

National Early Warning Score 2. to Identify Sepsis in the Emergency Department. A Review of the Literature

Veronica Marosi^{1*}, George Gadda², Claudia Timoftica³, Annalisa Alberti⁴ and Anne Destrebecq⁵

¹Nurse, ASST Rhodense, Rho, Italy

²Nursing Coordinator, Niguarda Hospital, Milan, Italy

³Nursing Coordinator, ASST Rhodense, Rho, Italy

⁴CLI teaching director, Rho campus, University of Milan; Director Center for Nursing Culture and Research Experience- ASST Rhodense, Rho, Italy

⁵Full Professor of Nursing Sciences - University of Milan, Milan, Italy

*Corresponding author

Veronica Marosi, Nurse, ASST Rhodense, Rho, Italy.

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ABSTRACT

Aims: The aim of this study is to understand the described sensitivity and specificity in the literature of the NEWS2 score to identify early patients at developmental risk for sepsis through the use of the score in the intra-hospital triage phase, comparing it with the diagnostic accuracy of qSOFA: Quick Sequential [Sepsis-related] Organ Failure Assessment for sepsis with organ dysfunction, infection-related mortality, or ICU due to infection, especially in patients by priority code level 3, 4, and 5 as levels 1 and 2 represent absence or rapid deterioration of one or more vital functions and risk of impairment of vital functions, respectively.

Materials and Methods: The study is based on a literature review by querying four databases, including PubMed, Cinahl, Embase, and Cochrane Library and the Guidelines of the Regional Health Council of Tuscany Region (2016). The study also asks a question: Does the use of the NEWS 2 early warning system in intrahospital triage lead to early recognition and treatment of patients at high risk for sepsis?

Results: The NEWS is more accurate in predicting mortality or ICU admission due to infection within 72 hours than qSOFA and SIRS in patients suspected of sepsis at initial presentation to the emergency department. This will potentially aid in the early diagnosis of all patients at risk for ED deterioration, including those at risk for sepsis-related mortality.

Conclusions: The use of NEWS 2 is important because of the predictive power of urgent priority, increasing the ability to discriminate patients who may be worsening their condition, despite a priori being otherwise classified. Implementation of the NEWS 2 among hospital-wide triage procedures effectively predicts early mortality and detects high-risk patients.

Keywords: Early Warning Score, Vital Signs, qSOFA, NEWS2, Sepsis, SIRS

Introduction

Sepsis is one of the most important problems in medicine, because of its complexity, from pathophysiology to clinical and therapeutic aspects; it is a clinical condition that we are concerned about from several points of view: increasing incidence, difficulty of diagnosis, high mortality, time dependence, and important costs [1]. It is a complex syndrome, characterized by an abnormal activation of the body's immune system, which itself turns from being defensive into a cause of insult [2]. It can evolve into septic shock and multi-organ dysfunction. Prompt diagnosis and appropriate therapeutic intervention from the first hours after the onset of severe sepsis is a key determinant of patient survival. In recent years, considerable development has been observed in supportive therapies for patients with sepsis and septic shock (renal hemofiltration therapies, different ventilatory and cardiovascular support techniques) and antimicrobial and

anti-inflammatory therapy; however, mortality still remains high, representing the leading cause of death of hospitalized patients [2]. Sepsis is a global health problem and is the leading cause of death from infection, and early recognition and diagnosis of sepsis is necessary to prevent the transition into septic shock, which is associated with a 40% mortality rate. A particular criticality of sepsis is the fact that it has no specific target department, understood as an area of treatment and hospitalization, as may be neurology for stroke or cardiology for IMA (Acute Myocardial Infarction). Mortality from sepsis is five times higher than for stroke and 6-10 times higher than for SCA (Acute Coronary Syndrome) [2]. In Europe, severe sepsis and septic shock increase 37% and 15% of patients admitted to intensive care units, respectively, with a mortality rate of more than 50% of cases [2]. In the United States, the incidence of sepsis is 50-95 cases per 100,000 annually. This condition affects 2% of hospitalized patients and 10% of those admitted to the ICU. The incidence in Australia is 77 cases/100,000 population; in France it is 95 cases/100,000 population and in England 51

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cases/100,000 population. This syndrome mainly affects elderly patients, over 65 years of age and with co-morbidities [2].



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There are also predisposing factors for the development of sepsis:

- extreme ages;
- Type of infection and site of infection;
- co-morbidities (diabetes, cancer, kidney and liver failure, organ transplantation, malnutrition);
- sex (male);
- immunodeficiency (HIV or by drugs);
- Genetic factors and polymorphism of immunity-regulating genes. Shock develops in about 40% of patients with sepsis, and 60-80% of patients with septic shock die. Sepsis is a syndrome with a critical time course. In the early stages, although it is more difficult to identify, it is easily treated with timely diagnosis and appropriate treatment. In the advanced stages it is easier to recognize but more difficult to treat. There is no single diagnostic test that can diagnose sepsis and septic shock with certainty. Sepsis and septic shock are clinical syndromes, defined as a constellation of signs and symptoms, abnormalities identifiable by laboratory tests, and specific pathophysiological changes [2].

It is necessary for patients with suspected sepsis to be assigned a high priority code to avoid valuable time being lost while waiting before admission. The algorithm for suspected infection has been included in the new triage algorithms with the following objectives:

- Early identification of the patient with suspected infection and proper assignment of the priority number code through the use of precise tools
- Activation of the Sepsis Pathway within the high intensity area of the DEA.
- Awareness and sharing of nurses being an integral part of a team work

The algorithm takes into account warning elements and risk factors of immunodepression, etc [2]. Numerous scores have been developed for both the detection and prognosis of sepsis. These include the system inflammatory response syndrome (SIRS), Quick Sequential Organ Failure Assessment (qSOFA), and, most recently, the National Early Warning Score 2 (NEWS2).

The use of these scores helps in the identification of patients at risk of sepsis [3]. Since 1997, an early alert score (EWS) based on simple physiological parameters has been proposed for early

detection of patients developing critical illness, most hospitals have implemented weighted aggregate track and trigger systems. In 2007, the National Institute for Health and Clinical Excellence (NICE) recommended the use of six physiological parameters: systolic blood pressure (SBP), heart rate (HR), respiratory rate (RR), body temperature (BT), peripheral oxyhemoglobin saturation (SpO₂), and level of consciousness [4]. Supplemental oxygen administration to the patient was added to the six physiological parameters recommended by NICE [5]. This study had a major impact, and the Royal College of Physicians adopted and reported the first version of the National Early Warning Score (NEWS) in 2012 [5]. Patient safety is based on the assessment and timely actions of nurses. The Early Warning Score (EWS) was recommended and implemented to improve patient safety by ensuring that patient deterioration is recognized and addressed in the care health care. Despite the use of EWS, problems still exist in the detection of patient deterioration by nursing personal; errors in EWS and non-adherence to referral protocols have been highlighted [6]. The proposed pathway is applicable whenever a case of severe sepsis or septic shock is suspected in an adult patient [7]. Pregnant patients have their own pathway that already includes the use of MEOWS (Modified Early Obstetric Warning Scores). In December 2017, the Royal College of Physicians of London (RCPL) published an update to the National Early Warning Score guidelines, releasing the National Early Warning Score 2 (NEWS 2), which includes several changes relative to the NEWS vital sign detections. The NEWS system update was driven by 4 goals, one of which is how to use the early warning system to identify patients who are at risk for sepsis, have rapid clinical deterioration, and therefore require urgent clinical intervention. To address concerns about NEWS and type II respiratory failure (T2RF), NEWS 2 includes a new SpO₂ scoring scale for patients with/at risk of T2RF [8]. This scale, called the SpO₂ “2” scale, places importance on lower SpO₂ thresholds than NEWS and combines these lower thresholds with weights for supplemental oxygen use at higher SpO₂ levels, reflecting the concern of hyperoxemia-induced respiratory failure. Although the derivation of these thresholds has not been presented and NEWS 2 is not yet validated, NHS England has approved the use of NEWS 2 in the critical care area in an in- and out-of-hospital setting [9]. NEWS 2 adjustment for patients with/at risk of T2RF differs from NEWS in the assignment of weights to measured SpO₂ (NEWS weighs SpO₂ values less than 96%; NEWS2 less than 88%). In addition, for patients with/at risk of T2RF, NEWS 2 assigns weights for SpO₂ values greater than 92% when receiving oxygen [9].

The National Early Warning Score 2 (NEWS2) is the most internationally used and validated in the pre- and hospital setting. The NEWS 2 has a high predictive ability and is an excellent tool that helps professionals in clinical decision making. Risk levels have been re- fined by introducing the threshold value 5, which allows:

1. to place the diagnostic hypothesis of sepsis in any patient with confirmed infection, signs or symptoms of infection, or at high infectious risk.
2. to trigger activation of the medical emergency team for sepsis management [2].

The use of the score in all inpatients allows, independent of septic status, early framing of patients at high risk of rapid

deterioration of clinical condition and activating medical re-evaluation [2]. The review of the present study aims to highlight the ability of NEWS 2 to identify early patients at evolving risk of sepsis during Intrahospital Triage by comparing the diagnostic accuracy of qSOFA and NEWS2 for sepsis with organ dysfunction, infection-related mortality, or ICU due to infection.

Materials and Methods

A literature review was conducted on digital sources using the following scientific databases: PubMed, CINAHL, Cochrane Library, Embase (Figure 1). The search considered articles published in the last 10 years. Early warning score, vital signs, qSOFA, NEWS2, sepsis, and Boolean OR/AND operators were used in the search, along with the MeSH thesaurus for PubMed and Keywords specific to each database.

The limits set were:

- Age > 18 years
- Publication period: last 10 years
- Language: English/Italian

Mixed methods studies that included attendants in emergency rooms were included. The samples recruited in the investigations of this review included adult caregivers with a mean age of 64 years, predominantly male, mostly with concomitant heart disease, and an in-hospital mortality from type II respiratory insufficiency of 54 %. All studies that included pediatric patients and pregnant women were excluded from the search. The search identified a total of 1,237 articles distributed in four scientific databases. After screening of duplicates and articles not pertinent by Title and Abstract, 19 full-text articles evaluated for eligibility were identified, of which 9 met the inclusion criteria as they focused on the care of the septic or at-risk patient in the emergency room according to the National Early Warning Score 2 guidelines. The articles are: one multicenter database study [Marco A. F. Pimentel], one observational study [Lisa Mellhammar], four retrospective studies [Shannon M. Fernando], [Luke E Hodgson], [Hassan Zaidi], and [Omar A. Usman], three multicenter observational prospective cohort studies [Francisco Martin-Rodriguez], [Walter Spagnolli], and [Matthew M Churpek].

Results

Main results Characteristics of the assisted

- The average age of those assisted is 64 (range 54-74)
- The most represented gender is male (63%)
- The largest ethnic group represented is other ethnic groups (18%)
- The most commonly encountered comorbidities are related to heart disease
- Intra-hospital mortality for patients with type II respiratory failure is 52 percent

Secondary Results

Performance metrics of the three scoring systems (News and News 2) for predicting the primary outcome in the three risk groups:

1. With documented type II respiratory failure
2. At risk for the onset of type II respiratory failure
3. Not at risk for the onset of Respiratory Failure Type II, which include the area under the receiver operating characteristic

curve (AUROC), with 95% confidence interval (CI), and sensitivity, specificity, and positive predictive value values at a threshold of 5 and 7.

At the 5- and 7-point cut-offs, the positive predictive values were higher for NEWS2 than for NEWS. In the second evaluation of risk stratification scores for sepsis NEWS 2 was superior to qSOFA in screening for the composite outcome; sepsis with organ dysfunction, infection-related le- gated mortality, or intensive care due to infection.

NEWS 2 had significantly higher AUC, 0.70 (95% CI 0.65-0.74) compared with qSOFA, AUC 0.62 (95% CI 0.57 - 0.67) $p=0.02$. The superiority of NEWS 2 with respect to qSOFA was true among both infected (Cohort A) and undifferentiated (Cohort B) patients.

Discussion and Conclusions

The purpose of the study is to highlight whether the New Early Warning Score 2 succeeds in early identification of patients at developmental risk of sepsis during the intraoperative triage phase within the emergency within the emergency. The samples recruited in the investigation in this review include adult caregivers predominantly male, at developmental risk of sepsis, of any ethnicity, mostly with concomitant heart disease. The studies included in this review agree that the New Early Warning Score 2 is effective for the rapid identification of patients at risk for sepsis. In the evaluation of risk stratification scores for sepsis within emergency rooms, the NEWS 2 was superior to the qSOFA in screening for the composite outcome; sepsis with organ dysfunction, infection-related mortality, or intensive therapy due to infection. The superiority of NEWS 2 over qSOFA was tested among both infected and undifferentiated patients. In agreement with the finding of Seymour et al. within Lisa Mellhammar's observational study, accuracy did not improve with the addition of lactate to qSOFA [4].

HBP (High Blood Pressure) has previously been shown to be superior to lactate in predicting sepsis, so the addition of HBP to qSOFA was tested. HBP significantly improved the performance of qSOFA in infected patients but NEWS 2 still performed better. NEWS has previously been shown to be superior to qSOFA for the detection of sepsis within the ER. NEWS 2 differs from NEWS by the inclusion of different SaO2 scales and the addition of altered consciousness, as a result, the area under the curve (AUC) is higher for NEWS 2 than qSOFA in this study. The higher AUC in infected patients for both scores, which were due to higher specificities but lower sensitivities, is likely multifactorial. Of particular importance was the fact that cohort A was more homogeneous, consisting only of infected patients and also because of differences in inclusion criteria [4]. Whether or not a study determines a value risk stratification score depends strongly on the outcome chosen. Many previous studies regarding qSOFA have used mortality as the primary outcome. However, focusing only on mortality implies that worsening physiological outcomes are not clinically important. As the long- term effects of sepsis have become more apparent, the development of sepsis itself is an important outcome.

Compared with studies with mortality as the primary outcome, the AUC and sensitivity of qSOFA were somewhat lower in this

study, however, this agreed with previous studies using sepsis as the primary outcome [4]. Evaluation with reference to the most severely ill patients could lead to overestimation of sensitivity and negative predictive value. A recent study by Usman et al. used severe sepsis as an outcome, but with the AUC higher for qSOFA than in the present study [4]. The inclusion of central nervous dysfunction in the outcome and the shorter period evaluated for sepsis probably contributed to the higher AUC; for several patients in this observational study by Lisa Mellhammar, sepsis was detected after eight hours. Although a very high specificity was found, the low sensitivity of two qSOFA points diminishes its usefulness in an ER setting when screening for a condition such as sepsis, which aims to capture all potential patients for rapid treatment. Thirty-day mortality was included as a secondary outcome. Mortality in both cohorts was low, generating wide confidence intervals for 30-day mortality [4]. In addition, when evaluating the effect of adding lactate to the stratification scores, the risk assessment, hyperlactatemia was excluded from the definition of sepsis. It is possible that other parameters, such as vital signs that were present in the scores and definition of sepsis, may also bias the results. However, this bias is unavoidable because there is no gold standard diagnostic test for sepsis with which the different scores can be compared. Instead, one method to probe this bias would be to address predictive validity, which assesses the relative performance of scores based on their ability to identify patients at increased risk for downstream events associated with the condition of interest. In this context, attributable mortality (adjusted for known risk factors) could have been performed. However, it was felt that this approach did not significantly reduce bias [4].

The multicenter database study by Marco A. F. Pimentel is the first study to evaluate NEWS2 performance in hospitalized patients who have documented type 2 respiratory failure (T2RF) or are at risk for it [9]. For the primary outcome - in-hospital death within 24 hours of observation - at the suggested Royal College of Physicians (RCPL) cut-offs of 5 and 7 points, positive predictive values (PPV) were higher for NEWS2 than for NEWS [9]. Modified scores were suggested to account for chronically altered physiology in patients with respiratory disease [9]. This study focuses on the groups of patients for whom the new SpO2 scoring "scale" in NEWS 2 has been provided [9]. The study demonstrates that the combined use of NEWS2 and hospital triage can help to identify patients at high risk of early death, including those who a priori were not emergencies or resuscitation cases. The results are consistent with those of previous studies, where the combination of NEWS2 physiological and clinical data along with additional hospital-level data during triage within the emergency department improves the predictive ability of the models studied [10]. NEWS 2 represents a validated and easy-to-use system. Similarly, the ER is making a major effort to improve its ability to adequately screen patients and quickly detect the most serious cases, for which structured triage systems are an optimal tool [10]. Several studies on the Early Warning Score can be found in the literature, but NEWS 2 was chosen because it is currently the most widely used in PhEMS and has a high literature consistency [10]. Mortality at 2, 7 and 30 days from any cause was set as the main outcome variable, neglecting deaths outside this window and outside the hospital [10]. Patients who did not need to be transported to the hospital or who were evacuated to basic life support units for minor

conditions (after being seen by a physician) were excluded to maximize the homogeneity of the patient cohort [10]. In the prospective multicenter observational cohort study by Matthew M Churpek attests that the NEWS had a higher description than the qSOFA when using the same definition of suspected infection as in the original paper by Seymour et al. Within the study, the NEWS, an early warning score designed for use in general wards in all patients, is accurate and more precise than both the SIRS and qSOFA [11]. SOFA was less accurate than these scores, probably because it includes several laboratory parameters, which might not be readily available at the beginning of a patient's hospitalization, and in this study only data up to the time of initial suspicion of infection [11]. In Luke E Hodgson's retrospective study, the SpO2 adjustments of NEWS2 aim to improve safety for patients with hypercapnic respiratory failure who would normally have an SpO2 range of 88-92% [12]. NEWS is well validated in multiple patient settings and provides standardization with all the advantages of this approach. In fact, respiratory patients were included in the NEWS-derived study and in a similar earlier early warning score. A recent large Danish study found similar declines in sensitivity for 48-hour mortality and intensive care unit (ICU) admission and found that records downgraded by NEWS changes in a lower call threshold were more frequently followed by 48-hour mortality or ICU admission than records with an unmodified NEWS in the same score threshold; this suggests that the purpose of NEWS, which detects deterioration, may be compromised by the changes [12]. The NEWS system update was driven by 4 objectives, one of which is how to use the early warning system to identify patients at risk of sepsis, who have rapid clinical deterioration and therefore require urgent clinical intervention. To address concerns about NEWS and type II respiratory insufficiency (T2RF), NEWS 2 includes a new SpO2 scoring scale for patients with/at risk of T2RF [8]. In conclusion, we recommend the use of NEWS 2 for clinical urgency definition regarding the selection of patients at risk of sepsis as it has higher and more accurate discrimination.

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