ORIGINAL RESEARCH

Correlation Between Central Vein Smoke Ultrasonography and Thrombus Elasticity Graphy in Severe Patients

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ABSTRACT

Objective • The objective of this study was to analyze the correlation between central vein smoke ultrasonography (CVSU) and thrombus elasticity graphy (TEG).

Methods • A retrospective analysis was made on 300 severe patients with smoky echo changes (SECs) in the internal jugular and femoral veins who were admitted to the hospital from January 2021 to March 2022. According to the ultrasound results, all patients were divided into Group A (n = 75), Group B (n = 75), Group C (n = 75), and Group D (n = 75). TEG examination, ultrasound examination, routine coagulation test were received. The coagulation function and TEG index were compared and analyzed in each group, and their correlation was analyzed.

Results • The trends of R value and K value of TEG index of patients in different groups were the same. The R value and K value in group D were the highest, followed by group C, and the lowest in group A; while those in groups C and D exhibited great differences with $P < .05$ to those in groups A and B. The PT, TT, APTT, and FIB of patients in groups C and D were much higher based on the values in groups A and B. R-value was positively correlated with APACHEII (0.678), TT (0.198), and APTT (0.187), and negatively associated with PT (-0.008), D-D (-0.315), and FDP (-0.298). K value presented a positive correlation with APACHEII (0.692) and TT (0.342) but a negative correlation with PT (-0.187), APTT (-0.053), D-D (-0.497), and FDP (-0.453). Positive correlations were observed between α and PT (0.198), APTT (0.046), D-D (0.602), and FDP (0.532), while negative correlations were found between α and APACHEII (-0.398) and TT (-0.315). MA was positively correlated with PT, D-D, and FDP but negatively with APACHEII, TT, and APTT.

Conclusion • TEG parameters had an obvious correlation with the coagulation function test, which can effectively evaluate the CVSU in severe patients. The ultrasonic signs can be undertaken as clinical hypercoagulability detection indicators in severe patients and intervention indicators for early thrombosis prevention in the future, they can guide clinicians to make the best treatment plan for severe patients. (*Altern Ther Health Med.* 2024;30(1):426-433).

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INTRODUCTION

Venous thromboembolism (VTE) includes pulmonary embolism (PE) and deep vein embolism (DVT), which not only increases the treatment difficulties of the primary disease but also the follow-up problems caused by treatment costs and anticoagulation and other related treatments. The lower extremity veins, especially the proximal femoral veins, are the most common.[1,2] In recent years, it has been reported that clinical PE caused by embolus source of the vena cava, including the head and internal jugular vein system, is not rare.[3,4] PE is a serious clinical event and one of the most common causes of sudden clinical death. With the popularization of pulmonary artery CT angiography and other technologies, the detection rate of PE has increased significantly, and it is no longer a rare disease previously considered.[5] However, the clinical symptoms of PE are varied, and a considerable number of patients have no warning symptoms. Therefore, it may be necessary to search for a pre-thrombotic warning symptom or laboratory indicator, that is, to seek an effective point of early clinical prevention of VTE. In the intensive care unit (ICU), severe patients with coagulopathy are very common, and the prognosis is poor. In addition, such patients have a higher

probability of PE and DVT than patients in common wards, so hypercoagulability of blood is an important issue requiring more attention in ICU.[6,7] Traditional coagulation function monitoring indexes cannot meet the current clinical needs, especially in the monitoring of blood hypercoagulability.[8,9]

Ultrasonic signs can be used as an early monitoring indicator of clinical blood hypercoagulability and even an indicator of early prevention and intervention of VTE in the future.[12] Smoky echo change (SEC) ultrasound screening of central vein in ICU severe patients is convenient and easy to obtain clinically. The clinical significance of SEC detected by central vein ultrasonography in severe ICU patients are not clear. In recent years, central vein smoke ultrasonography (CVSU) has developed rapidly in China, and bedside ultrasound assessment of severe patients has become increasingly popular in many units.[10] The internal jugular vein and femoral vein are superficial, and the blood vessels are relatively exposed, so CVSU examination is very convenient and easy to implement. Due to the CVSU examination is cheap, non-invasive, convenient, and easy access, ultrasonic signs used as an early monitoring indicator of clinical blood hypercoagulability or even an indicator of early prevention and intervention of VTE in the future, will have important clinical significance.[11] However, the clinical significance of this ultrasound sign is not clear at present, so it has not attracted enough clinical attention, and relevant epidemiological data are also lacking.

The thrombus elasticity graphy (TEG) is a device that dynamically monitors TEG thrombus images. It is sensitive, fast, and can be used alongside the bed, making it easy to operate during the detection. In recent years, the application of TEG in the detection of coagulation dysfunction in ICU patients has shown good clinical value. Relevant studies on sepsis, severe trauma, severe pneumonia, patients with blood purification, and cardiovascular and cerebrovascular embolic diseases suggest that it has advantages over traditional indicators in diagnosis and intervention monitoring to reflect the full picture and immediacy of coagulation function.[13,14] Meta studies have also shown that TEG detection may be used as a clinical method to predict VTE in the future.[15] Some studies believe that SEC in the heart and vascular lumen shown by ultrasound is the result of orderly distribution when blood flow is slow and red blood cells accumulate and lose fast laminar flow, which is a pre-thrombotic state.[16] It is generally believed that atrial SEC in patients with atrial fibrillation indicates blood stasis, which is related to thrombotic events and tends to be anticoagulant therapy. However, it has not been proved that isolated SEC can effectively predict thrombotic events.[17] It has been reported in recent years that SEC detected by ultrasound in central veins such as internal jugular vein and femoral vein is not uncommon and may be related to clinical embolism events.[18] Studies suggest that internal jugular vein SEC may also be related to carotid atherosclerosis.[19] There is insufficient evidence on the need for continuous monitoring and treatment of SEC detected by central vein ultrasound. So, analyze the correlation between CVSU and TEG, exploring convenient and easy access early monitoring indicator for sever patients is important.

Based on this, the objective of this study is to investigate the correlation between CVSU findings and TEG parameters in severe ICU patients..

PATIENTS AND METHODS

Research objects

This is a retrospective cohort study, a total of 300 severe patients with SEC in internal jugular vein and femoral vein treated in the hospital from January 2021 to March 2022 were enrolled. There were 152 males and 148 females, ranging from 53 years old to 76 years old, with an average age of (57.3 ± 8.53 years old). The average body mass index (BMI) was (22.86 ± 4.19) kg/m^2. According to the ultrasound results, all patients were divided into Group A (n = 75), Group B (n = 75), Group C (n = 75), and Group D (n = 75).

Inclusion criteria: (1) All subjects were severe patients with SEC in central vein by bedside ultrasound; (2) Age ≥ 18 years old newly admitted to ICU who meet the requirements of the hospital; (3) Internal jugular vein puncture catheterization and femoral vein puncture examination were performed 24 hours after admission; (4) All patients were received ultrasound and TEG examination when they were admitted to the hospital; (5) Volunteer to join the study; (6) Patients did not have contrast allergy; and (7) patients who can actively cooperate with the inspection.

Exclusion criteria: (1) Language communication disorders, patients with senile dementia or cognitive impairment; (2) Anticoagulant or antiplatelet drugs or thrombolytic therapy were used in the past week; (3) Patients with long-term bedridden condition before intensive care unit; (4) Patients undergoing stone hormone therapy; (5) Patients taking aspirin, low molecular weight heparin and other anticoagulant drugs; and (6) Patients with cerebral hemorrhage, trauma, and blood system disease history.

General basic information about patients was retrospectively recorded and collected, all data were recorded in customized study forms. The general data of the 4 groups in gender, age, weight, and so on were analyzed; Group A were SEC patients, including 50 males and 25 females, with an average value of (53.3 ± 4.31 years) and an average body mass index of (24.06 ± 1.19) kg/m^2, group B were patients with mild SEC, included 30 males and 45 females, with (50.6 ± 7.03) years as an average value and an average body mass index of (23.69 ± 3.92) kg/m^2. In Group C, patients with severe SEC, the ultrasound exploration of blood flow in at least one site presented continuous dense smoke eddy current development or SEC was detected in all four sites; it was mild, including 30 males and 45 females, with an average age of (51.4 ± 6.32 years). The average BMI was 23.91 ± 3.17 kg/m^2. Group D were patients with thrombosis, including 36 males and 39 females, with an average age of (50.8 ± 5.18 years) and an average BMI of (24.06 ± 3.86) kg/m^2. There was no difference in preoperative basis among patients from different groups ($P > .05$), which was comparable. Vital signs were stable in both groups, and no obvious contraindications were detected.

In this work, patients who fully met the inclusion criteria accepted the experimental regulations and signed experimentally informed consent, and the study was approved by the Ethics Committee of the Second Affiliated Hospital of Jiaxing University. (Supplementary table 1)

TEG examination

Use TCA-6000 thrombus scale map of Zhejiang Shengyu Medical Technology Co. Ltd. to test patients. 0.1 mL calcium chloride and 0.3 mL sodium citrate anticoagulant whole blood were thoroughly mixed, and then 0.36 mL activated blood was added into the injection cup of TEG instrument for testing, and the main parameters of TEG were detected, respectively. These included coagulation reaction time (R-value), coagulation angle (α) value, coagulation time (K value), coagulation index (CI), maximum amplitude (MA) value, and LY30 reflecting fibrinolysis.

The R-value reflecting the coagulation time, which represents the activation of coagulation factors and mainly reflects the functional activity and quantity of coagulation factors. K value and only angle represent the dynamic process of clot formation, and K value represents the time of clot formation, that is, the time used for clot formation to the amplitude of 20mm, which mainly reflects the activity of platelets, coagulation factors and the quality of fibrinogen. α Angle refers to the angle between the tangent line and the horizontal line from the formation point of a blood clot, namely the end point of R, to the maximum curve arc of the graph.

Ultrasound examination

The Italian Yum! Mylab Gold 25 echocardiography was selected for examination. The instrument is equipped with different frequency conversion probes, such as CA123-5 and IOE323, and the probe frequency is 5-8 MHz or 2.5-5 MHZ. The device also contained Electrocardiograph (ECG) monitoring leads and an automatic image storage device.

To examine femoral veins, subjects were supine with mild external rotation and abduction of lower limbs. The internal jugular vein was taken in the supine or lateral position, and the probe was taken on both sides of the control group along the direction of the blood vessel. The scan could be performed from near to far after the transverse incision. In the left decubitus position, some severe patients may adopt the semi-seated position.

Routine coagulation test

Fasting blood sampling was performed on the day of hospitalization or in the morning of the next day for venous blood examination. Sodium citrate containing 0.2 mL 3.2% was placed in a vacuum tube to fully soothe the vascular venous blood. 1.8 mL was placed in a fully automatic coagulation instrument (CS5100, Sisen Meikang Co., Ltd) for detection. Coagulation index The coagulation index test on the date of ultrasound examination or the closest to the examination date was selected. If there was one or more abnormalities in the coagulation index, it was regarded as abnormal CI.

Indicators to be observed

I. The general information of each enrolled patient was recorded, including age, gender, Apache II score, and the presence of catheter implants in the central vein of the main diagnosis department. Finally, the TEG parameters of the four groups were statistically analyzed to determine whether there was a significant difference, and the correlation between central vein SEC and TEG test results in severe patients was analyzed.

II. The main parameters of TEG in each patient were recorded according to the screening results, including R-value, α value, K value, comprehensive CI, and MA value. A shortened R-value meant a high coagulation state indicating high coagulation factor activity; while a prolonged R value meant a lack of coagulation factor or existence of anticoagulant substances. The maximum thrombus mainly reflected the aggregation function of platelets; the larger the value, the higher the platelet aggregation function, namely, the high coagulation state. The smaller the value, the lower the platelet aggregation function, namely, the low coagulation state. A low K value was accompanied by an increase in α Angle, indicating a high level of fibrinogen, that is, in a high coagulation state. A decrease in α Angle accompanies a high K value, that is, a low level of fibrinogen, that is, in a low coagulation state. CI value was an index of coagulation parameters of a comprehensive response

III. The relative index of thrombin loss as prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT), fibrin/fibrinogen degradation products (FDP), and D-dimer. These coagulation indexes were commonly used in clinical practice to evaluate the coagulation function.

IV. Clinical indicators were traced to calculate all patients' Acute Physiological and Chronic Health Rating Scale (APACHE II) score within 24 hours after admission. APACHE II score evaluated the severity of critically ill patients.

V. The predictive value of catheter-related thrombosis (CRT) was analyzed using area under the curve (AUC) for TEG and conventional coagulation indicators.

Statistical analysis

Statistical Product and Service Solutions (SPSS) 19.0 (SPSS Inc., Chicago, IL, USA) was utilized for data processing. Measurement data were represented by mean ± standard deviation ($\bar{x} \pm s$), and classification variables were represented by percentage or rate. Spearman correlation coefficient (R-value) analysis and Logic regression analysis were employed for correlation detection between SEC and TEG, and the test level was set at 0.05, and $P < .05$ was statistically significant.

RESULTS

Catheterization History

The statistical results of catheterization history in different groups are illustrated in Figure 1. In group A, 4 patients had a catheterization history, accounting for 5.33%. 6 patients with mild SEC had a catheterization history (8.0%), and 8 patients with moderate SEC had a catheterization

Figure 1. Statistical results of catheterization. (Left figure: statistical results of catheterization history in different groups; right figure: statistical results of catheterization location)

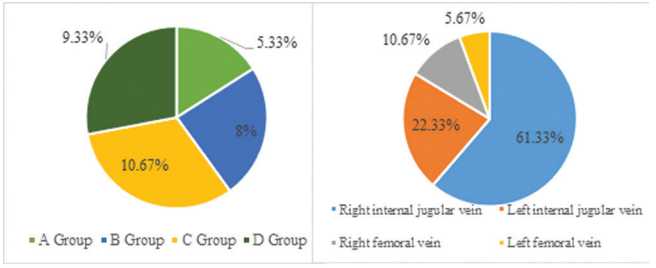
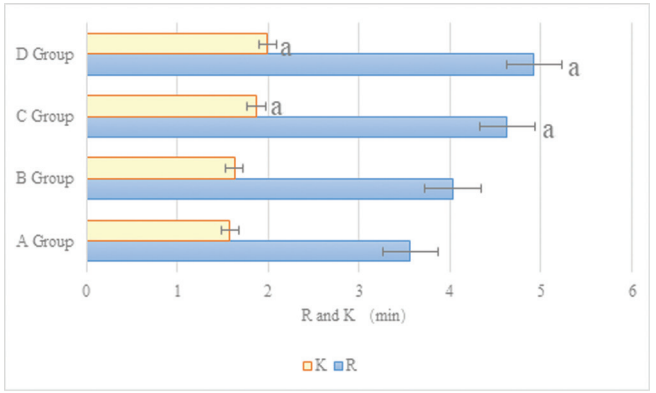


Figure 2. Comparison results of K value and R value in various groups.

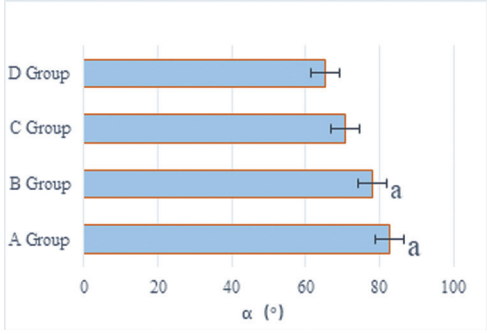


[a]meant a sharp difference with $P < .05$ to group A and group B)

Figure 3. MA and CI values of patients from different groups.

[a] and [b] meant the comparison revealed a difference with $P < .05$.)

Figure 4. Results of α value comparison of patients from various groups.



[a]meant the difference between patients with SEC and mild SEC in α value showed $P < .05$.

history, accounting for 10.67%. In group D, 7 patients had a history of catheterization, accounting for 9.33%.

The statistical results of catheterization location were demonstrated in the right figure in Figure 1. The right internal jugular vein was the most common, with 184 cases (61.33%), followed by the left internal jugular vein 67 cases (22.33%). The third was the right femoral vein, with 32 cases (10.67%), and the least was the left femoral vein, with 17 cases, accounting for 5.67%.

TEG indicators

The R and K trends under the TEG index were the same for all patients from different groups. The R and K values in group D were the highest, followed by those in group C, and those were the lowest in SEC patients. The differences in the R and K values of the groups C and D were great based on those in SEC patients and mild SEC patients and exhibited differences with $P < .05$. The above results were detailed in Figure 2.

In Figure 3, the MA value was (62.7 ± 9.17) mm, (58.2 ± 6.08) mm, (53.7 ± 5.43) mm, and (49.5 ± 4.31) mm in groups A, B, C, and D, respectively. The difference between groups A and B exhibited a significance with $P < .05$, and between them, groups C and D presented the same significance with $P < .05$.

As given in Figure 3, the CI value was (0.28 ± 0.14) mm in Group A, was (0.37 ± 0.08) mm in Group B, was (0.51 ± 0.13) mm in Group C, and was (0.49 ± 0.21) mm in Group D. The differences from patients with severe SEC or with thrombosis to those with SEC or mild SEC were great and presented significances with $P < .05$.

As compared in Figure 4, the α value was (82.7 ± 8.29)°, (78.2 ± 7.86)°, (70.7 ± 8.18)°, and (65.3 ± 7.36)° in the groups A - D, respectively. The difference between patients with SEC and those with mild SEC was observable, and the α values of patients with SEC and mild SEC were greatly different from those with severe SEC and thrombosis. The comparisons here all exhibited a difference with $P < .05$.

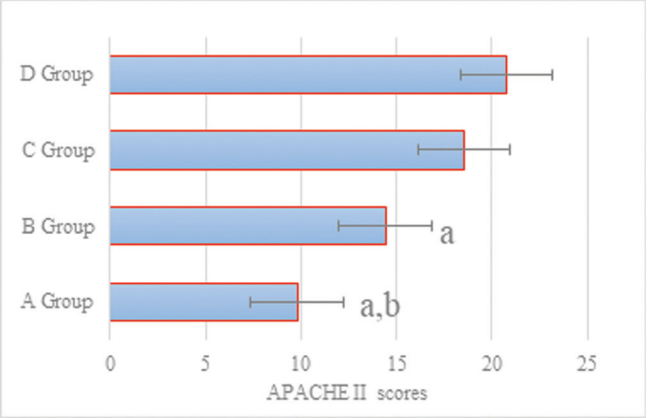
APACHE II scores

Figure 5 was a comparison of APACHE II scores of patients. APACHE II score of patients with SEC in group A was (9.81 ± 8.07) points, that of those with mild SEC was (14.42 ± 8.81) points, that of those with severe SEC was (18.53 ± 8.37) points, and that in group D for patients with thrombosis was (20.78 ± 8.16) points. The APACHE II score in patients with SEC was sharply different from that of those with mild SEC in group B, exhibiting a difference with $P<0.05$, and that in patients with SEC and mild SEC was greatly different that of patients with severe SEC and thrombosis, presenting an observable difference with $P < .05$. Patients with severe SEC and thrombosis were severity.

D-dimer

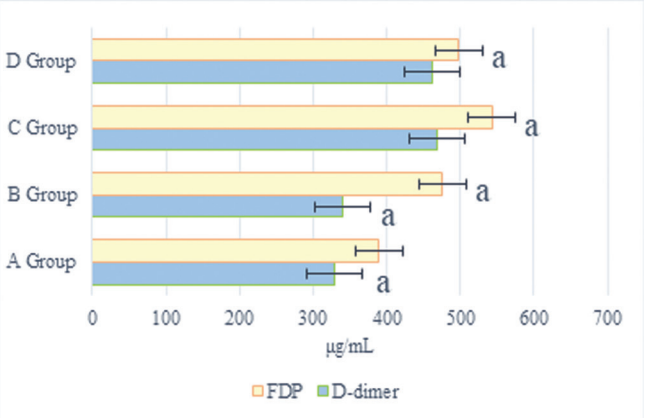
The D-dimer of patients from different groups was compared in Figure 6. The D - dimer values for patients with SEC, mild SEC, severe SEC, and thrombosis were (329 ± 28.3) mu g/L, (341 ± 30.1) mu g/L, (468 ± 38.7) mu g/L, and

Figure 5. Illustration of APACHE II scoring results.



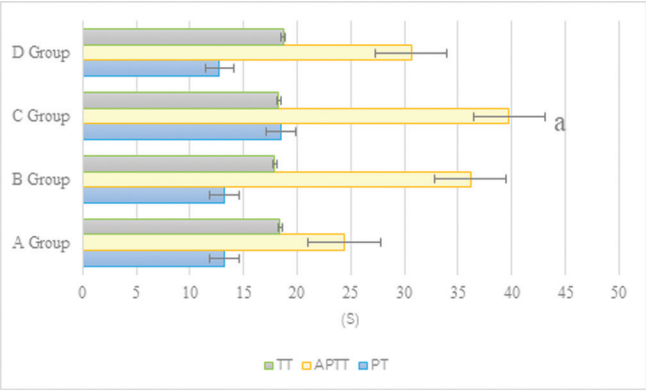
[a]meant the scores in group A and group B were remarkably different from those in the groups C and D, and
[b]meant the score in the group A exhibited a difference with $P < .05$ based on that in the group B.

Figure 6. D-dimer scores of the patients with different diseases.



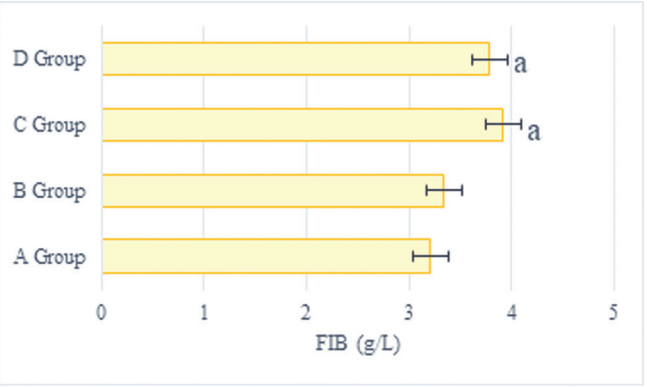
[a]meant that values of SEC and mild SEC patients were greatly different from those for the severe SEC and thrombosis patients, exhibiting a difference with $P < .05$.

Figure 7. Values of PT, TT, and APTT of patients from various groups.



[a]meant that the comparison exhibited a difference with $P < .05$.)

Figure 8. Results of FIB comparative analysis.



[a]meant a difference with $P < 0.05$

(462 ± 27.6) mu g/L, respectively. The D-dimer values of SEC and mild SEC patients were greatly different from those for the severe SEC and thrombosis patients, and the comparison here exhibited a difference with $P < .05$.

The comparison results of FDP are given in Figure 6, too. The FDP values for patients with SEC, mild SEC, severe SEC, and thrombosis were (389.25 ± 32.7) mu g/L, (476.23 ± 41.15) mu g/L, (543.53 ± 37.4), and (498 ± 42.6) mu g/L, respectively. The FDP values of SEC and mild SEC patients were greatly different from those for the severe SEC and thrombosis patients, and the comparison here exhibited a difference with $P < .05$.

Coagulation indexes

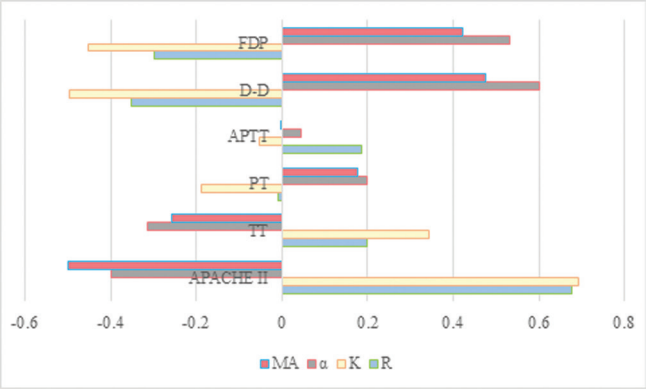
As disclosed in Figure 7, the TT comparison results showed that the TT of patients with SEC, mild SEC, severe SEC, and thrombosis were (18.4 ± 3.51) s, (17.9 ± 2.91) s, (18.3 ± 3.12) s, and (18.7 ± 3.22) s, respectively, with no remarkable difference among all groups ($P > .05$).

The PT was (13.25 ± 3.72) s for SEC patients in the Group A, (13.23 ± 3.51) s for mild SEC patients in group B, (18.53 ± 4.41) s for severe SEC patients in group C, and (12.78 ± 3.92) s for thrombosis patients in the group D. The difference among all patients from different groups showed no visible difference with $P > .05$.

The results of APTT comparison showed that it was (24.42 ± 6.72) s for SEC patients, (36.18 ± 5.18) s for mild SEC patients, (39.76 ± 6.73) s for severe SEC patients, and (30.65 ± 7.02) s for thrombosis patients in group D. The difference in APTT value between severe SEC patients and patients in other groups was sharp, with a significance of $P < .05$. APTT may be related to vein smoke in severe patients.

In the comparison results, the FIB of SEC patients in the Group A was (3.21 ± 0.53) s, that of mild SEC patients in the Group B was (3.34 ± 0.47) s, that of severe SEC patients in group C was (3.92 ± 0.37) s, and that for thrombosis patients in the group D was (3.79 ± 0.46) s. The difference between patients with severe SEC and thrombosis and those with SEC and mild SEC was great ($P < .05$). Figure 8 illustrates the above results. FIB may be related to vein smoke in severe patients.

Figure 9. Correlation between TEG parameters and coagulation parameters.



[a]meant a great difference was found to the Ctrl group.

Figure 10. ROC curves.

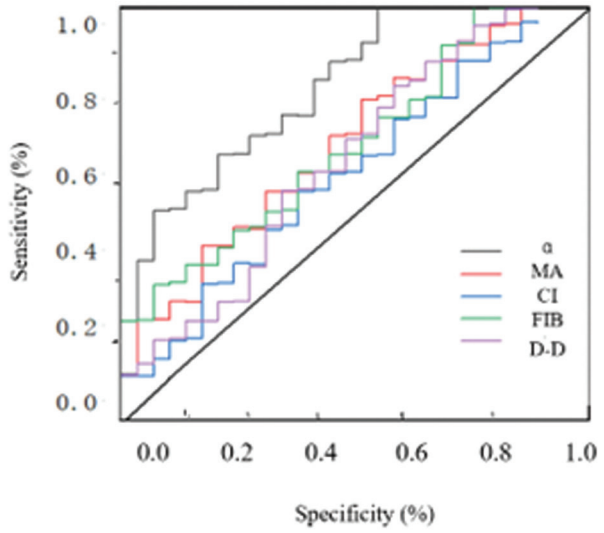


Table 1. MA, D-D, α, and FIB after catheterization

Variable	AUC	95% CI	Sensitivity (%)	Specificity (%)	*P* value
α	0.702	0.487 ~ 0.872	100	43.1	.012
MA	0.813	0.587 ~ 0.876	72	73.3	.001
CI	0.723	0.601 ~ 0.796	96	43.2	.019
FIB	0.845	0.573 ~ 0.817	67	92.1	.001
D-D	0.809	0.593 ~ 0.867	96	59.5	.001

Correlation analysis

The correlation between TEG index and the conventional coagulation index was analyzed, and the results were summarized as follows. The R-value was positively linked with APACHE II, TT, and APTT, with correlation coefficients of 0.678, 0.198, and 0.187, respectively, and were negatively associated with PT, D-D, and FDP with correlation coefficients of -0.008, -0.351, and -0.298, respectively. The K value exhibited positive correlations with APACHE II and TT (0.692 and 0.342, respectively) and negative correlations to PT, APTT, D-D, and FDP (-0.187, -0.053, -0.497, and -0.453). The correlations of α value with PT, APTT, D-D, and FDP were positive with coefficients of 0.198, 0.046, 0.602, and 0.532, respectively, but were negative with APACHE II and TT with coefficients of -0.398 and -0.315, respectively. MA was positively correlated with PT, D-D, and FDP (0.176, 0.476, and 0.421, respectively) and negatively linked to APACHE II, TT, and APTT (-0.498, -0.256, and -0.0.001, respectively). TEG-related indexes correlated with routine blood coagulation tests. The specific correlations are demonstrated in Figure 9.

CRT evaluation of TEG and coagulation indicators

MA, D-D, CI, α, and FIB of patients after catheterization were shown in Table 1, and these values predicted the occurrence of ROC, as displayed in Figure 10. AUC of α was 0.702, the sensitivity was 100%, and the specificity was 43.1%. The AUC of MA was 0.813, with a sensitivity and a specificity of 72% and 73.3%, respectively. The AUC of CI was 0.723, exhibiting a sensitivity of 96% and a specificity of 43.2%. The AUC of FIB was 0.845, the sensitivity was 67%, and the specificity was 92.1%. The AUC, sensitivity, and specificity of D-D were 0.809, 96%, and 59.5%, respectively.

DISCUSSION

SEC was first used in ultrasonography and later began to be used in blood vessels, where smoke echo in the descending aorta has been shown to be a risk factor for myocardial ischemia and ischemic cerebral infarction. Thromboembolism is possible due to smoke echo elevation in left atrium.[20] In the case of thrombosis or not, the change of smoke echo in lower limb veins also means changes in coagulation indexes, which some studies have confirmed.[21] Under the condition of low shear stress in blood flow, smoke echo occurs in lower limb veins. SEC has some relationship with blood flow velocity and cardiovascular inner diameter to a certain extent. When smoke echo appears, blood flow velocity will slow down and cardiovascular inner diameter will widen.[22] In the ultrasound imaging of the patient, it is concluded that there would be dense point-like weak echo images in the proximal segment of the vein, and slow flow occurred along with breathing, especially in the femoral vein. The main reason may be that the location is relatively shallow, the lumen is relatively wide, and the blood flow velocity would be slow, so the ultrasound development imaging would be smoke echo. This work evaluated the correlation between the ultrasound signs and TEG results in severe ICU patients through a comparative analysis of the screening results of ultrasound signs and TEG results.

TEG only needs to collect a small amount of whole blood from patients to measure their clotting status. This allows TEG to assess their condition and prognosis effectively, allowing physicians to target patients with interventions as quickly as possible. TEG is a kind of instrument for dynamic detection of the coagulation process, which can comprehensively examine coagulation function. Through TEG index parameters, the abnormal situation of the coagulation function can be understood, and the cause of the abnormal coagulation function can be clarified. The routine coagulation test can only reflect the changes of the patient's coagulation function, and the combination of the two can more clearly reflect the abnormal coagulation function. In

severe patients CVSU, the parameters of TEG can be understood through the images presented. The most important parameter of TEG is the R-value reflecting the coagulation time, K value and α Angle represent the dynamic process of clot formation, the normal value of α Angle is 53° ~ 72°,[23,24] The maximum amplitude MA represents absolute clot strength and reflects fibrinogen (FDP) and platelet function, with a normal value of 50 ~ 70 mm. These parameters together show the whole process of the coagulation cascade, including the dynamic information from coagulation initiation to fibrin formation, platelet aggregation, fibrin crosslinking, and clot dissolution, which has become an important test method for monitoring coagulation function in clinical practice.

In this work, the coagulation indexes of patients were analyzed according to the differences in SEC in the vascular lumen. No great differences were observed between SEC and SEC mild patients, while the differences between SEC and SEC mild and SEC severe patients and thrombosis groups were extremely obvious, indicating that coagulation indexes were related to vein smoke of severe patients like ultrasound development. TEG indicators analyzed in this work disclosed that TEG had obvious differences between K, R, MA, and α values of patients in the SEC, mild, and severe SEC groups. Measures of TEG were shown to be associated with the outcome of severe patients. PT measures the time required for plasma coagulation in response to exposure to tissue factors and can be used to assess exogenous and co-coagulation pathways. In this work, PT conditions of patients in 4 were analyzed, and there was a significant difference between group C and other groups. However, all groups had no significant differences in TT and APTT. The higher the values of K, R, PT, APTT, and FIB, and the lower the values of MA and α, the more serious the patients' disease is. The thrombus bomb chart index can replace the conventional coagulation function index to evaluate the disease of severe patients. Louis et al.[25] used TEG to investigate that enoxaparin administration did not prevent deep vein thrombosis and found that the TEG-adjusted dose of enoxaparin caused a significant increase in antithrombin activity, which had nothing to do with deep vein thrombosis formation. Brown RS used TEG to analyze thrombus division products in adult patients undergoing primary coronary bypass graft surgery. After CPB, the group that took tranexamic acid had better platelet function and less fibrinolytic system activation. It can provide good guidance for clarifying patients' postoperative bleeding and blood transfusion.[26] These studies all showed TEG was able to do a good job of inspecting patients.

The clinic's APACHE II score is mainly adopted to evaluate the severity of critically ill patients. In this work, the APACHE II score in group A was significantly lower than that in group C and group D. In addition, the difference between SEC and SEC mild groups exhibited a great difference, but significant difference between SEC severe and thrombosis groups and SEC mild groups was observed. Correlation analysis told that R and K values were positively correlated with TEG index, and α was negatively correlated with MA. Correlation of the R value was positive to APACHEII, TT, and APTT but was negative to PT, D-D, and FDP. K value exhibited a positive association with APACHE II and TT but a negative relationship with PT, APTT, D-D, and FDP. α value was positively related to PT, APTT, D-D, and FDP. Negative correlation with APACHEII and TT, MA was positively correlated with PT, D-D, and FDP but negatively linked with APACHE II, TT, and APTT. The results showed a certain degree of correlation between TEG-related indexes and routine blood coagulation tests. In routine blood coagulation tests, PT, MA, and CI could all show the maximum strength and stability of blood clot formation. This further demonstrates that TEG can provide effective reference indicators for severe patients and has high predictive value. Agren et al.[27] described that TEG and routine methods can be used to assess TEG in patients with perioperative bleeding. Wang et al.[28] indicated that some TEG parameters were significantly correlated with conventional coagulation tests, but the consistency was poor. The diagnostic sensitivity of the two methods for patients with bleeding was low, TEG could not replace conventional coagulation tests, and the optimal method that could reflect bleeding risk was still uncertain. Zia et al.[29] identified children with rare hemorrhagic disorders and predicted bleeding phenotypes. This also indicates that TEG has a good screening effect, and more comprehensive and objective observation results can be obtained by the fusion of thrombolysis and routine coagulation tests, providing a good prognosis for patients. TEG parameters are significantly correlated with thrombus function and may be used as a clinical method to predict VTE, which enables effective evaluation of severe patients' CVSU. The ultrasound signs may be as clinical hypercoagulability detection in severe patients and intervention indicators for early thrombosis prevention in the future and provide a theoretical basis for the early prevention and intervention of VTE.

Limitations

This was a single-center study, and the sample size of this study is small. The selection bias and any other potential biases that might have affected the results, although the findings of this study need to be confirmed by a larger sample size study in the future, they still provide a valuable theoretical basis and reference for clinical practice. In the future, prospective studies, larger sample sizes, or more indicators investigate the evalution of thrombus function can further confirm and promote its clinical application.

CONCLUSION

In this work, TEG parameters exhibited an obvious correlation with thrombus function, which was able to effectively evaluate severe patients using CVSU. The ultrasonic signs can be undertaken as clinical hypercoagulability detection indicators in severe patients and intervention indicators for early thrombosis prevention in the future, and

the SEG indicators can provide clinicians with the best treatment plan for severe patients. TEG parameters and CVSU as evaluation indictors should be consider in clinical, which provides a reference for the thrombus function for severe patients.

CONFLICT OF INTERESTS

The authors declared no conflict of interest.

AUTHOR CONTRIBUTIONS

QW ,JCand ZL designed the study and performed the experiments, YZ, CZ,LS and QZ collected the data, YS and JS analyzed the data, QW and JC prepared the manuscript. All authors read and approved the final manuscript.

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REFERENCES

1. Konstantinides SV, Torbicki A, Agnelli G, et al; 2014 ESC guidelines on the diagnosis and management of acute pulmonary embolism. *Eur Heart J*. 2014;35(43):3033-3069, 3069a. doi:10.1093/eurheartj/ehu283
2. Adamik B, Gozdzik W, Jakubczyk D, Welna M, Kübler A. Coagulation abnormalities identified by thromboelastometry in patients with severe sepsis: the relationship to endotoxemia and mortality. *Blood Coagul Fibrinolysis*. 2017;28(2):163-170. doi:10.1097/MBC.0000000000000572
3. Sukernik MR, West O, Lawal O, et al. Hemodynamic correlates of spontaneous echo contrast in the descending aorta. *Am J Cardiol*. 1996;77(2):184-186. doi:10.1016/S0002-9149(96)90593-7
4. Robba C, Battaglini D, Ball L, et al. Coagulative Disorders in Critically Ill COVID-19 Patients with Acute Distress Respiratory Syndrome: A Critical Review. *J Clin Med*. 2021;10(1):140. doi:10.3390/jcm10010140
5. Levi M, Schultz M. Coagulopathy and platelet disorders in critically ill patients. *Minerva Anestesiol*. 2010;76(10):851-859.
6. Hsu HY, Chung CP, Chen SY, Chiang YY, Hu HH. Spontaneous echo contrast in internal jugular veins: a probable indicator for systemic inflammation and a prothrombotic state. *Ultrasound Med Biol*. 2012;38(6):926-932. doi:10.1016/j.ultrasmedbio.2012.02.003
7. Liang C, Yang Y, He Z, et al. Comparison between thromboelastography and the conventional coagulation test in detecting effects of antiplatelet agents after endovascular treatments in acute ischemic stroke patients: A STROBE-compliant study. *Medicine (Baltimore)*. 2020;99(10):e19447. doi:10.1097/MD.0000000000019447
8. González-Torrecilla E, García-Fernández MA, Pérez-David E, Bermejo J, Moreno M, Delcán JL. Predictors of left atrial spontaneous echo contrast and thrombi in patients with mitral stenosis and atrial fibrillation. *Am J Cardiol*. 2000;86(5):529-534. doi:10.1016/S0002-9149(00)01007-9
9. Yasuoka Y, Naito J, Hirooka K, et al. Right atrial spontaneous echo contrast indicates a high incidence of perfusion defects in pulmonary scintigraphy in patients with atrial fibrillation. *Heart Vessels*. 2009;24(1):32-36. doi:10.1007/s00380-008-1084-3
10. Goswami KC, Yadav R, Rao MB, Bahl VK, Talwar KK, Manchanda SC. Clinical and echocardiographic predictors of left atrial clot and spontaneous echo contrast in patients with severe rheumatic mitral stenosis: a prospective study in 200 patients by transesophageal echocardiography. *Int J Cardiol*. 2000;73(3):273-279. doi:10.1016/S0167-5273(00)00235-7
11. Rittoo D, Sutherland GR, Currie P, Starkey IR, Shaw TR. A prospective study of left atrial spontaneous echo contrast and thrombus in 100 consecutive patients referred for balloon dilation of the mitral valve. *J Am Soc Echocardiogr*. 1994;7(5):516-527. doi:10.1016/S0894-7317(14)80009-6
12. Choi JC, Oh YH, Kim JG, et al. Spontaneous echo-contrast in the internal jugular veins of patients with ischemic stroke. *J Clin Ultrasound*. 2015;43(7):431-437. doi:10.1002/jcu.22249
13. Onozuka H, Muraki M, Mikami T, et al. Prevalence and clinical importance of spontaneous echo contrast within the carotid artery in patients with ischemic cerebrovascular disease. *J Ultrasound Med*. 2007;26(2):169-177. doi:10.7863/jum.2007.26.2.169
14. Yamamura O, Miyoshi Y, Hiraki S, et al. Spontaneous echo contrast in descending aorta correlates with low blood-flow velocity in carotid arteries and hemostatic abnormalities. *Angiology*. 2001;52(11):749-758. doi:10.1177/000331970105201104
15. Kaymaz C, Ozdemir N, Kýrma C, Ozkan M. Spontaneous echo contrast in the descending aorta in patients without aortic dissection: associated clinical and echocardiographic characteristics. *Int J Cardiol*. 2002;85(2-3):271-276. doi:10.1016/S0167-5273(02)00185-7
16. Kaul P. Spontaneous retrograde dissection of ascending aorta from descending thoracic aorta--a case review. *Perfusion*. 2011;26(3):215-222. doi:10.1177/0267659110395804
17. Liu K, Zhou Y, Xie W, et al. Handgrip exercise reduces peripherally-inserted central catheter-related venous thrombosis in patients with solid cancers: A randomized controlled trial. *Int J Nurs Stud*. 2018;86:99-106. doi:10.1016/j.ijnurstu.2018.06.004
18. de Wet IS. Proceedings: postero-medial release in club foot. *J Bone Joint Surg Br*. 1975;57(2):257-258.
19. Connelly CR, Van PY, Hart KD, et al. Thrombelastography-Based Dosing of Enoxaparin for Thromboprophylaxis in Trauma and Surgical Patients: A Randomized Clinical Trial. *JAMA Surg*. 2016;151(10):e162069. doi:10.1001/jamasurg.2016.2069
20. Van PY, Cho SD, Underwood SJ, Morris MS, Watters JM, Schreiber MA; Thrombelastography versus AntiFactor Xa levels in the assessment of prophylactic-dose enoxaparin in critically ill patients. *J Trauma*. 2009;66(6):1509-1515, 1515-1517. doi:10.1097/TA.0b013e3181a51e33
21. Malinoski D, Jafari F, Ewing T, et al. Standard prophylactic enoxaparin dosing leads to inadequate anti-Xa levels and increased deep venous thrombosis rates in critically ill trauma and surgical patients. *J Trauma*. 2010;68(4):874-880. doi:10.1097/TA.0b013e3181d32271
22. Matsumoto T, Wada H, Tamaru S, et al. Central venous catheter-related thrombosis after replacement therapy for intracranial bleeding in a patient with afibrinogenaemia. *Haemophilia*. 2008;14(1):153-156. doi:10.1111/j.1365-2516.2007.01564.x
23. Bahl A, Karabon P, Chu D. Comparison of Venous Thrombosis Complications in Midlines Versus Peripherally Inserted Central Catheters: Are Midlines the Safer Option? *Clin Appl Thromb Hemost*. 2019;25:1076029619839150. doi:10.1177/1076029619839150
24. Santos FKY, Flumignan RLG, Areias LL, et al. Peripherally inserted central catheter versus central venous catheter for intravenous access: A protocol for systematic review and meta-analysis. *Medicine (Baltimore)*. 2020;99(30):e20352. doi:10.1097/MD.0000000000020352
25. Louis SG, Van PY, Riha GM, et al; Thromboelastogram-guided enoxaparin dosing does not confer protection from deep venous thrombosis: a randomized controlled pilot trial. *J Trauma Acute Care*. 2014;76(4):937-942, 942-943. doi:10.1097/TA.0000000000000165
26. Brown RS, Thwaites BK, Mongan PD. Tranexamic acid is effective in decreasing postoperative bleeding and transfusions in primary coronary artery bypass operations: a double-blind, randomized, placebo-controlled trial. *Anesth Analg*. 1997;85(5):963-970. doi:10.1213/00000539-199711000-00003
27. Ågren A, Wikman AT, Holmström M, Östlund A, Edgren G. Thromboelastography (TEG®) compared to conventional coagulation tests in surgical patients--a laboratory evaluation. *Scand J Clin Lab Invest*. 2013;73(3):214-220. doi:10.3109/00365513.2013.765960
28. Wang Z, Li J, Cao Q, Wang L, Shan F, Zhang H. Comparison Between Thromboelastography and Conventional Coagulation Tests in Surgical Patients With Localized Prostate Cancer. *Clin Appl Thromb Hemost*. 2018;24(5):755-763. doi:10.1177/1076029617724229
29. Zia AN, Chitlur M, Rajpurkar M, et al. Thromboelastography identifies children with rare bleeding disorders and predicts bleeding phenotype. *Haemophilia*. 2015;21(1):124-132. doi:10.1111/hae.12481

Supplementary Table 1. Baseline characteristics of patients

Factor	Group A (n = 75)	Group B (n = 75)	Group C (n = 75)	Group D (n = 75)
Males	50(66.7)	30(40.0)	30(40.0)	36(48.0)
Age	53.3 ± 4.31	50.6 ± 7.03	51.4 ± 6.32	50.8 ± 5.18
Body mass index	24.06 ± 1.19	23.69 ± 3.92	23.91 ± 3.17	24.06 ± 3.86