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Dynamic coagulability after injury: Is delaying venous thromboembolism chemoprophylaxis worth the wait?

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Abstract

BACKGROUND: Severely injured patients often progress from early hypocoagulable to normal and eventually hypercoagulable states, developing increased risk for venous thromboembolism (VTE). Prophylactic anticoagulation can decrease this risk, but its initiation is frequently delayed for extended periods due to concerns for bleeding. To facilitate timely introduction of VTE chemoprophylaxis, we characterized the transition from hypo- to hypercoagulability and hypothesized that trauma-induced coagulopathy resolves within 24 hours after injury.

METHODS: Serial blood samples were collected prospectively from critically injured patients for 120 hours after arrival at an urban Level I trauma center. Extrinsic thromboelastometry maximum clot firmness was used to classify patients as hypocoagulable (HYPO, <49 mm), normocoagulable (NORM, 49–71 mm), or hypercoagulable (HYPER, >71 mm) at each time point. Changes in coagulability over hospital course, VTE occurrence, and timing of prophylaxis initiation were analyzed.

RESULTS: 898 patients (median Injury Severity Score, 13; mortality, 12%; VTE, 8%) were enrolled. Upon arrival, 3% were HYPO (90% NORM, 7% HYPER), which increased to 9% at 6 hours before down-trending. Ninety-seven percent were NORM by 24 hours, and 53% were HYPER at 120 hours. Median maximum clot firmness began in the NORM range, up-trended gradually, and entered the HYPER range at 120 hours. Patients with traumatic brain injury (TBI) followed a similar course and were not more HYPO at any time point than those without TBI. Failure to initiate prophylaxis by 72 hours was predicted by TBI and associated with VTE development (27% vs 16%, $p < 0.05$).

CONCLUSIONS: Regardless of injury pattern, trauma-induced coagulopathy largely resolves within 24 hours, after which hypercoagulability becomes increasingly more prevalent. Deferring

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AUTHORSHIP

J.J.S., L.Z.K., and M.J.C. designed this study. L.Z.K., A.S.C., R.A.C., and M.J.C. collected the data, which J.J.S., L.Z.K., and M.J.C. analyzed and interpreted. J.J.S. wrote the manuscript, which L.Z.K., A.S.C., R.A.C., and M.J.C. critically revised.

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DISCLOSURE

The authors declare no conflicts of interest.

initiation of chemoprophylaxis, which is often biased toward patients with intracranial injuries, is associated with VTE development.

Keywords

Trauma-induced coagulopathy; hypercoagulability; venous thromboembolism; chemoprophylaxis; thromboelastometry

Dysregulated coagulation, either hypo- or hypercoagulability, occurs in more than half of severely injured patients and is associated with increased morbidity and mortality.¹ Although changes in coagulation are multifactorial and vary among patients, the early postinjury period is often characterized by a hypocoagulable state known as trauma-induced coagulopathy (TIC).^{2,3} Trauma-induced coagulopathy results directly from tissue injury and shock; can be exacerbated iatrogenically by hypothermia, acidosis, and hemodilution during resuscitation; and facilitates uncontrolled hemorrhage.²⁻⁴ Patients who survive can become hypercoagulable with increased risk for venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE).⁵⁻⁸ These complications lead to prolonged hospitalizations, excess costs, and greater mortality.^{9,10}

The transition from hypo- to hypercoagulability after physiologic stress was first recognized in 1914 by Walter Cannon,¹¹ but despite much work over the last century to characterize and manage these contradictory states,^{1-8,10,12-20} the timing of this change remains poorly understood. One reason is that conventional coagulation tests like international normalized ratio and partial thromboplastin time cannot detect hypercoagulability. Because it is unknown when patients progress to normal and then hypercoagulable states, surgeons face a dilemma when determining the time to initiate prophylactic anticoagulation, which can decrease the risk of VTE.^{18,19} Concerns for thrombosis must be weighed against those for bleeding; consequently, introduction of VTE chemoprophylaxis is often delayed.

Increased use of viscoelastic hemostatic assays like thromboelastography (TEG) and thromboelastometry (TEM) in trauma has furthered our understanding of changes in coagulation after injury. Unlike conventional, plasma-based tests, viscoelastic assays quantify whole-blood clot formation and degradation and can identify hypercoagulability.²¹ Given these advantages, we used serial TEMs in this prospective study to characterize the transition from hypo- to hypercoagulability and determine the time to resolution of TIC, which might facilitate initiation of VTE chemoprophylaxis. We hypothesized that coagulopathic patients progress to a normal or hypercoagulable state within 24 hours after injury.

METHODS

This study was a secondary analysis of a larger prospective cohort study. From October 2010 to May 2016, serial blood samples were collected prospectively from patients meeting criteria for highest-level trauma activation at Zuckerberg San Francisco General Hospital, the only Level I trauma center in San Francisco, California. Samples were obtained upon arrival and at 6, 12, 24, 48, 72, 96, and 120 hours thereafter until the patient was transferred from the intensive care unit (ICU) or died. Patients were excluded if they were younger than

18 years, pregnant, incarcerated, transferred from another hospital, or taking outpatient anticoagulant or antiplatelet medications. Informed consent was obtained for study enrollment under a protocol approved by the Committee on Human Research at the University of California San Francisco.

Our procedures for sample collection and laboratory analysis have previously been described.²² Extrinsic thromboelastometry (EXTEM) was performed on each sample to assess clot function following activation with tissue factor using a ROTEM *delta* hemostasis analyzer (Tem International GmbH; Munich, Germany). Parameters measured by EXTEM included clotting time (CT; the time from the start of the test to initial clot formation; normal range, 42–74 seconds), alpha angle (α ; the slope of the tracing, which represents the rate of clot formation; normal range, 63–81 degrees), and maximum clot firmness (MCF; the greatest amplitude of the tracing, which illustrates clot strength; normal range, 49–71 mm).²³ These results were obtained only for research and were not known by clinicians. Maximum clot firmness and its TEG equivalent, maximum amplitude (MA), reflect platelet-fibrin interactions, a component involved in both clot formation and degradation, and have been shown to correlate with hypercoagulability in trauma and other surgical populations.^{24–28} Therefore, in this study, MCF was used to evaluate overall coagulability and classify patients as hypocoagulable (HYPO, <49 mm), normocoagulable (NORM, 49–71 mm), or hypercoagulable (HYPER, >71 mm) at each time point. Maximum clot firmness greater than 71 mm has been associated with thromboembolic events in another series.²⁵

Demographic, injury, resuscitation, and outcome data were also collected prospectively for all patients. Venous thromboembolisms consisted of symptomatic DVT or PE at any time during admission, which were confirmed by ultrasound or computed tomography angiogram, respectively. These diagnostic tests were ordered only if clinical suspicion warranted; routine surveillance was not conducted. The diagnosis of traumatic brain injury (TBI) required radiographic evidence of intracranial injury on computed tomography or magnetic resonance imaging and head Abbreviated Injury Scale (AIS) score greater than 3. Acute respiratory distress syndrome was determined using the Berlin Definition,²⁹ which included blinded, two-physician adjudication of chest radiographs during the first 8 days of admission as previously described.³⁰ Multiorgan failure was defined using the Denver Postinjury Multiple Organ Failure Score.³¹

Changes in coagulability over hospital course, VTE occurrence, and timing of chemoprophylaxis initiation were analyzed. Summary statistics are reported as median with interquartile range for continuous data and as percentage for binary data. Univariate differences between groups were evaluated with Wilcoxon rank-sum or Kruskal-Wallis tests for continuous data and the Fisher exact test for binary data. Multivariate logistic regression was performed to identify independent predictors of chemoprophylaxis initiation or VTE while controlling for age, sex, injury severity, and shock. A $p < 0.05$ was considered significant, except when adjusted for multiple comparisons using Bonferroni correction. Statistical analyses were performed with Stata/SE 15 (StataCorp, College Station, Texas).

RESULTS

Study Population

During the 6-year period, 898 patients were enrolled (Table 1). These patients were mostly male (83%) with a median age of 35 years, representing a typical trauma population. They had a median Injury Severity Score of 13 and median base deficit of 2.3. Fifty-seven percent sustained blunt trauma, and 31% experienced TBI. Seventy-one patients (8%) developed a symptomatic VTE at any point during admission. Overall mortality was 12%.

Initial Coagulability

Upon arrival, 3% of patients were HYPO, 90% NORM, and 7% HYPER (Table 2). Accordingly, HYPO patients were coagulopathic by other conventional and viscoelastic parameters with elevated international normalized ratio (1.4 vs 1.1 vs 1.1), prolonged CT (101 vs 59 vs 52 seconds), and reduced α (54 vs 72 vs 79 degrees) and had lowest platelet count and fibrinogen compared with NORM and HYPER patients (all $p < 0.02$ for multiple comparisons). HYPO patients had lowest Glasgow Coma Scale score (9 vs 14 vs 15), greatest degree of shock (base deficit, 6.0 vs 1.6 vs 3.8), and highest mortality (47% vs 11% vs 2%; all $p < 0.02$ for multiple comparisons). The percentage of female patients was highest in the HYPER cohort. Initial hypercoagulability was not associated with VTE (4% vs HYPO 0% vs NORM 6%; $p > 0.02$ for multiple comparisons).

Changes in Coagulability Over Hospital Course

We began by examining how the prevalence of hypocoagulability evolved over the first 5 days after injury (Fig. 1). Consistent with previous studies on TIC, a group of patients were HYPO early in their hospital course. This proportion peaked at 9% at 6 hours before declining significantly to 6% at 12 hours and to 2% at 24 hours, after which it remained less than 1%. Ninety-seven percent of patients were NORM by 24 hours. After this time, however, normocoagulability down-trended. We observed this change because 24 hours was an inflection point for hypercoagulability, which was 7% at arrival and escalated significantly to 24% at 72 hours, to 34% at 96 hours, and to 53% at 120 hours.

As a corollary to overall coagulability, we analyzed the trends of each EXTEM parameter over the first 5 days for the entire population (Fig. 2). Median MCF began in the NORM range, increased gradually after 6 hours, and entered the HYPER range at 120 hours. While CT and α remained within normal limits throughout the study, α followed a similar course to MCF, approaching the threshold between normocoagulability and hypercoagulability after 48 hours.

To explore the relationship between injury pattern and coagulability, patients were categorized into three groups: no TBI, isolated TBI, and polytrauma (TBI and AIS score ≥ 3 in at least one body region other than head or face). At each time point, the individual proportions of HYPO and HYPER patients were not different among these three groups (all $p > 0.02$ for multiple comparisons).

Coagulability and Thromboembolic Events

Of the 71 patients with a symptomatic VTE, 36 (51%) developed a DVT, and 35 (49%) developed a PE. Venous thromboembolisms affected 25% of patients who were HYPER at 48 hours, 26% at 72 hours, 30% at 96 hours, and 28% at 120 hours; however, these rates were not significantly different from those of NORM patients at the same time points.

Timing of Chemoprophylaxis Initiation

Sixteen percent of inpatients at 24 hours had received their first dose of VTE chemoprophylaxis, 44% at 48 hours, 71% at 72 hours, 88% at 96 hours, and 99% at 120 hours. Because coagulopathy had largely resolved by 24 hours, we were interested in whether the decision to withhold anticoagulation was associated with the development of a symptomatic VTE (Fig. 3). Venous thromboembolism incidence was lower for inpatients who had received prophylaxis by 72 hours (16%) than for those who had not (27%, $p < 0.05$). This advantage persisted at 96 hours (16% vs 40%, $p < 0.05$) and 120 hours (19% vs 50%); however, at the latter time point, the number of patients who were still admitted and had not received prophylaxis was too small to detect statistical significance.

After establishing that failure to initiate prophylaxis by 72 hours is associated with VTE development, we compared patients who had and had not received their first dose of prophylaxis by that time (Table 3). Those who had not received prophylaxis experienced more blunt trauma (88% vs 60%) and were more severely injured (Injury Severity Score, 29 vs 21), especially with intracranial (head AIS score, 4 vs 0; TBI, 70% vs 27%; Glasgow Coma Scale score, 11 vs 14) and orthopedic (71% vs 48%) injuries (all $p < 0.05$). They had longer hospital (21 vs 15 days) and ICU (12 vs 6 days) stays and fewer ventilator-free days (22 vs 25, all $p < 0.05$). This cohort whose anticoagulation was withheld was not more coagulopathic at arrival (HYPO, 0% vs 1%) or 72 hours (2% vs 0%, all $p > 0.05$). After we controlled for age, sex, injury severity, and shock with logistic regression analysis, TBI and orthopedic injury remained independent predictors of delayed prophylaxis.

DISCUSSION

The purpose of the current study was to characterize the changes in coagulation over the first 5 days after injury. While a subset of patients in this critically injured cohort experienced a brief period of hypocoagulability, 98% of patients were in a normal or hypercoagulable state by 24 hours, confirming our hypothesis. Hypercoagulability became increasingly more prevalent at subsequent time points, exceeding 50% among patients still in the ICU at 5 days, and these trends occurred independently of injury pattern. Although hypercoagulability on TEM did not correlate with thromboembolic events in this series, failure to initiate prophylactic anticoagulation by 72 hours, which was biased toward patients with intracranial injuries, was associated with VTE development.

Originally thought to result primarily from large-volume resuscitation, TIC is now understood as a complex endogenous response to tissue injury and hypoperfusion.^{2,3,12-14} This response disrupts the balance between clot formation and degradation that normally serves to stop hemorrhage while preventing microvascular thrombosis. As the balance is

restored, patients can shift in a continuum between hypo- and hypercoagulable states over time. Despite much interest in deranged coagulation at isolated time points, only a few studies have accounted for the dynamic nature of coagulation status as patients progress through their hospital course, and they have focused on trends in hypercoagulability.^{6,20,21} Our longitudinal study is unique in this respect. We described the trend in hypocoagulability and determined that TIC rarely persists beyond 24 hours. The increasing prevalence of hypercoagulability after that time is consistent with MA⁶ but not reaction time (TEG equivalent of CT)²⁰ data obtained at other institutions.

The lack of an independent association between hypercoagulability on TEM and eventual VTE diagnosis conforms with the mixed findings on this topic in the trauma literature. Kashuk et al.⁵ and Cotton et al.²⁶ have observed that elevated G and MA values, respectively, on TEG correlate with thromboembolic events. However, Schreiber et al.²⁰ and Van Haren et al.³² have reported that TEG values do not predict VTE occurrence. Several factors might explain our results. Growing recognition of PEs found incidentally or in the absence of DVT suggests that the time VTEs are identified might not correspond with the time they develop,^{33–35} and the use of protocolized VTE screening is varied among studies examining the clinical significance of hypercoagulability on viscoelastic assays. Since we did not screen, our true VTE incidence could have been higher. While we can conclude that blood becomes more prone to clotting as time from injury increases, we also appreciate that thrombosis is multifactorial and is influenced by the other components of Virchow's triad, stasis and endothelial damage, in addition to biochemical clot strength.

Despite this issue, the increased risk of VTE after trauma remains well-established, along with the effectiveness of prophylactic anticoagulation in decreasing this risk.^{7,8,18,19} The decision to initiate or defer chemoprophylaxis must be individualized based on multiple considerations including the status of anatomic and coagulopathic bleeding and planned procedures. After certain injuries like intracranial hemorrhages and blunt solid abdominal organ injuries, it is common to withhold anticoagulation empirically due to concerns for bleeding, but this practice is not evidence-based. Interrupting prophylaxis even by one dose is associated with DVT,³⁶ and in the current study, we delineated the consequences of delaying initiation of prophylaxis by each day. Seventy-two hours was the point at which failure to initiate prophylaxis became associated with VTE development, and orthopedic injury and TBI were independent predictors of the decision not to anticoagulate. The latter finding is interesting because, although TBI is thought to promote a severe, prolonged coagulopathy that necessitates deferring prophylaxis, no differences in coagulability were shown among patients with no TBI, isolated TBI, and polytrauma at any time point in this study.

Because time to resolution of TIC is most often less than 24 hours, this study provides additional support, but not complete justification, for earlier initiation of VTE chemoprophylaxis. One consideration we did not address is the safety of early anticoagulation in patients with injuries regarded high-risk for persistent or delayed bleeding, which has been the focus of previous work. In the setting of acute TBI, starting low-molecular-weight heparin (LMWH) or unfractionated heparin by 72 hours has retrospectively been shown not to increase radiographic progression of intracranial

hemorrhage or the rate of subsequent neurosurgical interventions, and it decreased the risk of VTE compared with delayed anticoagulation.^{37,38} Like-wise, introducing LMWH 24 hours after intracranial hemorrhage had been deemed stable on imaging did not result in new or expanded lesions.³⁹ Similar studies have demonstrated the efficacy and safety of early prophylaxis after spine fractures,⁴⁰ blunt solid abdominal organ injuries,^{41,42} and major vascular injuries.⁴³

We recognize several limitations of this study beyond those inherent in its prospective observational design. The TEM thresholds we used were based on reference ranges determined by the manufacturer using healthy patients,²³ and while MCF greater than 71 mm has been associated with thromboembolic events in a surgical population,²⁵ the clinical applicability of these thresholds has not been established in a trauma population. Patient attrition due to death and discharge from the ICU created a survivor bias and might have hindered our ability to detect statistical significance at later time points. Lastly, coagulation status at each time point was not controlled for the effects of prior resuscitation and blood transfusions.

Although viscoelastic assays have been shown to improve survival when used to guide resuscitation in trauma,¹⁵ their role in the management of the injured patient *after* correction of coagulopathy remains unclear and should be addressed in future work. Three studies have explored whether TEG could direct dosing of VTE chemoprophylaxis, but all were underpowered and failed to demonstrate a benefit over standard-dose LMWH.^{44–46} The most recent of these studies was a multicenter randomized controlled trial in which 185 patients were administered either 30 mg of enoxaparin twice daily or enoxaparin dose-adjusted to achieve a change in reaction time between standard and heparinase TEGs of 1–2 minutes,⁴⁵ which had previously been associated with no DVT occurrence.⁴⁷ Despite finding no difference in VTE rate between groups in this trial, the authors noted a lower overall VTE incidence than in their smaller pilot study (6.5% vs 14.9%),⁴⁶ which they attributed partially to shorter time to prophylaxis initiation (1.0 vs 2.7 days). When this observation is considered in the context of the current study, we speculate that absence or resolution of coagulopathy on TEG or TEM might facilitate earlier prophylaxis initiation on an individual-patient basis.

Therefore, while we support continued investigation into the use of viscoelastic assays in guiding *how* to prophylax, future studies should also evaluate prospectively their efficacy and safety in directing *when* to prophylax. These same questions about using TEG and TEM to determine when and how to prophylax could also be asked for other conditions for which we anticoagulate trauma patients, like blunt cerebrovascular injuries. Finally, while the current study provides clinical insight into the dynamics of dysregulated coagulation after injury, further elucidating the biologic mechanisms behind the transition from hypo- to hypercoagulability remains the key to targeted treatment in these high-risk patients.

CONCLUSIONS

Based on the results of this study, we conclude that TIC largely resolves within 24 hours, after which hypercoagulability becomes increasingly more prevalent. These trends occur

independently of injury pattern. Deferring initiation of prophylactic anticoagulation, which is often biased toward patients with intracranial and orthopedic injuries, is associated with VTE development. Further studies should examine the efficacy and safety of timing introduction of VTE chemoprophylaxis based on correction of coagulopathy.

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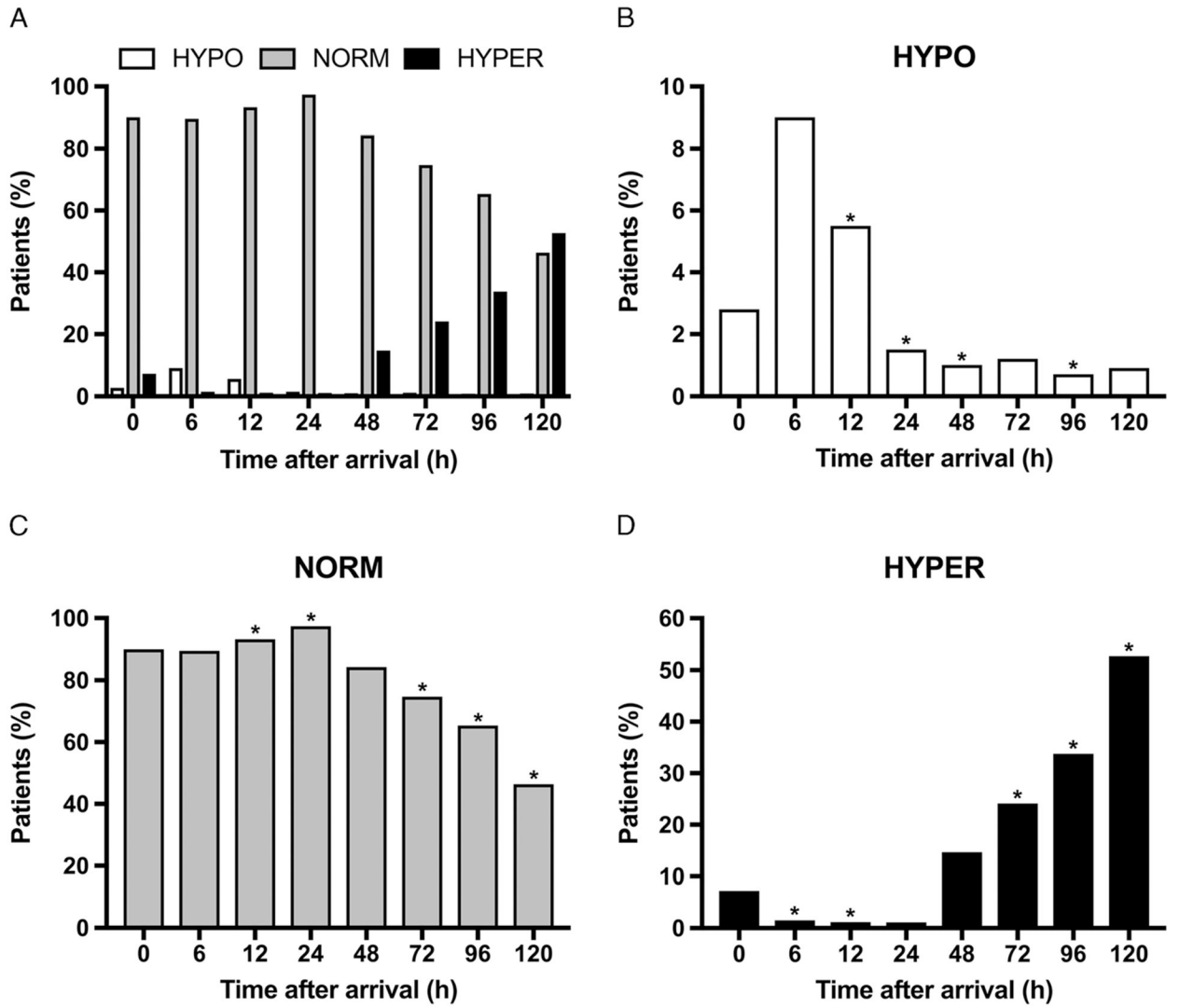


Figure 1. Changes in coagulability over hospital course. Proportions of HYPO, NORM, and HYPER patients at each time point are depicted collectively in (A) and individually in HYPO (B), NORM (C), and HYPER (D). * $p < 0.05$ when compared with previous time point; HYPER (MCF >71 mm); HYPO (MCF <49 mm); NORM (MCF, 49–71 mm).

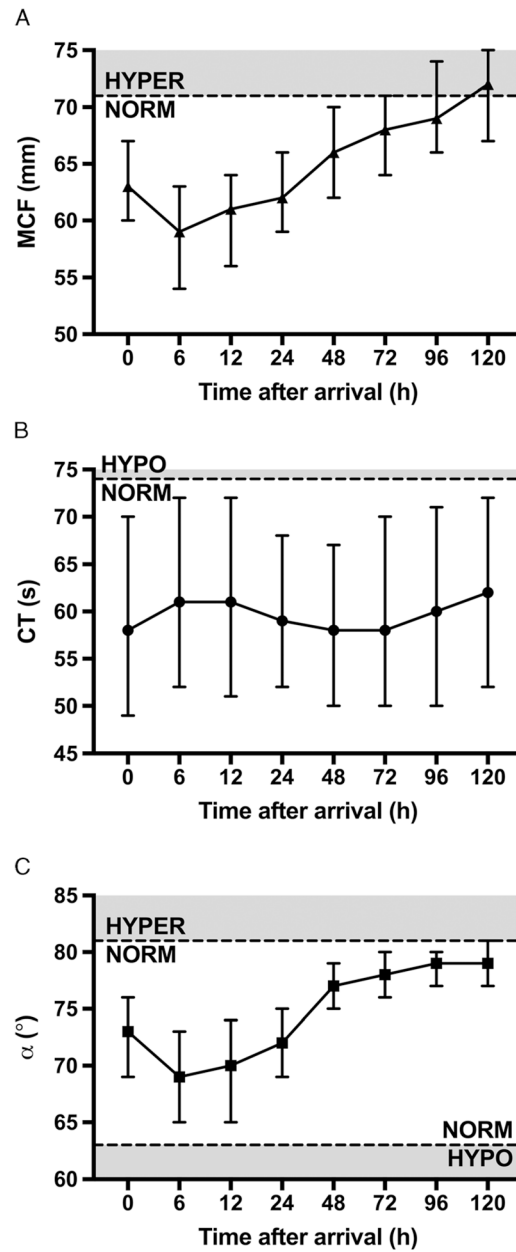


Figure 2. Trends in thromboelastometry parameters over first 5 days. (A) Maximum clot firmness (*MCF*; normal range, 49–71 mm). (B) Clotting time (*CT*; normal range, 42–74 seconds). (C) Alpha angle (α ; normal range, 63–81 degrees).

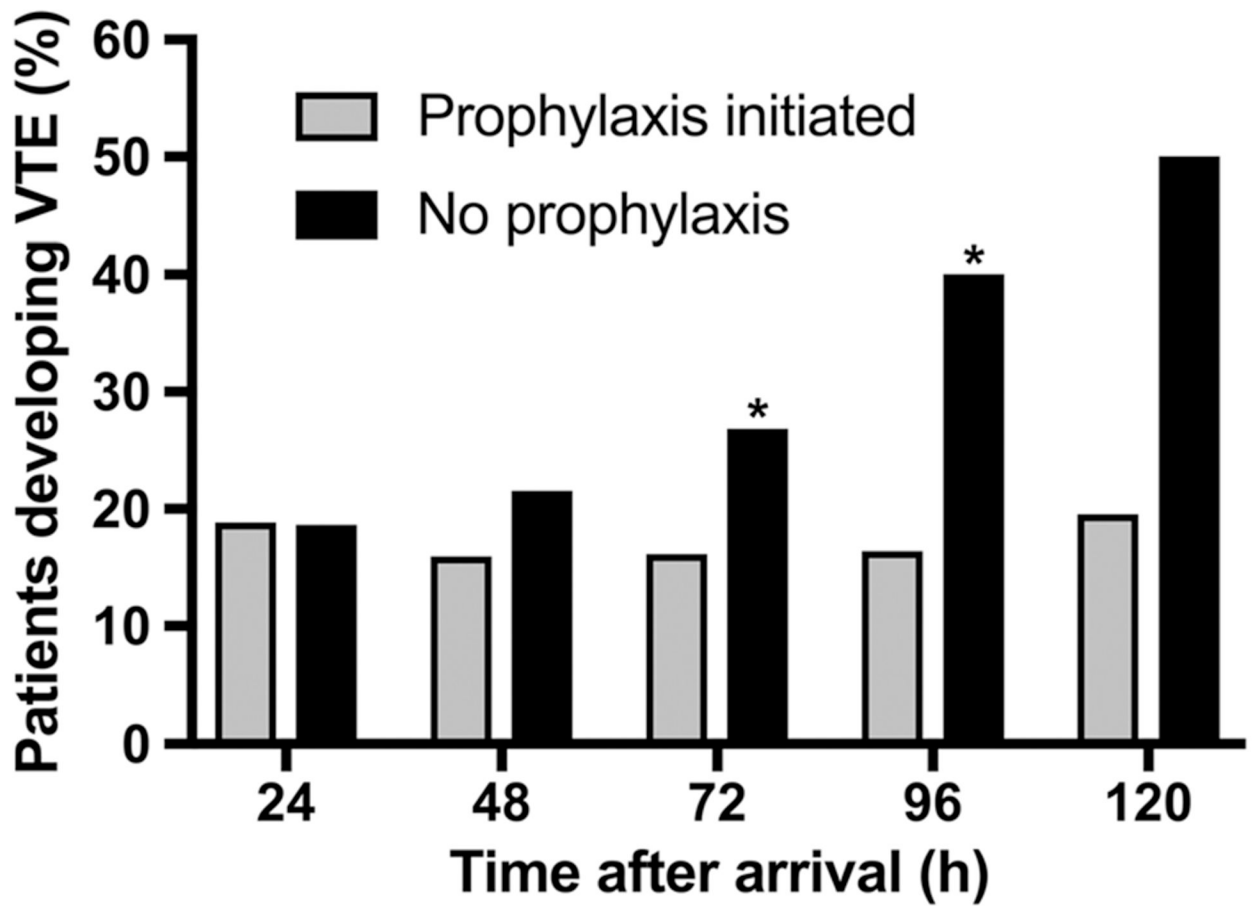


Figure 3. Venous thromboembolism development by timing of chemoprophylaxis initiation. At each time point, patients who had received their first dose of prophylaxis are compared with those who had not. * $p < 0.05$.

TABLE 1.

Characteristics of Study Population

n = 898	
Demographics	
Age, y	35 (25, 50)
Male	83%
BMI, kg/m ²	25.9 (23.2, 29.4)
Injury	
Blunt mechanism	57%
ISS	13 (4, 26)
Head AIS score	0 (0, 4)
TBI	31%
Orthopedic injury	33%
GCS score	14(8, 15)
Coagulopathy and resuscitation	
INR	1.1 (1.0, 1.2)
PTT, s	27.6 (25.5, 30.4)
Platelet count, × 10 ⁹ /L	272 (225, 322)
Fibrinogen, mg/dL	212 (165, 276)
D-dimer, µg/mL	1.3 (0.4, 6.3)
Base deficit	2.3 (0.7, 6.4)
EXTEM CT, s	58 (49, 70)
EXTEM α, degrees	73 (69, 76)
EXTEM MCF, mm	63 (60, 67)
EXTEM ML, %	14(10, 18)
Crystalloid, first 24 h, mL	3,750 (2,000, 5,798)
RBC, first 24 h, units	0 (0, 2)
Plasma, first 24 h, units	0 (0, 1)
Platelets, first 24 h, units	0 (0, 0)
VTE prophylaxis	54%
Outcomes	
Hospital LOS, d	6 (2, 16)
ICU LOS, d	2 (0, 6)
Ventilator-free days, first 28 d	27 (22, 28)
ARDS	15%
VTE	8%
MOF	10%
Mortality	12%

α, alpha angle; ARDS, acute respiratory distress syndrome; BMI, body mass index; GCS, Glasgow Coma Scale; INR, international normalized ratio; ISS, Injury Severity Score; LOS, length of stay; ML, maximum lysis; MOF, multiorgan failure; PTT, partial thromboplastin time; RBC, red blood cells.

TABLE 2.

Comparison of Patients by Initial Coagulability

	HYPO (3%)	NORM (90%)	HYPER (7%)	P
Demographics				
Age, y	40 (23, 64)	33 (24, 48)	41 (32, 57)	0.007
Male	89%	86%	60%	<0.001
BMI, kg/m ²	28.7 (25.2–31.3)	25.9 (23.2–29.3)	28.9 (24.1–32.8)	0.012
Injury				
Blunt mechanism	53%	52%	52%	1.000
ISS	13(1,35)	10 (1, 26)	8(1,11)	0.051
Head AIS score	0 (0, 4)	0 (0, 3)	0 (0, 3)	0.278
TBI	32%	26%	23%	0.752
Orthopedic injury	16%	29%	25%	0.432
GCS score	9 (3, 14)	14 (9, 15)	15 (10, 15)	0.012
Coagulopathy and resuscitation				
INR	1.4 (1.1, 1.8)	1.1 (1.0, 1.2)	1.1 (1.0, 1.1)	<0.001
PTT, s	29.9 (26.3, 50.3)	27.6 (25.5, 30.2)	27.4 (25.2, 30.8)	0.050
Platelet count, × 10 ⁹ /L	202(151,279)	270 (225,315)	334 (302, 434)	<0.001
Fibrinogen, mg/dL	152(112, 208)	213 (165,276)	307(251,405)	<0.001
D-dimer, µg/mL	6.2 (0.8, 7.4)	0.8 (0.3, 5.1)	0.8 (0.3, 2.1)	0.038
Base deficit	6.0 (2.6, 12.8)	1.6 (1.2, 5.3)	3.8 (1.8, 9.2)	0.001
EXTEM CT, s	101 (82, 160)	59 (50, 69)	52 (42, 63)	<0.001
EXTEM α, degrees	54 (50–61)	72 (69, 75)	79 (77, 81)	<0.001
EXTEM MCF, mm	45 (37, 47)	63 (60–66)	73 (72–75)	<0.001
EXTEM ML, %	16 (8, 100)	14 (10, 18)	12 (9, 17)	0.031
Crystalloid, first 24 h, mL	3,725 (2,871, 6,466)	3,046 (1,200, 5,200)	2,900 (1,000, 5,975)	0.214
RBC, first 24 h, units	1 (0, 15)	0 (0, 1)	0 (0, 0)	0.015
Plasma, first 24 h, units	0 (0, 9)	0 (0, 0)	0 (0, 0)	0.067
Platelets, first 24 h, units	0 (0, 2)	0 (0, 0)	0 (0, 0)	0.062
VTE prophylaxis	11%	49%	38%	0.045
Outcomes				

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	HYPO (3%)	NORM (90%)	HYPER (7%)	p
Hospital LOS, d	2(1,4)	4 (2, 11)	4 (1, 10)	0.127
ICU LOS, d	1 (0, 3)	1(0,4)	1 (0, 2)	0.505
Ventilator-free days, first 28 d	1 (0, 27)	28 (25, 28)	28 (27, 28)	<0.001
ARDS	56%	12%	6%	0.003
VTE	0%	6%	4%	0.810
MOF	11%	7%	4%	0.514
Mortality	47%	11%	2%	<0.001

α , alpha angle; AIS, Abbreviated Injury Scale; ARDS, acute respiratory distress syndrome; BMI, body mass index; GCS, Glasgow Coma Scale; HYPER, hypercoagulable (MCF >71 mm); HYPO, hypocoagulable (MCF <49 mm); INR, international normalized ratio; ISS, Injury Severity Score; LOS, length of stay; MCF, maximum clot firmness; ML, maximum lysis; MOF, multiorgan failure; NORM, normocoagulable (MCF 49–71 mm); PTT, partial thromboplastin time; RBC, red blood cells.

TABLE 3.

Comparison of Inpatients Who Did and Did Not Receive VTE Chemoprophylaxis by 72 Hours

	Prophylaxis Initiated (71%)	No Prophylaxis (29%)	<i>p</i>
Blunt mechanism	60%	88%	<0.001
ISS	21(13, 29)	29 (22, 35)	<0.001
Head AIS score	0 (0, 4)	4 (3, 5)	<0.001
TBI	27%	70%	<0.001
Orthopedic injury	48%	71%	0.001
GCS score	14(8, 15)	11 (7, 14)	0.001
Vasopressors, day 3	27%	49%	<0.001
HYPO, arrival	1%	0%	1.000
HYPO, 72 h	0%	2%	0.365
Hospital LOS, d	15(9, 26)	21 (15, 33)	<0.001
ICU LOS, d	6 (3, 14)	12 (7, 18)	<0.001
Ventilator-free days, first 28 d	25 (18, 27)	22 (14, 25)	<0.001

AIS, Abbreviated Injury Scale; GCS, Glasgow Coma Scale; HYPO, hypocoagulable (MCF <49 mm); ISS, Injury Severity Score; LOS, length of stay.

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