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Relationship between systemic immune inflammation index and systemic inflammation response index values and prognosis in patients with burns

Serap Samut Bulbul[1], Alper Ceylan[2], Metin Ocak[3], Selim Gorgum[4], Tolga Pamuk[5], Mesut Oterkus[6]

[1]Samsun University Faculty of Medicine, Department of Pediatric Surgery, Samsun, Türkiye
[2]Samsun Training and Research Hospital, Department of General Surgery, Samsun, Türkiye
[3]Samsun University Faculty of Medicine, Department of Emergency Medicine, Samsun, Türkiye
[4]Samsun Training and Research Hospital, Department of Microbiology and Clinical Microbiology, Samsun, Türkiye
[5]Zonguldak Gynecology and Pediatrics Hospital, Department of Pediatric Surgery, Zonguldak, Türkiye
[6]Malatya Turgut Özal University Faculty of Medicine, Department of Anaesthesiology and Reanimation, Malatya, Türkiye

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Abstract

To determine the relationship between systemic immune inflammation index (SyII) and systemic inflammation response index (SyIRI) values and prognosis in adult and pediatric cases treated for deep partial thick and full thick burns. A total of 358 cases were enrolled in the study, and their SyII and SyIRI indices at the time of hospital admission were retrospectively calculated using medical record data. The mean SyII (4610.7 vs. 1874.9; p=0.001) and SyIRI (20.8 vs. 7.3; p<0.001) values in the deceased group were notably higher than in the surviving group. SyII (p=0.006 and p<0.001, respectively) and SyIRI (p<0.001 for both) values were found to be independent risk factors in terms of both hospital stay longer than 30 days and mortality. SyIRI and SyII values of those with electrical burns were 4.7 ± 4.7 and 1507.2 ± 1380.4, respectively. SyIRI and SyII values of those with thermal burns were 8.7 ± 11.7 and 2147.8 ± 2711.4, respectively. A statistically significant difference was observed in SyIRI values between thermal and electrical burns (p=0.034), while SyII values did not differ significantly. The study shows that the risk of prolonged hospital stays, and mortality is higher in cases with severe burns with higher SyII and SyIRI values measured at the time of admission to the hospital. However, in terms of burn types, SyIRI is a more effective marker in distinguishing thermal burns from electrical burns.

Keywords: Burn, systemic immune inflammation index, systemic inflammation response index, prognosis, mortality

Introduction

A burn is damage to the skin or internal organs caused by physical or chemical agents such as heat, chemicals, radiation, or electricity. Although a burn is an acute injury, it can lead to longterm complications due to the chronicity of the inflammatory response and delayed wound healing. The inflammatory response in burns begins in the first minutes of injury and is an important part of wound healing. The inflammatory response promotes wound healing by increasing blood flow to the injury site, activating the immune system, and ensuring the migration of cells that promote wound healing [1,2]. In the early stages of the inflammatory response, mast cells and neutrophils arrive at the site of injury and secrete cytokines, chemokines, and other inflammatory mediators. These mediators stimulate the migration and activation of inflammatory cells. A chronic inflammatory response in burns may lead to delayed wound healing and long-term complications. Factors that contribute to the chronicity of the inflammatory response include the severity of the injury, injury duration, and wound infection [1-3].

Systemic inflammation is a complex physiological response that plays a crucial role in the development of various illnesses and leads to elevated levels of inflammatory markers in the blood. Systemic inflammation can increase disease risk and severity and affect prognosis. Measurement of systemic inflammation

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Corresponding Author: Mesut Oterkus, Malatya Turgut Özal University Faculty of Medicine, Department of Anaesthesiology and Reanimation, Malatya, Türkiye
Email: mesutoterkus@hotmail.com

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markers may play a crucial role in the diagnosis and treatment of inflammatory illnesses and can provide important information about prognosis [4-6].

The systemic immune inflammation index (SyII), obtained by multiplying the platelet and neutrophil counts splatted by the lymphocyte count, is a new biomarker of some malignancies and inflammatory diseases [4-7]. SyII has diagnostic value in some cancers, such as colorectal cancer and cervical cancer, and some diseases such as hepatic steatosis and rheumatoid arthritis [4-6]. SyII has also been shown to have a prognostic value in some severe cases, such as predicting the prognosis of cancer immunotherapy, prognosis in bladder cancer, short and longterm prognosis after acute ischemic stroke, and prognosis in cervical cancer [5-9]. SyII can provide predictive information about mortality in some cases, such as arteriosclerotic cardiovascular disease and sepsis [9,10]. SyII was also shown to have a diagnostic value in children in some diseases, such as metabolic syndrome in children with obesity, osteosarcoma, and acute appendicitis [11-13].

The Systemic Inflammation Response Index (SyIRI), reckoned by multiplying neutrophil and monocyte counts and dividing by the lymphocyte number, reflects the balance between the body's inflammatory activity and immune function [14-18]. Previous studies have indicated that SyIRI may offer valuable insights not only in the diagnosis of certain diseases, but also in assessing clinical severity, predicting prognosis, and estimating mortality risk [18-21].

Changes in the counts of neutrophils, monocytes, lymphocytes, and platelets are well-known in patients with severe burns [1-3]. However, as far as we could determine, it has not been shown whether there is a meaningful difference between patients who die and survive and those who stay in the hospital longer or for shorter periods in terms of the ratios of these cell counts, amongst patients with severe burns. The primary objective of this study was to investigate the association between SyII and SyIRI values measured at admission and clinical outcomes, including prolonged hospital stay and mortality, in adult and pediatric patients with severe burns.

Material and Methods

This retrospective, single-center study was conducted at a tertiary burn center between October 2019 and October 2023. This study was approved by the Samsun University Clinical Research Ethics Committee (No: SÜKAEK-2023-20/18, Date: 01 Novembr 2023). A total of 358 patients (children and adults) received inpatient treatment in our hospital's burns center and burns intensive care unit (ICU) due to deep partial thickness and full-thickness burns, and those with a total burn surface area (TBSA) of 20% and over were included in the study. All patients in our study had thermal (flames, hot liquids, hot solid objects etc.) and electrical burns. There were no patients with chemical or radiation burns. Patients with inhalation injury were excluded from the study. Inhalation injury was not observed in our pediatric patients, and adult patients with inhalation injury were excluded to avoid its confounding effect on prognosis. Information about the patients and laboratory findings were obtained from hospital records. All patients received standard burn care according to institutional protocols, including initial assessment, fluid resuscitation, wound care, and surgical interventions when clinically indicated. As this study was retrospective, treatment strategies were not standardized or analyzed as study variables. SyII and SyIRI values were calculated for each patient by obtaining data from the complete blood count performed within the first 24 hours after hospital admission.

Ills with deep partial thick and full-thick burns of all ages, admission within the first 24 hours of being burned, patients with thermal and electrical burns were determined as inclusion criteria. Exclusion criteria selected as outpatients receiving treatment in polyclinic, patients with superficial, superficial partial-thickness, and deep tissue burns, patients with concomitant trauma.

The following formulas were used to calculate SyII and SyIRI values:

SyII=(Platelet count x Neutrophil count) / (Lymphocyte count)

calculated as follows:

SyIRI=(Neutrophil count x Monocyte count) / (Lymphocyte count)

Statistical Analysis

All statistical evaluations were completed taking advantage of SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Datum was summarized as counts and percentages. Pearson's Chi-square test was utilized for categorical comparisons. The Kolmogorov-Smirnov test was utilized to verify the normality of continuous datum. Non-normally distributed variables were analyzed with the Mann-Whitney U test. Correlations between continuous variables were defined via Pearson's correlation analysis. Logistic regression identified factors associated with increased hospital stay and mortality. The predictive ability of SyII and SyIRI cutoff points for mortality was evaluated using ROC curve analysis. Findings were interpreted at a 95% confidence level, with significance set at $p<0.05$. Bonferroni adjustments were applied when multiple comparisons were made

Results

The mean age of the patients was 30.5 ± 27.9 years, and 221 (61.7%) were male. A total of 30 (8.4%) patients died of their burns. The thermal burn rate was 94.7% (n=339), and the electrical burn rate was 5.3% (n=19). A statistically meaningful difference was found between SyIRI values according to burn type ($p=0.034$). No statistically meaningful difference was found between SyII values according to burn type ($p>0.05$) (Table 1). A statistically meaningful difference was found in terms of age groups according to burn type ($p<0.001$) (Table 2).

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Table 1. Comparison of age groups according to burn type

Age (years)	Total		Electrical burn		Thermal burn		p
	n	%	n	%	n	%	
0-6	129	36.0	0	0.0	129	38.1	
6-18	34	9.5	2	10.5	32	9.4	
18-45	77	21.5	12	63.1	65	1.2	**<0.001**
45-65	68	19.0	4	21.1	64	18.8	
65+	50	14.0	1	5.3	49	14.5	

Table 2. Comparison of SyII and SyIRI values according to burn type

Variables	Electrical burn (n=19) Mean ± SD	Thermal burn (n=339) Mean ± SD	p
SyII	1507.2 ± 1380.4	2147.8 ± 2711.4	0.198
SyIRI	4.7 ± 4.7	8.7 ± 11.7	0.034

*The Mann-Whitney U test. **SD: Standard deviation, SyII: Systemic Immune Inflammation Index, SyIRI: System Inflammation Response Index

A total of 157 (43.9%) of the patients were aged younger than 18 years, 108 (30.2%) patients were treated in the burns ICU, and 111 (31.0%) patients were hospitalized for more than 30 days. The ratio of those aged over 18 years among the deceased was notably higher than in the surviving group (96.7% vs. 56.1%; p<0.001). The ratio of those receiving treatment in the burns ICU in the deceased group was found to be notably higher than in the surviving group (66.7% vs. 26.8%; p<0.001) (Table 3). Compared with survivors, deceased patients were significantly older, had a greater TBSA involvement, and exhibited markedly higher SyII (4610.72 ± 5208.84 vs. 1874.85 ± 2105.07) and SyIRI (20.83 ± 24.73 vs. 7.28 ± 8.47) values (all p<0.001). In contrast, no significant differences were observed between the groups in terms of sex, length of hospital stay, or cause of burn (Table 4). In the correlation analysis, SyII was found to be notably positively correlated with age (p<0.001; r=0.241) and hospital LOS (p=0.001; r=0.18). Additionally, SyIRI was found to be notably positively correlated with age (p<0.001; r=0.275) and hospital LOS (p<0.001; r=0.262). Age and hospital LOS were notably correlated (p=0.002; r=0.162) (Table 5). In the logistic regression analysis, age (p<0.001), treatment unit (p<0.001), SyII (p=0.006), and SyIRI (p<0.001) values were found to be independent risk factors for hospital LOS than 30 days and mortality. Hospital LOS did not emerge as an independent predictor of mortality (p=0.967) (Table 6).

Table 3. Distribution of variables in terms of survivor and deceased patients

Variables		Total		Survived		Deceased		p
		n	%	n	%	n	%	
Total		358	100	328	91.6	30	8.4	
Sex	**Male**	221	61.7	206	62.8	15	50.0	0.167
	Female	137	38.3	122	37.2	15	50.0	
Age (years)	**<18**	157	43.9	156	47.6	1	3.3	<0.001
	18+	201	56.1	172	52.4	29	96.7	
Age (years)	**0-6**	123	34.4	122	37.2	1	3.3	<0.001
	6-18	34	9.5	34	10.4	0	0.0	
	18-45	79	22.1	73	22.3	6	20.0	
	45-65	69	19.3	62	18.9	7	23.3	
	65+	53	14.8	37	11.3	16	53.3	
Unit	**Burns unit**	250	69.8	240	73.2	10	33.3	<0.001
	Burns ICU	108	30.2	88	26.8	20	66.7	
Hospital stay	**1-10 days**	87	24.3	75	22.9	12	40.0	0.013
	11-30 days	160	44.7	154	47.0	6	20.0	
	>30 days	111	31.0	99	30.2	12	40.0	

*The Chi-square test was used. **ICU: intensive care unit

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Table 4. Comparison of demographic and clinical characteristics according to survival status

Variables	Survived (Mean ± SD)	Deceased (Mean ± SD)	p
Age (years)	27.57 ± 26.36	62.97 ± 23.80	**<0.001**
Age (years) (+18), n (%)	172 (52.4)	29 (96.7)	**<0.001**
Length of hospital stay (days)	27.44 ± 25.69	27.23 ± 26.36	0.441
Hospital stay (>30 days), n (%)	99 (30.2)	12 (40.0)	0.266
Sex (Female), n (%)	122 (37.2)	15 (50.0)	0.167
Total body surface area (%)	28.61 ± 8.04	75.10 ± 9.74	**<0.001**
Cause of burn, n (%)			
Thermal	316 (94.0)	29 (96.7)	0.471
Electric	20 (6.0)	1 (3.3)	
Total body surface area, n (%)			
20-30	210 (62.5)	0 (0.0)	
30-40	89 (26.5)	0 (0.0)	**<0.001**
≥40	37 (11.0)	30 (100.0)	
SyII	1874.85 ± 2105.07	4610.72 ± 5208.84	**0.001**
SyIRI	7.28 ± 847	20.83 ± 24.73	**<0.001**

*The Mann-Whitney U test. **Sd: Standard deviation, SyII: Systemic Immune Inflammation Index, SyIRI: System Inflammation Response Index

Table 5. Correlation analysis of SyII and SyIRI with age and length of hospital stay

Variables	r/p	Age	SyII	SyIRI
SyII	**r**	0.241		
	p	<0.001		
SyIRI	**r**	0.275	0.846	
	p	<0.001	<0.001	
Hospital stay	**r**	0.162	0.18	0.262
	p	0.002	0.001	<0.001

Pearson's correlation analysis was used. SyII: Systemic Immune Inflammation Index, SyIRI: System Inflammation Response Index

Table 6. Logistic regression analyses

Variables	Reference category	P	Exp(B) (Odds ratio)	Lower (95% CI)	Upper (95% CI)
In terms of >30 days of hospital stay					
Sex	Male	0.902	1.03	0.65	1.63
Age	0 age	<0.001	1.01	1.01	1.02
Unit	Burn unit	<0.001	3.01	1.87	4.84
SyII	0-1000	0.006	1.15	1.04	1.27
SyIRI	0-5	<0.001	1.28	1.12	1.45
In terms of mortality					
Sex	Male	0.171	1.69	0.80	3.57
Age	0 age	<0.001	1.05	1.03	1.07
Unit	Burn unit	<0.001	5.46	2.46	12.11
SyII	0-1000	<0.001	1.24	1.11	1.38
SyIRI	0-5	<0.001	1.34	1.16	1.54
Hospital stay	1 day	0.967	1.00	0.99	1.01

Logistic regression analysis was used. SyII: Systemic Immune Inflammation Index, SyIRI: System Inflammation Response Index

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ROC analysis revealed that a SyII threshold of 2471.4 predicted mortality with a sensitivity of 60% and a specificity of 75.6% (p=0.001; AUC=0.681; 95% CI: 0.558-0.804) (Figure 1). A SyIRI threshold of 13.15 was found to predict mortality with a sensitivity of 56.7% and a specificity of 86.0% (p<0.001; AUC=0.719; 95% CI: 0.608-0.830) (Figure 2). There were no meaningful differences between the patients who died within the first 30 days and those who died after 30 days in terms of the mean SyII (p=0.305) and SyIRI (p=0.172) values.

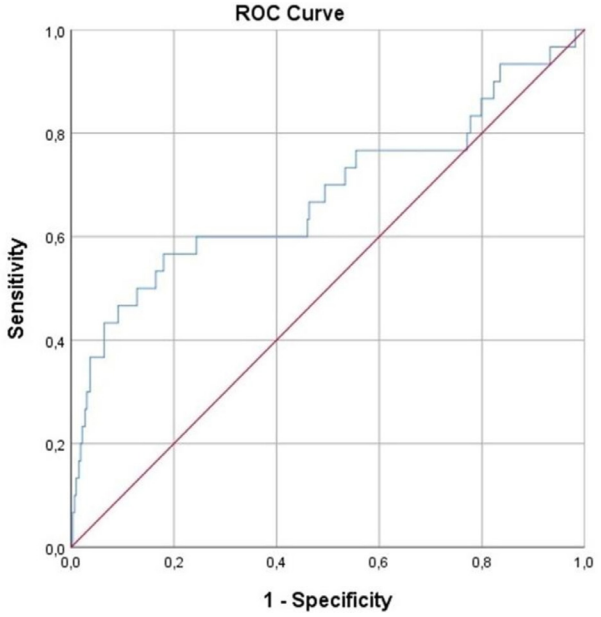

Figure 1. The sensitivity and specificity of value for SyII value in predicting mortality

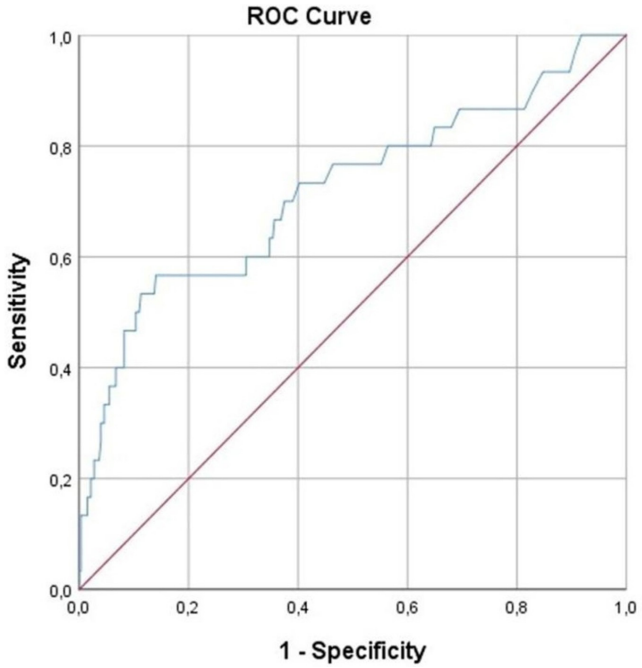

Figure 2. The sensitivity and specificity of value for SyIRI value in predicting mortality

No statistically meaningful difference was found between SyII and SyIRI values in terms of 30 day mortality in individuals aged 18-45, 45-65, and 65+ years (p>0.05). Statistical analysis could not be performed in the 0-6- and 6-18-years age groups because only one patient died.

According to Spearman's correlation analysis, there was no statistically meaningful difference between burn depth and SyII and SyIRI values (r:0.079, p=0.242 and r:0.031, p=0.647, respectively).

Discussion

In cases of severe burns, a severe inflammation condition is observed in the body. In this case, the severity of local and systemic inflammation varies depending on the severity of the burn, the duration of exposure to the burn, and the width of the burn area. This situation closely affects the prognosis [2,3]. In this study, the relationship between the system-ic inflammation indices SyII - SyIRI and hospital stay and mortality in patients with burns was shown.

A considerable difference was observed between groups regarding age distribution; patients aged above 18 years were predominant among the non-survivors (96.7%), while this rate was notably lower in the survivor group (56.1%). In addition, the mean age of the deceased patients was found to be notably higher than in the surviving group. In logistic regression analyses, age was found to be an independent risk factor in terms of hospital stay longer than 30 days and mortality, and age and hospital stay duration were found to be positively and notably correlated. All these findings show that age is a determinant of prognosis in patients with severe burns, and as age increases, hospital LOS becomes notably longer, and the risk of mortality increases notably.

We found that the mean hospital LOS was similar between those who died and those who survived, that the rate of those who were hospitalized for 1-10 days and longer than 30 days in those who died was notably higher than in those who survived, and that the duration of hospital stay was not an independent risk factor for mortality. This was because those with critical clinical conditions died in the first days of admission, and most of the other patients with severe burns were hospitalized for a very long time, and therefore, these findings show that the duration of hospitalization was not a direct determinant in terms of mortality. We also found that the mean SyII and SyIRI values did not differ between those who died within 30 days of admission and those who died after.

During severe burns, the number of lymphocytes in the blood stays largely the same, but there is an extreme overcompensation of neutrophils (and monocytes) from the bone marrow [22,23]. This is called a left shift. Mainly neutrophils migrate towards the wound area, and to a lesser extent, lymphocytes [24]. The burn injury process differed from normal wound healing in that immune cells continued to increase rather than returning

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to baseline levels. Following a burn injury, the initial phase of the immune response involves neutrophils and macrophages migrating to the wound site. Derived from the bloodstream and continuously replenished by the bone marrow, these cells are essential for clearing necrotic tissue and combating pathogens via phagocytosis and the production of reactive oxygen species. During the inflammatory phase, these innate immune cells enhance the inflammatory response by releasing soluble mediators that recruit additional immune cells to the site of injury. As the response evolves, T lymphocytes from lymphoid organs and anti-inflammatory macrophages contribute to the resolution of inflammation, thereby limiting further tissue damage [1,22-25]. In the context of trauma, specific T cell subtypes (Th1 and Th17) contribute to inflammation enhancement, whereas others (Th2 and regulatory T cells or Tregs) are involved in its resolution. Maintaining a balanced interaction among these T cell subsets is essential for an effective transition from inflammation to tissue repair. In standard wound healing processes—such as those following minor injuries—neutrophils undergo apoptosis, and macrophages transition from a pro-inflammatory phenotype to a reparative one, thereby restoring homeostasis and initiating the proliferative phase of skin regeneration [1,22-25]. However, in burn injuries, the tightly regulated immune response becomes dysregulated and prolonged. The burn-induced hyperinflammatory state leads to a marked increase in circulating immune cells, pro-inflammatory cytokines, and acute-phase reactants. In pediatric patients with severe burns, serum concentrations of interleukin IL-6, IL-8, granulocyte colony-stimulating factor, and monocyte chemoattractant protein-1 are markedly elevated, reflecting a heightened inflammatory response. These cytokine level increments are dependent on the injury size within 24-48 hours after trauma. Thermal injury also triggers a rapid increase in bone marrow-derived endothelial progenitor cells within the peripheral circulation, a response that correlates with the severity of the burn [22-25]. In the scope of this study, we aimed to show whether the counts of these cells differed between the prognosis groups at the time of admission, meaning the very first hours of the burn process.

It has been stated that in cases where an inflammatory response occurs, an increase in SyII values is observed due to an increase in the production of neutrophils and platelets in the serum and the withdrawal of lymphocytes from the circulation and migration to-wards the inflammation area [5-13]. It has been shown that SyII values provide important information in the diagnosis5,6 and prediction of prognosis of some diseases [7-10]. In the current study, the mean SyII value was substantially higher in the deceased group compared to the survivors (4610.7 vs. 1874.9), and SyII demonstrated a positive correlation with the length of hospital stay. Furthermore, SyII was identified as an independent risk factor for both prolonged hospitalization exceeding 30 days and increased mortality. Moreover, a SyII threshold of 2471.4 was found to predict mortality with a sensitivity of 60% and a specificity of 75.6%. All these findings show that the SyII value is higher in patients with more severe clinical presentation and higher mortality risk.

It has been shown that in the event of inflammation, SyIRI values increase due to in-creased production of neutrophils and monocytes and the recruitment of lymphocytes to the inflammation area [14-21]. It has been reported that the SyIRI can be used as a biomarker in the diagnosis of some diseases [14-17] and in predicting prognosis [19-21]. Biyik et al. [14] reported elevated mean SyII and SyIRI values in patients with acute pancreatitis and acute kidney injury. Lin et al. [15] demonstrated that in patients with ischemic stroke, SyII and SyIRI values were significantly elevated in those with atrial fibrillation compared to those without. Xu et al. [16] found that SyIRI levels were elevated in patients with rheumatoid arthritis compared to healthy individuals. Wang et al. [17] reported an association between elevated SyIRI values and an increased risk of metabolic disorders and cardiovascular diseases. Dziedzic et al. [18] demonstrated that SyIRI levels were associated with diagnostic categories, showing the highest values in patients with acute coronary syndrome, significantly exceeding those observed in individuals with stable coronary artery disease. Zhang et al. [19] reported that SyIRI was associated with all cause of mortality in patients with stroke, and that rising SyIRI was accompanied by rising mortality. Zhou et al. [20] found that SyIRI was an independent prognostic indicator for acute ischemic stroke. Additionally, Xia et al. [21] found that elevated SyII and SyIRI values were associated with an increased risk of both all cause and cardiovascular mortality in a cohort of over 42.000 patients. In the current study, the mean SyIRI value was substantially higher in the deceased group compared to the surviving group (20.8 vs. 7.3), and SyIRI was found to be positively correlated with hospital LOS. SyIRI was identified as an independent risk factor for both prolonged hospitalization exceeding 30 days and increased risk of mortality. Furthermore, a SyIRI threshold of 13.15 was found to predict mortality with a sensitivity of 56.7% and a specificity of 86.0%. All these findings indicate that patients with SyIRI values stay in the hospital longer and have a higher risk of mortality. The ROC analyses were performed as exploratory tools to assess the discriminative ability of admission SyII and SyIRI values for mortality and were not intended to replace multivariable prognostic modeling.

When SyII and SyIRI values were compared statistically according to burn types, we found that SyIRI values differed between thermal and electrical burns; however, this finding was descriptive and not intended for diagnostic differentiation. However, the small number of patients with electrical burns may have affected our results. We believe that studies with more patients with different burn types will be more enlightening on this subject. Therefore, the prognostic implications of SyII and SyIRI in pediatric burn patients should be interpreted with caution, and our conclusions primarily apply to the adult population.

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Limitations

Because the research design was retrospective and based on data from a single center, the findings may not be fully generalizable to other populations. The results need to be verified in a prospective study with a large sample from multiple centers. SyII and SyIRI values may vary morphologically among burn types. Although we analyzed this, the relatively small number of patients may have affected our results. In addition, this study evaluates pediatric and adult patients together. Because there is only one mortality rate in children under 18 years of age, the mortality-prognosis relationship of SyII and SyIRI values in children has not been clarified. SyII and SyIRI values were examined at a single time. It was not examined whether these markers fluctuated in the following days and weeks. It may be important to take these variations into account to reach more comprehensive conclusions.

Conclusion

The present study demonstrates that patients with severe burns who have higher SyII and SyIRI values measured at the time of hospital admission are at an increased risk of prolonged hospitalization and mortality. These findings suggest that SyII and SyIRI reflect the magnitude of the systemic inflammatory response in severe burn injury and are associated with worse clinical outcomes. These indices may therefore be useful as readily available adjunctive markers for early risk stratification and closer clinical monitoring in patients with severe burns.

Ethical Approval
Approved by the Samsun University Clinical Research Ethics Committee (No: SÜKAEK-2023-20/18, Date: 01 November 2023).

Patient Consent
Informed consent was waived due to the retrospective design.

Conflict of Interest
The authors declare no conflict of interest.

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