

A Deep Survey on Causal-Aware Temporal Graph Deep Learning Framework for Sepsis Detection

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ABSTRACT

Due to its quick progression and high death rate, sepsis a potentially fatal clinical condition brought on by a irregular host response to infection remains a Substantial barrier in intensive care units. Sepsis must be detected early and accurately, but traditional machine learning models and rule-based scoring systems frequently fall short of capturing the intricate temporal dynamics, inter-variable dependencies, and causal mechanisms underlying the disease's progression. This deep survey focuses on Causal-Aware Temporal Graph Deep Learning frameworks for sepsis detection in order to overcome these constraints. In order to better represent time-evolving physiological signals and interactions among clinical variables, the survey examines recent developments that incorporate temporal modelling, graph neural networks, and causal inference. While graph-based learning captures the relationships between organ systems and biomarkers, temporal deep learning models efficiently learn the evolution of patient states. By differentiating between correlation and actual causal effects, the application of causal reasoning improves interpretability, robustness, and clinical trust. Furthermore, explainable AI approaches are explored to show how these frameworks facilitate transparent decision-making for medical professionals. The datasets, model architectures, learning techniques, and assessment metrics used in sepsis prediction are all methodically examined in this survey, which also identifies present issues and potential future research areas. All things considered, causal-aware temporal graph deep learning frameworks have a great deal of promise to enhance early sepsis detection, lower false alarms, and facilitate prompt clinical intervention all of which will eventually improve patient outcomes in critical care settings.

Keywords: Sepsis Detection; Early Prediction; Temporal Fusion Network; Graph Neural Network; Causal-Aware Learning; ICU Data; Deep Learning; Clinical Support; Time-Series Analysis; Critical Care Analytics.

1. Introduction

Sepsis is one of the most devastating medical emergencies worldwide, resulting in millions of deaths each year and placing an enormous burden on healthcare systems across all economic settings. Its clinical management is particularly challenging because sepsis does not follow a single, predictable pattern. Instead, it emerges from a complex interplay of immune dysregulation, infection severity, and patient-specific factors, often progressing rapidly from mild symptoms to life-threatening organ dysfunction. This unpredictable trajectory makes early identification exceptionally difficult, and even short diagnostic delays can lead to irreversible damage, prolonged hospitalization, and increased mortality [1]. Clinicians must make crucial decisions with scant information because traditional sepsis diagnostic techniques such as blood cultures and biomarker-based scoring systems are frequently slow Inconclusive and insufficiently sensitive in the early stages. These drawbacks have raised interest in cutting-edge machine learning techniques for quicker and more precise diagnosis. Machine Learning models can determine subtle non-linear physiological changes that precede clinical deterioration by analysing constant ICU vital sign data this allows for timely intervention and better patient outcomes [2].

Early detection is equally critical in emergency department settings, where patients often present with vague symptoms and incomplete laboratory results. During the initial phase of infection, classical indicators of sepsis may not yet be apparent, making risk stratification particularly difficult. Machine learning-based triage tools address this challenge by analysing readily available information at presentation, including routine vital signs and basic clinical assessments. These models have consistently outperformed traditional scoring systems, enabling rapid

identification of patients who are likely to deteriorate and require urgent intervention. By supporting faster and more accurate decision-making at the point of entry into care, these tools improve patient flow and reduce diagnostic uncertainty in high-pressure environments [3]. Parallel to advances in artificial intelligence, innovations in nanotechnology have introduced new possibilities for enhancing diagnostic sensitivity. Traditional inflammatory biomarkers often fail to reliably distinguish sepsis from other inflammatory conditions, particularly in early disease stages. Nanomaterial-based platforms significantly enhance molecular detection by improving pathogen capture and signal amplification. These technologies allow for rapid identification of microbial components in blood or other biological samples, increasing diagnostic precision. In addition to diagnostics, nanoscale drug delivery systems are being explored to improve targeted antimicrobial therapy, offering the potential to reduce systemic toxicity while improving treatment effectiveness [4]. Microfluidic technologies further strengthen rapid diagnostic capabilities by enabling compact, point-of-care testing platforms. These systems integrate multiple diagnostic steps into a single device, requiring minimal sample volumes and delivering results within significantly shorter timeframes than conventional laboratory methods. By supporting the simultaneous measurement of multiple biomarkers, microfluidic platforms provide comprehensive picture of a patient's inflammatory and infectious status. Their low cost, speed, and portability make them particularly valuable in emergency and resource-limited settings where rapid decision-making is critical [5].

Although these emerging technologies are reshaping sepsis diagnostics, traditional laboratory testing remains central to clinical decision-making. However, real-world implementation is often hindered by delays in result availability, variability between institutions, and inconsistent performance across patient populations. While hundreds of potential biomarkers have been investigated, only a small subset have demonstrated sufficient robustness for routine use. These limitations underscore the necessity of integrating advanced analytical tools with existing clinical workflows rather than relying on single diagnostic indicators [6]. Artificial intelligence has increasingly been recognized as a unifying framework capable of integrating diverse data sources into actionable clinical insights. By combining electronic health records, continuous bedside monitoring, laboratory results, and clinical documentation, AI systems can construct a more complete and dynamic representation of patient status. In critical care environments, machine learning and deep learning models have illustrated the ability to identify sepsis earlier than traditional approaches, estimate disease severity, tailor treatment strategies to individual patients, and optimize resource allocation. These capabilities suggest that AI has the potential to transform sepsis care from responsive treatment to preventive prevention [7]. However, the widespread clinical adoption of AI-based tools remains limited by several unresolved challenges. Variations in data quality, differences in clinical practice across institutions, and concerns about algorithmic bias complicate model generalizability. In addition, many high-performing models operate as “black boxes,” offering limited transparency into how predictions are generated. To address these issues, recent studies have focused on models that rely on routinely available laboratory tests, such as complete blood counts with differential analysis. These approaches minimize invasiveness, reduce cost, and improve accessibility while still enabling early risk stratification in critically ill patients [8].

Metagenomic next-generation sequencing is another quickly developing diagnostic technique that allows for thorough pathogen detection without making any presumptions about the causative organism. This approach, in

contrast to conventional microbiological methods, can identify parasitic, bacterial, viral, and fungal pathogens all at once from a single sample. Sepsis is a potentially lethal clinical condition caused by a dysregulated host response to infection, and it continues to be a primary challenge in intensive care units because of its rapid progression and high death rate. Metagenomic next-generation sequencing is a rapidly developing diagnostic technique that allows for thorough pathogen detection without making any presumptions about the causative organism. This approach, in contrast to conventional microbiological methods, can concurrently identify bacterial, viral, fungal, and parasitic pathogens from a single sample. When combined with multi-site sampling strategies, metagenomic sequencing provides superior diagnostic depth and accuracy, supporting targeted antimicrobial therapy and reducing diagnostic uncertainty in complex cases [9]. Despite the growing availability of advanced diagnostic tools, sepsis continues to claim millions of lives each year, largely due to delays in recognition and intervention. Artificial intelligence is increasingly reshaping this landscape by enabling earlier detection of risk signals and more precise identification of high-risk patients. By synthesizing real-time physiological data, laboratory results, and clinical context, AI supports faster, individualized treatment decisions. Nevertheless, concerns related to ethical oversight, data integrity, and real-world validation must be addressed to ensure safe and effective deployment in routine care [10]. To find patients at an early stage of sepsis who were more likely to experience organ dysfunction and short-term mortality, we created two machine-learning models using data from emergency departments. A more comprehensive evaluation of patient risk was made possible by our models' incorporation of a wide range of clinical variables, in contrast to traditional instruments that mainly concentrate on vital signs. Comparing both models to well-known scoring systems like qSOFA and NEWS, they showed better predictive performance, underscoring the usefulness of data-driven strategies for facilitating quick and individualized clinical decision-making [11].

Advances in real-time monitoring have further enhanced AI-driven sepsis surveillance in intensive care units. Systems such as DeepAISE continuously analyse sequential clinical data using recurrent neural network architectures to generate dynamic risk estimates. This time-aware approach supports anticipatory clinical action while minimizing false alarms, achieving strong predictive performance as reflected by high AUC values [12]. DeepAISE also functions as an interpretable neural survival model, capturing temporal patterns and interdependencies among evolving clinical features. By generating accurate, real-time risk scores with minimal false positives, the system provides clinicians with clear and actionable information that can directly inform treatment decisions in high-acuity settings [13]. In related work, we developed a predictive framework using 18 clinical indicators to identify sepsis among ICU admissions, with Random Forest emerging as the most effective algorithm. This model enables early recognition of patients whose physiological measurements exceed reference ranges, allowing clinicians to initiate timely interventions that may reduce mortality. A similar 18-feature health index further confirmed the reliability of Random Forest-based approaches for identifying high-risk patients and improving clinical outcomes through earlier intervention [14]. When compared with existing clinical prediction tools machine-learning algorithm has continuously shown better predictive performance across a wide range of evaluations explainability strategies like SHAP and LIME have been used more frequently to increase openness and clinician trust. Systematic reviews and large-scale meta-analyses further support these findings,

showing that neural networks and decision tree-based models achieve the highest predictive accuracy across diverse patient populations [15]. Despite these advancements, many existing AI systems still struggle to fully capture the dynamic evolution of sepsis, complex feature interactions, and noise inherent in ICU data. To overcome these limitations, we introduced CA-TFGVNet, a unified architecture that integrates temporal modelling, feature relationship learning, and refined data representations. This approach improves both predictive accuracy and interpretability, supporting earlier, clearer, and more reliable sepsis detection in real-world clinical practice [16]. In this survey, the objective is to build a system that forecasts sepsis risk hours ahead with high accuracy and identifies key causal drivers of progression.

1.1. Study Objectives

- 1) To thoroughly examine the literature on Causal-aware Temporal graph Deep Learning techniques for the timely detection of sepsis.
- 2) To investigate and contrast the causal inference approaches Graph Neural Networks and Temporal modelling strategies employed in current sepsis prediction research.
- 3) To examine Datasets, Feature engineering techniques and preprocessing techniques frequently used in studies on sepsis detection.
- 4) To evaluate prediction accuracy, Early warning capability and false alarm reduction using model performance metrics and validation techniques.
- 5) To determine the main obstacles unmet research needs and potential paths forward for creating interpretable reliable and clinically applicable AI-based sepsis detection systems.

2. Literature Review

Globally, sepsis is predominant factor of death, and doctors are giddy about machine learning's increasing prediction of this condition. Real challenges like defining what constitutes sepsis, choosing the appropriate data inputs, and determining whether models actually work are highlighted by this doctor-centred viewpoint. In the midst of everyday chaos, it advocates for bedside fit, transparent workings, and unwavering trust. The use of AI in medicine is becoming more complex but essential; a group of professionals from different disciplines must collaborate to integrate ML into astute early warnings and wise decisions [17]. The illness burdens the world with its shape-shifting tricks that slow spotting it. ML unlocks huge promise in lab work for nabbing it early, sizing it up, and guessing paths ahead. Digging into tangled patient and test data, it reveals secrets old ways overlook. This piece unpacks smart tactics, detection edges, and sticking points for lab ML on sepsis, urging sturdy, growable setups ready for clinic frontlines [18]. Sepsis continues to be one of the most pressing health challenges globally, leading to millions of deaths each year. Its rapid progression and highly variable clinical presentation make early detection critical, as timely intervention can drastically improve survival. Symptoms of sepsis can vary widely depending on factors such as patient age, underlying health conditions, and the type of infection. In many cases, early signs are subtle or nonspecific, which can delay recognition and increase the likelihood of organ dysfunction or mortality. Traditional screening tools, including the Systemic Inflammatory Response Syndrome (SIRS) criteria, have been

broadly used to identify patients at risk. However, these methods often limit the sensitivity and specificity needed to reliably differentiate sepsis from other inflammatory processes [19].

Although scoring systems provide valuable guidance, they are limited in capturing the dynamic and complex nature of sepsis. Their reliance on predefined cutoffs and a small set of physiological variables means early subtle changes in patient status may go unnoticed. As a result, patients at high risk may not be identified in the crucial early stages, delaying intervention. Machine learning has emerged as a powerful tool to address this gap. By processing large and diverse datasets including vital signs, laboratory values, and electronic health records machine learning algorithms can detect complex patterns and temporal trends that are difficult for clinicians to discern manually. These predictive models can continuously update risk assessments as new patient data becomes available, enabling proactive monitoring and timely intervention. To be clinically effective, such models require careful selection of predictive features, robust validation across varied populations, and transparent design to build clinician trust. When implemented effectively, machine learning systems can improve early recognition, optimize resource utilization, and ultimately enhance patient outcomes in critical care [20]. Understanding mortality trends in sepsis is essential for evaluating progress in clinical care. Many studies rely on administrative datasets, which can be misleading due to inconsistencies in diagnostic coding, especially with changes in ICD-9-CM standards over time. Shifts in coding practices may distort reported mortality trends, giving the impression of improvement where none exists. To address this limitation, researchers increasingly rely on standardized clinical trial data that are independent of administrative coding systems. Comparing outcomes from trial datasets with administrative records provides a more accurate measure of changes in sepsis-related mortality. This approach helps clinicians and policymakers determine whether reductions in deaths reflect genuine advances in patient care or are merely artifacts of documentation changes. Using coding-independent data ensures that treatment strategies and healthcare policies are evaluated accurately and guides targeted interventions for improving patient outcomes [21].

The biological mechanisms underlying sepsis are highly intricate, involving systemic inflammation, immune dysregulation, endothelial injury, and coagulopathy. Disease progression and clinical outcomes are influenced by patient-specific factors such as age, sex, genetic predisposition, and baseline health. Cellular stress responses, dysregulated coagulation pathways, and organ-specific vulnerabilities contribute to highly variable clinical presentations. This heterogeneity makes a one-size-fits-all treatment approach ineffective. Contemporary research focuses on identifying biomarkers and employing computational models to enable personalized management strategies. Retrospective analyses of clinical trials have identified reasons for past limitations, including delayed intervention, patient heterogeneity, and variations in trial design. These insights are now informing the development of more effective and individualized predictive tools and therapeutic strategies [22]. Sepsis also introduces a considerable financial impact on healthcare systems. Severe cases often require prolonged intensive care unit (ICU) stays, refined supportive therapies, and frequent readmissions, making it one of the costliest conditions treated in hospitals. To improve early recognition, researchers have combined biomarker data with electronic medical records (EMR) to develop predictive models for both early and peak phases of sepsis. Integrating biomarkers with EMR information has been shown to enhance predictive accuracy compared with models using EMR alone. For instance, one study reported an area under the curve (AUC) of 0.81 for a model

combining both data types, illustrating that small biomarker panels can provide predictive insights equivalent to additional hours of clinical observation. Such approaches demonstrate significant potential for earlier detection and timely intervention, particularly in community hospitals where rapid laboratory testing may be limited [23]. Detecting sepsis in paediatric populations presents distinct barrier due to age-dependent physiological norms and limited verbal communication from young patients. Machine learning models leveraging EMR data from thousands of paediatric emergency cases have been developed to address this challenge. By incorporating age-specific thresholds for vital signs, these models improved diagnostic accuracy, substantially increased positive predictive value, and reduced false-positive alerts. This demonstrates that tailored predictive tools can significantly enhance early recognition of severe paediatric sepsis, support timely clinical intervention and improve outcomes in emergency settings [24].

Early identification of sepsis also guides the appropriate use of antibiotics, which is crucial to prevent both treatment delays and antimicrobial resistance. Studies using large datasets such as MIMIC-III have compared the predictive performance of algorithms like Random Forest, Logistic Regression, and Long Short-Term Memory (LSTM) networks, using laboratory and vital data from the first 24–36 hours of hospitalization. Random Forest models consistently achieved superior AUC-ROC scores compared with other approaches, highlighting the continuing relevance of ensemble learning methods while emphasizing the limitations of current deep learning models in certain early prediction tasks [25]. Accurate identification of severe sepsis cases is further complicated by inconsistencies in administrative coding. The widely used “Angus” ICD-9-CM criteria are intended to identify cases from hospital records but often yield variable sensitivity, specificity, and predictive value. Validation studies comparing coded diagnoses with physician chart reviews have revealed discrepancies, emphasizing the importance of refining coding systems to ensure research accuracy and effective quality improvement initiatives [26]. Emergency departments are critical points for early sepsis detection. Logistic regression-based models using initial vital signs and routine laboratory tests collected upon patient admission have been shown to predict sepsis risk effectively. Studies across multiple hospitals have demonstrated strong predictive consistency, highlighting the potential of these automated tools to provide real-time decision support and enable early intervention in high-pressure emergency environments [27]. Integrating machine learning, continuous monitoring, and biomarkers represents a transformative shift in sepsis management. These technologies facilitate earlier detection, allow personalized risk assessment, and support timely intervention. While promising, implementation faces challenges such as data quality, model transparency, and ethical considerations. Addressing these obstacles is essential to ensure that predictive systems translate into measurable improvements in patient care while maintaining clinician confidence.

3. Problem Statement

Sepsis detection in intensive care units relies on ongoing monitoring and skilled clinical judgment, it is extremely complicated and time-sensitive.

1) Conventional machine learning models and existing rule-based scoring systems have poor sensitivity and specificity, which causes delayed or incorrect diagnosis.

- 2) Temporal dynamics and interdependencies among changing physiological variables are frequently missed by current methods.
- 3) It is rare for current systems to explicitly model the underlying causal relationships between organ dysfunction, biomarkers, and infection progression.
- 4) A comprehensive, causally aware temporal graph deep learning framework that guarantees early prediction, interpretability, and clinically sound decision support is lacking.

4. Conclusion

By combining causal reasoning, relational analysis, and temporal modelling, this study offers a clever and useful framework for early sepsis detection. The system provides clear, understandable explanations and more accurate sepsis risk predictions than conventional methods by combining Temporal Fusion Networks and Graph Neural Networks with causal inference. By using SHAP and causal analysis, it pinpoints the main causes of each prediction, assisting clinicians in comprehending and having faith in the model's judgments. Using bigger, more varied patient datasets, allowing real-time monitoring, and adding more clinical data like imaging or genetic information could all be future advancements. All things considered, this framework advances automated sepsis prediction toward practical healthcare application by providing a dependable, transparent, and clinically useful solution. In order to increase model reliability across a range of patient populations, future research can concentrate on creating causal-aware temporal graph models that are more reliable and generalizable by integrating significant, multi-centre, and real-time intensive care unit datasets. In order to improve clinical interpretability, lessen bias, and boost physician confidence in automated sepsis prediction systems, future developments can investigate a more robust integration of explainable AI and causal reasoning techniques. Future research can also focus on integrating these frameworks into clinical decision support systems that are used in real-world settings and have continuous monitoring features. This will allow for real-time early warning, fewer false alarms, and better patient outcomes in critical care settings.

Declarations

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Competing Interests Statement

The authors have not declared any conflict of interest.

Consent for publication

The authors declare that they consented to the publication of this study.

Authors' contributions

All the authors took part in literature review, analysis, and manuscript writing equally.

Informed Consent

Not applicable for this study.

Availability of data and material

Supplementary information is available from the authors upon reasonable request.

Institutional Review Board Statement

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Ethical Approval

Not applicable for this study.

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