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ORIGINAL ARTICLE

Blood coagulation test abnormalities in trauma patients detected by sonorheometry: a retrospective cohort study

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Abstract

Background: Traumatic hemorrhage guidelines include point-of-care viscoelastic tests as a standard of care. Quantra (Hemosonics) is a device based on sonic estimation of elasticity via resonance (SEER) sonorheometry to assess whole blood clot formation.

Objectives: Our study aimed to assess the ability of an early SEER evaluation to detect blood coagulation test abnormalities in trauma patients.

Methods: We conducted an observational retrospective cohort study with data collected at hospital admission of consecutive multiple trauma patients from September 2020 to February 2022 at a regional level 1 trauma center. We performed a receiving operator characteristic curve analysis to determine the ability of the SEER device to detect blood coagulation test abnormalities. Four values on the SEER device were analyzed: clot formation time, clot stiffness (CS), platelet contribution to CS, and fibrinogen contribution to CS.

Results: A total of 156 trauma patients were analyzed. The clot formation time value predicted an activated partial thromboplastin time ratio of >1.5 with an area under the curve (AUC) of 0.93 (95% CI, 0.86-0.99). The AUC of the CS value in detecting an international normalized ratio of prothrombin time of >1.5 was 0.87 (95% CI, 0.79-0.95). The AUC of fibrinogen contribution to CS to detect a fibrinogen concentration of <1.5 g/L was 0.87 (95% CI, 0.80-0.94). The AUC of platelet contribution to CS to detect a platelet concentration of <50 G/L was 0.99 (95% CI, 0.99-1.00).

Conclusion: Our results suggest that the SEER device may be useful for the detection of blood coagulation test abnormalities at trauma admission.

KEYWORDS
blood coagulation test, critical care, hemorrhage, multiple traumas, thromboelastography

Essentials

- Viscoelastic tests are now part of the management of bleeding in trauma.
- Quantra is a viscoelastic test device based on an ultrasonic (sonic estimation of elasticity via resonance [SEER]) analysis of clot formation.
- We analyzed the ability of a SEER test to detect blood coagulation test abnormalities in trauma.
- The performance of the SEER device was acceptable to detect hypocoagulability thresholds.

1 | INTRODUCTION

Each year, 4.6 million deaths worldwide are related to major bleeding after trauma [1]. Early trauma resuscitation focuses on bleeding control and management of trauma-induced coagulopathy [2,3]. Acute traumatic coagulopathy has been reported in 20% to 30% of patients with severe trauma and has been associated with massive transfusion, organ failure, and increased mortality [3,4]. These blood coagulation disorders can lead to major hemorrhages from coagulation factor dilution and consumption, decreased fibrinogen concentration, platelet impairment, and excess fibrinolysis [2,5,6].

Standard blood coagulation tests, including prothrombin time (PT), platelet count, and Clauss fibrinogen concentration, remain the standard of care. However, standard blood coagulation tests have at least 2 limitations. First, the time needed to obtain the results of these tests may lead to delayed management [7]. Second, they provide information on specific coagulation functions that could appear quantitatively preserved in early blood loss despite an inappropriate qualitative function in the case of whole blood clot formation [7–9].

Traumatic hemorrhage guidelines include the concept of "point-of-care" coagulation and the viscoelastic test (VET) as a new standard of care [2,10,11]. Data on the use of VET as a point-of-care coagulation system have suggested a significant gain in the time required to achieve resuscitation goals associated with a significant reduction in the transfusion of allogeneic products; however, the effects on mortality were inconclusive [2,8,12,13].

To date, VET devices have included thrombelastography (TEG, Haemonetics) and rotational thromboelastometry (ROTEM, TEM International GmbH). These 2 devices use mechanical resistances generated over time by clot formation around a metallic pine in a whole blood sample [14]. These devices can detect acute traumatic coagulopathy and predict the use of massive transfusions with acceptable accuracy [2,15]. Another VET device is the Quantra system (Hemosonics), which assesses clot formation on the basis of the sonic estimation of elasticity via resonance (SEER) sonorheometry, a method that uses ultrasound to measure changes in the viscoelastic properties of whole blood during *ex vivo* coagulation [16,17]. A focused ultrasound pulse is transmitted into the blood sample to create a sharewave, causing the sample to resonate when a clot begins to form. The clot vibrations generate a series of ultrasound pulses that are transmitted and then analyzed [17]. This device assesses the clotting time, the clot stiffness, and its lysis [17].

During severe hemorrhages, several studies have shown a strong correlation among the SEER device, standard blood coagulation tests, and VET devices [18–20]. To date, no data have been available regarding the ability of a SEER device to detect acute traumatic coagulopathy during the early phase of trauma management. The main objective of our study was to assess the ability of an early SEER evaluation to detect blood coagulation test abnormalities in trauma patients. The second objective was to assess the ability of the SEER device to detect thrombocytopenia and to explore the correlation between SEER test values and standard blood coagulation test values.

2 | METHODS

We conducted a monocentric observational retrospective analysis with data collected from September 1, 2020, to February 28, 2022, at a regional level 1 trauma center (Hôpital Nord, Marseille, France). We adhered to the Strengthening the Reporting of Observational Studies in Epidemiology statement for observational studies [21].

All trauma patients aged >16 years at risk of blood coagulation test abnormalities; receiving, at hospital admission, a simultaneous SEER evaluation; and undergoing standard blood coagulation tests were eligible for inclusion in the study. Patients who were transferred from another hospital or from the emergency department and those with test sampling errors (eg, insufficient blood volume and lack of patient identification) were excluded from the analysis. This study received the approval of a national ethics committee (IRB-00012254-2022-021). Patient consent was waived for this study, but they were given appropriate information about the use of their data according to French law [22].

2.1 | Sampling technique and measurements

At patients' admission, whole blood samples were systematically collected in a 2.7-mL citrated tube (BD Vacutainer) from an arterial line according to international recommendations and the local protocol. As recommended by the guidelines, the patients underwent coagulation evaluations using a VET device (the Quantra system) and standard blood coagulation tests [2]. Four values obtained from the SEER device were analyzed: 1) initiation of clot time expressed in seconds (normal range defined by the manufacturer, 110-166 seconds), 2) clot stiffness expressed in hecto Pascals (hPa) (normal range, 13.0-33.2 hPa), 3) fibrinogen contribution to clot stiffness (normal range, 1.0-3.7 hPa), and 4) platelet contribution to clot stiffness

(normal range, 11.9-29.8 hPa). Multivial cartridges were used for the analysis (Q-Stat).

In whole blood, initiation of clot time is measured by the presence of kaolin, an activator of the intrinsic pathway [17]. It reflects the functional status of coagulation factors that lead to fibrin formation and is related to the concentration of coagulation factors implicated in the intrinsic pathway [17]. Clot stiffness was measured in the presence of thromboplastin (an activator of the extrinsic pathway) and polybrene (an inhibitor of heparin). It combines information about extrinsic coagulation factors, fibrinogen concentration, and platelet concentration [17,23]. The contribution of fibrinogen to clot stiffness is measured in the presence of thromboplastin and polybrene with the addition of a high dose of an antiplatelet agent (abciximab) to inhibit platelet function. The difference between clot stiffness and fibrinogen contribution to clot stiffness expresses platelet contribution to clot stiffness [17,18,23]. The SEER device is used to analyze clot stability to lysis (CSL) (given as percentage; normal range, 93%-100%) and to detect potential hyperfibrinolysis using a dedicated cartridge (Q-Stat). The result, which is calculated in percentage, is the normalized difference between clot stiffness over time in the absence of tranexamic acid and the corresponding changes in clot stiffness in the presence of tranexamic acid in a dedicated channel on analysis [17].

Standard blood coagulation tests, including PT, international normalized ratio (INR), activated partial thromboplastin time (aPTT) ratio compared with control mean, fibrinogen assay (STAR MAX, Diagnostica Stago), and platelet count (XN9000, Sysmex), were performed within the shortest possible time after arterial sampling [2].

2.2 | Data collection

The following data were collected from medical files: demographics (age, sex, weight, and height) and history of anticoagulant and/or antithrombotic use before admission. We collected data on injury severity scores (ISS), Northern French Alps Trauma System (TRENAU) grades, sequential organ failure assessment scores, prehospital fluid volume resuscitation, and the use of tranexamic acid. TRENAU grades were defined as follows: 1) A, unstable despite resuscitation (a systolic arterial pressure of <90 mmHg despite the use of 1000 mL of fluid expansion or norepinephrine and/or an oxygen saturation of <90% despite mechanical ventilation or high flow oxygen); 2) B, stabilized after prehospital resuscitation; 3) C, stable with high kinetic circumstances (a fall of ≥6 m, an estimated velocity of impact of ≥60 km/h, and victim killed in the same accident) or a medical history of anticoagulant therapy or significant chronic pathology (eg, coronary heart disease) [24]. Data on hemodynamic features at the time of hospital admission were collected, including systolic and diastolic blood pressures, heartbeats per minute, and use of norepinephrine. The type of trauma (penetrating or blunt) was reported, such as the presence of free fluid at initial ultrasound examination, initial Glasgow coma scale score, and use of invasive mechanical ventilation. Initial body temperature, initial hemoglobinemia, ionized calcium, D-dimer concentration, and arterial lactate concentration at hospital admission were reported. The number of blood products transfused (red cells, plasma, and platelets), the volume of fluid expansion during the first 24 hours of treatment, and the vital status at 24 hours and 28 days after admission were also reported.

2.3 | Trauma admission protocol

This protocol was applied to all patients who were admitted for trauma, having been directly transferred from a prehospital setting. In accordance with recommendation guidelines and our local protocol, initial support for trauma patients was provided in our intensive care unit (ICU) within the first 30 minutes after admission: clinical examination, initial imaging assessment (echography, chest and pelvis x-ray, and whole body computed tomography according to patient stability), and equipment (arterial and venous catheter), as previously published [25–27]. The administration of tranexamic acid was performed according to guidelines [2].

An algorithm was provided to the physician in charge to guide the administration of coagulation products (plasma, platelets, and fibrinogen) on the basis of the SEER results and clinical status. Its usage was not mandatory. Because the SEER device protocol had been implemented only recently in our center, the physician was allowed to refer to the results of either the SEER or the standard blood coagulation tests to guide coagulation management.

In case the physician in charge referred to the standard blood coagulation tests, the following thresholds were used to guide the administration of blood products: 1) hemoglobin between 70 and 90 g/L, 2) platelets >50 G/L (or >100 G/L if active bleeding or traumatic brain injury), 3) fibrinogen >1.5 g/L, and 4) INR or aPTT <1.5 ratio. These thresholds were used to guide the administration of red cell pack, platelets concentrate, fibrinogen, and fresh frozen plasma, respectively, according to the European guidelines for the management of bleeding trauma [2]. In the case of an expected massive transfusion, a ratio of fresh frozen plasma/red blood cells of at least 1:2 was recommended [2]. Massive transfusion was defined as the need for ≥10 red blood cell transfusions during the first 24 hours.

Calcium and temperature were normalized whenever it was possible. Norepinephrine was started if the systolic blood pressure was <90 mmHg or the mean arterial blood pressure was <60 mmHg (80 mmHg in cases of traumatic brain injury) despite vascular filling. Emergency surgery or embolization was performed depending on the bleeding origin and the patient's stability.

2.4 | Definitions

We defined blood coagulation test abnormalities on the basis of European guidelines; a deficit in the coagulation factor was defined as an INR of >1.5 or an aPTT ratio of >1.5 of the control [2]. Fibrinogen deficiency was defined as a concentration of ≤1.5 g/L, and thrombocytopenia was defined as a concentration of platelets of ≤50 G/L [2]. These thresholds were defined as therapeutic goals in the guidelines

for the transfusion of fresh frozen plasma, fibrinogen concentrate, or platelets [2]. The primary objective was to determine the ability of the SEER test values to detect blood coagulation test abnormalities, as defined above. Thus, the following associations were assessed: clot time as a surrogate of the aPTT ratio of >1.5 (intrinsic pathway), clot stiffness as a surrogate of the INR of >1.5 (extrinsic pathway), fibrinogen contribution to clot stiffness as a surrogate of the fibrinogen concentration of <1.5 g/L, and platelet contribution to clot stiffness as a surrogate of the platelet concentration of <50 G/L [2,28]. The secondary objectives were as follows: 1) to determine the ability of platelet contribution to clot stiffness to detect the thrombocytopenia threshold, defined as <100 G/L and <150 G/L, and 2) to determine the association between the SEER tests and the corresponding blood coagulation test values, as described in the primary objective.

2.5 | Data analysis

Quantitative values were described as medians (25th and 75th interquartile). Qualitative values were described as numbers and percentages. The time required to obtain the results of the laboratory tests and the SEER device was recorded. The time required to assess the SEER values was analyzed retrospectively by extracting data from the last 50 patients (the maximum number of logs registered in the device for this data) and compared using a Student's *t*-test.

The number of patients required to construct a receiver operating characteristic (ROC) curve with an area under the curve (AUC) of 0.75, an accuracy of 0.1, and a risk probability of 5% has been reported to be between 50 and 100, depending on the occurrence of the event to be detected [29]. In our study, the sample size calculation was not conducted because of its retrospective design. We considered that ≥100 patients would be enough to construct ROC curves for an event occurrence of ≥20%, according to the published method [28–30].

By constructing ROC curves, we determined the ability of the SEER values to detect the occurrence of the primary outcomes (aPTT ratio, >1.5; INR, >1.5; fibrinogen concentration, <1.5 g/L; platelet concentration, <50 G/L). ROC curves and AUC were used to evaluate test accuracy [29,30]. The best cutoff value was calculated for each test using the Youden index method [30]. Thresholds for a sensitivity and specificity of ≥90% were also calculated [29,31], in addition to positive and negative predictive values.

To evaluate the ability of the SEER values to predict the occurrence of secondary outcomes, we used the same method described earlier for platelet concentrations of ≤100 G/L and ≤150 G/L. Finally, an exploratory correlation analysis was performed to compare the SEER values and the results of the blood coagulation tests using the Pearson correlation coefficient (r) [32]. For the comparison, we conducted the same analysis in the subgroup population of the most serious patients who had been classified "unstable" according to the TRENAU triage method [24,33]. Descriptive and correlation analyses were performed using SPSS V20 (IBM Corp). ROC curve analysis and cutoff determination were performed using the pROC library with R, version 3.2.3 (https://www.r-project.org).

3 | RESULTS

Over the study period, 431 adult patients were directly admitted for trauma; 353 were men (82%) with a median age was 39 years (26-55 years) and a median ISS of 20 (9-28); 168 (39%) patients received blood transfusion, and the mortality rate was 14% at day 28. From this cohort, 156 trauma patients met the inclusion criteria by undergoing simultaneous blood coagulation and SEER test and were analyzed (Figure 1). One hundred and thirty (84%) patients were men, with a median age of 35 years (24-54 years) (Table 1). The median ISS was 22 (10-37), and 85 (55%) patients were classified as "unstable" on admission (TRENAU A). Blood transfusion within the first 24 hours of admission was required for 72 (47%) patients, including 21 (14%) patients who received massive transfusions. Mortality was 11% and 19% at 24 hours and 28 days, respectively, after ICU admission. All of the 30 patients who died at 28 days were classified as "unstable" on admission. Causes of death were exsanguination (n = 15), traumatic brain injury (n = 11), multivisceral deficiency (n = 3), and septic shock (n = 1). All patients received a tranexamic acid infusion before their admission. Primary outcomes occurred in 17%, 23%, 24%, and 3% of patients, respectively, as follows: aPTT ratio, >1.5; INR, >1.5; fibrinogen concentration, <1.5 g/L; and thrombocythemia, <50 G/L (Table 1). The results of the blood coagulation tests were obtained in a median time of 53 minutes (41-75 minutes). Regarding the SEER device, results were obtained significantly faster. Results for clot time, clot stiffness, and analysis of CSL were obtained respectively in 5 minutes (4-6 minutes) ($P < .001$), 11 minutes (11-12 minutes) ($P < .001$), and 48 minutes (41-55 minutes) ($P = .01$). Notably, none of the patients exhibited hyperfibrinolysis.

The performances of the SEER device in predicting the occurrence of primary outcomes are presented in Table 2 and Figure 2. The clot time value predicted an aPTT ratio of ≥1.5, with an AUC of 0.93 (95% CI, 0.86-0.99; $P = .001$). The best cutoff value was 144 seconds, with a sensitivity of 0.88 (95% CI, 0.69-1.00) and a specificity of 0.94 (95% CI, 0.78-0.99). The AUC of clot stiffness to predict an INR of ≥1.5 was 0.87 (95% CI, 0.79-0.95; $P = .001$). The best cutoff was 13.3 hPa, with a sensitivity of 0.81 (95% CI, 0.65-0.95) and a specificity of 0.89 (95% CI, 0.72-0.98) (Figure 2, Table 2). The AUC of fibrinogen contribution to clot stiffness to detect a fibrinogen concentration of ≤1.5 g/L was 0.87 (95% CI, 0.80-0.94; $P = .005$). The best cutoff for fibrinogen contribution to clot stiffness was 1.0 hPa, with a sensitivity of 0.84 (95% CI, 0.70-0.97) and a specificity of 0.82 (95% CI, 0.64-0.90) (Figure 2, Table 2). The highest AUC of the SEER values was in platelet contribution to clot stiffness to detect platelet concentration of ≤50 G/L, with an AUC of 0.99 (95% CI, 0.99-1.00; $P < .001$). The best cutoff value was 4.1 hPa, with a sensitivity of 1.00 (95% CI, 1.00-1.00) and a specificity of 0.99 (95% CI, 0.98-1.00) (Figure 2, Table 2).

The secondary endpoint results are summarized in Table 2, including the diagnostic performance of the SEER values in detecting

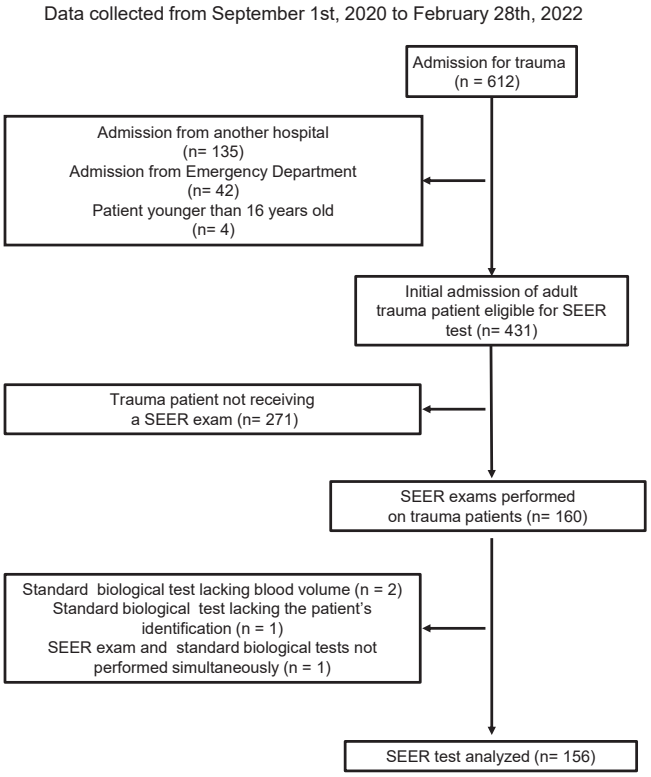

FIGURE 1 Flowchart of the study population. SEER, sonic estimation of elasticity via resonance.

platelet counts of ≤100 and ≤150 G/L. Correlations between the SEER values and the blood coagulation tests were moderate to high (Figure 3). The results for the subgroup of unstable patients at ICU admission (TRENAU A) are shown in Supplementary Tables 1 and 2. No significant differences were found between these results and the results obtained for the entire cohort.

4 | DISCUSSION

Our study shows for the first time that an early SEER evaluation detected blood coagulation test abnormalities with good accuracy in trauma patients. Based on the results of the ROC curve analysis, the SEER values (clot time, clot stiffness, fibrinogen contribution to clot stiffness, and platelet contribution to clot stiffness) detected their related blood coagulation test abnormality thresholds with high specificity and high negative predictive value as follows: aPTT ratio, >1.5; INR, >1.5; fibrinogen concentration, <1.5 g/L; and platelet concentration, <50 G/L. Similar results were observed in the subgroup of patients with life-threatening conditions (TRENAU A).

To the best of our knowledge, no previous study has described the performances of the SEER device in detecting blood coagulation test abnormalities in trauma. The results of our study showed that the performances of the SEER device were comparable with the values obtained from conventional VET devices. In a meta-analysis, ROTEM showed a range of sensitivity from 70% to 100% and a specificity from 58% to 100% to detect blood coagulation test abnormalities, depending on the value chosen at 5, 10, or 15 minutes [34]. In another study, Nascimento et al [35] found a sensitivity of 33% and a specificity of 95% of TEG in detecting hypocoagulability in trauma patients, compared with an INR of >1.5.

In a large prospective cohort, Chow et al [28] found that TEG predicted the occurrence of an INR of >1.5 and aPTTs of ≥40 seconds with AUCs of 0.80 and 0.85, respectively, using an R-time of ≥3.9 minutes. Despite the good performance of the device, the authors emphasized that this threshold was inside the range of the normal values of the device [28]. In our study, we defined the best thresholds of clot time (144 seconds) and clot stiffness (13.3 hPa) to detect the occurrence of an increased aPTT ratio and INR, both of which were within the normal ranges of the SEER device (104-166 seconds and 13-33 hPa, respectively). Because this difference may be confusing at the bedside, there is a need for clinical validation of nonpathological SEER values in a specific trauma population.

Several previous studies have reported the ability of conventional VET devices to detect fibrinogen deficiency in trauma patients [2,36]. A review showed that the AUCs of conventional VET devices in detecting fibrinogen deficiency in trauma patients ranged from 0.70 to 0.95, depending on the threshold used (1.0, 1.5, or 2.0 g/L) [36]. For this purpose, the performance of the SEER device described in our results seems to be in line with that of other VET devices.

Regarding thrombocytopenia, trauma guidelines advise that conventional VET devices may be useful for obtaining information about platelet dysfunction, even in cases of normal platelet counts [2,13]. To date, only a few studies have reported the ability of VET devices to

TABLE 1 Description of the cohort and initial values at admission.

Variables	Whole cohort (n = 156)	TRENAU A (n = 85)
Male (%)	130 (84)	67 (80)
Age (y)	35 (24-54)	39 (21-55)
SAPS II	42 (25-57)	55 (42-75)
Time between first medical contact and admission (min)	65 (51-90)	63 (50-88)
Antithrombotic medication (%)	11 (7)	7 (8)
Anticoagulant medication (%)	4 (3)	2 (2)
ASA score (%)		
1	97 (63)	51 (60)
2	41 (26)	26 (30)
3	9 (6)	8 (10)
Penetrating trauma (%)	28 (18)	10 (12)
TRENAU grade (%)		
A[a]	85 (55)	85 (100)
B[b]	39 (25)	-
C[c]	31 (20)	-
Initial Glasgow scale score	15 (4-15)	8 (3-14)
Heart rate (bpm)	97 (80-118)	100 (75-120)
Systolic blood pressure (mmHg)	120 (100-140)	105 (81-133)
Body temperature (°C)	36.5 (35.4-37.0)	36.0 (34.7-37.0)
Invasive mechanical ventilation (%)	85 (55)	71 (83)
Norepinephrine (%)	69 (44.5)	63 (74)
ISS	22 (10-37)	34 (20-43)
SOFA score	5 (1-8)	8 (5-10)
Prehospital fluid volume (mL)	1000 (500-1000)	1000 (500-1500)
Initial hemoglobin (g/dL)	12.1 (10.2-14.0)	11.3 (9.6-13.3)
Initial thrombocythemia (G/L)	222 (187-282)	214 (160-254)
Frequency of platelets count <50 G/L (%)	5 (3)	5 (6)
Frequency of platelets count <100 G/L (%)	7 (5)	7 (8)
Frequency of platelets count <150 G/L (%)	24 (16)	20 (24)
aPTT ratio	1.0 (0.9-1.2)	1.1 (1.0-1.5)
Frequency of aPTT ratio >1.5 (%)	26 (17)	24 (28)
INR	1.2 (1.1-1.5)	1.3 (1.1-1.7)
Frequency of INR >1.5 (%)	36 (23)	31 (37)
Fibrinogen (g/L)	2.0 (1.5-2.6)	1.8 (1.3-2.3)
Frequency of fibrinogen <1.5 g/L (%)	37 (24)	29 (34)
Lactatemia (mmol/L)	2.3 (1.4-4.1)	2.7 (1.8-7.1)
Ionized calcemia (mmol/L)	1.1 (1.1-1.2)	1.08 (1.02-1.14)
D-dimer (ng/mL)	220 (110-700)	380 (190-1150)
CT (s)	119 (104-138)	126 (110-146)
CS (hPa)	16.3 (12.8-20.4)	14.4 (9.8-18.6)
PCS (hPa)	15.1 (11.9-18.8)	13.7 (9.5-17.3)
FCS (hPa)	1.3 (0.9-1.8)	1.1 (1.7-0.7)
CSL (%)	99 (97-100)	98 (92-100)
Fluid volume in the first 24 h (mL)	1500 (1000-3000)	2000 (1000-3500)
Transfusion in the first 24 h (%)	72 (47)	53 (62)
Massive transfusion[d] (%)	21 (14)	18 (21)
Number of units received in the transfused population		
Red blood cell (unit)	5 (2-10)	6 (3-11)
Fresh frozen plasma (unit)	4 (2-8)	6 (2-9)
Platelets concentrate (unit)	1 (0-1)	1 (0-2)
Length of stay in ICU (when alive)	8 (3-11)	11 (5-19)
Death at day 1 (%)	17 (11)	17 (20)
Death at day 28 (%)	30 (19)	30 (35)
Reason of death on day 28		
Exsanguination (n)	15	15
Traumatic brain injury (n)	11	11
Multivisceral deficiency (n)	3	3
Septic shock (n)	1	1

Results are presented as number and percentage or median and 25th to 75th IQR. Analysis was based on 156 patients in the whole cohort and 85 patients in the TRENAU A subgroup.

aPTT, activated partial thromboplastin time; ASA, American Society of Anesthesiologist; CS, clot stiffness; CSL, clot stability to lysis; CT, clot time; FCS, fibrinogen contribution to clot stiffness; hPa, hecto Pascal; ICU, intensive care unit; INR, international normalized ratio; ISS, injury severity score; PCS, platelet contribution to clot stiffness; SAPS, simplified acute physiology score; SOFA, sequential organ failure assessment; TRENAU, Northern French Alps Trauma System.

[a]A grade: unstable despite resuscitation.

[b]B grade: stabilized after resuscitation.

[c]C grade: stable with high kinetic circumstances (a fall of ≥6 m, an estimated velocity of impact of ≥60km/h, and victim killed in the same accident) or medical history of anticoagulant therapy or significant chronic pathology (eg, coronary heart disease).

[d]Massive transfusion was defined by the need for at least 10 red blood cell units in the first 24 hours after admission.

TABLE 2 Performance of sonorheometric values to predict the occurrence of primary and secondary outcomes.

	AUC	Best cutoff	Sensitivity	Specificity	PPV	NPV	Cutoff for sensitivity >90	Cutoff for specificity >90
Ability of CT to predict								
aPTT >1.5	0.93 (0.86–0.99)	144 s	0.88 (0.69–1.00)	0.94 (0.78–0.99)	0.73 (0.46–0.96)	0.97 (0.94–1.00)	<130	>143
Ability of CS to predict								
INR >1.5	0.87 (0.79–0.95)	13.3 hPa	0.81 (0.65–0.95)	0.89 (0.72–0.98)	0.70 (0.50–0.93)	0.94 (0.89–0.98)	>16.0	<13.0
Ability of FCS to predict								
Fibrinogen <1.5 g/L	0.87 (0.80–0.94)	1.0 hPa	0.84 (0.70–0.97)	0.82 (0.64–0.90)	0.59 (0.45–0.72)	0.94 (0.90–0.99)	>1.4	<0.8
Ability of PCS to predict								
Platelets <50 G/L	0.99 (0.99–1.00)	4.1 hPa	1.00 (1.00–1.00)	0.99 (0.98–1.00)	0.67 (0.29–1.00)	1.00 (1.00–1.00)	>4.1	<4.1
Platelets <100 G/L	0.84 (0.60–1.00)	4.35 hPa	0.86 (0.57–1.00)	0.99 (0.76–1.00)	0.70 (0.13–0.97)	0.99 (0.97–1.00)	>12.6	<6.4
Platelets <150 G/L	0.87 (0.78–0.96)	11.8 hPa	0.83 (0.66–0.96)	0.86 (0.75–0.95)	0.54 (0.42–0.76)	0.97 (0.94–0.99)	>14.2	<10.1

The analysis was based on 156 patients.

aPTT, activated partial thromboplastin time ratio; AUC, area under the curve; CS, clot stiffness; CT, clot time; FCS, fibrinogen contribution to clot stiffness; hPa, hecto Pascals; INR, international normalized ratio; NPV, negative predictive value; PCS, platelet contribution to clot stiffness; PPV, positive predictive value.

detect the thrombocytopenia threshold in trauma patients. A large observational study showed that conventional VET devices had a sensitivity of 70% in detecting platelet concentrations of ≤100 G/L in a trauma population [8]. Rugeri et al [37] reported that thromboelastometry was able to detect a platelet count of ≤50 G/L with a sensitivity of 100% and a specificity of 83%. To our knowledge, no external validation of our findings is available in the literature. In our study, thrombocythemia of ≤50 G/L occurred in only 5 patients. However, these results must be confirmed in a study with a larger cohort.

Interestingly, the SEER device provided results for the coagulation function in 11 to 12 minutes, while the results of the blood coagulation tests were obtained in an average of 53 minutes after sampling. These results are in line with those reported for other VET devices [8,38]. The shorter time allows for earlier decisions about the need for transfusions and the type of product required, which can affect patient outcomes [8].

In the studied trauma patients, we found moderate to high correlations between the SEER values and the blood coagulation test values, especially between the fibrinogen contribution to clot stiffness and the Clauss fibrinogen dosage. However, we were not able to confirm this finding because there are still no external data on correlations between SEER values and standard biological test values in a trauma population. Of note, in large-volume blood loss spinal surgery, Naik et al [18] showed that the Clauss fibrinogen method was highly correlated with SEER values (r = 0.77; 95% CI, 0.66-0.85) [39].

Regarding the correlation between platelet contributions to clot stiffness value and platelet count, the same group found high correlations between platelet contributions to clot stiffness and platelet count (r = 0.83; 95% CI, 0.76-0.89) [18]. In our results, we found a moderate to high correlation between platelet contributions to clot stiffness value and platelet count (Supplementary Table 2). The discrepancy between the SEER evaluation and the platelet count was more pronounced in a count of ≥200 G/L (Figure 3 and Supplementary Table 2).

We hypothesize that the correlation between the SEER values of platelet contribution to clot stiffness and standard biological values should be interpreted with caution in cases of severe acute traumatic coagulopathy. Platelet contribution to clot stiffness is calculated as clot stiffness minus fibrinogen contribution to clot stiffness. In the case of multiple deficiencies of coagulation factors, platelet contributions to clot stiffness could be underestimated. Indeed, the SEER clot stiffness calculation is based on the addition of thromboplastin to whole blood [16,17]. In a standard blood coagulation test, thromboplastin is used to measure PT/INR in plasma. In whole blood, it is similar to a global blood coagulation test, leading to clot formation that takes into account the concentration of fibrinogen and platelets [16,17]. This explains why clot stiffness must be considered a surrogate for INR and not its perfect substitute. A low fibrinogen or platelet concentration may alter the clot formation in vitro, even without a specific coagulation factor deficiency, leading to decreased clot stiffness. This indicates the need for a stratified approach based on different coagulation profiles in a larger study cohort [9].

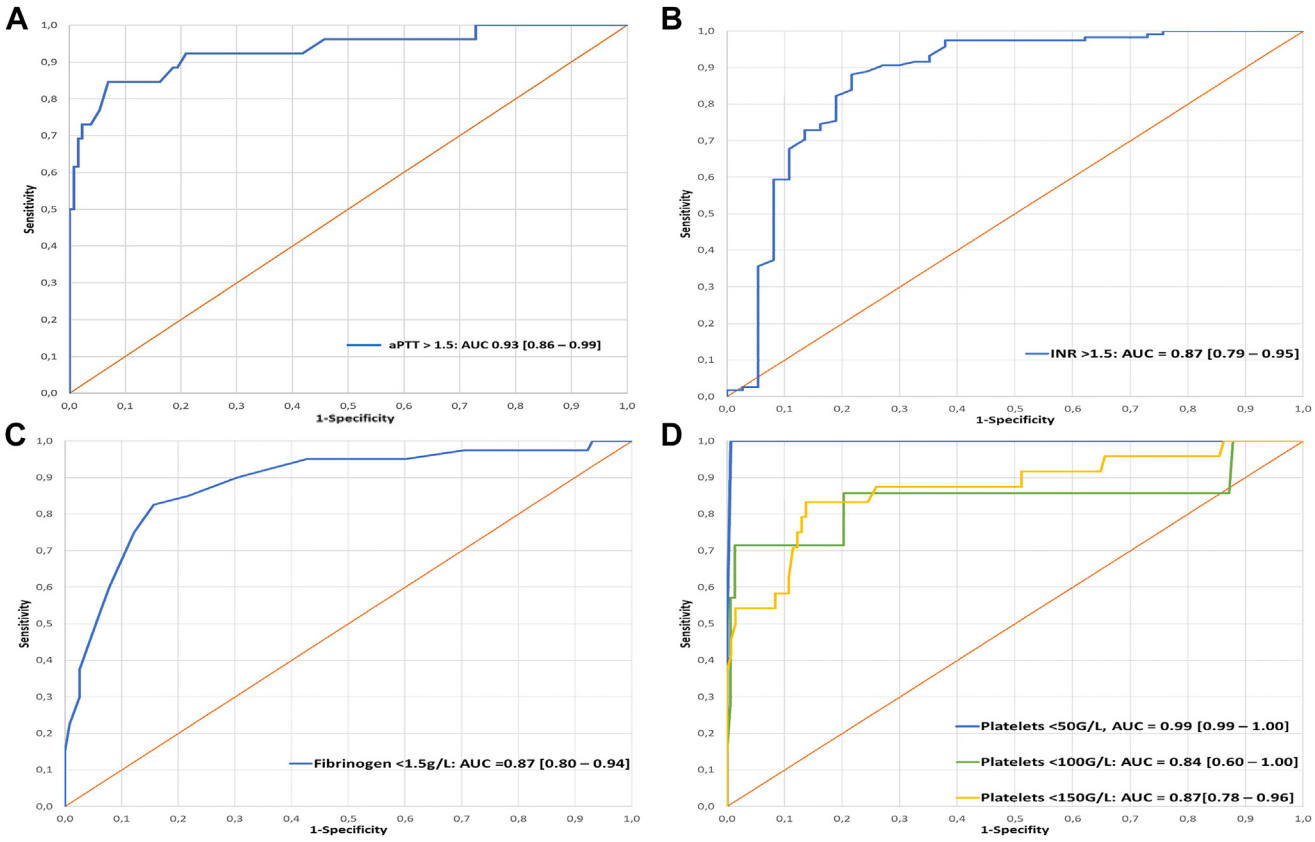

FIGURE 2 Receiving operator characteristic curve analysis of the primary outcomes. (A) The curve represents the ability of clot time to detect an activated partial thromboplastin time (aPTT) >1.5 of the control. (B) The curve represents the ability of clot stiffness to detect an international normalized ratio (INR) of >1.5. (C) The curve represents the ability of fibrinogen contribution to clot stiffness to detect a fibrinogen concentration of ≤1.5 g/L. (D) The curve represents the ability of platelet contribution to clot stiffness to detect a platelet concentration of 50, 100, and 150 G/L or less. Analysis was based on 156 patients. AUC, area under the curve.

Regarding the evaluation of hyperfibrinolysis, our results are inconclusive. Biological diagnoses of hyperfibrinolysis require specific biologic markers that were not evaluated in our standard care (plasmin antiplasmin complexes and α2-antiplasmin) [9,40]. All of the analyzed patients received tranexamic acid as the standard of care, and the SEER values regarding CSL were in the normal range. This low occurrence of hyperfibrinolysis is in line with recent studies, and VET markers, such as LYS30 (in the ROTEM device), are commonly used to diagnose it [9,40]. To date, only 1 study has reported a very high correlation between LYS30 and CSL (r = 0.95) in a cohort of 56 trauma patients. However, specific studies are needed to confirm the ability of CSL to detect hyperfibrinolysis [41].

Our study has several limitations. Its retrospective design may have given rise to bias that could not be taken into account during the analysis. We limited these biases by collecting prospective data and applying a pragmatic design based on blood samples that were gathered before any type of transfusion or coagulation treatment (except tranexamic acid). Furthermore, clot stiffness was used as a surrogate for INR in our study to lead plasma transfusions, which could not be analyzed without considering fibrinogen concentration and platelet count. Another limitation is the heterogeneity of the patient's severity in reflecting real-life conditions. As shown in a previous cohort study, the French trauma system tends to admit patients even without clinical evidence of severity to limit undue deaths of trauma patients who present with situational evidence of severe accidents (eg, high velocity, death of another patient, etc.) [42]. In our study, 25% of our patients had low-grade severity (TRENAU C), which is in line with previous studies [42]. We tried to limit the bias of heterogeneity by conducting a subgroup analysis of a greater number of severe patients. As noted in the method, use of the SEER device was not mandatory during the study period, resulting in a large proportion of patients admitted during the period not receiving a SEER test at admission. This bias may impact the generalizability of our results, particularly for stable patients who may have been underreported. Moreover, the administration of blood products may have been inconsistent due to the coexistence of 2 transfusion protocols based either on SEER values or on laboratory tests. This limitation did not bias our results because all transfusions were performed after blood samples were obtained. Furthermore, the aim of this study was not to compare 2 transfusion strategies but to determine thresholds of interest for SEER tests. Information about the sociocultural determinants of the health of the studied population (including ethnicity) is missing because of our local legislation, which may have limited the assessment of the generalizability of the study findings. Finally,

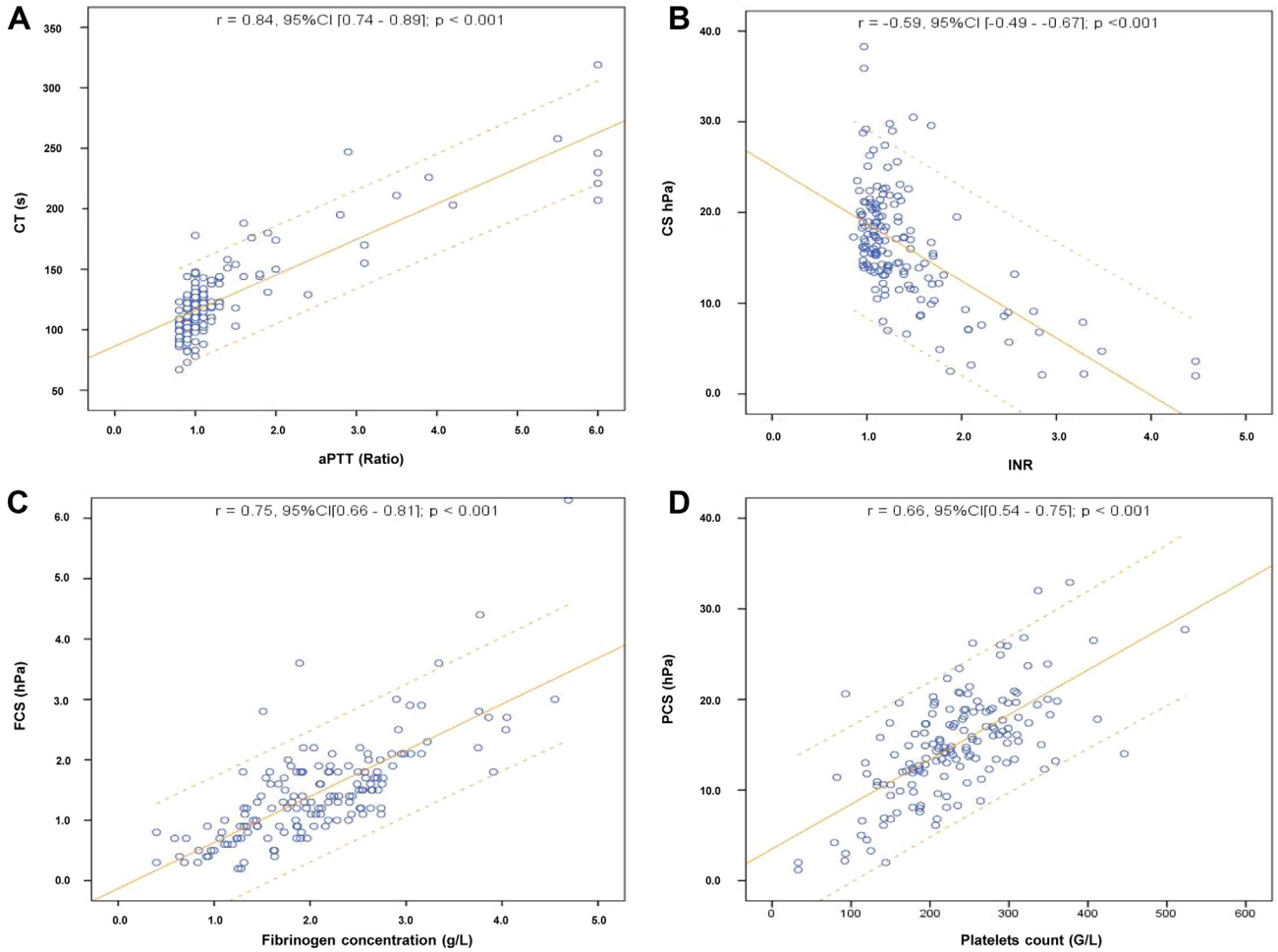

FIGURE 3 Results of correlation analysis. (A) Represents Pearson's correlation coefficient between clot time (CT) and activated partial thromboplastin time (aPTT) ratio with control. (B) Represents Pearson's correlation coefficient between clot stiffness (CS) and the international normalized ratio (INR). (C) Represents Pearson's correlation coefficient between fibrinogen contribution to clot stiffness (FCS) and fibrinogen concentration obtained from the laboratory test. (D) Represents Pearson's correlation coefficient between platelet contribution to clot stiffness (PCS) and platelet count obtained from the laboratory test. The analysis was based on 156 patients.

because the study was conducted at a single center, external validation is required to confirm and generalize our findings.

5 | CONCLUSION

Our results suggest that the SEER device can be used as a VET device for initial detection of blood coagulation test disorders in trauma patients. We found reasonable performances of the SEER device in detecting a aPTT ratio of >1.5, an INR of >1.5, a fibrinogen concentration of <1.5 g/L, and a platelet count of <50 G/L. However, the cutoff values that corresponded to the blood coagulation test disorders were within or close to the normal range of the SEER tests. Therefore, we conclude that the SEER device may be useful for detecting blood coagulation test abnormalities within a short period of time on admission of trauma patients but that threshold values should be interpreted with caution pending further prospective data.

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ETHICS STATEMENT

This study received the approval of a national ethics committee (IRB-00012254-2022-021). Patient consent was waived for this study, but they were given appropriate information about the use of their data according to French law.

AUTHOR CONTRIBUTIONS

G.D. and M.L. conceived the study. G.D., M.F., C.G., I.L., C.A., and B.L. collected the data. G.D. and F.A. performed the statistical analysis. M.L. supervised the study. G.D. and M.F. wrote the manuscript. C.G.,

I.L., C.A., B.L., P.A., and L.Z. edited the manuscript. C.G., I.L., C.A., B.L., P.A., L.Z., and M.L. made the corrections. G.D. reviewed the manuscript.

RELATIONSHIP DISCLOSURE

M.L. received fees from AOP Orphan Phamaceuticals France and Aspen for symposiums and from Gilead and Ambu for consulting. The other authors declare no conflicts of interest.

DATA AVAILABILITY

Data are available on reasonable demand.

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SUPPLEMENTARY MATERIAL

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