HİTİT MEDICAL JOURNAL
HİTİT ÜNİVERSİTESİ TIP FAKÜLTESİ DERGİSİ

e-ISSN: 2687-4717 Cilt|Volume: 6 • Sayı|Issue: 3 - Ekim|October 2024

The Predictors of Outcome in Patients that Require Management in Intensive Care Units: A Narrative Review

Yoğun bakım ünitelerinde tedavi gerektiren hastalarda prognostik belirteçler: Derleme

İbrahim Karagöz[1] | Bahri Özer[2] | Gülali Aktaş[3]

[1]Abant Izzet Baysal University, Department of Anesthesiology and Reanimation, Bolu, Türkiye.
[2]Abant Izzet Baysal University, Department of General Surgery, Bolu, Türkiye.
[3]Abant Izzet Baysal University, Department of Internal Medicine, Bolu, Türkiye.

Sorumlu Yazar | Correspondence Author
Gülali Aktaş
draliaktas@yahoo.com
Address for Correspondence: Abant Izzet Baysal University, Department of Internal Medicine, Golkoy, 14030, Bolu, Türkiye.

Makale Bilgisi | Article Information
Makale Türü | Article Type: Derleme | Review
Doi: https://doi.org/10.52827/hititmedj.1443663
Geliş Tarihi | Received: 28.02.2024
Kabul Tarihi | Accepted: 13.06.2024
Yayım Tarihi | Published: 14.10.2024

Atıf | Cite As
Karagöz İ, Özer B, Aktaş G. The Predictors of Outcome in Patients that Require Management in Intensive Care Units: A Narrative Review. Hitit Medical Journal 2024;6(3):367-378 https://doi.org/10.52827/hititmedj.1443663

Hakem Değerlendirmesi: Alan editörü tarafından atanan en az iki farklı kurumda çalışan bağımsız hakemler tarafından değerlendirilmiştir.
Etik Beyanı: Makale Derleme türünde olduğundan etik kurul onayına gerek yoktur.
İntihal Kontrolleri: Evet (iThenticate)
Çıkar Çatışması: Yazarlar çalışma ile ilgili herhangi bir çıkar çatışması olmadığını beyan etmişlerdir.
Şikayetler: hmj@hitit.edu.tr
Katkı Beyanı: Fikir/Hipotez: BO, GA Tasarım: BO, GA Veri Toplama/Veri İşleme: IK, BO Veri Analizi: IK, GA Makalenin Hazırlanması: BO, GA.
Hasta Onamı: Çalışma derleme türünde olduğundan hasta onamına gerek yoktur.
Finansal Destek: Bu çalışma ile ilgili herhangi bir finansal kaynaktan yararlanılmamıştır.
Telif Hakı & Lisans: Dergi ile yayın yapan yazarlar, CC BY-NC 4.0 kapsamında lisanslanan çalışmalarının telif hakkını elinde tutar.

Peer Review: Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
Ethical Statement: Not applicable
Plagiarism Check: Yes (iThenticate)
Conflict of Interest: The authors declared that, there are no conflicts of interest.
Complaints: hmj@hitit.edu.tr
Authorship Contribution: Idea/Hypothesis: BO, GA Design: BO, GA Data Collection/Data Processing: IK, BO Data Analysis: IK, GA Manuscript Preparation: BO, GA.
Informed Consent: Not applicable.
Financial Disclosure: There are no financial funds for this article.

The Predictors of Outcome in Patients that Require Management in Intensive Care Units: A Narrative Review

ABSTRACT
Intensive care units stand as the frontline battlegrounds where medical warriors combat the most critical illnesses and injuries. Within the labyrinth of intensive care units, where every moment teeters between life and death, prognostic markers emerge as beacons of guidance amidst uncertainty. In recent years, researchers have identified several novel mortality predictors in the intensive care population. In this review, we aimed to examine the clinical and laboratory markers that have been proposed in recent years to evaluate prognosis in the intensive care unit population and to review the literature on this topic. Management of patients in intensive care units is a dynamic process and reliable risk stratification models and prognostic markers are needed for this purpose. Novel prognostic indicators could serve as reliable diagnostic and prognostic tools in critically ill patients.
Keywords: Intensive care, marker, mortality, predictor, prognosis.

ÖZET
Yoğun bakım üniteleri, tıbbi savaşçıların en kritik hastalıklar ve yaralanmalarla mücadele ettiği ön cephe savaş alanlarıdır. Her anın yaşamla ölüm arasında gidip geldiği yoğun bakım ünitelerinin labirentinde, belirsizlik ortamında yol gösterici işaretler olarak prognostik belirteçler ortaya çıkıyor. Son yıllarda araştırmacılar yoğun bakım popülasyonunda birçok yeni mortalite belirteçleri tespit etmektedirler. Bu derlemede, yoğun bakım ünitesi popülasyonunda prognozu değerlendirmek için son yıllarda önerilen klinik ve laboratuvar belirteçlerin incelenmesi ve bu konuyla ilgili literatürün gözden geçirilmesi amaçlandı. Yoğun bakım ünitelerindeki hastaların yönetimi dinamik bir süreçtir ve bu amaçla güvenilir risk sınıflandırma modellerine ve prognostik belirteçlere ihtiyaç vardır. Yeni prognostik göstergeler, kritik hastalarda güvenilir tanı ve prognostik araçlar olarak hizmet edebilir.
Anahtar Sözcükler: Belirteç, mortalite, öngördürücü, prognoz, yoğun bakım.

Introduction

The struggle against serious conditions takes place in intensive care units (ICUs). Subjects in ICU require more careful management and swiftness in interventions. Patients in ICU are vulnerable and need to round-the-clock care, monitored with precision, and supported with a delicate balance of science and compassion (1). Since the population in ICU requires prompt and attentive care, markers for prediction of outcome of those patients need to emerge. These indicators should serve well in assessing the progress of the patients' treatment and forecasting their future outlook. Biomarkers and prognostic indicators shed light on the path for clinicians, aiding in navigating the fine line between decision-making and care planning for ICU patients (2). In recent years, researchers have identified several novel mortality predictors in the intensive care population, leveraging advanced statistical techniques, biomarkers, and data-driven approaches. Some of these include machine learning models, serum biomarkers, genetic markers, multiomic approaches, physiological indices, and dynamic predictors (3, 4). In this current review, our objective was to analyze the clinical and laboratory indicators that have been suggested in recent years for assessing prognosis among patients in the intensive care unit, and to survey the existing literature concerning this subject.

Machine Learning Models

Advanced machine learning algorithms have been devised to discern intricate patterns within the mortality rates of intensive care patients and to scrutinize extensive datasets encompassing these individuals. These models include a wide range of clinical variables, such as vital signs, laboratory values, and demographic factors, to predict patients' prognoses with high accuracy. These models include automatic algorithms, decision-making models, kidney damage prediction models and survival prediction models (5-8).

Biomarkers

Emerging markers like procalcitonin, copeptin, and soluble trigger receptor expressed on myeloid cells (sTREM-1) demonstrate potential in forecasting mortality among critically ill patients (9-11). These biomarkers reflect underlying inflammatory processes, severity of infection, and organ dysfunction, providing valuable information about the patient's prognosis.

Genetic Markers

Variations in genetics might influence individuals' susceptibility to critical illness and their prognosis within the intensive care unit. Genome-wide association studies (GWAS) have pinpointed genetic markers linked to heightened mortality risk in conditions such as sepsis, acute respiratory distress syndrome, and septic shock (12-14).

Multiomic Approaches

The molecular mechanisms underlying the diseases of critically ill patients are possible by integrating data from multiple omics platforms, including genomics, transcriptomics, proteomics and metabolomics. Within this context, multiomic analyses have uncovered fresh biomarkers and therapeutic targets linked to mortality among the intensive care unit population (4, 15).

Physiological Indices

New physiological indices such as the Shock Index, Oxygenation Index, and Sequential Organ Failure Assessment (SOFA) score provide quantitative measurements of hemodynamic instability, respiratory failure, and organ dysfunction, respectively. Therefore, they assist clinicians in evaluating disease severity and forecasting the likelihood of death in critically ill patients (16-18).

Dynamic Predictors

Dynamic variables, such as changes in clinical parameters over time (e.g., trends in vital signs, laboratory values, and severity scores), provide valuable prognostic information in the intensive care unit (19). Monitoring dynamic indicators allows early detection of clinical deterioration and timely intervention to improve patient prognosis. APACHE-II score is among these dynamic markers (20). The identification of new determinants of mortality in the critical care population represents a significant advance in critical care medicine. With the integration of the latest technologies and innovative approaches, it is aimed to improve risk stratification, optimize treatment strategies and ultimately improve survival rates in critically ill patients.

Laboratory Markers of Prognosis in ICU

New indicators based on laboratory markers in the critical care population include a range of biomarkers and laboratory data-derived measurements that

provide valuable information regarding patient prognosis. Some examples may include procalcitonin, C-reactive protein, lactate, troponin, blood urea nitrogen and creatinine, hemogram-derived indices, and inflammatory cytokines. These markers have been examined in assessing outcomes of patients in intensive care.

Procalcitonin

Bacterial infections and systemic inflammation trigger the release of procalcitonin (PCT), which is a peptide precursor of calcitonin (21). Elevated PCT has been associated with increased mortality in critically ill patients, particularly those with sepsis and septic shock (22). It is also useful in deciding treatment. Monitoring PCT levels can aid in early detection of infection and guide antibiotic therapy decisions (23).

Procalcitonin is a valuable indicator of sepsis and systemic inflammation. PCT levels increase in response to bacterial infections and systemic inflammation, making it a valuable marker in identifying sepsis and other infectious conditions in intensive care patients. High PCT levels are associated with the presence and severity of bacterial infections and help clinicians distinguish between infectious and noninfectious causes of systemic inflammation. Procalcitonin also allows dynamic monitoring of the condition of patients in intensive care. Serial measurement of PCT levels provides valuable information about the patient's response to treatment and resolution of the infection. A decrease in PCT levels over time is indicative of a positive response to treatment; persistently high or increasing PCT levels may indicate ongoing infection or treatment failure. Dynamic monitoring of PCT levels helps clinicians optimize antibiotic therapy and identify patients at higher risk of adverse outcomes.

Procalcitonin holds prognostic significance in cases of sepsis and septic shock. Elevated levels of PCT upon admission to the intensive care unit or during the initial phases of sepsis have been linked to heightened disease severity and poorer outcomes. High PCT levels are associated with higher mortality rates, longer hospital stays, and increased rates of organ dysfunction in septic patients. Monitoring PCT levels can help clinicians assess the severity of infection, predict patient outcomes, and guide treatment decisions, including antibiotic therapy. Procalcitonin has an important action in prognosis and management decisions in ICU population. It provides valuable information about the presence and severity of infection, predicts patient outcomes, and guides antibiotic therapy. Integrating PCT measurement into clinical practice enhances patient care, promotes antibiotic stewardship, and mitigates the burden of antibiotic-resistant infections in the intensive care unit.

C-reactive protein

C-reactive protein (CRP) is an acute phase reactant produced by the liver in response to inflammation. High CRP levels are associated with a wide variety of inflammatory conditions, including diabetic nephropathy, thyroiditis, diabetic neuropathy, and hepatitis (24-27). Moreover, a recent work found association between Covid-19 mortality and CRP based inflammatory markers (28). CRP has also shown an association with heightened mortality rates among critically ill patients (29). Serial measurement of CRP levels can help assess the severity of inflammation and monitor response to therapy.

Lactate

Lactate is a byproduct of anaerobic metabolism and serves as a marker of tissue hypoperfusion and organ dysfunction (30). High levels of lactate, especially in cases of sepsis and septic shock, correlate with higher mortality rates among ICU patients. Additionally, lactate clearance, representing the speed at which lactate levels diminish with treatment, has emerged as a prognostic factor in critically ill patients (31-33).

Troponin

Troponin is a marker of myocardial injury and is commonly elevated in patients with acute coronary syndromes and other cardiac conditions. Heightened troponin levels have been linked to elevated mortality rates in critically ill patients, especially among those diagnosed with sepsis and acute respiratory distress syndrome (34, 35). Serial measurement of troponin levels can help identify patients at higher risk of adverse cardiac events.

Creatinine and Blood Urea Nitrogen

Creatinine and blood urea nitrogen (BUN) are markers of renal function and are commonly monitored in critically ill subjects. Elevated levels of creatinine and BUN are associated with acute kidney injury

(AKI) and increased mortality in the ICU (36, 37). Changes in renal function over time can help predict patient outcomes and guide renal replacement therapy decisions.

Inflammatory cytokines

Inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-alpha), and interleukin-8 (IL-8) play key roles in the immune response and inflammatory cascade (38). High levels of these cytokines have been associated with increased mortality, especially in critically ill patients with sepsis and systemic inflammatory response syndrome (SIRS) (39). Measurement of cytokine levels may help identify patients at higher risk for poor outcomes and guide immunomodulatory therapy. New mortality predictors based on laboratory indices in the intensive care population provide valuable information for risk stratification, treatment guidance, and prognosis in critically ill subjects. Integrating these biomarkers into clinical practice may help improve patient outcomes and optimize resource allocation in the ICU.

Interleukin-6

Interleukin-6 (IL-6) plays a critical role in the inflammatory response and has emerged as an important biomarker for prognosis in the intensive care unit (ICU) population. It has important actions in assessing the severity of the disease (40). IL-6 is a pro-inflammatory cytokine produced by various cell types, including immune cells, endothelial cells, and fibroblasts, in response to infection, tissue damage, or inflammation. Elevated levels of IL-6 in the bloodstream indicate the presence and severity of systemic inflammation, a common occurrence in critically ill patients afflicted with conditions like sepsis, septic shock, and acute respiratory distress syndrome (ARDS) (41). High levels of IL-6 have been associated with increased disease severity and worse outcomes in ICU patients (42). Elevated IL-6 levels have been linked to an increased risk of mortality, prolonged hospital stays, and higher rates of organ dysfunction across various critical illnesses. Monitoring IL-6 levels may help clinicians identify patients at higher risk of adverse outcomes and guide treatment decisions. IL-6 levels measured early in the course of critical illness have prognostic value in predicting the patient (43). Numerous studies have indicated that elevated IL-6 levels upon admission to the intensive care unit or during the initial phases of the disease are correlated with heightened mortality and poorer outcomes among critically ill patients. Additionally, IL-6 levels may be linked to the occurrence of complications such as acute kidney injury (AKI), acute respiratory failure, and multiple organ dysfunction syndrome. Given its central role in the inflammatory response, IL-6 has emerged as a potential therapeutic target in critical care medicine (44). Strategies aimed at modulating IL-6 activity, such as the use of IL-6 inhibitors or monoclonal antibodies targeting the IL-6 receptor, are being investigated for their potential to alleviate inflammation and improve outcomes in critically ill patients.

Interleukin-8

Interleukin-8 (IL-8) is a potent chemokine involved in the recruitment and activation of neutrophils, which are key factors in the inflammatory response (45). In the ICU population, IL-8 has been associated with a variety of critical illnesses and serves as a marker of prognostic significance. IL-8 is released in response to infection, tissue damage, and inflammation. In critically ill patients, elevated IL-8 levels often reflect the presence of systemic inflammation, especially in conditions such as sepsis, septic shock, and acute respiratory distress syndrome (46). Sustained release of IL-8 may lead to excessive inflammatory response, contributing to tissue damage and organ dysfunction. High levels of IL-8 have been associated with increased disease severity and worse outcomes in intensive care patients. Elevated IL-8 levels upon admission to the intensive care unit or during the initial phases of critical illness have been correlated with elevated mortality rates, prolonged hospital stays, and increased incidence of organ failure (47). Tracking IL-8 levels can aid clinicians in gauging the extent of inflammation and forecasting patient outcomes. IL-8 has been demonstrated to contribute to the development of organ dysfunction in critically ill patients (48). Excessive levels of IL-8 may contribute to endothelial dysfunction, microvascular damage, and the development of acute lung injury. IL-8-mediated neutrophil recruitment and activation may also contribute to tissue damage in other organs such as the kidneys, liver, and gastrointestinal tract.

Strategies aimed at modulating IL-8 activity are being investigated for their potential to improve outcomes in critically ill patients (49). Hence, monitoring IL-8 levels could assist in directing clinical management and pinpointing patients who might gain from specific therapeutic interventions targeting the modulation of the inflammatory response.

Tumor necrosis factor-alpha

Tumor necrosis factor-alpha (TNF-alpha) is an inflammatory cytokine that holds a pivotal role in immune response and inflammation. In the critical care population, TNF-alpha has been studied extensively for its role and prognostic significance in various critical illnesses (50). It is produced primarily by activated macrophages and other immune cells in response to infection, tissue damage, or inflammation. In critically ill patients, elevated TNF-alpha levels often reflect the presence of systemic inflammation, especially in conditions such as sepsis, septic shock, and acute respiratory distress syndrome (51). TNF-alpha contributes to the recruitment and activation of immune cells, leading to amplification of the inflammatory response. High TNF-alpha levels have been associated with increased disease severity and worse outcomes in intensive care patients. Elevated TNF-alpha levels upon admission to the intensive care unit or during the initial phases of critical illness have been correlated with elevated mortality rates, prolonged hospital stays, and increased incidence of organ failure (52). Monitoring TNF-alpha levels can help clinicians assess the severity of inflammation and predict the outcome of the patients. TNF-alpha has been demonstrated to contribute to the pathogenesis of organ dysfunction in critically ill individuals. Overproduction of TNF-alpha can result in endothelial dysfunction, microvascular damage, and the onset of multiple organ failure (53). TNF-alpha-mediated inflammation contributes to tissue damage in various organs, including the lungs, kidneys, liver, and gastrointestinal tract.

There are also novel inflammatory indexes that have been used in various clinical conditions, including assessing the outcome of the critically ill patients. These include systemic inflammatory index (SII), Hemoglobin-Albumin-Lymphocyte-Platelet (HALP) score, uric acid to HDL cholesterol ratio (UHR), and prognostic nutritional index (PNI).

Systemic Inflammatory Index

In the field of modern medicine, the systemic inflammatory index stands out as a versatile tool that serves as both a diagnostic aid and a prognostic indicator in a wide disease variety. Based on the complex interplay of immune responses in the body, this index provides invaluable information about the severity and progression of various medical conditions. From acute infections to chronic inflammatory disorders, the systemic inflammatory index provides a quantitative measurement of the body's inflammatory burden, guiding healthcare professionals in their decision-making processes.
The systemic inflammatory index plays a crucial role in inflammatory conditions, serving as a quantitative measure of the body's overall inflammatory response (54, 55). In such instances, the immune system undergoes dysregulation, resulting in an overabundance of pro-inflammatory cytokines and other mediators. The systemic inflammatory index (SII), frequently derived from indicators like C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and white blood cell count (WBC), furnishes clinicians with an overview of the systemic inflammatory condition. SII assists in diagnosing inflammatory conditions. Elevated levels of inflammatory markers can indicate the presence and severity of inflammation, helping clinicians differentiate between inflammatory and non-inflammatory conditions (56). Additionally, SII serves as a prognostic indicator, offering insights into the progression and severity of inflammatory diseases. High levels of inflammatory markers may indicate a more aggressive disease course or an increased risk of complications. Furthermore, SII is useful in guiding treatment decisions by monitoring the response to therapy. Changes in inflammatory marker levels over time can indicate the effectiveness of treatment and help clinicians adjust therapeutic strategies accordingly.

Hemoglobin-Albumin-Lymphocyte-Platelet (HALP) Score

HALP score is a composite index obtained from hemoglobin, albumin, lymphocyte and platelet levels in the blood. This score acts as a prognostic marker in Hemoglobin levels and indicates the oxygen carrying capacity of the blood. Low hemoglobin levels (anemia) may reflect underlying chronic diseases, nutritional

deficiencies, or bone marrow disorders. Albumin is a protein synthesized by the liver and serves as a marker of nutritional status and liver function. Low albumin levels may indicate malnutrition, liver disease, inflammation, or other underlying chronic conditions. Lymphocytes are a type of white blood cell that plays a role in the body's immune response. Decreased lymphocyte count may indicate impaired immune function, chronic infections, autoimmune diseases, or bone marrow disorders. Platelets are blood cells that play a role in clotting and wound healing. Abnormal platelet counts may indicate bleeding disorders, inflammatory conditions, or bone marrow disorders.

The HALP score combines these four components to provide a comprehensive assessment of the patient's nutritional and inflammatory status. Low HALP score, indicating low hemoglobin and albumin levels and/or high lymphocyte and platelet levels; It is associated with increased mortality and poor outcomes in a variety of diseases, including cancer, cardiovascular disease, chronic kidney disease, and sepsis (57). Clinicians use the HALP score as a prognostic tool to assess disease severity, predict clinical outcomes, and guide treatment decisions. It helps identify high-risk patients who may need more intensive monitoring or aggressive interventions to improve their prognosis. Additionally, monitoring changes in HALP score over time can provide valuable information about the patient's response to treatment and disease progression (58, 59).

In the intensive care population, HALP score serves as a valuable prognostic tool for assessing the severity of illness and predicting clinical outcomes. Low hemoglobin levels in critically ill patients can indicate various conditions such as anemia, hemorrhage, or impaired oxygen delivery (60). Monitoring hemoglobin levels as part of the HALP score helps clinicians identify patients who may require blood transfusions or additional interventions to optimize oxygenation and tissue perfusion. Serum albumin levels are commonly decreased in critically ill subjects because of factors such as inflammation, fluid shifts, and nutritional deficiencies. Low albumin levels are associated with increased morbidity and mortality in the ICU population. The HALP score incorporates albumin as a marker of nutritional status and disease severity, helping clinicians assess the overall inflammatory and metabolic state of critically ill patients (61). Changes in lymphocyte counts can reflect the degree of immune dysregulation and inflammatory response in critically ill patients. Lymphopenia is common in severe infections, sepsis, and systemic inflammatory syndromes. Monitoring lymphocyte counts, as part of the HALP score, aids in identifying patients with compromised immune function and predicting outcomes (62). Platelet counts are closely monitored in the ICU population due to their role in hemostasis and thrombosis. Thrombocytopenia, characterized by low platelet counts, can occur secondary to sepsis, disseminated intravascular coagulation (DIC), or drug-induced thrombocytopenia (63). Elevated platelet counts may indicate underlying inflammation or a hypercoagulable state (64). Including platelet counts in the HALP score allows clinicians to assess coagulation status and predict the risk of bleeding or thrombotic events in critically ill patients.

Uric acid to HDL-cholesterol Ratio (UHR)

The ratio of uric acid to high-density lipoprotein (HDL) cholesterol is a novel metabolic and inflammatory marker. Uric acid is a byproduct of purine metabolism and has antioxidant properties but can also contribute to inflammation when present in excess. HDL cholesterol, often referred to as "good" cholesterol, has anti-inflammatory and antioxidant properties and helps remove excess cholesterol from the bloodstream. UHR's diagnostic and prognostic role have been studied in various conditions such as hypertension, hepatic steatosis, type 2 DM, thyroiditis, metabolic syndrome, prediabetes, diabetic kidney disease and even new onset diabetes (65-70). UHR stands as a potential prognostic indicator in critically ill patients, especially among those diagnosed with sepsis and systemic inflammatory response syndrome. Uric acid and HDL cholesterol both contribute to inflammation and oxidative stress (71).

In critically ill patients, UHR has been proposed as a marker of oxidative stress and inflammation. Elevated levels of uric acid and decreased levels of HDL cholesterol are common in conditions such as sepsis and SIRS, where inflammation and oxidative stress play key roles in pathogenesis. UHR may reflect the balance between pro-inflammatory and

anti-inflammatory processes in these patients.

Studies have suggested that a higher UHR is associated with increased disease severity and worse outcomes in critically ill patients (72). Elevated UHR has been correlated with higher mortality rates, longer hospital stays, and increased rates of complications such as acute kidney injury, acute respiratory distress syndrome, and multi-organ dysfunction syndrome. The UHR holds promise as a reliable marker of prognosis in critically ill subjects, providing insights into disease severity and predicting clinical outcomes. Further research is needed to better understand the mechanisms underlying this ratio and its potential as a therapeutic target in critical care medicine.

Prognostic nutritional index (PNI)

The prognostic nutritional index (PNI) is a parameter that reflects both the nutritional and immunological status of the individual. In the context of inflammation, PNI may be a useful tool in assessing the severity and prognosis of inflammatory conditions (73). PNI includes serum albumin levels, which are commonly used as markers of nutritional status. During inflammation, as in acute or chronic diseases, there is often a decrease in serum albumin due to factors such as decreased synthesis, increased catabolism, or leakage into tissues. A low serum albumin level indicates malnutrition or inflammatory processes (74). PNI also includes the lymphocyte count, which reflects the body's immune response. Inflammation can lead to changes in lymphocyte number due to factors such as cytokine release, cell migration and apoptosis (75). The decrease in lymphocyte count is often associated with systemic inflammation and immune suppression. PNI provides a comprehensive assessment of the patient's condition by combining markers of both nutritional and immunological status. In inflammatory conditions, a low PNI is associated with worse prognosis, including increased risk of complications, longer hospital stay, and higher mortality rates. It serves as a prognostic indicator of patient outcomes. Monitoring changes in PNI over time may also help assess response to treatment in inflammatory conditions. Improvements in PNI may indicate successful management of inflammation, whereas persistent or worsening low PNI may indicate treatment failure or disease progression. In summary, the prognostic nutritional index (PNI) is a valuable tool in assessing the nutritional and immunological status of patients with inflammation. It provides information about prognosis, helps guide treatment decisions, and can be used to monitor response to treatment.

In intensive care patients, the prognostic nutritional index (PNI) plays an important role in assessing disease severity, predicting outcomes, guiding nutritional interventions, and monitoring response to treatment. ICU patients often experience significant physiological stress and metabolic changes. Including markers of both nutritional status (such as serum albumin) and immune function (such as lymphocyte count), PNI provides a comprehensive assessment of the patient's overall condition. Low PNI at the time of intensive care unit (ICU) admission may indicate higher disease severity and increased risk of complications (76). PNI serves as a prognostic indicator for intensive care patients. Several studies have shown that a low PNI is associated with worse outcomes in critically ill patients, including increased mortality, longer ICU stays, and higher complication rates. Therefore, PNI may help clinicians identify patients who may require closer monitoring or more aggressive interventions (76). Adequate nutrition is essential for the recovery of critically ill patients. However, many intensive care patients are at risk of malnutrition due to factors such as hypermetabolism, catabolism, and decreased oral intake. PNI can guide nutritional assessment and support strategies by identifying patients at higher risk of malnutrition. Patients with low PNI may benefit from early initiation of enteral or parenteral nutrition to prevent further deterioration of nutritional status and improve clinical outcomes. Monitoring changes in PNI over time can help assess the patient's response to treatment and nutritional support. While improvements in PNI may indicate a positive response to treatment, a decreasing PNI may signal treatment failure or ongoing physiological stress. Regular monitoring of PNI allows clinicians to adjust treatment plans and nutritional support strategies accordingly (77). PNI can be used to risk stratify critical care patients and help clinicians prioritize resources and interventions based on disease severity and predicted outcomes.

Patients with low PNI may require more intensive monitoring, aggressive nutritional support, or early intervention to reduce complications and improve prognosis. Overall, the prognostic nutritional index (PNI) is a valuable tool in the management of intensive care patients, providing valuable information on disease severity, prognosis, nutritional status, and response to treatment. Its integration into clinical practice can help optimize patient care and improve outcomes in the critical care setting.

Hemogram Indices

Hemogram indices have been reported as reliable diagnostic markers of inflammation in various conditions. For instance, aside from its function in detecting anisocytosis, RDW has been proposed as a new inflammatory indicator in several inflammatory conditions, such as functional bowel conditions, autoimmune diseases, rheumatoid arthritis, degenerative vertebral conditions, malignancy, autoimmune hepatitis, gastrointestinal conditions, and even Covid-19 infection (78-81). Another example could be mean platelet volume (MPV), which has been linked to type 2 DM, diabetic nephropathy, hypothyroidism, infections, vertebral discopathies, irritable bowel disease, gastrointestinal conditions, rheumatoid arthritis, obesity, mortality in ICU population, and liver fibrosis (82-85). All of these conditions are associated with inflammation as intensive care management does.

Recent studies on critically ill patients revealed that hemogram markers could be used as prognostic indicators. Mean platelet volume, which refers the size of circulating thrombocytes, has been suggested as a marker of outcome in patients in ICU (86). Another study suggested use of hemogram markers as screening and prognosis tools in ICU patients (87). These indices were also useful in detecting patients with poor prognosis in Covid-19 patients that require intensive care management (88). These data suggest that hemogram markers are reliable prognostic markers for patients in ICU.

Conclusion

Management of patients in ICU is a dynamic process and reliable risk stratification models and prognostic markers are needed for this purpose. Novel prognostic indicators could serve as reliable diagnostic and prognostic tools in critically ill subjects.

References

1. Greenberg SM, Ziai WC, Cordonnier C, et al. 2022 Guideline for the Management of Patients With Spontaneous Intracerebral Hemorrhage: A Guideline From the American Heart Association/American Stroke Association. Stroke. 2022;53(7):e282-e361.
2. Wazir H, Abid M, Essani B, et al. Diagnosis and Treatment of Liver Disease: Current Trends and Future Directions. Cureus. 2023;15(12):e499-e522.
3. Jentzer JC, Kashou AH, Murphree DH. Clinical applications of artificial intelligence and machine learning in the modern cardiac intensive care unit. Intelligence Based Medicine. 2023 ;7(1):89-100.
4. Garduno A, Cusack R, Leone M, Einav S, Martin-Loeches I. Multi-Omics Endotypes in ICU Sepsis Induced Immunosuppression. Microorganisms. 2023;11(5): 11-19.
5. Delahanty RJ, Kaufman D, Jones SS. Development and Evaluation of an Automated Machine Learning Algorithm for In-Hospital Mortality Risk Adjustment Among Critical Care Patients. Critical Care Medicine. 2018;46(6):e481-e488.
6. Johnson AE, Ghassemi MM, Nemati S, et al. Machine Learning and Decision Support in Critical Care. Proceedings of the Institute of Electrical and Electronics Engineers. 2016;104(2):444-466.
7. Koyner JL, Carey KA, Edelson DP, Churpek MM. The Development of a Machine Learning Inpatient Acute Kidney Injury Prediction Model. Critical Care Medicine. 2018;46(7):1070-1077.
8. Houthooft R, Ruyssinck J, van der Herten J, et al. Predictive modelling of survival and length of stay in critically ill patients using sequential organ failure scores. Artificial Intelligence in Medicine. 2015;63(3):191-207.
9. Jafari M, Fazeli F, Sezavar M, et al. Role of Procalcitonin in the Prognosis of Mortality in Patients Admitted to the Intensive Care Unit: A Review Study. Tanaffos. 2021;20(4):296-305.
10. Martino M, Arnaldi G. Copeptin and stress. Endocrines. 2021;2(4):384-404.
11. François B, Lambden S, Fivez T, et al. Prospective evaluation of the efficacy, safety, and optimal biomarker enrichment strategy for nangibotide, a TREM-1 inhibitor, in patients with septic shock (ASTONISH): a double-blind, randomised, controlled, phase 2b trial. Lancet Respirtory Medicine. 2023;11(10):894-904.
12. Hernandez-Beeftink T, Guillen-Guio B, Lorenzo-Salazar JM, et al. A genome-wide association study of survival in patients with sepsis. Critical Care. 2022;26(1):341-346.

13. Hamilton FW, Thomas M, Arnold D, et al. Therapeutic potential of IL6R blockade for the treatment of sepsis and sepsis-related death: A Mendelian randomisation study. Public Library of Science Medicine. 2023;20(1):41-74.
14. Guillen-Guio B, Lorenzo-Salazar JM, Ma SF, et al. Sepsis-associated acute respiratory distress syndrome in individuals of European ancestry: a genome-wide association study. Lancet Respirtory Medicine. 2020;8(3):258-266.
15. Liao SY, Casanova NG, Bime C, et al. Identification of early and intermediate biomarkers for ARDS mortality by multi-omic approaches. Scientific Reports. 2021;11(1):74-88.
16. Maheshwari K, Nathanson BH, Munson SH, et al. Abnormal shock index exposure and clinical outcomes among critically ill patients: A retrospective cohort analysis. Journal of Critical Care. 2020;57:5-12.
17. Sauthier M, Tuli G, Jouvet PA, et al: A Continuous and Noninvasive Method to Estimate Pao(2) and Oxygenation Index. Crit Care Explorations. 2021;3(10):40-46.
18. Pölkki A, Pekkarinen PT, Takala J, et al. Association of Sequential Organ Failure Assessment (SOFA) components with mortality. Acta anaesthesiologica Scandinavica. 2022;66(6):731-741.
19. Deasy J, Liò P, Ercole A. Dynamic survival prediction in intensive care units from heterogeneous time series without the need for variable selection or curation. Scientific Reports. 2020;10(1):221-229.
20. Tian Y, Yao Y, Zhou J, et al. Dynamic APACHE II Score to Predict the Outcome of Intensive Care Unit Patients. Frontiers in Medicine. 2021;8:744-749.
21. Gregoriano C, Heilmann E, Molitor A, et al. Role of procalcitonin use in the management of sepsis. Journal of thoracic disease. 2020;12(1):5-15.
22. Webb AL, Kramer N, Stead TG, et al. Serum Procalcitonin Level Is Associated with Positive Blood Cultures, In-hospital Mortality, and Septic Shock in Emergency Department Sepsis Patients. Cureus. 2020;12(4):78-82.
23. Schuetz P. How to best use procalcitonin to diagnose infections and manage antibiotic treatment. Clinical Chemistry and Laboratory Medicine. 2023;61(5):822-828.
24. Bilgin S, Kurtkulagi O, Atak Tel BM, et al. Does C-reactive protein to serum Albumin Ratio correlate with diabEtic nephropathy in patients with Type 2 dIabetes MEllitus? The CARE TIME study. Primary Care Diabetes. 2021;15(6):1071-1074.
25. Demirkol ME, Aktas G. C-reactive protein to LymphocytE count ratio could be a reliable mArkeR of thyroiditis; the CLEAR-T study. Precision Medical Sciences. 2022;11(1):31-34.
26. Aktas G. Serum C-Reactive Protein to Albumin Ratio as a Reliable Marker of Diabetic Neuropathy in Type 2 Diabetes Mellitus. Biomolecules and biomedicine. 2024.
27. Demirkol ME, Aktas G, Bilgin S, et al. C-reactive protein to lymphocyte count ratio is a promising novel marker in hepatitis C infection: the clear hep-c study. Revista da Associação Médica Brasileira. 2022;68(6):838-841.
28. Demirkol ME, Bilgin S, Kahveci G, et al. La proporcion de proteina C reactiva a linfocitoE es un marcador confiable en pacientes con infeccion por COVID-19; el estudio CLEAR COVID. Cirugia Y Cirujanos. 2022;90(5):596-601.
29. Karagoz I, Ozer B, Ital I, et al. C-reactive protein-to-serum albumin ratio as a marker of prognosis in adult intensive care population. Bratislava medical journal. 2023;124(4):277-279.
30. Li X, Yang Y, Zhang B, et al. Lactate metabolism in human health and disease. Signal Transduction and Targeted Therapy. 2022;7(1):305.
31. Park IH, Yang JH, Jang WJ, et al. Clinical significance of lactate clearance in patients with cardiogenic shock: results from the RESCUE registry. Journal of Intensive Care. 2021;9(1):63-66.
32. Kabra R, Acharya S, Kumar S. Serum lactate levels in critically Ill patients: An early marker to be targeted. Journal of the Scientific Society. 2022;49(3):246-250.
33. Muthukumar V, Arumugam PK, Narasimhan A, et al. Blood Lactate And Lactate Clearance: Refined Biomarker And Prognostic Marker In Burn Resuscitation. Annals of Burns Fire Disasters. 2020;33(4):293-298.
34. Larcher R, Besnard N, Akouz A, et al. Admission High-Sensitive Cardiac Troponin T Level Increase Is Independently Associated with Higher Mortality in Critically Ill Patients with COVID-19: A Multicenter Study. Journal of Clinical Medicine. 2021;10(8):12-20
35. Jayasimhan D, Foster S, Chang CL, et al. Cardiac biomarkers in acute respiratory distress syndrome: a systematic review and meta-analysis. Journal of Intensive Care. 2021;9(1):36-40
36. Van der Slikke EC, Star BS, de Jager VD, et al. A high urea-to-creatinine ratio predicts long-term mortality independent of acute kidney injury among patients hospitalized with an infection. Scientific Reports. 2020;10(1):149-156.
37. Li X, Zheng R, Zhang T, et al. Association between blood urea nitrogen and 30-day mortality in patients with sepsis: a retrospective analysis. Annals of Palliative Medicine. 2021;10(11):11653-11663.
38. Arnaldez FI, O'Day SJ, Drake CG, et al. The Society for Immunotherapy of Cancer perspective on regulation of interleukin-6 signaling in COVID-19-related systemic inflammatory response. Journal of Immunother Cancer. 2020;8(1):12-16
39. Yan Y, Hu Y, Wang X, et al. The predictive prognostic values

of serum interleukin-2, interleukin-6, interleukin-8, tumor necrosis factor-α, and procalcitonin in surgical intensive care unit patients. Annals of Translational Medicine. 2021;9(1):56-60
40.Dhar SK, K V, Damodar S, et al. IL-6 and IL-10 as predictors of disease severity in COVID-19 patients: results from meta-analysis and regression. Heliyon. 2021;7(2):55-61.
41. Battaglini D, Robba C, Fedele A, et al. The Role of Dysbiosis in Critically Ill Patients With COVID-19 and Acute Respiratory Distress Syndrome. Frontiers Medicine . 2021;8(1):671-714.
42.Guirao JJ, Cabrera CM, Jiménez N, et al. High serum IL-6 values increase the risk of mortality and the severity of pneumonia in patients diagnosed with COVID-19. Molecular Immunology. 2020;128:64-68.
43. Lavillegrand JR, Garnier M, Spaeth A, et al. Elevated plasma IL-6 and CRP levels are associated with adverse clinical outcomes and death in critically ill SARS-CoV-2 patients: inflammatory response of SARS-CoV-2 patients. Annals of Intensive Care. 2021;11(1):9-12.
44.McElvaney OJ, Curley GF, Rose-John S, et al. Interleukin-6: obstacles to targeting a complex cytokine in critical illness. Lancet Respirotory Medicine. 2021;9(6):643-654.
45. Cambier S, Gouwy M, Proost P. The chemokines CXCL8 and CXCL12: molecular and functional properties, role in disease and efforts towards pharmacological intervention. Cellular and Molecular Immunology. 2023;20(3):217-251.
46.Hu Q, Hao C, Tang S. From sepsis to acute respiratory distress syndrome (ARDS): emerging preventive strategies based on molecular and genetic researches. Bioscience Reports. 2020;40(5):1-9
47. Bülow Anderberg S, Luther T, Berglund M, et al. Increased levels of plasma cytokines and correlations to organ failure and 30-day mortality in critically ill Covid-19 patients. Cytokine. 2021;138:83-89.
48.Ishikawa S, Teshima Y, Otsubo H, et al. Risk prediction of biomarkers for early multiple organ dysfunction in critically ill patients. BioMed Central Emergency Medicine. 2021;21(1):132-142
49.Cutuli SL, Carelli S, Grieco DL, De Pascale G. Immune Modulation in Critically Ill Septic Patients. Medicina (Kaunas). 2021;57(6):552-563
50.Fatani SH, Alkhatib KH, Badr H, et al. Association of TNF-α-308 (G >A) (rs1800629) Gene Polymorphism with Adverse Outcomes of Sepsis in Critically Ill Patients. DNA and Cell Biology. 2020;39(9):1723-1729.
51. Ilias I, Vassiliou AG, Keskinidou C, et al. Changes in Cortisol Secretion and Corticosteroid Receptors in COVID-19 and Non COVID-19 Critically Ill Patients with Sepsis/Septic Shock and Scope for Treatment. Biomedicines. 2023;11(7):1801-1806
52. Gharamti AA, Samara O, Monzon A, et al. Proinflammatory cytokines levels in sepsis and healthy volunteers, and tumor necrosis factor-alpha associated sepsis mortality: A systematic review and meta-analysis. Cytokine. 2022;158:156-167.
53. Medina-Leyte DJ, Zepeda-García O, Domínguez-Pérez M, et al. Endothelial Dysfunction, Inflammation and Coronary Artery Disease: Potential Biomarkers and Promising Therapeutical Approaches. International Journal of Moleculer Sciences. 2021;22(8).
54. Yang YL, Wu CH, Hsu PF, et al. Systemic immune-inflammation index (SII) predicted clinical outcome in patients with coronary artery disease. European Journal of Clinical Investigation. 2020;50(5):132-140.
55. Fois AG, Paliogiannis P, Scano V, et al. The Systemic Inflammation Index on Admission Predicts In-Hospital Mortality in COVID-19 Patients. Molecules. 2020;25(23):5725-5736
56. Taslamacioglu Duman T, Ozkul FN, Balci B. Could Systemic Inflammatory Index Predict Diabetic Kidney Injury in Type 2 Diabetes Mellitus? Diagnostics (Basel). 2023;13(12):2063-2074
57. Tian M, Li Y, Wang X, et al. The Hemoglobin, Albumin, Lymphocyte, and Platelet (HALP) Score Is Associated With Poor Outcome of Acute Ischemic Stroke. Frontiers Neurology. 2020;11:610-618.
58. Antar R, Farag C, Xu V, et al. Evaluating the baseline hemoglobin, albumin, lymphocyte, and platelet (HALP) score in the United States adult population and comorbidities: an analysis of the NHANES. Frontiers in Nutrition. 2023;10:120-134.
59. Xu H, Zheng X, Ai J, Yang L. Hemoglobin, albumin, lymphocyte, and platelet (HALP) score and cancer prognosis: A systematic review and meta-analysis of 13,110 patients. International Immunopharmacology. 2023;114(1):1094-1099.
60.Manal M, Naglaa M, Kareem MF, et al. Anemia in Critically Ill Patients; Prevalence and Prognostic Implications. The Medical Journal of Cairo University. 2020;88(12):2121-2129.
61. Eckart A, Struja T, Kutz A, et al. Relationship of Nutritional Status, Inflammation, and Serum Albumin Levels During Acute Illness: A Prospective Study. The American Journal of Medicine. 2020;133(6):713-722.
62. Cai L, Zhou X, Wang M, et al. Predictive Nomogram for Severe COVID-19 and Identification of Mortality-Related Immune Features. The Journal of Allergy and Clinical Immunology in Practice. 2021;9(1):177-184.
63. Santoshi RK, Patel R, Patel NS, et al. A Comprehensive Review of Thrombocytopenia With a Spotlight on Intensive Care Patients. Cureus. 2022;14(8):27718-27729.

64. Amgalan A, Othman M. Hemostatic laboratory derangements in COVID-19 with a focus on platelet count. Platelets. 2020;31(6):740-745.
65. Aktas G, Khalid A, Kurtkulagi O, et al. Poorly controlled hypertension is associated with elevated serum uric acid to HDL-cholesterol ratio: a cross-sectional cohort study. Postgraduate Medicine. 2022;134(3):297-302.
66. Kosekli MA, Kurtkulagii O, Kahveci G, et al. The association between serum uric acid to high density lipoprotein-cholesterol ratio and non-alcoholic fatty liver disease: the abund study. Revista Associaçao Medica Brasileira (1992). 2021;67(4):549-554.
67. Aktas G, Kocak MZ, Bilgin S, et al. Uric acid to HDL cholesterol ratio is a strong predictor of diabetic control in men with type 2 diabetes mellitus. Aging Male. 2020;23(5):1098-1102.
68. Kurtkulagi O, Tel BMA, Kahveci G, et al. Hashimoto's thyroiditis is associated with elevated serum uric acid to high density lipoprotein-cholesterol ratio. Romanian Journal of Internal Medicine. 2021;59(4):403-408.
69. Kocak MZ, Aktas G, Erkus E, et al. Serum uric acid to HDL-cholesterol ratio is a strong predictor of metabolic syndrome in type 2 diabetes mellitus. Revista Associaçao Medica Brasileira (1992). 2019;65(1):9-15.
70. Aktas G, Yilmaz S, Kantarci DB, et al. Is serum uric acid-to-HDL cholesterol ratio elevation associated with diabetic kidney injury? Postgraduate Medicine. 2023;135(5):519-523.
71. Hu X, Liu J, Li W, et al. Elevated serum uric acid was associated with pre-inflammatory state and impacted the role of HDL-C on carotid atherosclerosis. Nutrition ,Metabolism and Cardiovasculer Diseases. 2022;32(7):1661-1669.
72. Montero-Chacón LB, Padilla-Cuadra JI, Chiou SH, et al. High-Density Lipoprotein, Mean Platelet Volume, and Uric Acid as Biomarkers for Outcomes in Patients With Sepsis: An Observational Study. Journal of Intensive Care Medicine. 2020;35(7):636-642.
73. Aktas G. Association between the Prognostic Nutritional Index and Chronic Microvascular Complications in Patients with Type 2 Diabetes Mellitus. Journal of Clinical Medicine. 2023;12(18):52-59
74. Sheinenzon A, Shehadeh M, Michelis R, et al. Serum albumin levels and inflammation. International Journal of Biological Macromolecules. 2021;184:857-862.
75. Noack M, Miossec P. Importance of lymphocyte-stromal cell interactions in autoimmune and inflammatory rheumatic diseases. Nature Reviews Rheumatology. 2021;17(9):550-564.
76. Wang Z, Zhao L, He S. Prognostic nutritional index and the risk of mortality in patients with hypertrophic cardiomyopathy. International Journal of Cardiology. 2021;331:152-157.
77. Mulazzani GEG, Corti F, Della Valle S, et al. Nutritional Support Indications in Gastroesophageal Cancer Patients: From Perioperative to Palliative Systemic Therapy. A Comprehensive Review of the Last Decade. Nutrients. 2021;13(8):2766-2777
78. Aktas G, Alcelik A, Tekce BK, et al. Red cell distribution width and mean platelet volume in patients with irritable bowel syndrome. Gastroenterology Review/Przegląd Gastroenterologiczny. 2014;9(3):160-163.
79. Aktas G, Sit M, Dikbas O, et al. Could red cell distribution width be a marker in Hashimoto's thyroiditis? Experimental and Clinical Endocrinology & Diabetes. 2014;122(10):572-574.
80. Cakır L, Aktas G, Mercimek OB, et al. Are red cell distribution width and mean platelet volume associated with rheumatoid arthritis. Biomedical Research. 2016;27(2):292-294.
81. Aktas G, Sit M, Karagoz I, et al. Could Red Cell Distribution Width be a Marker of Thyroid Cancer? Journal of College Physicians Surgeons Pakistan. 2017;27(9):556-558.
82. Duman TT, Aktas G, Atak B, et al. Is mean platelet volume to platelet ratio a promising indicator of diabetic regulation in type 2 diabetes mellitus. The Journal of Medical Research. 2018;4(3):137-139.
83. Kocak MZ, Aktas G, Erkus E, et al. Mean Platelet Volume to Lymphocyte Ratio as a Novel Marker for Diabetic Nephropathy. Journal of College Physicians Surgeons Pakistan. 2018;28(11):844-847.
84. Bilgin S, Tel BMA, Kahveci G, et al. Hypothyroidism is strongly correlated with mean platelet volume and red cell distribution width. National Journal of Health Sciences. 2021;6(1):7-10.
85. Aktas G, Sit M, Tekce H, et al. Mean platelet volume in nasal polyps. West Indian Medical Journal. 2013;62(6):515-518.
86. Karagoz I, Aktas G, Yoldas H, et al. Association Between Hemogram Parameters and Survival of Critically Ill Patients. Journal of Intensive Care Medicine. 2019;34(6):511-513.
87. Liberski PS, Szewczyk M, Krzych Ł J. Haemogram-Derived Indices for Screening and Prognostication in Critically Ill Septic Shock Patients: A Case-Control Study. Diagnostics (Basel). 2020;10(9):638-647
88. Velazquez S, Madurga R, Castellano JM, et al. Hemogram-derived ratios as prognostic markers of ICU admission in COVID-19. BioMed Central Emergency Medicine. 2021;21(1):1-9.