Challenge Journal of Perioperative Medicine

Research Article

Early detection of acute kidney injury in critically ill burn patients: Evaluating the predictive role of serum and urinary NGAL

Izzet Alatli [a,*], Buket Kocaman Akbay [b]

[a] *Department of Anesthesiology and Reanimation, Darıca Farabi Education and Research Hospital, İstanbul, Türkiye*
[b] *Department of Algology, Antalya Training and Research Hospital, Antalya, Türkiye*

ABSTRACT

Background: Early detection of acute kidney injury (AKI) in critically ill burn patients is crucial for improving outcomes. Neutrophil gelatinase-associated lipocalin (NGAL) has emerged as a promising biomarker for early AKI detection. This study aimed to evaluate the efficacy of serum and urinary NGAL levels in predicting AKI in burn patients admitted to the intensive care unit (ICU).

Methods: A prospective observational study was conducted on 31 burn patients admitted to the burn ICU. Serum and urinary NGAL levels were measured at admission (0 hours) and at 12, 24, 36, 48, and 72 hours post-admission. AKI was defined using the RIFLE and AKIN criteria. Renal replacement therapy (RRT) requirements, mortality, and other clinical parameters were recorded. Statistical analyses were performed to assess the correlation between NGAL levels and AKI development.

Results: Of the 31 patients, 48.4% required RRT, and 45.2% died. Serum NGAL levels at 0 and 12 hours were significantly higher in patients who developed AKI ($p<0.05$). A serum NGAL cutoff of 251 ng/ml was identified as a significant predictor of AKI ($p<0.05$). Urinary NGAL levels did not show significant predictive value for AKI. Mortality was significantly associated with higher burn surface area, increased fluid requirements, and higher SOFA and APACHE II scores ($p<0.01$).

Conclusion: Serum NGAL levels are elevated early in burn patients who develop AKI, suggesting its potential as a predictive biomarker. Urinary NGAL did not show significant predictive value. Further studies with larger cohorts are needed to validate these findings and explore the role of NGAL in guiding early interventions in burn patients.

ARTICLE INFO

Article history:
Received – January 12, 2025
Revision requested – February 11, 2025
Revision received – February 16, 2025
Accepted – February 25, 2025

Keywords:
Critically ill patients
Burn
NGAL
Kidney injury
Renal replacement therapy
Mortality

Citation: Alatli I, Kocaman Akbay B. Early detection of acute kidney injury in critically ill burn patients: Evaluating the predictive role of serum and urinary NGAL. *Chall J Perioper Med.* **2025**; 3(1):8–13.

1. Introduction

Acute kidney injury (AKI) is a serious and common complication in critically ill burn patients, significantly increasing morbidity, mortality, and long-term health complications [1,2]. The kidneys are particularly vulnerable in burn injuries due to a combination of factors, including systemic inflammation, hypovolemia, nephrotoxic drug exposure, and muscle breakdown leading to rhabdomyolysis. Given the high risk of AKI in burn patients and its association with poor outcomes, early detection is crucial for guiding timely interventions and improving prognosis [3,4]. Traditionally, AKI is diagnosed using markers such as serum creatinine and urine output. However, these conventional markers have significant limitations. Serum creatinine, for instance, does not rise until substantial kidney damage has already occurred, making it a delayed rather than an early indicator of injury. Urine output, while commonly monitored, can be influenced by factors like aggressive fluid resuscitation, systemic inflammation, and changes in hemodynamics, limiting its reliability as a sole diagnostic tool. These challenges highlight the urgent need for more sensitive and specific biomarkers that can detect AKI at an

* *Corresponding author*. E-mail address: doc4161@gmail.com (I. Alatli)
ISSN: 2980-292X / DOI: https://doi.org/10.20528/cjpm.2025.01.002

earlier stage, allowing for timely therapeutic interventions.

Neutrophil gelatinase-associated lipocalin (NGAL) has emerged as a promising biomarker for the early detection of AKI. NGAL is a small protein released by renal tubular epithelial cells in response to injury, and its levels rise rapidly in both blood and urine within hours of kidney damage—long before changes in serum creatinine occur [5,6]. Previous studies have demonstrated that NGAL can predict AKI in various critically ill populations, including patients undergoing cardiac surgery, those with sepsis, and individuals with contrast-induced nephropathy [7,8]. These findings suggest that NGAL could serve as an early warning signal, enabling clinicians to initiate protective measures such as optimizing fluid management, avoiding nephrotoxic agents, and considering early renal replacement therapy (RRT) when necessary.

Despite the growing evidence supporting NGAL as a biomarker for AKI in critically ill patients, its role in burn patients remains unclear. The pathophysiology of AKI in burns differs from other settings due to the interplay of systemic inflammation, large-volume fluid shifts, direct renal insults, and tissue injury, which may alter NGAL kinetics. Additionally, there is uncertainty regarding whether serum or urinary NGAL is a more reliable predictor of AKI in this population, as factors such as increased vascular permeability and altered renal protein handling in burn-induced systemic inflammatory responses may affect urinary NGAL levels differently.

We hypothesized that NGAL levels would rise earlier than traditional AKI markers such as serum creatinine and urine output, making it a valuable tool for early detection in critically ill burn patients. Therefore, this study aimed to evaluate the predictive value of serum and urinary NGAL levels for AKI in this high-risk population. By exploring the role of NGAL in burn patients, we sought to provide new insights into early AKI diagnosis and contribute to improved clinical management strategies, ultimately leading to better patient outcomes.

2. Materials and Methods

This study was conducted at the Burn Intensive Care Unit of Dr. Lütfi Kırdar Kartal Training and Research Hospital between April 1, 2011, and April 1, 2012, with approval from the local ethics committee (KEAHEK, March 21, 2011, No: 03/11). The study was designed as a prospective analytical observational study to evaluate the effectiveness of neutrophil gelatinase-associated lipocalin (NGAL) as a biomarker for the early detection of acute kidney injury (AKI) in burn patients. Inclusion and Exclusion Criteria: Patients were eligible for inclusion if they met the following criteria: (1) age ≥18 years, (2) admission to the Burn ICU within 24 hours of burn injury, (3) TBSA burned ≥20%, and (4) informed consent provided. Exclusion criteria comprised: (1) pre-existing chronic kidney disease (CKD), (2) pregnancy or lactation, (3) incomplete clinical data, and (4) refusal to participate.

Upon admission to the hospital, patients were initially evaluated in the emergency department. Following initial interventions, they were assessed for additional trauma and clinical findings by a multidisciplinary team before being admitted to the burn intensive care unit. After routine monitoring, central venous catheterization and arterial cannulation were performed to facilitate fluid resuscitation and hemodynamic monitoring. Fluid resuscitation was initiated based on parameters such as body weight and the percentage of total body surface area (TBSA) affected by burns.

Blood and urine samples were collected at admission (0 hours) and at 12, 24, 36, 48, and 72 hours post-admission according to a standardized protocol. Concurrently, hemodynamic parameters, urine output, the volume of crystalloids and colloids administered within 72 hours, the use of inotropic agents, the duration of renal replacement therapy (RRT), and lactate and creatinine levels measured from venous blood gas samples were recorded. Urine samples collected for the study were not centrifuged, while serum samples were centrifuged at 5000 rpm for 4 minutes. The plasma fraction was then transferred to Eppendorf tubes and stored at -80 °C for further analysis.

To assess morbidity and mortality, the Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation II (APACHE-II) scores were recorded at 24 and 48 hours. The AKIN (Acute Kidney Injury Network) and RIFLE (Risk, Injury, Failure, Loss, End-stage) criteria were used to define AKI and were evaluated at 12, 24, 36, 48, and 72 hours. NGAL levels in blood and urine samples were measured using the ELISA method (Human Neutrophil Gelatinase-Associated Lipocalin/Lipocalin-2 ELISA Kit; Adipo Bioscience, Inc., Santa Clara, USA).

2.1. Statistical analysis

Statistical analyses were performed using SPSS for Windows, version 15.0. The normality of the data distribution was assessed using the Kolmogorov-Smirnov test, and all parameters were found to be normally distributed. Descriptive statistics (mean, standard deviation, frequency) were used to summarize the data. For quantitative data, comparisons between groups were performed using the Student's t-test, while within-group comparisons were analyzed using the paired sample t-test. Qualitative data were compared using the chi-square test or Fisher's exact test, as appropriate. Sensitivity and specificity analyses were conducted to determine the optimal cutoff value for serum NGAL. Pearson's correlation test was used to evaluate relationships between variables. A p-value of <0.05 was considered statistically significant.

3. Results

The study included 31 patients (26 males, 5 females) with a mean age of 32.9 ± 17.6 years. The mean burn surface area was 51.3%, with flame burns being the most common etiology (54.8%). Inhalation injury was present in 12.9% of patients. Burn severity was predominantly second- and third-degree in all patients, with total body

surface area (TBSA) involvement ranging from 20% to 100% (mean: 51.3%). Primary Outcomes: AKI developed in 22.5% of patients based on RIFLE criteria and 18% based on AKIN criteria. Serum NGAL levels at 0 and 12 hours were significantly higher in patients who developed AKI ($p<0.05$) (Table 1, Fig. 1). A serum NGAL cutoff of 251 ng/ml was identified as a significant predictor of AKI ($p<0.05$). However, urinary NGAL levels did not show significant predictive value for AKI (Table 2, Fig. 2). Secondary Outcomes: RRT was required in 48.4% of patients, with a mean duration of 6.3 ± 4.7 days. Mortality was 45.2%, with higher burn surface area, increased fluid requirements, and higher SOFA and APACHE II scores being significant predictors of mortality ($p<0.01$). Inotropic support was required in 51.6% of patients and was associated with higher mortality ($p<0.01$) (Table 3).

Among the cohort, 17 patients were successfully discharged following recovery, whereas 14 patients succumbed to their injuries. While the types of burns varied, flame burns were the most common (n=17, 54.8%), followed by electrical burns (n=12, 38.7%), inhalation burns (n=4, 12.9%), scald burns (n=2, 6.4%), and burns caused by hot oil (n=1, 3.2%). Notably, two patients with electrical burns had no discernible entry or exit wounds. Some patients sustained combined burn injuries: three had both flame and inhalation burns, one had flame and electrical burns, and another had scald and inhalation burns.

In patients with suspected inhalation injury, clinical findings such as singed nasal hairs, soot deposition in the upper airways, mucosal hyperemia, and edema were carefully evaluated. Additionally, bedside bronchoscopy was performed by the pulmonology team to confirm the diagnosis. One patient was diagnosed with thoracic fractures due to multiple trauma.

Among the cohort, two patients had a history of coronary artery disease, diabetes mellitus, and hypertension; one patient had diabetes mellitus and hypertension; and another had schizophrenia, for which they were undergoing treatment at the time of admission following a suicide attempt. The remaining 26 patients had no known comorbidities aside from burn injuries. None of the patients had a history of chronic kidney disease.

Table 1. Relationship between serum NGAL levels and creatinine levels.

Time point	Correlation coefficient (R)	p-value
0 hour	0.433	0.015*
12 hours	0.443	0.013*
24 hours	0.140	0.454
36 hours	0.279	0.151
48 hours	0.332	0.091
72 hours	0.159	0.449

*Pearson correlation analysis
* $p<0.05$

Table 2. Relationship between urinary NGAL levels and creatinine levels.

Time point	Correlation coefficient (R)	p-value
0 hour	0.352	0.056
12 hours	0.195	0.302
24 hours	0.124	0.513
36 hours	0.211	0.282
48 hours	0.351	0.072
72 hours	0.232	0.264

Table 3. Distribution of inotropic use, mortality, and RRT.

Parameter	Presence (n)	Presence (%)	Absence (n)	Absence (%)
Inotropic use	16	51.6	15	48.4
Mortality	14	45.2	17	54.8
RRT	15	48.4	16	51.6

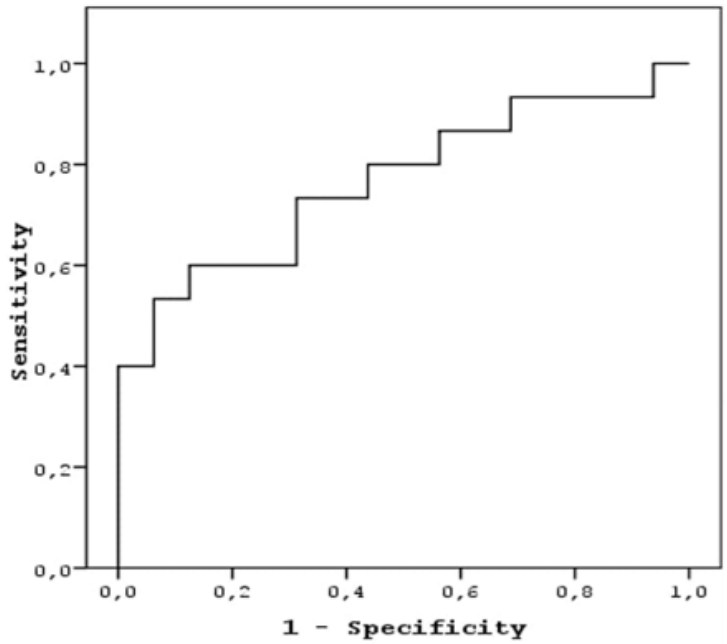

Fig. 1. ROC curve for serum NGAL: Graph representation of sensitivity vs. 1-specificity.

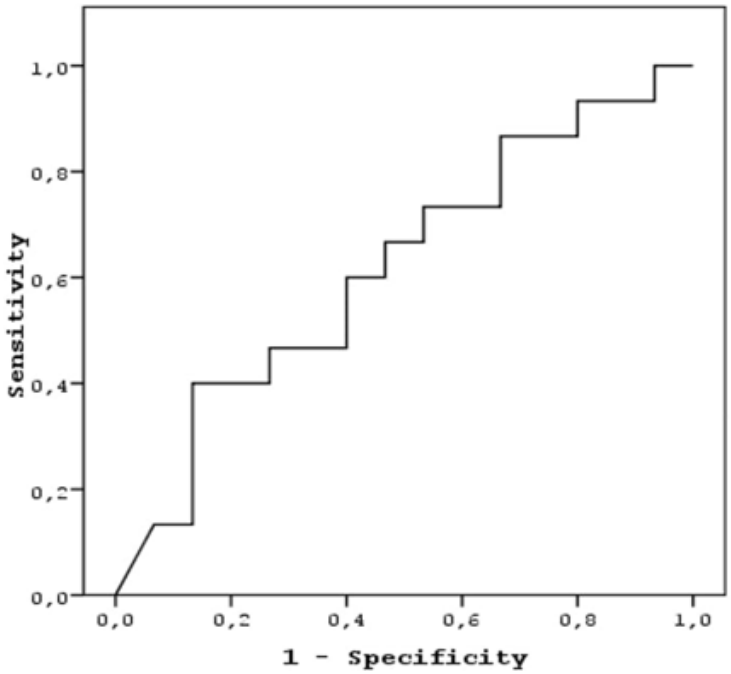

Fig. 2. ROC curve for urinary NGAL: Graph representation of sensitivity vs. 1-specificity.

4. Discussion

This study highlights that serum NGAL levels rise early in burn patients who develop acute kidney injury (AKI), suggesting its potential as a predictive biomarker. The strong correlation between serum NGAL levels and AKI development aligns with findings from other critically ill populations, such as those undergoing cardiac surgery, sepsis patients, and individuals with contrast-induced nephropathy [6,8,9]. However, urinary NGAL did not show significant predictive value in our cohort, likely due to the complex pathophysiology of burn-related AKI, which involves systemic inflammation, hypovolemia, and nephrotoxic insults [10,11].

NGAL is a small protein released from renal tubular cells in response to injury, and its levels increase rapidly in both serum and urine following AKI [5]. In our study, serum NGAL levels at admission (0 hours) and 12 hours post-admission were significantly higher in patients who developed AKI, with a cutoff value of 251 ng/ml demonstrating strong predictive accuracy ($p<0.05$). This finding is consistent with previous studies in cardiac surgery and critically ill patients, where NGAL predicted AKI 24–48 hours before serum creatinine levels rose [7,9]. The early rise in NGAL levels likely reflects tubular injury before significant changes in glomerular filtration rate (GFR) occur, making it a valuable tool for early AKI detection [6]. However, urinary NGAL did not demonstrate

significant predictive value in our cohort. This discrepancy may stem from the unique pathophysiology of burn-related AKI, which includes systemic inflammation, hypovolemia, and nephrotoxic insults [10]. Additionally, the heterogeneous nature of burn injuries and the varying degrees of severity in our cohort may have influenced the results. Further studies with larger, more homogeneous cohorts are needed to explore the role of urinary NGAL in burn patients.

The high mortality rate in our cohort (45.2%) underscores the severity of burn injuries and the critical importance of early AKI detection. AKI is a common complication in burn patients, with reported incidences ranging from 1% to 36%, depending on the population and diagnostic criteria used [12,13]. In our study, nearly half of the patients (48.4%) required renal replacement therapy (RRT), highlighting the urgent need for early identification and intervention in this population.

The association between higher SOFA and APACHE II scores and mortality emphasizes the role of multi-organ dysfunction in burn-related outcomes. Patients with larger burn surface areas and increased fluid requirements were more likely to develop AKI and require RRT, consistent with previous studies. Early identification of high-risk patients using biomarkers like NGAL could facilitate timely interventions, such as optimizing fluid management, avoiding nephrotoxic agents, and initiating RRT when indicated.

5. Limitations

This study has several limitations. Its single-center design and small sample size limit the generalizability of the findings. Additionally, the heterogeneous nature of burn injuries and the inclusion of patients with varying degrees of severity may have influenced the results. The lack of a standardized protocol for RRT initiation and the use of different RRT modalities (e.g., continuous vs. intermittent) may also have affected outcomes. Future studies should aim to include larger, more homogeneous cohorts and standardize RRT protocols to better evaluate the predictive value of NGAL in burn patients. Further research is needed to validate the role of NGAL in guiding early interventions in burn patients. Studies should explore the utility of NGAL in combination with other biomarkers, such as cystatin C, kidney injury molecule-1 (KIM-1), and interleukin-18 (IL-18), to improve the accuracy of AKI prediction [9, 14]. Additionally, the impact of early interventions guided by NGAL levels on patient outcomes, such as mortality, length of ICU stay, and long-term renal function, should be investigated.

6. Conclusions

Serum NGAL is a promising biomarker for early AKI detection in burn patients. Its ability to predict AKI before significant changes in serum creatinine makes it a valuable tool for early intervention. However, urinary NGAL did not show significant predictive value in our cohort, likely due to the complex pathophysiology of burn-related AKI. Further studies with larger cohorts are needed to validate these findings and explore the role of NGAL in guiding early interventions in burn patients.

Acknowledgements

None declared.

Funding

The authors received no financial support for the research, authorship, and/or publication of this manuscript.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this manuscript.

Author Contributions

All of the authors made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; were involved in drafting the manuscript or revising it critically for important intellectual content; and gave final approval of the version to be published.

Data Availability

The datasets created and/or analyzed during the current study are not publicly available, but are available from the corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

This study was approved by the local ethics committee of Dr. Lütfi Kırdar Kartal Training and Research Hospital (KEAHEK, March 21, 2011, No: 03/110). Written informed consent was obtained from the participants. All methods were performed in accordance with relevant guidelines and regulations.

REFERENCES

1. Palmieri T, Lavrentieva A, Greenhalgh DG. Acute kidney injury in critically ill burn patients. Risk factors, progression and impact on mortality. *Burns*. **2010**;36(2):205-11.
2. Witkowski W, Kawecki M, Surowiecka-Pastewka A, Klimm W, Szamotulska K, Niemczyk S. Early and Late Acute Kidney Injury in Severely Burned Patients. *Med Sci Monit*. **2016**;22:3755-63.
3. Park J, Kym D, Kim M, Cho YS, Hur J, Chun W, et al. Pioneering predictions of AKI and AKIN severity in burn patients: a comprehensive CBC approach. *Sci Rep*. **2024**;14(1):675.
4. Emami A, Javanmardi F, Rajaee M, Pirbonyeh N, Keshavarzi A, Fotouhi M, et al. Predictive Biomarkers for Acute Kidney Injury in Burn Patients. *J Burn Care Res*. **2019**;40(5):601-5.
5. Nickolas TL, O'Rourke MJ, Yang J, Sise ME, Canetta PA, Barasch N, et al. Sensitivity and specificity of a single emergency department measurement of urinary neutrophil gelatinase-associated lipocalin for diagnosing acute kidney injury. *Ann Intern Med*. **2008**;148(11):810-9.
6. Devarajan P. Emerging biomarkers of acute kidney injury. *Contrib Nephrol*. **2007**;156:203-12.
7. Wagener G, Gubitosa G, Wang S, Borregaard N, Kim M, Lee HT. Urinary neutrophil gelatinase-associated lipocalin and acute kidney injury after cardiac surgery. *Am J Kidney Dis*. **2008**;52(3):425-33.
8. Mishra J, Ma Q, Kelly C, Mitsnefes M, Mori K, Barasch J, et al. Kidney NGAL is a novel early marker of acute injury following transplantation. *Pediatr Nephrol*. **2006**;21(6):856-63.
9. Haase M, Bellomo R, Devarajan P, Schlattmann P, Haase-Fielitz A. Accuracy of neutrophil gelatinase-associated lipocalin (NGAL) in

diagnosis and prognosis in acute kidney injury: a systematic review and meta-analysis. *Am J Kidney Dis*. **2009**;54(6):1012-24.
10. Srisawat N, Lawsin L, Uchino S, Bellomo R, Kellum JA. Cost of acute renal replacement therapy in the intensive care unit: results from The Beginning and Ending Supportive Therapy for the Kidney (BEST Kidney) study. *Crit Care*. **2010**;14(2):R46.
11. Cruz DN, de Cal M, Garzotto F, Perazella MA, Lentini P, Corradi V, et al. Plasma neutrophil gelatinase-associated lipocalin is an early biomarker for acute kidney injury in an adult ICU population. *Intensive Care Med*. **2010**;36(3):444-51.
12. Mustonen KM, Vuola J. Acute renal failure in intensive care burn patients (ARF in burn patients). *J Burn Care Res*. **2008**;29(1):227-37.
13. Chung KK, Juncos LA, Wolf SE, Mann EE, Renz EM, White CE, et al. Continuous renal replacement therapy improves survival in severely burned military casualties with acute kidney injury. *J Trauma*. **2008**;64(2 Suppl):S179-85; discussion S85-7.
14. Parikh CR, Jani A, Mishra J, Ma Q, Kelly C, Barasch J, et al. Urine NGAL and IL-18 are predictive biomarkers for delayed graft function following kidney transplantation. *Am J Transplant*. **2006**;6(7):1639-45.