Correlation between Serum Biomarkers and Disease Severity in Critically Ill Patients: Predicting Outcomes in the ICU

Turki K. Ainosah[1], Sarah A. Alanazi[2], Khalaf F. Alanazi[3], Loai A. Alqahtany[4], Fatemah A. Alanazi[5]

Health Affairs at the Ministry of National Guard

Abstract

Objective: This study investigates the correlation between serum biomarkers and disease severity in critically ill patients, focusing on their predictive value for patient outcomes in an ICU setting.

Methods: A prospective cohort study was conducted with 120 critically ill patients admitted to a tertiary hospital ICU. Serum levels of biomarkers including lactate, interleukin-6 (IL-6), C-reactive protein (CRP), procalcitonin, and D-dimer were measured at admission. Correlations with APACHE II and SOFA scores were analyzed, and predictive values for ICU mortality and length of stay were assessed.

Results: Elevated lactate and IL-6 levels showed strong correlations with higher APACHE II ($r = 0.71$, $r = 0.62$) and SOFA scores ($r = 0.68$, $r = 0.59$), and were significant predictors of ICU mortality (lactate OR = 2.25, $p < 0.001$; IL-6 OR = 1.85, $p = 0.02$). CRP, procalcitonin, and D-dimer also correlated with disease severity, but less robustly.

Conclusions: Lactate and IL-6 are valuable biomarkers for assessing disease severity and predicting outcomes in critically ill patients. Their integration into clinical practice can enhance risk stratification and guide therapeutic decisions in the ICU.

Keywords: Serum biomarkers, lactate, interleukin-6, disease severity, ICU outcomes, predictive value, critically ill patients.

Introduction

In the intensive care unit (ICU), critically ill patients often require continuous monitoring to assess disease progression and guide therapeutic interventions. Serum biomarkers, measurable indicators of biological processes, have become invaluable tools for predicting disease severity and patient outcomes in these settings (Pierrakos& Vincent, 2010). These biomarkers provide real-time information on the physiological state of patients and can signal the onset of complications, such as sepsis, acute respiratory distress syndrome (ARDS), or multi-organ failure (Kellum et al., 2016).

Several serum biomarkers, such as C-reactive protein (CRP), procalcitonin, lactate, and interleukin-6 (IL-6), have been widely studied for their ability to predict disease severity in critically ill patients. For example, elevated levels of procalcitonin are commonly associated with bacterial infections and sepsis, and its levels often correlate with the severity of infection (Teggert et al., 2020). Similarly, lactate has been shown to be a

reliable indicator of tissue hypoxia and is frequently used to assess the likelihood of organ failure and mortality (Suetrong& Walley, 2016). Despite the growing use of these biomarkers, their predictive value and correlation with patient outcomes remain areas of ongoing research, particularly regarding which biomarkers are the most reliable indicators of disease progression in the ICU.

The ability to predict outcomes using serum biomarkers would enable clinicians to identify high-risk patients earlier, optimize treatment strategies, and potentially improve survival rates. However, there is a need for more comprehensive studies that examine the correlation between specific biomarkers and clinical outcomes in a diverse range of critically ill patients. This study aims to explore the relationship between commonly used serum biomarkers and disease severity in ICU patients, with the goal of assessing their predictive value for patient outcomes, including recovery, complications, or mortality.

Research Questions
1. Which serum biomarkers are most strongly correlated with disease severity in critically ill patients?
2. How accurately can these biomarkers predict patient outcomes in the ICU?
3. Are there specific patterns in biomarker levels that indicate disease progression or worsening in ICU patients?

Literature Review

1. Importance of Biomarkers in Critical Care

Serum biomarkers have become an essential component of critical care medicine, providing valuable insight into the physiological processes occurring in critically ill patients. Biomarkers are measurable substances in the blood that reflect normal or pathological processes and can be used to monitor disease progression, predict outcomes, and guide treatment decisions (Marshall et al., 2009). In the ICU, where rapid and accurate decision-making is vital, biomarkers offer clinicians a non-invasive means of evaluating patient status and adjusting interventions accordingly (Pierrakos& Vincent, 2010).

2. Commonly Studied Biomarkers in Critical Care

Several biomarkers have been extensively studied for their correlation with disease severity and patient outcomes in critical care settings. Among the most widely researched are C-reactive protein (CRP), procalcitonin, lactate, and interleukin-6 (IL-6), all of which are associated with inflammation, infection, and organ dysfunction in critically ill patients.

-C-Reactive Protein (CRP): CRP is an acute-phase protein produced by the liver in response to inflammation. Elevated CRP levels have been found to correlate with systemic inflammation, sepsis, and multi-organ failure (Pepys & Hirschfield, 2003). Studies have demonstrated that higher CRP levels are associated with poorer outcomes, including increased mortality, in ICU patients (Zhang and Ni, 2011).

-Procalcitonin: Procalcitonin is another important biomarker used in critical care, particularly for the diagnosis and monitoring of bacterial infections and sepsis. Procalcitonin levels rise significantly in response to systemic bacterial infections, making it a reliable indicator of infection severity (Lindstrom and Wong, 2014). Studies have shown that procalcitonin-guided therapy can help reduce unnecessary antibiotic use while accurately predicting sepsis-related outcomes (Teggert et al., 2020).

-Lactate: Lactate is a byproduct of anaerobic metabolism and is commonly used as an indicator of tissue hypoxia and shock in critically ill patients. Elevated lactate levels are strongly correlated with increased

mortality in ICU patients, particularly those with sepsis or shock (Suetrong& Walley, 2016). Lactate clearance, or the reduction of lactate levels over time, has also been used as a prognostic tool to assess the effectiveness of therapeutic interventions and predict patient outcomes (Jansen et al., 2009).

-Interleukin-6 (IL-6): IL-6 is a pro-inflammatory cytokine that plays a key role in the immune response to infection and injury. Elevated IL-6 levels are associated with sepsis, systemic inflammation, and multi-organ failure, and have been linked to worse outcomes in critically ill patients (van der Poll et al., 2017). IL-6 levels are also predictive of the severity of conditions such as acute respiratory distress syndrome (ARDS) and sepsis, making it a valuable biomarker in the ICU (Kellum et al., 2016).

3. Biomarkers and Disease Severity

The correlation between serum biomarker levels and disease severity has been a focus of several studies in critical care medicine. Research has shown that biomarkers such as CRP, procalcitonin, and lactate are reliable indicators of disease severity in conditions such as sepsis, ARDS, and multi-organ failure. For example, higher lactate levels are associated with more severe organ dysfunction and an increased risk of mortality (Suetrong& Walley, 2016). Similarly, elevated procalcitonin levels have been correlated with the severity of bacterial infections and sepsis, providing clinicians with a tool to assess the progression of the disease and the need for aggressive interventions (Lindstrom and Wong, 2014).

Moreover, combining multiple biomarkers to create a “biomarker panel” has been suggested as a more effective strategy for predicting disease severity and outcomes. Studies have indicated that combining markers such as CRP, IL-6, and lactate can improve the accuracy of predictions regarding patient outcomes, particularly in complex cases like sepsis or multi-organ failure (Jansen et al., 2009).

4. Predictive Value of Biomarkers for Patient Outcomes

Biomarkers not only provide insight into disease severity but also have significant predictive value for patient outcomes. Numerous studies have highlighted the role of biomarkers in predicting mortality, the likelihood of recovery, and the risk of complications in critically ill patients.

-Prognostic Value of Lactate: Elevated lactate levels have long been associated with poor outcomes in critically ill patients. Several studies have demonstrated that high lactate levels on ICU admission are predictive of increased mortality, particularly in patients with sepsis or septic shock (Casserly et al., 2015). Furthermore, lactate clearance has been shown to be a valuable indicator of treatment response, with higher lactate clearance rates associated with better outcomes (Jansen et al., 2009).

-Procalcitonin in Sepsis: Procalcitonin has emerged as a key biomarker for predicting outcomes in sepsis. Elevated procalcitonin levels have been associated with worse outcomes, including higher mortality rates, in septic patients (Teggert et al., 2020). Studies suggest that serial measurements of procalcitonin can be used to guide therapy and predict the risk of complications or treatment failure.

-CRP as a Marker of Recovery: CRP is frequently used to monitor the inflammatory response in critically ill patients. Decreasing CRP levels over time have been associated with patient recovery, while persistently elevated levels may indicate ongoing infection or complications (Pepys & Hirschfield, 2003). Studies have shown that CRP dynamics can be used to assess the effectiveness of treatments and predict long-term outcomes (Zhang and Ni, 2011).

5. Gaps in Research

While the role of biomarkers in predicting disease severity and outcomes in critically ill patients has been well-established, there are several gaps in the literature. One area that requires further research is the use of biomarker panels to improve the accuracy of outcome predictions. Although individual biomarkers such as lactate and procalcitonin have shown promise, combining multiple biomarkers may offer a more comprehensive approach to predicting patient outcomes. Additionally, more studies are needed to explore the role of emerging biomarkers and how they can be integrated into clinical practice to improve patient care.

Serum biomarkers play a critical role in assessing disease severity and predicting patient outcomes in the ICU. Biomarkers such as CRP, procalcitonin, lactate, and IL-6 have proven to be valuable tools for monitoring critically ill patients, guiding therapeutic interventions, and predicting recovery or mortality. However, further research is needed to explore the full potential of biomarker panels and emerging biomarkers in improving the accuracy of outcome predictions in the ICU.

Methodology

This prospective observational study was conducted in the intensive care unit (ICU) of a large tertiary hospital to assess the correlation between serum biomarkers and disease severity in critically ill patients. The study aimed to determine how specific biomarkers could predict patient outcomes and the progression of critical illnesses, such as sepsis, acute respiratory distress syndrome (ARDS), and multi-organ failure.

Study Design

A prospective observational design was employed to explore the relationship between serum biomarkers and disease severity in ICU patients. Patients were followed from the time of ICU admission until discharge or death, and serum biomarkers were measured at various points throughout their ICU stay. The study spanned six months, from January to June 2022.

Participants

A total of 120 critically ill patients were recruited for the study based on the following inclusion and exclusion criteria:

-Inclusion Criteria:

- Adult patients (≥ 18 years) admitted to the ICU with a diagnosis of sepsis, ARDS, or multi-organ failure.
- Patients expected to stay in the ICU for at least 48 hours.
- Patients for whom informed consent was obtained from themselves or their legal representatives.

-Exclusion Criteria:

- Patients with a do-not-resuscitate (DNR) order.
- Patients with terminal illnesses with a life expectancy of less than 48 hours.
- Patients with known chronic conditions that could significantly alter baseline biomarker levels (e.g., chronic liver disease, end-stage renal disease).

The study sample was diverse, consisting of patients of different age groups, gender, and clinical conditions, providing a broad view of critically ill patient populations. The sample size of 120 patients was determined to achieve adequate statistical power for correlation analyses between serum biomarkers and clinical outcomes.

Biomarkers Measured

The following serum biomarkers were selected based on their relevance to critical illness and their use in previous studies:

-C-Reactive Protein (CRP): To assess inflammation.
-Procalcitonin: To detect bacterial infections and sepsis.
-Lactate: To measure tissue hypoxia and metabolic acidosis.
-Interleukin-6 (IL-6): To monitor systemic inflammation and immune response.
-D-dimer: To assess coagulopathy and thrombotic risk.

Blood samples were collected at baseline (within 24 hours of ICU admission) and at specified intervals (Day 3, Day 5, and Day 7) or until patient discharge or death. Samples were analyzed in the hospital's laboratory using standardized methods to ensure accuracy and consistency in biomarker measurement.

Data Collection

In addition to serum biomarker measurements, clinical data were collected to assess disease severity and patient outcomes. The following data points were recorded for each patient:

-Demographic Information: Age, gender, pre-existing medical conditions.
-Clinical Data: Vital signs, diagnosis, type of critical illness (e.g., sepsis, ARDS), comorbidities, and interventions (e.g., mechanical ventilation, vasopressors).
-Disease Severity Scores: The Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA) scores were calculated at ICU admission and throughout the patient's stay to quantify disease severity.
-Patient Outcomes: Length of ICU stay, complications (e.g., secondary infections, organ failure), and mortality rates.

Outcome Measures

The primary outcomes of the study were the correlation between serum biomarker levels and disease severity, as measured by APACHE II and SOFA scores, and the prediction of patient outcomes, including ICU length of stay, complications, and mortality.

The secondary outcome was to assess the predictive value of specific biomarkers for disease progression, such as whether trends in biomarkers (e.g., rising or declining levels) over time were associated with clinical deterioration or recovery.

Statistical Analysis

Data analysis was conducted using SPSS software, version 25.0. The following statistical methods were employed:

-Descriptive Statistics: Mean and standard deviation (SD) for continuous variables (e.g., age, biomarker levels) and frequencies and percentages for categorical variables (e.g., gender, diagnosis).
-Correlation Analysis: Pearson's or Spearman's correlation coefficients were calculated to assess the relationship between biomarker levels and disease severity scores (APACHE II and SOFA) and patient outcomes.

-Regression Analysis: Multivariate logistic regression was used to identify independent predictors of mortality, ICU length of stay, and complications, with biomarker levels as covariates.
-Survival Analysis: Kaplan-Meier survival curves were generated to evaluate the association between serum biomarker levels and mortality. Log-rank tests were used to compare survival outcomes between groups with different biomarker levels.

Ethical Considerations
The study was approved by the ethics committee. Informed consent was obtained from each patient or their legal representatives prior to inclusion in the study. To ensure patient confidentiality, all personal and clinical data were de-identified and stored securely. Only authorized members of the research team had access to patient records and biomarker data.

Limitations
While the study provides valuable insights into the correlation between serum biomarkers and disease severity, several limitations should be noted. First, the study was conducted in a single tertiary hospital, which may limit the generalizability of the findings to other settings. Additionally, biomarker levels were measured at predetermined intervals, which may not fully capture rapid changes in critically ill patients. Future studies could benefit from larger, multi-center samples and more frequent biomarker monitoring to account for dynamic changes in critically ill patients.

Findings

1. Patient Demographics and Clinical Characteristics
A total of 120 critically ill patients were included in the study. The mean age of the participants was 62 ±15 years, and 55% of the patients were male. The most common diagnoses were sepsis (45%), acute respiratory distress syndrome (ARDS) (30%), and multi-organ failure (25%). The average APACHE II score at admission was 23.8 ±6.5, and the average SOFA score was 9.5 ±3.4.

Table 1. Patient Demographics and Clinical Characteristics

Characteristic	Value
Number of patients	120
Age (mean ±SD)	62 ±15 years
Gender (Male/Female)	66 (55%) / 54 (45%)
Common Diagnoses	Sepsis (45%), ARDS (30%), Multi-organ failure (25%)
APACHE II score (mean ±SD)	23.8 ±6.5
SOFA score (mean ±SD)	9.5 ±3.4
ICU Mortality	32%
ICU Length of Stay (mean)	14 ±7 days

2. Biomarker Levels and Disease Severity
The serum biomarker levels measured at admission (Day 1) showed a strong correlation with disease severity scores (APACHE II and SOFA scores). Lactate and IL-6 were the most strongly correlated with higher severity scores, while CRP and procalcitonin also demonstrated significant correlations.

Table 2. Correlation Between Biomarker Levels and Disease Severity

Biomarker	Mean Level (±SD)	APACHE II Correlation (r)	SOFA Correlation (r)
C-Reactive Protein (CRP)	160 ±40 mg/L	0.45 ($p < 0.001$)	0.43 ($p < 0.001$)
Procalcitonin	8.5 ±4.2 ng/mL	0.52 ($p < 0.001$)	0.49 ($p < 0.001$)
Lactate	4.1 ±1.9 mmol/L	0.71 ($p < 0.001$)	0.68 ($p < 0.001$)
Interleukin-6 (IL-6)	100 ±45 pg/mL	0.62 ($p < 0.001$)	0.59 ($p < 0.001$)
D-dimer	3.4 ±1.8 mg/L	0.39 ($p < 0.05$)	0.41 ($p < 0.05$)

The results show that lactate had the strongest correlation with both the APACHE II score ($r = 0.71$) and the SOFA score ($r = 0.68$), indicating that higher lactate levels were associated with more severe disease. IL-6 and procalcitonin also showed moderate-to-strong correlations, suggesting their usefulness in assessing disease severity in critically ill patients.

3. Biomarkers and Patient Outcomes

Biomarker levels at admission were also analyzed to predict patient outcomes, including ICU length of stay, complications, and mortality. Elevated lactate and IL-6 levels were significantly associated with higher mortality rates and longer ICU stays.

Table 3. Biomarker Levels and Patient Outcomes

Biomarker	Survivors (Mean ± SD)	Non-survivors (Mean ±SD)	p-value
C-Reactive Protein (CRP)	135 ±35 mg/L	175 ±45 mg/L	0.04
Procalcitonin	7.2 ±3.8 ng/mL	10.1 ±4.9 ng/mL	0.03
Lactate	3.5 ±1.5 mmol/L	5.2 ±2.1 mmol/L	<0.001
Interleukin-6 (IL-6)	82 ±35 pg/mL	120 ±50 pg/mL	0.02
D-dimer	2.8 ±1.5 mg/L	4.2 ±2.0 mg/L	0.04

Non-survivors had significantly higher levels of lactate (5.2 ±2.1 mmol/L) compared to survivors (3.5 ±1.5 mmol/L, $p < 0.001$), as well as elevated IL-6 levels (120 ±50 pg/mL in non-survivors vs. 82 ±35 pg/mL in survivors, $p = 0.02$). CRP, procalcitonin, and D-dimer also showed significant differences between survivors and non-survivors, although the correlations were weaker compared to lactate and IL-6.

4. Predictive Value of Biomarkers

Multivariate logistic regression analysis was conducted to assess the predictive value of serum biomarkers for ICU mortality. After adjusting for confounding factors (e.g., age, gender, comorbidities), lactate and IL-6 remained significant independent predictors of mortality.

Table 4. Multivariate Logistic Regression for Predicting ICU Mortality

Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Lactate	2.25	1.45 - 3.56	<0.001
Interleukin-6 (IL-6)	1.85	1.10 - 3.12	0.02

C-Reactive Protein (CRP)	1.30	0.88 - 1.92	0.07
Procalcitonin	1.15	0.75 - 1.72	0.09
D-dimer	1.12	0.76 - 1.78	0.11

Lactate was the strongest predictor of mortality, with an odds ratio (OR) of 2.25 ($p < 0.001$), indicating that for each 1 mmol/L increase in lactate, the odds of mortality more than doubled. IL-6 was also a significant predictor (OR 1.85, $p = 0.02$), further supporting its role in predicting patient outcomes in the ICU.

5. Lactate Clearance and Recovery

In addition to absolute biomarker levels, lactate clearance (the rate at which lactate levels decrease over time) was analyzed as a potential predictor of recovery. Patients who survived had a higher lactate clearance rate over the first 48 hours of ICU admission compared to non-survivors.

Table 5. Lactate Clearance and Outcomes

Outcome	Lactate Clearance (%)	p-value
Survivors	35 ±12%	<0.001
Non-survivors	18 ±9%	

Patients who survived demonstrated significantly higher lactate clearance (35 ±12%) compared to non-survivors (18 ±9%, $p < 0.001$). This finding suggests that early lactate clearance may be a useful marker for predicting recovery in critically ill patients.

Summary of Findings

- Lactate and IL-6 levels were the strongest predictors of disease severity and patient outcomes in ICU patients, with high levels associated with worse outcomes and increased mortality.
- CRP, procalcitonin, and D-dimer were also significantly correlated with disease severity but had weaker predictive value compared to lactate and IL-6.
- Lactate clearance was a valuable marker for assessing the likelihood of recovery, with higher clearance rates associated with better outcomes.

Discussion

This study explored the correlation between serum biomarkers and disease severity in critically ill patients, focusing on their predictive value for patient outcomes, including ICU length of stay, complications, and mortality. The results demonstrate that specific biomarkers, particularly lactate and interleukin-6 (IL-6), have a strong association with disease severity and can serve as valuable tools for predicting clinical outcomes in the ICU.

Lactate as a Predictor of Disease Severity and Mortality

Lactate emerged as the strongest predictor of both disease severity and mortality in critically ill patients. The significant correlations between lactate levels and APACHE II ($r = 0.71$) and SOFA scores ($r = 0.68$) highlight its role in assessing the extent of organ dysfunction and metabolic distress. This is consistent with previous studies, which have established lactate as a reliable indicator of tissue hypoxia, shock, and poor perfusion (Casserly et al., 2015; Suetrong& Walley, 2016). The elevated lactate levels observed in non-survivors further reinforce its prognostic value, as critically ill patients with persistently high lactate levels had significantly worse outcomes.

The finding that lactate clearance was significantly higher in survivors compared to non-survivors (35% vs. 18%, $p < 0.001$) is particularly noteworthy. Early lactate clearance has been shown to predict improved outcomes, as it reflects the body's ability to restore normal tissue perfusion and resolve metabolic acidosis (Jansen et al., 2009). This study supports the use of lactate clearance as a dynamic marker for monitoring patient recovery, suggesting that it could be used to guide therapeutic interventions aimed at improving patient outcomes.

Interleukin-6 (IL-6) and Systemic Inflammation

IL-6, a pro-inflammatory cytokine, was also identified as a strong predictor of disease severity and mortality. Elevated IL-6 levels were associated with higher APACHE II and SOFA scores, as well as increased mortality, in critically ill patients. These findings align with previous studies that have shown IL-6 to be a key mediator of systemic inflammation, particularly in conditions such as sepsis and ARDS, where it contributes to immune dysregulation and multi-organ failure (van der Poll et al., 2017).

Given its strong correlation with both disease severity and outcomes, IL-6 may be a useful biomarker for identifying high-risk patients early in the course of their ICU stay. Monitoring IL-6 levels could help clinicians identify patients who are at greater risk of complications, allowing for timely and targeted interventions. The role of IL-6 in the pathogenesis of critical illness also makes it a potential therapeutic target, as reducing IL-6 levels through anti-inflammatory treatments may improve patient outcomes.

Other Biomarkers: CRP, Procalcitonin, and D-dimer

While lactate and IL-6 were the strongest predictors in this study, other biomarkers, including CRP, procalcitonin, and D-dimer, also demonstrated significant correlations with disease severity and patient outcomes, although to a lesser extent. Elevated CRP levels were associated with higher APACHE II and SOFA scores, indicating its role as a marker of systemic inflammation. Procalcitonin, commonly used as a diagnostic tool for bacterial infections, was significantly higher in non-survivors and patients with sepsis, supporting its use in assessing infection severity and guiding antibiotic therapy (Lindstrom and Wong, 2014).

D-dimer, an indicator of coagulation and thrombotic activity, was also elevated in non-survivors, suggesting a link between coagulopathy and poor outcomes. However, its correlation with disease severity was weaker compared to lactate and IL-6. This finding suggests that while D-dimer is useful for assessing thrombotic risk, it may not be as robust a predictor of overall disease progression in critically ill patients.

Clinical Implications

The findings of this study have several important implications for clinical practice in the ICU. First, the strong predictive value of lactate and IL-6 highlights the potential for these biomarkers to guide early clinical decision-making and risk stratification. Lactate clearance, in particular, could be used as a marker of treatment response, allowing clinicians to adjust therapeutic strategies based on the patient's recovery trajectory.

Second, the combination of multiple biomarkers may offer greater predictive accuracy than relying on a single biomarker. Although lactate and IL-6 were the most reliable predictors in this study, integrating other biomarkers such as CRP, procalcitonin, and D-dimer could improve the overall assessment of disease severity and outcomes. The development of biomarker panels or scoring systems that incorporate several markers may help improve early detection of high-risk patients and enhance personalized care.

Strengths and Limitations

This study's strengths include its prospective design and comprehensive analysis of multiple biomarkers in a large cohort of critically ill patients. By measuring biomarkers at different time points during the ICU stay, the study captured dynamic changes in biomarker levels, providing valuable insights into their role in predicting disease progression.

However, several limitations should be noted. The study was conducted in a single tertiary hospital, which may limit the generalizability of the findings to other healthcare settings. Additionally, while the study identified correlations between biomarkers and outcomes, it did not explore causal relationships. Future research should focus on longitudinal studies with larger, multi-center populations to confirm these findings and assess the impact of interventions targeting biomarker modulation on patient outcomes.

Future Directions

Further research is needed to investigate the utility of emerging biomarkers in critical care, as well as the potential for combining biomarkers into predictive models. Additionally, studies exploring the use of biomarker-guided therapies, such as interventions aimed at reducing lactate or IL-6 levels, could provide new approaches to improving outcomes in critically ill patients.

Conclusion

In conclusion, this study demonstrates that serum biomarkers, particularly lactate and IL-6, are valuable predictors of disease severity and patient outcomes in the ICU. These biomarkers can help clinicians identify high-risk patients early, guide therapeutic interventions, and improve decision-making in critical care. Incorporating biomarkers into clinical practice offers the potential for more personalized and effective patient management, ultimately improving outcomes for critically ill patients.

References

1. Casserly, B., Phillips, G. S., Schorr, C., Dellinger, R. P., Townsend, S. R., Osborn, T. M., ... & Levy, M. M. (2015). Lactate measurements in sepsis-induced tissue hypoperfusion: results from the Surviving Sepsis Campaign database. *Critical care medicine*, *43*(3), 567-573.
2. Jansen, T. C., van Bommel, J., & Bakker, J. (2009). Blood lactate monitoring in critically ill patients: a systematic health technology assessment. *Critical care medicine*, *37*(10), 2827-2839.
3. Kellum, J. A., Chawla, L. S., Keener, C., Singbartl, K., Palevsky, P. M., Pike, F. L., ... & Angus, D. C. (2016). The effects of alternative resuscitation strategies on acute kidney injury in patients with septic shock. *American journal of respiratory and critical care medicine*, *193*(3), 281-287.
4. Marshall, J. C., & Reinhart, K. (2009). Biomarkers of sepsis. *Critical care medicine*, *37*(7), 2290-2298.
5. Lindstrom, S. T., & Wong, E. K. C. (2014). Procalcitonin, a valuable biomarker assisting clinical decision-making in the management of community-acquired pneumonia. *Internal medicine journal*, *44*(4), 390-397.
6. Pepys, M. B., & Hirschfield, G. M. (2003). C-reactive protein: a critical update. *The Journal of clinical investigation*, *111*(12), 1805-1812.
7. Pierrakos, C., & Vincent, J. L. (2010). Sepsis biomarkers: a review. *Critical care*, *14*, 1-18.
8. Suetrong, B., & Walley, K. R. (2016). Lactic acidosis in sepsis: it's not all anaerobic: implications for diagnosis and management. *Chest*, *149*(1), 252-261.
9. Teggert, A., Datta, H., & Ali, Z. (2020). Biomarkers for point-of-care diagnosis of sepsis. *Micromachines*, *11*(3), 286.

10. van der Poll, T., van de Veerdonk, F. L., Scicluna, B. P., &Netea, M. G. (2017). The immunopathology of sepsis and potential therapeutic targets. *Nature Reviews Immunology*, *17*(7), 407-420.
11. Zhang, Z., & Ni, H. (2011). C-reactive protein as a predictor of mortality in critically ill patients: a meta-analysis and systematic review. *Anaesthesia and intensive care*, *39*(5), 854-861.