

# The importance of inflammatory indices in the early diagnosis and prognostic evaluation of patients with crush syndrome

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## ABSTRACT

**Aims:** The increase in natural disasters has led to a higher incidence of crush injuries among individuals. Consequently, the development of disaster medicine in recent years has been accompanied by a rise in crush syndrome cases. In disaster medicine management, there is a need for rapid diagnostic and prognostic biomarkers in such cases. Creatine kinase (CK) and C-reactive protein (CRP) are among the most commonly used biomarkers for assessing the inflammatory process. In recent years, novel inflammatory indices such as the Systemic Inflammatory Response Index (SIRI), the Systemic Immune-inflammation Index (SII), and the Pan-immune-Inflammatory Value (PIV) have been shown to play a significant role in the rapid diagnostic and prognostic evaluation of various diseases. In this study, we aimed to determine the diagnostic value and clinical significance of the SII, SIRI, and PIV indices in the diagnosis of crush syndrome.

**Methods:** This retrospective observational study was conducted on patients diagnosed with crush syndrome who were affected by the earthquake that occurred in Hatay on February 6, 2023, and who were admitted to Ankara Etlik City Hospital between January 1 and December 31, 2023. The included patients were analyzed in terms of laboratory parameters and inflammatory indices and were compared with a control group.

**Results:** In the patient group included in the study, markers of inflammation, tissue damage, and metabolic disturbances were found to be significantly higher compared to the control group. Notably, levels of CRP, WBC, neutrophils, CK, AST, ALT, BUN, and potassium were markedly elevated, while calcium and pH levels were reduced. Systemic inflammatory indices such as SII, SIRI, PIV, and NLR were also found to be higher in the patient group. In logistic regression analysis, only the SIRI variable was identified as an independent predictor. ROC analyses demonstrated that parameters such as AST, ALT, and SIRI had high diagnostic power. The findings indicate that systemic inflammation and pathophysiological processes are more pronounced in the patient group.

**Conclusion:** The data obtained demonstrate that inflammatory indices play an important role in the diagnosis of crush syndrome. In particular, the SIRI may provide a stronger diagnostic value compared to other inflammatory indices. Therefore, the use of SIRI as a biomarker for early diagnosis and management of crush syndrome could be beneficial in clinical practice.

**Keywords:** Crush syndrome, early diagnosis, inflammation, creatine kinase, biomarker, earthquake

## INTRODUCTION

The term "crush" refers to compression or crushing. Crush syndrome describes a condition in which the trunk or extremities of the body are exposed to an external compressive force.<sup>1</sup> Historically, in 1941, Bywaters and Beall<sup>2</sup> reported that many patients injured during the Blitz bombings died due to acute renal failure. They later identified a link between muscle damage caused by compression and the development of acute renal failure, coining the term "crush syndrome".<sup>2</sup> Causes of crush injuries include natural disasters

such as earthquakes, as well as industrial, construction, or agricultural accidents.<sup>3-5</sup>

Following a compressive force, muscle injuries may occur in the affected regions, potentially accompanied by muscle necrosis, neurological dysfunction, and edema. As a result, crush syndrome can lead to acute kidney injury (AKI) and even multiple organ failure. Prolonged exposure to compression can cause cellular death, particularly



myonecrosis. Although individuals may appear stable after being rescued, the sudden release of potassium, phosphorus, and myoglobin into circulation from damaged tissues can trigger fatal ventricular fibrillation.<sup>6</sup>

The compression of skeletal muscles can result in AKI and, subsequently, rhabdomyolysis—a condition often associated with fatal outcomes. Nephrotoxic products released during rhabdomyolysis, together with tubular obstruction, contribute to AKI. Additionally, hypotension and hypoperfusion may exacerbate acute tubular necrosis. Other factors that increase mortality include advanced age and extensive muscle injury. Therefore, elevated levels of parameters such as serum potassium, aspartate aminotransferase (AST), and creatine kinase (CK), which indicate the severity of muscle injury, reflect both the extent of tissue damage and the severity of the clinical condition.<sup>7</sup>

Recent studies have shown that systemic inflammatory response syndrome (SIRS), triggered by muscle injury, may exacerbate tissue damage. It is suggested that this may create a vicious cycle. Following trauma, immune cells accumulate and become activated at the injury site. Activated lymphocytes, macrophages, and neutrophils contain enzymes in their intracellular granules that produce reactive oxygen species (ROS). Macrophages, which are rich in growth factors and cytokines, significantly contribute to ROS production. While ROS can intensify tissue damage, they also play a role in enhancing immune responses against tissue injury. Paradoxically, macrophages are involved in both muscle cell damage and regeneration.<sup>8</sup>

When the immune system detects danger signals released from injured tissues, inflammation is initiated.<sup>9</sup> This process leads to the release of inflammatory cytokines and ROS, activating lymphocytes, macrophages, and neutrophils, thereby exacerbating local tissue injury.<sup>10</sup> Numerous pro-inflammatory cytokines and chemokines are involved in the pathogenesis of skeletal muscle injury. Some of these inflammatory cytokines may enter systemic circulation and cause inflammation in distant tissues and organs.<sup>11</sup>

Among biomarkers derived from neutrophil, lymphocyte, and monocyte counts, the Systemic Inflammatory Response Index (SIRI) and the Systemic Immune-inflammation Index (SII) have previously been used in evaluating the prognosis of neoplastic diseases.<sup>12,13</sup> SII and SIRI incorporate multiple well-known inflammatory markers that reflect the balance between inflammation and immune response.<sup>14</sup>

Inflammation plays a key role in the pathogenesis of skeletal muscle injury in crush syndrome, and C-reactive protein (CRP) is the most widely used inflammatory marker. A newer parameter, the Pan-immune-Inflammatory Value (PIV), has emerged as a comprehensive and practical index for evaluating inflammation in clinical practice. Moreover, it has been shown to be associated with poor prognosis in various chronic diseases.<sup>15-17</sup>

## METHODS

This study was designed as a retrospective analysis and was approved by the Ankara Etlik City Hospital Clinical Researches Ethics Committee (Date: 26.04.2023, Decision No: AEŞH-EK1-2023-099). All procedures were carried out in accordance with the ethical rules and the principles of

the Declaration of Helsinki. The study included patients diagnosed with crush syndrome who were affected by the earthquake that occurred in Hatay on February 6, 2023, and who were admitted to Ankara Etlik City Hospital between January 1 and December 31, 2023.

Demographic, clinical, and laboratory data of the patients were obtained from electronic medical records and hospital case report forms. The cases were divided into two groups: patients diagnosed with crush syndrome, and volunteers who had experienced crush injuries but did not develop the syndrome. Informed consent was obtained from both patient and control groups. Initial admission values were extracted from the hospital's "keydata" system. The results of both groups were compared. In all groups, the following parameters were analyzed: urea, creatinine, calcium, phosphorus, potassium, CK, AST, alanine aminotransferase (ALT), white blood cell (WBC) count, neutrophil count (NEU), lymphocyte count (LYMPH), monocyte count (MONO), platelet (PLT) count, neutrophil-to-lymphocyte ratio (NLR), SII, SIRI, PIV, CRP, pH, and lactate levels.

In the evaluation of cases diagnosed with crush syndrome, demographic data as well as clinical and laboratory findings were assessed. The control group included patients who had experienced crushing trauma but did not develop crush syndrome. The number of affected extremities, duration of entrapment under debris, and whether fasciotomy, dialysis, or intubation were performed were analyzed. Patients who did not survive (deceased cases) were also included in the analysis.

The following cases were excluded from the study: patients under the age of 18; pregnant patients who had experienced crushing injuries; patients admitted more than 24 hours after injury; patients who had experienced crushing trauma but had normal CK levels; patients with chronic renal failure undergoing routine hemodialysis; and patients who did not consent to participate in the study.

## Diagnostic Criteria

The diagnosis of crush syndrome was established based on the clinical and laboratory findings of patients who had sustained crush injuries. Patients who had muscle damage due to crushing, presented clinical symptoms, and had CK levels >5000 U/L were included in the study. The study cohort consisted of 63 patients diagnosed with crush syndrome and 49 individuals who had experienced crushing injuries but did not develop the syndrome (control group).

Inflammatory indices were calculated using the following formulas:

- $SII = \text{Platelet count} \times \text{neutrophil count} / \text{lymphocyte count}$
- $SIRI = \text{Neutrophil count} \times \text{monocyte count} / \text{lymphocyte count}$
- $PIV = \text{Neutrophil count} \times \text{monocyte count} \times \text{platelet count} / \text{lymphocyte count}$

## Statistical Analysis

The data analysis of the study was conducted using The Statistical Package for Social Sciences (SPSS) for Windows, Version 23 (IBM Corp., Armonk, NY, USA). To evaluate the distribution characteristics of the variables, both analytical tests (Kolmogorov-Smirnov and Shapiro-Wilk tests) and visual methods (histogram inspection) were used. Descriptive

statistics were presented as mean±standard deviation for normally distributed variables and median (interquartile range [IQR]) for non-normally distributed variables.

For comparisons between groups, the Student's t-test was used for parametric variables, while the Mann-Whitney U test was employed for non-parametric variables. For categorical variables, the Chi-square test or, when appropriate, Fisher's exact test was used.

To assess relationships between variables, correlation analysis was performed. The Pearson correlation coefficient was used for parametric variables, while the Spearman correlation coefficient was applied for non-parametric variables. Variables showing strong correlations in the correlation analysis were evaluated for multicollinearity risk, and Variance Inflation Factor (VIF) values were examined for each independent variable. Variables with VIF>5 were excluded from the model. A multivariate logistic regression analysis was then conducted using variables deemed appropriate in terms of multicollinearity.

To evaluate the discriminatory power of laboratory and inflammatory indices used in the diagnosis of crush syndrome, a receiver operating characteristic (ROC) curve analysis was conducted, and optimal cutoff values were calculated for parameters such as NLR, SII, SIRI, and PIV. Additionally, differences between the areas under the curve (AUC) of the ROC curves were compared using the DeLong test.

A p-value <0.05 was considered statistically significant in all analyses.

## RESULTS

A total of 112 cases were included in the study. Among the participants, 56.3% were in the patient group and 43.8% were in the control group. Regarding gender distribution, 34.8% of the cases were female and 65.2% were male. Fasciotomy was performed at the scene in 18.8% of the cases, while 81.3% did not undergo fasciotomy. The proportion of patients requiring dialysis was 17.9%, whereas 82.1% did not require dialysis. Intubation was required in 5.4% of the cases, and 94.6% were followed without intubation. The mortality (exitus) rate in the study group was 9.8%, while 90.2% of the patients were discharged alive (Table 1).

**Table 1.** Descriptive characteristics of the study group

Variable	Category	n	%
Group	Control	49	43.8
	Patient	63	56.3
Sex	Female	39	34.8
	Male	73	65.2
Fasciotomy on site	No	91	81.3
	Yes	21	18.8
Dialysis	No	92	82.1
	Yes	20	17.9
Intubated	No	106	94.6
	Yes	6	5.4
Deceased	No	101	90.2
	Yes	11	9.8

The mean age of the patient group was 40.9±17.1 years, while that of the control group was 44.3±18.2 years. Among inflammatory markers, CRP levels were significantly higher in the patient group (129.2±90.4 mg/L) compared to the control group (62.3±64.6 mg/L) (p<0.001). Similarly, WBC and neutrophil counts were significantly elevated in the patient group (WBC: 16.2±6.6 vs. 9.2±3.0×10<sup>3</sup>/μL; NEU: 12.9±5.9 vs. 6.4±3.0×10<sup>3</sup>/μL; p<0.001). Levels of CK and liver enzymes (AST, ALT) were also markedly higher in the patient group. Kidney function indicators, such as BUN and creatinine, were significantly elevated in patients (p<0.001).

Among electrolytes, potassium levels were increased and calcium levels were decreased in the patient group. Lactate levels were higher in patients (2.4±2.3 mmol/L) than in controls (1.7±1.1 mmol/L). The average duration of entrapment under debris was significantly longer in the patient group (17.6±20.5 hours) compared to the control group (3.9±11.4 hours) (p<0.001).

In comparisons between the two groups, most biochemical and hematological parameters showed statistically significant differences. Inflammatory and tissue damage markers were markedly elevated in the patient group. Levels of CRP, WBC, neutrophils, monocytes, CK, AST, ALT, BUN, and potassium were significantly higher (all p<0.001), while calcium and pH levels were lower (p=0.001 and p=0.016, respectively). Additionally, systemic inflammatory indices such as SII, SIRI, PIV, and NLR were significantly elevated in the patient group (p<0.001). The duration of entrapment under debris was significantly longer in the patient group (mean: 17.6 hours; p<0.001). No statistically significant differences were observed in PLT and LYMPH levels between the groups (p>0.05).

These findings indicate that systemic inflammation, tissue damage, and metabolic disruption were more pronounced in the patient group compared to the control group (Table 2).

The correlation analysis between the variable crush and various laboratory parameters revealed numerous significant positive associations. The strongest positive correlations were observed with WBC (r=0.548), NEU (r=0.560), CK (r=0.482), and MONO (r=0.474), indicating a notable increase in inflammatory and tissue damage markers in the patient group (all p<0.001). Additionally, CRP, AST, ALT, BUN, potassium (K), SII, SIRI, PIV, NLR, and the duration of entrapment also demonstrated significant positive correlations with the presence of crush syndrome (p<0.01).

Conversely, calcium (r=-0.351, p<0.001) and pH (r=-0.221, p=0.019) levels were negatively correlated with the crush variable, suggesting that lower levels of these homeostatic parameters are associated with patients diagnosed with crush syndrome.

In summary, a strong positive correlation exists between the crush variable and inflammatory markers (WBC, NEU, SII, CRP, SIRI, NLR), as well as metabolic parameters (BUN, K). In contrast, inverse correlations were found with calcium and pH, supporting the presence of more prominent systemic inflammation, metabolic disturbance, and tissue injury in the patient group compared to controls (Table 3).

**Table 2.** Distribution of basic laboratory and clinical data by group

Variable	Control mean±SD	Control median (IQR)	Control min-max	Patient mean±SD	Patient median (IQR)	Patient min-max	p (2-tailed)
Age (years)	44.33±18.20	45.0 (32)	18–85	40.89±17.12	40.0 (25)	18–90	0.320
CRP (mg/L)	62.35±64.60	39.0 (97)	1–266	129.21±90.41	120.0 (86)	18–400	<0.001
WBC (×10 <sup>3</sup> /μL)	9.17±3.05	8.71 (3.08)	4.17–22.97	16.17±6.60	14.30 (8.80)	5.30–36.20	<0.001
NEU (×10 <sup>3</sup> /μL)	6.38±2.99	5.88 (2.79)	2.26–19.88	12.91±5.88	11.50 (8.20)	3.40–29.60	<0.001
MONO (×10 <sup>3</sup> /μL)	0.77±0.29	0.71 (0.37)	0.33–1.59	1.35±0.68	1.20 (0.70)	0.30–3.90	<0.001
LYMPH (×10 <sup>3</sup> /μL)	1.80±0.82	1.70 (1.24)	0.64–4.30	1.80±0.86	1.60 (1.20)	0.39–4.49	0.830
PLT (×10 <sup>3</sup> /μL)	254.82±93.48	255.0 (110.5)	94–592	229.83±85.88	217.0 (102.0)	81–455	0.116
CK (U/L)	392.63±266.08	359.0 (406)	41–952	42975.89±51661.56	24346.0 (50749)	1200–260334	<0.001
AST (U/L)	68.14±145.50	34.0 (27)	9–782	702.54±857.25	578.0 (751)	49–6419	<0.001
ALT (U/L)	39.61±60.04	20.0 (26)	8–358	271.29±392.95	158.0 (236)	19–2819	<0.001
BUN (mg/dl)	35.99±29.11	29.1 (27)	2–152	66.91±49.33	47.0 (74)	5–208	<0.001
Serum creatinine (mg/dl)	1.87±6.94	0.73 (0.42)	0.24–49.0	2.00±2.06	1.00 (1.97)	0.30–8.20	0.005
Potassium (K, mmol/L)	4.12±0.70	4.04 (0.6)	3.1–7.5	4.96±1.30	4.40 (1.6)	3.4–8.7	<0.001
Calcium (Ca, mg/dl)	8.64±0.80	8.61 (0.8)	5.8–9.9	7.90±1.12	8.00 (1.9)	5.6–10.0	0.001
pH	7.41±0.07	7.42 (0.08)	7.11–7.52	7.36±0.13	7.40 (0.10)	6.60–7.53	0.016
Lactate (mmol/L)	1.66±1.11	1.40 (0.68)	0.64–8.04	2.40±2.35	1.70 (1.40)	0.50–16.90	0.042
Time under debris (hr)	3.94±11.43	0.0 (2)	0–48	17.58±20.54	6.0 (27)	0–80	<0.001
SII	1117.96±933.29	879.0 (811)	192–4908	1999.26±1418.32	1554.0 (1889.08)	357.47–6685.0	<0.001
SIRI	3.51±3.48	3.00 (3.00)	0.00–22.00	13.34±13.52	8.60 (12.58)	1.81–70.20	<0.001
PIV	927.00±1181.90	598.0 (609.5)	132–7804	3149.05±3686.48	2131.8 (3528.86)	301.47–20568.60	<0.001
NLR	4.60±3.42	3.55 (3.72)	0.93–13.76	9.11±6.76	7.18 (5.93)	1.74–32.56	<0.001

SD: Standard deviation, IQR: Interquartile range, CRP: C-reactive protein, BUN: Blood urea nitrogen, WBC: White blood cell, AST: Aspartate aminotransferase, NEU: Neutrophil, ALT: Alanine aminotransferase, MONO: Monocyte, SII: Systemic Immune-inflammation Index, LYMPH: Lymphocyte, SIRI: Systemic Inflammatory Response Index, PLT: Platelet, PIV: Pan-immune Inflammation Value, CK: Creatine kinase, NLR: Neutrophil-to-lymphocyte ratio, K: Potassium, Ca: Calcium

**Table 3.** Pearson correlations between crush syndrome and other variables

Variable	r	p-value
Age	-0.097	0.307
CRP	0.386	<0.001
WBC	0.548	<0.001
NEU	0.560	<0.001
MONO	0.474	<0.001
PLT	-0.139	0.145
LYMPH	-0.002	0.981
SII	0.338	<0.001
SIRI	0.427	<0.001
PIV	0.361	<0.001
BUN	0.348	<0.001
Serum creatinine (KREA)	0.013	0.894
Potassium (K)	0.360	<0.001
Calcium (Ca)	-0.351	<0.001
AST	0.439	<0.001
ALT	0.363	<0.001
pH	-0.221	0.019
Lactate	0.190	0.044
Duration under debris (hr)	0.343	0.001
NLR	0.377	<0.001

CRP: C-reactive protein, SII: Systemic Immune-inflammation Index, WBC: White blood cell, SIRI: Systemic Inflammatory Response Index, NEU: Neutrophil, PIV: Pan-immune-Inflammation Value, MONO: Monocyte, NLR: Neutrophil-to-lymphocyte ratio, LNF: Lymphocyte, PLT: Platelet

According to the results of the correlation analysis, a high level of positive correlation was identified among certain variables, indicating a potential risk of multicollinearity. Prior

to model development, the VIF values for all independent variables were assessed. The final logistic regression model was constructed using variables that remained within acceptable limits for multicollinearity.

In this multivariable model, only the SIRI (Systemic Inflammation Response Index) variable was found to be statistically significant ( $\beta=0.269$ ,  $p=0.026$ ,  $OR=1.308$ , 95% CI: 1.032–1.660). This finding indicates that even when controlling for the effects of other variables, SIRI independently increases the likelihood of being in the patient group and stands out as the strongest predictor in the model (Table 4).

According to the ROC analysis, many biochemical and hematological parameters were found to have high diagnostic power in distinguishing the patient group from the control group. AST (AUC=0.968) and ALT (AUC=0.940) were identified as the parameters with the highest discriminative ability. These were followed by duration under debris (AUC=0.876), neutrophil count (AUC=0.852), WBC (AUC=0.849), SIRI (AUC=0.811), and monocyte count (AUC=0.792). These results indicate that inflammatory and tissue damage markers were significantly elevated in the patient group and possess strong diagnostic discriminative value.

Parameters with moderate diagnostic power included BUN (AUC=0.731), NLR-2 (AUC=0.746), and potassium (AUC=0.712), while creatinine (AUC=0.676) and lactate (AUC=0.603) demonstrated lower discriminative ability. The fact that calcium (AUC=0.289) and pH (AUC=0.358) values were below 0.5 indicates an inverse relationship, suggesting



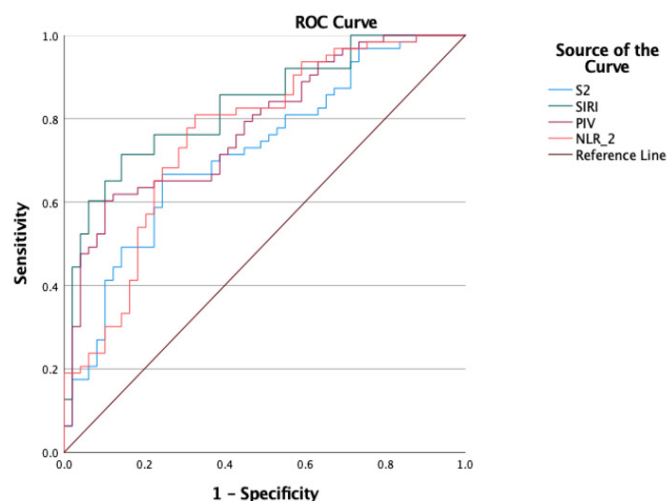
**Table 4.** Logistic regression analysis results (dependent variable: group=patient)

Predictor variable	$\beta$ (estimate)	SE	z	p-value	Odds ratio	95% CI (lower-upper)
Intercept	0.5663	4.0891	0.138	0.890	1.762	0.0006–5327.79
SII	-0.000206	0.000507	-0.407	0.684	1.000	0.999–1.000
SIRI	0.2687	0.1210	2.221	0.026	1.308	1.032–1.660
NLR	-0.0930	0.1560	-0.597	0.551	0.911	0.671–1.240
Potassium (K)	0.3992	0.4324	0.923	0.356	1.491	0.639–3.480
Calcium (Ca)	-0.3497	0.3651	-0.958	0.338	0.705	0.345–1.440
Duration under debris (hours)	0.0456	0.0245	1.862	0.063	1.047	0.998–1.100

SE: Standard error, CI: Confidence interval, SII: Systemic Immune-inflammation Index, SIRI: Systemic Inflammatory Response Index NLR: Neutrophil-to-lymphocyte ratio

that lower levels of these parameters were associated with the patient group (Figure, Table 5).

In conclusion, the ROC analysis revealed that indicators of inflammatory response (WBC, NEU, MONO, SII, SIRI, NLR), tissue damage (AST, ALT), and metabolic deterioration (BUN, K, Ca, pH) possessed strong discriminative power in the patient group. These findings support that, in clinical evaluation, parameters such as CK, AST, ALT, and duration under debris stand out prognostically.



**Figure.** ROC curve  
ROC: Receiver operating characteristic

In the pairwise comparisons of ROC curves, the SII parameter was found to have significantly lower discriminative power compared to SIRI and PIV ( $p < 0.001$  and  $p = 0.010$ , respectively). In contrast, no statistically significant difference was observed between SII and NLR ( $p = 0.155$ ).

SIRI was found to have a significantly higher AUC value than NLR ( $p = 0.014$ ), while no significant difference was noted between PIV and NLR ( $p = 0.611$ ).

These results indicate that the SIRI index is one of the strongest discriminative parameters in terms of inflammation and prognosis, whereas SII has a more limited diagnostic capability (Table 6).

## DISCUSSION

Crush syndrome is a serious clinical condition characterized by systemic damage caused by compressive force applied externally to the trunk, extremities, or other parts of the body. This trauma results in extensive musculoskeletal tissue damage, which can lead to limb loss and organ dysfunction.

**Table 5.** ROC analysis results

Variable	AUC	SE	p-value	95% CI (lower-upper)
CRP	0.777	0.055	<0.001	0.669–0.884
WBC	0.849	0.044	<0.001	0.764–0.935
NEU	0.852	0.044	<0.001	0.765–0.938
MONO	0.792	0.050	<0.001	0.694–0.889
SII	0.710	0.057	0.001	0.598–0.821
SIRI	0.811	0.047	<0.001	0.720–0.903
PIV	0.764	0.052	<0.001	0.662–0.866
BUN	0.731	0.054	<0.001	0.624–0.837
Serum creatinine (KREA)	0.676	0.058	0.006	0.563–0.789
Potassium (K)	0.712	0.055	0.001	0.604–0.819
Calcium (Ca)	0.289	0.054	0.001	0.182–0.395
AST	0.968	0.021	<0.001	0.926–1.000
ALT	0.940	0.027	<0.001	0.887–0.993
pH	0.358	0.060	0.028	0.241–0.476
Lactate	0.603	0.062	0.111	0.482–0.723
Time under debris (hrs)	0.876	0.045	<0.001	0.788–0.965
NLR	0.746	0.056	<0.001	0.636–0.856

SE: Standard error, CI: Confidence interval, ROC: Receiver operating characteristic, AUC: Areas under the curve, CRP: C-reactive protein, BUN: Blood urea nitrogen, WBC: White blood cell, ALT: Alanine aminotransferase, NEU: Neutrophil, NLR: Neutrophil-to-lymphocyte ratio, MONO: Monocyte, SII: Systemic Immune-inflammation Index, SIRI: Systemic Inflammatory Response Index, PIV: Pan-immune Inflammation Value, AST: Aspartate aminotransferase

**Table 6.** Comparison of AUC differences between ROC curves

Comparison (test pair)	z	p (2-tailed)	AUC difference	SE	95% CI (lower-upper)
SII-SIRI	-3.510	<0.001	-0.112	0.289	-0.174–0.049
SII-PIV	-2.575	0.010	-0.062	0.296	-0.108–0.015
SII-NLR	-1.422	0.155	-0.042	0.302	-0.099–0.016
SIRI-PIV	2.221	0.026	0.050	0.280	0.006–0.095
SIRI-NLR	2.446	0.014	0.070	0.286	0.014–0.126
PIV-NLR	0.509	0.611	0.020	0.295	-0.056–0.096

SE: Standard error, CI: Confidence interval, ROC: Receiver operating characteristic, AUC: Areas under the curve, SII: Systemic Immune-inflammation Index, SIRI: Systemic Inflammatory Response Index, PIV: Pan-immune Inflammation Value, NLR: Neutrophil-to-lymphocyte ratio

Post-traumatic muscle damage causes significant changes in blood parameters, notably a marked elevation in CK levels, which correlates with the severity of the disease. In recent years, inflammatory indices developed to assist in the diagnostic process of various diseases have also been evaluated for their potential utility in diagnosing crush syndrome.

This study aimed to investigate the diagnostic value and prognostic role of inflammatory indices in crush syndrome.

Accordingly, we sought to determine the role of the SII, the Systemic Inflammation Response Index (SIRI), and the PIV in diagnosing crush syndrome and to evaluate their correlation with CK, CRP, WBC, and neutrophil-lymphocyte ratio (NLR).

Previous studies have investigated the use of various scoring systems and indices in diagnosing crush syndrome. However, studies examining the role of SII, SIRI, and PIV specifically in crush syndrome remain limited.

In cases of crush syndrome, an increased number of affected extremities and more extensive muscle injury are associated with a higher risk of AKI, increased need for hemodialysis, and significantly elevated CK levels. In our study, 17.9% of all patients exposed to crush injury required hemodialysis, which is consistent with previous research. CK levels in our cohort increased proportionally to the severity of muscle damage. Consequently, AKI may develop in these patients. Elevated CK may serve as an early indicator of AKI. A significant correlation was observed between CK and inflammatory indices, suggesting that these indices may be used as prognostic markers for disease severity.

Ischemia-reperfusion injury plays a critical role in the pathogenesis of crush syndrome. Restoration of blood flow to ischemic muscle tissue triggers an inflammatory response, with neutrophils being the first immune cells to infiltrate the affected area, becoming activated within minutes. In our study, similarly, patients with severe muscle damage showed significant elevations in inflammatory indices.

The pathophysiology of crush syndrome includes renal failure due to rhabdomyolysis, electrolyte imbalances, fatal arrhythmias, and SIRS. In our findings, patients with elevated renal function test results (BUN, creatinine) and abnormal electrolyte levels (potassium) also exhibited significant increases in inflammatory indices.

Neutrophils, lymphocytes, monocytes, and platelets—key components of the immune system—respond to systemic inflammation, trauma, and physiological stress. The neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), SII, SIRI, and PIV are considered prognostic markers in inflammatory processes. Moreover, early changes in neutrophil and lymphocyte counts (<6 hours) may reflect systemic inflammation more rapidly than traditional markers like WBC and CRP. Therefore, due to their practicality and low cost, inflammatory indices can be used to support clinical decision-making.

In a study by Wang and colleagues,<sup>27</sup> inflammatory indices were found to be clinically significant in predicting the occurrence and severity of pneumonia in patients with intracerebral hemorrhage. Similarly, our study demonstrated a meaningful correlation between inflammatory indices and the patient group. Thus, inflammatory indices may be practically used to predict the severity of crush syndrome in affected individuals.

According to the ROC curve analysis conducted in our study, neutrophil (AUC=0.852), WBC (AUC=0.849), SIRI

(AUC=0.811), and monocyte (AUC=0.792) levels showed high diagnostic power in differentiating patients with crush syndrome. Pairwise comparisons of AUC values revealed that SIRI had higher AUC values compared to other indices, indicating its superior diagnostic utility in identifying crush syndrome among patients exposed to crush injuries.

In recent years, the use of inflammatory indices in predicting disease prognosis has garnered increasing attention. For instance, in a cross-sectional study by Li et al.,<sup>28</sup> SIRI was found to possess the highest discriminatory capacity and accuracy in predicting chronic kidney disease and low glomerular filtration rate (GFR). Consistently, our study also found that SIRI had significant diagnostic utility and a high AUC value in crush syndrome.

In a retrospective cohort study by Zhang et al.,<sup>29</sup> SIRI was found to positively correlate with stroke severity. In our logistic regression analysis, SIRI was identified as an independent predictor of the likelihood of having crush syndrome. This suggests that patients with elevated CK levels also had high SIRI values. Therefore, SIRI may be a valuable marker for both diagnosis and severity assessment in patients exposed to crush injury.

In a retrospective observational study by Yaman et al.,<sup>18</sup> the McMahon score was used to predict mortality in earthquake-related rhabdomyolysis. The study demonstrated that in disasters such as earthquakes, the McMahon score plays an important role in rapid decision-making regarding mortality prediction. Similarly, our study showed that in patients affected by natural disasters, SIRI and other inflammatory indices may serve as useful markers in rapid diagnosis and severity assessment of crush syndrome.

### Limitations

- The sample size was relatively small; thus, validation of the study findings could be enhanced with a larger cohort.
- The study was conducted retrospectively.
- The number of fatal cases (exitus) was limited, preventing a reliable statistical assessment of mortality prediction.

### CONCLUSION

Natural disasters occurring around the world—especially earthquakes—frequently expose individuals to compressive forces. In disaster and emergency medicine, the importance of rapid and effective decision-making mechanisms is increasingly emphasized over time. In this context, our study suggests that inflammatory indices may serve as useful tools in the diagnostic process and prognostic evaluation of patients exposed to crush injuries in natural disasters such as earthquakes.

Among these indices, the SIRI stands out as the most effective and significant marker. Since it can be calculated using early and routinely obtained blood test results, it may accelerate the diagnostic process. Furthermore, it is easy to compute and does not incur additional cost.

With these characteristics, SIRI may be used as a practical and cost-effective biomarker for both diagnosis and prognosis in patients with crush syndrome during natural disasters.

## ETHICAL DECLARATIONS

### Ethics Committee Approval

Was approved by the Ankara Etlik City Hospital Clinical Researches Ethics Committee (Date: 26.04.2023, Decision No: AEŞH-EK1-2023-099).

### Informed Consent

As this was a retrospective study, formal written informed consent was not required and was therefore not obtained.

### Peer Review Process

This manuscript was subject to external peer review.

### Conflict of Interest

The authors declare no conflicts of interest related to this study.

### Financial Disclosure

The authors received no financial support for the conduct or publication of this research.

### Author Contributions

All authors contributed significantly to the study's conception, design, data acquisition, analysis, and interpretation. All authors reviewed and approved the final version of the manuscript.

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