

Investigation of the Value of Coagulation Parameters in Thromboembolic Events Among Patients Not Receiving Anticoagulant Therapy

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ABSTRACT

Objective: The main causes of thromboembolic events are atherosclerosis, vascular endothelial injury, and hypercoagulability. Coagulation is activated through two basic mechanisms, including intrinsic and extrinsic pathways, leading to thrombin production as a result of a series of enzymatic reactions. The intrinsic pathway is evaluated with activated partial thromboplastin time (APTT) and extrinsic pathway with prothrombin time (PT). This study aimed to investigate the relationship between thromboembolic diseases and coagulation parameters.

Material and Methods: Patients diagnosed with acute ischemic stroke (AIS) (n=216), acute coronary syndrome (ACS) (n=25), pulmonary thromboembolism (PTE) (n=15), and patients without an emergency pathology (n=71) (Control Group) in the emergency department were retrospectively reviewed in the period from 01 November 2016 to 31 March 2019.

Results: The APTT (25.61±5.93 sec), PT (12.05±2.26 sec), and INR (1.04±0.19) values of the AIS group were statistically significantly lower compared to APTT (27.98±3.21 sec), PT (12.58±2.18 sec), and INR (1.10±0.15) values of the control group (p = <0.001, <0.001 and <0.001 respectively). Similarly, the APTT (27.15±8.97 sec), PT (12.26±2.75 sec), and INR (1.03±0.25) values of the ACS group were statistically significantly lower compared to those of the control group (p=0.012, 0.030, and 0.001, respectively). There was no statistically significant difference between the PTE group and control group in terms of APTT, PT, and INR values (p= 0.133, 0.758, and 0.711, respectively).

Conclusion: Shortened APTT levels in cases without a history of anticoagulant use at the time of admission can be considered to be a predictive and effective tool for clinicians in arterial embolic events (AIS and ACS).

Key words: Activated Partial Thromboplastin Time, Acute Coronary Syndrome, Acute Ischemic Stroke, International Normalized Ratio, Prothrombin Time, Pulmonary Thromboembolism

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INTRODUCTION

Despite great progress in the diagnosis and management of thromboembolic diseases, the recognition of them still challenging for emergency physicians. The main causes of thromboembolic events are atherosclerosis, vascular endothelial injury, and hypercoagulability. Coagulation is activated through two basic mechanisms, including intrinsic and extrinsic pathways, leading to thrombin production as a result of a series of enzymatic reactions. The intrinsic and common pathways are evaluated with activated partial thromboplastin time (APTT) and extrinsic and common pathways with prothrombin time (PT)(1). The APTT is a medical test that characterizes blood coagulation and measures the time necessary to generate fibrin from initiation of the intrinsic pathway. Normal APTT times require the presence of the following coagulation factors: I, II, V, VIII, IX, X, XI, and XII. Dysregulation of the intrinsic pathway would be expected to contribute to thromboembolic disease (2,3).

Shortening of the APTT is considered to have clinical relevance with an increased risk of thromboembolism (4).

This study aimed to investigate the relationship between thromboembolic diseases and coagulation parameters.

MATERIAL and METHODS

Patients diagnosed with acute ischemic stroke (AIS), acute coronary syndrome (ACS), and pulmonary thromboembolism (PTE) in the emergency department in the period from 01 November 2016 to 31 March 2019 were retrospectively reviewed. This study included a total of 327 patients, including those diagnosed with AIS (n=216), ACS (n=25), and PTE (n=15) in the emergency room, who did not receive anticoagulant therapy for any reason in the past, and 71 control patients with no history of stroke, coroner artery disease, or pulmonary thromboembolism.

Patients with, coagulopathic disorders, renal failure and use of anticoagulants (warfarin and heparin) were excluded. The APTT, PT, and international normalized ratio (INR) values of the patients, which were measured at the time of admission, were recorded and compared between the groups for statistical analysis.

Laboratory Assays: PT-INR, and APTT (Sysmex CS-2500, Kobe 651-0073 Japan) were measured in the emergency biochemistry laboratory.

Power analysis: The sample size was calculated with an alpha value of 0.05, 80% power, an enrollment ratio of 1, and APTT values of 28.5 in group 1 (control group) and 26.9 in group 2 (patients with venous thromboembolism), yielding that 48 patients in either group making a total of 96 participants would be included in the study (5).

Statistical analyses: The categorical variables were presented as frequency and percentages. Continuous variables were presented as mean \pm standard deviation. The Kolmogorov Smirnov test was used for testing whether the variables were distributed normally. Student's t-test was used for binary comparison of continuous variables conforming to the normal distribution, Mann-Whitney U test for non-compliant ones, and Chi-square test for comparison of categorical data. A p-value of < 0.05 was considered statistically significant. The statistical analysis software was SPSS Statistics for Windows, version 22.0 (SPSS Statistics for Windows, Version 22.0. IBM Corp., Armonk, N.Y., USA)..

RESULTS

Two hundred and sixteen AIS patients, 25 ACS patients, 15 PTE patients and 71 controls were included in the study. The clinical characteristics of patients and controls are presented in Table 1. Significant differences were observed between the controls and patients in age, sex, hypertension, and diabetes mellitus. The APTT (25.61 ± 5.93 sec), PT (12.05 ± 2.26 sec), and INR (1.04 ± 0.19) values of the AIS group were found to be statistically significantly lower compared to the APTT (27.98 ± 3.21 sec), PT (12.58 ± 2.18 sec), and INR (1.10 ± 0.15) values of the control group (p values were <0.001 , <0.001 , and <0.001 , respectively). Similarly, the APTT (27.15 ± 8.97 sec), PT (12.26 ± 2.75 sec), and INR (1.03 ± 0.25) values of the ACS group were found to be statistically significantly lower compared to those of control group (p values were 0.012, 0.030, and 0.001, respectively). No statistically significant difference was observed between the APTT (27.89 ± 9.76 sec), PT (12.66 ± 1.42 sec), and INR (1.12 ± 0.16) values of the PTE group and those of the control group (p values were 0.133, 0.758, and 0.711, respectively) (Table 2).

Figure 1: Study Flow Chart

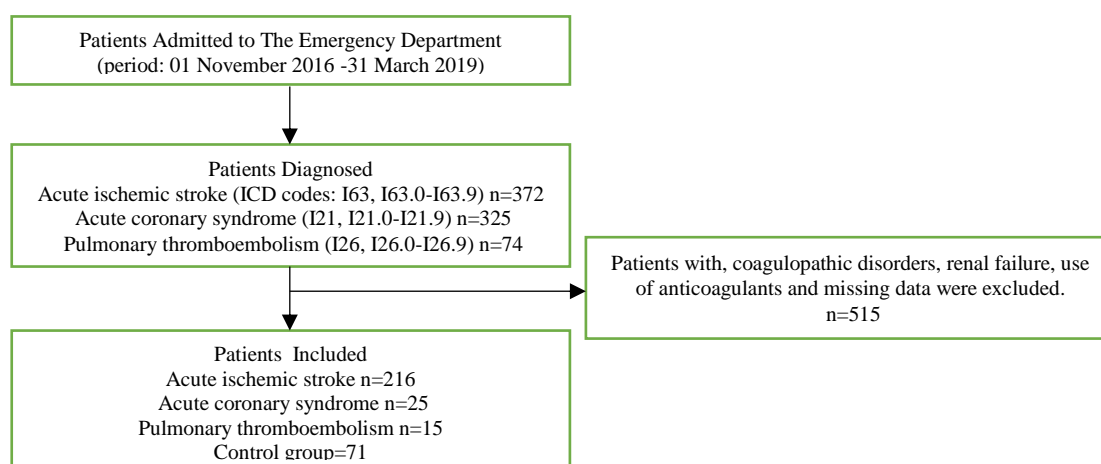


Table 1: Demographics of The Patients

	Patients (AIS, ACS, PTE) n=266	Control Group (n=71)	P value
Age, year	69.4±12.7	65.4±17.1	0.035*
Male Sex, %	63.9 (170)	46.4 (33)	0.013**
Hypertension, %	59 (157)	43.7 (31)	0.03**
Diabetes mellitus, %	40.9 (109)	21.1 (15)	0.003**

ACS: acute coronary syndrome, AIS: acute ischemic stroke, APTT: activated partial thromboplastin time, INR: international normalized ratio, PT: prothrombin time, PTE: pulmonary thromboembolism *Student t test, **Chi-square analysis

Table 2: Comparison of the Groups

Coagulation parameters	AIS (n=216)	ACS (n=25)	PTE (n=15)	Control group (n=71)	(p*)	AIS vs Control (p **)	ACS vs Control (p **)	PTE vs Control (p **)
APTT (sec.)	25.61±5.93	27.15±8.97	27.89±9.76	27.98±3.21	<0.001	<0.001	0.012	0.133
PT (sec.)	12.05±2.26	12.26±2.75	12.66±1.42	12.58±2.18	<0.001	<0.001	0.030	0.758
INR	1.04±0.19	1.03±0.25	1.12±0.16	1.10±0.15	<0.001	<0.001	0.001	0.711

ACS: acute coronary syndrome, AIS: acute ischemic stroke, APTT: activated partial thromboplastin time, INR: international normalized ratio, PT: prothrombin time, PTE: pulmonary thromboembolism, *Kruskal Wallis, **Mann-Whitney U Test

DISCUSSION

There are studies in the literature examining the relationship between APTT AIS, ACS, and PTE (1,5,6). To the best of our knowledge, our study is the first study to examine these three diseases at once.

The most important cause of stroke occurs when a thrombus occludes or obstructs a brain artery. Lin et. al investigated the association of the shortened APTT with AIS in their study. They concluded that shortened APTT was a marker for thrombosis and could be used to evaluate AIS severity and neurological prognosis. In their study, the reference range for APTT was 23.3-39.3 seconds and the mean normal value was 28.4 seconds. Therefore they defined the shortened APTT as the APTT of fewer than 28.4 seconds (1). Similarly, in our study, it was found that the APTT time was significantly shorter in the AIS group compared to the control group.

In the study investigating the relationship between APTT and ACS, Abdullah et al. reported that the presence or absence of shortened APTT can be used as a positive or negative predictive marker in patients with suspected coronary artery disease (7). In the study investigating the relationship between APTT and ACS by Anvari et al., it was reported that significantly shortened APTT times were detected in STEMI or non-STEMI patients compared to the control group (6). Similar to both studies, in our study, the APTT time was significantly shorter in the ACS group compared to the control group.

Venous thrombosis and arterial thrombotic disease have traditionally been thought of as separate processes; however, they share many similarities in pathophysiology and risk factors (8). In their study, Tripodi et al. compared the relationship between VTE and APTT. Shortened APTT was evaluated as a risk factor for VTE regardless of thrombophilia and factor 8 level (5). Differently, in our study, when the VTE group was compared with the control group, no statistically significant difference was found between them in terms of APTT durations. We consider that the reason we obtained different results is due to the difference in assessment methods.

Tripodi et al. used the APTT ratio (test value/reference value) as the evaluation parameter and determined 0.87 as the cut-off value. In our study, we compared the groups in terms of mean APTT results without determining any cut-off value.

Limitations: This study has the following limitations. First patients were tested after their thrombotic episodes. Second, the role played by high levels of coagulation factors in shortening the APTT could not be evaluated, even if the conditions were known to affect the test (patients with, coagulopathic disorders, renal failure, and use of anticoagulants) were excluded.

CONCLUSION

Shortened APTT levels in cases without a history of anticoagulant use at the time of admission can be considered to be a predictive and effective tool for clinicians in arterial embolic events (AIS and ACS). We recommend that multicentre prospective cohort studies with a larger patient population investigating coagulation parameters in cases with PTE, which is induced by venous occlusion should be conducted in the future.

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Ethical issues: All authors declare originality of research.

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