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Evaluation of Coagulopathy Frequency and Risk Factors in Trauma Patients in the Intensive Care Unit

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Abstract

Background: Posttraumatic coagulopathy is a common problem; however, the risk factors are not fully known.
Objectives: This study aimed to retrospectively determine the frequency of coagulopathy related to trauma, as well as risk factors and their effects, on prognosis among patients admitted to the intensive care unit (ICU) after trauma.
Methods: In total, 184 patients who were admitted to the 20-bed general adult ICU of Ankara Yıldırım Beyazıt University Medical Faculty Hospital between 2011 and 2017 after trauma were retrospectively analyzed. Two groups were selected by examining the laboratory results of the patients (considering the 1st- and 3rd-day platelet count), Prothrombin Time (PT), activated Partial Thromboplastin Time (aPTT), and International Normalized Ratio (INR) values with and without trauma-associated coagulopathy.
Results: The mean age of 184 patients included in the study was obtained at 41.77±16.91 years. The majority of the patients (n=149; 81%) were male. Coagulopathy was detected in 78 (42.4%) patients (on the first day [n=60; 32.6%] and on the third day [n=18; 9.8%]). It was found that patients with coagulopathy had more comorbidities (OR=3.080; %95 CI: 1.033-9.176), lower Glasgow Coma Score (GCS) (OR: 0.890; %95 CI: 0.827-0.957), lower Revised Trauma Score (RTS) (OR=0.699; %95 CI: 0.568-0.862), higher Acute Physiology and Chronic Health Evaluation-II (APACHE-II) score (OR=1.092; %95 CI: 1.041-1.145), lower albumin values (OR:0.392; %95 CI: 0.203-0.758), and higher 28-day mortality (P<0.005), compared to patients without coagulopathy.
Conclusion: In this study, co-morbidity, high APACHE-II, low GCS, RTS, and albumin levels were determined as independent risk factors for the development of post-traumatic coagulopathy. Since it is not possible to change the risk factors of critical trauma patients, such as GCS and co-morbidity, it is taught that the prevention of risk factors, such as hypoalbuminemia, with appropriate approaches can reduce the incidence of coagulopathy, as well as the mortality rate.

Keywords: Coagulopathy, Trauma, Trauma-induced coagulopathy

1. Background

Trauma-induced coagulopathy (TIC) has been defined initially in 2013 in major trauma patients. In these patients, who have a TIC frequency of 10% to 25%, a four-fold increase in mortality risk has been notified with a higher transfusion requirement, compared to patients having normal coagulation (1). Therefore, it is vital to distinguish the risk factors that cause TIC.

The cause of TIC has not been quite understood yet. Certain studies that have been carried out regarding this subject point out six factors in the development of this complication, including tissue damage/trauma, hypoperfusion, hemodilution, hypothermia, acidosis, and inflammation (2). Acidosis and hypothermia can cause coagulopathy by various mechanisms (3). Excessive fluid resuscitation has been shown to be harmful in post-traumatic hemorrhages (4). It has been notified via certain research studies that TIC is an endogenic event that starts prior to a medical intervention (5). This feature sets this condition apart from consumption coagulopathy or dilutional coagulopathy which are well-known in trauma patients (6). Early diagnosis of patients having risk for TIC might be the primary and vital step in preventing TIC by examining clinical findings and laboratory results. Early detection of TIC's risk factors, measures taken against these factors, as well as the initiation of therapy, might be effective for severely injured patients.

2. Objectives

This study aimed to search whether or not the frequency of coagulopathy and its risk factors have effects on mortality among patients admitted to the intensive care unit (ICU) after trauma.

3. Methods

Hospital/Patient record system and files of 184 patients admitted to the general adult 20-bed ICU of Ankara Yıldırım Beyazıt University Medical Faculty Hospital after trauma between January 2011 and September 2017 have been examined retrospectively. Patients that were under 18 years old, those who had coagulopathy anamnesis beforehand, cases with liver diseases, or patients whose coagulation values had not

been controlled during the first three days were excluded from the study.

After reviewing the literature, many differences were found in laboratory values for coagulopathy. This study is based on both the reference range of the hospital and the literature (7-9). Accordingly, patients have been separated into two groups (with and without coagulopathy). Patients with thrombocyte count <100 000/μL on the first and third days, Prothrombin Time (PT) >16 s, activated Partial Thromboplastin Time (aPTT)>40 s, and International Normalized Ratio (INR)>1.6 were accepted as having coagulopathy.

The recorded information included age, gender, co-morbidities, anticoagulant usage history, Revised Trauma Score (RTS), Glasgow Coma Score (GCS), Acute Physiology and Chronic Health Evaluation (APACHE-II) Score, trauma reason (in-vehicle traffic accident, out-of-vehicle traffic accident, battery, gunshot/firearm injuries, and falling from a height), whether or not having multiple trauma or single organ trauma, blood and blood transfusion administered until coagulopathy has been detected, posttraumatic surgical operation, cardiac resuscitation or intubation history until coagulopathy has been detected, length of hospitalization and length of ICU stay, at which day coagulopathy was detected (if detected), hypothermia, hyperthermia, whether the patient became infected or not, and 28-day mortality. Moreover, complete blood count on the first and third days, coagulation parameters (PT, PTT, INR, D-dimer, Fibrinogen), albumin, liver and kidney function tests, and blood gas values of patients have been evaluated in this study.

The data were analyzed in SPSS software (Version 20, SPSS Inc. Chicago IL. USA) through descriptive statistics that were presented as mean±SD or median (minimum-maximum) for continuous variables. The nominal variables were also expressed as frequency and percentages (%). The Chi-square test was used to compare categorical variables between groups, and the independent sample t-test was utilized for parametric data in comparing digital values. Non-parametric values were evaluated employing the Mann-Whitney U test. Moreover, univariate and multivariate logistic regression analyses were performed to assess the association between coagulopathy and the risk factors findings. A P-value of <0.05 was considered statistically significant.

4. Results

Out of 184 patients, coagulopathy was detected in 78 (42.4%) cases (on the first day [32.6%] and the third day [9.8%]). When patients with and without coagulopathy were compared; It was determined that co-morbidities were higher (p<0.05) and albumin values were lower (p<0.05) in patients who developed coagulopathy. Furthermore, 23.1% of the patients who developed coagulopathy had accompanying diseases, and this rate was 9.4% in patients without coagulopathy. Coagulopathy was observed in 26 patients out of 45 having a GCS score of less than 8 (Table 1). When patients with and without coagulopathy were compared, TIC was observed more frequently in patients who were intubated in the first three days after trauma and patients who had cardiopulmonary resuscitation (CPR) (P=0.029 and P=0.039, respectively) (Table 1).

Table 1. The Assessment of Groups According to Demographic Characteristics and Other Features

Parameters	With coagulopathy (n=106)	Without coagulopathy (n=78)	P-value
Age (years)	40.3 ± 15.9 (15-83)	43.6 ± 18.3 (16-88)	0.194
Gender (F/M)	20 (18.8) / 86 (81.2)	15 (19.2) / 63 (80.8)	0.951
Co-morbidities	10 (9.4)	18 (23.1)	0.013
GCS (<8)	19 (17.9)	26 (33.3)	0.017
APACHE-II Score	15.8 ± 6 (5-36)	19.6 ± 6.9 (7-37)	0.421
RTS (<5)	16 (15.1)	22 (28.2)	0.115
Number of patients having post-traumatic surgery	63 (59.4)	54 (69.2)	0.172
Number of patients having post-traumatic CPR	1 (0.9)	5 (6.4)	0.039
Number of patients having post-traumatic intubation	64 (60.3)	59 (75.6)	0.029
Presence of hypothermia	6 (5.6)	7 (8.9)	0.386
Presence of hyperthermia	7 (6.6)	10 (12.8)	0.150
Presence of infection	28 (26.4)	30 (38.4)	0.082
Causes of Trauma			
IVTA	61 (57.5)	28 (35.8)	
OVTA	13 (12.3)	12 (15.4)	
Battery/Assault	2 (1.9)	2 (2.6)	0.393
Gunshot wounds	3 (2.8)	8 (10.3)	
Falling down from a height	18 (17)	23 (29.5)	
Other	9 (8.5)	5 (6.4)	
Mortality (28 days)	3 (2.8)	15 (19.2)	<0.001
Length of (hospital) stay	19.7 ± 18 (3-120)	28.6 ± 35 (3-193)	0.374
Length of stay in ICU	14.2 ± 18 (2-120)	22.3 ± 35 (2-193)	0.483

Continuous variables are expressed as mean±SD (minimum-maximum values) and categorical variables are expressed as frequency (percentage). Continuous variables were compared using the student t-test or Mann-Whitney U test, and categorical variables were compared using Pearson's chi-square test or Fisher exact test. Statistically significant P-values are in bold. RTS: Revised Trauma Score. APACHE-II: Acute Physiology and Chronic Health Evaluation. GCS: Glasgow Coma Scale. CPR: Cardiopulmonary Resuscitation. IVTA: In-Vehicle Traffic Accident OVTA: Out-of-Vehicle Traffic Accident

After examining the relationship between the coagulopathy and the reason for trauma, TIC was observed more frequently in patients having a gunshot wound (P=0.036) in patients that fell from a height (P=0.044), and in patients who had in-vehicle traffic accident (P=0.004). A statistically significant result has not been obtained between TIC and patients who had out-of-vehicle traffic accidents and patients who have been battered due to other trauma reasons (P>0.05) (Table 1).

A 28-day mortality has been observed in 18 out of 184 patients studied (9.7%) and 15 out of 78 patients who developed coagulopathy (19.2%). A significant difference has been detected in the mortality rate of patients who had TIC, compared to patients that did not have TIC (P<0.001) (Table 1). From the laboratory values, it has been detected that albumin and hematocrit values are lower in the group having coagulopathy, and the pH value of blood gas is more acidotic, compared to the group without coagulopathy.

No statistical significance was observed on other laboratory values (P>0.05) (Table 2).

In Table 3, univariate logistic regression analysis was applied to determine the factors affecting coagulopathy in patients. As a result of univariate logistic regression analysis, it was understood that co-morbidities (OR=2.880; %95 CI: 1.246-6.655), lower GCS (OR=0.890; %95 CI: 0.827-0.957), and RTS (OR=0.699; %95 CI: 0.568-0.862), higher APACHE-II score (OR=1.092; %95 CI: 1.041-1.145), lower albumin (OR=0.304; %95 CI: 0.193-0.480), and hematocrit values (OR=0.919; %95 CI: 0.879-0.961) are the factors affecting the coagulopathy. As a result of the univariate logistic regression analysis, these factors with a P-value below 0.25 were included in the multivariate logistic regression analysis. Enter method was used in multivariate logistic regression analysis. According to the multivariate logistic regression analysis result, it was understood that the presence of comorbidity (OR=3.080; %95 CI: 1.033-9.176) and low albumin value (OR=0.392; %95 CI: 0.203-0.758) predicted coagulopathy.

Table 2. The Assessment of Laboratory Values of Cases in the Group

Parameters	With coagulopathy (n=106)	Without coagulopathy (n=78)	P-value
White Blood Cells 1st day (K/uL)	15.6 ± 5.2 (7.2-29)	14.9 ± 6.2 (2.5-30.4)	0.425
White Blood Cells 3rd day (K/uL)	10.9 ± 4.5 (3.5-28)	10.9 ± 5.6 (2.8-30.9)	0.173
Hematocrit 1st day (%)	37.4 ± 6.2 (24.7- 53)	33.2 ± 7.9 (14.1-59)	0.322
Hematocrit 3rd day (%)	29.5 ± 5.7 (20-44.8)	26.6 ± 4.2 (17-40)	0.005
AST 1st day (U/L)	112 ± 154 (5-1104)	229 ± 684 (12-6045)	0.226
AST 3rd day (U/L)	79.8 ± 127 (13-1210)	384 ± 1076 (14-7252)	0.576
ALT 1st day (U/L)	101.3 ± 180 (3-1104)	155 ± 323 (6-2505)	0.223
ALT 3rd day (U/L)	70.3 ± 110 (8-895)	252 ± 618 (6-3816)	0.442
Urea 1st day (mg/dL)	34.9 ± 13 (11-98)	40.2 ± 20.8 (14-119)	0.244
Urea 3rd day (mg/dL)	29.1 ± 14.4 (5.1-67)	43.2 ± 30.1 (6.6-130)	0.171
Creatinine 1st day (mg/dL)	0.93 ± 0.3 (0.3-2.8)	1.07 ± 0.5 (0.5-3.4)	0.312
Creatinine 3rd day (mg/dL)	0.7 ± 0.2 (0.27-2.3)	1.2 ± 1 (0.3-4.7)	0.076
Albumin 1st day (g/dL)	3.7 ± 0.7 (1.4-4.9)	3 ± 0.7 (1.6-4.7)	0.018
Albumin 3rd day (g/dL)	3.1 ± 0.5 (2.1-4.3)	2.8 ± 0.4 (1.8- 3.9)	0.299
pH 1st day	7.35 ± 0.10 (7.01-7.49)	7.32 ± 0.10 (6.8-7.50)	0.031
pH 3rd day	7.41 ± 0.04 (7.30-7.52)	7.40 ± 0.08 (6.97-7.50)	0.291
Lactate 1st day (mmol/L)	2.3 ± 1.8 (0.16-9.9)	3.2 ± 2.3 (0.3- 12.2)	0.129
Lactate 3rd day (mmol/L)	1.0 ± 0.6 (0.2-3.4)	1.6 ± 2.1 (0.27-15)	0.135
HCO3 1st day (mmol/L)	22.0 ± 3.5 (14.9-41)	20.2 ± 5.3 (7.2- 48)	0.431
HCO3 3rd day (mmol/L)	26.7 ± 4.9 (19-59)	24.3 ± 5 (7.8-46)	0.468

Continuous variables are expressed as mean±SD (minimum-maximum values). Continuous variables were compared using the student t-test or Mann-Whitney U test. Statistically significant P-values are in bold. AST: Aspartate aminotransferase. ALT: Alanine aminotransferase. HCO3: Bicarbonate

Table 3. Logistic Regression Analysis

	Univariate Logistic Regression					Multivariate Logistic Regression (Forward LR)				
	Wald	p	OR	95% C.I.for OR		Wald	p	OR	95% C.I.for OR	
				Lower	Upper				Lower	Upper
Age	1.686	0.194	1.012	0.994	1.029	0.635	0.426	0.990	0.967	1.014
Gender	0.004	0.951	0.977	0.464	2.056					
Co-morbidities	6.126	0.013	2.880	1.246	6.655	4.077	0.043	3.080	1.033	9.176
Infections	2.994	0.084	1.741	0.929	3.263	0.001	0.994	1.003	0.449	2.240
CPR	3.182	0.074	7.192	0.823	62.843	0.180	0.672	1.813	0.116	28.339
GKS	9.934	0.002	0.890	0.827	0.957	0.053	0.818	1.021	0.855	1.219
RTS	11.239	0.001	0.699	0.568	0.862	0.691	0.406	0.799	0.470	1.357
APACHE-II	12.856	<0.001	1.092	1.041	1.145	1.984	0.159	1.051	0.981	1.126
Albumin	26.213	<0.001	0.304	0.193	0.480	7.760	0.005	0.392	0.203	0.758
Hematocrit	13.562	<0.001	0.919	0.879	0.961	0.635	0.425	0.974	0.914	1.038

Wald: test statistics. OR: odds ratio. Cox and Snell R2'si 0.223. Nagelkerke R2'si 0.302. Statistically significant p-values are in bold CPR: Cardiopulmonary Resuscitation. GCS: Glasgow Coma Scale. RTS: Revised Trauma Score. APACHE-II: Acute Physiology and Chronic Health Evaluation

5. Discussion

TIC development risk might be predicted by examining the demographic characteristics, laboratory findings, or clinical features of patients admitted to the ICU after trauma. In this study, the incidence of coagulopathy after trauma was higher than that mentioned in other studies in the literature. The presence of comorbidity and low albumin values were determined as independent risk factors for the development of coagulopathy.

In our study, the frequency of TIC development is 42.4% (n=78), and this ratio is higher than that in other studies reported in the literature in general. In the studies carried out in Europe, Australia, and Africa the ratios were 34%, 9%, and 54%, respectively (10-12). Differences in this ratio in our study and other studies might be originated from the differences in the definition of coagulopathy, as well as the nature of trauma (minor or major) included in the study. In addition, since this is a retrospective study, information about posttraumatic anticoagulant usage might be insufficient, and patients might also have been included in the study with unknown posttraumatic anticoagulant usage. Since D-dimer and fibrinogen levels were not examined on each patient, cases whose DIC (Disseminated Intravascular Coagulopathy) table was not differentiated might have been included in the study as well.

Accompanying diseases are among the predisposition factors in the formation of inflammation as a result of tissue damage (10). Coagulopathy is a common case due to frequently-used antiplatelet or anticoagulant drugs on accompanying diseases, such as cerebrovascular accidents and coronary artery diseases (9). In our study, the presence of an accompanying disease was discovered as a risk factor in TIC development as well.

Hypothermia takes an important place in the pathophysiology of coagulopathy. When GCS is under 8, coagulopathy is observed more often due to the high risk of hypothermia (13). In a study conducted on patients with head trauma, significant negative correlations were observed among the PT, PTT, INR, and GCS scores (14). In our study, the patients were also separated into two groups of GCS≤8 and GCS>8. By determining GCS≤8, 33% of patients had coagulopathy, and it was determined that low GCS is a risk factor for TIC that was in line with the findings of studies in the literature.

When we examined other scoring systems, usually AIS (Abbreviated Injury Score) and ISS (Injury Severity Score) were mentioned in studies. However, in our study, anatomic scoring was not examined due to a lack of data. Instead, the correlation between coagulopathy and RTS was investigated using GCS, the rate of respiration, and systolic blood pressure. In our study, coagulopathy was found to be associated with both GCS and low RTS. In a study carried out by MacLeod et al., it was emphasized that early TIC might be detected in patients even having a normal RTS score (15). In another study, the role of RTS was mentioned in predicting hypofibrinogenemia in blunt trauma patients (16). APACHE-II score is one of the most calculated scoring systems in the ICUs. In our study, consistent with other studies, the APACHE-II score was found to be high. A 10-year retrospective study showed that an APACHE-II score of >16.5 could be considered a poor prognostic indicator in multiple trauma patients (17).

Tissue hypoperfusion might exacerbate TIC utilizing activated protein c. A successful resuscitation on the other hand prevents the hypoperfusion of tissues (18). The prediction model created for acute traumatic coagulopathy by Peltan et al. contains CPR and intubation (19). It was also detected that coagulopathy was more observed in patients that had been intubated or had posttraumatic CPR. This finding emphasizes the effect of hypoperfusion and acidosis on coagulopathy development once again.

In accordance with the European Guideline on Management of Major Bleeding and Coagulopathy Following Trauma, physicians have to clinically assess the extent of traumatic hemorrhage by examining the physiology of the patient, anatomical injury pattern, the reason for trauma, and the patient's response to initial resuscitation (20). Knowing the reason for the trauma would provide useful information to identify patients having major bleeding risks at an early stage. College of American Surgeons defines a 6-m (20 ft) threshold as a “critical threshold for a fall height” regarding major injuries including bleeding (21). In a study by Savioli et al., the most common cause of trauma was traffic accidents (68%), and it was found that TIC was more common in patients with head and abdominal trauma (22). In our study, the ratio of patients diagnosed with coagulopathy is as follows; in-vehicle traffic accidents (35.8%), falling from height (29.5%), out-of-vehicle traffic accidents (15.4%), and gunshot wounds (10.3%). Statistically, coagulopathy was more frequently observed in gunshot wounds, falling from a height, and in-vehicle traffic accidents. Since our study is retrospective, we were not able to access the information regarding the height of falls of patients who fell from height.

Acidosis and hypothermia can cause coagulopathy by various mechanisms (3). In our study, we also examined the correlation of hypothermia, hyperthermia, infection, and acidosis status with coagulopathy. No correlation was found among hypothermia, hyperthermia, and infection status; however, we have observed acidosis more frequently in patients having developed coagulopathy.

In the study carried out by Mujuni et al., the risk of mortality was higher in the TIC group (29.3%), than in the non-coagulopathic group. It was also detected

that coagulopathy was a strong mortality determinant in trauma patients and a predictor of morbidity (12). Survived patients with early coagulopathy have developed 3 to 4 times more organ failure than those without coagulation complications, and this cause higher mortality rates (23). In a study on 3,114 patients with traumatic brain injury, mortality rates were 50.4% and 17.3% in patients with and without coagulopathy, respectively (24). In our study, the mortality rate was obtained at 2.8% in patients without TIC and 19.2% in patients with TIC. It should be mentioned that mortality was higher in patients with TIC.

Serum albumin level at emergency department admission is a significant predictor of in-hospital complications in geriatric trauma patients (25). In a cohort study on 30,732 patients, low albumin levels were associated with increased short- and long-term mortality (26). In our study, it was determined that coagulopathy patients had a lower albumin level. It can be said that hypoalbuminemia may be one of the reasons for the development of post-traumatic coagulopathy.

It is recommended to apply erythrocyte suspension, fresh frozen plasma, and platelet ratio while administering blood products to prevent TIC. In our Clinic, the trauma-related hemorrhage method is applied according to this protocol.

The early diagnosis and treatment of posttraumatic coagulopathy are vital to decreasing both morbidity and mortality. If we know the risk factors of TIC, we can reduce the risk of coagulopathy by taking precautions.

5.1. Limitations

The retrospective nature of our study imposed certain limitations. The DIC panel was not differentiated since the D-dimer and fibrinogen levels of each patient admitted with trauma were not checked. Patients with DIC might have been accepted as TIC. Since there was no access to detailed information regarding fluid resuscitation, coagulopathy induced by hemodilution or colloids was not differentiated.

6. Conclusion

If the risk factors of TIC are known, the risk of coagulopathy can be reduced by taking precautions. Since it is not possible to change the risk factors of critical trauma patients, such as GCS and co-morbidity, it is taught that the prevention of risk factors, such as hypoalbuminemia with appropriate approaches, can reduce the incidence of coagulopathy, as well as the mortality rate.

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Footnotes

Conflicts of Interest: The authors declare that there is no conflict of interest.
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