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'Door-to-prophylaxis' as a novel quality improvement metric in prevention of venous thromboembolism following traumatic injury

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ABSTRACT

Objective Venous thromboembolism (VTE) risk reduction strategies include early initiation of chemoprophylaxis, reducing missed doses, weight-based dosing and dose adjustment using anti-Xa levels. We hypothesized that time to initiation of chemoprophylaxis would be the strongest modifiable risk for VTE, even after adjusting for competing risk factors.

Methods A prospectively maintained trauma registry was queried for patients admitted July 2017–October 2021 who were 18 years and older and received emergency release blood products. Patients with deep vein thrombosis or pulmonary embolism (VTE) were compared to those without (no VTE). Door-to-prophylaxis was defined as time from hospital arrival to first dose of VTE chemoprophylaxis (hours). Univariate and multivariate analyses were then performed between the two groups.

Results 2047 patients met inclusion (106 VTE, 1941 no VTE). There were no differences in baseline or demographic data. VTE patients had higher injury severity score (29 vs 24), more evidence of shock by arrival lactate (4.6 vs 3.9) and received more post-ED transfusions (8 vs 2 units); all $p<0.05$. While there was no difference in need for enoxaparin dose adjustment or missed doses, door-to-prophylaxis time was longer in the VTE group (35 vs 25 hours; $p=0.009$). On multivariate logistic regression analysis, every hour delay from time of arrival increased likelihood of VTE by 1.5% (OR 1.015, 95% CI 1.004 to 1.023, $p=0.004$).

Conclusion The current retrospective study of severely injured patients with trauma who required emergency release blood products found that increased door-to-prophylaxis time was significantly associated with an increased likelihood for VTE. Chemoprophylaxis initiation is one of the few modifiable risk factors available to combat VTE, therefore early initiation is paramount. Similar to door-to-balloon time in treating myocardial infarction and door-to-tPA time in stroke, "door-to-prophylaxis time" should be considered as a hospital metric for prevention of VTE in trauma.

Level of evidence Level III, retrospective study with up to two negative criteria.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Many factors have been identified, which are associated with increased venous thromboembolism (VTE) risk.
⇒ Many of these factors are not modifiable risk factors.
⇒ Earlier initiation is associated with decreased VTE incidence, but the hourly risk of delay in initiation of chemoprophylaxis has yet to be defined.

WHAT THIS STUDY ADDS

⇒ In this retrospective study that included 2047 severely injured patients, every hour delay from time of arrival to chemoprophylaxis initiation increased the likelihood of VTE by 1.5%.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Delay in chemoprophylaxis initiation is associated with VTE and is one of the few modifiable risk factors.
⇒ "Door-to-prophylaxis" time should be considered as a hospital metric in prevention of VTE in trauma to ensure timely initiation of VTE chemoprophylaxis.

INTRODUCTION

Venous thromboembolism (VTE), which includes deep vein thrombosis (DVT) and pulmonary embolism (PE), is a well-recognized complication after trauma.[1–4] Balancing the risk of bleeding with VTE mitigation continues to plague those who are traumatically injured.[5–9] Numerous strategies to reduce VTE risk have included early initiation of chemoprophylaxis (CP),[5–7] reducing missed doses,[10] weight-based dosing[11] and dose adjustment using serum anti-Factor-Xa (anti-Xa) levels.[12] Despite these strategies, patients continue to be afflicted by VTE.

The foundation of VTE prevention is CP, most commonly in the form of subcutaneous enoxaparin or unfractionated heparin.[13] Injury patterns such as intracranial hemorrhage, blunt solid organ injury and spine injuries have historically precluded immediate initiation of CP.[5 6 8 9] However, delayed initiation of CP beyond 72 hours has been shown in previous studies to carry a threefold increase in VTE risk.[14] Recent major national guidelines recommend starting CP within 48 hours for nearly all injury patterns.[8 15 16] Despite evidence to support the safety and efficacy of "early" initiation of CP within 48 hours, many centers struggle with

initiating CP within this time period.[17] Institutional CP protocols are commonly lacking, placing patients at risk for VTE,[17] and furthermore, the risk of unnecessarily prolonging CP initiation in severely injured patients by the hour is undefined.

Providers have limited control on many of the factors that have been shown to decrease VTE risk, specifically missed CP doses and time to goal anti-Xa. Time to initiation of CP, however, is a modifiable risk factor, which has the potential to improve patient outcomes. We hypothesized that prophylaxis initiation time would be the strongest modifiable risk for VTE, after adjusting for competing risk factors.

METHODS

Database design and patient population

Our Institutional Review Board approved this study. The study site prospectively maintains an extensive trauma database of all patients seen by the trauma service who receive blood products. All patients are included in the database regardless of presenting data or outcomes. Patient demographics, injury mechanism and severity, prehospital and presenting vitals, resuscitation type and volume, interventions, outcomes and dispositions are all collected prospectively. We evaluated all adult patients with trauma (>17 years of age) admitted between July 2017 and October 2021 who (1) received emergency-release blood products in prehospital or emergency (ED) setting and (2) arrived as the highest level trauma activation. Patients on known home anticoagulation medications, clopidogrel or known to have pre-existing DVT or PE were excluded.

Definitions and outcomes

VTE was defined as the presence of either a PE, a DVT or both after admission. PE was defined as those events detected by helical CT angiography (CTA) of the chest obtained for clinical suspicion and recorded in the Division of Acute Care Surgery's Morbidity and Mortality database. Similarly, DVT was defined as those events detected by duplex ultrasonography. Our institution does not perform DVT screening, therefore these studies were obtained for clinical suspicion only and recorded in the Division of Acute Care Surgery's Morbidity and Mortality database. PE location within the pulmonary arterial tree was documented and classified based on the most proximal clot noted (in the setting of multiple locations). DVT thrombus was also characterized as below knee, above knee, upper extremity or internal jugular veins. Patients diagnosed with PE or DVT on admission were not included. Patients with VTE were assigned to the *VTE* group, while those without were assigned to the *no VTE* cohort. *Door-to-prophylaxis* was defined as time from hospital arrival to first dose of VTE CP (measured in hours). Hospital, intensive care unit (ICU) and ventilator-free days were all calculated on a 30-day time frame.

Institutional VTE CP protocols

At the authors' institution, CP initiation and dosing are administered based on institutional protocols derived from current literature review, which are agreed on between trauma surgery, neurosurgery and orthopedic surgery. Enoxaparin is the CP medication of choice unless renal function precludes safe administration (glomerular filtration rate <30 mL/min), in which heparin (UH) is used. Patients weighing less than 45 kg are given 20 mg of enoxaparin. Patients weighing between 45 kg and 89 kg, 30 mg of enoxaparin is administered. For patients weighing over 90 kg, 40 mg is utilized and for those over 130 kg, 50 mg is given. All enoxaparin regimens are administered every 12 hours. If heparin is needed due to renal dysfunction, 5000 units of UH is given every 8 hours for patients less than 90 kg and 7500 units for those over 90 kg. Enoxaparin dosage is adjusted based on peak anti-Xa assay measured after the third dose of enoxaparin (goal of 0.2–0.4 international unit/mL).

CP is initiated immediately unless there is a contraindication such as solid organ injury, intracranial hemorrhage or spine fractures requiring an emergent operation. Patients with non-operative solid-organ injury are administered CP 24 hours from admission. In patients with intracranial hemorrhage, a stability CT head is obtained (6 hours after injury) and CP is started 24 hours after the stability scan. Spine fractures requiring emergent operative intervention receive CP 24 hours after operative completion.

Statistical analysis

Univariate and multivariate analyses were performed between the two groups. Continuous data are presented as medians with 25th and 75th IQR with comparisons between groups performed using the Wilcoxon rank sum (Mann-Whitney U test). Categorical data are reported as proportions and, where appropriate, tested for significance using χ^2 or Fisher exact tests. The primary data analysis evaluated each hour delay in receipt of the first dose of CP on development risk for VTE. All statistical tests were two tailed with $p<0.05$ set as significant.

Purposeful regression modeling was then used to construct a multivariate logistic regression model evaluating the development of VTE during hospital stay. This was done using the technique of purposeful selection of covariates described by Hosmer and Lemeshow.[18] In an effort to minimize the risk of falsely identifying significant results with multiple comparisons, all variables were prespecified and judged *a priori* to be clinically sound. Independent variables were entered into stepwise regression that generated variables of significance. These were then applied to a multivariate logistic regression analysis evaluating these variables and the variable of interest, door-to-prophylaxis time by hour. STATA MP statistical software (V.17; College Station, Texas) was used for analysis.

RESULTS

During the study period, 2047 patients met inclusion. We then separated these patients into the 106 who developed VTE and the 1941 who did not (no VTE). Of the 106 patients with VTE, 68 were diagnosed with PE, 38 with DVT and 14 with both PE and DVT. When evaluating the location of clot within the patients with PE, 10 patients had clot within the pulmonary trunk or right/left pulmonary artery (15%), 23 patients had clot in a lobar artery (34%), 25 patients had segmental clot (36%) and 10 had clot in subsegmental arteries (15%). Of the 38 patients diagnosed with DVT, 22 patients were found to have clot above the knee (58%), 4 below the knee (11%), 11 in the upper extremity (29%) and 1 had clot within the internal jugular vein (2%).

There were no differences in baseline or demographic data (table 1). However, patients with VTE had higher chest, abdomen and extremity abbreviated injury scale (AIS) scores as well as overall injury severity score (ISS). There was no difference in field vital signs or prehospital focused assessment with sonography in trauma results (table 2). There was also no difference in prehospital fluid administered or whole blood transfused, but the VTE cohort received more red blood cells and plasma in the prehospital setting. When we evaluated all patients in the study,

Table 1 Comparison of baseline data, demographics, and injury severity between patients diagnosed with VTE during admission and those without VTE

	VTE (n=106)	No VTE (n=1941)	P value
Median age, years	36 (26, 58)	37 (25, 54)	0.692
Median BMI	26 (23, 30)	26 (23, 31)	0.678
Male sex	67%	72%	0.301
White race	39%	38%	0.881
Blood group O	59%	51%	0.118
Blunt mechanism of injury	73%	70%	0.519
Median head AIS	3 (0, 4)	3 (0, 4)	0.994
Median chest AIS	3 (2, 4)	3 (1, 3)	0.003
Median abdomen AIS	3 (2, 4)	2 (0, 4)	<0.001
Median extremity AIS	3 (2, 3)	2 (2, 3)	0.019
Median ISS	29 (20, 38)	24 (14, 34)	<0.001

AIS, abbreviated injury scale; BMI, body mass index; ISS, injury severity score; VTE, venous thromboembolism.

the risk for VTE increased in a steady, linear fashion over time as CP initiation was delayed (figure 1).

The VTE group arrived more tachycardic than the no VTE patients, but there were no differences in arrival blood pressure or Glasgow Coma Scale (table 3). Arrival laboratory values were also similar between groups with the exception of higher lactate and lower lysis by rapid thrombelastography. Similar to prehospital transfusions, the VTE group had more transfusions of red blood cells, plasma and platelets in both the emergency department (ED) and post-ED settings.

While there was no difference in need for enoxaparin dose adjustment or missed doses, door-to-prophylaxis time was longer in the VTE group (table 4). VTE patients had a higher rate of complications compared with the no VTE cohort, but no difference in survival. The VTE group also had less hospital, ICU and ventilator-free days.

Multivariate regression analysis was then performed. We began evaluating independent variables including age, gender, race, ISS, ED vitals and labs, transfusions and system issues related to increased VTE risk (need for anti-Xa dose adjustment, missed doses). These variables were then entered into stepwise regression that generated five variables of significance (age, male sex, lactate, post-ED transfusions and ISS). These were then applied to a multivariate logistic regression analysis evaluating these five variables and door-to-prophylaxis time by hour. Controlling for these five variables, every hour delay from time of arrival increased likelihood of VTE by 1.5% (table 5). When transferred patients were removed from the model, the associated VTE risk with door-to-prophylaxis time was unchanged (OR 1.015, 95% CI 1.007 to 1.021, p<0.001).

Table 2 Comparison of field vital signs and resuscitation volumes between groups

	VTE (n=106)	No VTE (n=1941)	P value
Median scene HR	118 (91, 139)	110 (90, 129)	0.062
Median scene SBP	106 (91, 134)	109 (87, 131)	0.970
Median scene GCS	13 (6, 15)	13 (3, 15)	0.671
Field FAST(+)	40%	47%	0.204
Median field fluid, mL	0 (0, 500)	0 (0, 250)	0.638
Median field RBC, U	0 (0, 0)*	0 (0, 0)	0.014
Median field plasma, U	0 (0, 0)†	0 (0, 0)	0.050
Median field WB, U	0 (0, 0)	0 (0, 1)	0.238

90 90th and 95th percentile VTE: (2, 2) vs No VTE (1, 2).
†90± 90th and 95th percentile VTE: (1, 2) vs No VTE (1, 1).
FAST, focused assessment with sonography of trauma; GCS, Glasgow Coma Scale; HR, heart rate; mL, milliliters; RBC, red blood cells; SBP, systolic blood pressure; U, units; VTE, venous thromboembolism; WB, whole blood.

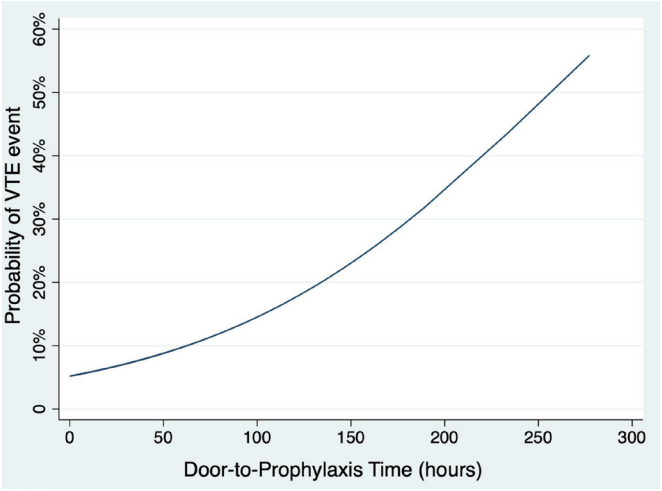

Figure 1 Probability of developing VTE during admission as a function of time from hospital arrival to first dose of VTE chemoprophylaxis. VTE, venous thromboembolism.

Table 3 Comparison of arrival vital signs, initial laboratory values, ED and post-ED transfusions between patients diagnosed with VTE during admission and those without VTE

	VTE (n=106)	No VTE (n=1941)	P value
Arrival HR	112 (96, 134)	107 (86, 126)	0.036
Arrival SBP	109 (84, 130)	106 (90, 126)	0.698
Arrival GCS	13 (3, 15)	14 (3, 15)	0.446
Arrival hemoglobin g/dL	12.1 (11.0, 13.3)	12.5 (10.8, 13.9)	0.114
Arrival platelet count	204 (142, 261)	217 (161, 271)	0.185
Arrival base excess	−5 (−10 to −1)	−4 (−8 to −2)	0.190
Arrival lactate, mmol/L	4.6 (3.2, 6.7)	3.9 (2.6, 6.0)	0.038
Arrival rTEG ACT, seconds	113 (105, 121)	113 (105, 121)	0.142
Arrival r-TEG angle, degrees	72 (67, 75)	73 (68, 76)	0.164
Arrival r-TEG MA, mm	62 (56, 67)	63 (58, 68)	0.196
Arrival r-TEG LY-30, %	0.1 (0.0, 1.1)	0.4 (0.0, 1.6)	0.034
ED RBC, U	1 (0, 5)	1 (0, 2)	<0.001
ED plasma, U	1 (0, 5)	1 (0, 2)	0.006
ED platelets, U	0 (0, 1)	0 (0, 0)	0.005
ED WB, U	0 (0,1)	0 (0,1)	0.467
TXA administration, %	6.3	1.9	<0.001
Post-ED RBC, U	8 (3, 19)	2 (0, 6)	<0.001
Post-ED plasma, U	5 (2, 14)	0 (0, 3)	<0.001
Post-ED platelets, U	1 (0, 3)	0 (0, 1)	<0.001
Post-ED WB, U	0 (0, 0)	0 (0, 0)	0.449

*All data presented as medians with IQR in parenthesis.
ACT, activated clotting time; ED, emergency department; GCS, Glasgow Coma Scale; g/dL, grams per deciliter; HR, heart rate; LY-30, Percent amplitude reduction (lysis) 30 minutes after MA; MA, maximal amplitude; mm, millimeters; mmol/L, millimoles per liter; RBC, red blood cells; r-TEG, rapid thrombelastography; SBP, systolic blood pressure; TXA, tranexamic acid; U, units; VTE, venous thromboembolism; WB, whole blood.

Table 4 Univariate comparison of risk factors for VTE and outcomes between groups

Prophylaxis type	VTE (n=106)	No VTE (n=1941)	P value
Enoxaparin	54%	69%	0.001
Unfractionated heparin	23%	13%	
Therapeutic anticoagulation	17%	3%	
None	6%	15%	
Enoxaparin requiring anti-Xa adjustment	38%	30%	0.083
Door-to-prophylaxis time, hours	35 (14, 51)	25 (11, 41)	0.009
Median missed enoxaparin doses	1 (0, 3)	0 (0, 2)	0.406
Acute renal failure	21%	11%	0.004
Pneumonia	41%	19%	<0.001
Sepsis	56%	23%	<0.001
Acute respiratory failure	74%	51%	<0.001
Median hospital-free days	0 (0, 13)	15 (0, 24)	<0.001
Median ICU-free days	1 (0, 23)	25 (0, 30)	<0.001
Median ventilator-free days	4 (0, 28)	28 (0, 30)	<0.001
30-day survival	88%	86%	0.728

ICU, intensive care unit; VTE, venous thromboembolism.

Several variables of pertinent interest (CP medication choice, abdominal AIS instead of ISS, LY-30 and tranexamic acid (TXA) exposure) were inserted into the model to evaluate significance. With respect to use of heparin for prophylaxis, we added this to the MLR model with no change in the impact on door-to-prophylaxis time and risk of VTE (OR 1.012, 95% CI 1.005 to 1.017; p<0.001). The use of heparin (rather than enoxaparin) demonstrated non-significance (OR 1.07, 95% CI 0.60 to 1.90; p=0.824). When we dropped ISS from our MLR model and added abdominal AIS, the impact of door-to-prophylaxis time and risk of VTE remained the same (OR 1.012, 95% CI 1.001 to 1.019; p=0.006). An increase in abdominal AIS was associated with increased, but not significant, risk of VTE (OR 1.16; 95% CI 0.97 to 1.38; p=0.068). When LY-30 was added to the model, change in percentage of lysis was not associated with subsequent development of VTE (OR 0.98, 95% CI 0.94 to 1.01; p=0.314). When shutdown was dichotomized to LY-30 less than or greater than 0.9%, there was also no significant difference (OR 1.31, 95% CI 0.83 to 2.07; p=0.240). Finally, when TXA administration was added into the model, TXA exposure increased the association of door-to-prophylaxis time with VTE (OR 1.023; 95% CI 1.003 to 1.043, p=0.014).

DISCUSSION

In our retrospective review of severely injured polytrauma patients who received emergency release blood products, prolonged CP initiation time was significantly associated with an increased likelihood for symptomatic VTE. Every hour in CP initiation delay from time of arrival increased the likelihood of VTE by 1.5%, even after adjusting for injury surrogate variables. To the authors' knowledge, no prior research has defined risk by the hour of CP initiation delay in a severely injured population.

Table 5 Multivariate regression analysis evaluating independent variables predicting development of VTE during hospital stay

	OR	95% CI	P value
Door-to-prophylaxis, hours	1.015	1.004 to 1.023	0.004
Age, years	0.98	0.951 to 1.020	0.403
Male sex	0.56	0.171 to 1.889	0.357
ISS	1.02	0.974 to 1.061	0.439
Post-ED transfusions, units	1.05	1.009 to 1.095	0.016
Lactate	0.83	0.647 to 1.064	0.197

ED, emergency department; ISS, injury severity score.

Post-traumatic VTE reduction strategies are numerous and multifaceted. First, the optimal CP agent has been debated for over two decades. Kakaar *et al* showed in 1977 that UH dosed every 8 hours decreased the incidence of DVTs and fatal PEs in the surgical patient population.[19] Furthermore, this form of prophylaxis was not associated with any increased bleeding complications. Despite good evidence of UH's utility, it was not widely adopted in the trauma population. In 1996, Geerts *et al* compared enoxaparin to UH every 12 hours in a double-blinded randomized control study that revealed enoxaparin was superior at reducing DVT.[13] Due to concerns in that study for ineffective UH dosing (every 12 hours vs every 8 hours), multiple studies were carried out over the following two decades to refute or validate the study's findings.[20–22] It is now generally accepted that enoxaparin is favored to be superior to UH and is reflected in several national guidelines as the CP agent of choice.[15 16]

In an attempt to risk stratify trauma patients and guide CP initiation, several VTE risk assessment models were created. Two notable models are the Greenfield Risk Assessment Profile and Trauma Embolic Scoring System. The models suggest patients calculated to be at high risk should receive CP. However, Zander *et al* revealed in a trauma population undergoing routine lower extremity ultrasound surveillance, patients developed DVT despite being deemed low risk by the models.[23] Ultimately, VTE risk models for trauma are cumbersome to calculate and underperform in prediction of VTE, likely because DVT and PE are often different entities and not always related (ie, pulmonary thrombosis).[4 24–26] Consequently, the risk assessment models have been abandoned by many centers and national guidelines, leaving providers with limited options to reduce VTE risk.[15 16]

The next risk reduction strategies center around appropriate dosing. It is now known that missing more than one dose of CP increases odds of VTE eightfold.[10] Administration compliance is, therefore, a huge priority, but patients miss doses for a multitude of reasons that providers can not always control. However, effective dosing is something that is controllable. Historically, 30 mg of enoxaparin given every 12 hours was the gold standard.[13] Although this one-size-fits all approach seems simple, there was concern that medication metabolism/elimination differs among patients and a single universal starting dose may not be effective. With the advent of anti-Xa monitoring, dose adjustment is possible to ensure adequate DVT prophylaxis is being achieved. Numerous studies have now shown that weight-based dosing and dose adjustments based off anti-Xa reduce VTE risk.[12 27] These strategies are now supported by multiple recent national guidelines.[15 16]

Despite using all available known strategies noted above, our data in severely injured patients with trauma demonstrated that over 5% of our patients suffered a DVT or PE. Unlike previous research, this study provides associated VTE risk with each hour of delay in CP initiation. Our study population consisted of bleeding patients requiring blood product resuscitation, in which balancing hemostasis with hypercoagulability is most difficult. Once hemostasis has been achieved, providers should be mindful that unnecessary delays in initiation can be costly. Unlike other studies, associated risk with delay in CP has now been quantified, to better inform our decision-making on whether to delay or initiate. Similar to recent literature gap analyses, our study echoes the sentiment that CP initiation timing is one of the few

modifiable risk factors providers have control over, so striving to find the optimal timing to initiate CP to reduce VTE burden is significant.[28 29]

In other aspects of medicine, metrics or "audit filters" have been established in an effort to improve patient outcomes. Interestingly, two examples of such disease processes involve clot, most notably myocardial infarction and ischemic stroke. Door-to-balloon time and door-to-needle time have been coined in the treatment timing of myocardial infarction and ischemic stroke, respectively.[30 31] Time to reperfusion has unequivocally been shown to improve morbidity and mortality in these patient subsets.[30 31] This study suggests a demand signal exists within the realm of CP initiation after traumatic injury, with known gaps in VTE CP guidelines or compliance with those guidelines. Ideally, an effective process audit filter for "door-to-prophylaxis" time would improve compliance with CP initiation nationwide, ultimately to reduce VTE and the morbidity associated with it. Additionally, if hospitals abided by these measures, and VTE still occurred, a need for nationwide process improvement, in place of individual penalties, would be more justifiable.

The primary limitations of this study are inherent due to its retrospective design. First, the study population's extremity AIS was moderate to severe, which splints and bandages limit the diagnostic accuracy for DVTs. Additionally, our center does not perform routine DVT surveillance to capture asymptomatic DVTs, so the actual incidence of VTE is most certainly higher than 5%.[32] Furthermore, with our institution's high overall injury severity, CTAs of the chest are obtained somewhat liberally, so this may account for the differences in VTE incidence compared with national averages. Second, transferred patients from other emergency rooms who received emergency release blood products were captured by the database. While there were very few of these, it is likely that their door-to-prophylaxis time does not take into account the extended prehospital time and may under-represent the door-to-prophylaxis time association with VTE in this subset of patients. However, when removing transferred patients from the model, the associated risk of CP delay remained significant. Furthermore, the associated VTE risk with each hour of delay of CP may not be a linear, therefore the inflection point at which the optimal time to administer CP to reduce VTE risk remains unknown. Also, we demonstrated an association between several risk factors and VTE, notably blood transfusions and injury severity. These risk factors have their own risk associated and are often related to one another.[33 34] Thus, the VTE cohort was more injured and critically ill, and it is possible that unmeasured covariates (such as specific injury patterns) influenced this relationship. While it is known that not all traumatic injuries carry the same VTE risk, we felt by including all injury patterns, our findings would be more generalizable and allowed us to weigh CP initiation timing against all other risk factors. Finally, this is a single institution's experience in a severely injured population, and the results may not be generalizable. Further research is required to validate our findings.

CONCLUSIONS

The current retrospective study of severely injured patients with trauma, who received emergency release blood products, found that increased door-to-prophylaxis time was significantly associated with an increased likelihood for developing symptomatic VTE. Unlike previous research, this study found an associated risk with each hour of delay increasing VTE likelihood by 1.5%. CP initiation is one of the few modifiable risk factors available to combat VTE and early initiation appears critical. In the severely injured and actively bleeding patient where holding CP is necessary, CP initiation should be considered as early as safety permits. While validation in future studies is required, similar to door-to-balloon time in treating myocardial infarction and door-to-needle time in stroke, "door-to-prophylaxis time" should be considered as a quality improvement metric for prevention of VTE in trauma.

Contributors J-MVG, TWC, DEL, CWK, JKB and MS were responsible for data collection, literature search, study design and data interpretation. JVG, TWC, CWK, TJP and BAC were involved in study design, data analysis, manuscript writing and revisions. BAC was involved in all aspects of the manuscript production. J-MVG is responsible for the overall content as the guarantor.

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