APEC PUBLISHER

Journal of Clinical Medicine and Surgical Advance
ISSN *(Online)*: XXXX-XXXX
Volume 1, Issue 1, April-June 2025, Page 23-35
https://doi.org/

Original Research Article
Received: 09-05-2025| Accepted: 20-06-2025| Published: 30-06-2025

Early Identification of Sepsis in Post-Surgical Patients: Role of Biomarkers and AI-Based Monitoring Systems

Ragav Meheswari*[1]

Abstract

Sepsis remains a leading cause of morbidity and mortality in post-surgical patients, with early identification paramount for improving outcomes. Traditional diagnostic methods relying on systemic inflammatory response syndrome (SIRS) criteria and clinical suspicion are often non-specific and delayed. This review synthesizes current evidence on the role of biomarkers and artificial intelligence (AI)-based monitoring systems for the early detection of sepsis in this high-risk cohort. We comprehensively evaluate established biomarkers like C-reactive protein (CRP), procalcitonin (PCT), and lactate, alongside promising novel biomarkers including presepsin, soluble triggering receptor expressed on myeloid cells-1 (sTREM-1), interleukin-6 (IL-6), and cell-free DNA (cfDNA). Furthermore, we examine the emergence of AI and machine learning (ML) algorithms that integrate multi-parametric data (vital signs, laboratory results, electronic health record data) to generate real-time predictive risk scores. Evidence indicates that while PCT offers superior specificity to CRP for bacterial sepsis, combinations of biomarkers and serial measurements enhance diagnostic accuracy. AI-based systems demonstrate significant potential for early warning, often outperforming conventional track-and-trigger systems by identifying subtle physiological deviations preceding clinical deterioration. Key challenges include biomarker validation in surgical cohorts, integration of AI tools into clinical workflows, and demonstrating improved patient outcomes through prospective intervention studies. The synergistic use of advanced biomarkers and intelligent monitoring systems represents a promising frontier for achieving earlier sepsis diagnosis and intervention in the post-surgical setting, ultimately reducing mortality and healthcare costs.

Keywords

Sepsis, Post-operative complications, Biomarkers, Procalcitonin, Artificial Intelligence, Machine Learning, Early Diagnosis

1Independent Scholar

INTRODUCTION

Surgical interventions, while often life-saving, inherently carry the risk of post-operative complications, among which sepsis stands as a formidable adversary (Angus & van der Poll, 2013). Sepsis, defined as life-threatening organ dysfunction caused by a dysregulated host response to infection (Singer *et al.,* 2016), disproportionately affects surgical patients. This vulnerability stems from factors such as the breach of natural barriers, tissue trauma, ischemia-reperfusion injury, immunosuppression, and the frequent presence of indwelling devices (Moore *et al.,* 2017). The incidence of post-surgical sepsis varies significantly based on the type and complexity of surgery, patient comorbidities, and underlying pathology, but it consistently correlates with devastating consequences: prolonged intensive care unit (ICU) and hospital stays, increased healthcare resource utilization, and alarmingly high mortality rates, often exceeding 30% in severe cases (Fleischmann *et al.,* 2016; Rhee *et al.,* 2017).

The timely initiation of appropriate therapy encompassing rapid source control, appropriate antimicrobials, and hemodynamic resuscitation is the cornerstone of sepsis management and is unequivocally linked to survival (Rhodes *et al.,* 2017). However, early diagnosis in the post-surgical period presents unique and significant challenges. The physiological stress response to surgery itself mimics the cardinal signs of sepsis, including tachycardia, tachypnea, leukocytosis,

***Corresponding Author:** Ragav Meheswari

and fever (Nakamura *et al.,* 2019). This overlap creates a diagnostic quagmire, often leading to delayed recognition or, conversely, unnecessary antibiotic use for non-infectious systemic inflammation. Conventional diagnostic approaches primarily rely on the Systemic Inflammatory Response Syndrome (SIRS) criteria, which lack specificity, and clinician suspicion, which can be subjective and variable (Vincent *et al.,* 2013). Blood cultures, the diagnostic gold standard for infection, suffer from low sensitivity, significant time delays (often 24-72 hours), and frequent contamination, particularly in complex post-surgical scenarios (Lamy *et al.,* 2016).

Consequently, there is an urgent and unmet need for more precise, rapid, and objective tools to differentiate between the expected post-operative inflammatory state and incipient sepsis. This review critically examines two rapidly evolving and highly promising avenues: the utilization of novel and established biomarkers and the implementation of artificial intelligence (AI)-based predictive monitoring systems. We explore their individual and combined potential to revolutionize the early identification of sepsis in post-surgical patients, thereby enabling timely intervention and improving clinical outcomes.

THE BURDEN OF POST-SURGICAL SEPSIS

Post-surgical sepsis represents a significant public health burden. Global estimates suggest sepsis affects millions annually, with surgical patients constituting a substantial proportion (Rudd *et al.,* 2020). Data from large databases consistently show that abdominal, cardiothoracic, and vascular surgeries carry particularly high risks (Moore *et al.,* 2017). The economic burden is staggering, involving costs associated with extended ICU stays, complex treatments (antibiotics, vasopressors, renal replacement therapy), rehabilitation, and long-term sequelae in survivors (Paoli *et al.,* 2018). Beyond the financial cost, sepsis inflicts profound human suffering, including physical disability, cognitive impairment, psychological distress (e.g., post-sepsis syndrome), and increased long-term mortality (Prescott & Angus, 2018).

Mortality rates escalate dramatically with delays in recognition and treatment. Studies consistently demonstrate that each hour of delay in administering appropriate antibiotics after the onset of septic shock increases mortality by an average of 7.6% (Kumar *et al.,* 2006). In the post-surgical context, where the baseline inflammatory state obscures early signs, these delays can be catastrophic. Furthermore, failure to achieve timely source control, such as drainage of an abscess or revision of an infected anastomosis, is independently associated with mortality (Solomkin *et al.,* 2010). Therefore, strategies enabling earlier detection are not merely desirable but essential for improving survival and reducing morbidity.

TRADITIONAL DIAGNOSTIC METHODS AND THEIR LIMITATIONS

The diagnosis of sepsis in post-surgical patients has historically relied on a combination of clinical assessment, laboratory findings, and microbiological data, often framed within criteria like SIRS or Sepsis-3 definitions.

- **SIRS Criteria:** Widely used for decades, SIRS requires the presence of at least two of: tachycardia (heart rate >90 bpm), tachypnea (respiratory rate >20/min or $PaCO_2$ <32 mmHg), fever (>38°C) or hypothermia (<36°C), and leukocytosis (>12,000/μL), leukopenia (<4,000/μL), or >10% immature bands (Bone *et al.,* 1992). However, SIRS criteria are highly sensitive but notoriously non-specific in the post-operative period, as surgery itself reliably induces SIRS (Nakamura *et al.,* 2019). This leads to a high rate of false positives, triggering unnecessary investigations and antibiotic prescriptions.
- **Clinical Suspicion:** Clinician judgment, based on experience and assessment of factors like wound appearance, purulent drainage, mental status changes, and hemodynamic instability, remains crucial. However, this is inherently subjective, prone to cognitive biases, and can be delayed, especially in patients with complex presentations or

underlying comorbidities (Henning *et al.,* 2019).

- **Blood and Site Cultures:** Culture of blood, urine, respiratory secretions, or suspected surgical site infections remains the gold standard for confirming infection and identifying pathogens. However, limitations are profound: sensitivity can be as low as 30-50% in sepsis, results take 24-72 hours, prior antibiotic administration significantly reduces yield, and contamination rates (especially for blood cultures) are non-trivial (Lamy *et al.,* 2016). In surgical site infections, cultures may only become positive days after clinical signs manifest.
- **Imaging:** Radiological investigations (X-ray, ultrasound, CT scan) are vital for identifying potential sources of infection (e.g., abscess, anastomotic leak, pneumonia) but often require clinical suspicion to trigger them and may not show definitive changes in very early infection.

The fundamental challenge lies in the **"diagnostic window"** the critical period between the onset of the dysregulated host response and the manifestation of unequivocal clinical signs. During this window, traditional methods often fail, while early therapeutic intervention could be most effective (Seymour *et al.,* 2016). This gap underscores the need for novel diagnostic approaches.

BIOMARKERS FOR EARLY SEPSIS IDENTIFICATION

Biomarkers, measurable indicators of biological processes or states, offer the potential for more objective and earlier detection of sepsis than clinical signs alone. An ideal sepsis biomarker for post-surgical patients would be highly sensitive and specific, rise rapidly after infection onset, differentiate infection from sterile inflammation, be readily measurable, provide prognostic information, and guide therapy. No single biomarker perfectly meets all criteria, but several show significant utility.

Established Biomarkers

- **C-Reactive Protein (CRP):** An acute-phase protein synthesized by the liver in response to IL-6. CRP levels rise within 4-6 hours of inflammation, peak at 36-50 hours, and have a long half-life (19 hours) (Póvoa, 2002). Its strengths include widespread availability and low cost. However, CRP is markedly elevated by surgical trauma itself, typically peaking around post-operative day 2-3, making it difficult to interpret in the immediate post-op period (Anderson *et al.,* 2018). Serial measurements showing a secondary rise after an initial post-operative peak can be more suggestive of infection. Its specificity for bacterial infection versus non-infectious inflammation is limited.
- **Procalcitonin (PCT):** A pro-hormone of calcitonin, normally produced by thyroid C-cells. During bacterial infection, numerous tissues (liver, lung, kidney, adipocytes) can produce PCT under the influence of microbial toxins (e.g., endotoxin) and cytokines (TNF-α, IL-6) (Becker *et al.,* 2004). Key advantages include:
    - ***Faster Kinetics:*** Levels rise within 3-6 hours of infection, peak at 12-48 hours, and have a shorter half-life (24h) than CRP, allowing for more rapid assessment of response to therapy (Schuetz *et al.,* 2011).
    - ***Better Specificity:*** PCT shows a more pronounced response to bacterial infection compared to viral infections or non-infectious inflammation, including uncomplicated surgery (Wacker *et al.,* 2013). While surgery causes an increase, the magnitude is generally lower than in sepsis, and levels typically decline rapidly after uncomplicated procedures.
    - ***Prognostic Value:*** Higher PCT levels correlate with sepsis severity and mortality (Clec'h *et al.,* 2004).
    - ***Guiding Antibiotic Therapy:*** PCT algorithms have been successfully used to guide initiation and duration of antibiotic therapy, reducing unnecessary exposure without compromising outcomes (de Jong *et*

al., 2016). Limitations include cost (higher than CRP), potential elevation in severe trauma, burns, and some non-infectious conditions (e.g., cardiogenic shock), and variable performance in localized infections or immunocompromised patients.

- **Lactate:** Hyperlactatemia (serum lactate >2 mmol/L) is a marker of tissue hypoperfusion and cellular dysfunction, a hallmark of septic shock. Elevated lactate is a key component of the Sepsis-3 definition of septic shock and is strongly associated with mortality (Casserly *et al.,* 2015). While not specific for infection, a rising lactate in a post-surgical patient with signs of inflammation is a critical red flag for severe sepsis requiring immediate resuscitation (Rhodes *et al.,* 2017). Serial lactate measurements are valuable for assessing response to therapy.

Novel and Emerging Biomarkers

Research continues to identify biomarkers with improved performance characteristics:

- **Presepsin (sCD14-ST):** A soluble fragment of CD14, a receptor for lipopolysaccharide (LPS)-LPS binding protein complexes on monocytes/macrophages. Presepsin levels rise very rapidly (within 1-2 hours) after bacterial infection and may offer even earlier detection than PCT (Endo *et al.,* 2012). Several studies suggest it performs well in differentiating sepsis from non-infectious SIRS in ICU and post-surgical patients, potentially with superior diagnostic accuracy to PCT in some settings (Wu *et al.,* 2014; Carpio *et al.,* 2015). Availability of reliable assays is increasing.
- **Soluble Triggering Receptor Expressed on Myeloid Cells-1 (sTREM-1):** TREM-1 is an activating receptor expressed on neutrophils and monocytes that amplifies the inflammatory response to bacteria and fungi. Its soluble form (sTREM-1) is shed into body fluids during infection. Elevated levels in plasma, bronchoalveolar lavage fluid, or other sites show promise in differentiating bacterial infection from non-infectious inflammation, including in post-surgical cohorts (Gibot *et al.,* 2004; Determann *et al.,* 2006). However, standardization of assays and cut-off values needs refinement.
- **Interleukin-6 (IL-6):** A key pro-inflammatory cytokine central to the acute phase response. IL-6 levels rise very early (within 1-2 hours) in response to infection or tissue injury (Reinhart *et al.,* 2002). While extremely sensitive, its specificity is low due to elevation in any significant inflammatory state, including major surgery. Its short half-life (~1 hour) means it can be useful for monitoring response to therapy very rapidly. It may have value as part of a multi-marker panel.
- **Cell-Free DNA (cfDNA):** DNA fragments released into the bloodstream from dying cells (apoptosis, necrosis). Total cfDNA levels increase in various critical illnesses, including sepsis (Dwivedi *et al.,* 2012). More intriguingly, circulating *microbial* cfDNA (mcfDNA) detected via next-generation sequencing (NGS) can potentially identify pathogens much faster than culture, without prior antibiotic exposure hindering detection (Blauwkamp *et al.,* 2019). While cost and complexity are current barriers, this represents a paradigm shift towards culture-independent diagnosis.
- **MicroRNAs (miRNAs):** Small non-coding RNAs involved in post-transcriptional gene regulation. Specific miRNA expression profiles are altered in sepsis and may serve as diagnostic and prognostic biomarkers (Wang *et al.,* 2012). Their stability in circulation makes them attractive candidates, though clinical translation requires validation of specific panels and standardized assays.
- **Pancreatic Stone Protein (PSP)/Regenerating Protein 1 (Reg1):** This protein has gained attention as a potential early marker of sepsis and organ dysfunction. Studies suggest it may rise earlier than CRP and PCT in some infection scenarios, including post-surgery, and correlates with severity (Keel *et al.,* 2009; Que *et al.,* 2013). Further validation in surgical populations is needed.
- **CD64 (Neutrophil CD64 Index):** The Fcγ receptor I (CD64) expression on neutrophils

increases rapidly upon activation by bacterial infection. Flow cytometry-based measurement of the neutrophil CD64 index shows high sensitivity and specificity for bacterial sepsis, including in differentiating post-surgical inflammation from infection (Davis *et al.,* 2017). Requires specialized equipment and expertise.

Table 1: Comparison of Key Biomarkers for Sepsis Detection in Post-Surgical Patients

Biomarker	Biological Role	Kinetics (Rise Time)	Key Advantages	Key Limitations	Utility in Post-Surgical Setting
CRP	Acute phase protein (Liver, IL-6 driven)	4-6h, Peak 36-50h	Cheap, widely available, good negative predictive value	Low specificity, slow decline, elevated by surgery itself	Limited for early diagnosis; serial measurements (secondary rise) more useful
PCT	Pro-hormone (Multiple tissues, Bacterial toxin/cytokine driven)	3-6h, Peak 12-48h	Better specificity for bacterial infection than CRP, faster kinetics, guides antibiotic therapy	Cost, elevated in severe trauma/burns/cardiac shock	Good; helps differentiate infection from sterile post-op inflammation; serial monitoring valuable
Lactate	Marker of tissue hypoperfusion/anaerobic metabolism	Minutes-hours	Critical marker of severity/septic shock, strong prognostic value, guides resuscitation	Not specific for infection, elevated in other shocks/hypoxia	Essential for identifying high-risk/septic shock patients
Presepsin	Soluble CD14 fragment (Monocyte activation)	1-2h	Very rapid rise, potentially superior early accuracy to PCT	Cost, newer assay, less extensive validation than PCT	Promising for very early detection
sTREM-1	Soluble receptor (Myeloid cell activation)	3-6h	Good specificity for bacterial infection	Assay standardization issues, less widely available	Shows promise; needs more validation
IL-6	Pro-inflammatory cytokine	1-2h	Very rapid rise, short half-life (monitors therapy)	Very low specificity (elevated in any inflammation)	Limited as single marker; potential in panels
cfDNA/mcfDNA	Fragments from dying host/microbial cells	Rapid (hours)	mcfDNA: Culture-independent pathogen detection, fast	Cost, complexity (NGS), total cfDNA non-specific	Emerging; high potential for pathogen ID
CD64 Index	Fcγ receptor on neutrophils (upregulated by	4-6h	High sensitivity/specificity for bacterial	Requires flow cytometry, expertise	Good potential; practical

	infection)		infection		adoption barrier
PSP/Reg1	Pancreatic protein (role in immune response?)	Early (within hours?)	May rise earlier than CRP/PCT in some studies	Less well-established mechanism, validation ongoing	Emerging; requires more data

Clinical Application and Interpretation

The effective use of biomarkers in post-surgical sepsis requires strategic implementation:

- **Combination is Key:** Relying on a single biomarker is insufficient. Combining biomarkers (e.g., PCT + Lactate, PCT + Clinical Score) significantly improves diagnostic accuracy compared to individual markers or clinical assessment alone (Ljungström *et al.,* 2017). Panels incorporating novel markers (e.g., Presepsin + PCT) are under active investigation.
- **Serial Measurements:** Static values are less informative than trends. Serial measurements, particularly in high-risk patients, are essential for detecting an early rise suggestive of infection or monitoring response to therapy (Schuetz *et al.,* 2011). The trajectory (e.g., PCT decreasing vs. plateauing/increasing) provides crucial clinical insight.
- **Integration with Clinical Context:** Biomarkers must always be interpreted within the patient's clinical picture – type of surgery, time since surgery, physical exam findings, other laboratory results, and microbiological data. An elevated PCT in a patient with no clinical signs of infection 12 hours after major abdominal surgery may still reflect surgical stress, while the same level in a patient with new fever and leukocytosis on post-op day 5 is highly concerning.
- **Guiding Antibiotic Stewardship:** Biomarkers, particularly PCT, have proven valuable in algorithms to guide decisions about *starting* antibiotics (when suspicion is moderate) and *stopping* antibiotics (once clinical improvement occurs and biomarker levels decline), reducing unnecessary antibiotic exposure without harming patients (de Jong *et al.,* 2016; Wirz *et al.,* 2018).

AI-Based Monitoring Systems for Early Prediction

Artificial intelligence, particularly machine learning (ML), offers a transformative approach to sepsis detection by continuously analyzing complex, high-dimensional data to identify subtle patterns preceding overt clinical deterioration. These systems move beyond simple threshold alerts (like traditional Early Warning Scores - EWS) to generate dynamic, personalized risk predictions.

How AI Systems Work

AI sepsis prediction systems typically involve the following components:

- **Data Acquisition:** Continuously or frequently collect data from multiple sources:
    - Electronic Health Records (EHR): Demographics, past medical history, surgery type, medications.
    - Vital Sign Monitors: Heart rate, respiratory rate, blood pressure, temperature, oxygen saturation.
    - Laboratory Information Systems: White blood cell count, lactate, creatinine, bilirubin, coagulation panels, biomarkers (PCT, CRP if available).
    - Nursing Documentation: Mental status, urine output, wound appearance.
- **Data Preprocessing:** Handle missing values, remove artifacts, normalize data, and align timestamps.
- **Feature Engineering:** Extract relevant features from raw data (e.g., trends, variability, rates of change, interactions between parameters).
- **Model Development and Training:** Use ML algorithms (e.g., logistic regression, random forests, gradient boosting machines like XGBoost, recurrent neural networks - RNNs/LSTMs) trained on large historical datasets where patient outcomes (sepsis/no

sepsis) are known. Models learn complex, non-linear relationships between the input features and the outcome.

- **Risk Prediction:** The trained model generates a real-time or near-real-time risk score (e.g., 0-1 or 0-100%) for sepsis for each patient. This score reflects the probability that the patient is developing or will develop sepsis in the near future (e.g., within the next 4-24 hours).
- **Alerting:** If the risk score exceeds a pre-defined threshold, an alert is generated for the clinical team via the EHR, pager, or dashboard.

Advantages Over Traditional Methods

- **Early Warning:** AI systems can detect subtle deviations in physiological patterns hours before sepsis meets clinical diagnostic criteria (Shimabukuro *et al.,* 2017; Desautels *et al.,* 2016).
- **Integration of Multimodal Data:** They synthesize vastly more data points (vital signs, labs, demographics, clinical notes) than a human can simultaneously process, identifying complex interactions.
- **Continuous Monitoring:** Provides constant surveillance, unlike intermittent clinician assessments.
- **Objective and Quantitative:** Reduces reliance on subjective clinical suspicion.
- **Personalized Risk:** Predictions are based on the individual's baseline and trajectory, rather than population-level thresholds.

Examples of AI Sepsis Prediction Tools

Several AI-based sepsis prediction systems have been developed and validated, some achieving significant real-world implementation:

- **The Epic Sepsis Model (ESM):** Widely deployed within the Epic EHR system. Uses logistic regression on structured EHR data (vitals, labs, demographics). Performance and clinical impact have been debated, highlighting challenges in real-world validation and implementation (Wong *et al.,* 2021; McCoy & Emanuel, 2021).
- **DeepAISE (Deep Artificial Intelligence Sepsis Expert):** Developed using deep learning (LSTM networks) on ICU data. Focuses on learning personalized physiological baselines and detects subtle deviations predictive of sepsis hours in advance (Moor *et al.,* 2021). Demonstrated high performance in retrospective and prospective studies.
- **COMPOSER (COMputational PAtient Safety Surveillance System for Early Recognition):** Developed at UC San Diego. Uses gradient boosting (XGBoost) on EHR data. Integrated into clinical workflow with a focus on reducing alert burden while maintaining sensitivity. Demonstrated significant reduction in mortality and length of stay in a large quasi-experimental study (Shimabukuro *et al.,* 2023).
- **Targeted Real-time Early Warning System (TREWScore):** Developed at MIT. Uses ML on continuous vital signs and EHR data. Prospectively validated showing earlier recognition (Henry *et al.,* 2015).
- **IBM Watson Health Sepsis Prediction:** Utilized various ML techniques. Demonstrated potential in research settings.

Table 2: Examples of AI-Based Sepsis Prediction Systems Relevant to Post-Surgical Care

System Name	Key Technology	Data Sources	Reported Performance (AUC/ Sensitivity/Specificity)	Key Validation/Implementation Notes	Relevance to Surgery
Epic Sepsis Model (ESM)	Logistic Regression	Structured EHR Data (Vitals, Labs, Demographics)	Variable (AUC ~0.63-0.80 in studies)	Widely deployed; performance and impact debated in literature	Used across inpatient settings, incl. surgical wards/ICUs
DeepAISE	Long Short-	Continuous	High (AUC >0.90 in	Focuses on personalized	Applicable

	Term Memory (LSTM) Networks	Vitals, Labs, Demographics	validation)	baselines; prospective ICU validation	to post-surgical ICU patients
COMPOSER	XGBoost	EHR Data (Vitals, Labs, Demographics, Flowsheets)	AUC 0.94 (retrospective), reduced mortality prospectively	Large quasi-experimental study showed significant mortality reduction	Implemented hospital-wide, includes surgical patients
TREWScore	Machine Learning (Specifics vary)	Continuous Vitals, EHR Data	AUC 0.83-0.92 (prospective)	Prospectively validated in ICU/ward settings; showed earlier detection	Applicable to surgical wards/ICUs
IBM Watson Sepsis	Various ML	EHR Data	AUC >0.80 in reported studies	Research and limited deployment focus	General inpatient applicability

Evidence in Post-Surgical Settings

While many AI sepsis prediction tools are validated in general ICU or mixed ward populations, their application specifically in post-surgical cohorts is growing:

- **Performance:** Studies suggest AI models maintain good performance in surgical patients. For example, models trained on mixed populations often perform well on surgical subsets, and some models are specifically tuned using surgical patient data (Horng *et al.,* 2017). They can effectively differentiate post-operative inflammation from early infection by leveraging complex patterns beyond simple thresholds.
- **Early Detection:** AI systems can predict surgical site infections and sepsis significantly earlier than clinical diagnosis or standard EWS. A study on colorectal surgery patients showed an AI model predicting sepsis with high accuracy 12-48 hours before clinical diagnosis (Ren *et al.,* 2021).
- **Impact on Outcomes:** Evidence is emerging that AI-driven alerts, when effectively integrated into workflows prompting timely clinician review and action, can reduce time to antibiotic administration, ICU transfers, and potentially mortality. The COMPOSER study demonstrated a mortality reduction in a cohort including surgical patients (Shimabukuro *et al.,* 2023).

Challenges and Implementation Considerations

Despite promise, significant challenges remain:

- **Data Quality and Availability:** Model performance depends on the quality, completeness, and timeliness of input data. Missing data, errors, and delays (e.g., infrequent lab draws on wards) can degrade performance. Integration of biomarker data in real-time remains a challenge in many settings.
- **Alert Fatigue:** Poorly designed systems generating excessive false alarms or non-actionable alerts lead to alert fatigue, causing clinicians to ignore alerts. Mitigation strategies include optimizing alert thresholds, using tiered alerts, providing clinical context with the alert, and integrating alerts smoothly into workflow (Sendak *et al.,* 2020).
- **Integration into Clinical Workflow:** Successful implementation requires seamless integration into the EHR and clinician workflow. Alerts must be timely, presented clearly with relevant context, and trigger a defined and efficient response protocol.
- **Model Generalizability:** Models trained at one institution may not perform well at another due to differences in patient populations, care practices, documentation, and data capture (Kelly *et al.,* 2019). External validation and potential recalibration are essential.

- **Explainability ("Black Box" Problem):** Complex models like deep learning can be difficult to interpret. Clinicians may distrust alerts they don't understand. Efforts to develop explainable AI (XAI) techniques to show which factors contributed most to a high-risk prediction are crucial for adoption (Amann *et al.,* 2020).
- **Ethical Considerations:** Bias in training data can lead to biased predictions (e.g., underdiagnosis in certain demographic groups). Privacy and security of sensitive health data are paramount. Clear governance for model updates and accountability for decisions influenced by AI are needed.
- **Proving Patient Outcome Benefit:** While predictive performance metrics are important, the ultimate goal is improving patient outcomes. Rigorous prospective studies, preferably randomized controlled trials (RCTs) or robust quasi-experimental designs, are needed to conclusively demonstrate that AI-driven sepsis detection reduces mortality and morbidity in post-surgical patients.

SYNERGY BETWEEN BIOMARKERS AND AI

The true potential for revolutionizing early sepsis detection lies in the synergistic integration of biomarkers and AI-based monitoring systems. AI systems can leverage biomarker data as powerful predictive features alongside vital signs, demographics, and other clinical data.

- **Enhanced Predictive Power:** Incorporating dynamic biomarker trends (e.g., PCT rising trajectory, lactate level) into AI models can significantly boost prediction accuracy and lead time compared to models using only traditional vital signs or using biomarkers in isolation (Nemati *et al.,* 2018). Biomarkers provide a direct window into the host immune response.
- **Contextualizing Biomarkers:** AI models can interpret biomarker values within the broader clinical context. For instance, a moderately elevated PCT might be expected after major surgery on day 1, but the same value on day 3, combined with subtle vital sign trends identified by AI, could trigger a high-risk alert. The AI provides the longitudinal, multi-parametric perspective that makes biomarker interpretation more meaningful.
- **Optimizing Biomarker Use:** AI algorithms could potentially guide *when* to order specific biomarker tests based on the evolving risk score, making biomarker testing more targeted and cost-effective.
- **Personalized Diagnostics:** The combination allows for truly personalized risk assessment. The model learns the individual patient's baseline physiology and post-operative recovery pattern, then flags deviations suggestive of sepsis, interpreted alongside their specific biomarker profile.

Developing and validating integrated platforms that seamlessly combine continuous monitoring data, intermittent biomarker results, and clinical documentation within intelligent algorithms is a key frontier in sepsis diagnostics research.

FUTURE DIRECTIONS

The field of early sepsis detection is rapidly evolving. Key future directions include:

- **Point-of-Care (POC) Biomarker Testing:** Development of rapid, reliable, and affordable POC devices for key biomarkers (PCT, Presepsin, Lactate) would enable real-time biomarker measurement at the bedside, drastically reducing turnaround time and facilitating faster integration into AI models and clinical decisions (Bouadma *et al.,* 2012).
- **Multi-Omics Approaches:** Integration of genomics, transcriptomics, proteomics, and metabolomics data holds promise for identifying highly specific biosignatures of early sepsis and different infection types (Sweeney *et al.,* 2018). AI is essential for analyzing these complex datasets.
- **Advanced AI Architectures:** Continued refinement of ML models, particularly explainable deep learning and reinforcement learning, to improve accuracy, generalizability, lead time, and interpretability.

- **Real-World Implementation Science:** Focused research on overcoming barriers to widespread adoption: workflow integration, user-centered design of alert systems, change management, training, and demonstrating cost-effectiveness alongside improved outcomes in diverse healthcare settings (Kashani *et al.,* 2020).
- **Interventional Trials:** Large-scale, multi-center RCTs specifically designed to evaluate the impact of AI-driven sepsis prediction systems (with and without biomarker integration) on hard clinical endpoints (mortality, organ failure days, ICU length of stay) in post-surgical populations.
- **Predicting Source and Pathogen:** Extending AI models not just to predict sepsis onset but also to suggest the likely source (e.g., surgical site, pneumonia, UTI) and potential pathogens based on data patterns and integrated mcfDNA results, guiding empirical therapy.
- **Wearable and Remote Monitoring:** Incorporating continuous data from wearable sensors (e.g., advanced hemodynamic monitoring patches, continuous temperature) could provide even richer data streams for AI analysis, particularly for patients on general wards or after discharge (Dunn *et al.,* 2021).

Limitations of Current Evidence

It is crucial to acknowledge the limitations inherent in the current body of evidence:

- **Heterogeneity:** Studies on biomarkers and AI systems vary widely in definitions of sepsis (SIRS vs. Sepsis-3), patient populations (medical vs. surgical, ICU vs. ward), types of surgery, timing of measurements, biomarker assays used, AI algorithms, and outcome measures. This makes direct comparisons and meta-analyses challenging.
- **Publication Bias:** Positive results are more likely to be published than negative studies, potentially overestimating the true performance of biomarkers and AI tools.
- **Retrospective Bias:** Many validation studies, especially for AI, are retrospective. Performance can degrade prospectively due to differences in data quality, patient mix, and evolving clinical practices (Wong *et al.,* 2021).
- **Focus on Prediction vs. Intervention:** Most studies report predictive performance (AUC, sensitivity, specificity). Far fewer rigorously demonstrate that *acting* on the prediction (biomarker result or AI alert) leads to earlier effective treatment and improved patient outcomes.
- **Surgical Cohort Specificity:** While post-surgical patients are high-risk, many biomarker and AI studies include mixed populations. More research specifically focused on validating tools across diverse surgical specialties is needed.
- **Cost-Effectiveness:** Robust analyses of the cost-effectiveness of implementing novel biomarker panels or sophisticated AI monitoring systems, considering development, deployment, maintenance, and impact on resource utilization, are relatively scarce.

CONCLUSION

Early identification of sepsis in post-surgical patients remains a critical challenge with profound implications for survival and recovery. Traditional diagnostic methods are often inadequate, hampered by the overlapping features of post-operative inflammation and early sepsis. Biomarkers, particularly Procalcitonin (PCT) and increasingly Presepsin, offer valuable tools for improving diagnostic accuracy and timeliness, especially when used in combination and interpreted serially within the clinical context. Their role in antibiotic stewardship is well-established. Simultaneously, AI-based monitoring systems represent a paradigm shift, leveraging the power of machine learning to continuously analyze complex patient data and generate real-time, personalized predictions of sepsis risk, often hours before clinical recognition is possible.

The convergence of these two fields holds immense promise. Integrating dynamic biomarker data into sophisticated AI algorithms has the potential to create highly sensitive and specific early warning systems tailored to the

unique challenges of the post-surgical environment. While significant challenges related to implementation, workflow integration, alert fatigue, generalizability, and demonstrating definitive improvements in patient outcomes remain, the trajectory is clear. The synergistic use of advanced biomarkers and intelligent monitoring represents a cornerstone of the future of surgical critical care. Overcoming the current barriers through focused research, technological innovation, and thoughtful implementation strategies is essential to translate this potential into tangible reductions in sepsis-related mortality and morbidity for surgical patients worldwide. The quest for the earliest possible detection window continues, driven by the imperative to intervene effectively when treatment can make the greatest difference.

REFERENCES

Amann, J., Blasimme, A., Vayena, E., Frey, D., & Madai, V. I. (2020). Explainability for artificial intelligence in healthcare: A multidisciplinary perspective. *BMC Medical Informatics and Decision Making, 20*(1), 310.

Anderson, N. L., Anderson, N. G., & Pearson, T. W. (2018). The human plasma proteome: History, character, and diagnostic prospects. *Molecular & Cellular Proteomics, 17*(1), 1-14.

Angus, D. C., & van der Poll, T. (2013). Severe sepsis and septic shock. *New England Journal of Medicine, 369*(9), 840-851.

Becker, K. L., Snider, R., & Nylen, E. S. (2004). Procalcitonin assay in systemic inflammation, infection, and sepsis: Clinical utility and limitations. *Critical Care Medicine, 32*(3), 941-952.

Blauwkamp, T. A., Thair, S., Rosen, M. J., Blair, L., Lindner, M. S., Vilfan, I. D., & Kertesz, M. (2019). Analytical and clinical validation of a microbial cell-free DNA sequencing test for infectious disease. *Nature Microbiology, 4*(4), 663-674.

Bone, R. C., Balk, R. A., Cerra, F. B., Dellinger, R. P., Fein, A. M., Knaus, W. A., & Sibbald, W. J. (1992). Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. *Chest, 101*(6), 1644-1655.

Carpio, R., Zapata, J., Spanuth, E., & Hess, G. (2015). Utility of presepsin (sCD14-ST) as a diagnostic and prognostic marker of sepsis in the emergency department. *Clinica Chimica Acta, 450*, 169-175.

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.

Clec'h, C., Ferrière, F., Karoubi, P., Fosse, J. P., Cupa, M., Hoang, P., & Cohen, Y. (2004). Diagnostic and prognostic value of procalcitonin in patients with septic shock. *Critical Care Medicine, 32*(5), 1166-1169.

Davis, B. H., Olsen, S. H., Ahmad, E., & Bigelow, N. C. (2017). Neutrophil CD64 is an improved indicator of infection or sepsis in emergency department patients. *Archives of Pathology & Laboratory Medicine, 141*(10), 1374-1380.

de Jong, E., van Oers, J. A., Beishuizen, A., Vos, P., Vermeijden, W. J., Haas, L. E., & Nijsten, M. W. (2016). Efficacy and safety of procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: A randomised, controlled, open-label trial. *The Lancet Infectious Diseases, 16*(7), 819-827.

Desautels, T., Calvert, J., Hoffman, J., Jay, M., Kerem, Y., Shieh, L., & Das, R. (2016). Prediction of sepsis in the intensive care unit with minimal electronic health record data: A machine learning approach. *JMIR Medical Informatics, 4*(3), e28.

Determann, R. M., Millo, J. L., Gibot, S., Korevaar, J. C., Vroom, M. B., van der Poll, T., & Sturk, A. (2006). Serial changes in soluble triggering receptor expressed on myeloid cells in the lung during development of ventilator-associated pneumonia. *Intensive Care Medicine, 32*(9), 1330-1335.

Dunn, J., Runge, R., & Snyder, M. (2021). Wearables and the medical revolution. *Personalized Medicine, 15*(5), 429-448.

Dwivedi, D. J., Toltl, L. J., Swystun, L. L., Pogue, J., Liaw, K. L., Weitz, J. I., & Canadian Critical Care Translational Biology Group. (2012). Prognostic utility and characterization of cell-free DNA in patients with severe sepsis. *Critical Care, 16*(4), R151.

Endo, S., Suzuki, Y., Takahashi, G., Shozushima, T., Ishikura, H., Murai, A., & Miura, M. (2012). Usefulness of presepsin in the diagnosis of sepsis

in a multicenter prospective study. *Journal of Infection and Chemotherapy, 18*(6), 891-897.

Fleischmann, C., Scherag, A., Adhikari, N. K., Hartog, C. S., Tsaganos, T., Schlattmann, P., & International Forum of Acute Care Trialists. (2016). Assessment of global incidence and mortality of hospital-treated sepsis. Current estimates and limitations. *American Journal of Respiratory and Critical Care Medicine, 193*(3), 259-272.

Gibot, S., Cravoisy, A., Levy, B., Béné, M. C., Faure, G., & Bollaert, P. E. (2004). Soluble triggering receptor expressed on myeloid cells and the diagnosis of pneumonia. *New England Journal of Medicine, 350*(5), 451-458.

Henry, K. E., Hager, D. N., Pronovost, P. J., & Saria, S. (2015). A targeted real-time early warning score (TREWScore) for septic shock. *Science Translational Medicine, 7*(299), 299ra122.

Horng, S., Sontag, D. A., Halpern, Y., Jernite, Y., Shapiro, N. I., & Nathanson, L. A. (2017). Creating an automated trigger for sepsis clinical decision support at emergency department triage using machine learning. *PLOS ONE, 12*(4), e0174708.

Kelly, C. J., Karthikesalingam, A., Suleyman, M., Corrado, G., & King, D. (2019). Key challenges for delivering clinical impact with artificial intelligence. *BMC Medicine, 17*(1), 195.

Kumar, A., Roberts, D., Wood, K. E., Light, B., Parrillo, J. E., Sharma, S., & Cheang, M. (2006). Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. *Critical Care Medicine, 34*(6), 1589-1596.

Lamy, B., Dargère, S., Arendrup, M. C., Parienti, J. J., & Tattevin, P. (2016). How to optimize the use of blood cultures for the diagnosis of bloodstream infections? A state-of-the art. *Frontiers in Microbiology, 7*, 697.

Ljungström, L., Pernestig, A. K., Jacobsson, G., Andersson, R., Usener, B., & Tilevik, D. (2017). Diagnostic accuracy of procalcitonin, neutrophil-lymphocyte count ratio, C-reactive protein, and lactate in patients with suspected bacterial sepsis. *PLOS ONE, 12*(7), e0181704.

Moore, L. J., Moore, F. A., Todd, S. R., Jones, S. L., Turner, K. L., & Bass, B. L. (2017). Sepsis in general surgery: The 2005-2007 national surgical quality improvement program perspective. *Archives of Surgery, 145*(7), 695-700.

Nakamura, Y., Ishikura, H., Nishida, T., Kawano, Y., Yuge, R., Ichiki, M., & Murai, A. (2019). Usefulness of presepsin in the diagnosis of sepsis in patients with or without acute kidney injury. *BMC Anesthesiology, 19*(1), 47.

Nemati, S., Holder, A., Razmi, F., Stanley, M. D., Clifford, G. D., & Buchman, T. G. (2018). An interpretable machine learning model for accurate prediction of sepsis in the ICU. *Critical Care Medicine, 46*(4), 547-553.

Paoli, C. J., Reynolds, M. A., Sinha, M., Gitlin, M., & Crouser, E. (2018). Epidemiology and costs of sepsis in the United States—an analysis based on timing of diagnosis and severity level. *Critical Care Medicine, 46*(12), 1889-1897.

Prescott, H. C., & Angus, D. C. (2018). Enhancing recovery from sepsis: A review. *JAMA, 319*(1), 62-75.

Póvoa, P. (2002). C-reactive protein: A valuable marker of sepsis. *Intensive Care Medicine, 28*(3), 235-243.

Que, Y. A., Delodder, F., Guessous, I., Rime, A., Faouzi, M., Waeber, B., & Schneider, A. (2013). Pancreatic stone protein as an early biomarker predicting mortality in a prospective cohort of patients with sepsis requiring ICU management. *Critical Care, 17*(5), R114.

Reinhart, K., Bauer, M., Riedemann, N. C., & Hartog, C. S. (2012). New approaches to sepsis: Molecular diagnostics and biomarkers. *Clinical Microbiology Reviews, 25*(4), 609-634.

Ren, Y., Loftus, T. J., Datta, S., Ruppert, M. M., Liu, S., Guan, Z., & Bihorac, A. (2021). Performance of a machine learning algorithm using electronic health record data to predict postoperative complications and report on a mobile platform. *JAMA Network Open, 5*(5), e2211973.

Rhee, C., Dantes, R., Epstein, L., Murphy, D. J., Seymour, C. W., Iwashyna, T. J., & CDC Prevention Epicenter Program. (2017). Incidence and trends of sepsis in US hospitals using clinical vs claims data, 2009-2014. *JAMA, 318*(13), 1241-1249.

Rhodes, A., Evans, L. E., Alhazzani, W., Levy, M. M., Antonelli, M., Ferrer, R., & Dellinger, R. P. (2017). Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. *Intensive Care Medicine, 43*(3), 304-377.

Rudd, K. E., Johnson, S. C., Agesa, K. M., Shackelford, K. A., Tsoi, D., Kievlan, D. R., &

Naghavi, M. (2020). Global, regional, and national sepsis incidence and mortality, 1990-2017: Analysis for the Global Burden of Disease Study. *The Lancet, 395*(10219), 200-211.

Schuetz, P., Christ-Crain, M., Thomann, R., Falconnier, C., Wolbers, M., Widmer, I., & ProHOSP Study Group. (2011). Effect of procalcitonin-based guidelines vs standard guidelines on antibiotic use in lower respiratory tract infections: The ProHOSP randomized controlled trial. *JAMA, 302*(10), 1059-1066.

Seymour, C. W., Liu, V. X., Iwashyna, T. J., Brunkhorst, F. M., Rea, T. D., Scherag, A., & Angus, D. C. (2016). Assessment of clinical criteria for sepsis: For the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA, 315*(8), 762-774.

Shimabukuro, D. W., Barton, C. W., Feldman, M. D., Mataraso, S. J., & Das, R. (2017). Effect of a machine learning-based severe sepsis prediction algorithm on patient survival and hospital length of stay: A randomised clinical trial. *BMJ Open Respiratory Research, 4*(1), e000234.

Shimabukuro, D. W., Feldman, M. D., Barton, C. W., Das, R., & Mataraso, S. J. (2023). Effect of a machine learning-based alert system on sepsis mortality and length of stay: A prospective controlled clinical trial. *Critical Care Medicine, 51*(2), 225-234.

Singer, M., Deutschman, C. S., Seymour, C. W., Shankar-Hari, M., Annane, D., Bauer, M., & Angus, D. C. (2016). The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA, 315*(8), 801-810.

Solomkin, J. S., Mazuski, J. E., Bradley, J. S., Rodvold, K. A., Goldstein, E. J., Baron, E. J., & Bartlett, J. G. (2010). Diagnosis and management of complicated intra-abdominal infection in adults and children: Guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Clinical Infectious Diseases, 50*(2), 133-164.

Sweeney, T. E., Azad, T. D., Donato, M., Haynes, W. A., Perumal, T. M., Henao, R., & Khatri, P. (2018). Unsupervised analysis of transcriptomics in bacterial sepsis across multiple datasets reveals three robust clusters. *Critical Care Medicine, 46*(6), 915-925.

Vincent, J. L., Opal, S. M., Marshall, J. C., & Tracey, K. J. (2013). Sepsis definitions: Time for change. *The Lancet, 381*(9868), 774-775.

Wacker, C., Prkno, A., Brunkhorst, F. M., & Schlattmann, P. (2013). Procalcitonin as a diagnostic marker for sepsis: A systematic review and meta-analysis. *The Lancet Infectious Diseases, 13*(5), 426-435.

Wang, H., Zhang, P., Chen, W., Feng, D., Jia, Y., & Xie, L. (2012). Evidence for serum miR-15a and miR-16 levels as biomarkers that distinguish sepsis from systemic inflammatory response syndrome in human subjects. *Clinical Chemistry and Laboratory Medicine, 50*(8), 1423-1428.

Wirz, Y., Meier, M. A., Bouadma, L., Luyt, C. E., Wolff, M., Chastre, J., & Schuetz, P. (2018). Effect of procalcitonin-guided antibiotic treatment on clinical outcomes in intensive care unit patients with infection and sepsis patients: A patient-level meta-analysis of randomized trials. *Critical Care, 22*(1), 191.

Wong, A., Otles, E., Donnelly, J. P., Krumm, A., McCullough, J., & DeTroyer-Cooley, O. (2021). External validation of a widely implemented proprietary sepsis prediction model in hospitalized patients. *JAMA Internal Medicine, 181*(8), 1065-1070.

Wu, C. C., Lan, H. M., Han, S. T., Chaou, C. H., Yeh, C. F., & Liu, S. H. (2014). Comparison of diagnostic accuracy in sepsis between presepsin, procalcitonin, and C-reactive protein. *American Journal of Emergency Medicine, 35*(1), 1-5.

Conflict of Interest: No Conflict of Interest

Source of Funding: Author(s) Funded the Research

How to Cite: Meheswari, R. (2025). Early Identification of Sepsis in Post-Surgical Patients: Role of Biomarkers and AI-Based Monitoring Systems. *Journal of Clinical Medicine and Surgical Advance, 1*(1), 23-35.