Early detection of sepsis in urgent and emergency services: integrative review

Detecção precoce de sepse nos serviços de urgência e emergência: revisão integrativa

Detección temprana de la sepsis en servicios de urgencia y emergencia: revisión integradora

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ABSTRACT
Objective: to identify elements that support the construction of a clinical protocol for early detection of sepsis in urgent and emergency services. **Method:** integrative literature review, from 2017 to June 2021, in the Medical Literature Analysis and Retrieval System Online, National Library of Medicine, Scientific Electronic Library Online, Scopus and Web of Science. **Results:** 193 articles were found and nine composed the final sample. The elements identified were: recommendations from the surviving sepsis campaign; screening and opening of protocol by nurse; trainings; warning systems, use of systemic inflammatory response syndrome criteria; response teams or protocol manager; early warning score; checklist of verification; multiprofessional communication and antibiotic list. **Conclusion:** the results contribute to care for septic patients in urgent and emergency services, favoring positive outcomes, based on early recognition and timely application of the initial treatment.
Descriptors: Emergency Medical Services; Emergency Nursing; Sepsis; Early Diagnosis; Clinical Protocols.

RESUMO
Objetivo: identificar elementos que subsidiam a construção de protocolo clínico para detecção precoce de sepse em serviços de urgência e emergência. **Método:** revisão integrativa da literatura, do período de 2017 a junho de 2021, nas bases *Medical Literature Analysis and Retrieval System Online*, *National Library of Medicine*, *Scientific Eletronic Library Online, Scopus e Web of Science*. **Resultados:** foram encontrados 193 artigos e selecionados nove que compuseram a amostra final. Os elementos identificados foram: recomendações da campanha de sobrevivência à sepse; triagem e abertura de protocolo por enfermeiro; treinamentos; sistemas de alerta, uso dos critérios da síndrome da resposta inflamatória sistêmica; times de resposta ou gerente de protocolo; escore de alerta precoce; *check-list* de verificação; comunicação multiprofissional e lista de antibióticos. **Conclusão:** os resultados contribuem para assistência ao paciente séptico em serviços de urgência e emergência, favorecendo desfechos positivos, a partir do reconhecimento precoce e aplicação oportuna do tratamento inicial.
Descritores: Serviços Médicos de Emergência; Enfermagem em Emergência; Sepse; Diagnóstico Precoce; Protocolos Clínicos.

RESUMEN
Objetivo: identificar elementos que apoyen la construcción de un protocolo clínico para la detección temprana de sepsis en servicios de urgencia y emergencia. **Método:** revisión integradora de la literatura, de 2017 a junio de 2021, en las bases de datos *Medical Literature Analysis and Retrieval System Online, National Library of Medicine, Scientific Electronic Library Online, Scopus* y *Web of Science*. **Resultados:** se encontraron 193 artículos de los cuales nueve compusieron la muestra final. Los elementos identificados fueron: recomendaciones de la campaña supervivencia a la sepsis; cribado y apertura de protocolo por enfermero; capacitaciones; sistemas de alerta, uso de los criterios del síndrome de respuesta inflamatoria sistémica; equipos de respuesta o gerente de protocolo; puntuación de alerta temprana; lista de verificación de verificación; comunicación multiprofesional y listado de antibióticos. **Conclusión:** los resultados contribuyen a la atención de los pacientes sépticos en los servicios de urgencia y emergencia, favoreciendo resultados positivos, basados en el reconocimiento temprano y la aplicación oportuna del tratamiento inicial.
Descriptores: Servicios Médicos de Urgencia; Enfermería de Urgencia; Sepsis; Diagnóstico Precoz; Protocolos Clínicos.

INTRODUCTION

Sepsis is characterized by the presence of organ dysfunction resulting from the body's unregulated response to infection, in which there is risk of death, which may culminate in septic shock[1]. Worldwide, between 20 and 30 million people per year are affected by sepsis, with an estimate of 24,000 cases a day[2]. The Global Burden of Disease Study, analyzing 109 million deaths in 195 countries from 1990 to 2017, revealed nearly 48.9 million records of sepsis and 11 million deaths from the disease, representing 19.7% of the global deaths[3].

A relevant study carried out in 2017 in Brazil, the Sepsis Prevalence Assessment Database (SPREAD), indicated that 37% of the septic patients were admitted to intensive care units (ICUs), followed by emergency services with 34% of the cases and 47% mortality[4]. Sepsis is a global priority at the expense of its high incidence, prevalence, mortality[5] and financial impact on health expenditures[6], even in urgency and emergency services, the patient's gateway to the Urgency and Emergency Care Network (*Rede de Atenção às Urgências e Emergências*, RUE) in Brazil.

Thus, once sepsis is diagnosed, stabilization measures are a priority and should be initiated in a multimodal way, until the patient is referred to a hospital service, minimizing negative outcomes. As sepsis worsens over time, evolving to septic shock, its early identification is the most important step for timely treatment and better prognosis[7]. In this sense, development and implementation of managed protocols is essential in programs for improvement and quality of care[8], impacting on a reduction in the number of deaths by up to 16%[2].

Clinical protocols are descriptive of specific situations of care and of the care process, which list operational details and specifications that lead to clinical decision-making[9], helping to standardize care, promoting patient safety by minimizing errors[10]. They are instruments built from scientific evidence, in the technological and economic assessment of the health services, whose effectiveness is linked to the specific needs of the target audience, the professionals' expectations and the reality of the service[11].

The prevalence of sepsis protocols for patients hospitalized in the ICU stands out, observing a gap in those directed to the care context in urgency and emergency care. With the hypothesis that better scientific evidence is essential for the elaboration of clinical protocols as a starting point, and considering the epidemiology of sepsis, it is justified to carry out this integrative review, which aimed at identifying elements that support the elaboration of a clinical protocol for early detection of sepsis in urgency and emergency services.

METHOD

This is an integrative literature review conducted in six phases, namely: (I) definition of the hypothesis and guiding question; (II) sampling or search in the literature; (III) categorization of the studies; (IV) evaluation of the studies included in the review; (V) interpretation of the results, and (VI) knowledge synthesis[12].

The guiding question was elaborated based on the Problem, Concept and Context (PCC) strategy[13], where: P - Characterization of the elements supporting the elaboration of the clinical protocols, C - Early detection of sepsis, and C - Urgency and emergency services. The following question was raised: Which elements support the elaboration of clinical protocols for the early detection of sepsis in urgency and emergency services?

The bibliographic survey was carried out in July 2021, in the following databases: Medical Literature Analysis and Retrieval System Online (MEDLINE) through the Virtual Health Library (*Biblioteca Virtual em Saúde*, BVS), National Library of Medicine (PubMed), Scientific Electronic Library Online (SciELO), Scopus and Web of Science, with application of the following Descriptors in Health Sciences for the Portuguese language and of the Medical Subject Headings for the English language: *Sepse*; *Protocolos Clínicos* and *Serviços Médicos de Emergência* (with their corresponding equivalents in English: Sepsis, Clinical Protocols, and Emergency Medical Services). Crossings between the controlled descriptors were made by using the Boolean operator ''AND'', resulting in the following search strategy: *Sepse*/Sepsis AND *Protocolos clínicos*/Clinical protocols AND *Serviços Médicos de Emergência*/Emergency Medical Services.

The inclusion criteria were as follows: original and full articles published from January 2017 to June 2021, in Portuguese, English and/or Spanish, which answered the guiding question, and which were available in full online. This time frame was chosen because the last international consensus on sepsis was published in 2016 (*The Third International Consensus Definitions for Sepsis and Septic Shock - Sepsis-3*[1]). The articles excluded were those belonging to the editorial or review category, as well as those not relevant to the central theme and conducted with adolescents, children and/or neonates.

Search, analysis and inclusion of the publications were performed by two independent researchers, initially by reading the titles and abstracts. Subsequently, the eligible studies were read in full, and those that did not answer the research question were included to comprise the *corpus* of the integrative review. In case of disagreements, a third researcher was consulted. For selection of the studies, the *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) protocol flowchart[14] was applied.

For categorization of the articles, data collection and extraction of information from the texts, a synoptic chart was created, containing the following items: article number, author(s), country and year of publication, study title, objectives, method and level of evidence. The level of evidence was established according to the parameters of the *Oxford Centre for Evidence-Based Medicine*[15]. The elements identified in the publications for early detection of sepsis in urgency and emergency services were grouped for the synthesis, analysis and discussion of the diverse evidence.

RESULTS

A total of 193 articles were found in the primary search. After applying the exclusion and eligibility criteria, nine studies[16-24] comprised the final sample of this review, as presented in Figure 1.
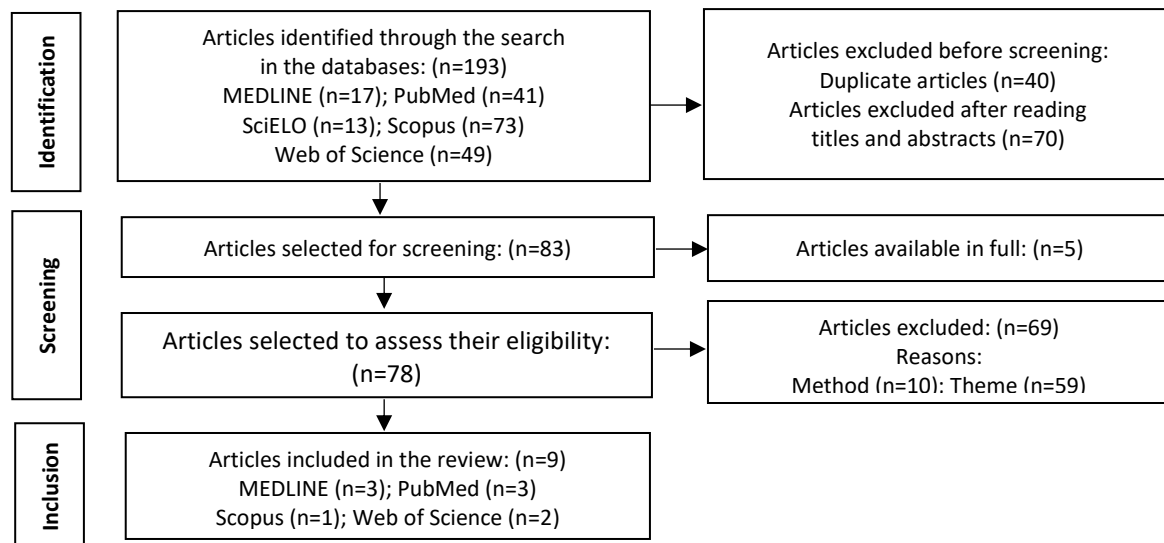
FIGURE 1: Flowchart corresponding to the selection of the articles included in the review. Curitiba, PR, Brazil, 2021.
Source: The authors (2021).

Figure 2 shows prevalence of publications in 2017[16-18], in the English language[16-19,21-23], from Central American countries[18-19,21,23], and intervention research studies[16,18-19,21-22]. Three articles were available in MEDLINE[18-19,22], another three in PubMed[21,23-24], one in Scopus[17] and two in Web of Science[16,20].

Article	Author, country and year of publication	Title	Synthesis of the objectives	Method and level of evidence
A1[16]	Arabi YM et al. Saudi Arabia, 2017.	*The impact of a multifaceted intervention including sepsis electronic alert system and sepsis response team on the outcomes of patients with sepsis and septic shock.*	To describe the results of a multifaceted intervention on the sepsis or septic shock outcomes.	Cohort study. Level 2B.
A2[17]	Groot BD et al. Netherlands, 2017.	*Inclusion of emergency department patients in early stages of sepsis in a quality improvement programme has the potential to improve survival: a prospective dual-centre study.*	To assess the impact on mortality exerted by a quality improvement program, in initial stages of sepsis when compared to advanced stages.	Prospective and observational study. Level 2C.
A3[18]	McColl T et al. Canada, 2017.	*Implementation of emergency department sepsis bundle and system redesign: a process improvement initiative.*	To assess the effects of a sepsis management package on patients' mortality.	Cohort study. Level 2B.
A4[19]	McDonald CM et al. Canada, 2018.	*Sepsis now a priority: a quality improvement initiative for early sepsis recognition and care.*	To develop a triage algorithm to improve the quality of the care provided to patients with sepsis.	Cohort study. Level 2B.
A5[20]	Scheidt SN et al. Brazil, 2018	*Sepsis management protocol implantation at the Emergency Department of the Campos Gerais Regional University Hospital.*	To assess the care protocol corresponding to sepsis management and to characterize the patients subjected to clinical evaluation.	Cross-sectional and descriptive study. Level 2C.
A6[21]	Moore WR et al. USA, 2019.	*Improving 3-hour sepsis bundle care outcomes: implementation of a nurse-drive sepsis protocol in the emergency department.*	To assess the impact of the protocol; to develop a checklist for communication; and to monitor the treatment needs.	Cohort study. Level 2B.
A7[22]	Rosenqvist M et al. Sweden, 2020.	*Improved outcomes after regional implementation of sepsis alert: a novel triage model.*	To assess the results of the triage model.	Cohort study. Level 2B.
A8[23]	Whitfield PL et al. USA, 2020.	*Implementation of an adult code sepsis protocol and its impact on SEP-1 core measure perfect score attainment in the ED.*	To assess the impact of the protocol.	Observational study. Level 2C.
A9[24]	Borguezam CB et al. Brazil, 2021.	*Managed clinical protocol: impact of implementation on sepsis treatment quality indicators.*	To assess the impact of the managed clinical protocol for sepsis on the treatment quality indicators.	Observational and epidemiological study. Level 2C.

FIGURE 2: Synthesis of the articles included in the integrative review. Curitiba, PR, Brazil, 2021.
Source: The authors (2021).

Research Article
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Artículo de Investigación

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Ten elements were identified to elaborate clinical protocols, aiming at early detection of sepsis in urgency and emergency services; each element was presented by at least two of the nine studies in the sample (Figure 3).

Element	Article
Recommendations of the Surviving Sepsis Campaign	A1, A2, A3, A4, A5, A6, A7, A8 and A9
Triage and Protocol Opening by Nurses	A2, A3, A4, A5, A6, A7, A8 and A9
Sepsis Training or Campaigns	A2, A3, A4, A5, A6, A7 and A9
Electronic Warning or Indication in the Medical Chart	A1, A2, A3, A4, A6 and A8
Criteria of the Systemic Inflammatory Response Syndrome	A1, A3, A4, A5 and A8
Sepsis Response Teams or Protocol Manager	A1, A7 and A9
Early Warning Score	A7*, A8** and A9**
Checklist	A6 and A9
List of Antibiotics	A3 and A4
Multiprofessional Communication	A6 and A7

FIGURE 3: Elements supporting detection of sepsis for inclusion in clinical protocols at urgency and emergency services. Curitiba, PR, Brazil, 2021.
Source: The authors (2021).
Note: *Rapid Emergency Triage and Treatment System, **Sequential Organ Failure Score.*

DISCUSSION

Recommendations of the Surviving Sepsis Campaign

Treatment of septic patients in emergency services is equally opportune to the care of those with cardiovascular diseases, whose purpose is to favor the initiation of actions at early stages, improve the clinical outcomes and minimize mortality[18].

The Surviving Sepsis Campaign (SSC), launched in 2004, was an important milestone in the topic since, from consensus meetings between experts and a systematic review, recommendations were listed, based on early goal-directed resuscitation from the first six sepsis recognition hours[25]. These guidelines were revised in 2008, 2012 and 2016, with the implementation of a 1-hour treatment bundle, developed in 2018[26,27], with a new update in 2021[28], constituting the most current evidence for the management of septic patients.

Protocols based on the SSC recommendations contribute to improving the disease identification process, timely treatment and minimization of septic complications and mortality[19,24]; early identification is considered the gold standard for managing the syndrome[21], and the Campaign is a prominent reference in the studies included in this review for the development of clinical protocols[16-24].

The main elements of the Campaign refer to the measurement of lactate to identify tissue hypoperfusion; collection of two pairs of blood cultures to identify the infecting microorganism; administration of broad-spectrum antibiotics to cover empirical treatment; administration of crystalloid fluids to restore hypovolemia; and administration of vasopressors in septic shock, volume-refractory hypotension, or hyperlactatemia. The time to implement these measures can vary between 1 and 3 hours[27,28].

The protocols supported by the Campaign's recommendations exerted a positive impact on adherence to the sepsis resuscitation package, reducing the time for triage, measuring lactate, collecting blood cultures, infusing fluids and administering antibiotics[16-19,21-24]. In terms of mortality, intervention studies with the protocol have shown to reduce it when associated with managed sepsis treatment[16-18,23], especially because of the 14-fold increase in the patient's chances of receiving the package of measures within a period of one hour, with an impact on all treatment indicators[24]. One-hour antibiotic administration increased from 22% to 90% after triage[22], and the compliance rate for all elements of the treatment rose from 30.7% to 71.3%[23], with the same strategy.

Such results evidence the international reference for the standardization of concepts and for sepsis identification and treatment, as well as they solidify the relevance and operationalization in the elaboration of protocols in urgency and emergency services, especially to the fact that using the Campaign's recommendations in protocols and the corresponding evaluation of the results show the positive impact on the care offered to septic patients.

In this sense, the use of the SSC recommendations to develop clinical protocols should be encouraged and applied outside the hospital, reiterating the SPREAD data, where emergency services account for 34% of the admissions of septic patients[4], highlighting the importance of developing protocols for this care context.

Triage and Protocol Opening by Nurses

The nurse's performance in triage of the patient, identification of the risks and opening of the research protocol was identified in eight of the productions analyzed[17-24]. Timely triage, prioritizing medical care, based on changes in the vital signs[19,21], and clinical history becomes essential in urgency and emergency services.

In Brazil, the Emergency Care Units are part of the RUE, and triage is performed by the nurse, using a risk classification system, requiring clinical and technical knowledge, as well as managerial and decision-making skills, to ensure the necessary safety and rigor for the role[29]. The literature reveals that there is an impact and effectiveness of the protocol applied in the triage by nurses, with an improvement in overall compliance with all treatment metrics, such as antibiotic administration, test collection, implementation of initial measures and during the hospitalization period[21].

A retrospective cohort research study, with development of an algorithm with nurse-initiated treatment orders during emergency triage of a patient with suspected sepsis, allowed for improvements in the care process through greater compliance with resuscitation packages, awareness raising regarding identification, and timely treatment[19].

In this way, professional nurses, qualified to perform clinical triage through generalist training and as care managers, assist in the diagnosis of sepsis cases, which require fast and assertive decision-making[30].

Training or Educational Campaigns

The implementation of sepsis protocols requires training or application of educational campaigns to guide the professionals and standardize the care provided, especially regarding early identification of signs and symptoms[20]. Training of the team exerts an impact on the patients' survival and optimizes the implementation of early diagnosis actions[24].

Studies that implemented protocols with application of training sessions[17-22,24], or educational campaigns[18], observed an impact on the awareness of the team.

Electronic Warning or Indication in the Medical Chart

Electronic warnings or indications in medical records are strategies widely used in emergency services[22]; generated from the inclusion of abnormal signs in the electronic system, they contribute to the early detection of sepsis and support decision-making, as they overcome deficiencies in human processes[16]. These tools assist in the team's effective communication, with emphasis on the complexity of the work process experienced in emergency units.

By increasing the team's awareness regarding early treatment initiation, it is a strategy associated with a better outcome for septic patients[16]. Likewise, the use of sepsis warnings showed a significant reduction in the period of time between triage, requesting antimicrobial therapy and applying the empirical treatment[23].

Use of the Criteria of the Systemic Inflammatory Response Syndrome

The criteria of the Systemic Inflammatory Response Syndrome (SIRS) were listed in several studies of this review, constituting one of the strategies that favor detection of sepsis[16,18-20,23]. The criteria are as follows: temperature $>38°C$ or $<36°C$, heart rate >90 bpm/min, respiratory rate >20 brpm/min or carbon dioxide partial pressure <32 mmHg and leukocyte count $>12,000/mm^3$ or $<4,000/mm^3$ or $>10\%$ of rods. The presence of two or more of these criteria can indicate sepsis[1].

The frequent use of the SIRS criteria in patient triage can be attributed to the results of studies, prior to *Sepsis 3*, dating from 2016[1], whose document considers the SIRS criteria as very sensitive. However, even if they are no longer required for the diagnosis of sepsis, they assist in the detection, especially in countries with limited resources, with a high degree of agreement among expert judges[31]. In this sense, use of the SIRS criteria can be useful for urgency and emergency services, considering that they are often environments without laboratory resources, and the available clinical criteria can be used.

Sepsis Response Teams or Protocol Manager

Sepsis response teams consist of professionals from multiple areas, trained to care for patients with acute organic deterioration and activated to identify and implement clinical protocols[32], reducing variation in care and increasing reliability of the assistance provided[16].

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With the same objective, the sepsis protocol manager is responsible for assisting in the detection and carrying out of initial treatment measures, making it possible to increase by eight times the chances of the patient receiving treatment in 1 hour, reducing mortality by 10.33%[24]. Considering the care context of this review, in urgency and emergency services, physicians and nurses are trained professionals, and routinely comprise care teams, which may be assigned this responsibility.

Use of Early Warning Score

Diagnosis of sepsis in the emergency service can be difficult, given the unspecific and subtle symptoms, unknown infection source and lack of resources, especially laboratory ones, causing many patients to be diagnosed at late stages[18]. It is necessary to use valid triage mechanisms at the patient's admission, and vital signs are fundamental in this process. The early warning scores stand out, developed with the objective of facilitating and providing opportunities for prior recognition of conditions that deteriorate biological variables[33] which, when grouped, make up a weighted score, providing opportunities for the assessment of organic deterioration[34]. Such warnings are considered as a useful care standard in emergency services[22].

Some of the relevant scores cited in the studies included in this review were the following: *Rapid Emergency Triage and Treatment System*[22] (REETS) and *Sequential Organ Failure Score*[23-24] (SOFA). REETS combines vital signs and symptoms to stratify the patients' risk[22], while SOFA is applied to define the presence of organ dysfunction by evaluating six organ systems: respiratory, hepatic, cardiovascular, neurological, renal and coagulation. Each system is assigned an indicator to which zero to four points are attributed, counted within a 24-hour period. Such score provides a mortality prognosis[1] and is useful to differentiate patients in the emergency services when more specific measures are not available.

Both scores are useful in the Emergency context. However, SOFA needs laboratory tests for its full application[33]. REETS can be easily applied at the patient's admission[22], just like the *quick Sequential Organ Failure Assessment* (qSOFA), usually used at the bedside in Brazil, with fast applicability of the heart rate, respiratory frequency and level of consciousness variables[33]. By using these scores, according to the service profile and demand, suspected sepsis can be identified, increasing the detection rate of the problem and its early treatment.

Checklist

Sepsis checklists are instruments that contribute to care quality, especially in services with difficulties allocating exclusive human resources for the management of clinical protocols. In a protocol implementation study, with development of a checklist to assist in the treatment of patients with sepsis, it was observed that its use increased by four times the chance of the patient receiving the treatment measures in 1 hour, contributing to a 22.75% reduction in mortality[24].

A number of researchers investigated compliance of the application of the sepsis treatment package by using the DART checklist: **D**etect, **A**ct, **R**eassess and **T**itrate. The tool supported tracking progression of the measures and contributed to the team's communication about the care provided, with emphasis on the transitions and transfers[21].

List of Antibiotics

Antimicrobial therapy is one of the main cornerstones for the treatment of septic patients. The availability of lists of antimicrobials, comprising the clinical protocol, contributes to the physician's best decision[19]. Making them available favors empirical therapy and the most adequate choice regarding the confirmed or presumable infection source, indicating local resistance patterns[18].

It is reiterated that, in addition to being based on scientific evidence, elaboration of the clinical protocol must consider the reality of the service and the needs of the target population[11]. In this sense, it is important to know the resistance/sensitivity profile of the bacteria, most frequently identified in the community or service for which the protocol is intended.

Multiprofessional Communication

Multiprofessional communication improves treatment outcomes for septic patients, reinforcing adherence to the initial resuscitation measures, time sensitivity, and effectiveness in managing the problem. In addition to that, strategies that add communication processes among the professionals provide safer care measures, transitions and transfers[21]. Information about administration of antibiotics should be shared, as well as test results and the patients' responses in relation to the therapeutic measures[29]. Such feedback between professionals engages care[22], contributing to patient safety.

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Study limitations

As a limitation of this review, we point to the reduced number of articles about the theme of sepsis found in the Urgency and emergency scope. However, this limitation indicates the importance and need of conducting new studies in this knowledge area.

Conclusion

Ten elements were identified that contribute to the timely detection of sepsis, with emphasis for the SSC recommendations, use of electronic warnings, application of early warning scores, inclusion of the sepsis protocol team/manager, training to promote knowledge and awareness of the team, and triage systematization with protocol opening by nurses.

Application of these elements must be guided by the characteristics of the target audience, the health service and the human resources, with a view to contributing to the advancement of care quality indicators.

The contributions of this study, for health and nursing, are based on the identification of elements that support the elaboration of a clinical protocol for early detection and treatment of sepsis directed to the urgency and emergency context, favoring positive outcomes.

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