Editorial

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AI integration in sepsis care: a step towards improved health and quality of life outcomes

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Introduction

Sepsis is a life-threatening condition caused by the body's dysregulated immune response to infections, which may lead to body-wide inflammation, tissue damage, organ failure, and even death[1]. The characteristic features include tachycardia, tachypnea, hypotension, tissue hypoxia, delirium, etc. Septic shock is the last stage of sepsis. High-risk individuals include the elderly, children, and patients with compromised immune systems[1]. In US hospitals, sepsis is the third most common cause of death. In 2019, it accounted for more than 75% of deaths aged 65 or above[2]. Early diagnosis, identification of underlying etiology, and timely therapeutic interventions play crucial roles in sepsis management. Time is the most critical factor as with each 1 h treatment delay, mortality increases by 8%[3].

Early diagnosis still poses an obstacle in initiating early treatment therapies. Several blood tests are performed to diagnose the underlying etiology but no single diagnostic test is 100% certain. These diagnostic tests include blood culture tests, and blood levels of essential biomarkers such as procalcitonin (PCT), lactate, cytokines, and C-reactive protein, etc[4]. Essential biomarkers are also used to assess the efficacy of the treatment regimen[5].

Treatment strategies for sepsis include the use of antibiotics within the first few hours of septic shock or sepsis with no shock, fluid therapies to treat hypotension and maintain adequate tissue perfusion, removal of abscess or any dead tissue[6], vasopressors if blood pressure does not resolve[4], supportive care such as mechanical ventilation for respiratory failure and renal therapies for acute kidney injury[4]. Immunomodulators can also be used as sepsis dysregulated immune response, so with agents like corticosteroids immune response can be altered[4].

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Artificial intelligence in critical care

The need for early detection of sepsis has encouraged researchers to make use of sophisticated analytical tools such as artificial intelligence (AI)[7]. AI makes machines capable of simulating intelligence and endows machines with human-like capabilities such as learning, reasoning, problem-solving, and decision-making. AI algorithms such as machine learning and deep learning are being harnessed for early detection and alerting physicians to impending sepsis. The application of AI as an early warning system earned a significant role in critical care.

Researchers at John Hopkins University developed an ML-based Targeted Realtime Early Warning System (TREWS)[7] that detects symptoms hours before than most traditional methods. TREWS first combines the medical history of patients with current symptoms and lab values to predict the likelihood of sepsis hours before and then suggests the antibiotic regimen. TREWS, first deployed in 2018, has achieved an AUC (Area under the curve) of 0.97 and significantly reduced the mortality rate. Previously an algorithm, ESM (Epic sepsis model)[8], was introduced as an analytical tool for sepsis prediction. The ESM was validated in retrospective study involving 27 697 patients who underwent 38 455 hospitalizations at Michigan Medicine, between 6 December 2018 and 20 October 2019. The study population included 7% (2552) sepsis patients. During initial validation, the ESM demonstrated poor discriminative ability for predicting sepsis onset, with an AUC of 0.63 (95% CI). However, sensitivity analysis that included model scores up to 3 h postsepsis onset demonstrated improved discriminative ability with an AUC of 0.80 (95% CI) indicating that ESM is better at detecting sepsis concurrently or shortly after clinical diagnosis rather than providing an early prediction about sepsis onset.

In Adams *et al.*'s study[7], the outcomes for 6877 sepsis patients, including 2366 high-risk patients, who had a TREWS alert prior to receiving antibiotics regimen were retrospectively analyzed. Patients with confirmed TREWS alerts and antibiotics therapy within 3 h of alert had 3.3% adjusted absolute risk reduction (ARD) and 18.7% adjusted relative risk reduction (RRR) with 95% CI for in-hospital mortality. Patients with confirmed TREWS alerts and antibiotic regimen within 3 h of alert also had better SOFA (Sequential Organ Failure Assessment) scores indicating reduction in organ failure progression and shorter duration of hospital stay. Adams *et al.* study demonstrated the benefits of early intervention following TREWS alerts. The high-risk cohort had more pronounced improvements in SOFA scores along with 4.5% (95% CI) ARD and 13.19% (95% CI) RRR in patients with confirmed alerts within 3 h for in-hospital mortality as compared to high-risk patients with no confirmed alerts.

Recently, SepsisFinder[9], another ML-based model was developed to predict the sepsis onset. SepsisFinder was validated using electronic health record (EHR) data consisting of 8038 sepsis cases classified as per Sepsis-3 criteria. The cohort was divided into a training set (67.9%) and a validation set (32.2%). On Validation dataset, the SepsisFinder demonstrated better discriminative abilities with an AUC of 0.95 (95% CI) than traditional scoring system, NEWS2 (National Early Warning Score) and gradient boosting decision tree (GBDT). SepsisFinder also predicted sepsis-onset earlier than NEWS2 and GBDT, that is, median 7.3 h before onset.

Although, TREWS[7] and SepsisFinder[9] holds promises for improving critical care in hospitals. However, notable limitations of the validation studies include single-centered and observational nature lacking randomization. As the control group lacks patients without sepsis, it may have included patients with no sepsis to avoid any selection bias to influence the study's findings[7]. Therefore, there is need for randomized control trials (RCTs) to validate benefits of these ML models. Additionally, the FDA[10] only clears 'locked' AI algorithms (algorithms with core structure, training methods or data sources not alterable by end-users and give same results when same input applied each time) and both TREWS and SepsisFinder are propriety algorithms, which may make large-scale implementation of these alert systems challenging. Additionally, the cost-effectiveness of these models must be evaluated to prevent overpricing which may keep hospitals from purchasing these devices.

In conclusion, sepsis is associated with high mortality rates. Early diagnosis and treatment are the key to reducing sepsis-related deaths and improving patient outcomes. The potential of advanced analytical AI tools can be harnessed for early prediction of sepsis onset. In retrospective studies, machine learning models namely TREWS and SepsisFinder demonstrated better performance in early prediction of sepsis onset. These AI systems may help improve health outcomes and quality of life in patients with sepsis. However, further research is required to realize the full benefits of these machine learning techniques to solve the mystery of sepsis in emergency management.

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