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MID-REGIONAL PRO-ADRENOMEDULLIN (MR-proADM) AS A DIAGNOSTIC AND PROGNOSTIC BIOMARKER IN EARLY SEPSIS: A NARRATIVE REVIEW

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ABSTRACT

Sepsis is a critical medical condition resulting from an inappropriate host response to infection, often leading to organ dysfunction and high mortality. Early diagnosis remains a significant clinical challenge due to the nonspecific nature of initial symptoms and the limited efficacy of conventional biomarkers. Commonly used markers, such as C-reactive protein (CRP) and procalcitonin (PCT), provide useful information on inflammation and bacterial infections but do not adequately reflect vascular dysfunction or predict clinical deterioration.

Mid-regional proadrenomedullin (MR-proADM) has recently gained importance as a biomarker reflecting both inflammatory processes and impaired vascular integrity. As a stable fragment of proadrenomedullin, it indirectly represents the activity of adrenomedullin, a peptide involved in maintaining endothelial function and circulatory homeostasis. Evidence from observational studies indicates that MR-proADM levels increase early in the course of infection and correlate with disease progression, organ failure, and risk of death.

Compared to traditional biomarkers, MR-proADM appears to offer better prognostic performance, particularly in identifying patients at risk of severe complications. Its association with endothelial damage and microcirculatory dysfunction makes it particularly relevant to the pathophysiology of sepsis.

In summary, MR-proADM may be a valuable complement to existing diagnostic tools, aiding early risk stratification and clinical decision-making. Further studies are needed to standardize its use and confirm its role in routine practice.

KEYWORDS

Sepsis, MR-proADM, Proadrenomedullin, Biomarkers, Endothelial Dysfunction, Procalcitonin, C-reactive Protein, Prognosis, Intensive Care, Emergency Medicine

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1. Introduction

Sepsis is a life-threatening condition characterized by a disturbed organism response to infection. This finally leads to acute multi-organ dysfunction. Despite significant advances in medicine, especially intensive care, sepsis remains one of the leading causes of death among hospitalized patients worldwide. The clinical presentation of sepsis is largely nonspecific, especially in the initial stages of the disease. This often leads to delays in diagnosis, which also leads to delays in initiating appropriate treatment. This is strongly associated with the patient's subsequent prognosis, so early clinical recognition of sepsis is a key prognostic factor – the sooner appropriate treatment is initiated, the greater the chance for complete recovery.

Currently, traditional diagnostic methods rely on the observation of clinical symptoms and standard laboratory parameters of inflammation, such as CRP and procalcitonin. Unfortunately, these parameters lack sufficient sensitivity and specificity to enable diagnosis of the disease in its very early course of disease. Therefore, there is growing interest in the use of circulating biomarkers, which provide more accurate and much faster information regarding disease severity, progression, and prognosis. Among the commonly used biomarkers, C-reactive protein (CRP) and procalcitonin (PCT) remain the primary parameters used in clinical practice to assess the risk of sepsis. CRP is a widely available and sensitive, yet nonspecific, inflammatory biomarker that increases relatively slowly – CRP levels in the blood begin to rise after approximately 6 hours, and peak concentrations are not reached until more than 36 hours later. This indicates that CRP, despite its usefulness, does not enable the beginning of sepsis. Procalcitonin has a higher specificity for bacterial infections and its concentration changes are more dynamic than CRP, but it does not reliably reflect endothelial injury, tissue hypoperfusion or the degree of multiple organ failure.

In recent years, mid-regional proadrenomedullin (MR-proADM) has emerged as a clinical relevant biomarker in the context of sepsis. MR-proADM is a stable fragment of the proadrenomedullin precursor molecule, from which the biologically active peptide adrenomedullin is derived.

Adrenomedullin plays a crucial role in the regulation of vascular tone, endothelial barrier function, and modulation of inflammatory responses. However, due to its extremely short half-life and instability in plasma, direct measurement of adrenomedullin is not clinically meaningful. Instead, MR-proADM is used as a surrogate marker reflecting the activity of the adrenomedullin system. Importantly, MR-proADM demonstrates high stability in the circulation, making it suitable for routine laboratory assessment. Its concentration increases in response to infection and inflammation, particularly in conditions associated with endothelial impairment and hemodynamic instability. This biological profile suggests that MR-proADM may provide complementary information to conventional biomarkers by integrating both inflammatory and vascular pathophysiological pathways.

Accumulating evidence indicates that MR-proADM is not only a diagnostic biomarker but also a strong predictor of poor prognosis in patients with sepsis. Its ability to mirror hemodynamic instability and microcirculatory disturbance may explain its improved prognostic performance compared with traditional inflammatory markers.

2. Methodology

This study is a narrative review with elements of a structured and systematic literature search. The aim of our study is to assess the diagnostic and prognostic value of the MR-proADM biomarker in patients with suspected or confirmed sepsis. The criteria include early disease identification and risk assessment.

2.1 Literature Search Strategy

Publicly available databases of scientific publications from the platforms listed below were searched:

- PubMed
- Scopus
- Web of Science

The search covered publications from 2000 to December 2025. Keywords used in various combinations included: “MR-proADM”, “mid-regional proadrenomedullin”, “sepsis”, “biomarkers”, “prognosis”, “endothelial dysfunction”, “procalcitonin”, and “C-reactive protein”.

Additionally, the reference lists of all included studies were searched to identify other relevant publications that were not included in the original search..

2.2 Inclusion and Exclusion Criteria

Studies were included if they:

- involved adult patients (≥ 18 years),
 - focused on suspected or confirmed sepsis,
 - evaluated MR-proADM as a diagnostic or prognostic biomarker,
 - compared MR-proADM with other biomarkers or clinical scoring systems,
 - were original research articles or peer-reviewed reviews.
- Studies were excluded if they:
- were not published in English,
 - were case reports, editorials, letters, or commentaries,
 - lacked full-text availability,
 - did not report clinically relevant outcomes,
 - focused exclusively on pediatric populations.

2.3 Study Selection and Data Extraction

A total of several dozen studies meeting the inclusion criteria were identified and analyzed. The majority of these studies were prospective or retrospective observational studies conducted in intensive care units (ICUs) and emergency departments (EDs).

Data extracted from each study included:

- study design,
- patient population,
- diagnostic and prognostic performance of MR-proADM,
- comparison with other biomarkers (CRP, PCT, IL-6),
- association with clinical outcomes such as mortality, organ failure, and ICU admission.

2.4 Study Populations

Across the included literature, patient populations were heterogeneous and included:

- patients with suspected sepsis in emergency settings,
- patients with confirmed sepsis or septic shock,
- critically ill patients admitted to intensive care units,
- patients with varying infectious etiologies, including pneumonia and bloodstream infections.

2.5 Biomarkers and Clinical Parameters Assessed

In most studies, MR-proADM was evaluated alongside established inflammatory and prognostic markers, including:

- C-reactive protein (CRP),
- procalcitonin (PCT),
- interleukin-6 (IL-6),
- lactate,
- clinical scoring systems such as SOFA (Sequential Organ Failure Assessment) and APACHE II.

Table 1. Characteristics of Included Studies (Summary Overview)

Study Type	Setting	Population	Main Focus
Prospective observational	ICU	Septic and septic shock patients	Prognostic value of MR-proADM
Retrospective cohort	ED	Suspected infection patients	Early diagnosis and risk stratification
Multicenter studies	ICU/ED	Heterogeneous sepsis populations	Comparison with CRP and PCT
Systematic reviews	Clinical research databases	Mixed adult populations	Overall biomarker performance

2.6 Methodological Considerations

Due to the observational nature of most included studies, heterogeneity in study design, patient selection, and biomarker measurement techniques was significant. This variability limits direct comparability of results but allows for a broader synthesis of existing evidence regarding the clinical utility of MR-proADM.

3. Results

A review of the scientific literature largely demonstrates that mid-regional pro-adrenomedullin (MR-proADM) is a highly valuable biomarker in the context of early sepsis, particularly for early risk stratification and the assessment of disease severity. The findings can be grouped into four main thematic areas: (1) early diagnostic performance, (2) association with disease severity, (3) prognostic value, and (4) comparison with established biomarkers.

3.1 Early Diagnostic Performance of MR-proADM

Many reviewed studies have indicated that MR-proADM levels increase early in the development of sepsis, often significantly preceding significant increases in commonly used inflammatory biomarkers such as CRP. This early increase appears to be closely related to endothelial activation, microcirculatory disturbances, and the systemic inflammatory response.

Unlike CRP, which typically exhibits delayed kinetics, MR-proADM demonstrates a more rapid response to physiological stress, making it a potentially valuable biomarker for the early detection of patients at risk of sepsis progression.

Importantly, elevated MR-proADM levels have been observed not only in confirmed cases of sepsis but also in patients presenting to the emergency department with suspected infection, which also significantly impacts its usefulness in early triage.

3.2 Association with Disease Severity

Various studies have observed correlations between MR-proADM levels and the severity of sepsis. Elevated levels of the biomarker have been observed in patients with conditions such as:

- septic shock
- multi-organ dysfunction syndrome (MODS)
- severe hemodynamic instability
- requirement for vasopressor support
- admission to intensive care units

This specific correlation significantly indicates that MR-proADM presents not only inflammatory activation but also the degree of endothelial instability and circulatory failure.

Elevated MR-proADM levels are correlated with worsening clinical status. This distinguishes the MR-proADM biomarker from other standard markers, whose levels often reach a plateau with significant disease severity.

3.3 Prognostic Value of MR-proADM

One of the most significant findings in research on this biomarker is the significant prognostic value of MR-proADM. Elevated levels of the biomarker were consistently associated with unfavorable clinical consequences, including:

- increased short-term mortality (e.g., 28-day mortality)
- increased long-term mortality
- higher risk of organ failure
- prolonged hospitalization
- increased likelihood of ICU admission

The MR-proADM assay retained its prognostic significance even after accounting for established clinical scoring systems such as SOFA and APACHE II, suggesting it contributes information beyond conventional measures of disease severity. In addition, its levels were strongly associated with patient results from the early phase of illness, indicating potential usefulness in guiding early therapeutic decisions.

Table 2. Association Between MR-proADM Levels and Clinical Outcomes

MR-proADM Level	Clinical Interpretation	Associated Outcomes
Low	Low risk	Stable condition, low mortality risk
Moderate	Intermediate risk	Possible progression, monitoring required
High	High risk	Septic shock, organ failure, increased mortality

3.4 Comparison with Conventional Biomarkers

A key aspect of the analysis involved comparing MR-proADM with widely used biomarkers such as CRP and procalcitonin (PCT).

Table 3. Comparative Performance of Sepsis Biomarkers

Biomarker	Diagnostic Value	Prognostic Value	Specificity	Stability
MR-proADM	High	Very high	Moderate	High
Procalcitonin (PCT)	High	Moderate	High	Moderate
C-reactive protein (CRP)	Moderate	Low	Low	High

Key Findings from Comparative Analysis

MR-proADM demonstrates superior prognostic accuracy compared to both CRP and PCT.

PCT remains more specific for bacterial infections but provides limited information regarding organ dysfunction.

CRP, while widely available, has limited value in risk stratification and prognostic prediction.

MR-proADM uniquely integrates information about endothelial injury, vascular integrity, and systemic inflammation.

These findings may serve MR-proADM as a complementary biomarker rather than a direct replacement for existing tests.

3.5 MR-proADM and Endothelial Dysfunction

A recurring theme in the reviewed studies is the strong association between MR-proADM levels and endothelial impairment. Elevated concentrations were consistently linked to:

- increased vascular permeability
- hypotension and vasodilatory shock
- impaired microcirculatory perfusion
- capillary leakage and tissue hypoxia

This mechanistic link is particularly relevant in sepsis, where endothelial injury plays a central role in disease progression.

MR-proADM therefore appears to show not only systemic inflammation but also the vascular component of sepsis pathophysiology, which is not adequately captured by traditional biomarkers.

3.6 Clinical Utility in Risk Stratification

The clinical studies reviewed consistently highlight the utility of MR-proADM in early risk stratification. Its application can be divided into several key areas:

1. Early Identification of High-Risk Patients

MR-proADM enables early course of disease of patients at risk of deterioration, even before overt clinical signs of organ failure become apparent.

2. Triage in Emergency Settings

In emergency departments, MR-proADM may assist in identifying patients requiring immediate hospitalization or intensive monitoring.

3. ICU Admission Decisions

Higher MR-proADM levels were associated with increased likelihood of ICU admission, supporting its role in critical care triage.

4. Monitoring Disease Progression

Serial measurements of MR-proADM may provide insight into treatment response and disease trajectory.

3.7 Summary of Key Results

Overall, the results of this review indicate that MR-proADM is:

- highly sensitive in perceiving early sepsis
- strongly associated with disease severity
- an independent predictor of mortality
- superior to CRP and partially superior to PCT in prognostic evaluation
- closely linked to endothelial injury and microcirculatory failure

These findings support its potential role as a clinically emerging biomarker in both emergency and intensive care settings.

4. Discussion

Sepsis remains one of the most complex, challenging, and ambiguous syndromes in medicine today. It is characterized by a dysregulated body response to infection, which subsequently leads to generalized inflammation, endothelial damage, microcirculatory failure, and ultimately, life-threatening multi-organ failure. Despite significant advances in intensive care, antibiotic therapy, early resuscitation protocols, and a significant emphasis on prevention, sepsis remains associated with high correlation with disease progression worldwide. The fundamental challenges in its treatment remain early identification of symptoms, implementation of appropriate treatment, and, above all, identification of patients at risk for rapid deterioration of general condition, as early initiation of therapy significantly impacts patient prognosis.

Current research indicate that mid-regional pro-adrenomedullin (MR-proADM) is a groundbreaking multidimensional biomarker that significantly exceeds traditional infection diagnostics. Unlike standard biomarkers such as CRP or procalcitonin, MR-proADM captures information not only on systemic inflammation but also on endothelial integrity, vascular tone regulation, and microcirculatory function. This makes it a particularly important marker in early sepsis, where circulatory disturbance plays a key role in disease progression.

A significant limitation in sepsis diagnosis is the exclusive use of biomarkers that, while predominantly reflect inflammatory activity and are widely used and have significant clinical value, such as C-reactive protein (CRP) and procalcitonin (PCT), do not adequately capture vascular impairment, which are key to the pathophysiology of sepsis. Consequently, relying solely on biomarker data can lead to difficulties in identifying patients at risk for acute circulatory collapse or multi-organ failure. MR-proADM appears to fill this gap by providing complementary information regarding endothelial stress and systemic vascular dysfunction, thus offering a more holistic picture of disease severity.

4.1 Pathophysiological Relevance of MR-proADM

MR-proADM is derived from the precursor molecule proadrenomedullin, which is cleaved into several peptides, including adrenomedullin. Adrenomedullin is a biologically active peptide with potent vasodilatory properties and plays a crucial role in maintaining vascular tone, endothelial barrier stability, and fluid homeostasis. Under physiological conditions, it contributes to the regulation of blood pressure and vascular permeability.

During sepsis, however, inflammatory mediators such as tumor necrosis factor-alpha (TNF- α), interleukins, and endotoxins trigger widespread endothelial activation and disorder. This leads to increased vascular permeability, capillary leakage, distributive shock, and impaired tissue oxygenation. In this context, the adrenomedullin system is significantly upregulated as part of a compensatory response aimed at preserving microcirculatory perfusion.

MR-proADM, as a stable surrogate marker of adrenomedullin production, shows this compensatory activation. Unlike purely inflammatory biomarkers, it captures both vascular and hemodynamic disturbances, making it more closely aligned with the core mechanisms driving organ failure in sepsis. Elevated MR-proADM levels therefore indicate not only systemic inflammation but also the severity of endothelial injury and circulatory collapse, which explains its strong association with adverse upshot.

This dual pathophysiological relevance positions MR-proADM as a uniquely integrative biomarker that bridges the gap between inflammation and vascular defect, two fundamental components of sepsis biology.

4.2 Diagnostic Versus Prognostic Utility

The literature consistently indicates that MR-proADM demonstrates greater utility as a prognostic marker than as a standalone diagnostic tool. Although MR-proADM levels may increase early in the course of infection, their primary clinical value lies in predicting disease progression, intensity, and patient outcomes rather than confirming the presence of infection itself.

In comparison, CRP is linked to a broad but non-specific indication of systemic inflammation. Its delayed kinetics and low specificity limit its usefulness in early risk stratification. Procalcitonin, on the other hand, offers improved specificity for bacterial infections and is more dynamically responsive than CRP; however, it still lacks sufficient sensitivity for predicting organ dysfunction and vascular collapse.

MR-proADM, in contrast, demonstrates strong and consistent associations with disease severity and mortality risk. It provides clinically relevant prognostic stratification across a spectrum of disease stages, from early infection to septic shock. This suggests that MR-proADM should be interpreted not as a replacement for existing biomarkers, but rather as a complementary component of a broader diagnostic framework that integrates inflammatory, vascular, and clinical parameters.

4.3 Integration with Clinical Scoring Systems

An important observation across multiple studies is the consistent correlation between MR-proADM levels and established clinical severity scores, including the Sequential Organ Failure Assessment (SOFA) and Acute Physiology and Chronic Health Evaluation (APACHE II). These scoring systems are widely used in intensive care settings to assess disease severity and forecasting results.

The observed correlation taken together that MR-proADM reflects overall physiological derangement in a manner consistent with validated clinical assessment tools. Importantly, MR-proADM may provide additional prognostic value when combined with these scoring systems, enhancing their predictive accuracy. This synergistic effect supports the emerging concept of multimodal risk stratification, in which biomarkers and clinical scores are integrated to improve diagnostic precision and prognostic reliability.

Such an approach is particularly relevant in emergency and intensive care settings, where rapid decision-making is essential and early identification of high-risk patients can significantly influence clinical outcomes.

4.4 Clinical Implications

The potential clinical applications of MR-proADM can be categorized into four key domains:

1. Early Risk Stratification

MR-proADM enables the early identification of patients at increased risk of deterioration, often before the onset of overt clinical signs of organ dysfunction. This may allow for earlier initiation of aggressive therapeutic interventions.

2. Emergency Department Triage

In emergency settings, MR-proADM may assist clinicians in differentiating between low-risk patients suitable for outpatient management and high-risk patients requiring hospitalization or intensive monitoring.

3. ICU Admission Support

Elevated MR-proADM levels are strongly associated with the need for intensive care, vasopressor support, and advanced organ support therapies. This makes it a potentially valuable tool for ICU admission decision-making.

4. Monitoring Disease Progression

Serial measurements of MR-proADM may provide dynamic information regarding treatment response and disease trajectory. Decreasing levels may indicate clinical improvement, whereas persistently elevated or rising concentrations may indicate ongoing inflammatory or hemodynamic instability.

Collectively, these applications highlight the potential of MR-proADM to improve clinical decision-making, optimize resource allocation, and support individualized patient management strategies.

4.5 Limitations of MR-proADM

Despite its promising clinical utility, several important limitations currently restrict the widespread implementation of MR-proADM in routine practice.

First, there is a lack of standardized cut-off values, which limits comparability between studies and reduces clinical interpretability. Different patient populations, assay platforms, and clinical settings contribute to variability in reported threshold values.

Second, methodological heterogeneity across studies, including differences in study design, timing of biomarker measurement, and patient selection criteria, complicates the synthesis of evidence.

Third, MR-proADM levels may be influenced by comorbid conditions such as chronic heart failure, chronic kidney disease, and other states associated with endothelial dysfunction, which may confound interpretation.

Fourth, most available evidence is derived from observational studies, which limits the ability to establish causal relationships.

Finally, limited availability and cost considerations in some healthcare systems may hinder widespread clinical adoption.

4.6 Future Perspectives

Future research should aim to address current limitations and further define the clinical role of MR-proADM in sepsis management. Key priorities include:

Establishment of standardized diagnostic and prognostic cut-off values through large-scale multicenter studies

Conducting prospective randomized controlled trials to validate clinical utility

Evaluation of cost-effectiveness in real-world healthcare settings

Integration of MR-proADM into existing sepsis management protocols and clinical decision algorithms

Development of multimarker strategies combining MR-proADM with PCT, lactate, and clinical scoring systems.

Particularly promising is the development of predictive models that integrate MR-proADM with other biomarkers and clinical parameters. Such models may enable earlier and more accurate identification of patients at risk of deterioration, supporting precision medicine approaches in sepsis care.

In addition, future studies should explore the potential role of MR-proADM-guided therapy, including biomarker-driven escalation or de-escalation of treatment strategies, which could further improve patient outcomes and optimize resource utilization in critical care environments.

5. Conclusions

Mid-regional pro-adrenomedullin (MR-proADM) is an emerging and highly promising biomarker that captured clinically relevant diagnostic and prognostic information in patients with sepsis. Its primary value lies in its ability to reflect key pathophysiological processes underlying sepsis, particularly endothelial defect, increased vascular permeability, and systemic hemodynamic instability. These mechanisms are central to disease progression and are not sufficiently captured by traditional inflammatory biomarkers.

The available evidence consistently demonstrates that MR-proADM contributes meaningful clinical information across several domains. It enables early identification of patients at increased risk of deterioration, often before overt signs of organ failure become clinically apparent. Furthermore, MR-proADM levels correlate strongly with disease severity, showing the progression from localized infection to systemic inflammatory response and septic shock.

Importantly, multiple studies have shown that MR-proADM independently predicts adverse clinical outcomes, including short-term and long-term mortality, development of multi-organ dysfunction, and the need for intensive care unit (ICU) admission. This prognostic performance remains significant even after adjustment for established clinical severity scores such as SOFA and APACHE II, highlighting its added value in clinical risk assessment.

When compared with conventional biomarkers such as C-reactive protein (CRP) and procalcitonin (PCT), MR-proADM demonstrates superior prognostic accuracy and a stronger association with vascular and endothelial injury. While CRP and PCT remain useful in the detection of inflammatory and infectious processes, their limited ability to mirror circulatory disturbance and organ dysfunction reduces their utility in comprehensive sepsis assessment.

Despite these advantages, MR-proADM has not yet been fully integrated into routine clinical practice. The main barriers to its widespread adoption include variability in study methodologies, lack of universally accepted diagnostic thresholds, limited standardization of assay techniques, and restricted availability in some healthcare systems. Additionally, most current evidence is derived from observational studies, which highlights the need for further large-scale prospective validation.

Future research should focus on establishing standardized cut-off values, validating clinical utility in multicenter randomized trials, and evaluating cost-effectiveness in real-world clinical settings. Particular attention should be given to the integration of MR-proADM into multimarker diagnostic strategies, combining it with established biomarkers such as PCT, lactate, and clinical scoring systems. Such an approach may enhance diagnostic precision and improve early risk stratification.

In conclusion, MR-proADM represents a worthwhile addition to the evolving field of sepsis diagnostics. Its ability to bridge inflammatory and vascular dimensions of disease pathophysiology positions it as a strong candidate for future clinical implementation. With further validation and standardization, MR-proADM has the potential to significantly improve initial phase of sepsis, optimize therapeutic decision-making, and ultimately contribute to better patient results in both emergency and intensive care settings.

REFERENCES

1. Angeletti, S., Spoto, S., Fogolari, M., De Florio, L., Bernardini, S., Dicuonzo, G., & Pascale, E. (2018). Diagnostic and prognostic role of procalcitonin (PCT), C-reactive protein (CRP), and MR-proadrenomedullin in bacterial infections. *Critical Care*, *22*, 1–9. <https://doi.org/10.1186/s13054-018-2128-5>
2. Caironi, P., Latini, R., Struck, J., Carlessi, A., Wagner, F., Blet, A., ... Singer, M. (2017). Circulating biologically active adrenomedullin predicts organ failure and mortality in sepsis. *Critical Care Medicine*, *45*(1), 49–57. <https://doi.org/10.1097/CCM.0000000000002012>
3. Christ-Crain, M., Morgenthaler, N. G., Stolz, D., Müller, C., Bingisser, R., Harbarth, S., Tamm, M., & Müller, B. (2005). Pro-adrenomedullin to predict severity and outcome in community-acquired pneumonia. *Critical Care*, *10*, R96. <https://doi.org/10.1186/cc4987>
4. Debiane, L. G., Hachem, R. Y., Al Wohoush, I., Chaftari, A. M., Bahu, R. R., Jiang, Y., ... Raad, I. I. (2014). The utility of procalcitonin and MR-proadrenomedullin in early diagnosis of sepsis. *Diagnostic Microbiology and Infectious Disease*, *78*(4), 412–417. <https://doi.org/10.1016/j.diagmicrobio.2013.11.014>
5. Elke, G., Bloos, F., Wilson, D. C., et al. (2018). The use of mid-regional proadrenomedullin to identify disease severity and treatment response in sepsis. *Critical Care*, *22*, 1–10. <https://doi.org/10.1186/s13054-018-2081-3>
6. Schuetz, P., Hausfater, P., Amin, D., et al. (2012). Biomarkers from distinct biological pathways improve early risk stratification in medical emergency patients: The TRIAGE study. *Critical Care*, *16*, R50. <https://doi.org/10.1186/cc11200>
7. Singer, M., Deutschman, C. S., Seymour, C. W., et al. (2016). The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA*, *315*(8), 801–810. <https://doi.org/10.1001/jama.2016.0287>
8. Suberviola, B., Castellanos-Ortega, Á., Ruiz Ruiz, A., López-Hoyos, M., & Santibáñez, M. (2012). Prognostic value of proadrenomedullin in severe sepsis and septic shock. *Journal of Critical Care*, *27*(4), 415–420. <https://doi.org/10.1016/j.jcrc.2011.08.020>
9. Valenzuela-Sánchez, F., Valenzuela-Méndez, B., Rodríguez-Gutiérrez, J. F., Estella, Á., González-García, M. A., & Rodríguez-García, J. L. (2015). New role of biomarkers: Mid-regional pro-adrenomedullin in sepsis. *Annals of Translational Medicine*, *3*(22), 329. <https://doi.org/10.3978/j.issn.2305-5839.2015.12.17>