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Utility of Thromboelastography to Identify Hypercoagulability in Lung Cancer Related Ischemic Stroke Patients

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Abstract

Lung cancer related hypercoagulability could increase the risk of ischemic stroke. Routine coagulation tests may have limited capacity in evaluating hypercoagulability. The aim of this study was to investigate the ability of thromboelastography (TEG) in the identification of hypercoagulability in patients with lung cancer and cryptogenic ischemic stroke (LCIS). Between January 2016 and December 2018, whole citrated blood from LCIS patients (n = 35) and age- and gender-matched lung cancer patients and healthy volunteers were used for TEG and routine coagulation tests. The coagulation indicator and clinical data were compared among the 3 groups. There were 27/35 (77.14%) on TEG and 18/35 (51.43%) on routine coagulation tests of LCIS patients who had evidence of hypercoagulability. The detection rate of hypercoagulability by TEG in LCIS patients was higher than routine coagulation tests ($P = 0.018$). Comparing with lung cancer patients and healthy controls, LCIS patients have a significantly higher maximum amplitude (MA), fibrinogen, and D-dimer. Multivariate analysis showed that D-dimer and MA were significantly associated with ischemic stroke in lung cancer patients. ROC curve showed that the area under the curve of TEG (0.790 $\pm$ 0.048, 95% CI: 0.697-0.864) was significantly higher than routine coagulation tests (0.673 $\pm$ 0.059, 95% CI: 0.572-0.763) ($P = 0.04$) in identifying hypercoagulability in LCIS patients. Therefore, TEG could identify hypercoagulability in LCIS patients and healthy controls. Identification of hypercoagulability in lung cancer patients by TEG may be helpful to prevent the occurrence of LCIS.

Keywords

lung cancer, ischemic stroke, thromboelastography, hypercoagulability

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Introduction

Thromboembolic event is the second most common cause of mortality in advanced cancer patients.[1] Traditionally, the main consideration has been given to venous thrombotic events. Recently, Blann and Dunmore[2] outlined that approximately 25% of all PubMed citations on thrombosis are arterial thrombosis, including ischemic stroke. Lung cancer is the most common type of cancer, with the highest risk of ischemic stroke.[3] It was reported that the risk of ischemic stroke in lung cancer patients is 1.43 times higher than general population, indicating that lung cancer itself may be an etiologic of ischemic stroke, known as lung cancer related ischemic stroke (LCIS).[4] Increasing studies had suggested that cancer related hypercoagulability may be the principal mechanism for ischemic stroke in patients with lung cancer.[5,6] Given the development of cancer therapy and the extended survival of lung cancer patients, the incidence of LCIS may increase. Once ischemic stroke occurs in cancer patients, or vice versa, neurological outcomes significantly worsen and prognosis tends to be poor.[7] Accordingly,

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precise and timely monitoring to guide coagulation management has important clinical implications.

Previously, routine coagulation tests, such as prothrombin time (PT), activated partial thromboplastin time (APTT), fibrinogen (FIB), etc. can only partially analyze a certain stage of coagulation process or a certain coagulation product.[8,9] Therefore, conventional diagnostic methods remain poor assays for dynamic assessment of clot strength in whole blood. In contrast, thromboelastography (TEG) first described in 1948 is a sensitive blood coagulation assay that analyzes the kinetics of clot formation, from the initial fibrin threads to fibrinolysis.[10] Clinically, TEG has been successfully used for coagulation assessment in trauma, perioperative care, liver transplantation.[11,12] Moreover, it has been expanded into oncology area and has been indicated to identify hypercoagulability and predict thromboembolic complications in prostate cancer patients and lung cancer patients.[13-15] However, the application of TEG in evaluating coagulation function of LCIS patients has not been reported.

In this study, we aimed to assess coagulation status recorded by TEG and routine coagulation tests in LCIS patients. We also analyzed the correlation between TEG parameters and routine coagulation data. We hypothesized that TEG may be superior to routine coagulation tests in identifying hypercoagulability of LCIS patients. This study may contribute to a more targeted method to anticoagulant prophylaxis and detect those at high risk of ischemic stroke in patients with lung cancer in the future.

Materials and Methods

Patients

This study was approved by the Medical Ethics Committee of First Affiliated Hospital of Guangxi Medical University (No 2013 KY 108). Written informed consent was obtained from all participants for their anonymized information to be published in this article. Between January 2016 and December 2018, 108 consecutively adult patients with active lung cancer who experienced acute ischemic stroke were evaluated at the First and second Affiliated Hospital of Guangxi Medical University for this study. Based on previous studies, lung cancer related ischemic stroke (LCIS) in the present study was defined as patients with lung cancer and cryptogenic ischemic stroke.[5,16] Patients with cerebrovascular diseases other than cryptogenic ischemic stroke were excluded in the present study. Moreover, patients with metastatic brain cancer, preexisting coagulation disorders, patients with anticoagulant therapy or surgical history within 3 weeks before ischemic stroke onset, and patients with incomplete clinical data were also excluded. According to this protocol, 53 patients with large-artery atherosclerosis stroke, 6 patients with cardiac embolism stroke, 9 patients with metastatic brain cancer and 5 patients with surgery within 1 week were excluded. Finally, 35 patients out of 108 were suitable to be enrolled in the study.

The diagnosis of acute ischemic stroke referred to the American Heart Association diagnostic criteria for stroke.[17] With reference to TOAST criteria (Trial of Org 10172 in Acute Stroke Treatment),[18] ischemic stroke etiology was classified as large artery atherosclerosis stroke, cardiac embolism stroke, small vessel stroke, stroke of other determined etiology and stroke of undetermined etiology. Lung cancer have been objectively confirmed by histologically or cytologically testing and were all symptomatic.

Controls

Due to variability in the values of TEG parameters in healthy volunteers reported in the literature,[19,20] we obtained TEG samples from age- and sex-matched healthy controls (HC group) from physical examination center at the First Affiliated Hospital of Guangxi Medical University. To identify independent risk factors of ischemic stroke in lung cancer patients, age-, sex- and cancer progression matched patients with active lung cancer who admitted to the same hospital during the same period were recruited and served as LC group. The exclusion criteria were similar to LCIS group.

Blood Specimen Collection

Once acute ischemic stroke occurred in lung cancer patients, 7-10 ml citrated venous blood samples (1:9 trisodium citrate 3.2%: blood) were withdrawn from them prior to stroke treatment within 6 hours. Venous blood samples were withdrawn from healthy volunteers when they did physical examination in our hospital. Once lung cancer patients were confirmed, venous blood samples were withdrawn from them before surgery therapy. The blood was held at room temperature and taken for processing within 2 hours of collection, which was used for TEG, routine coagulation tests, complete blood count and biochemical examination.

Routine Coagulation Tests and TEG

Laboratory screening were performed in all patients. Routine coagulation tests included prothrombin time (PT), activated partial thromboplastin time (APTT), thrombin time (TT) and fibrinogen (FIB) and plasma D-dimer. Complete blood count included white blood cell (WBC), hemoglobin (HB) and platelet counts (PLT).

TEG was performed using a TEG® 5000 Analyzer (Haemoscope Corporation, Skokie, IL, U.S.) using the intrinsic pathway activator kaolin (Haemonetics Corp.). In brief, 1 ml of citrated blood was added to 1 vial of kaolin. After mixing gently by inversion, 340 ml of this solution was added to the standard specimen cup. Then, 20 ml of 0.2 mol/L calcium was added to the standard specimen cup to remove the effect of citrate and the procedure was started without delay. TEG variables analysis included reaction time (R-time), clot formation time (K-time), α-angle, maximum amplitude (MA), and coagulation index (CI). LY30, measures the fibrinolytic system. All the TEG were performed by the same operator who was trained on the procedure. Quality-control checks were performed according to the manufacturer's instruction.

Table 1. Demographic Characteristics and Routine Coagulation Tests of 3 Groups.

Characteristic	LCIS patients (n = 35)	Lung cancer patients (n = 35)	Healthy controls (n = 35)	*P*
Age (yr)	65.77 ± 7.12	64.11 ± 8.45	63.29 ± 6.93	0.646*
Male, n (%)	26 (74.29)	26 (74.29)	26 (74.29)	1.000#
WBC ($\times 10^9$/L)	7.67 ± 1.89	7.26 ± 1.71	6.81 ± 1.19	0.090†
PLT ($\times 10^9$/L)	298.05 ± 95.08	292.49 ± 95.33	246.89 ± 70.88[b]	0.017*
HB (g/L)	120.33 ± 16.06	119.57 ± 18.13	124.83 ± 10.18	0.074†
PT (s)	11.5 (10.7-12.4)	11.3 (10.6-11.8)	11.2 (10.9-11.7)	0.402†
APTT (s)	29.78 ± 3.40	30.43 ± 3.90	30.74 ± 6.15	0.674*
TT (s)	11.97 ± 1.55	11.81 ± 1.49	11.96 ± 1.44	0.887*
FIB (g/L)	4.88 (3.68-6.00)	4.03 (3.44-4.90)[b]	3.61 (3.00-4.35)[a]	0.000†
D-dimer (μg/mL)	0.69 (0.27-5.21)	0.28 (0.18-0.86)[b]	0.20 (0.11-0.36)[a]	0.000†

Data were expressed as mean ± standard deviation (SD) or median (interquartile range) or *n* (%) as appropriate.
*One-way ANOVA test, †Kruskal-Wallis *H* test, #With chi-square test.
[a]$P < 0.01$, [b]$P < 0.05$ compared with LCIS group.
Abbreviations: LCIS, lung cancer related-ischemic stroke; WBC, white blood cell; PLT, platelet count; HB, hemoglobin; PT, prothrombin time; APTT, activated partial thromboplastin time; TT, thrombin time; FIB, fibrinogen.

In TEG analysis, hypercoagulability is indicated by shorter R-time and K-time, increased α-angle, MA and coagulation index. In this study, hypercoagulability was defined by having at least 3 abnormal TEG parameters. TEG parameters were considered abnormal if they existed outside the median (interquartile range) of the healthy controls. The presence of coagulopathy was evaluated by 2 experienced hematology and coagulation specialists.

Sample Size

Based on Navi's findings that the 6-month cumulative incidence of ischemic stroke was 3.0% in patients with cancer compared with 1.6% in control patients,[4] in our 1:1 matched case-control study, we estimated that we would need 28 subjects in each group to detect a statistically significant difference with 80% power at 5% level of significance (2-tailed).

Baseline Data Collection

We recorded age and gender, vascular risk factors such as hypertension, diabetes, hyperlipidemia, prior stroke, coronary artery disease and current smoking, lung cancer data (pathological types, tumor stage, treatment such as radiotherapy, chemotherapy and surgery), ischemic stroke data (stroke etiology, infarcts patterns and severity of focal neurological deficits) and cranial CT/magnetic resonance images (MRI)/diffusion-weighted image (DWI). Tumor were staged according to the TNM classification of American Joint Committee on Cancer.[21] Severity of focal neurological deficits were assessed by the National Institutes of Health Stroke Scale (NIHSS).

Statistical Analysis

All statistical analysis was performed using SPSS version 20.0 and GraphPad prism version 5.0. Categorical variables were described as frequency (percentage) and continuous variables as mean (SD) or median (interquartile range). Comparison among 3 groups were performed by one-way ANOVA with LSD post hoc test, Kruskal-Wallis test (Bonferroni adjusted post hoc) for continuous variables, and χ^2 test or Fisher's exact tests for categorical variables as appropriate. Correlations between continuous variables were assessed by Spearman's correlation coefficient. Variables with $P < 0.05$ in univariate analyses were entered to stepwise logistic regression analysis. The sensitivity and specificity of the TEG and routine coagulation test in evaluating coagulation states in patients and controls were calculated by receiver operating characteristic (ROC) curve. The ROC analysis utilized MedCalc v9.3 (MedCalc Software, Mariakerke, Belgium). Areas under ROC curves were compared using the DeLong method. Two-sided P value < 0.05 was considered statistically significant.

Results

Thirty-five LCIS patients (26 male, 9 female, mean age 65.77 ± 7.12 years) were recruited in this study. Meanwhile, 35 patients with lung cancer (LC group) and 35 healthy controls (HC group) were enrolled. Tables 1 and 2 showed the demographic, clinical and laboratory data for patients and controls. In this study, 27/35 (77.14%) of LCIS patients and 24/35 (68.57%) of lung cancer patients demonstrated evidence of hypercoagulability based on TEG. In routine coagulation tests, 18/35 (51.43%) of LCIS patients and 15/35 (42.85%) of lung cancer patients were hypercoagulability. Detection rate for hypercoagulability between TEG and routine coagulation test was statistically significant among LCIS patients ($P = 0.018$).

According to routine coagulation tests, the levels of PLT count, FIB and plasma D-dimer were significantly higher in LCIS group and LC group ($P < 0.05$). And the levels of FIB and plasma D-dimer were higher in LCIS group than that in LC group ($P < 0.05$). There were no significantly different among 3 groups with respect to WBC, PT, APTT and TT (Table 1).

One-way ANOVA showed significant differences among 3 groups with respect to R-time, K-time, α-angle, MA and

Table 2. The Clinical Data of Lung Cancer Related-Ischemic Stroke Patients.

Characteristic, n (%)	LCIS patients (n = 35)	Lung cancer patients (n = 35)	*P*
TNM Classification			
Stage I	3 (8.6%)	3 (8.6%)	1.000
Stage II	7 (20.0%)	8 (22.9%)	0.949
Stage III	9 (25.7%)	11 (31.4%)	0.650
Stage IV	16 (17.1%)	13 (37.1%)	0.411
Histopathological tissue type			
Adenocarcinoma	29 (82.9%)	27 (77.1%)	0.417
Squamous cell carcinoma	5 (14.3%)	6 (17.1%)	0.782
Small cell carcinoma	1 (2.9%)	2 (5.7%)	0.572
Cancer therapy			
Surgery	17 (48.6%)	13 (36.1%)	0.288
Chemotherapy	20 (57.1%)	21 (58.3%)	0.919
Radiotherapy	5 (14.3%)	6 (16.7%)	0.782
No anti-cancer therapy	10 (28.6%)	12 (33.3%)	0.664
Infarcts DWI patterns			
Single vascular territory	10 (28.6)	/	/
Multiple vascular territories	25 (71.4)	/	/
Admission NIHSS score	3-25	/	/

Abbreviations: LCIS, lung cancer related-ischemic stroke; DWI, diffusion-weighted image.

coagulation index (all $P < 0.05$). Post-hoc test showed that MA was significantly increased in LCIS group than that in LC group ($P = 0.011$) (Table 3 and Figure 1). There were not significant differences among patients with different pathological type and different cancer stages with respect to TEG parameters (Table 2).

Correlation analysis showed PLT count and FIB were significantly correlated with TEG parameters (Table 4), and FIB was strongly correlated with MA (r = 0.605) (Figure 2). No significant correlations were found between PT, APTT, TT and TEG parameters.

The levels of FIB, plasma D-dimer and MA that were significantly increased in LCIS group comparing with LC group were entered into multivariate models. The results revealed that plasma D-dimer (odds ratio [OR]: 1.002, 95% confidence interval [CI]: 1.001-1.003, $P = 0.012$) and MA (OR: 1.156, 95% CI: 1.033-1.294, $P = 0.017$) were independently associated with ischemic stroke in lung cancer patients.

In respect to identifying hypercoagulability in LCIS patients and lung cancer and healthy control, ROC curve showed that the area under the curve (AUC) of TEG was 0.795 ± 0.047, (95% CI: 0.704–0.868), the optimal cut-off value was 65.9, with a sensitivity of 60.00% and specificity of 89.4%, which was significantly higher than routine coagulation test 0.673 ± 0.059, (95% CI: 0.572–0.763) with sensitivity of 62.86%, specificity of 72.73% ($P = 0.04$) (Figure 3 and Figure 4).

Discussion

Our results suggested that hypercoagulability was the main cause of LCIS and that this hypercoagulability can be identified by TEG, which gave an added perspective to the diagnosis of hypercoagulability. We demonstrated that LCIS patients and lung cancer patients tended to be hypercoagulability by TEG, with decreased R-time and K-time while increased MA, angle and coagulation index. There was no difference in LY30 among 3 groups, indicating that hypercoagulability observed in LCIS patients and lung cancer patients were resulted from an enhanced tendency to clot formation rather than decreased activity in the fibrinolytic system. By multiple logistic regression and ROC analysis, we found that TEG was better for identifying hypercoagulability in LCIS patients than routine coagulation test.

Currently, there is great interest in the clinical applications of TEG. Nevertheless, the results of TEG in patients with cancer are still conflicting. Several studies suggested that TEG could use to identify hypercoagulability in various cancer and predict thromboembolic complications in colorectal, prostate and thyroid cancer patients.[13,14,22] However, there were also studies showed that no difference were found between patients with cancer and healthy controls, nor could TEG use to differentiate cancer patients with different stage or different pathological type.[11,15] It may be related to these studies carrying out on patients with mixed cancer or cancer patients at different stages. And some studies used only one of abnormal TEG parameters to define hypercoagulable state, which may be inadequate. In the present study, we studied in a single cancer and defined hypercoagulability by at least 3 abnormal TEG parameters. Therefore, we believed that our study was sufficient to demonstrate the value of the hypercoagulability that detected by TEG.

It is all known that routine coagulation tests, including PT, APTT, FIB and D-dimer are still widely used in hospitals, though they do not give information about the overall strength of the clot. So, it is unclear whether TEG test capable of completely reflecting the situations represented in routine coagulation tests. Previously, hyper-fibrinogenemia and thrombocytosis have been common reported in patients with cancer, and platelets and fibrinogen played important roles in cancer-induced hypercoagulability.[23] In line with these studies, we found that the levels of FIB, PLT count and plasma D-dimer were significantly higher in LCIS group than that in LC group and HC group. Significantly, we also found that FIB and PLT count were correlated with MA. The MA represents the contribution of platelet function and FIB and measures maximal clot strength. Recently, Wang et al identified the correlations of MA with the routine coagulation data.[24] Moreover, a study by Akay et al[10] correlated parameters of rotational TEG with routine coagulation tests in patients with cancer, which revealed maximum clot firmness (meaning MA) showed the strongest correlation with FIB and PLT count. Although the specific mechanism of hypercoagulability on these TEG required further exploration, MA

Table 3. Comparison of TEG Parameters Among 3 Groups.

TEG parameters	LCIS patients (n = 35)	Lung cancer patients (n = 35)	Healthy controls (n = 35)	*P*
R—time (min)	4.2 (3.3-4.7)	4.2 (3.4-4.8)	7.8 (6.1 to 8.9)[ac]	0.000[†]
K—time (min)	1.3 (1.1-2.1)	1.3 (1.0-1.7)	2.2 (2.0 to 3.9)[ac]	0.000[†]
α-angle (deg)	69.6 (55.5-74.5)	70 (57.5-74.5)	58.9 (44.5 to 62.7)[ac]	0.001[†]
MA (mm)	69.9 (65.6-71.9)	62.1 (59.6-65.7)[b]	57.5 (51.4 to 61.3)[ad]	0.000[†]
coagulation index	2.1 (0.5-2.8)	2.0 (0.5-2.8)	−2.2 (−5.4 to 0.8)[ac]	0.000[†]
LY30 (%)	0.3 (0.3-0.6)	0.2 (0.0-1.1)	0.0 (0.0 to 0.5)	0.234[†]

Data were expressed as median (interquartile range).
[†]Kruskal-Wallis *H* test.
[a]$P < 0.01$, [b]$P < 0.05$ compared with LCIS group, [c]$P < 0.01$, [d]$P < 0.05$ compared with LC group.
Abbreviations: TEG, thromboelastography; LCIS, lung cancer-related ischemic stroke; R-time, reaction time; K-time, clot formation time; MA, maximum amplitude; LY30, clot lysis at 30 minutes.

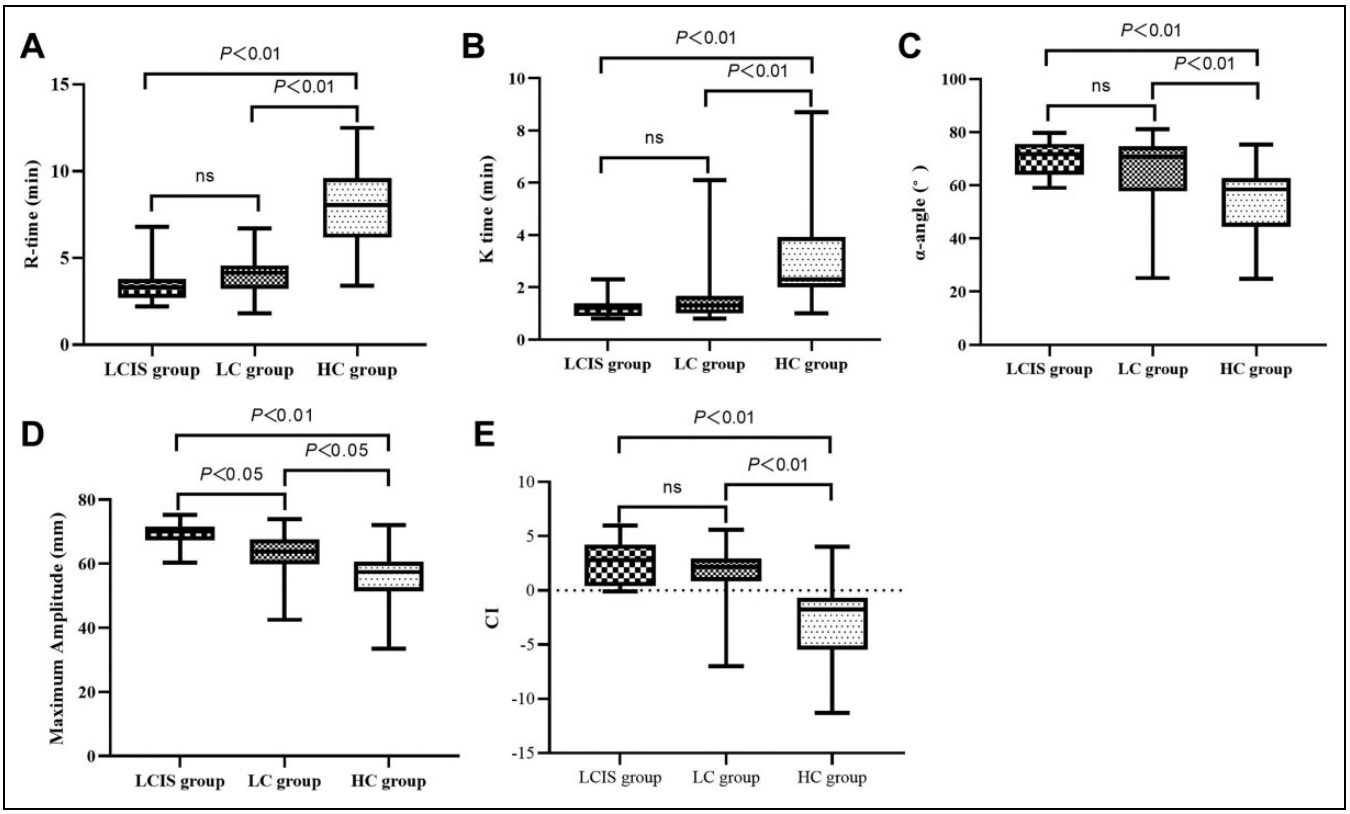

Figure 1. Comparison of major TEG parameters among 3 groups. R-time and K-time were significantly shorter while Angle, MA and CI levels were significantly higher in LCIS group and LC group than that in HC group (Kruskal-Wallis H test, $P < 0.05$). MA was significantly higher in LCIS group than that in LC group ($P = 0.011$). Abbreviations: TEG, thromboelastography; R-time, reaction time; K-time, clot formation time; MA, maximum amplitude; CI, coagulation index; LCIS, lung cancer related ischemic stroke; LC, lung cancer; HC, healthy control; ns, ns denotes not statistically different at $P = 0.05$.

appeared to be the most important TEG parameter for evaluating hypercoagulability in LCIS patients and lung cancer patients, which made TEG superior to routine coagulation tests.

Given high risk and serious sequelae of ischemic stroke in patients with cancer, many investigators have attempted to identify specific biomarkers of hypercoagulability in this patient population. Several laboratory evidences of hypercoagulability in cancer related stroke patients have been reported, including elevated levels of C-reactive protein, FIB, PLT count or leukocyte count, etc.[25,26] However, hypercoagulability is difficult to detect by routine coagulation tests unless the PLT count and FIB are markedly increased. In addition, higher levels of thrombin-antithrombin complex (TAT) and soluble fibrin monomer complex (SFMC) could serve as molecular markers of coagulation activation during cardiopulmonary bypass in patients who underwent aortic replacement surgery.[27] The TAT reflects the generation of thrombin through the prothrombinase

Table 4. Correlation Analyses of TEG Parameters and Routine Coagulation Tests.

		R-time (min)	Time (min)	α-Angle (deg)	MA (mm)	Coagulation index
PLT ($\times 10^9$/L)	R	−0.255	−0.274	0.251	0.570	0.336
	P	0.009	0.005	0.010	0.000	0.001
FIB (g/L)	R	−0.287	−0.340	0.298	0.605	0.388
	P	0.003	0.000	0.002	0.000	0.000

Abbreviations: PLT, platelet count; FIB, fibrinogen; MA, maximum amplitude; R-time, reaction time; K-time, clot formation time.

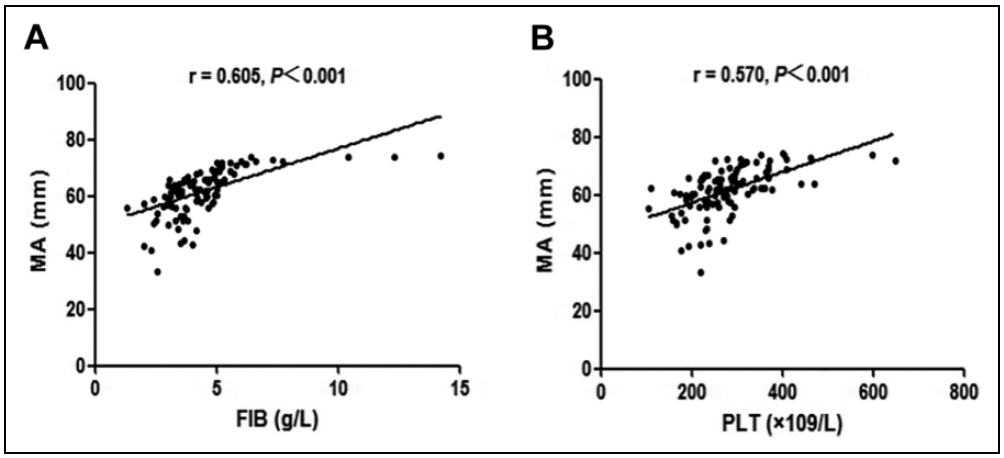

Figure 2. Correlations analysis between FIB and PLT with MA. A, MA value was significantly related to FIB. B, MA value was significantly related to PLT. Abbreviations: MA, maximum amplitude; FIB, fibrinogen; PLT, platelet count.

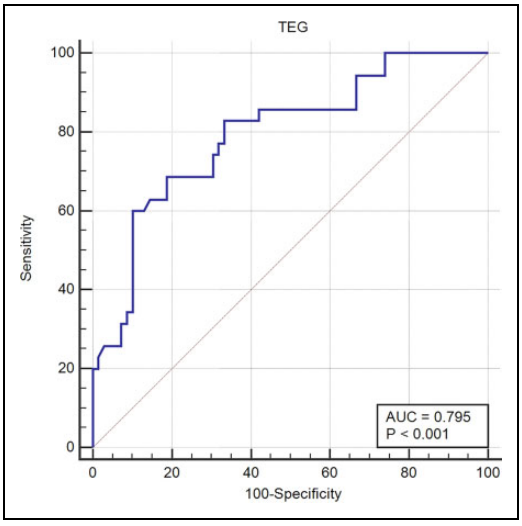

Figure 3. Receiver operating characteristic curve analysis of TEG in LCIS patients. The AUC was 0.795 ± 0.047 (95% CI: 0.704–0.868). The optimal cut-off value was 65.9. At this cut-off value, the sensitivity was 60.00% and the specificity was 89.40%. Abbreviations: TEG, thromboelastography; LCIS, lung cancer related ischemic stroke; AUC, Area under the curve.

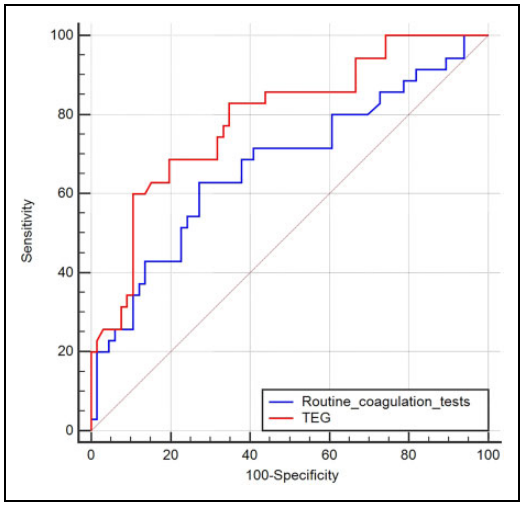

Figure 4. Receiver operating characteristic curve (ROC) analysis of TEG and routine coagulation tests in identifying hypercoagulability in LCIS patients. The area under the curve of TEG tracing was significantly larger than routine coagulation test ($P = 0.04$). Abbreviations: TEG, thromboelastography; LCIS, lung cancer related ischemic stroke; LY30, clot lysis at 30 minutes.

complex, and this reflects both extrinsic and intrinsic coagulation pathway activation. Whether TAT and SFMC can be served as biomarkers of hypercoagulability in patients with LCIS still needs further research in the future. Real-time monitoring of the coagulation status of cancer patients is challenging to clinicians. TEG is a global hemostatic test that can give immediate results reflecting platelet function, thrombin generation, fibrinogen levels, and fibrinolysis with bedside availability, which is not recorded by routine laboratory tests.[28] Recently, Toukh et al[14] demonstrated that the application of

TEG was valuable in predicting thrombotic complications (including transient ischemic attack and coronary artery disease) in prostate cancer patients. In the present study, increased MA and plasma D-dimer were independent predictors for ischemic stroke in lung cancer patients, and the areas under the ROC curve of TEG was significantly higher than routine coagulation tests. In the present study, these findings suggested that TEG may be superior to routine coagulation tests in evaluating hypercoagulability. Furthermore, the cut-off value of TEG revealed the degree of hypercoagulability in these subjects that may trigger the occurrence of ischemic stroke. As a result, clinicians can identify lung cancer patients who are at high risk of developing ischemic stroke based on this degree of hypercoagulability.

Although our results have significant implications, there is not without limitations. One limitation is that the relatively small size of patient population limited the generalizability of results for lung cancer patients with high risk of ischemic stroke. A larger, prospective, multicentered study with follow-up would be better to understand the ability of TEG in identifying hypercoagulability and may facilitate an ability to predict lung cancer patients those who may suffer ischemic stroke events. Another limitation is that the definition of hypercoagulability using TEG parameters has not been consistent yet. However, the presence of hypercoagulability was defined as at least 3 abnormal TEG parameters in this study, which was considered to be a relatively reliable definition.

In conclusion, the present study demonstrated that TEG may be superior to routine coagulation tests in identifying hypercoagulability of LCIS patients. Identification of hypercoagulability in lung cancer patients by TEG, especially MA, in lung cancer patients may help to detect those at high risk of ischemic stroke. Further studies should include a larger number of patients to confirm our findings and to determine if TEG can be applied on therapeutic interventions in this patient population.

Abbreviations

TEG: thromboelastography, LCIS: lung cancer and ischemic stroke, LC: lung cancer, HC: healthy controls, MA: maximum amplitude, PT: prothrombin time, APTT: activated partial thromboplastin time, TT: thrombin time, FIB: fibrinogen, PLT: platelet counts.

Authors' Note

Xuemei Quan, MD, and Qixiong Qin, MD, contributed equally to this work. XMQ, QXQ, and ZJL conceived and designed the research. HC, QQL, and CGM helped to screen patients and collect blood sample. QXQ, YC, and XTQ helped to perform TEG and collect the data. XMQ and QXQ analyzed the data and drafted the initial manuscript. ZJL and YFW critically revised the manuscript. ZJL provided financial support for this work. All authors read and approved the final manuscript.

Declaration of Conflicting Interests

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