Mediterranean Journal of Emergency Medicine
https://mjemonline.com/

MJEM
Mediterranean Journal of Emergency Medicine

Usefulness of shock index for prehospital triage of septic shock by the SAMU regulation

Jouffroy R, Saade A, Philippe P, Gueye P, Bloch-Laine E, Ecollan P, Carli P, Vivien B. Usefulness of shock index for prehospital triage of septic shock by the SAMU regulation. Med Emergency, MJEM 2020; 28:58-63.
DOI: 10.26738/MJEM.2017/MJEM28.2020/CT.CRE.150420

Key words: prehospital triage, SAMU regulation, septic shock, shock index

ABSTRACT

Introduction: Scoring systems were developed for risk-stratification of septic shock (SS) patients but their performance is poor in the prehospital setting.

Objective: The aim of this study was to evaluate the ability of the shock index (SI) in prehospital triage of SS patients to predict their admission in intensive care unit (ICU).

Methods: We performed a two months retrospective study of call records received by the Paris SAMU 75 regulation centerconcerning patients with presumed SS. The outcome was the in-ICU admission.

Results: Among the 30 642 calls received, 140 concerned patients with presumed SS were included. Twenty-two patients (16%) were admitted to ICU and 118 (84%) to the emergency department. The area under the curve (AUC) of the SI was 0.76 [0.65-0.86]. Using a threshold for SI > 0.9, the sensitivity was 82%, the specificity was 67%, the positive predictive value was 32% and the negative predictive value was 95%. After logistic regression analysis, the OR for SI > 0.9 reached 7.65 [2.33-35.00]. Using propensity score analysis, the odd-ratio (OR) for SI > 0.9 was 1.34 [1.15-1.52]. Results are expressed by OR with 95 percent confidence interval [95 CI].

Conclusion: Shock index is a reliable tool for risk stratification of SS patients managed in the prehospital setting. Using a threshold of one for the SI helps the screening of patients requiring ICU admission by the SAMU 15 regulation call centre. Prospective studies including SI in the decision-making process in the prehospital triage of SS patients are needed to validate these results.

Authors' affiliation:

Corresponding author: Romain Jouffroy, MD
Department of Anesthesia & Intensive Care Unit, SAMU, Hôpital Necker Enfants Malades 149 rue de Sèvres 75015 Paris, University Paris Descartes, France.
Departments of Anesthesia & Clinical Epidemiology and Biostatistics; Michael DeGroote School of Medicine; Faculty of Health Sciences, McMaster University, Hamilton, Ontario, Canada
Population Health Research Institute; David Braley Cardiac, Vascular and Stroke Research Institute; Perioperative Medicine and Surgical Research Unit, Hamilton, Ontario, Canada.
romain.jouffroy@gmail.com

Jouffroy R, MD[1,2,3], Saade A, MD, PhD[1], Philippe P, MD[1], Gueye P, MD, PhD[4], Bloch-Laine E, MD[5], Ecollan P, MD[6], Carli P, MD, PhD[1], Vivien B, MD, PhD[1]

1. Department of Anesthesia & Intensive Care Unit, SAMU, Hôpital Necker Enfants Malades 149 rue de Sèvres 75015 Paris, University Paris Descartes, France.
2. Department of Anesthesia & Clinical Epidemiology and Biostatistics; Michael DeGroote School of Medicine; Faculty of Health Sciences, McMaster University. Hamilton, Ontario, Canada.
3. Population Health Research Institute; David Braley Cardiac, Vascular and Stroke Research Institute; Perioperative Medicine and Surgical Research Unit; Hamilton, Ontario, Canada.
4. Prehospital Medical System, SAMU de Martinique, University Hospital Pierre Zobda Quitman, Fort-de-France Martinique, France
5. Emergency department, hospital Cochin 24 rue du faubourg saint Jacques, 75014 Paris France and emergency department – SMUR, Hospital Hôtel Dieu 1 place du parvis Notre-Dame 75004 Paris, France.
6. Intensive Care Unit, SMUR, Pitie Salpetrière Hospital, 47 boulevard de l'Hôpital 75013 Paris, France.

Article history / info:

Category: Case report
Received: Dec. 18, 2019
Revised: Feb. 12, 2020
Accepted: Apr. 15, 2020

Conflict of interest statement:

There is no conflict of interest to declare

Authors contribution:

- Study concept and design: Jouffroy. R
- Acquisition of data: Jouffroy R.
- Analysis and interpretation of data: Jouffroy R.
- Drafting of the manuscript: Jouffroy R.
- Critical revision of the manuscript for important intellectual content: all authors

INTRODUCTION

Sepsis remains a major public health issue with an overall mortality rate of 30% [1;2]. In the United States, annual sepsis incidence is around 240 per 100 000 inhabitants [3]. One-third to one-half of in-hospital deaths are related to septic shock [4], contributing to 180 000 deaths per year [5]. Each year, approximately 50% of intensive care unit (ICU) admissions are related to sepsis [6]. Thus, the epidemiology and the consequences of sepsis in terms of care-related morbidity and mortality are well described in the ICU [3;7]. The early diagnosis and initiation of appropriate treatments significantly decreased the mortality rate [8-13]. Nevertheless, if the in-hospital diagnosis is at ease using biological complementary examinations and score systems (SOFA, IGS2 for example), the prehospital diagnosis remains challenging.

In the prehospital setting, an adequate triage aims at avoiding "under-triage", i.e. admission to the emergency department (ED) when ICU admission is more appropriate, and "over-triage", i.e. admission to the ICU when ED admission isadequate [14].

In order to optimize the triage prior to ICU admission, many scoring systems as the modified Early Warning Score (MEWS) [15], the modified Robson Screening Tool (mRST) [16], the Prehospital Early Sepsis detection (PRESEP) [17], and the quick Sepsis-related Organ Failure Assessment score (qSOFA) [18] were evaluated to assess illness severity, and predict the prognosis and mortality of septic patients. In the prehospital setting, no accurate scoring system exists due to major discrepancies between studies [19-22]. Initially described in 1967, the shock index (SI) corresponds to the ratio between the heart rate and the systolic blood pressure. The normal range ranks between 0.5 to 0.7 in healthy adults. In the ED, in case of acute circulatory failure, an SI 1.0 was associated with poor outcome [23].

The objective of this study was to evaluate the ability of the SI at prehospital triage of septic shock patients to predict ICU admission.

METHODS

Study design

As previously described [24;25], in France, the management of out-of-hospital emergencies is based on the Service d'aide médicale d'urgence (SAMU), equivalent to the American pre-hospital emergency medical services (EMS). The SAMU hospital-based team is composed of switchboard operators and physicians reached dialing the national number "15".

Over the phone, the appropriate level of care is determined on patient's medical history and symptoms related by the patient or the witness. For life-threatening emergencies, a mobile intensive care unit (MICU) with a physician staffed, a nurse and an ambulance driver, and equipped with medical devices and drugs allowing the initial management of main organ deficiencies, is dispatched to the scene. For less severe cases, an emergency mobile team with fire brigade squads (EMT) or a basic life support ambulance is dispatched to the scene.

The patient's clinical evaluation is communicated to the regulating call centre by the MICU or the EMT to choose the appropriate orientation, e.g. transfer to the ED or to the ICU [26].

Study population

Between 2011, April 1st and May 31st, all calls received by the SAMU 75 centre call were recorded. A retrospective analysis using collected data from recorded phone calls was performed in order to identify all calls related to septic shock during the study period. Recorded calls related to septic shock were retrospectively included in the study. All patients with suspected infection (fever and/or hypothermia) and signs of shock (skin mottling and/or tachycardia and/or low blood pressure and/or tachypnea and/or cyanosis and/or confusion), and no alternative diagnosis, during prehospital assessment by a MICU/EMT/ambulance team were defined as related-sepsis and analyzed. Patients under 18 years old, pregnant women and patients with incomplete data were not included from the analysis.

Data collection

Patient's demographic characteristics, comorbidities, vital signs (systolic, diastolic and mean blood pressure, heart rate, respiratory rate, pulse oximetry, body core temperature and Glasgow coma scale (GCS) communicated to the SAMU regulation call centre over the phone by the MICU/EMT/Ambulance team were retrieved. Shock index (SI) was calculated by the ratio of prehospital heart rate on systolic blood pressure [27]. Patient hospital orientation (ED or ICU) and outcome were extracted from hospital medical reports or from the SAMU records. Infectious disease was suspected on prehospital clinical signs (systolic blood pressure, diastolic blood pressure, mean blood pressure, heart rate, respiratory rate, body temperature, pulse oximetry and GCS), based on the data extracted from prehospital records. The site of infection was suspected according to the prehospital clinical examination, whereas the final diagnosis was extracted from hospital medical record. Three researchers, two residents, and one emergency physician verified the diagnosis of sepsis. The primary outcome was ICU admission primarily, i.e. directly from the prehospital setting, or upon transfer from another department, i.e. after ED admission. Our ethical committee approved the protocol (Comité de Protection des personnes, Ouest 5, Paris - Number 2017-A00354-49) considered that consent of patients was waived for participation in this retrospective observational study.

Statistical analysis

For statistical analyses, a threshold for SI > 0.9 was chosen according to the literature [28-30]. Univariate analysis was conducted to evaluate the relationship between covariates and ICU admission. Results are expressed as mean with standard deviation for quantitative gaussian parameters and, as absolute value and percentage for qualitative parameters. Evaluation of the predictive accuracy of SI was assessed by receiver operator characteristic (ROC) with area under the curve (AUC) and 95 percent confidence interval (95 CI) obtained after a resampling procedure based on a smoothed bootstrap (n = 10 000) because of the small sample size. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for SI > 0.9.

A multivariable logistic regression including age, immunosuppression, prehospital GCS and prehospital respiratory rate was performed. Immunosuppression was defined by the presence of at least one of the followings: history of cancer, human immunodeficiency virus infection, diabetes mellitus, chronic renal failure, chronic obstructive pulmonary disease.

To reduce the effect of confounders, a propensity score analysis was performed using the "nearest" method [31]. Potential confounders included in the propensity score were as follows: age, immunosuppression, prehospital GCS and prehospital respiratory rate. For statistical testing, standardized mean deviation was used to reduce the influence of sample size on the p value [31]. Baseline characteristics included in the propensity score were compared between cases and controls by paired tests after matching. The average treatment effect was estimated using odds ratio (OR) with (95 CI) for ICU admission with SI > 0.9. All analyses were performed using R 3.4.2 (http://www.R-project.org; the R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Between 2011, April 1st and May 31st, the SAMU 75 regulation call centre received 30 642 calls (**Figure 1**) among which 140concerned patients with SS.

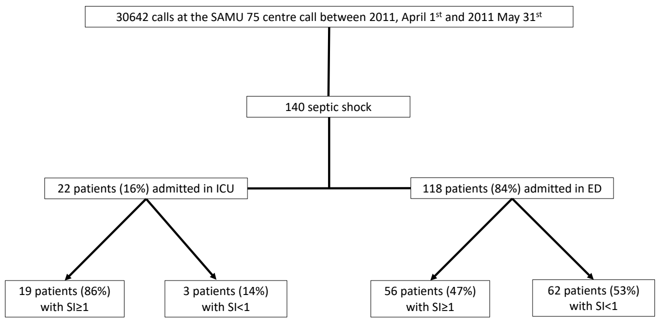

Figure 1: Flow chart of the study.

ICU: intensive care unit, ED: emergency department, SI: shock index

Septic shock patients' demographics and prehospital clinical characteristics are summarized in **Table 1**. Among the 140 patients analyzed 76 (54%) were male. The mean age was 64 ± 23 years old. Sixteen patients (11%) were transferred to the hospital by a mobile intensive care unit (MICU). Twenty-two (16%) patients were admitted to the ICU and 118 (84%) were admitted to the ED.

Results are expressed as mean with standard deviation for quantitative gaussian parameters, as median with interquartile range for quantitative non-normal parameters and, as absolute value and percentage for qualitative parameters. p-value

Table 1: Demographic and prehospital clinical characteristics of septic shock patients admitted to the ICU or the ED.

	Overall (n=140)	ICU (n=22)	ED (n=118)	*p-value*
Age (years)	64 ± 23	67 ± 14	64 ± 24	0.53
SBP (mmHg)	117 ± 28	96 ± 12	121 ± 28	**< 0.001***
DBP (mmHg)	67 ± 19	52 ± 14	69 ± 19	**< 0.001***
MBP (mmHg)	83 ± 21	67 ± 12	86 ± 21	**< 0.001***
HR (beats.min^{-1})	109 ± 21	112 ± 20	108 ± 21	0.46
RR (movements. min^{-1})	25 [22–28]	28 [25–30]	24 [21–28]	0.03
Pulse oximetry (%)	96 [90–98]	90 [83–94]	96 [92–98]	0.003*
Body core temperature (°C)	38.6 [37.9–39]	37.5 [36.7–38.5]	38.8 [38.1–39.3]	**< 0.001***
Glasgow coma scale	15 [15–15]	15 [15–15]	15 [15–15]	0.08
Shock index	1.0 ± 0.3	1.2 ± 0.2	0.9 ± 0.3	**< 0.001***
Male gender	76 (54%)	15 (68%)	61 (52%)	0.16
Immunosuppression	86 (61%)	19 (86%)	67 (57%)	0.02*
Shock index > 0.9	75 (54%)	19 (86%)	56 (47%)	**< 0.001***

Values are expressed as mean ± SD, median [interquartile range]
SBP = systolic blood pressure, DBP = diastolic blood pressure, MBP = mean blood pressure, HR = heart rate, RR = respiratory rate, ICU = intensive care unit, ED = emergency department,
* = p-value < 0.05 between ICU and ED SS patients.

corresponds to the comparison between patients admitted to the ED and to the ICU. Infection was microbiologically identified in 26 patients (19%). The suspected and confirmed origin of sepsis was mainly pulmonary, urinary and digestive (**Table 2**).

Table 2: Suspected and confirmed origin of sepsis.

	Suspected origin (n = 37)	Confirmed origin (n = 26)
Pulmonary	14 (37%)	15 (58%)
Urinary	12 (32%)	7 (27%)
Digestive	5 (14%)	4 (15%)
Cutaneous	1 (3%)	0 (0%)
Other	5 (14%)	NA

Data are expressed as absolute value with percentage.
NA=not applicable

Mortality at day-28 reached 24% (nine patients). All deaths were related to sepsis.

The AUC of the SI ROC curve (**Figure 2**) was 0.76 [0.65-0.86].

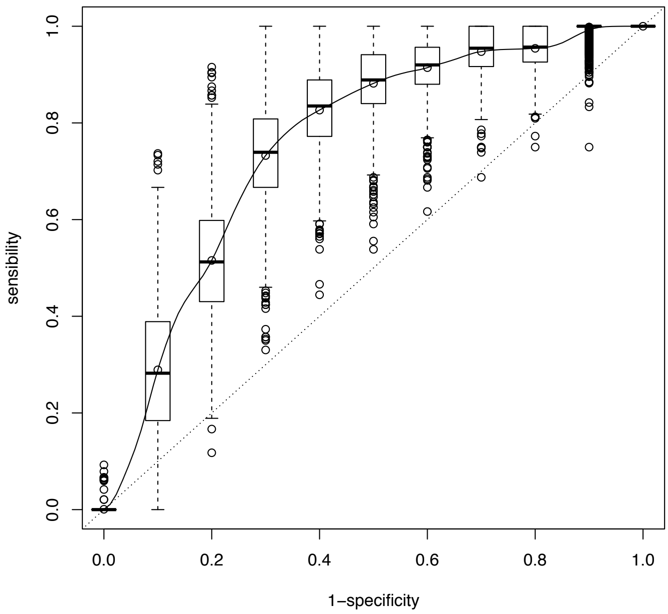

Figure 2: ROC curve of the shock index.

Using a threshold of SI > 0.9, the sensitivity was 82%, the specificity was 67%, the positive predictive value was 32% and the negative predictive value was of 95% for ICU admission.

In the logistic regression model, SI > 0.9 had an OR of 7.65 [2.33-35.00] and immunosuppression had an OR of 5.68 [1.68-26.72].

No covariates significantly differed between cases and controls after matching (**Table 3**).

Table 3: Comparison of predictive variable for ICU admission included in the propensity score before and after matching. Values are expressed as mean ± SD, median [interquartile range] or number (%).

	Before Matching n = 140			After Matching n = 115		
PS covariate	**Cases**	**Controls**	***p value***	**n = 115**	**Controls**	***p value***
	n = 22	n = 118		n = 19	n = 96	
Age	67 ± 14	64 ± 24	0.53	67 ± 14	63 ± 24	0.46
GCS	15 [15–15]	15 [15–15]	0.08	15 [15–15]	15 [15–15]	0.09
RR	28 [25–30]	24 [21–28]	0.03	28 [25–30]	24 [21–28]	0.05

PS: propensity score, GCS: Glasgow coma scale, RR: respiratory rate.

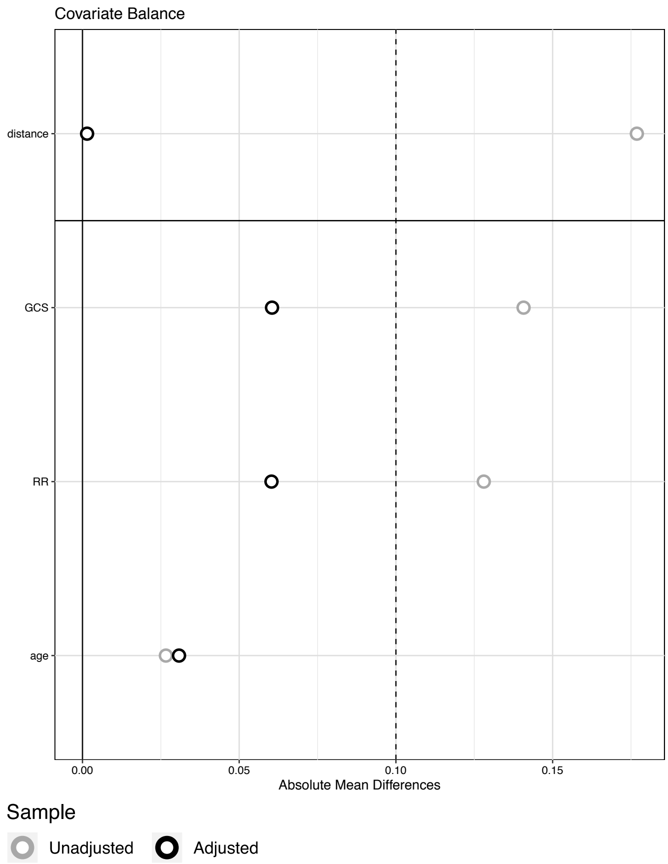

Figure 3: Standardized mean deviation between cases and controls after matching.

Standardized mean deviation between the groups are presented in **Figure 3**.

After adjusting for confounding factors using propensity score, OR for SI > 0.9 was 1.34 [1.15-1.52].

DISCUSSION

In this study, we observed that triage of patients with septic shock by the SAMU regulation call center using the shock index is reliable. A threshold of one helps distinguish patients who don't require ICU admission with a good negative predictive value. A SI > 0.9 at the SAMU regulation call center is associated with a 1.34-fold increase in ICU admission. SI appears to be a simple, easy and objective parameter to evaluate the risk of ICU admission in septic shock patients.

In the prehospital setting, excluding the unknown potential impact of the prehospital EMS, two targets, prior treatments instauration, may help to reduce the mortality rate of sepsis. The first target is the delay reduction between the first medical contact and the diagnosis, and the second target is the delay reduction before diagnosis establishment. In a previous study, Malbrainet al. reported that inappropriate management of septic patients could be harmful [14]. The management includes all steps between the disease occurrence and the end of the treatment including rehabilitation. Therefore, efficient screening and triaging are crucial for the early identification of SS patients to improve the global management of sepsis [9;13].

The qSOFA score performance and other score systems [17] widely used in the ICU and in the ED but lack of accuracy in the pre-hospital setting [32-34]. Because of the poor availability of biomarkers in the prehospital setting, to improve the accuracy of scores to detect septic patients with high risk of poor outcome, other tools are needed. The herein results suggests that the SI could be an efficient tool for the triage of septic patient by the SAMU regulation call center. In addition, the threshold of 1 for SI, used in this study, is simple to memorize and easy to remember in an emergency environment.

This study presents several limitations. First, it is a retrospective study with a small sample size. Second, the results are restricted to the Paris area and may not be extrapolated to other prehospital systems. Third, we did not identify patients taking beta-blockers for which the SI may not be appropriate and may have influenced our results. Fourth, specificity and positive predictive value of SI > 0.9 are quite low. Consequently, SI should only be used as a screening tool by the SAMU regulation call center to help the triage of SS patients.

CONCLUSION

Shock index is reliable to help the triage of SS patients in the prehospital setting. The use of the shock index in the prehospital chain of care may improve the management of SS patients upstream to their transfer to the hospital. Further studies including the shock index in the decision-making process for the prehospital triage of SS patients are needed to validate this tool.

REFERENCES

1. Ferrer R, Artigas A, Levy MM, Blanco J, Gonzalez-Diaz G, Garnacho-Montero J, et al. Improvement in process of care and outcome after a multicenter severe sepsis educational program in Spain. JAMA 2008; 299:2294-303.
2. Nguyen HB, Van Ginkel C, Batech M, Banta J, Corbett SW. Comparison of predisposition, insult/infection, response, and organ dysfunction, acute physiology and chronic health evaluation II, and mortality in emergency department sepsis in patients meeting criteria for early goal-directed therapy and the severe sepsis resuscitation bundle. J Crit Care 2012; 27:362-9.
3. Brun-Buisson C. The epidemiology of the systemic inflammatory response. Intensive Care Med 2000; 26:S64-74.
4. Liu V, Escobar GJ, Greene JD, Soule J, Whippy A, Angus DC, et al. Hospital deaths in patients with sepsis from 2 independent cohorts. JAMA 2014; 312:90-2.
5. Epstein L, Dantes R, Magill S, Fiore A. Varying estimates of sepsis mortality using death certificates and administrative codes - United States, 1999-2014. Morb Mortal Wkly Rep 2016; 65:342-5.
6. Blanco J, Muriel-Bombin A, Sagredo V, Taboada F, Gandia F, Tamayo L, et al. Incidence, organ dysfunction and mortality in severe sepsis: a Spanish multicentre study. Crit Care 2008; 12:R158.
7. Finfer S, Bellomo R, Lipman J, French C, Dobb G, Myburgh J. Adult-population incidence of severe sepsis in Australian and New Zealand intensive care units. Intensive Care Med 2004; 30:589-96.
8. Kumar A, Roberts D, Wood KE, Light B, Parrillo JE, Sharma S, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med 2006; 34:1589-96.
9. Leisman DE, Doerfler ME, Ward MF, Masick KD, Wie BJ, Gribben JL, et al. Survival Benefit and cost savings from compliance with a simplified 3-hour sepsis bundle in a series of prospective, multisite, observational cohorts. Crit Care Med 2017; 45:395-406.
10. Levy MM, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, et al. 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. Crit Care Med 2003; 31:1250-6.
11. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001; 345:1368-77.
12. Seymour CW, Gesten F, Prescott HC, Friedrich ME, Iwashyna TJ, Phillips GS, et al. Time to treatment and mortality during mandated emergency care for sepsis. N Engl J Med 2017; 376:2235-44.
13. Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, et al. Assessment of clinical criteria for sepsis: for the third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016; 315:762-74.
14. Malbrain ML, Marik PE, Witters I, Cordemans C, Kirkpatrick AW, Roberts DJ, et al. Fluid overload, de-resuscitation, and outcomes in critically ill or injured patients: a systematic review with suggestions for clinical practice. Anaesthesiol Intensive Ther 2014; 46:361-80.
15. Subbe CP, Kruger M, Rutherford P, Gemmel L. Validation of a modified early warning score in medical admissions. QJM 2001; 94:521-6.
16. Robson W, Nutbeam T, Daniels R. Sepsis: a need for prehospital intervention? Emerg Med J 2009; 26:535-8.
17. Bayer O, Schwarzkopf D, Stumme C, Stacke A, Hartog CS, Hohenstein C, et al. An early warning scoring system to identify septic patients in the prehospital setting: The PRESEP score. Acad Emerg Med 2015; 22:868-71.

18. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). JAMA 2016; 315:801-10.
19. Jouffroy R, Saade A, Carpentier A, Ellouze S, Philippe P, Idialisoa R, et al. Triage of septic patients using qSOFA criteria at the SAMU regulation: A retrospective analysis. Prehosp Emerg Care 2018; 22:84-90.
20. Jouffroy R, Saade A, Ellouze S, Carpentier A, Michaloux M, Carli P, et al. Prehospital triage of septic patients at the SAMU regulation: Comparison of qSOFA, MRST, MEWS and PRESEP scores. Am J Emerg Med 2018; 36:820-4.
21. Koyama S, Yamaguchi Y, Gibo K, Nakayama I, Ueda S. Use of prehospital qSOFA in predicting in-hospital mortality in patients with suspected infection: A retrospective cohort study. PLoS One 2019; 14:e0216560.
22. Tusgul S, Carron PN, Yersin B, Calandra T, Dami F. Low sensitivity of qSOFA, SIRS criteria and sepsis definition to identify infected patients at risk of complication in the prehospital setting and at the emergency department triage. Scand J Trauma Resusc Emerg Med 2017; 25:108.
23. Rady MY, Nightingale P, Little RA, Edwards JD. Shock index: a re-evaluation in acute circulatory failure. Resuscitation 1992; 23:227-34.
24. Jouffroy R, Saade A, Tourtier JP, Gueye P, Bloch-Laine E, Ecollan P, et al. Skin mottling score and capillary refill time to assess mortality of septic shock since pre-hospital setting. Am J Emerg Med 2019; 37:664-71.
25. Jouffroy R, Vivien B. Prehospital emergency care in sepsis: from the «door-to-antibiotic» to the «antibiotic-at-door» concept? Ann Am Thorac Soc 2019; 16:775-6.
26. Adnet F, Lapostolle F. International EMS systems: France. Resuscitation 2004; 63:7-9.
27. Allgöwer M BC. Schock index. Deutsche Medizinische Wodenschrift 1967; 46:1-10.
28. Berger T, Green J, Horeczko T, Hagar Y, Garg N, Suarez A, et al. Shock index and early recognition of sepsis in the emergency department: pilot study. West J Emerg Med 2013; 14:168-74.
29. Tseng J, Nugent K. Utility of the shock index in patients with sepsis. Am J Med Sci 2015; 349:531-5.
30. Yussof SJ, Zakaria MI, Mohamed FL, Bujang MA, Lakshmanan S, Asaari AH. Value of Shock Index in prognosticating the short-term outcome of death for patients presenting with severe sepsis and septic shock in the emergency department. Med J Malaysia 2012; 67:406-11.
31. Austin PC. Goodness-of-fit diagnostics for the propensity score model when estimating treatment effects using covariate adjustment with the propensity score. Pharmacoepidemiol Drug Saf 2008; 17:1202-17.
32. Churpek MM, Snyder A, Han X, Sokol S, Pettit N, Howell MD, et al. Quick sepsis-related organ failure assessment, systemic inflammatory response syndrome, and early warning scores for detecting clinical deterioration in infected patients outside the intensive care unit. Am J Respir Crit Care Med 2017; 195:906-11.
33. Dorsett M, Kroll M, Smith CS, Asaro P, Liang SY, Moy HP. qSOFA has poor sensitivity for prehospital identification of severe sepsis and septic shock. Prehosp Emerg Care 2017; 21:489-97.
34. Innocenti F, Tozzi C, Donnini C, De Villa E, Conti A, Zanobetti M, et al. SOFA score in septic patients: incremental prognostic value over age, comorbidities, and parameters of sepsis severity. Intern Emerg Med 2018; 13:405-12.