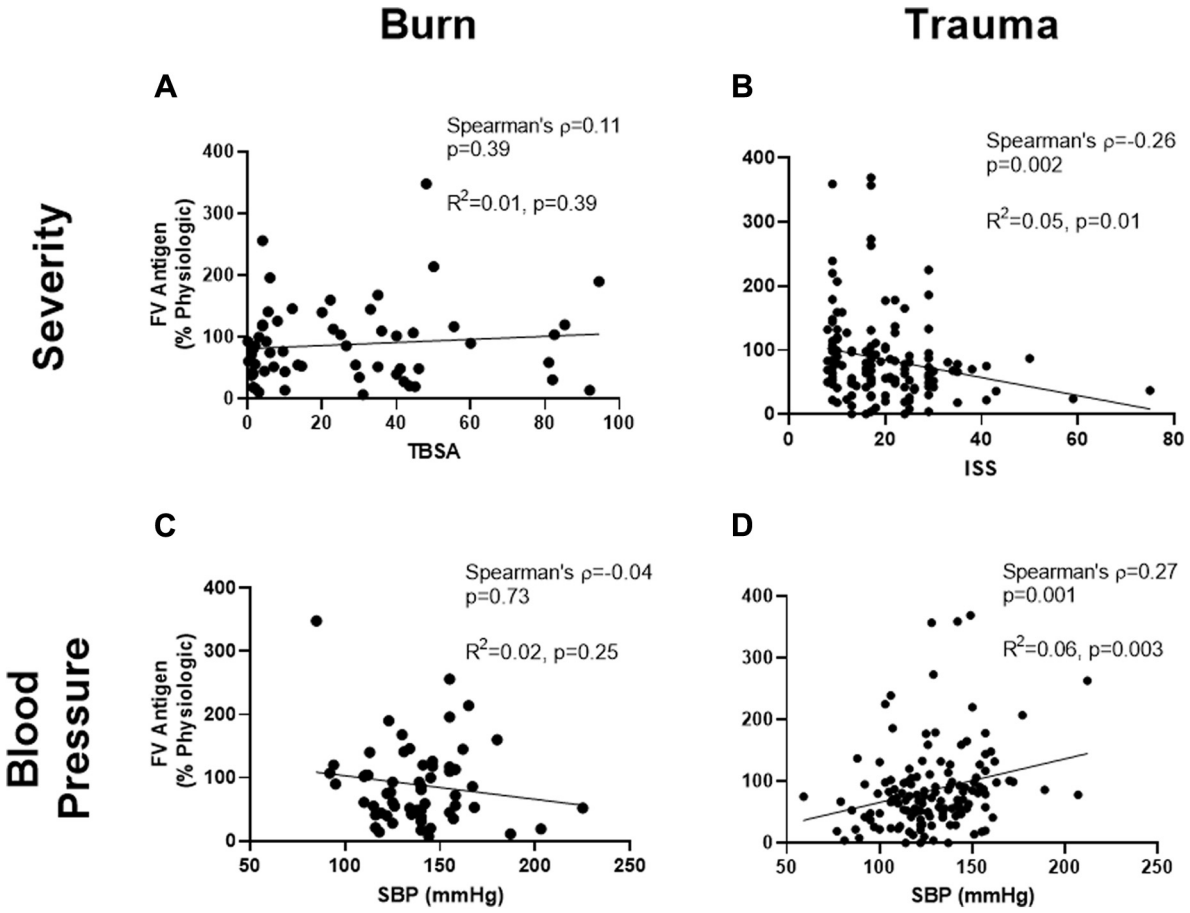

Fig. 1 – (A-D) Relationship between FV Antigen, injury type, severity, and blood pressure.

After adjusting for this confounder, trauma was associated with a three times higher likelihood for the presence of FV fragments [OR 3.26 (95% CI, 1.51-7.02); $P = 0.003$]. In the non-burn trauma population, 6% ($n = 8$) of samples exhibited the specific 30 kD aPC-derived FV fragment, which was not observed in any burn patient samples ($P = 0.11$) (Fig. 3B).

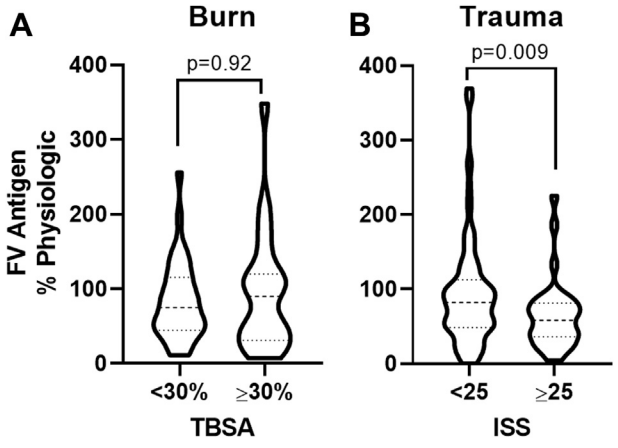

Fig. 2 – Factor V Antigen and injury severity. Factor V antigen by injury severity in (A) burn and (B) trauma patients.

Factor V antigen and degradation products in trauma patients with shock

Trauma patients with vital signs that met the criteria for ongoing shock (SBP $\leq$ 90 mmHg and HR $\geq$ 108 bpm; $n = 13$) were compared to trauma patients who did not meet these criteria. Admission FV antigen levels were significantly lower in the shock group (24%, IQR, 18.5%-58.5% *versus* 78%, 49%-106%; $P < 0.0001$; Fig. 4A). The proportion of patients with aPC-derived FV fragments was higher among trauma patients with vitals consistent with shock, but this did not reach statistical significance (15% *versus* 5%, $P = 0.17$; Fig. 4B).

Discussion

This is the first study to characterize FV antigen levels and proteolytically derived FV fragments as an indirect measure of aPC activity in patients with burn and nonburn traumatic injury. Admission FV antigen levels are similar between burn and nonburn trauma groups. The present study identifies an association between increasing injury severity (ISS) and decreasing admission FV antigen levels in nonburn trauma patients. In contrast, there was no association between burn injury severity (%TBSA) and admission FV antigen (Figs. 1A and B, 2). Similar patterns within injury subgroups were identified between SBP, a marker of perfusion, and FV antigen.

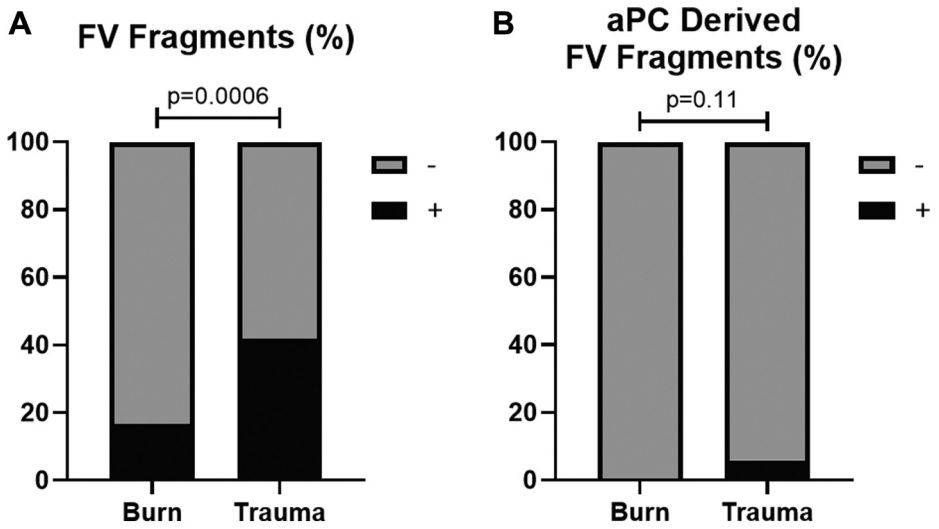

Fig. 3 – Proteolysis Derived FV Fragments. (A) Proportion of samples with any FV fragment (B) Proportion of samples with aPC-derived FV fragment.

There is a direct relationship between SBP and FV antigen in nonburn trauma. However, no significant association is found between these two variables in the burn population (Fig. 1C and D). The proportion of patient samples containing FV fragments was higher in nonburn trauma patients compared to burn patients (Fig. 3A). The aPC-derived FV fragment (30 kD) was identified only in trauma patient samples (Fig. 3B). Taken together, we present indirect evidence of aPC activity in trauma patient plasma that is associated with injury severity. This association is not observed among burn patients.

Given the relationship between trauma injury severity (ISS), clinical markers of perfusion (SBP), and FV antigen levels, trauma patients who met the criteria for hemorrhagic shock based on clinical parameters (SBP $\leq$ 90 mmHg and HR $\geq$ 108 bpm) were compared to those who did not meet these criteria.[27] Within the shock subgroup, FV antigen levels were significantly lower, and there was a trend toward a greater proportion of aPC-derived fragments (Fig. 4A and B). These findings suggest that hypoperfusion plays a role in FV and aPC dynamics after traumatic injury.

Our data reinforce previous findings on FV and its activity after trauma/burn. In a study of 203 trauma patients, Cohen *et al.* (2012) measured plasma levels of several coagulation factors after injury and found an inverse relationship between aPC and FV levels. Furthermore, elevated aPC levels were associated with increased hypoperfusion, injury severity, and poor outcomes.[11] Based on these findings, we expect increasing injury severity to be inversely correlated and blood pressure to be directly correlated with FV antigen as observed in this study. In a study of nine burn patients, Tejiram *et al.* (2016) measured factor activity with functional coagulation assays and found normal range FV activity in all patients on

Table 2 – Likelihood of FV fragments.

Univariate	FV fragments		aPC-derived FV fragment	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age at injury, each increase of 1 year	1.02 (1.00-1.04)	**0.01**	1.01 (0.97-1.05)	0.69
Gender, male *versus* Female	1.24 (0.63-2.44)	0.54	0.36 (0.09-1.49)	0.16
Race/Ethnicity				
African American *versus* Caucasian	0.14 (0.03-0.62)	**0.009**	-	
Hispanic *versus* Caucasian	0.27 (0.06-1.24)	0.09	-	
Other *versus* Caucasian	0.27 (0.06-1.24)	0.82	1.81 (0.20-16.02)	0.6
Body Mass Index	1.00 (0.95-1.06)	0.98	0.81 (0.67-0.98)	**0.03**
Time POI to blood draw, 5 min	1.00 (0.99-1.02)	0.43	0.96 (0.91-1.02)	0.17
Trauma *versus* Burn	3.35 (1.57-7.17)	**0.002**	-	0.94
Adjusted model: Adjusted for age				
Trauma *versus* Burn	3.26 (1.51-7.02)	**0.003**	-	

Significant *P*-values ($P < 0.05$) are bolded.
FV = factor V; aPC = activated protein C; POI = point of injury.

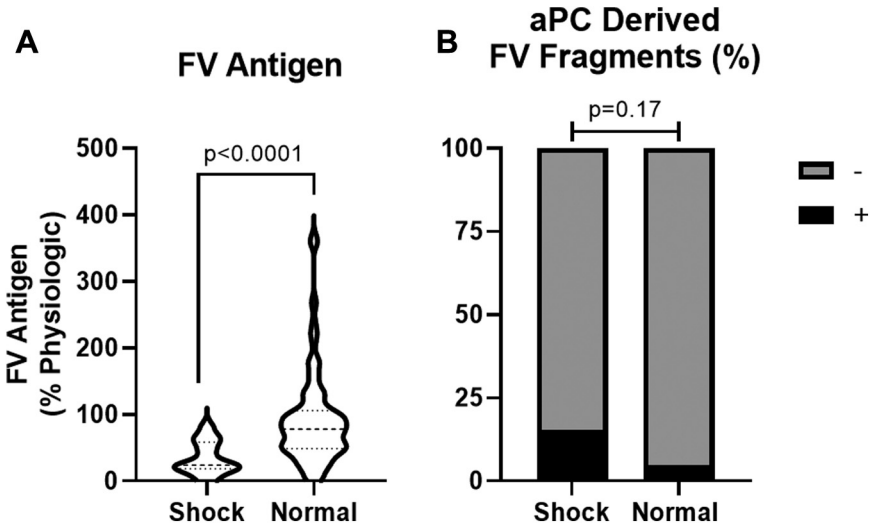

Fig. 4 – FV antigen in trauma patients with shock. (A) Factor V antigen levels (B) aPC derived FV fragments.

admission across a wide range (25%-95%) of %TBSA burn injury. Protein C levels were near normal on admission in patients who survived but significantly lower in patients who died of their injuries.[18] Based on these findings, we would not expect an association between FV antigen and %TBSA injury, or much evidence of aPC activity in burn patients, which is consistent with our results.

Burn and nonburn trauma groups differed significantly in race/ethnicity, the time between the point of injury and blood draw, need for mechanical ventilation, and overall mortality (Table 1). These differences are reflective of the heterogeneous demographic and catchment characteristics inherent to the hospitals involved in the study. In the present study, the regional burn center is situated in a relatively more metropolitan area compared to the trauma center. Due to differences in patient volume at the enrolling institutions, the number of patients in each group is not equal (~69% trauma and 31% burn). Although not balanced in terms of patient numbers, we believe that the best approach is to include all available patients in the analysis. Prehospital crystalloid volumes were approximately 400 mL higher in trauma patients ($P = 0.07$). Considering the similar age, gender distribution, and BMI in the two patient groups, we believe that this relatively small difference in prehospital fluid volume was not likely to influence the results with respect to either coagulopathy or FV fragments. However, crystalloid resuscitation and its impact on trauma and BIC is a target for future research.

The shorter times between the point of injury and blood draw among burn patients is likely a result of increased air ambulance traffic and shorter distances between accident scenes and the hospital. Regardless, after investigating and adjusting for these potential confounding factors, we still observe a higher likelihood for the presence of FV fragments among nonburn trauma patients. Burn and nonburn trauma have reliable intragroup measures of injury severity (%TBSA and ISS, respectively), but comparing intergroup injury severity is challenging. In order to categorize patients into high and low severity categories, we identified cut-offs in each measure associated with a critical injury. An ISS score of ≥25 is associated with mortality and is defined as critical.[28,29] Burn TBSA ≥30% are classified as severe, induce burn shock, and would likely be fatal without treatment.[30] We observed no difference in FV antigen levels between patients with high and low severity burn injury (Fig. 3A) and significantly lower FV antigen levels among patients with high severity trauma (Fig. 3B). Overall, injury severity was relatively high within the burn group; therefore, if an association between severity and FV antigen levels existed, we would expect to observe it within this cohort, despite the challenges of intergroup comparisons.

Burn and nonburn trauma patients experience tissue damage and physiologic disturbances related to their injuries and/or treatment and resuscitation.[2,8,10,31] These homeostatic insults induce coagulopathy that is associated with poor outcomes. Trauma researchers have implicated dysregulation in the Protein C pathway in acute traumatic coagulopathy, which is supported by the data presented here.[11] Acute traumatic coagulopathy develops after tissue damage, hemorrhage, and hypoperfusion and is characterized by hypocoagulability.[1] Acute BIC develops after tissue damage and inflammatory cascades and is characterized by hypercoagulability.[8] Conceptually, the mechanistic drivers of coagulopathy in burn and nonburn trauma are different. In the present study, hypoperfusion and increasing injury severity in the setting of trauma are associated with evidence of aPC pathway activity with reduced FV antigen levels, which is inferred as a sequelae of hemorrhage. Admission Hemoglobin levels were significantly lower within trauma patients when compared to burn patients, which supports the conclusion that hemorrhage may be a key driver in FV dynamics, and by extension, aPC activity in trauma patients. The data presented here suggest that, unlike nonburn trauma, dysregulation in the Protein C pathway is not a major driver of BIC. Understanding the pathophysiology of ATC has led to treatment algorithms that have improved patient outcomes. Research, diagnostics, and treatment options for BIC have lagged. This work provides evidence of different mechanisms of

coagulopathy in burn and nonburn trauma and highlights the need for burn-specific coagulopathy research.

Conclusion

Burn and nonburn trauma patients have similar plasma levels of FV antigen on admission. Increasing traumatic injury severity is associated with decreased FV antigen levels, and a greater proportion of trauma patient samples exhibit indirect evidence of activated Protein C activity by the presence of proteolytically degraded FV fragments. FV antigen levels are lower in trauma patients with ongoing shock. Burn severity is not associated with FV antigen levels. These data suggest that acute traumatic coagulopathy differs mechanistically from BIC.

Author Contributions

A.E.P., T.O., K.E.B., J.W.S. designed the study. T.O., M.C.B., M.D.K., D.E.B., K.F. collected data and performed the experiments. J.W.K., T.D.L. analyzed the data. J.W.K. wrote the manuscript. All authors were responsible for critical revisions and acceptance of the final version.

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Disclosure

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Supplementary Data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.jss.2021.12.049.

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