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Usefulness of presepsin as a prognostic indicator for patients with trauma in the emergency department in Korea: a retrospective study

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Purpose: Trauma is an important public health concern, and it is important to increase the survival rate of patients with trauma and enable them to return to society in a better condition. Initial treatment in the emergency department (ED) is closely associated with the prognosis of patients with trauma. However, studies regarding laboratory biomarker tests that can help predict the prognosis of trauma patients are limited. Presepsin is a novel biomarker of inflammation that can predict a poor prognosis in patients with sepsis. This study aimed to determine whether presepsin could be used as a prognostic indicator in patients with polytrauma.

Methods: The study included patients with trauma who had visited a single regional ED from November 2021 to January 2023. Patients who had laboratory tests in the ED were included and analyzed retrospectively through chart review. Age, sex, injury mechanism, vital signs, surgery, the outcome of ED treatment (admission, discharge, transfer, or death), and trauma scores were analyzed.

Results: Overall, 550 trauma patients were enrolled; 59.1% were men, and the median age was 64 years (interquartile range, 48.8–79.0 years). Patients in a hypotensive state (systolic blood pressure, <90 mmHg; n=39) had higher presepsin levels (1,061.5±2,522.7 pg/mL) than those in a nonhypotensive state (n=511, 545.7±688.4 pg/mL, P<0.001). Patients hospitalized after ED treatment had the highest presepsin levels (660.9 pg/mL), followed by those who died (652.0 pg/ mL), were transferred to other hospitals (514.9 pg/mL), and returned home (448.0 pg/mL, P=0.041).

Conclusions: Serum presepsin levels were significantly higher in trauma patients in a hypotensive state than in those in a nonhypotensive state. Additionally, serum presepsin levels were the highest in hospitalized patients with trauma, followed by those who died, were transferred to other hospitals, and returned home.

Keywords: Emergency treatment; Multiple trauma; Injuries; Human presepsin protein; Hypotension

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INTRODUCTION

Background

Trauma is a significant public health issue, with high prevalence and mortality rates, especially among young individuals who are socially and economically active [1]. The effects of traumatic injuries are staggering, accounting for over 40 million emergency department (ED) visits each year in the United States alone [2]. On a global scale, these injuries result in an alarming annual death toll of approximately six million people. Trauma continues to be the leading cause of death for both children and adults under the age of 46 years, representing nearly half of all fatalities within these age groups [1,3,4]. Therefore, it is crucial to improve the survival rates of trauma patients and facilitate their return to society in an improved condition.

Traumatic deaths are traditionally characterized by a trimodal pattern, with the initial treatment in the ED playing a significant role in the prognosis of trauma patients [5]. A variety of inflammatory cytokines contribute to traumatic deaths through the immune-inflammation cascade [4,6,7]. Despite the importance of this field, research is still limited, particularly in relation to laboratory biomarker tests that can predict the prognosis of trauma patients.

Presepsin (soluble CD14 [sCD14] subtypes, discovered in 2004) is a novel biomarker of inflammation that can predict a poor prognosis in patients with sepsis [8–16]. As a receptor of the lipopolysaccharide-binding protein (LPS-LBP) complex, sCD14 can trigger a series of signal transduction pathways and inflammatory cascades, leading to a systemic inflammatory response [4,17–19]. Several clinical studies examining the relationship between sCD14 and sepsis have demonstrated that sCD14 levels significantly increase in patients with sepsis and septic shock, compared to healthy individuals [20,21]. However, the specificity of sCD14 is low, and its levels are also significantly elevated in patients with coronary heart disease, heart failure, and liver cirrhosis [11].

Objectives

This study aimed to determine whether presepsin could be used as a prognostic indicator in patients with polytrauma.

METHODS

Ethics statement

This study was approved by the Institutional Research Board of Korea University Guro Hospital (No. 2023GR0364). The requirement for informed consent from the participants was waived due to the retrospective nature of the study. The study adhered to the principles of the Declaration of Helsinki.

Study design and setting

This study was carried out at Korea University Guro Hospital (Seoul, Korea) which was recognized as a level I trauma center in 2016 and currently functions as a regional trauma center in the city. The research encompassed 699 patients without any preexisting diseases who visited the ED between November 2021 and January 2023. Of these, 149 patients who were intoxicated were excluded, leaving data from 550 trauma patients for analysis. Patients deemed to be under the influence of substances during ED triage were not included in the study. Most of these patients were intoxicated due to alcohol, drugs, pesticides, and other substances. The study focused on patients who required blood tests in the ED, thus excluding those who visited for minor injuries or simple treatments. Trauma was classified as a physical injury caused by traffic accidents, falls, blunt injury, penetrating injury, or other causes (Table 1).

Clinical and laboratory variables were collected retrospectively from electronic medical and emergency medical services transport records. The baseline characteristics were collected at the time of ED triage and included age, sex, injury mechanism, vital signs, Glasgow Coma Scale score, surgery, and ED treatment results. All laboratory data, including presepsin, were collected at the ED at the initial presentation, and the data included the complete blood count and levels of lactic acid and inflammatory markers, including C-reactive protein (CRP), procalcitonin (PCT), and presepsin. We also calculated the Revised Trauma Score (RTS), Injury Severity Score (ISS), and Trauma Injury Severity Score (TRISS) as indicators of severity. Details about the outcomes of ED treatment (admission, discharge, transfer, and death) were also collected. Patients were divided into a hypotension group (systolic blood pressure [SBP], <90 mmHg) and a nonhypotension group (SBP, >90 mmHg) based on the SBP measured from the initial vital signs taken when the patient first presented to the ED.

Statistical analysis

IBM SPSS ver. 20.0 (IBM Corp) was used for the statistical analyses. The continuous variables are expressed as medians (interquartile ranges [IQRs]) or means ± standard deviations. Categorical variables are expressed as frequencies (percentages). In this study, analysis of variance and the t-test were used for data analysis. The t-test was used to compare mean differences between the

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Table 1. General characteristics of patients who visited the ED due to trauma

Variable	Hypotension (n=39)	Nonhypotension (n=511)	Total (n=550)	P-value
Sex				0.501
Male	25 (64.1)	300 (58.7)	325 (59.1)	
Female	14 (35.9)	211 (41.3)	225 (40.9)	
Age (yr)	59 (39.0–73.0)	65 (50.0–79.0)	64 (48.8–79.0)	<0.001
Vital sign				
Systolic blood pressure (mmHg)	70 (0–85.0)	135 (118.0–150.0)	132 (112.8–150.0)	0.166
Respiratory rate (breaths/min)	20 (20–24)	20 (20–20)	20 (20–20)	<0.001
Heart rate (beats/min)	88 (80–108)	86 (76–99)	86 (76–99)	0.049
Body temperature (°C)	36.0 (35.4–36.5)	36.7 (36.4–37.0)	36.6 (36.3–37.0)	0.114
SpO_2 (%)	96 (92–98)	98 (96–98)	98 (96–98)	<0.001
Glasgow Coma Scale	15 (13–15)	15 (15–15)	15 (15–15)	<0.001
Transport method				0.006
Public EMS	31 (79.5)	295 (57.7)	326 (59.3)	
Private ambulance service	3 (7.7)	66 (12.9)	69 (12.5)	
Other vehicles, walk-in, or unknown	5 (12.8)	150 (29.4)	155 (28.2)	
Laboratory result				
Hemoglobin (g/dL)	11.7 (8.7–13.3)	13.0 (11.4–14.2)	13.0 (11.2–14.1)	<0.001
White blood cells (10^3/μL)	11.5 (8.2–17.4)	8.5 (6.4–11.8)	8.8 (6.6–11.9)	<0.001
Lactic acid (mmol/L)	3.9 (2.2–7.5)	1.7 (1.1–2.4)	1.7 (1.2–2.6)	<0.001
Procalcitonin (ng/mL)	0.1 (0.04–1.30)	0.1 (0.04–0.40)	0.1 (0.04–0.40)	0.749
C-reactive protein (mg/L)	1.2 (0.6–6.4)	1.9 (0.5–18.4)	1.8 (0.5–16.9)	0.425
Presepsin (pg/mL)	566 (413.0–789.0)	404 (293.0–544.0)	409 (294.0–564.3)	<0.001
Trauma score				
Injury Severity Score	17 (6–27)	4 (1–10)	5 (1–10)	<0.001
Revised Trauma Score	6.4 (5.2–7.1)	7.8 (7.8–7.8)	7.8 (7.8–7.8)	<0.001
Trauma Injury Severity Score	93.8 (36.0–97.4)	98.3 (96.8–99.4)	98.3 (96.8–99.4)	<0.001
Mechanism of accident				-
Blunt trauma	2 (5.1)	55 (10.8)	57 (10.4)	
Same level falling	6 (15.4)	165 (32.3)	171 (31.1)	
Falling	7 (17.9)	104 (20.4)	111 (20.2)	
Car accident	1 (2.6)	23 (4.5)	24 (4.4)	
Motorbike rider	1(2.6)	21 (4.1)	22 (4.0)	
Bicycle and nonmotor transportation	4 (10.3)	31 (6.1)	35 (6.4)	
Penetrating injury	8 (20.5)	43 (8.4)	51 (9.3)	
Other	10 (25.6)	69 (13.5)	79 (14.4)	
Operation	14 (35.9)	126 (24.7)	140 (25.5)	0.120
ED treatment result				0.003
Admission	28 (71.8)	236 (46.2)	264 (48.0)	
Transfer	3 (7.7)	60 (11.7)	63 (11.5)	
Discharge	7 (17.9)	213 (41.7)	220 (40.0)	
Died	1 (2.6)	2 (0.4)	3 (0.5)	

Values are presented as number (%) or median (interquartile range). Percentages may not total 100 due to rounding.
ED, emergency department; SpO_2, saturation of peripheral oxygen; EMS, emergency medical services.

two groups. Statistical significance was set at $P < 0.05$.

RESULTS

This study included 699 patients without diseases who visited the ED during the study period. A total of 149 intoxicated patients were excluded, and data from 550 patients with trauma were analyzed (Fig. 1). Overall, 550 trauma patients were enrolled, of whom 59.1% were men, and the median age was 64 years (IQR, 48.8–79.0 years). Thirty-nine patients were in a hypotensive state and 511 were not. The proportion of men among patients with and without a hypotensive state was 64.1% and 58.7%, respec-

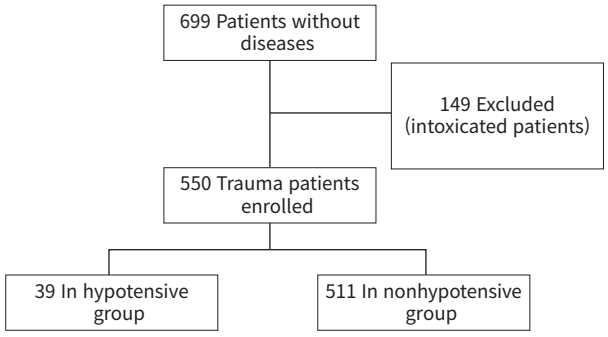

Fig. 1. Flowchart of enrolled patients.

tively. The median age of patients with and without hypotensive state was 59 years (IQR, 39–73 years) and 65 years (IQR, 50–79 years), respectively. No significant difference between the two groups in terms of initial SBP (P = 0.166), initial body temperature (P = 0.114), and PCT levels (P = 0.749) was observed. However, the initial respiratory rate (P < 0.001) and heart rate (P = 0.049) differed significantly between the two groups. In addition, the ISS (P < 0.001), RTS (P < 0.001), and TRISS (P < 0.001) showed significant between-group differences (Table 1).

Patients in a hypotensive state (SBP, <90 mmHg; n = 39) had higher presepsin levels (mean, 1,061.41 pg/mL; median, 566 pg/mL; IQR, 413–789 pg/mL) than those who were not (n = 511; mean, 545.7 pg/mL; median, 404 pg/mL; IQR, 293–544 pg/mL; P < 0.001) (Fig. 2, Table 1).

Patients hospitalized after ED treatment had the highest presepsin levels (660.87 pg/mL), followed by those who died (652.00 pg/mL), were transferred to other hospitals (514.95 pg/mL), and returned home (448.04 pg/mL, P = 0.041) (Fig. 3).

Fig. 4 shows the receiver operating characteristic (ROC) curve between presepsin level and patients with and without a hypotensive state, and the area under the ROC curve was 0.669.

Although not statistically significant, patients who underwent surgery had higher presepsin levels (630.2 pg/mL) than those who did not (523.8 pg/mL, P = 0.526). No significant difference was observed between patients with ISS above 15 (569.1 pg/mL) or below 15 (513.6 pg/mL, P = 0.887).

DISCUSSION

To the best of our knowledge, this study is the first to validate the usefulness of presepsin levels in trauma patients, marking its significance. Our findings revealed significant differences in presepsin levels depending on whether trauma patients were in a hypotensive state or not. Presepsin, a marker for the severity of various

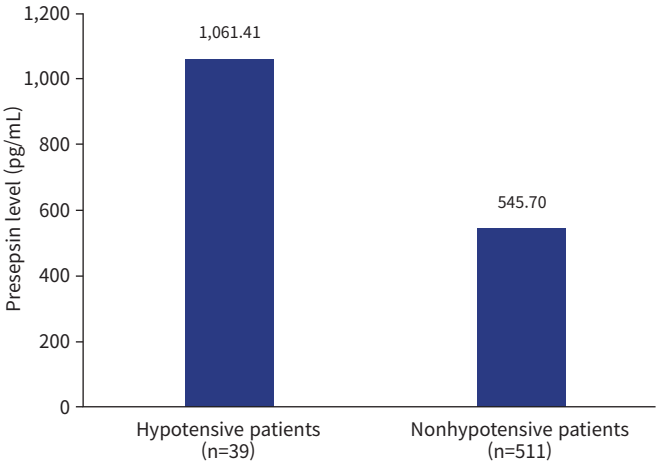

Fig. 2. Presepsin levels in hypotensive and nonhypotensive patients.

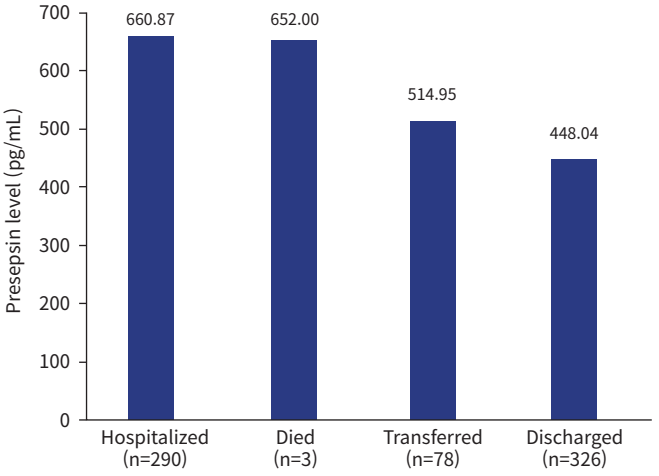

Fig. 3. Presepsin levels in patients classified by the outcome of emergency department treatment.

medical conditions, is typically considered to fall within a normal range of approximately 500 ng/L. In line with previous studies, our trauma patients in a hypotensive state displayed presepsin levels nearly double those of patients not in a hypotensive state. Importantly, presepsin levels were significantly higher in patients with severe outcomes, such as hospitalization or death, compared to those with less severe outcomes, like hospital discharge or transfer. Most patients transferred to other hospitals were transferred due to the perceived minor severity of their injuries. This marked difference suggests the potential of presepsin as a prognostic marker in trauma patients. Given these insights, presepsin shows promise as a valuable prognostic tool for traumatic injury.

As noted earlier, presepsin is a novel biomarker of inflamma-

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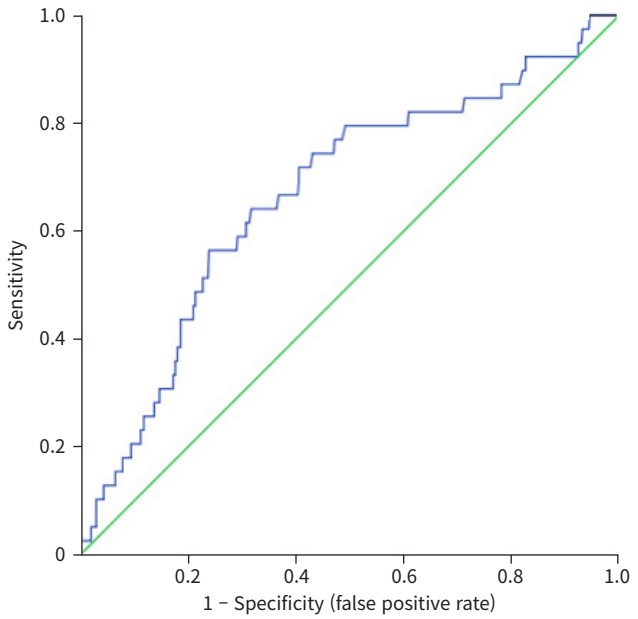

Fig. 4. The receiver operating characteristic (ROC) curve between presepsin levels and patients with and without a hypotensive state (area under the ROC curve, 0.669).

tion that has been widely studied recently and has high sensitivity and specificity for the diagnosis of bacterial infection [21–24]. This study demonstrated that elevated presepsin levels not only indicate a high suspicion of sepsis, but also predict a poor prognosis for patients with trauma. We also found that along with presepsin levels ($P < 0.001$), the initial lactic acid levels ($P < 0.001$) showed significant differences between patients with and without a hypotensive state. However, no significant differences between the two groups with respect to the initial PCT levels ($P = 0.749$) and CRP levels ($P = 0.425$) were observed. Further research is required to validate the potential use of CRP, PCT, and lactic acid levels as prognostic indicators in trauma patients. When assessing the relationship between inflammatory markers and prognosis, changes observed during follow-up can be as important as the initial increase. However, this study focused on the correlation between initial factors and prognosis in an ED setting, and therefore did not include data from several days post–initial assessment.

Patients with polytrauma can die through various pathophysiological pathways, which may or may not involve infectious components [25]. In an effort to maintain homeostasis, a trauma patient's body triggers an inflammatory cascade, which could potentially provide predictive indicators of outcomes through associated biomarkers. This same inflammatory cascade is activated in order to maintain physiological equilibrium during sepsis, infection, and trauma [4]. Given the current research on presepsin as an inflammatory biomarker in patients with sepsis and infection, we hypothesized that its levels might also be elevated in trauma patients, which led us to conduct this study.

According to a study by Zhang et al. [16], presepsin was effective for the diagnosis of sepsis, but has limitations as a standalone rule-out marker. In our study, presepsin exhibited differences between trauma patients with and without a hypotensive state and correlated with ED outcomes. However, further investigations, including comparisons with other markers and multiple regression analyses, are required.

Kang et al. [4] categorized trauma patients into two groups: those with infections and those without. They found that plasma presepsin levels within the first 3 days of admission were significantly higher only in the group with infections. Although presepsin shows promise as a superior biomarker for early differentiation of infection in trauma patients, the increase in PCT and CRP levels, as well as white blood cell counts due to trauma stress, necessitates caution when using these indicators for infection diagnosis. As Kang et al. [4] reported, markers that are elevated in infection and sepsis could also rise due to noninfectious trauma stress, thus requiring differentiation. Our study measured presepsin levels in all trauma patients, regardless of their infection status, and confirmed its elevation even in cases of simple trauma. Kang et al. [4] proposed that presepsin might react specifically in patients with trauma-related infections. However, our study suggests that presepsin might also respond to traumatic stress that is not related to infection. The commonly used biomarker CRP typically indicates an inflammatory response, but it is not specific to either infection or trauma. Conversely, PCT is often used as a biomarker for detecting infection, particularly bacterial infection, rather than trauma itself. In this study, we sought to determine whether presepsin could serve as a biomarker for trauma-induced hypotension, irrespective of infection.

In humans, presepsin is primarily produced by monocytes and macrophages [4,26]. This biomarker, along with others and white blood cells, displays unique elevation characteristics due to their individual production mechanisms. While white blood cells are the primary effector cells in the inflammatory response following trauma, their increase can also be a reaction to the stress induced by trauma, rather than a specific indication of a post-traumatic infection [4,27]. Levels of CRP and PCT act as indirect markers of the host-pathogen response, as they can rise in response to lipopolysaccharide or specific cytokines [4,28]. Procalcitonin is mainly released by the neuroendocrine cells of various organs, while CRP is predominantly produced by hepatocytes [4,29].

Consequently, both procalcitonin and CRP levels can escalate during the acute phase of systemic inflammation, which includes infection and trauma.

Limitations

This study had some limitations. First, it was a retrospective analysis carried out at a single tertiary trauma center, which may limit the generalizability of the results. Second, the study period was approximately 1 year and 2 months, potentially restricting the size of the patient cohort. Third, there was a lack of clinical data related to the course of treatment for trauma patients, including factors such as the length of hospital stay. Fourth, the study only included the initial lab results for presepsin levels, and thus, we were unable to confirm any pattern of fluctuation in relation to the trimodal phases of trauma. To address these limitations and strengthen our findings, further research involving larger multicenter prospective studies and the integration of comprehensive clinical data is recommended.

Conclusions

Serum presepsin levels were significantly higher in patients with trauma in a hypotensive state than in those in a nonhypotensive state. In addition, serum presepsin levels were the highest in hospitalized trauma patients, followed by those who died, were transferred to other hospitals, and returned home.

ARTICLE INFORMATION

Author contributions

Conceptualization: all authors; Data curation: SWK; Formal analysis: JYK; Methodology: SWK; Project administration: all authors; Visualization: SWK; Writing–original draft: SWK; Writing–review & editing: all authors. All authors read and approved the final manuscript.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Data availability

Data analyzed in this study are available from the corresponding author upon reasonable request.

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