IMPACT OF EARLY SEPSIS RECOGNITION AND MANAGEMENT IN THE EMERGENCY DEPARTMENT

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Abstract

Sepsis represents a frequent occurrence in the emergency department and a leading cause of admissions to intensive care units as well as mortality. Early management of sepsis and septic shock is pivotal for patient prognosis. Given that the Emergency Department (ED) serves as the initial point of contact for septic patients, emergency physicians hold a fundamental role in the early stages of patient care, involving accurate initial diagnosis, resuscitation, and prompt treatment. Assessing the patient's volume status, optimal hemodynamic resuscitation, and monitoring the patient's response are critical aspects of sepsis management in the emergency department. Close monitoring of vital signs, laboratory parameters, and treatment response is vital for guiding subsequent management decisions. Collaboration with other specialties such as critical care, infectious disease, and surgery is often necessary for comprehensive management of septic patients. Timely recognition and intervention in the ED can significantly influence patient outcomes and alleviate the burden of sepsis-related morbidity and mortality. Hence, continuous education and training of emergency physicians in sepsis management are essential for enhancing patient care and outcomes.

Keywords: Sepsis, Emergency Department, Septic Shock, Management, Mortality.

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Introduction

Sepsis is a major issue in many hospitalizations that result in death [1]. The majority of sepsis cases appear to occur outside of hospital settings [2], and these patients often report to ERs with a variety of symptoms, making diagnosis and detection difficult [3]. In the United States in 2011, sepsis accounted for 6.2% of all hospital expenses and was a leading cause of mortality.

Over the past several years, research and discussion have centred mostly on new sepsis definitions and early antibiotic therapy; however, issues linked to treatment delays in emergency rooms have gotten less attention. Sepsis is not identified early enough [4] and systematic screening and diagnostic processes for identifying it are not consistently carried out in accordance with current standards, according to previous research, which is primarily based on single case studies and smaller patient cohorts. Large-scale epidemiological research conducted recently shown that although sepsis mortality has declined, incidence is still rising. Timely identification of sepsis is crucial for effective treatment [5], and adhering to sepsis guidelines is linked to better results [6]. Since the relationship between the promptness of diagnostic tests and the duration of therapy has not been examined, the actual frequency of sepsis is probably underestimated.

Sepsis was designated as a global health priority by the World Health Assembly (WHA) and World Health Organization (WHO) in May 2017, and they enacted a resolution urging the 194 UN Member States to enhance sepsis prevention, diagnosis, and management [6]. Rivers et al. published their ground-breaking early-goal directed treatment (EGDT) trial in 2001. Nevertheless, EGDT did not lower the sepsis mortality rate when compared to standard treatment, according to three further multicenter randomized controlled trials (RCTs)[7]. The European Society of Intensive Care Medicine (ESICM) and the Society of Critical Care Medicine (SCCM) have released updated definitions of sepsis that are intended to aid in early detection and screening.

Nevertheless, prospective studies are still needed to confirm their advantages, and doctors still emphasize the need of administering antibiotics and fluids early on in the first resuscitation of sepsis patients. Increasing our understanding of these correlations may help with the numerous people who are brought to emergency rooms with sepsis and their first management. Furthermore, solid data demonstrating the degree to which diagnostic tests are postponed or neglected for sepsis patients who arrive at the emergency department are required [8].

Changes to the definition of sepsis:

Since 1992, the definition of sepsis has undergone several revisions. In 2016, the SCCM and ESICM updated the definitions of sepsis and septic shock, focusing on the dys-regulated host response to infection and organ failure. According to the revised criteria (Sepsis-3), patients with an increase of more than two Sequential Organ Failure Assessment (SOFA) points are classified as having sepsis. Septic shock is defined as refractory hypotension requiring vasopressors along with concomitant hyper-lactatemia (>2 mmol/L) despite adequate fluid resuscitation. The recommendations excluded severe sepsis, and rapid SOFA (qSOFA) was used for screening instead of the systemic inflammatory response syndrome (SIRS) [9].

The Sepsis-3 criteria were initially evaluated in derivation and validation datasets based on a large database. However, there are several issues with the criteria, and several organizations have not endorsed them. Firstly, the definition of sepsis did not consider lactate levels. Therefore, individuals with elevated lactate levels but no hypotension (or compensated septic shock) may be overlooked according to the Sepsis-3 criteria. In other words, people in the early stages of sepsis may go unnoticed. In a previous multicenter study, the prevalence of this phenotype (normotensive individuals with hyper-lactatemia) was 26% [10].

The Sepsis-3 data showed a 9.9% prevalence of normotensive hyper-lactatemia (>4 mmol/L), yet the 29.9% mortality rate was significant. This has led to doubts about the validity of the Sepsis-3 definitions. Additionally, as per the Sepsis-3 criteria, septic shock can only be diagnosed when both hyper-lactatemia and the need for vasopressors occur simultaneously. This means that until the patient experiences hypotension, the lactate level is not considered in the criteria. Moreover, in the absence of knowledge about the lactate level, an infected patient with hypotension might not be diagnosed with septic shock. This suggests that in resource-limited settings where lactate levels are not regularly available, the usefulness of the Sepsis-3 criteria is limited. Therefore, further prospective research is necessary to validate the Sepsis-3 criteria. Until then, it seems appropriate to continue using the current sepsis criteria [11].

Clinical Criteria for Sepsis

There is a documented correlation between sepsis screening and a lower death rate. In order to

enhance the early detection and treatment of sepsis, regular screening of possibly infected individuals who are likely to be septic is emphasized in both the 2012 and 2016 surviving sepsis campaign (SSC) guiding lines. They advise hospitals to implement a performance-based initiative that includes sepsis early detection and treatment. Since 1992, sepsis patients have been screened for and identified using the SIRS criteria. At least two of the four SIRS criteria need to be satisfied in order to diagnose sepsis. Nevertheless, SIRS is not specific enough for sepsis and can be induced by a number of infectious and noninfectious sources, making it too sensitive. As a result, some patients may meet SIRS criteria but not necessarily have sepsis, and vice versa. The Sepsis-3 Task Force replaced the idea of SIRS with qSOFA for sepsis screening in this situation. With just three factors, the qSOFA is a condensed version of the SOFA score. Patients with a qSOFA score of ≥2 should be evaluated for sepsis. With no need for laboratory testing, the qSOFA is a widely available instrument for use at the bedside that performs better in non-intensive care units (ICUs) than in ICUs. Its application in identifying infected patients outside of the ICU who are likely to be septic was suggested by the Sepsis-3 Task Force. A qSOFA score of ≥2 has a high specificity for organ dysfunctions, according to a recent prospective research, but its low sensitivity may restrict its utility as a bedside tool. The SIRS criteria are still applicable, according to the authors. Clinical data suggests that clinical indications or symptoms of acute deterioration or sepsis appear in individuals many hours before the situation deteriorates [12].

To identify patients who are at a high risk of worsening, early warning scores were created, such as the National Early Warning Score (NEWS), Early Warning Scoring System (EWSS), and Modified Early Warning Score (MEWS). These scores demonstrated a trend towards better outcomes, despite the lack of strong evidence based on solid data. When combined with an outreach service (such as rapid response teams or medical emergency teams), they make it easier to start the best treatments as soon as septic patients are identified. While respiratory or cardiac issues were the most frequent reason for these outreach teams to be activated, a research indicated that sepsis was the cause of activations in 19.9% of cases, and Early goal-directed therapy (EGDT) was used in 22.7% of cases. Remarkably, Churpek et al. examined a number of early warning scores—including qSOFA—among patients who weren't in the intensive care unit. When it came to predicting in-hospital death or ICU transfer, qSOFA outperformed SIRS, MEWS, and NEWS in terms of specificity and sensitivity. The SIRS criterion (≥2) yielded faster patient identification results than qSOFA. Consequently, the SIRS criteria are a sensitive and practical bedside tool for sepsis screening outside of the ICU, and the use of qSOFA may be premature [12].

Laboratory Findings

Evidence of organ dysfunction is more clinically useful in diagnosing the septic patient than SIRS criteria alone. The information utilized to determine the SOFA score is derived from serum laboratory monitoring, which is the most reliable method of identifying signs of organ failure. A complete blood count (CBC), comprehensive metabolic panel (CMP), lactic acid level, coagulation studies, and blood cultures are routine tests used to assess patients for sepsis. Additionally, cultures from questionable sources (such as sputum, urine, wounds, etc.) must to be collected and examined [13].

To assess the patient's acid-base balance and oxygenation, arterial blood gases can be taken. Only laboratory findings that specifically identify the causal pathogen are relevant to sepsis. In the absence of these, laboratory data are utilized to demonstrate organ function, oxygenation and volume status, and inflammation [13].

Leukocytosis, bandemia, thrombocytopenia, anemia, and hemoconcentration can all be assessed using the complete blood count (CBC). Hyperglycemia, renal and/or hepatic function, and electrolyte abnormalities can all be assessed with the CMP. In the absence of diabetes, a glucose level higher than 140 mg/dL is consistent with increased physiologic stress brought on by systemic diseases like sepsis. Even in the absence of hypotension or other indicators of shock, hyper-lactatemia with levels higher than 2 mmol/L can be a major signal of tissue hypo-perfusion [13]. When the activated partial thromboplastin time exceeds 60 seconds or the internalized normalized ratio is more than 1.5, coagulopathies can be recognized [8].

Prompt Interventions and Ideal CPR

The EGDT was developed to monitor central venous oxygen saturation (ScvO2, >70%), central venous pressure (8–12 mm Hg), mean arterial pressure (MAP, ≥65 mm Hg), and urine output continuously in order to diagnose sepsis early and optimize hemodynamic parameters in a timely manner. When given to patients with septic shock or severe sepsis prior to ICU admission, this protocolized therapy considerably lowered the in-hospital mortality rate and decreased the

frequency of multi-organ dysfunction when compared to conventional care [7].

Nonetheless, there was no discernible survival advantage over standard treatment in three multinational multicenter studies (Protocolized treatment for Early Septic Shock, Australasian Resuscitation in Sepsis Evaluation, and Protocolized Management in Sepsis). Additionally, the EGDT was linked to higher hospitalization costs rather than better outcomes than normal care in a meta-analysis of individual participants in the three RCTs [12].

As a result, the 2016 standards compromised the EGDT idea. However, patients in the standard care groups got a significant amount of fluids in these three RCTs, demonstrating the continued emphasis on first fluid resuscitation with crystalloids. When balanced crystalloids were used instead of saline, the rates of all-cause mortality, chronic renal insufficiency, and new dialysis treatments were considerably reduced. Instead, the 2016 recommendations place more emphasis on reassessing tissue perfusion and volume status following the first fluid resuscitation. This is due to a clear correlation between a greater death rate in sepsis patients and the maintenance of a positive daily fluid balance over an extended period of time. In this regard, the guidelines recommend measuring CVP, ScvO2, bedside cardiovascular ultrasound, and dynamic assessment of fluid responsiveness with passive leg raise or fluid challenge, or repeating assessments of vital signs, cardiopulmonary status, capillary refill time, pulse, and skin findings [14].

According to a population-based study conducted in the US, a decreased in-hospital mortality rate was linked to early central vein catheterization [15]. The three EGDT RCTs did, however, show that if septic patients received enough fluids and antibiotics on time, there was no advantage to invasive hemodynamic monitoring using CVP and ScvO2. Consequently, treatment CVP and ScvO2 objectives are not pre-specified in the 2016 SSC recommendations. CVP is not a reliable indicator of the fluid response and does not accurately reflect intravascular volume status. Instead, echocardiography provides a noninvasive way to evaluate the volume status in patients on mechanical ventilator support, and frequent measures of lactate (i.e., lactate clearance) allow assessment of the response to initial resuscitation [12].

The in-hospital mortality rate rises when empirical antibiotics are not administered promptly once sepsis is identified. According to a recent study by Liu et al, [16] individuals who got antibiotics within six hours had a higher risk of dying in the hospital if the medicines were started one hour later than planned. As a result, the SSC recommendations advise injecting empiric antibiotics intravenously after receiving blood culture findings within an hour. It is advised to treat with one or two broad-spectrum antibiotics and to de-escalate treatment as soon as clinical improvement or pathogen non-detection occurs.

Vasopressors are a part of the 6-hour sepsis bundle and are associated with a higher survival rate in patients with septic shock. Therefore, when initial fluid resuscitation fails to improve hypotension, norepinephrine should be given as the first line of treatment as soon as possible to maintain a mean arterial pressure of 65 mm Hg. Targeting a MAP of 80–85 mm Hg as opposed to 65–70 mm Hg did not improve the survival rate of patients with septic shock in an open-label randomized controlled trial [17]. Therefore, the goal MAP should be chosen based on the patient's state; patients with chronic hypertension may require a higher target, whereas those with uncontrollable bleeding due to trauma may require a lower target [12].

A target heart rate is not specified in the SSC recommendations for individuals with septic shock. But because tachycardia has so many negative repercussions, such diastolic dysfunction and myocardial ischemia, patients with septic shock should have their heart rates kept below normal limits. Recent research by Morelli et al. [18] showed that esmolol can be used to safely lower heart rate (target rate, 80–94 beats/min) without increasing adverse effects. It was also linked to a lower norepinephrine dosage and a lower death rate in septic shock patients when compared to the control group. More extensive research should be done to confirm these findings.

Fluid therapy

The first-line treatment for individuals experiencing septic shock is fluid delivery in conjunction with antibiotic therapy. By increasing the volume of stressed blood, this therapy aims to address hypovolemia. This will enhance cardiac preload and venous return, which will boost CO and, eventually, oxygen delivery. However, half of the patients would ultimately stop responding to fluid stimuli after the first stages of resuscitation. In this case, administering a fluid bolus might exacerbate the organ perfusion pressure by causing fluid buildup, reduced DO2, and impaired venous return. As a result, over time, several tests have been created to forecast a patient's fluid reactivity in septic shock cases. The passive leg raising (PLR) test is widely accepted among them due to its ease of use and special suitability for the

emergency department. A volume of approximately 300 mL of blood is delivered to the ventricles by lifting the patient's legs to a 45° position and lowering the trunk, which raises the cardiac preload. When a patient's CO rises by 10% or more above baseline, it is said that they are preload responsive and can exhibit an increase in CO after fluid is administered. It is advised to use a technique of continuous CO monitoring in order to identify the effects of a PLR test. But it's crucial to remember that every patient diagnosed with septic shock and admitted to the emergency department (ED) needs to be treated with a fluid bolus right away and be deemed fluid responsive [19].

In this regard, a heated discussion among practitioners was prompted by the 2016 SCC recommendations, which suggested a fixed dosage of 30 mL/kg of crystalloids within the first three hours. One may argue that, for a time-dependent illness like septic shock, the three hours prior to patient reevaluation was excessively long. However, the suggested dosage of fluid was thought to be very high and scarcely appropriate for all individuals [20].

The absence of reliable evidence to back up these suggestions further validated these worries. In order to address the necessity for septic patients to receive therapy right away, the 2018 SCC bundle update replaced the previously advised 3- and 6-hour bundles with an hour-1 bundle, which helped to partially settle this dispute. However, despite widespread support, no modifications to the protocol were implemented to allow for more personalized fluid delivery. Regarding this, Teboul and Monnet have recently suggested that, while closely monitoring the patient, begin fluid administration with an infusion of approximately 10 mL/kg within the first 30 to 60 minutes [21].

If the patient's tachypnea gets worse or their oxygen saturation drops, they should take less fluid. On the other hand, if symptoms such as skin mottling, elevated capillary reflectance time, or low arterial pulse pressure persisted after starting fluid therapy, then an increase in the infusion rate has to be taken into account. This strategy was completely supported because that the choice to prolong fluid administration should be made based on the patient's unique risk/benefit ratio and that the benefits of additional fluid infusion should be assessed utilizing dynamic assessments of preload response [22].

Antimicrobial Initiation

The first empirical antimicrobial treatment need to be comprehensive enough to address microorganisms identified in illnesses linked to healthcare settings. For first therapy, a broad-spectrum carbapenem such doripenem, imipenem/cilastatin, or meropenem is advised. One may also take into consideration an extended-range penicillin/b-lactamase inhibitor combination, such ticarcillin/clavulanate or piperacillin/tazobactam. Adding a third- or higher-generation cephalosporin should be taken into consideration if a multidrug regimen is necessary. For critically sick septic patients, an additional gram-negative agent is advised in addition to those already listed [23].

When MRSA is known or suspected, as in the case of cellulitis, vancomycin or another anti-MRSA drug should be administered. The addition of a macrolide or fluoroquinolone is most appropriate if Legionella is detected. The choice of antifungal medication should be tailored to the severity of the presenting illness if it is thought that the possibility of Candida being the cause of sepsis [23].

Vasopressors

The Sepsis-3 definitions state that the need for vasoactive medications is a clinical indicator of septic shock patients. Regarding this, the 2018 SSC bundle and the 2016 SSC recommendations both advise the early use of vasopressors in hypotensive septic patients in order to reverse the significantly reduced arterial tone [23].

Norepinephrine

The first-line vasoactive drug in the treatment of individuals experiencing septic shock is norepinephrine (NE). Its vaso-constrictive effect is primarily mediated by activating α1-adrenergic receptors, with minimal impact on heart rate [24].

A number of established rationales have contributed to the rising body of evidence supporting the necessity of early NE treatment in septic patients throughout time. The first and most evident is that patient prognosis is improved by either stopping or correcting hypotension, as persistent hypotension is one of the major risk factors for death [25].

The activation of α1-receptors on the venous side causes venous constriction and raises the volume of stressed blood, which is another argument in favor of early NE delivery [26]. Improved cardiac preload and increased venous return result from this. Notably, administering fluid in these circumstances ought to be more effective since it would be carried out in a higher pressurized venous system, which would operate on the stressed volume and, in the end, lower the dosage administered. Finally, cardiac contractility can be increased by NE injection because cardiac β1-

adrenergic receptors are still present on cardiac cells during the early stages of septic shock. The beneficial effect of NE is further enhanced by a concurrent rise in diastolic arterial pressure, or the left ventricular coronary artery perfusion pressure [27].

Several investigations have assessed the impact of early NE therapy in individuals with septic shock. Colon-Hidalgo and Bai's two retrospective investigations have demonstrated that the interval between NE onset and death is a reliable indicator of mortality. In this sense, early NE administration and NE administration only after fluid treatment has failed have been directly compared in the CENSER experiment. According to the trial's findings, early NE delivery is linked to better shock management throughout the first six hours (the primary outcome) [27].

It is generally agreed upon that NE should be administered at a dose that is titrated to achieve a mean arterial pressure of 65 mmHg. However, it's unclear if aiming for greater levels is a good idea. The SEPSISPAM research, which examined 65 mmHg vs. 85 mmHg as MAP targets, found no statistically significant differences in mortality in this aspect. Nevertheless, a higher MAP goal had a positive impact on renal function when the subgroup of individuals with a history of arterial hypertension was examined. Therefore, in patients suffering from septic shock and arterial hypertension, a task force of the European Society of Intensive Care Medicine (ESICM) has suggested that the first blood pressure objective be a MAP value greater than 65 mmHg. The usage of a second vasopressor is suggested when NE dosages more than or equal to 1 μg/Kg/min are necessary to treat refractory hypotension [27].

Other vasoactive agents

The 2016 SSC recommendations recommend adding vasopressin, a vasoactive drug, to normal extracorporeal shock (NE) in cases of refractory shock. This is done by decreasing adrenergic tone and increasing vasoconstriction via distinct receptor activation. In this regard, a meta-analysis revealed that while there were no differences in mortality, the risk of arrhythmic events, such as atrial fibrillation, was lower when vasopressin was linked to NE than when NE was used alone. But it's crucial to remember that not all nations have access to vasopressin [28].

Another second-line vasopressor that the 2016 SSC recommends using in the event of concomitant cardiac failure is epinephrine. The data that is currently available, however, indicates that there was no difference in patient survival between patients treated with NE plus dobutamine and those treated with epinephrine alone [23].

As per the previous guidelines, dopamine should not be used as a vasopressor or a renal protective medication at low dosages when managing septic patients. Compared to NE, it has been demonstrated that using it is linked to a higher risk of cardiac arrhythmias and death. At the moment, bradycardia is the only condition in which its usage is advised [29].

Time is of the essence

Time is one of the most crucial factors in fluid resuscitation. Delays in fluid resuscitation have been linked to death, according to several studies. This was corroborated by a cohort trial including 11,182 sepsis patients, which showed that administering fluids within 30 minutes of diagnosis reduced death. In the 30-minute group, the death rate was lower (24.5%). In a recent study, fluid delivery enhanced microvascular perfusion in the early phase of sepsis but not in the late phase, when the effects of Ringer's lactate solution or 4% albumin on the microvascular circulation were assessed. This provided reassurance that time is probably more crucial than the kind of fluid utilized.

Inter-professional Exchange of Information

Enhancing communication among all medical professionals attending to a septic patient also enhances the promptness, effectiveness, and general standard of treatment. The patient's appearance, any family members or next of kin who may be with them, the results of any diagnostic tests conducted, the treatments administered, and the patient's reaction to those therapies should all be shared with inpatient carers by carers starting therapy in the emergency department. Evaluation of sufficient source control can be facilitated by test findings that are relevant and may indicate the infectious source that inpatient providers are informed about. Moreover, the patient's reaction to fluid or vasopressor resuscitation is pertinent data that aids in maintaining continuity of treatment. Finally, but just as importantly, ED physicians should make sure the patient's family is included in the treatment plan and that their desires are conveyed in hand-off reports.

Conclusion

Patients with septic shock, severe sepsis, or both, have a high in-hospital mortality rate and an increased risk of organ failure and death. Prevention and early detection of sepsis are crucial until new emergency medications or therapies are

shown to be effective. Improving patient outcomes requires early implementation of the best medicines and increased adherence to sepsis bundles. Even with this increasing understanding, emergency physicians still face difficulties in managing septic shock, particularly in the early stages of therapy and diagnosis. Therefore, it is critical that emergency physicians understand the most recent developments in the care of septic patients. Future research on sepsis should examine the usage of an early consultation system and specialised hand-off communication tool for ED and critical care professionals in order to promote a seamless transfer of treatment, as the field of sepsis research continues to advance.Future research should also focus on developing new diagnostic tools and technologies to aid in the early identification of sepsis, as well as the development of targeted therapies to improve patient outcomes. Collaboration between emergency medicine and critical care teams will be essential in advancing the field of sepsis research and improving patient care. It is crucial for emergency professionals to stay updated on the latest evidence-based practices and guidelines for managing sepsis in order to provide the best possible care for patients. As new advancements in sepsis treatment and management continue to emerge, ongoing education and training for emergency providers will be essential to ensure optimal patient outcomes.

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