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Association of Serum Copeptin Levels with Hemorrhagic Shock Severity in Major Trauma Patients

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Abstract

Background

Hemorrhagic shock remains one of the leading causes of preventable death after trauma, and rapid identification of shock severity is essential for early resuscitation and transfusion planning. Copeptin (CPT), a stable surrogate marker of arginine vasopressin release, may reflect the physiological stress response associated with hemorrhage. This study aimed to evaluate the association between serum CPT levels and hemorrhagic shock severity in adult trauma patients.

Methods

This prospective observational biomarker study was conducted between September 2023 and September 2024 in a tertiary emergency department. Adult trauma patients were classified according to Advanced Trauma Life Support (ATLS) hemorrhagic shock stages. Serum CPT levels were measured using enzyme-linked immunosorbent assay (ELISA). Relationships between CPT levels, shock stage, Injury Severity Score (ISS), transfusion requirement, and laboratory parameters were analyzed. Receiver operating characteristic (ROC) analysis and multivariable logistic regression were performed to assess the discriminatory and independent predictive performance of CPT for advanced hemorrhagic shock (stage ≥ 2).

Results

A total of 103 trauma patients were included (54 major trauma, 49 minor trauma). Serum CPT levels were significantly higher in patients with major trauma compared with minor trauma (658.59 ± 70.03 vs. 587.81 ± 94.66 pg/mL, p = 0.001). CPT levels increased progressively with advancing hemorrhagic shock stage and demonstrated a moderate positive correlation with shock severity (Spearman r = 0.499, p < 0.001; Kendall tau-b r = 0.401, p < 0.001). ROC analysis for identifying advanced hemorrhagic shock showed an AUC of 0.705 (95% CI 0.61–0.81), with 76% sensitivity and 52% specificity at a cut-off value of 611.95 pg/mL. In multivariable logistic regression analysis, ISS remained independently associated with advanced hemorrhagic shock (OR 1.11, 95% CI 1.03–1.20, p = 0.006), whereas CPT did not retain independent significance after adjustment for ISS, hemoglobin, and base deficit.

Conclusions

Serum CPT levels were associated with hemorrhagic shock severity and transfusion requirement in trauma patients. Although CPT demonstrated moderate discriminatory performance for advanced hemorrhagic shock, its independent predictive value was limited after adjustment for overall trauma

severity. CPT may serve as an adjunctive exploratory biomarker in early trauma assessment rather than a standalone diagnostic tool.

Introduction

Background/rationale

According to the most recent data from the World Health Organization and the Centers for Disease Control and Prevention, more than nine people die every minute due to injury or violence. Each year, 5.8 million individuals of all ages die from unintentional injuries and violence [1].

Hemorrhage is the most prominent cause of preventable death following trauma. Identifying the source of bleeding, rapidly controlling it, and initiating resuscitative interventions to keep the injured patient alive constitute critical steps in evaluating and managing such cases. In patients with trauma, circulatory disturbance may result from various injuries. Blood volume, cardiac output, and hemorrhage are fundamental circulatory concerns that must be carefully examined. Rapid and accurate assessment of the hemodynamic status of a patient with trauma is a fundamental rule.

Shock is defined as inadequate perfusion and oxygenation of organs due to insufficiency and abnormalities in the circulatory system. The first rule of managing shock is to recognize its presence. Hemorrhage is the most common cause of shock in trauma cases. The body’s response to blood loss in patients with trauma involves fluid shifts between compartments, and these shifts should be considered when evaluating the response. It is also necessary to plan for changes associated with severe, prolonged shock and the pathophysiological consequences of resuscitation and reperfusion.

The diagnosis of shock in patients with trauma relies on clinical findings and laboratory tests. Clinical indicators that demonstrate the severity and extent of bleeding in these patients include level of consciousness, skin perfusion, and heart rate (Table 1). Base deficit and/or lactate levels are laboratory assessments that can be used to determine the presence and severity of shock.

Table 1
Signs and symptoms of hemorrhage by class.

Estimated blood loss	Class I	Class II	Class III	Class IV
	< 15%	15–30%	31–40%	> 40%
Heart rate (bpm)	↔	↔/↑	↑	↑/↑↑
Blood pressure	↔	↔	↔/↓	↓
Pulse pressure	↔	↓	↓	↓
Respiratory rate (beats/sec)	↔	↔	↔/↑	↑
Mental status	↔	↔	↓	↓↓
Urine output (mL/hour)	↔	↔	↓	↓
Base deficit*	0 to -2 mEq/L	-2 to -6 mEq/L	-6 to -10 mEq/L	-10 mEq/L or less
Need for blood products	Monitor	Possible	Present	Massive transfusion protocol

*Base excess is the quantity of base (HCO_3^-, in mEq/L) that is above or below the normal range in the body. A negative number is called a base deficit and indicates metabolic acidosis [2].

Arginine vasopressin (AVP), a neuropeptide stored in the posterior pituitary, is necessary to maintain vasomotor tone during shock and supports vasoconstriction via non-adrenergic pathways. During hemorrhagic shock, animal models have shown that 10–20% of AVP stores are rapidly released, leading to a significant acute increase in circulating levels [3–6]. Various studies have suggested that CPT, the C-terminal portion of the pre-pro vasopressin molecule, may serve as a reliable surrogate marker for AVP [7]. CPT concentrations correlate with vasopressin levels in both healthy volunteers and critically ill patients [8–10]. Therefore, CPT measurement during the resuscitation of hemorrhagic shock may provide insight into the underlying vasopressin response of the patient [11, 12].

Objectives

Primary Objective

The primary objective of this study was to investigate whether serum CPT levels correlate with the severity of hemorrhagic shock in adult trauma patients.

Secondary Objectives

Secondary objectives included assessing the association between CPT levels and transfusion requirements, the ISS, and the marker's diagnostic performance in discriminating between stages of

hemorrhagic shock.

Rationale and Clinical Relevance

Hemorrhagic shock remains a major determinant of early trauma mortality, and its rapid and accurate assessment is critical for guiding resuscitation strategies. This study aimed to identify a laboratory parameter—analogous to the base deficit obtained from arterial blood gas analysis—that could support clinicians in determining hemorrhagic shock severity. Establishing CPT as such a biomarker may enhance early recognition of trauma patients who require blood product replacement, facilitate appropriate triage to specialized trauma centers, and improve blood bank preparedness at receiving facilities. This is especially valuable for transferred patients whose shock severity cannot be reliably assessed through initial visual evaluation. Early identification of high-risk patients may ultimately contribute to faster access to life-saving blood products and improved clinical outcomes.

Methods

Study design

This prospective, biomarker accuracy study was conducted between September 15, 2023, and September 15, 2024, at the Emergency Medicine Department (ED) of Atatürk University Research Hospital and included 103 patients who presented with multiple traumas and met the inclusion criteria. The study commenced after receiving approval from the Atatürk University Clinical Research Ethics Committee (date: 07/09/2023, protocol code: B.30.2.ATA.0.01.00/1 and number: B.30.2.ATA.0.01.00/605). Written informed consent was obtained from all volunteers participating in the study. For patients who arrived unconscious, consent was obtained from their legal guardians. The study was conducted in accordance with the Declaration of Helsinki and good clinical practices.

Consecutive eligible patients were screened during the study period. Hemorrhagic shock stages were determined by emergency physicians according to ATLS 10th edition criteria using heart rate, systolic blood pressure, mental status, estimated blood loss, and base deficit values at ED admission.

Patient ISS's were performed by physicians who were the first to see the patient and manage the trauma, who had received ATLS training, and who had at least two years of experience as emergency medicine residents.

To evaluate pre-existing chronic diseases and potential coagulopathies that could affect patients' physiological responses to volume loss before trauma, the patients with trauma in our study were classified into five groups: hypertension, diabetes mellitus, asthma, malignancy, and none.

The trauma cases in the study were also categorized into five groups according to the volume of hydration with %0,9 isotonic solution they received: none, < 500 cc, 500–1.000 cc, 1.000–1.500 cc, and > 1.500cc.

Participants

The inclusion criteria for the patients were being aged over 18 years, not being pregnant, and having sustained multiple traumas with an Injury Severity Score (ISS) of > 16, thereby being classified as a major trauma case. Patients with multiple trauma, not being pregnant and ISS of < 16 were included in the control group as minor trauma cases.

During the study period, 150 patients presented to the ED of Atatürk University Research Hospital with complaints of having trauma. Patients were excluded due to multitrauma secondary to Cardiopulmonary arrest, status epilepticus, stroke, sepsis, hypoglycemia (blood glucose < 60 mg/dL), active intoxication, drug overdose, severe anemia (Hb < 8 g/dL) or a known hematological malignancy, end-stage renal or hepatic failure, pregnancy, or sufficient sample volume were excluded from the study. A total of 120 patients agreed to participate in the study. Of these, 8 were excluded due to incomplete data and missing case forms, and 9 were excluded due to improper storage of blood samples sent for laboratory analysis. (Fig. 1).

Post-hoc power analysis (ROC AUC):

To determine the statistical adequacy of the study, a post-hoc power analysis was conducted using G*Power software (version 3.1.9.7). Given the observed effect size of d = 0.85 for serum CPT levels, a significance level (alpha) of 0.05, and a total sample size of 103 (n = 49 for minor trauma; n = 54 for major trauma), the calculated power (1-beta) was 0.989. This indicates that the study had excellent robust statistical strength to detect significant differences between the two groups.

Biochemical Analysis

At the time of presentation, blood samples were collected from the patients as part of routine diagnostic testing. These blood samples were sent to the Medical Biochemistry Laboratory of Atatürk University Health Research and Application Center for analysis.

Blood samples were drawn into biochemistry tubes and centrifuged at 3.000 rpm for 10 minutes to separate the serum. After routine tests requested from the emergency department were completed, the amount required for CPT analysis was frozen at -80°C and stored until analysis. For routine parameters, the following laboratory results were recorded and utilized: hemoglobin, hematocrit, mean corpuscular volume (MCV), platelet count, international normalized ratio (INR), lactate, and base deficit.

All analyses were carried out at the Medical Biochemistry Laboratory of Atatürk University Health Research and Application Center. On the day of analysis, after the samples were thawed under appropriate conditions, CPT levels in the serum were measured using an enzyme-linked immunosorbent assay (ELISA) kit from A.B.T. (Cat. No. ABT1470 Hu, Atlas Biotechnology Co., Ltd., Ankara, Türkiye) according to the manufacturer's standard protocol. Measurements were conducted on an ELISA reader

device (BioTek PowerWave XS, USA) using the ELISA method. All samples were tested in duplicate, and their averages were used for statistical analysis. The intra- and inter-assay coefficients of variation of the kit were < 10%.

Statistical Analysis

The statistical analysis was conducted to evaluate the relationship between serum CPT levels and hemorrhagic shock stage, as well as resuscitation requirements, in patients with major trauma classified according to the ISS. Patients classified as having minor trauma based on ISS were designated as the control group. Comparative analyses between the study and control groups were performed to determine the association of serum CPT levels with hemorrhagic shock stage and resuscitation requirements in patients with multiple trauma.

Statistical analyses were performed using IBM SPSS Statistics (IBM Corp., Armonk, NY, USA). The normality of data distribution was assessed using the Kolmogorov–Smirnov test. Normally distributed variables were analyzed using the independent samples t-test or one-way analysis of variance (ANOVA), whereas non-normally distributed variables were evaluated using the Mann–Whitney U test or Kruskal–Wallis test, as appropriate. Categorical variables were compared using the chi-square test. Continuous variables were expressed as mean ± standard deviation (SD) and minimum–maximum values. A p-value of < 0.05 was considered statistically significant.

Receiver operating characteristic (ROC) curve analysis was performed to assess the predictive performance of serum CPT levels. Sensitivity, specificity, area under the curve (AUC), and optimal cut-off values were calculated. A p-value of < 0.05 was considered statistically significant.

Spearman and Kendall tau-b correlation analyses were performed for correlation analysis between shock phase and serum CPT levels.

Variables associated with hemorrhagic shock severity were evaluated using multivariable binary logistic regression analysis. Hemorrhagic shock stages were dichotomized as minor shock (stage 1) and advanced shock (stage ≥ 2). CPT, base deficit, hemoglobin, and ISS were entered simultaneously into the regression model. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. Model discrimination was assessed using receiver operating characteristic (ROC) curve analysis.

Results

A total of 103 patients were included in this prospective, observational, and analytical approach study.

According to trauma type, the age distribution was similar between the two groups (p = 0.914). We determined that serum CPT levels were significantly higher in patients with major trauma (p = 0.001). Hemoglobin levels were significantly lower in patients with major trauma (p = 0.001). INR values were significantly higher in the major trauma group (Z =-5.738, mean rank: 680.6 for major trauma, 334.30 for

minor trauma). Base deficit values were lower in minor trauma cases, while they were measured higher in the major trauma group, indicating a statistically significant difference (p = 0.001) (Table 2).

Table 2
Comparison of laboratory parameters according to trauma type (presented as mean ± SD and p-values)

Parameters	**Patients with Minor Trauma (n = 49)**	**Patients with Major Trauma (n = 54)**	**p**
Age	42.69 ± 12.83	42.40 ± 13.86	0.914
Hemoglobin (g/dL)	14.42 ± 1.87	12.82 ± 1.87	0.001*
Hematocrit (%)	42.06 ± 5.17	40.07 ± 4.32	**0.036**
MCV (fL)	83.16 ± 5.85	81.14 ± 7.51	0.133
Platelet count (10^3/Ul)	219.69 ± 42.3	215.66 ± 51.21	0.666
INR**	0.70–1.70	0.80–2.05	0.001*
Base deficit**	-4.0-6.0	-8.0-8.0	0.001*
CPT level (pg/mL)	587.81 ± 94.66	658.59 ± 70.03	0.001*

*Statistically significant p-value, **Non-normally distributed parameters, presented as minimum–maximum values. MCV: mean corpuscular volume, INR: international normalized ratio

Upon categorizing patients according to their hemorrhagic shock stages, no statistically significant difference in sex distribution was found among groups with shock stages 1, 2, and 3 (p = 0.797). Epidemiological and clinical variables of participants are shown in Table 3

Table 3
Epidemiological and clinical variables of participants

	Shock Stages			
	Stage 1	**Stage 2**	**Stage 3**	**p value**
Gender n(%)				0.797
Male	52 (50.5%)	15 (14.6%)	8 (7.8%)	
Female	21 (20.4%)	4 (3.9%)	3 (2.8%)	
Age (mean ± SD value)	42.10 ± 12.58	42.21 ± 15.51	46 ± 14.87	0.999[a] 0.643[b] 0.736[c]
Chronic Disease n(%)				0.775
None	61 (59.2%)	16 (15.4%)	11 (10.7%)	
Hypertension	6 (5.8%)	3 (2.8%)	0	
Diabetes mellitus	4 (3.9%)	0	0	
Asthma	1 (0.9%)	0	0	
Malignancy	1 (0.9%)	0	0	
Hidrasyon volüme n(%)				**0.001**
None	21 (20.4%)	3 (2.8%)	0	
< 500 cc	31 (30%)	1 (1.1%)	2 (1.9%)	
500–1,000 cc	16 (15.5%)	7 (6.8%)	7 (6.8%)	
1,000–1,500 cc	2 (1.9%)	7 (6.8%)	1 (1.1%)	
> 1,500 cc	3 (2.8%)	1 (1.1%)	1 (1.1%)	
Erythrocyte suspension unit n(%)				**0.001**
None	72 (69.9%)	12 (11.7%)	1 (0.9%)	
1	1 (0.9%)	6 (5.8%)	8 (7.8%)	
2	0	1 (0.9%)	1 (0.9%)	
3	0	0	1 (0.9%)	

[a]Shock Stage 1 vs. Shock Stage 2, [b]: Shock Stage 1 vs. Shock Stage 3, [c]Shock Stage 2 vs. Shock Stage 3

The proportion of trauma patients with chronic diseases was very low, and no significant bidirectional relationship was found between the presence of chronic disease and shock stage ($p = 0.775$). Only one patient was using rivaroxaban; therefore, no statistical analysis was performed for this subgroup.

We also evaluated the number of red blood cell transfusions administered to patients according to their shock stages and found a statistically significant relationship between the number of erythrocyte suspension units transfused and the shock stages ($p = 0.001$) (Table 3).

In the comparison of CPT levels based on hemorrhagic shock stages, serum CPT levels were found to be the lowest in patients with shock stage 1. It was determined that CPT levels in patients with shock stages 2 and 3 were significantly higher than those in stage 1, while there was no statistically significant difference between stages 2 and 3.

Table 4 presents the mean ± SD values and statistical comparisons of all laboratory parameters evaluated in patients from the three shock stage groups.

Table 4
Laboratory parameters and statistical significance levels according to hemorrhagic shock stages

Parameters	Shock Stage 1(n = 73)	Shock Stage 2 (n = 19)	Shock Stage 3 (n = 11)	p
Hemoglobin (g/dL)	14.17 ± 1.68	12.68 ± 2.13	11.23 ± 1.82	0.005[a] **0.001**[b] 0.086[c]
Hematocrit (%)	41.66 ± 4.68	40.97 ± 4.67	36.79 ± 4.23	0.831[a] **0.004**[b] 0,050[c]
MCV (fL)	83.30 ± 5.52	81.06 ± 6.99	75.90 ± 10.58	0.373[a] **0.002**[b] 0.094[c]
Platelet count (10^3/Ul)	218.63 ± 38.35	219.10 ± 48.20	208 ± 87.43	0.999[a] 0.767[b] 0.810[c]
INR	1.05 ± 0.16	1.33 ± 0.32	1.65 ± 0.25	**0.001**[a] **0.001**[b] **0.001**[c]
Base deficit*	-6.0 to -6.0	-8.0 to -8.0	-8.0 to -2.0	**0.001**[a] **0.001**[b] 0.085[c]
CPT (pg/mL)	597.79 ± 86.53	683.85 ± 56.52	703.16 ± 59.26	**0.001**[a] **0.001**[b] 0.798[c]

[a]Shock Stage 1 vs. Shock Stage 2, [b]: Shock Stage 1 vs. Shock Stage 3, [c]Shock Stage 2 vs. Shock Stage 3, *Non-normally distributed parameter, presented as minimum–maximum values. MCV: mean corpuscular volume, INR: international normalized ratio, CPT: CPT

In the correlation analysis between shock phase and serum CPT levels, we determined a moderate, positive, and statistically significant relationship according to both the Spearman rho ($r = 0.499$, $p < 0.001$) and Kendall tau-b ($r = 0.401$, $p < 0.001$) tests. Serum CPT levels were observed to increase as the shock phase progressed.

Evaluation of CPT levels according to hemorrhagic shock stages revealed that CPT levels increased as the shock stage advanced (Fig. 2).

Comparison of injury regions according to shock stages did not reveal any statistically significant relationship ($p = 0.42$). Stage 3 hemorrhagic shock was observed after injuries to the pelvis (37.5%), abdomen (20%), and extremities (13.3%). Injuries to the face (100%), head (84.6%), and chest (77.8%) were frequently observed in hemorrhagic shock stage 1.

The patient with the highest ISS value (50) was in stage 3 hemorrhagic shock, and it was observed that as ISS scores increased, the stages of hemorrhagic shock also increased, indicating a statistically significant correlation ($p = 0.001$). Among the 103 patients, only one case resulted in death. This patient had the highest ISS score, was in hemorrhagic shock stage 3, and had a CPT level of 703.19 pg/mL.

With a cut-off value of 611.95 pg/mL, serum CPT levels exhibited 76% sensitivity and 52% specificity in differentiating trauma cases by hemorrhagic shock stage, with a positive predictive value of 53% and a negative predictive value of 24% (AUC = 0.705, $p < 0.001$, 95% confidence interval 0.61–0.81, negative likelihood ratio = 0.47, positive likelihood ratio = 1.55) (Fig. 3).

To explore whether CPT remained independently associated with advanced hemorrhagic shock after adjustment for injury severity and laboratory parameters, a multivariable logistic regression model was constructed (Table 5).

Table 5
Multivariable logistic regression analysis for advanced hemorrhagic shock (stage ≥ 2)

Variable	OR	95% CI	p value
Copeptin (per 100-unit increase)	2.00	0.84–4.75	0.115
Base deficit	0.81	0.60–1.08	0.154
Hemoglobin	0.79	0.50–1.24	0.305
ISS	1.11	1.03–1.20	0.006*

Abbreviations: OR odds ratio, CI confidence interval, ISS Injury Severity Score.
*Statistically significant ($p < 0.05$).

In multivariable logistic regression analysis, ISS was independently associated with advanced hemorrhagic shock (OR 1.11, 95% CI 1.03–1.20, p = 0.006). Although CPT levels were elevated in patients with advanced shock, CPT did not retain independent significance after adjustment for ISS, hemoglobin, and base deficit. These findings suggest that the relationship between CPT and hemorrhagic shock severity may partly reflect overall trauma burden.

Although serum CPT demonstrated moderate discriminatory ability for advanced hemorrhagic shock in ROC analysis (AUC 0.705), CPT did not retain independent significance in multivariable logistic regression after adjustment for ISS, hemoglobin, and base deficit. This finding suggests that CPT levels may partly reflect overall trauma severity rather than hemorrhagic shock alone.

Discussion

In this study, we evaluated the relationship between serum CPT levels measured in patients with major trauma who presented to the hospital after multiple traumas and the stages of hemorrhagic shock, and its usability as a helpful biomarker in diagnosis. Our findings represent the first study demonstrating that serum CPT levels can be a helpful parameter in hemorrhagic shock staging and determining resuscitation fluid requirements.

Similar to the study by Yang et al., which discussed the relationship between acute traumatic coagulopathy and progressive hemorrhagic injury after traumatic brain injury and CPT levels, our study involved 103 patients. The age range of the population was as follows: 42.40 ± 13.86 years for patients with major trauma, 42.1 ± 12.5 years for hemorrhagic shock stage 1, 42.2 ± 15.5 years for stage 2, and slightly higher at 46 ± 14.8 years for stage 3. Compared to the study by Kleindienst et al., which mentioned the relationship between CPT levels and osmoregulation following brain trauma (with a mean age of 53 years), our population was younger.

Based on the data obtained from a comprehensive literature review, it was determined that in addition to CPT levels, several other parameters were investigated in trauma cases. These include blood and urine sodium, blood lactate and glucose, plasma fibrinogen, D-dimer, vasopressin (AVP), and C-reactive protein levels [11, 13-15]. In a study undertaken by Salvo et al., the median venous lactate concentration was reported as 2.05 mmol/L, whereas in our study, it was determined to be 1.05 mmol/L for stage 1, 1.33 mmol/L for stage 2, and 1.65 mmol/L for stage 3. Base deficit, which had not been previously studied as a marker for osmoregulation, hemodynamic stability, and hemorrhagic shock in trauma cases, was found to be statistically significant across all shock stages. This parameter, which has been incorporated into the literature through the most recent advanced trauma life support (ATLS) guidelines, was also measured in a manner consistent with expected hemorrhagic shock stages in the population studied [16].

The hemoglobin value decreased with increasing hemorrhagic shock stage and associated blood loss in patients (14.17–12.68–11.23 g/dL). While a statistically significant difference was found between stages 1 and 2 (p=0.005) and between stages 1 and 3 (p=0.001), no statistical significance was

observed between stages 2 and 3. The increase in CPT levels observed with the increase in the shock levels of the patients was accompanied by a decrease in the laboratory parameters Hb and Htc. The decrease in blood pressure due to bleeding led to an increase in arterial hypovolemia. It is thought that the baroreceptor stimulation, which occurs as a physiological response, also increased CPT release [17,18]. Struck et al. reported no significant correlation between hemoglobin and blood pressure values and CPT values. They suggested this might be related to the fact that the amount of bleeding was not excessive and shock had not yet developed in patients presenting to the emergency department. The difference between our findings and that of this study is thought to be related to the fact that patients presenting to the emergency department had lost significant amounts of blood and were in the advanced stage of shock [19]. In our study, the high number of patients in the initial stage of hemorrhagic shock, the early development of significant symptoms during bleeding, and the fact that many patients sought medical attention immediately after trauma before the onset of shock, thus contributing to a reduced incidence of advanced-stage shock. In patients with advanced-stage shock, rapid deterioration of tissue perfusion, changes in consciousness, and loss of physical strength may reduce their likelihood of seeking medical help and accessing healthcare systems if there is no witnessed trauma, potentially leading to a rarity of advanced-stage cases.

In line with these values, it was determined that the mean values of hematocrit and MCV decreased as the shock stage advanced. Moreover, hematocrit and MCV values statistically significantly differed between shock stages 1 and 3 ($p=0.004$ and 0.002, respectively).

Serum CPT levels, consistent with findings in other trauma studies, were found to be higher in major traumas with ISS > 16 [11] and, more importantly, were observed to increase in direct correlation with the progression of hemorrhagic shock stages, aligning with the primary objective of our study. Statistical significance was observed in the comparisons of CPT levels between shock stages 1 and 2 and between stages 1 and 3, but not between stages 2 and 3. We attribute this to the low number of patients in stages 2 and 3.

In a study by Demir et al. involving patients with head trauma [20], the measured CPT levels were 1.038 pg/mL for mild, 1.387 pg/mL for moderate, and 1.607 pg/mL for severe trauma. However, no analysis has previously been performed based on hemorrhagic shock staging in relation to injury regions; thus, the current study is expected to contribute to the literature in this area.

When trauma cases were analyzed according to the amount of hydration administered, it was notable that a total of 5 patients (three in stage 1 and one each in stages 2 and 3) received more than 1.500 cc of fluid. This is particularly striking because it is not a practice recommended in the ATLS guidelines. This finding points to the necessity of reinforcing and increasing the frequency of trauma management training aligned with ATLS standards. As the hemorrhagic shock stage increased, a reduction in fluid volume and a shift toward the use of blood products were observed, which is in accordance with ATLS guideline recommendations.

As the first study to compare CPT levels according to hemorrhagic shock stages, we believe that this research will make a significant contribution to the literature.

Limitations of the study

Homogenizing and increasing the distribution of cases across the hemorrhagic shock stages would enable more comprehensive studies yielding data with higher sensitivity and specificity. In our study, there were 11 patients in hemorrhagic shock stage 3 and no patients in stage 4. It is also considered that including the amount of urine output during the monitoring of trauma cases would improve the completeness of patient follow-up and improve the quality of the study by presenting all components of the hemorrhagic shock stage.

Conclusion

Consistent with the objective of this study, serum CPT levels measured in patients presenting to the emergency department with multiple traumas were found to correlate with their hemorrhagic shock stages and resuscitation needs. CPT appears to be a useful adjunctive exploratory biomarker for distinguishing between hemorrhagic shock stages 1 and 2, as well as between stages 1 and 3. It can support clinical evaluation and help guide the need for blood and blood product administration, even in the absence of direct patient observation. The ability of CPT levels to provide clinical insight into a patient's condition is expected to contribute to optimal case management, reduce trauma-related mortality rates, and minimize hospital stays.

Abbreviations

CPT: CPT

ATLS: Advanced Trauma Life Support

ELISA: Enzyme-Linked Immunosorbent Assay

ISS: Injury Severity Score

ROC: Receiver operating characteristic

AVP: Arginine vasopressin

ED: Emergency Medicine Department

ANOVA: ANalysis Of Variance

MCV: Mean Corpuscular Volume

INR: International Normalized Ratio

SPSS: Statistical Package for the Social Sciences

Declarations

Ethics approval and consent to participate

The study commenced after receiving approval from the Atatürk University Clinical Research Ethics Committee (date: 07/09/2023, protocol code: B.30.2.ATA.0.01.00/1 and number: B.30.2.ATA.0.01.00/605). Written informed consent was obtained from all volunteers participating in the study. For patients who arrived unconscious, consent was obtained from their legal guardians. The study was conducted in accordance with the Declaration of Helsinki and good clinical practices.

Consent for publication

There is not any identifying images or other personal or clinical details of participants are presented that compromise anonymity.

Competing Interests

No, there are no competing interests.

Conflict of Interest Statement

None of the authors have any conflicts of interest, either financially or in relation to industry.

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Author Contribution

Çalbay A: Conception, Design, Supervision, Materials, Data Analysis and/or Interpretation, Literature Review, Writer, Critical ReviewÇalbay MM: Conception, Materials, Literature Review, Critical ReviewBayramoğlu A: Conception, Supervision, Data Collection and/or Processing, Critical ReviewÖztürk N: Design, Supervision, Materials, Data Analysis and/or Interpretation, Critical Review

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None.

Data Availability

Data are available on reasonable request

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Figures

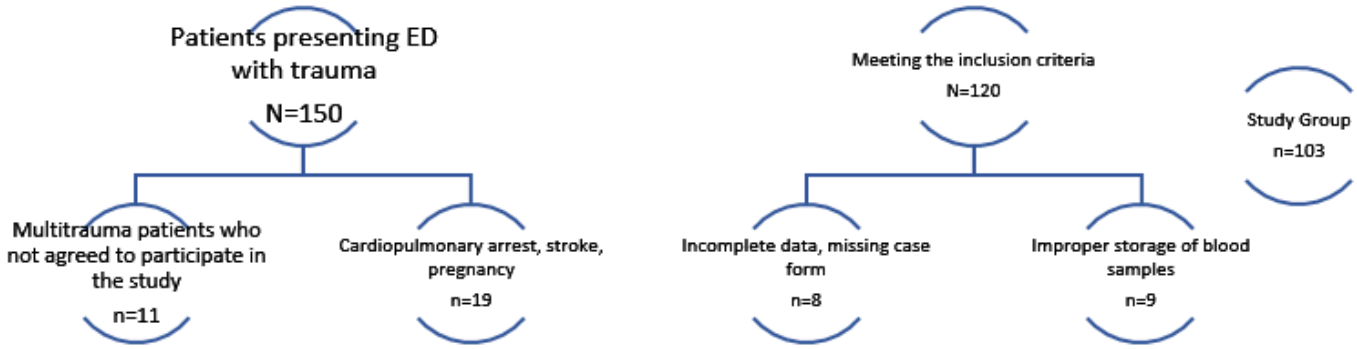


Figure 1

Flow diagram of participant selection

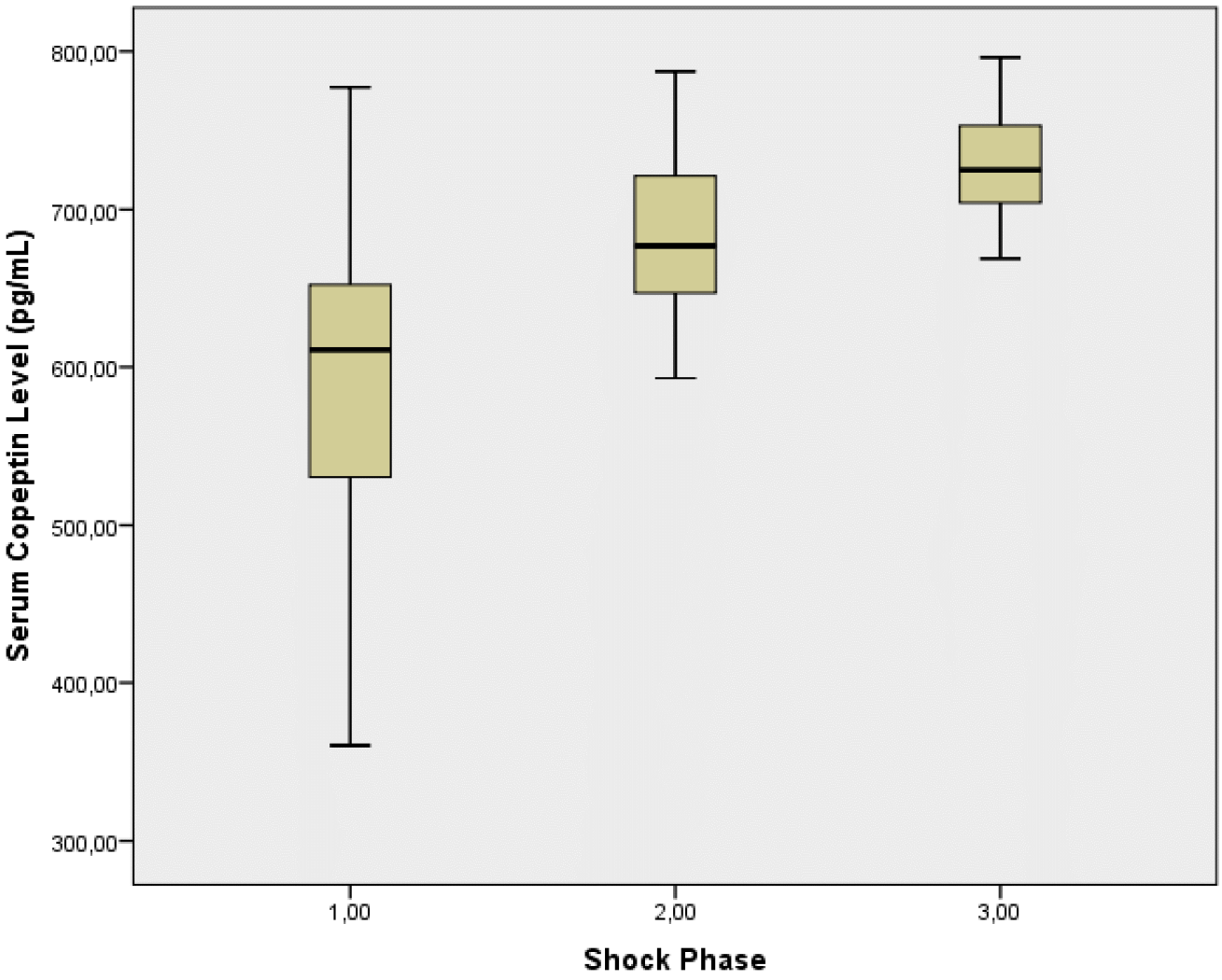


Figure 2

Serum CPT levels according to hemorrhagic shock stages

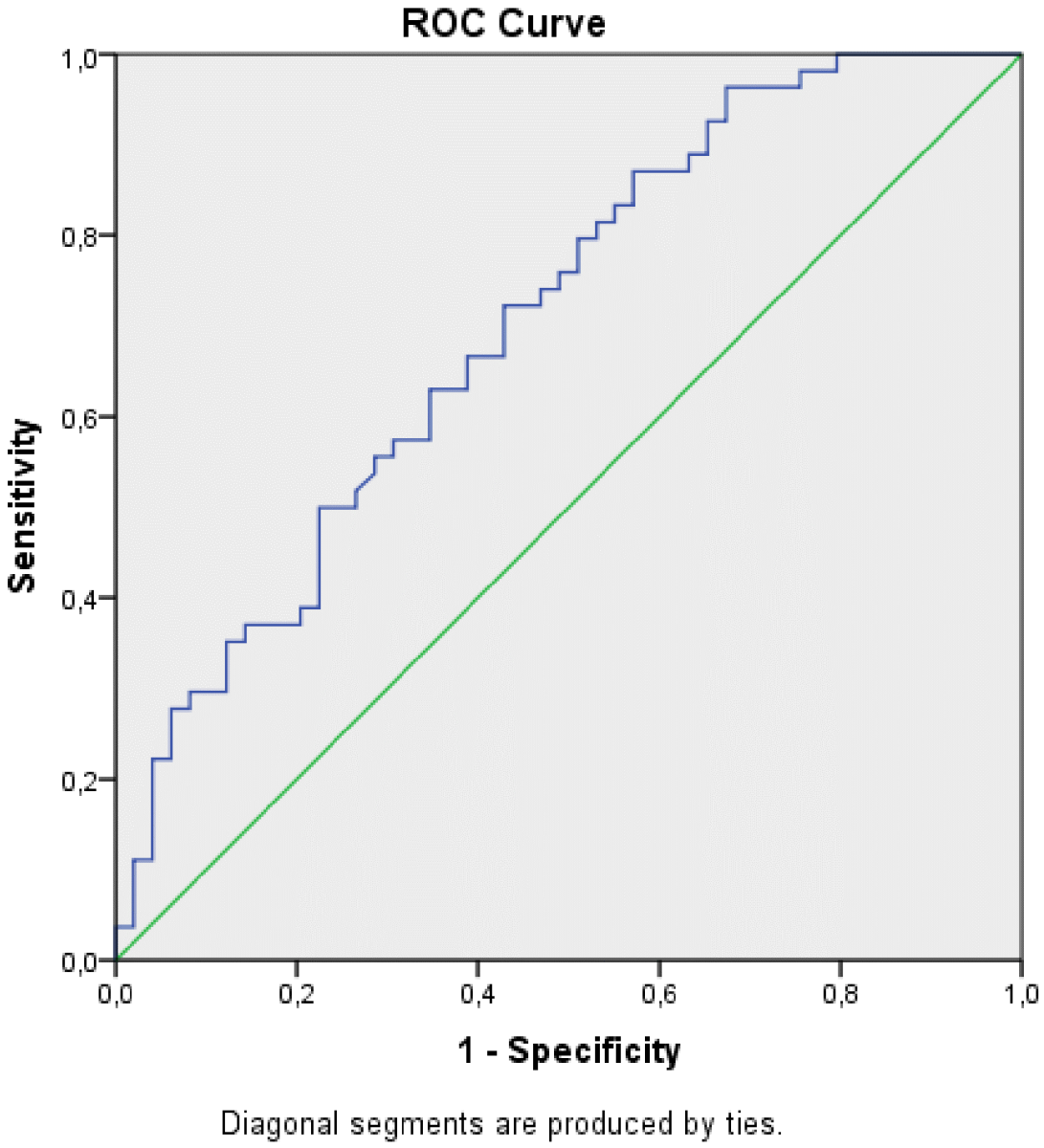


Figure 3

ROC analysis of serum CPT for identifying advanced hemorrhagic shock (stage ≥2)