



# Using mSIS, DNI, CRP, LDH and Albumin Levels for Predicting Burn-related Mortality

## Yanık İlişkili Mortalitenin Öngörülmesinde mSIS, DNI, CRP, LDH ve Albümin Seviyelerinin Kullanılması

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### Abstract

**Objective:** After major burn injury, patients suffer from massive systemic inflammatory response. Approximately 54% of burn-related deaths in modern burn units occur due to septic shock and multiple organ dysfunction syndrome instead of osmotic shock and hypovolemia, in 72 hours after admission. Early diagnosis and effective treatment of the sepsis would be a benefit for burn patients, especially those with severe burns. In this study, we aimed to use modified systemic inflammatory score (mSIS), C-reactive protein (CRP), delta neutrophil index (DNI), lactate dehydrogenase (LDH) and albumin (ALB) together to predict mortality of patients suffering from more than 30% of total body surface area (TBSA) burns.

**Method:** Between January 2020 and December 2020, the records of patients admitted to our center were analyzed retrospectively. Demographic and burn-related characteristics of patients and mortality were tabulated. DNI, CRP, serum ALB and LDH levels at the time of admission and discharge were also recorded. mSIS was calculated for all patients based on serum ALB levels and lymphocyte-to-monocyte ratio. The DNI, CRP, LDH and ALB levels both during admission and discharge were analyzed with ROC analysis.

**Results:** Totally 55 severe burn patients were admitted to burn intensive care unit in one year period. The mean age of the patients was 40.8 (18-89) years and the mean burned TBSA was 40.73%. There were 13 deaths with 23.6% mortality rate. The average length of stay for all patients was 35.3 days where all mortalities occurred after 72 hours of admission. Both admission and discharge CRP levels were significantly high for non-survivals ( $p=0.001$  and  $p=0.000$ , respectively). When LDH, ALB and DNI values were compared between the groups, while LDH and DNI discharge levels were significantly high and ALB levels were significantly low for non-survivals, there were no difference at the admission levels. The ROC curve analysis was performed for the eligibility of the inflammatory biomarkers to predict the mortality. Continued high levels

### Öz

**Amaç:** Majör yanık yaralanmalarından sonra hastalarda masif sistemik enflamatuvar yanıt görülmektedir. Modern yanık ünitelerinde yanığa bağlı ölümlerin yaklaşık %54'ü, ozmotik şok ve hipovolemi yerine başvurdan 72 saat sonra septik şok ve çoklu organ disfonksiyonu sendromu nedeniyle meydana gelmektedir. Sepsisin erken teşhisi ve etkin tedavisi, yanık hastalarında, özellikle ciddi yanıklarda fayda sağlayacaktır. Bu çalışmada toplam yanık vücut yüzey alanı (TVYA) %30'dan fazla olan hastalarda mortaliteyi tahmin etmek için sistemik enflamatuvar skor (mSIS), C-reaktif protein (CRP), delta nötrofil indeksi (DNI), laktat dehidrogenaz (LDH) ve albümini (ALB) birlikte kullanmayı amaçladık.

**Yöntem:** Ocak 2020 ile Aralık 2020 tarihleri arasında merkezimize başvuran hastaların hasta kayıtları geriye dönük olarak incelendi. Hastaların demografik ve yanık ile ilgili özellikleri mortalite varlığı durumuna göre analiz edilmiştir. Hasta kabulü ve taburculuk sırasındaki DNI, CRP, serum ALB ve LDH seviyeleri de kaydedildi. mSIS, tüm hastalar için serum ALB seviyelerine ve lenfosit-monosit oranına göre hesaplanmıştır. Hem yatış hem de taburculuk sırasında DNI, CRP, LDH ve ALB seviyeleri ROC analizi ile analiz edildi.

**Bulgular:** Bir yıllık süre içerisinde yanık yoğun bakım ünitesine toplam 55 ağır yanıklı hasta başvurdu. Hastaların ortalama yaşı 40,8 (18-89) yıl ve ortalama yanık TVYA'sı %40,73 idi. Hastaların 13'ü hayatını kaybetti (%23,6). Tüm hastalar için ortalama yatış süresi 35,3 gün olup, tüm ölümler başvurdan 72 saat sonra meydana gelmiştir. Hem yatış hem de taburculuk CRP düzeyleri ölen hastalar için anlamlı derecede yüksekti (sırasıyla  $p=0,001$  ve  $p=0,000$ ). Gruplar arasında LDH, ALB ve DNI değerleri karşılaştırıldığında, hayatını kaybeden hastalarda LDH ve DNI taburculuk düzeyleri anlamlı olarak yüksek, ALB anlamlı derecede düşüktü, ancak kabul düzeyleri arasında fark yoktu. Mortaliteyi tahmin etmek için enflamatuvar belirteçlerin uygunluğu için ROC eğrisi analizi yapıldı. Devam eden yüksek LDH, CRP ve DNI seviyeleri ve azalan ALB seviyelerinin (sırasıyla; 0,86, 0,92, 0,84) ölüm



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## Abstract

of LDH, CRP, and DNI and decreasing ALB levels predicts mortality better than abbreviated burn severity index and rBAUX according to the value of area under ROC curve (0.86, 0.92, 0.84, respectively).

**Conclusion:** Predicting the life expectancy of patient at the time of admission to the burn intensive care unit is the greatest help in deciding the treatment scheme. Burn severity scores are mostly used for mortality prediction, and widely used ones are based on TBSA and age. Sometimes, calculating the TBSA could be difficult especially for the patients referred from primary care. In regard to our study, accurate mortality prediction can be made with CBC, serum ALB and CRP levels and without TBSA. Moreover, during the intensive care unit stay, increasing levels of DNI, LDH and CRP levels and decreasing ALB levels should be alerting for mortality.

**Keywords:** Albumin, burn, CRP, DNI, LDH, mortality, mSIS

## Öz

oranını kısaltılmış yanık şiddet indeksi ve rBAUX'ten daha iyi tahmin ettiği görülmüştür.

**Sonuç:** Hastanın yanık yoğun bakım ünitesine kabul edildiği andaki yaşam beklentisinin tahmin edilmesi, tedavi şemasının belirlenmesinde en büyük yardımcıdır. Mortalite tahmini için çoğunlukla yanık şiddeti skorları kullanılır ve bunlardan yaygın olarak kullanılanları TVYA ve yaşa dayanmaktadır. Bazen özellikle birinci basamaktan sevk edilen hastalar için toplam vücut yüzey alanının (TBSA) hesaplanması zor olabilir. Bu çalışma ile TBSA'dan bağımsız olarak, sadece tam kan sayımı, serum ALB ve CRP seviyeleri ile mortalite tahmininin mümkün olabileceği gösterilmiştir. Ayrıca, yoğun bakımda kalış sırasında artan DNI, LDH ve CRP seviyeleri ve azalan ALB seviyeleri mortalite için alarm verici olmalıdır.

**Anahtar kelimeler:** Albümin, CRP, DNI, LDH, mortalite, mSIS, yanık

## Introduction

Burn injuries often result in extensive damage to the skin, which is the largest organ system, with resulting loss of the primary barrier to infection (1). After major burn injury, in addition to the lack of this barrier, patients also suffer from massive systemic inflammatory response, anemia, leukopenia, thrombocytopenia, and coagulopathy (2). Thus, although the severity and prognosis of burn injuries depend principally on the depth and size of the burn site, approximately 54% of burn-related deaths in modern burn units occur due to septic shock and multiple organ dysfunction syndrome instead of osmotic shock and hypovolemia, in 72 hours after admission (1,3). In patients with more than 20% burned total body surface area (TBSA), the incidence of sepsis is noted to be between 3% and 30% (1). Therefore, the early diagnosis and effective treatment of sepsis would be benefit for burn patients, especially for those with severe burns.

Previously lymphocyte-to-monocyte ratio (LMR), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio, delta neutrophil index (DNI), C-reactive protein (CRP), and preoperative serum albumin (ALB) levels have been reported as prognostic factors in various tumors, sepsis, and trauma (4-6). And recently modified systemic inflammatory score (mSIS) based on preoperative serum ALB levels found to be prognostic factor in some cancers (5). Some inexpensive and routinely performed tests have been reported as early predictors of systemic inflammatory response for severe burn patients separately (2,4,7,8). But to our best knowledge, no study has used those markers and mSIS as mortality predictors for severe burn victims together.

In this study, we aimed to use mSIS, CRP, DNI, LDH and ALB together to predict mortality of those patients who suffer from more than of 30% TBSA burns.

## Materials and Methods

Between January 2020 and December 2020, the records of patients admitted to our center were analyzed retrospectively after getting ethical approval from hospital ethical board (09/06/2021- E1-21-1838). Age, gender, burned TBSA, burn agent, burn depth, abbreviated burn severity index (ABSI), revised BAUX score (rBAUX) and mortality were tabulated. Lymphocyte, monocyte, neutrophil counts; DNI, CRP, serum ALB and LDH levels at the times of admission and discharge were also recorded. mSIS was calculated for all patients based on serum ALB levels and LMR. DNI, CRP, LDH and ALB level both during admission and discharge were analyzed with ROC analysis.

## Statistical Analysis

Data were given as mean  $\pm$  standard deviation for demographic and clinical data. The results were accepted with a 95% confidence interval and  $p < 0.05$  significance. Comparisons were made using t-tests and categorical data were analyzed using the Mann-Whitney U test. ROC curve analysis was used to compare the sensitivity and specificity of biomarkers with rBAUX and ABSI.

## Results

Total 55 severe burn patients were admitted to our burn intensive care unit in one year period. The mean age of the patients was 40.8 (18-89) years. The mean burned TBSA was 40.73%. Five of the patients had inhalation injury and

13 of the patients died (23.6%) (Table 1). The average length of stay for all patients was 35.3 days where all mortalities occurred after 72 hours of admission.

Table 2 summarizes the patients burn related characteristics including burn etiology, burn wound depth, rBAUX and ABSI scores.

ABSI and rBAUX scores were significantly high for the non-survival group ( $p=0.002$  and  $p=0.008$ , respectively). Although mSIS's at the time of admission and discharge were not significantly different between the survivals and non-survivals, both admission and discharge CRP levels were significantly higher for non-survivals ( $p=0.001$  and  $p=0.000$ , respectively). When LDH, ALB and DNI values were compared between the groups, LDH and DNI discharge levels were significantly higher and ALB levels were significantly lower for non-survivals although the admission levels were not significantly different between the groups (Table 3).

The ROC curve analysis was performed for the eligibility of the biomarkers to predict the mortality. Continued high levels of LDH, CRP, and DNI and decreasing ALB levels predicts mortality better than ABSI and rBAUX according to the value of area under ROC curve (0.86, 0.92, 0.84, respectively) (Figure 1, Table 4).

## Discussion

Although dramatic improvements have been made in the treatment of severe burns, the management of severely burned patients is still challenging. Predicting the life expectancy of the patient at the time of admission to the burn intensive care unit is the greatest help in deciding the treatment scheme. Recently, ABSI and rBAUX are the scoring systems commonly used as mortality predicting scores (9,10). Those burn severity scores are all based on the burned TBSA. Even though there are simple rules for calculating TBSA, it is mostly subjective as is human-related that real TBSA may be over/underestimated during the very first evaluation. Thermal injury may induce a marked systemic inflammatory response at early stage; however, SIRS scoring was not recommended by the American Burn Association (ABA) in burns, but there are still some controversial discussions on using the well-known inflammatory markers as a mortality predictor.

Dvorak et al. have concluded in their review that sepsis is the most potential mortality reason for severely burned patient (1). Recognizing sepsis by inflammatory markers at the very early stage may prevent patients suffering from septic complications. With this view, Wu et al. (11)

**Table 1. Patient characteristics**

| Characteristics          | Survival<br>n=42 | Non-survival<br>n=13 | Total<br>n=55 |
|--------------------------|------------------|----------------------|---------------|
| Age (years)              | 38 years         | 50 years             | 40.8 (18-89)  |
| Sex n (M/F)              | 30/12            | 7/6                  | 37/18         |
| Burned TBSA (%)          | 38.93%           | 46.54%               | 40.73%        |
| Inhalation injury, n (%) | 3 (7.1%)         | 2 (15.3%)            | 5 (9.1%)      |
| LOS (days)               | 39.7             | 21.2                 | 35.3          |
| ICU-LOS (days)           | 22.6             | 17.9                 | 20.4          |

TBSA: Total body surface area, ICU: Intensive care unit, LOS: Length of stay

**Table 2. Patients' burn-related characteristics**

|                 | Score                              | Frequencies | Percentage (%) |
|-----------------|------------------------------------|-------------|----------------|
| <b>rBAUX</b>    |                                    |             |                |
|                 | 40-50                              | 2           | 3.6            |
|                 | 50-60                              | 8           | 14.5           |
|                 | 60-70                              | 6           | 10.9           |
|                 | 70-80                              | 10          | 18.1           |
|                 | 80-90                              | 10          | 18.1           |
|                 | 90-100                             | 9           | 16.3           |
|                 | 100-110                            | 4           | 7.27           |
|                 | >110                               | 6           | 10.9           |
| <b>ABSI</b>     |                                    |             |                |
|                 | 4-5                                | 8           | 14.5           |
|                 | 6-7                                | 16          | 29             |
|                 | 8-9                                | 23          | 41.8           |
|                 | 10-11                              | 7           | 12.7           |
|                 | >12                                | 2           | 3.6            |
| <b>Depth</b>    |                                    |             |                |
|                 | 2 <sup>nd</sup> degree-superficial | 1           | 1.8            |
|                 | 2 <sup>nd</sup> degree-deep        | 17          | 30.9           |
|                 | 3 <sup>rd</sup> degree             | 37          | 67.3           |
| <b>Etiology</b> |                                    |             |                |
|                 | Scald                              | 11          | 20.0           |
|                 | Concentrated liquid                | 3           | 5.5            |
|                 | Fire                               | 25          | 45.5           |
|                 | Flushing                           | 2           | 3.6            |
|                 | Electric                           | 8           | 14.5           |
|                 | Chemical                           | 3           | 5.5            |
|                 | Contact                            | 1           | 1.8            |
|                 | Others                             | 2           | 3.6            |
|                 | <b>Total</b>                       | <b>55</b>   | <b>100.0</b>   |

ABSI: Abbreviated burn severity index, rBAUX: Revised BAUX score

**Table 3. Comparison of biomarkers' significance with ABSI and rBAUX**

|                       | Mortality | N  | Mean   | Std. deviation | Significance*  |
|-----------------------|-----------|----|--------|----------------|----------------|
| <b>ABSI</b>           | -         | 41 | 3.44   | 0.923          | <b>p=0.002</b> |
|                       | +         | 13 | 4.31   | 1.032          |                |
| <b>rBAUX</b>          | -         | 42 | 78.14  | 20.240         | <b>p=0.008</b> |
|                       | +         | 13 | 99.15  | 19.300         |                |
| <b>mSIS admission</b> | -         | 42 | 1.21   | 0.842          | p=0.156        |
|                       | +         | 13 | 1.62   | 0.506          |                |
| <b>mSIS discharge</b> | -         | 39 | 1.26   | 0.751          | p=0.474        |
|                       | +         | 13 | 1.46   | 0.519          |                |
| <b>CRP admission</b>  | -         | 42 | 60.03  | 60.233         | <b>p=0.001</b> |
|                       | +         | 13 | 161.38 | 99.006         |                |
| <b>CRP discharge</b>  | -         | 42 | 37.27  | 49.853         | <b>p=0.000</b> |
|                       | +         | 13 | 249.23 | 116.143        |                |
| <b>LDH admission</b>  | -         | 42 | 458.17 | 368.563        | p=0.797        |
|                       | +         | 13 | 414.54 | 200.009        |                |
| <b>LDH discharge</b>  | -         | 42 | 203.21 | 119.495        | <b>p=0.000</b> |
|                       | +         | 13 | 504.62 | 259.382        |                |
| <b>ALB admission</b>  | -         | 42 | 32.79  | 7.390          | p=0.26         |
|                       | +         | 13 | 27.15  | 6.619          |                |
| <b>ALB discharge</b>  | -         | 42 | 32.88  | 10.590         | <b>p=0.00</b>  |
|                       | +         | 13 | 23.77  | 5.019          |                |
| <b>DNI admission</b>  | -         | 40 | 4.492  | 12.3914        | p=0.232        |
|                       | +         | 13 | 6.685  | 7.5102         |                |
| <b>DNI discharge</b>  | -         | 42 | 1.210  | 3.5043         | <b>p=0.000</b> |
|                       | +         | 13 | 26.492 | 19.6571        |                |

\*Mann-Whitney U test, CRP: C-reactive protein, ABSI: Abbreviated burn severity index, LDH: Lactate dehydrogenase, DNI: Delta neutrophil index, ALB: Albumin, mSIS: Systemic inflammatory score

analyzed the prediction ability of SIRS score for severely burned patient, but they concluded SIRS score as having limited use for prognostic determinations. A 2018 study by Yan et al. (12) compared the ability of sepsis-3 SOFA score, ABA sepsis criteria, and Mann-Salinas novel predictors to diagnose sepsis based on positive blood or tissue cultures. Their study revealed that although the sepsis-3 criteria was the most predictive of the three, none of the criteria had the accuracy enough to be a diagnostic standard in burn patients (12).

Rafiezadeh Shahi et al. (4) reported that serum ALB levels slightly increased the accuracy of mortality predictions. Hu et al. (7) observed in their study that admission NLR above 14 was positively correlated with decreased survival, indicating a potential prognostic value of systemic inflammatory markers. In another clinical study, Osuka et al. (2) found early thrombocytopenia and lymphopenia to be independent risk factors for 60-day mortality in severely burned patients.

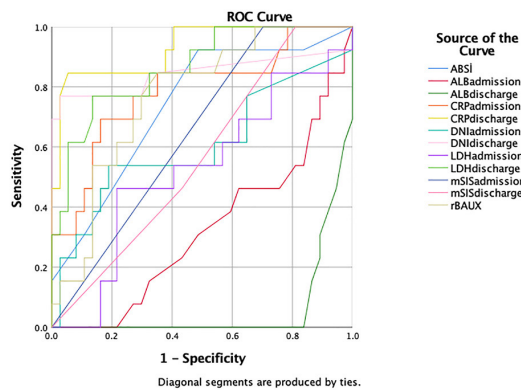
CRP is another biomarker of inflammation. In healthy individuals, the levels of CRP in plasma are almost undetectable, while more than 500 mg/L can be observed in patients with burn trauma. Its levels may further increase in burn patients with infection or sepsis, thus previous studies have suggested CRP as a good predictor of sepsis in burn patients (3). Kim and Ha (8) concluded that DNI might be used as an early marker of patients with burn sepsis. Our study showed that high and steady CRP levels are a mortality predictor.

From our literature review, we found that most of the inflammatory biomarkers and systemic inflammation

**Table 4. Area under the curve**

| Test result variable (s) | Area  | Std. error <sup>a</sup> | Asymptotic sig. <sup>b</sup> | Asymptotic 95% confidence interval |             |               |
|--------------------------|-------|-------------------------|------------------------------|------------------------------------|-------------|---------------|
|                          |       |                         |                              | Lower bound                        | Upper bound | Cut-off value |
| <b>ABSI</b>              | 0.738 | 0.080                   | 0.011                        | 0.581                              | 0.895       | 4.5           |
| <b>ALB admission</b>     | 0.323 | 0.085                   | 0.060                        | 0.157                              | 0.490       | 17.5 (g/L)    |
| <b>ALB discharge</b>     | 0.060 | 0.031                   | 0.000                        | 0.000                              | 0.122       | 15.5 (g/L)    |
| <b>CRP admission</b>     | 0.787 | 0.079                   | 0.002                        | 0.632                              | 0.942       | 185.5 (mg/L)  |
| <b>CRP discharge</b>     | 0.928 | 0.043                   | 0.000                        | 0.844                              | 1.000       | 176 mg/L      |
| <b>DNI admission</b>     | 0.605 | 0.104                   | 0.264                        | 0.402                              | 0.808       | 13.4 (%)      |
| <b>DNI discharge</b>     | 0.845 | 0.088                   | 0.000                        | 0.673                              | 1.000       | 9.3 (%)       |
| <b>LDH admission</b>     | 0.526 | 0.095                   | 0.782                        | 0.339                              | 0.713       | 479.5 (U/L)   |
| <b>LDH discharge</b>     | 0.864 | 0.058                   | 0.000                        | 0.750                              | 0.977       | 524.5 (U/L)   |
| <b>mSIS admission</b>    | 0.649 | 0.079                   | 0.114                        | 0.493                              | 0.804       | 1.5           |
| <b>mSIS discharge</b>    | 0.565 | 0.086                   | 0.486                        | 0.397                              | 0.734       | 0.5           |
| <b>rBAUX</b>             | 0.768 | 0.071                   | 0.004                        | 0.630                              | 0.907       | 98            |

ABSI: Abbreviated burn severity index, LDH: Lactate dehydrogenase, DNI: Delta neutrophil index, ALB: Albumin, mSIS: Systemic inflammatory score, CRP: C-reactive protein, <sup>a</sup>: Under the non-parametric assumption, <sup>b</sup>: Null hypothesis: True area=0.5



**Figure 1.** ROC curve analysis of inflammatory markers, ABSI and rBAUX score

*ABSI: Abbreviated burn severity index, LDH: Lactate dehydrogenase, DNI: Delta neutrophil index, ALB: Albumin, mSIS: Systemic inflammatory score, CRP: C-reactive protein*

scores were used for mortality prediction for burn patients. However, none of those studies had discussed mSIS, DNI, CRP, LDH, and ALB levels together comparing with ABSI and rBAUX.

In our study, we found that using those biomarkers during the admission, mortality prediction could be done as accurate as using ABSI or rBAUX. But, more importantly, the high levels of those biomarkers during discharge are more significant for predicting mortality and continuing high levels of DNI, CRP, LDH levels and continuing low levels of ALB should be alerting for severe burn patients.

## Conclusion

Most widely used burn severity scores are based on TBSA and age. Sometimes, calculating the TBSA could be difficult especially for the patients referred from primary care. According to our study, calculations without TBSA, just with CBC, serum ALB and CRP levels, can make almost accurate mortality prediction possible. Moreover, during the intensive care unit stay, increasing levels of DNI, LDH and CRP and decreasing ALB levels should be alerting for mortality.

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## Ethics

**Ethics Committee Approval:** Between January 2020 and December 2020, the records of patients admitted to our center were analyzed retrospectively after getting

ethical approval from Ankara City Hospital ethical board (09/06/2021- E1-21-1838).

**Informed Consent:** Retrospective study no need for consent.

**Peer-review:** Externally peer-reviewed.

## Authorship Contributions

Concept: M.A., A.E.A., Design: M.A., A.E.A., Data Collection or Processing: M.A., A.E.A., Analysis or Interpretation: M.A., A.E.A., Literature Search: M.A., A.E.A., Writing: M.A., A.E.A.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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