Submitted: 06 September, 2022 Accepted: 01 December, 2022 Published: 08 May, 2023 DOI:10.22514/sv.2023.029

Open Access
Signa Vitae

ORIGINAL RESEARCH

The role of thromboelastogram (TEG) and routine coagulation indexes in evaluating the severity of acute pancreatitis in the early stage of onset

Wenmei Liang[1,*], Tonghua Liu[1], Minmin Gong[1]

[1]Department of Critical Care Medicine, The Affiliated Hospital of Zunyi Medical University, 563000 Zunyi, Guizhou, China

***Correspondence**
sandy33619@163.com
(Wenmei Liang)

Abstract

To study the role of thromboelastogram (TEG) and routine coagulation indexes in evaluating the severity of acute pancreatitis (AP) in the early stage of onset. A total of 123 patients with acute pancreatitis treated at our hospital from January 2018 to January 2021 were divided into three groups according to their disease severity. We analyzed the correlation and prognostic significance of TEG, routine coagulation indexes and blood platelet (PLT) count with disease severity. The clot reaction time (R-value), clot generation time (K-value), maximum width value (MA-value) and clot generation rate (α-angle) between the three groups were significantly different ($p < 0.05$). The level of prothrombin time (PT), D-dimer (D-D) and fibrinogen (FIB) and PLT count of the mild group were significantly different from the moderate and severe group as well as between the moderate and severe group ($p < 0.05$). Spearman correlation analysis showed that α-angle, MA-value, PT, D-D, activated partial thromboplastin time (APTT) and FIB were positively correlated, while platelet count, R-value and K-value were negatively correlated with the severity of AP. According to the follow-up results, 110 patients were divided into the survival (n = 95) or the death (n = 15) group. The R- and K-values in the survival group were significantly higher than those in the death group, while the α angle, MA-value, PT, APTT, D-D and FIB in the death group were significantly lower than those in the death group ($p < 0.05$). The severity and prognosis of patients with AP were directly related to the degree of coagulation disorder, and TEG combined with routine coagulation indexes demonstrated high evaluation significance for determining the severity and prognosis of AP patients.

Keywords

Thromboelastogram; Routine coagulation indexes; Acute pancreatitis; Severity of disease

1. Objects and methods

1.1 Basic information

This study was a retrospective review of adult patients with AP who underwent treatment at the Affiliated Hospital of Zunyi Medical University Hospital from January 2018 to January 2021. To assess the severity of AP, the "Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus" was consulted [1]. The diagnostic criteria for AP were as follows: (1) the pancreatitis was characterized by abdominal pain (persistent or radiating to the back); (2) serum amylase or lipase was elevated at least three times the upper limit of normal (ULN); (3) computed tomography (CT), magnetic resonance imaging (MRI) or transabdominal ultrasonography showing typical AP imaging results. At least two of the above three features were required to be present for diagnosing AP.

The study inclusion criteria were: (1) having at least two of the above three diagnostic criteria, (2) the presence of symptoms of acute abdominal pain, fever, nausea and vomiting, and (3) patients or family members provided signed informed consent. The exclusion criteria were: (1) patients with a history of thrombotic and hemorrhagic diseases, (2) the presence of hepatic and renal insufficiency as well as cardiovascular or cerebrovascular diseases, (3) patients with combined immune system, hematological and infectious diseases, (4) end-stage malignant diseases, (5) recent use of non-steroidal anti-inflammatory drugs or anticoagulants, (6) psychiatric diseases or medical history, (7) incomplete clinical data, and (8) poor compliance to treatment.

1.2 TEG and routine coagulation indexes testing

Briefly, 5 mL of fasting venous blood was collected from patients within 12 hours after admission to our hospital. The Haemonetics TEG 5000 Thrombelastograph Analyzer (Haemonetics Corp, Braintree, MA, USA) was used for TEG testing. Each TEG index, including clot reaction time (R-value), clot generation time (K-value), clot generation rate (α-angle) and maximum width value (MA-value), was recorded in detail. For routine coagulation index testing, the levels of prothrombin time (PT), activated partial thromboplastin time (APTT), D-dimer (D-D) and plasma fibrinogen (FIB) were investigated using the fully automatic CS2000 Hemagglutination Analyzer (SYSM EX, Kobe, Japan) and matching reagents. Their blood platelet (PLT) count was determined using the MEDONIC CA620 Blood Cell Analyzer (Boule, Domnarvsgatan 4, SE-163 53 Spånga, Sweden).

1.3 Observation indexes

The TEG, routine coagulation indexes and blood PLT count of patients in each group were compared. Then, the correlation between TEG, routine coagulation indexes, blood PLT count and disease severity was analyzed, and their significance on the prognosis of AP patients was evaluated.

1.4 Statistical analysis

The SPSS (v22.0, International Business Machines Corporation, Chicago, IL, USA) statistical software was used for data analysis. Continuous data are described as (n (%)) according to the χ^2 test, and measurement data are expressed as $\bar{x} \pm s$. The *t*-test was used to compare differences between groups, and analysis of variance (ANOVA) was used to analyze the differences between multiple groups. The correlation between TEG, routine coagulation indexes and disease severity was analyzed using Spearman's correlation analysis. $p < 0.05$ was used to indicate statistical differences.

2. Results

2.1 Baseline characteristics of AP patients

A total of 123 AP patients admitted to our hospital from January 2018 to January 2021 were selected and divided into 3 groups: mild (n = 45), moderate (n = 42) and severe (n = 36) according to their disease severity. Our analysis showed that the clinical data of the three groups were homogeneous ($p > 0.05$) (Table 1).

2.2 Comparison of TEG parameters between different groups of patients

Comparative analysis of the R-value, K-value, α-angle and MA-value between the three groups ($p < 0.05$) showed that patients in the severe group had the lowest R-value and K-value but the highest α-angle and MA-value, while those from the mild group had the highest R-value and K-value but lowest α-angle and MA-value (Table 2).

2.3 Comparison of routine coagulation indexes and blood PLT counts between different groups of patients

The levels of PT, APTT, D-D, FIB and PLT counts were also compared between the three groups ($p < 0.05$). The results revealed that all routine coagulation indexes were highest in the severe group except for PLT count, which was the lowest. Comparatively, opposite results were obtained for the mild group. In addition, the level of APTT in the mild and moderate groups was not statistically significant ($p > 0.05$), while the levels of PT, D-D, FIB and PLT were significantly different between the two groups ($p < 0.05$). All indexes compared between the mild and severe group or the moderate and severe group were statistically significant ($p < 0.05$) (Table 3).

2.4 Analysis of the correlation between TEG, routine coagulation indexes and disease severity

Spearman analysis was used to assess the correlation between each index and disease severity. Our results showed that the α-angle, MA-value, PT, APTT and the levels of D-D and FIB were positively correlated with the severity of AP (r = 0.798, 0.813, 0.805, 0.885, 0.815 and 0.820, respectively, $p < 0.001$). However, PLT counts, R-value and K-value were negatively correlated with AP severity (r = -0.817, -0.824 and -0.830, respectively, $p < 0.001$) (Table 4).

2.5 Association of TEG and routine coagulation indexes with the survival of AP patients

In this study, during the 1-year follow-up visits, 2 patients were lost to follow-up, and 1 died due to other diseases. Thus, a total of 110 patients were successfully followed, demonstrating a follow-up rate of 89.43%. According to the follow-up results, the 110 patients were divided into a survival group (n = 95) or a death group (n = 15). Patients in the survival group had significantly higher R- and K-values but significantly lower α-angle, MA-value, PT, APTT and levels of D-D and FIB than those in the death group ($p < 0.05$) (Table 5).

2.6 Analysis of the value of TEG and routine coagulation indexes for disease severity and prognosis assessment

Further analysis comparing the R-value, K-value, α-angle, MA-value, PT, APTT, D-D and FIB using individual assays demonstrated higher sensitivity and specificity when the indexes were combined in determining the severity of AP and patients' prognoses ($p < 0.05$) (Table 6).

3. Discussion

AP is a relatively common clinical disorder of the digestive system associated with cholelithiasis, biliary infection and pancreatic duct obstruction [2]. It is an inflammatory disease in which pancreatin is activated in the pancreas by multiple etiologies, causing a local or systemic reaction in the pancreatic tissues [3]. In clinics, a greater variation in the status of AP

TABLE 1. Comparison of clinical data of patients in the three groups ($\bar{x} \pm s$).

Variables	Case	Gender (male/female)	Age (yr)	Body mass index (kg/m^2)
Mild group	45	25/20	54.00 ± 6.21	20.50 ± 1.12
Moderate group	42	23/19	54.50 ± 6.19	20.50 ± 1.10
Severe group	36	20/16	54.50 ± 6.17	21.00 ± 1.08
F value		0.005	0.093	2.623
p value		0.940	0.911	0.077

TABLE 2. Comparison of TEG parameters in patients from each group ($\bar{x} \pm s$).

Variables	Case	R-value (min)	K-value (min)	A-angle (°)	MA-value (mm)
Mild group	45	6.89 ± 0.78	1.99 ± 0.45	65.30 ± 5.74	66.98 ± 7.02
Moderate group	42	5.10 ± 0.95	1.39 ± 0.74	69.35 ± 6.85	69.47 ± 8.85
Severe group	36	4.32 ± 1.02	0.87 ± 0.70	72.38 ± 7.54	73.99 ± 8.12
F value		86.062	31.387	11.468	7.755
p value		0.000	0.000	0.000	0.001

R-value: clot reaction time; K-value: clot generation time; A-angle: clot generation rate; MA-value: maximum width value.

TABLE 3. Comparison of routine coagulation indexes and blood platelet counts of patients from each group ($\bar{x} \pm s$).

Variables	Case	PT (s)	APTT (s)	D-D (mg/L)	FIB (g/L)	PLT ($\times 10^9$/L)
Mild group	45	13.85 ± 1.14	28.92 ± 5.10	1.50 ± 0.71	2.43 ± 1.08	100.20 ± 35.60
Moderate group	42	14.30 ± 1.11	30.05 ± 6.62	1.78 ± 0.69	4.05 ± 1.01	78.89 ± 25.33
Severe group	36	16.85 ± 1.20	52.30 ± 5.84	3.69 ± 0.70	5.89 ± 1.05	50.10 ± 23.20
F value		76.502	193.058	111.351	109.138	29.864
p value		0.000	0.000	0.000	0.000	0.000
t mild *vs.* moderate		1.863	0.895	1.863	7.213	3.196
p mild *vs.* moderate		0.022	0.124	0.022	0.000	0.000
t mild *vs.* severe		11.497	19.219	13.881	14.505	7.291
p mild *vs.* severe		0.000	0.000	0.000	0.000	0.000
t moderate *vs.* severe		9.743	15.617	12.106	7.876	5.201
p moderate *vs.* severe		0.000	0.000	0.000	0.000	0.000

PT: prothrombin time; APTT: activated partial thromboplastin time; D-D: D-dimer; FIB: fibrinogen; PLT: blood platelet.

TABLE 4. Analysis of the correlation between TEG, routine coagulation indicators and disease severity.

Indexes	Severity of AP	
	r	*p* value
a-angle	0.798	0.033
MA-value	0.813	0.020
PT	0.805	0.025
APTT	0.885	0.008
D-D	0.815	0.018
FIB	0.820	0.014
PLT	−0.817	0.017
R-value	−0.824	0.012
K-value	−0.830	0.010

AP: acute pancreatitis; α-angle: clot generation rate; MA-value: maximum width value; PT: prothrombin time; APTT: activated partial thromboplastin time; D-D: D-dimer; FIB: fibrinogen; PLT: blood platelet; R-value: clot reaction time; K-value: clot generation time.

TABLE 5. Analysis of TEG and routine coagulation indexes in patients with different prognostic conditions.

Variables	Case	R-value (min)	K-value (min)	a-angle (°)	MA-value (mm)	PT (s)	APTT (s)	D-D (mg/L)	FIB (g/L)
Survival group	95	5.88 ± 1.04	1.92 ± 0.56	65.88 ± 3.04	63.65 ± 8.52	12.85 ± 2.59	31.89 ± 7.02	1.59 ± 0.90	3.44 ± 1.35
Death group	15	3.24 ± 0.85	1.56 ± 0.81	76.08 ± 9.25	77.53 ± 8.49	16.77 ± 5.52	54.10 ± 10.01	4.92 ± 0.90	6.06 ± 1.40
t value		9.340	2.166	8.393	5.866	4.51	10.694	13.317	6.951
p value		0.000	0.033	0.000	0.000	0.000	0.000	0.000	0.000

R-value: clot reaction time; K-value: clot generation time; α-angle: clot generation rate; MA-value: maximum width value; PT: prothrombin time; APTT: activated partial thromboplastin time; D-D: D-dimer; FIB: fibrinogen.

TABLE 6. Analysis of the value of TEG and routine coagulation indexes for the assessment of disease severity and prognosis.

Indexes	Severity of AP			Prognosis			
	95% CI	Sensitivity (%)	Specificity (%)	95% CI	Sensitivity (%)	95% CI	Specificity (%)
A-angle (°)	0.733∼0.840	74.21	68.23	0.735∼0.841	75.20	0.740∼0.812	69.20
MA-value (mm)	0.735∼0.868	75.02	69.33	0.738∼0.852	74.66	0.745∼0.849	70.11
R-value (min)	0.768∼0.855	72.01	70.51	0.769∼0.856	73.36	0.773∼0.849	71.20
K-value (min)	0.552∼0.678	62.52	61.30	0.458∼0.632	52.52	0.439∼0.648	60.33
PT (s)	0.798∼0.886	69.62	70.20	0.754∼0.888	69.98	0.750∼0.892	70.21
APTT (s)	0.810∼0.932	75.65	71.20	0.818∼0.935	76.20	0.828∼0.920	71.35
D-D (mg/L)	0.795∼0.889	71.21	72.20	0.854∼0.954	74.52	0.861∼0.943	70.21
FIB (g/L)	0.820∼0.963	76.85	70.33	0.865∼0.987	75.50	0.871∼0.979	71.54
Combined	0.885∼0.996	91.20	88.95	0.875∼0.994	91.23	0.886∼0.988	88.86

AP: acute pancreatitis; A-angle: clot generation rate; MA-value: maximum width value; R-value: clot reaction time; K-value: clot generation time; PT: prothrombin time; APTT: activated partial thromboplastin time; D-D: D-dimer; FIB: fibrinogen; CI: Confidence intervals.

patients is usually observed, as most mild AP patients can be cured after active treatments. However, patients with severe AP often suffer from acute morbidity and rapid disease progression and are highly susceptible to multiple organ failure; thus, they have a mortality rate of up to 30% [4]. Therefore, early assessment of the condition and disease severity are important to provide a reliable basis for developing a targeted treatment strategy and improving patients' prognoses.

In the early stages of AP, the pancreas releases a large amount of cytokines and inflammatory mediators, which can activate the coagulation pathway and initiate the exogenous and endogenous coagulation pathways, leading to disorders of coagulation function in patients [5]. Previous studies showed that the severity of AP and the development of complications were closely associated with the degree of dysfunction in the coagulation system [6, 7]. PT, APTT, FIB, D-D and other biomarkers can be used as indicators to assess routine coagulation function in clinics to effectively reflect the coagulation function of patients in the initial coagulation stage. APTT and PT have the advantages of no blood cell involvement in the detection process and do not involve the influence of PLT aggregation and adhesion on coagulation function. Comparatively, FIB can reflect the change in quantity but not in its function. D-D is a marker of secondary fibrinolysis, and its alterations in organisms suggest the possible formation of microcirculatory thrombosis secondary to the alteration of fibrinolysis [8, 9]. In this study, we found differences in the levels of PT, APTT, D-D and FIB as well as blood PLT counts between patients with different severity of AP. This finding indicates that a more severe patient condition would result in higher levels of coagulation indicators, thus, urging the need for a timely targeted treatment plan. However, reports have shown that the assessment of the severity and prognosis of AP using coagulation indexes alone could have some clinical limitations [8].

In the thromboelastogram, R-value can effectively reflect the activity of clotting factors, while K-value and α-angle can effectively reflect the rate of clot formation, and MA-value and G-value can reflect the maximum intensity of clot formation [10, 11]. In this present study, the data showed statistical differences in R-values, K-values, α-angle and MA-values between the three groups of patients with different severity of AP. In addition, thromboelastography parameters were significantly different in patients with mild, moderate and

severe AP. Previous studies also reported that the coagulation function of AP patients was disordered and directly related to the severity of the disease [12]. Additionally, we hypothesize that the underlying mechanism might be due to significantly higher levels of PLT and fibrinogen in the plasma of patients with severe AP, resulting in stronger and more stable blood clots and a faster clot formation rate [8, 9]. In addition, the results of our study also showed that α-angle, MA-value, PT, APTT, D-D and FIB were positively correlated with AP disease severity ($p < 0.001$), while PLT, R-value, and K-value were negatively correlated with AP disease severity ($p < 0.001$). The results also suggested that TEG and routine coagulation indexes have a certain relationship with AP disease severity, which might be important in assessing the severity of a patient's disease.

The results of this study showed that the R- and K-values of patients in the survival group were significantly higher than those in the death group, while the α-angle and MA-value were significantly lower than those in the death group. The data suggested that the degree of TEG indexes disorders in AP patients significantly correlated with the prognosis of the disease, similar to the study of ChengFan *et al.* [13].

4. Conclusions

In this study, we found that α-angle, MA-value, PT, APTT, D-D, FIB level and blood PLT counts were positively correlated with AP disease severity, while R-value and K-value were negatively correlated with AP disease severity. Therefore, TEG combined with routine coagulation indexes might be important in assessing AP severity and patients' prognosis. In the future, we aim to further explore the underlying mechanism of the coagulation system in pancreatitis-associated lung injury.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

WL—designed the research study. TL—performed the research and analyzed the data. MG—wrote the manuscript. All authors read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was obtained from the Ethics Committee of the Affiliated Hospital of Zunyi Medical University (Approval no. KLL-2022-698). Written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

ACKNOWLEDGMENT

We thank the peer reviewers for their valuable suggestions.

FUNDING

This work was supported by Science and Technology Fund Project of Guizhou Provincial Health Commission (Grant No. gzwkj2023-114).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

[1] Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, *et al*. Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013; 62: 102–111.

[2] Wang G, Gao C, Wei D, Wang C, Ding S. Acute pancreatitis: etiology and common pathogenesis. World Journal of Gastroenterology. 2009; 15: 1427.

[3] Garg PK, Singh VP. Organ failure due to systemic injury in acute pancreatitis. Gastroenterology. 2019; 156: 2008–2023.

[4] Mederos MA, Reber HA, Girgis MD. Acute pancreatitis. JAMA. 2021; 325: 382.

[5] Dumnicka P, Maduzia D, Ceranowicz P, Olszanecki R, Drożdż R, Kuśnierz-Cabala B. The interplay between inflammation, coagulation and endothelial injury in the early phase of acute pancreatitis: clinical implications. International Journal of Molecular Sciences. 2017; 18: 354.

[6] Fan C, Song Y, Wang X, Mao C, Xiong Y. Identification of early derangements of coagulation, hematological and biochemical profiles in patients with acute pancreatitis. Clinical Biochemistry. 2022; 109–110: 37–43.

[7] Li Q, Liu C, Ling L, Huang X, Chen S, Zhou J. Association between coagulation function and prognosis in patients with acute pancreatitis. Nan Fang Yi Ke Da Xue Xue Bao. 2022; 42: 1006–1012. (In Chinese)

[8] Badhal SS, Sharma S, Saraya A. Prognostic significance of D-dimer, natural anticoagulants and routine coagulation parameters in acute pancreatitis. Tropical Gastroenterology. 2012; 33: 193–199.

[9] Liu C, Zhou X, Ling L, Chen S, Zhou J. Prediction of mortality and organ failure based on coagulation and fibrinolysis markers in patients with acute pancreatitis. Medicine. 2019; 98: e15648.

[10] Othman M, Kaur H. Thromboelastography (TEG). Methods in Molecular Biology. 2017; 26: 533–543.

[11] Whiting D, DiNardo JA. TEG and ROTEM: technology and clinical applications. American Journal of Hematology. 2014; 89: 228–232.

[12] Florkiewicz H, Korolko A, Bielak J. Blood clotting disorders in acute pancreatitis. Polski Tygodnik Lekarski. 1969; 24: 521–523. (In Polish)

[13] Fan C, Song Y, Wang X, Mao C, Xiong Y. Identification of early derangements of coagulation, hematological and biochemical profiles in patients with acute pancreatitis. Clinical Biochemistry. 2022; 109–110: 37–43.

How to cite this article: Wenmei Liang, Tonghua Liu, Minmin Gong. The role of thromboelastogram (TEG) and routine coagulation indexes in evaluating the severity of acute pancreatitis in the early stage of onset. Signa Vitae. 2023; 19(3): 132-136. doi: 10.22514/sv.2023.029.