Original Article

J Trauma Inj 2023;36(2):114-120
https://doi.org/10.20408/jti.2022.0050

Journal of Trauma and Injury JTI

pISSN 2799-4317 • eISSN 2287-1683

The practicality of interleukin-6 in prognosis of blunt chest trauma in Korea: a retrospective study

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Purpose: There are many studies on the practicality of interleukin-6 (IL-6) as a prognostic predictor in patients with multiple severe traumas. However, few studies focus on the practicality of IL-6 in patients with chest trauma. So, this study investigated whether IL-6 is effective as a prognostic factor in patients with blunt chest trauma.

Methods: A total of 44 blunt chest trauma patients who visited the regional trauma center from July to December 2021 were included in this retrospective study. Blood IL-6 levels were measured immediately after emergency room admittance (IL-6 E) and 24 hours after trauma (IL-6 24). To determine whether IL-6 levels can predict the clinical course and prognosis of patients with blunt chest trauma, the correlation between IL-6 (IL-6 E and IL-6 24) and the trauma score system, Injury Severity Score, Thoracic Trauma Severity Score, and Pulmonary Contusion Score, intensive care unit (ICU) stay period, and total hospitalization period were analyzed.

Results: IL-6 E showed a good correlation with Injury Severity Score (P=0.505), Thoracic Trauma Severity Score (P=0.597), Pulmonary Contusion Score (P=0.493), ICU stay period (P=0.762), and total hospitalization period (P=0.662). However, IL-6 24 had a relatively low correlation compared to IL-6 E. Therefore, IL-6 E showed useful results for predicting the prognosis of patients with blunt chest trauma.

Conclusions: Early plasma IL-6 levels (IL-6 E) can predict the injury severity of blunt chest trauma, length of ICU stay, and total hospitalization period.

Keywords: Interleukin-6; Thoracic injury; Injury Severity Score

Received: September 5, 2022
Revised: September 29, 2022
Accepted: November 12, 2022

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INTRODUCTION

The Injury Severity Score (ISS), New Injury Severity Score (NISS), Revised Trauma Score (RTS), Trauma and Injury Severity Scale (TRISS), and Glasgow Coma Scale are widely used in evaluating trauma severity and are designed to predict the progress and prognosis of acute severe trauma patients [1]. In a study by Orhon et al. [2], the ISS, NISS, RTS, and TRISS were useful for predicting trauma patients' mortality. The NISS, RTS, and TRISS were also significantly correlated with intensive care unit (ICU) treatment period, and the TRISS was highly correlated with mechanical ventilation time in trauma ICU treatment patients [2].

The systemic inflammatory immune response in acute blunt trauma patients is an important pathophysiological mechanism for tissue damage, and the amplified inflammatory response can cause multiple organ failure syndromes [3]. Tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6) are well known as the major cytokines that cause such systemic inflammatory reactions [3]. When multiple organ failure occurs in trauma patients, the duration of ICU treatment and the period of artificial ventilator treatment are prolonged, which increases the long-term mortality and the risk of functional disability [4–7]. Other studies have reported that increased IL-6 and IL-8 levels and reduced IL-4 levels in the early stage of trauma can cause systemic inflammatory response syndromes, acute respiratory distress syndrome, and multiorgan failure syndrome, which can increase morbidity and mortality [8].

To determine whether the IL-6 level in the blood was effective for prognosis in early trauma patients, Qiao et al. [9] performed a meta-analysis of studies evaluating IL-6 levels and the prognosis of trauma patients. As a result, the blood IL-6 level tested within 24 hours after trauma was effective in predicting posttraumatic complications, especially the occurrence of multiple organ failure syndromes [9]. Gebhard et al. [10] periodically measured the blood IL-6 levels in the first 24 hours after trauma in severe trauma patients and found they were correlated with the ISS.

Thoracic trauma is associated with 60% of severe multiple trauma patients and has a 20% to 25% mortality rate [11]. Depending on the mechanism of injury, chest trauma is divided into blunt and penetrating wounds, and blunt injuries account for about 70% [11]. The proportion of blunt thoracic injuries is about 15% of all trauma patients, and when accompanied by pulmonary contusions, 10% to 15% mortality is observed depending on the accompanying damage [11].

In the past, there have been many studies showing that IL-6 levels in the blood are effective in predicting the prognosis of patients with multiple traumas caused by acute blunt injuries [9]. However, there have been few studies on IL-6 in blunt chest trauma. In a study of 208 patients who visited a level I trauma center, Taniguchi et al. [12] showed that IL-6 levels in the blood tested immediately after arrival in the emergency room were correlated with the duration of ICU treatment and the Abbreviated Injury Scale (AIS) in the chest, abdomen, and musculoskeletal system. Other studies have shown that IL-6 and surfactant protein-D levels were associated with complications in patients with multiple rib fractures and lung contusion with blunt chest injuries [13].

Therefore, the purpose of this study was to investigate whether the initial IL-6 level in blunt chest trauma patients was effective as a predictor of progress and prognosis. In blunt chest trauma patients who visited the trauma center, the IL-6 values were collected immediately after emergency room admittance (IL-6 E) and 24 hours after trauma (IL-6 24). Statistical analysis was conducted to determine whether the IL-6 values were correlated with the ISS, Thoracic Trauma Severity Score (TTSS), Pulmonary Contusion Score (PCS), ICU treatment period, and total hospitalization period.

METHODS

Ethics statements

The study was approved by the Institutional of Review Board of Cheju Halla General Hospital (No. 2002-L05-01). This study is a retrospective study of patient medical records. Hence, written informed consent was not needed.

Research subject

Among the trauma patients who visited the regional trauma center from July 1 to December 31, 2021, those with acute blunt chest injury were identified, and their medical records were reviewed retrospectively. Patients with traumatic brain and spinal cord injuries, musculoskeletal injury of AIS 3 or higher, and abdominal injuries requiring surgery were excluded. For all patients with chest injuries who visited the regional trauma center, a basic blood IL-6 test was performed at the time of the emergency room visit and 24 hours after the injury. After reviewing the medical records, patients with missing test results and who visited the emergency room for more than 3 hours after trauma were excluded from the study. A total of 44 patients were selected for the study, excluding patients with inflammatory diseases and malignant tumors as underlying diseases and patients who underwent cardiopulmonary resuscitation.

Measure and definition

The medical records of the included patients were reviewed for IL-6 E and IL-6 24, and the ISS, PCS, and TTSS values of each patient were calculated. Then, the number of days of treatment in the ICU (ICU stay) and the total number of days in the hospital (total hospitalization period) were calculated for each patient.

The level of IL-6 in the blood was tested by electrochemiluminescence immunoassay analysis using the Cobas e 411 equipment (Hitachi, Tokyo, Japan) at the Department of Laboratory Medicine at Cheju Halla General Hospital, and the results were reported within 60 minutes after requesting the test.

The ISS is an anatomically-based consensus severity score sys-

tem standardized by the Association for the Advancement of Automotive Medicine and the International Trauma Association. This scoring system divides the body into six parts to obtain the AIS value for each part, and the squares of the AIS values for the three most severe parts are summed.

The PCS was devised by Kim et al. [14] using chest computed tomography (CT). In this grading method, both lungs were divided into quadrants, and the right upper and middle lobes were included in one lobe, and the right lower, left upper, and lower left lobes were separate quadrants each. Each lobe was given 0 to 3 points for the degree of lung contusion on the chest CT, and the scores of each lobe were summed up (0–12 points total) to obtain the PCS. The combined score was determined as follows: 0 to 2 as mild, 3 to 5 as moderate, and 6 to 12 as severe [14].

The TTSS was described by Pape et al. [15]. Compared to the AIS or Lung Injury Scale, the TTSS is a system that is more suitable for thoracic trauma patients [15]. The TTSS consists of five items, the PaO2/FiO2 ratio, number of rib fractures, grade of lung contusion, pleural involvement, and patient's age. The sum of the scores of the five items ranges from a minimum of zero points and a maximum of 25 points [15].

Statistical analysis

IBM SPSS ver. 20.0 (IBM Corp) was used for the statistical analysis of the collected data. The IL-6 E, IL-6 24, ISS, PCS, TTSS, ICU stay, and total hospitalization period were calculated, and descriptive statistics were performed. A bivariate correlation analysis was performed to determine whether there was a correlation between each variable. A multivariate linear regression analysis was performed to test the causality between IL-6 and treatment outcomes (ICU stay and total hospitalization period). A Pearson's correlation was used, and a P-value less than 0.05 was defined as statically significant. The variance inflation factor was used to evaluate multicollinearity.

RESULTS

A total of 44 blunt chest trauma patients were selected for the study. The average age of the patients was 59.3 ± 15.8 years old, and the male to female ratio was 1.44:1. The average ISS was 14.4 ± 8.0, TTSS was 8.6 ± 3.7, and PCS was 2.7 ± 2.3. The IL-6 E value of the patient group 474.7 ± 745.9 pmol/L, and the IL-6 24 value was268.0 ± 531.6 pmol/L, showing a larger standard deviation than the average value (Table 1, Figs. 1, 2).

Only the blunt chest injury was present in 24 patients (55.6%). Eight patients (17.8%) had orthopedic fractures, two patients (4.4%) had orthopedic fractures and spleen injuries, three patients (6.7%) had facial bone fractures, three patients (6.7%) had vertebral fractures, two patients (4.4%) had liver injuries, one patient (2.2%) had a pelvic bone fracture, and one patient (2.2%) had a skull fracture (Table 2).

To determine whether an IL-6 test can predict the clinical course and prognosis of patients with blunt chest trauma, the correlation between IL-6 (IL-6 E, IL-6 24) and the trauma score system, ICU stay period, and total hospitalization period was analyzed (Table 3).

IL-6 E levels showed a high correlation with the ISS, TTSS (Table 3, Figs. 3, 4), and PCS, which can predict the patient`s prognosis. IL-6 E levels were also highly correlated with the ICU stay and total hospitalization periods, which are determined by the patient`s treatment result (Table 3, Figs. 5, 6). IL-6 24 levels were correlated with the TTSS, ICU stay, and total hospitalization period but had no correlation with the ISS and PCS. A multivariable linear regression analysis was performed with IL-6 E levels, the ISS, and the TTSS as independent variables to confirm the causality of IL-6 E levels with the ICU stay and total hospitalization period (Table 4).

The causality of IL-6 E levels was well explained with the ICU stay (standardized β coefficient, 0.424; $P < 0.001$) and with total hospitalization periods (standardized β coefficient, 0.345; $P < 0.010$). The variance inflation factors among the ISS, TTSS, and IL-6 E levels were under 10.

DISCUSSION

In this study, the level of IL-6 tested immediately after visiting the

Table 1. Basic characteristics of patient and result of study (n=44)

Characteristic	Value
Sex ratio	1.44:1
Age (yr)	59.3±15.8
Injury Severity Score	14.4±8.0
Thoracic Trauma Severity Score	8.6±3.7
Pulmonary Contusion Score	2.7±2.3
Intensive care unit stay (day)	1.8±3.5
Total hospitalization period (day)	24.2±16.1
IL-6 E (pmol/L)	474.7±745.9
IL-6 24 (pmol/L)	268.0±531.6

Values are presented as mean±standard deviation, unless otherwise indicated.
IL-6 E, interleukin-6 levels measured immediately after the emergency room admittance; IL-6 24, interleukin-6 levels measured at 24 hours after trauma.

https://doi.org/10.20408/jti.2022.0050

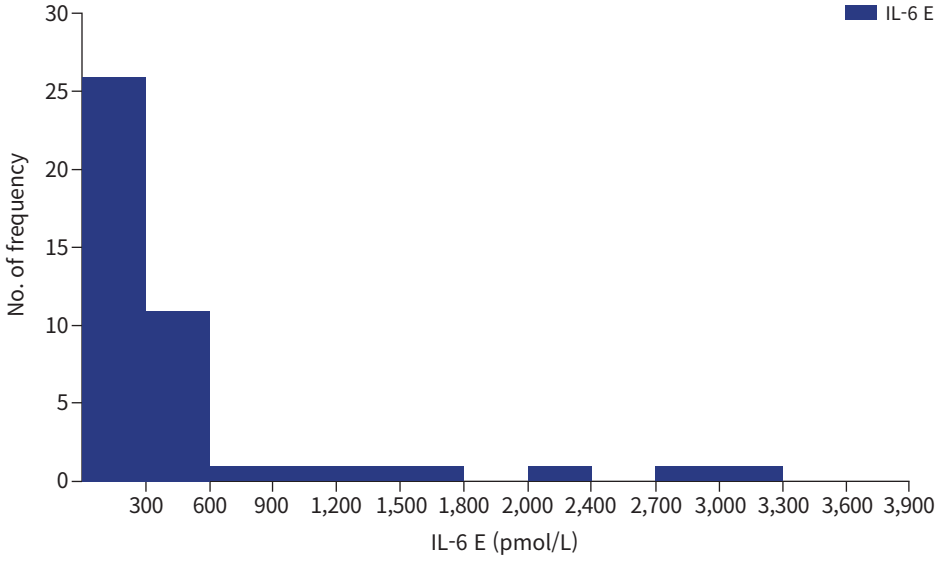

Fig. 1. Interleukin-6 levels measured immediately after the emergency room admittance (IL-6 E; n=44). SD, standard deviation.

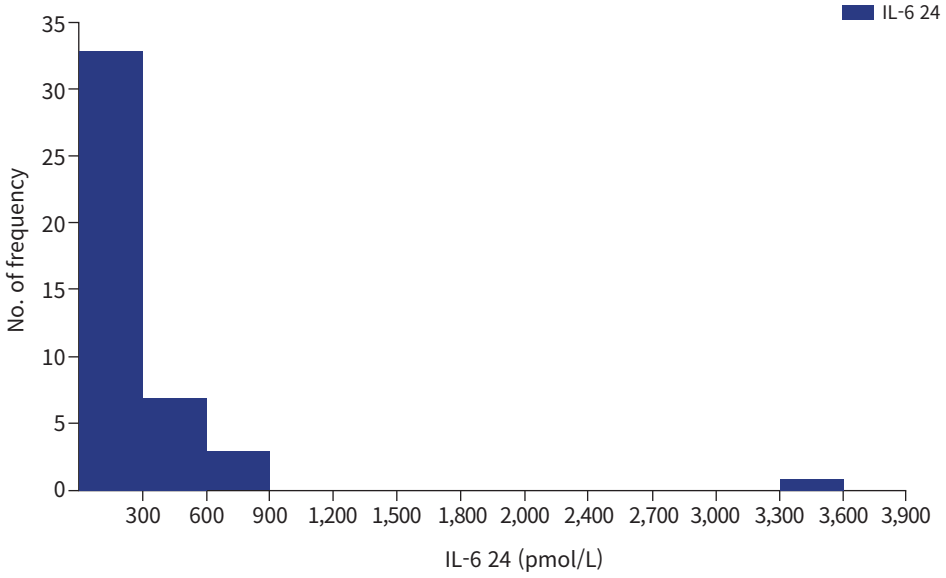

Fig. 2. Interleukin-6 levels measured at 24 hours after trauma (IL-6 24; n=44). SD, standard deviation.

emergency room of a patient with a blunt chest injury was found to be correlated with various indicators related to chest injuries, such as the ISS, TTSS, and PCS. In addition, it was found that there was a correlation between IL-6 E levels and the duration of ICU stay and the total hospitalization periods. IL-6 24 levels were correlated with the TTSS, ICU stay, and total hospitalization periods.

In several previous studies, blood IL-6 levels tested within 24 hours in multiple trauma patients were reported to have a high correlation with the trauma severity score (correlation coefficient, 0.46–0.61) [10,12,16]. In this study, which focused on patients with chest trauma, only the IL-6 E level was correlated with the ISS (correlation coefficient, 0.505), and not the IL-6 24 level. Also, in this study, the IL-6 E level showed a good correlation with the TTSS (0.597) and PCS (0.493), whereas IL-6 24 level showed a correlation with only the TTSS (0.398). These results show that the IL-6 E level is more valuable than the IL-6 24 level in predicting the severity of the initial chest trauma.

A number of studies have evaluated the association between an increase in serum IL-6 levels and multiple organ failure syndromes in trauma patients [17–19]. Frink et al. [19] analyzed the association between the levels of TNF-α, IL-6, IL-8, and IL-10 in

Table 2. Associated injury (n=44)

Associated injury	No. (%)
Thorax injury only	24 (54.5)
Fracture of extremity	8 (18.2)
Fracture of extremity and spleen injury	2 (4.5)
Facial bone fracture	3 (6.8)
Fracture of spine	3 (6.8)
Liver injury	2 (4.5)
Pelvic bone fracture	1 (2.3)
Simple skull fracture	1 (2.3)

Table 3. Correlation between IL-6 and injury scores and treatments outcomes

Variable	IL-6 E (n=44)	IL-6 24 (n=44)
ISS		
Pearson correlation	0.505**	0.117
P-value	<0.001	0.45
TTSS		
Pearson correlation	0.597**	0.398**
P-value	<0.001	0.007
PCS		
Pearson correlation	0.493**	0.28
P-value	0.001	0.065
ICU stay		
Pearson correlation	0.762**	0.556**
P-value	<0.001	<0.001
Total hospitalization period		
Pearson correlation	0.662**	0.389**
P-value	<0.001	0.009

IL-6, interleukin-6; IL-6 E, interleukin-6 levels measured immediately after the emergency room admittance; IL-6 24, interleukin-6 levels measured at 24 hours after trauma; ISS, Injury Severity Score; TTSS, Thoracic Trauma Severity Score; PCS, Pulmonary Contusion Score; ICU, intensive care unit.
**P<0.01.

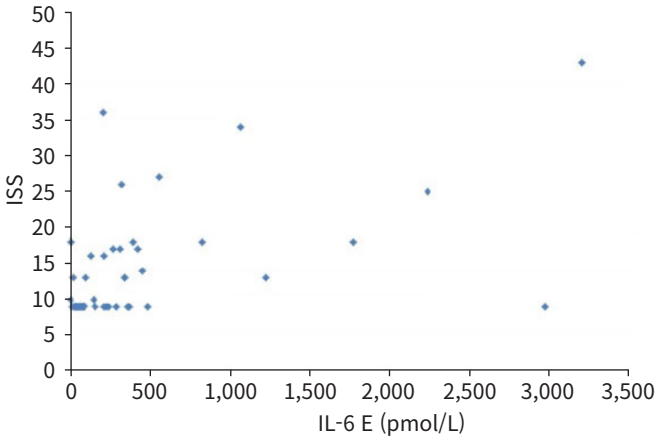

Fig. 3. Scatterplot between Injury Severity Score (ISS) and interleukin-6 levels measured immediately after the emergency room admittance (IL-6 E).

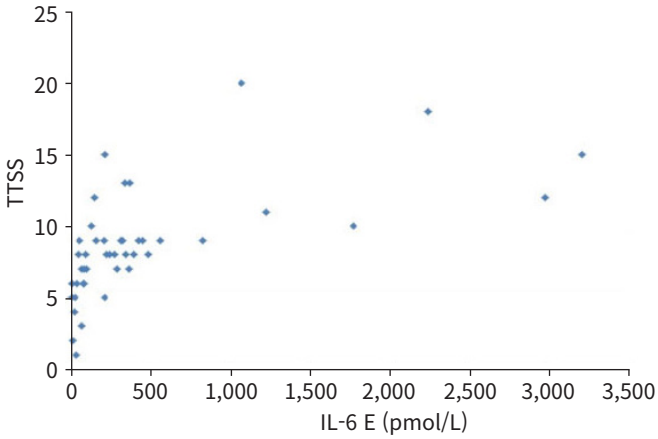

Fig. 4. Scatterplot between Thoracic Trauma Severity Score (TTSS) and interleukin-6 levels measured immediately after the emergency room admittance (IL-6 E).

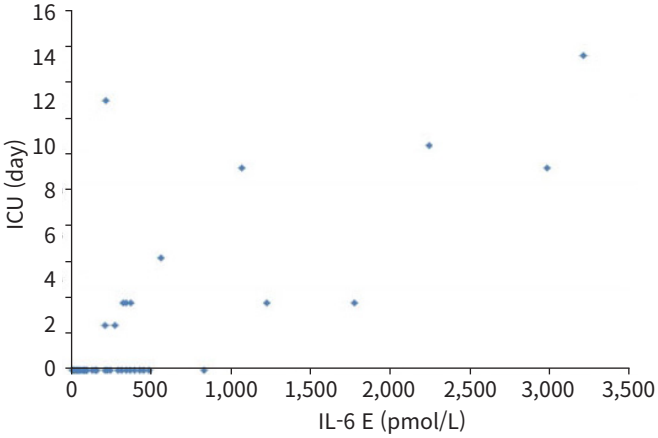

Fig. 5. Scatterplot between intensive care unit (ICU) stay and interleukin-6 levels measured immediately after the emergency room admittance (IL-6 E).

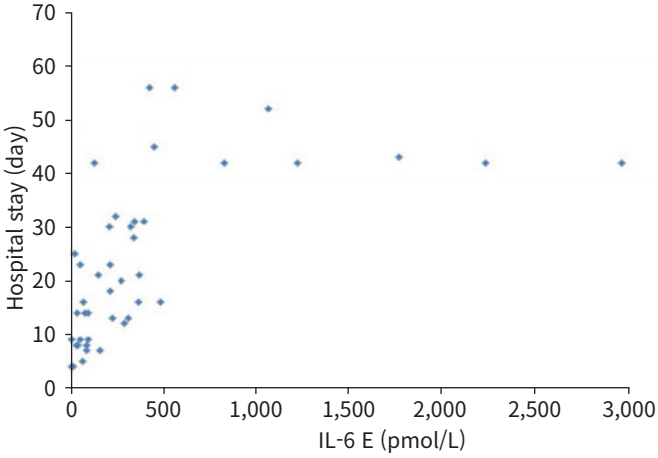

Fig. 6. Scatterplot between total hospitalization periods and interleukin-6 levels measured immediately after the emergency room admittance (IL-6 E).

https://doi.org/10.20408/jti.2022.0050

Table 4. Multivariable linear regression analysis

Variable	β	Standardized β	P-value
Intensive care unit stay			
ISS	0.091	0.208	0.040
TTSS	0.369	0.391	0.001
IL-6 E	0.007	0.424	<0.001
Total hospitalization period			
ISS	0.771	0.387	0.003
TTSS	0.871	0.203	0.128
IL-6 E	0.027	0.345	0.010

ISS, Injury Severity Score; TTSS, Thoracic Trauma Severity Score; IL-6 E, interleukin-6 levels measured immediately after the emergency room admittance.

the blood of early trauma patients and the occurrence of multiple organ failure syndrome. The researchers reported that IL-6 was the most useful predictor of multiple organ failure [19]. Similarly, Jastrow et al. [17] and Cuschieri et al. [18] reported that the area under the curve (AUC) value of the correlation between blood IL-6 levels was high in predicting multiorgan dysfunction syndrome in the early stage of trauma (Jastrow et al. [17]: n = 48; blood IL-6 levels 4–8 hours after admission to the ICU; AUC, 0.816; Cuschieri et al. [18]: n = 79; blood IL-6 levels over 12 hours; AUC, 0.749; 95% confidence interval, 0.643–0.855). The occurrence of multiorgan dysfunction syndrome in patients with multiple trauma due to blunt injury prolongs the patients' ICU treatment period and increases the incidence of complications [4,5]. In a study by Taniguchi et al. [12], the ICU treatment period was prolonged, and the mortality rate increased 28 days after hospitalization in a group of multiple blunt trauma patients with increased serum IL-6 E levels. This study on patients with blunt chest trauma showed a correlation between the increase in IL-6 E and IL-6 24 levels and the length of treatment in the ICU and total hospitalization period. This result is similar to the previous studies conducted on multiple trauma patients.

According to past studies, blood IL-6 levels in patients with acute multiple trauma begin to rise immediately after injury and reach a peak within 6 hours after trauma [8,10]. Other studies investigated the association between the level of IL-6 in the blood within 4 to 12 hours after arriving at the emergency room, the trauma severity score, and the patient's clinical course and reported that blood IL-6 levels are useful for determining patient prognosis [8,10,19]. However, based on the results of these studies, the IL-6 levels obtained 4 to 12 hours after arrival at the hospital do not predict the severity and clinical course. According to the statistics of the regional trauma center, for most trauma patients, diagnosis and immediate necessary surgical and/or interventional procedures and the severity and clinical prognosis are completed within 4 to 12 hours after trauma [20]. Thus, the results of this study confirm that IL-6 E levels correlate well with the trauma scoring system, and patient treatment outcomes show that IL-6 E levels are valuable as a diagnostic aid to help determine the treatment direction and predict the course of treatment for acute chest trauma patients.

This study has two limitations. First, although blunt chest trauma was the main injury, there is a possibility that IL-6 levels may be affected depending on the accompanying injuries to other body parts. Second, IL-6 levels continuously change over time after trauma. Therefore, the time it takes for each patient to arrive at the emergency room after trauma can affect the test results and cause statistical errors.

In patients with acute blunt thoracic trauma, higher the level of blood IL-6 E level correlate with the severity of the trauma and lung damage, and the duration of ICU treatment and hospitalization are likely to increase. Therefore, patients with high IL-6 E levels need more active observation and treatment to prevent trauma complications.

NOTES

Conflicts of interest

The authors have no conflicts of interest to declare.

Funding

None.

Data sharing statement

The data of this article are available from the corresponding author upon reasonable request.

Author contributions

Conceptualization: JWO; Data curation: JWO, TYL; Formal analysis: MC; Writing–original draft: JWO; Writing–review & editing: all authors. All authors read and approved the final manuscript.

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