American Journal of Emergency Medicine 49 (2021) 331–337

Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Time for a prehospital-modified sequential organ failure assessment score: An ambulance–Based cohort study

Francisco Martín-Rodríguez, PhD [a,b,*], Ancor Sanz-García, PhD [c,**], Carlos del Pozo Vegas, MD, PhD [d], Guillermo J. Ortega, PhD [c], Miguel A. Castro Villamor, MD, PhD [b], Raúl López-Izquierdo, MD, PhD [e]

[a] Unidad Móvil de Emergencias Valladolid I, Gerencia de Emergencias Sanitarias, Gerencia Regional de Salud de Castilla y León (SACYL), Spain
[b] Centro de Simulación Clínica Avanzada, Departamento de Medicina, Dermatología y Toxicología, Universidad de Valladolid, Spain
[c] Unidad de Análisis de Datos (UAD) del Instituto de Investigación Sanitaria del Hospital de la Princesa (IIS-IP), Madrid, Spain
[d] Servicio de Urgencias, Hospital Clínico Universitario de Valladolid, Gerencia Regional de Salud de Castilla y León (SACYL), Spain
[e] Servicio de Urgencias, Hospital Universitario Rio Hortega de Valladolid, Gerencia Regional de Salud de Castilla y León (SACYL), Spain

ARTICLE INFO

Article history:
Received 26 March 2021
Received in revised form 17 June 2021
Accepted 20 June 2021
Available online xxxx

Keywords:
Clinical decision-making
Short-term mortality
Emergency medical services
Organ dysfunction scores
Prehospital care

ABSTRACT

Background: To adapt the Sequential Organ Failure Assessment (SOFA) score to fit the prehospital care needs; to do that, the SOFA was modified by replacing platelets and bilirubin, by lactate, and tested this *modified* SOFA (mSOFA) score in its prognostic capacity to assess the mortality-risk at 2 days since the first Emergency Medical Service (EMS) contact.
Methods: Prospective, multicentric, EMS-delivery, ambulance-based, pragmatic cohort study of adults with acute diseases, referred to two tertiary care hospitals (Spain), between January 1st and December 31st, 2020. The discriminative power of the predictive variable was assessed through a prediction model trained using the derivation cohort and evaluated by the area under the curve (AUC) of the receiver operating characteristic (ROC) on the validation cohort.
Results: A total of 1114 participants comprised two separated cohorts recruited from 15 ambulance stations. The 2-day mortality rate (from any cause) was 5.9% (66 cases). The predictive validity of the mSOFA score was assessed by the calculation of the AUC of ROC in the validation cohort, resulting in an AUC of 0.946 (95% CI, 0.913–0.978, $p < .001$), with a positive likelihood ratio was 23.3 (95% CI, 0.32–46.2).
Conclusions: Scoring systems are now a reality in prehospital care, and the mSOFA score assesses multiorgan dysfunction in a simple and agile manner either bedside or en route. Patients with acute disease and an mSOFA score greater than 6 points transferred with high priority by EMS represent a high early mortality group.
Trial registration: ISRCTN48326533, Registered October 312,019, Prospectively registered (doi:https://doi.org/10.1186/ISRCTN48326533).

1. Introduction

The quick and effective characterization of patients with high-risk of short-term mortality has been one of the main challenges for health systems. That is why the use of scoring systems such as the Sequential Organ Failure Assessment (SOFA) has become a standard clinical practice in intensive care units (ICU) [1,2], having proven its usefulness in very diverse clinical contexts [3,4,5].

Such success of the SOFA score has led to being used in non-ICU settings [6] and, through modifications, the score was lately simplified and adapted to encompass broader clinical contexts, finally developing the quick-SOFA (qSOFA) [1].

Due to its simplicity, the qSOFA score has been implemented by the Emergency Medical Services (EMS) as an alert trigger in cases of suspected infection to detect possible sepsis, although with limited diagnostic accuracy [7]. This restriction together a limited range of pathologies in which can be applied have boosted the National Early Warning Score (NEWS) as new gold standard in the realm of the EMS [8]. In fact, the NEWS can be used, not only as a trigger for sepsis but also as a trigger of clinical deterioration in a wider range of pathologies [9,10].

The development of small, robust, and reliable point-of-care testing (POCT) has allowed its use in prehospital care [11,12]. For instance, prehospital lactate measured by POCT is a good predictor of poor

* Correspondence to: F. Martín-Rodríguez, School of Medicine, Valladolid University, C/Ramón y Cajal, 7. 47005, Valladolid, Spain.
** Correspondence to: A. Sanz-García, Unidad de Análisis de Datos (UAD), Instituto de Investigación Sanitaria del Hospital de la Princesa (IIS-IP), Calle Diego de Leon, 62, 28006 Madrid, Spain.
E-mail addresses: fmartin@saludcastillayleon.es (F. Martín-Rodríguez), ancor.sanz@salud.madrid.org (A. Sanz-García).

https://doi.org/10.1016/j.ajem.2021.06.042

prognosis, since it provides information about the anaerobic metabolism [13].

In the prehospital environment, on the other side, healthcare workers must react quickly and precisely to acute diseases, facing many times very heterogeneous syndromes; in such situations, the identification of patients at high risk of short-term mortality becomes rather tough [14,15,16].

The aim of the present work was to adapt the SOFA score in accordance with the prehospital arena and compare this modified score to other risk stratification tools used in this environment.

2. Methods

2.1. Study design and settings

This is a prospective, multicentric, EMS-delivery, ambulance-based, pragmatic cohort study of combined data from the EMS units and hospitals from January 1 through December 31, 2020. This EMS is operated by the Public Health System of Castilla-León (SACYL), the primary health authority. The study was carried out in the province of Valladolid, with a reference population of 524,204 inhabitants, located in an area of 8111 km^2, with a demographic density of 64.19 inhabitants/km^2. The typical demographics are elderly adults in urban and peri-urban locations, with a reduced incidence of events in rural and more remote areas. EMS operates in the province with one helicopter emergency medical service (HEMS), four advanced life support (ALS) and fourteen basic life support (BSL), which refer patients to the three hospitals in the region (two tertiary university hospitals and one small general district hospital). The number of emergency calls received by EMS in Valladolid during the last year was 134,033. HEMS handled 51 cases, ALS evacuated 8631 patients, and BLS reported 40,688 cases. The study involved three ALS, fourteen BLS, and two tertiary university hospitals. The selection of the vehicles was conditioned to the POCT availability, and subsequently, the hospitals were selected as the centers where those selected vehicles refer to.

The ALS units are made up of two emergency medical technician (EMT), an emergency registered nurse (ERN), and a physician, all of them performing standard advanced life support maneuvers in accordance with protocols on the scene or *en route,* e.g., advanced cardiac, trauma and pediatric life support, advanced airway management (orotracheal intubation, use of videolaryngoscope, noninvasive mechanical ventilation, surgical airway, hemorrhage-pneumothorax decompression), fluid and drug administration, immobilization, ultrasound, fibrinolysis, point-of-care testing. The BLS is made up of two EMT who perform assisted transfers after prior evaluation by an ALS physician, developing restricted competencies, e.g., basic cardiac, trauma and pediatric life support, immobilization, basic airway management (suctioning of secretions, administration of oxygen by noninvasive methods and balloon resuscitation and oropharyngeal cannula ventilation, without the use of invasive airway management devices) and, use of semiautomatic defibrillator monitor.

2.2. Participants

All calls for help to the 1–1-2 emergency number that were dispatched by an ALS were screened for eligibility. Any request for emergency assistance is received by an EMT at the emergency call center. The EMT collects data on affiliation, geolocation, and symptoms, and transfers the case to a physician. Based on a simple assessment, the consultant physician assigns the most appropriate resource for the emergency (medical dispatch): HEMS, ALS, BLS, a combination of these, or simply resolves the situation by telephone consultation. Certain incidents such as heart attacks, cardiorespiratory arrest, stroke, polytrauma, poisoning, suspected sepsis, or any pathology that the call center physician determines, are immediately attributed to an ALS. The system is two-way: the ALS physician, after the pertinent evaluation, may consider that the evaluation can be performed safely at BLS; and the BLS EMTs, in the presence of complex cases, may request the presence of the ALS at the scene.

All adult patients (aged ≥18 years old), with any acute disease, evaluated by the ALS physician, and transferred by ambulance (either ALS or BLS) to the ED were eligible. Cases of cardiorespiratory arrest upon arrival at the scene, end-stage patients documented by a specialist report, pregnant women, intravenous line impossibility, patients discharged in situ (after the evaluation by the ALS physician, their transfer to hospital was not necessary), situations with risk at the scene for the team (e.g., weapons, fire, explosions), and patients in whom, despite all attempts, it was not possible to obtain informed consent were excluded from this study.

2.3. Outcomes

The outcome was in-hospital mortality at any time in between patient admission at the ED and two days after that, i.e., the outcome should be considered as the cumulative mortality during the first 48 h. This mortality period is widely accepted in similar studies as the early-mortality window [17,18].

2.4. Data sources and predictors.

Epidemiological variables -sex, age, intervention times-, basal set of vital signs -respiratory rate, oxygen saturation, supplemental oxygen administered prior to the ALS arrival at the scene, systolic, diastolic, and mean blood pressure, heart rate, temperature, and Glasgow coma scale-, and analytical variables (glucose, lactate, creatinine) were collected by the RN during the first contact with the patient, either at the scene or *en route*.

With the objective of adapting the SOFA score to the prehospital care requirements when patients are transferred in ambulance, a prehospital SOFA was modified by using lactate instead of platelets and bilirubin, for which POCTs are unavailable.

The respiratory rate was calculated by listening the respiratory cycles for 30 s and, in case of doubt or irregular rhythm, for one minute. Oxygen saturation, systolic, diastolic, and mean blood pressure, and heart rate were taken with the LifePAK® 15 monitor-defibrillator (Physio-Control, Inc., Redmond, USA). The temperature was measured with ThermoScan® PRO 6000 thermometer (Welch Allyn, Inc., Skaneateles Falls, USA). After that, an intravenous line was placed and 1.5 ml of venous blood was taken using the epoc® Blood Analysis System (Siemens Healthcare GmbH, Erlangen Germany), obtaining creatinine, lactate, and glucose levels.

To make a link between EMS medical records and hospital's electronic medical records, an exact match was made with 5 of the following extractors: name and surname, sex, age, day, arrival time, incident code, ambulance code and/or health care card number. EMS medical records that were unable to be linked were excluded.

After the follow-up period, the following hospital variables were recorded: Charlson comorbidity index, ICU inpatients, 2-day in-hospital mortality, and the final diagnosis (based on the International Classification of Diseases 11th Revision).

By using those variables, the scores analyzed in this study were calculated.

2.5. mSOFA score calculation

Previous to the scores determination, the whole cohort was randomly divided -preserving the original outcome distribution- in derivation and validation cohort. The predictive score mSOFA was built using the derivation cohort and its validity was assessed by using the validation cohort.

The weights and categories for each variable of the mSOFA score are as follows:

(i) The points for each category of the pulse oximetry saturation/fraction of inspired oxygen ratio (SaFi), Glasgow Coma Scale, and

creatinine were the same as the ones described in the original score [1] [19]. (ii) The mean blood pressure (MBP) was used for the cardiovascular state, in particular, one-point was assigned to patients with MBP less than 70 mmHg, and 0 otherwise. (iii) Prior administration of catecholamines (dopamine or norepinephrine) was discarded because it is improbable or even unknown at the assistance scene.

(iv) Platelets and bilirubin, for which POCTs, are unavailable, were replaced by lactate, a biomarker with a proven ability to predict the risk of short-term mortality [20-22] was added to the mSOFA in order to include the anaerobic metabolism state. The following cut-offs were chosen by considering both clinical and bibliographic criteria: ≤ 2 mmol/L, > 2 to 3, > 3 to 4, > 4 to 6, and > 6 mmol/ [23-25]. The weight and subsequent points given to each category of lactate were determined by considering the estimate obtained from the logistic regression of lactate levels vs. the outcome, and adapting them to the range 0–4 points, as are the other parameters of the SOFA score.

Lastly, the final score resulted from the sum of points in each variable (Table 1).

2.6. Statistical methods

The final outcomes and predictors were compiled by independent investigators of each hospital through the review of the patients' electronic medical records. The main outcome was blinded to the clinical investigators in charge of data collection. The collected data was stored in a database created using the software IBM SPSS Statistics for Apple version 20.0. (IBM Corp, Armonk USA). The database was purified by means of logical tests, the presence of extreme values, and the detection of missing data, resulting in a total of 27 variables.

Normality tests were performed on all the quantitative variables (Shapiro-Wilk and Lilliefors tests). Quantitative variables were described as median and interquartile range (25th–75th percentile). The categorical variables were described using absolute frequencies and percentages.

For the comparison of means of quantitative variables, the Mann-Whitney *U* test was used; the Chi-square test was used for 2×2 contingency tables to assess the association or dependency relationship between qualitative variables. Fisher's exact test was used when it was necessary.

The area under the curve (AUC) of the receiver operating characteristic (ROC) of the score in the validation cohort was used to assess the predictive validity of it. The *p* value of the hypothesis test (H0: AUC = 0.5) and its corresponding 95% confidence interval (CI) were also assessed. Further statistical characteristics such as: positive predictive value, negative predictive value, positive likelihood ratio, negative likelihood ratio, odds ratio, and diagnostic accuracy were determined. Additionally, to compare mSOFA with NEWS and qSOFA, a Delong's test and a decision curve analysis were used in the same training cohort both AUC of the ROC.

The data were analyzed using our own codes and base functions in R, version 4.0.3 (http://www.R-project.org; the R Foundation for Statistical Computing, Vienna, Austria).

Table 1
Modified Sequential organ failure assessment score (mSOFA).

	Points				
	0	1	2	3	4
Respiratory, SaFi	>302	<302	<221	<142	<67
Cardiovascular, MAP (mmHg)	≥70	<70			
Renal, Creatinine (mg/dl)	<1.2	1.2–1.9	2.0–3.4	3.5–4.9	>5.0
Neurologic, GCS (points)	15	13–14	10–12	6–9	<6
Metabolic, Lactate (mmol/L)	<2	2.1–3	3.1–4	4.1–6	>6

SaFi: pulse oximetry saturation/fraction of inspired oxygen ratio; MAP: mean arterial pressure; GCS: Glasgow coma scale.

2.7. Ethics approval and consent to participate

This study was approved by the Health Research Ethics Board of Hospital Universitario Rio Hortega and Hospital Clínico Universitario of Valladolid (reference: PI-049-19 and PI-GR-19-1258), followed the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) [26] statement and registered in the World Health Organization's International Clinical Trials Registry Platform (ICTRP) (doi.org/10.1186/ISRCTN48326533).

As a pre-study phase, all participants had to read and sign the informed consent. The physician of the ALS was responsible of obtaining the primary consent during the first contact with the patient at the scene. This consent was valid for the entire study and its subsequent follow-up. In cases where the patient was unable to understand the document, a relative or legal guardian signed it. If consent was not obtained despite previous attempts, a research associate from each hospital made another attempt during the patient's stay in the ED. If consent was not obtained, the patient was excluded from the study.

3. Results

3.1. Patient characteristics

During the study period, 1796 patients were recruited from 15 ambulance stations (1 ALS and 14 BLS). A total of 682 cases were excluded because they did not meet the inclusion criteria (Additional file 1: Supplementary Fig. 1), resulting in a final cohort of 1114 cases. Among the excluded patients, 15 cases were due to the impossibility of obtaining the consent and 22 cases because the EMS medical records cannot be linked. The median age was 69 years (IQR, 52–81 years), 486 (43.6%) were females. The 2-day mortality rate (from any cause) was 5.9% (66 cases). The clinical-epidemiological characteristics of the patients and the differences between survivors and non-survivors are shown in Table 2. From the analysis of the differences between survivors and non-survivors it can be seen that there were statistically significant differences for all the variables except for sex, arrival and transfer times, time zone, heart rate, temperature, and final diagnosis. In particular, all the components of mSOFA presented highly significant differences for survivors and non-survivors ($p < .001$).

3.2. mSOFA accuracy

The mortality distribution according to mSOFA score and the predicted probability of mortality are shown in Fig. 1. A score <6 presented an overall mortality lower than 10%, whereas the mortality overcame the 50% for a score greater than 8.

The predictive validity of the mSOFA score was assessed by the calculation of the AUC of ROC in the validation cohort (Fig. 2), resulting in an AUC of 0.946 (95% CI: 0.913–0.978, p < .001). Further details of the score also provided information regarding its validity: the specificity was 80.2% (95% CI: 63.6% – 96.7%), the sensitivity was 61.7% (95% CI: 41% – 82.4%), the positive predictive value was 52.6 (95% CI, 31.9–71.2), the negative predictive value was 97.5 (95% CI, 96.2–98.8), the positive likelihood ratio was 23.3 (95% CI, 0.32–46.2) and the negative likelihood ratio was 0.42 (95% CI, 0.2–0.63).

When comparing the curves (Additional file 1: Supplementary Fig. 2), the mSOFA presented a higher AUC (AUC = 0.946 (95% CI: 0.913–0.978)) when compared to NEWS (AUC = 0.890 (95% CI: 0.831–0.949)) ($p = .018$ vs mSOFA) and to qSOFA (AUC = 0.754 (95% CI, 0.650–0.858)) ($p < .001$ vs mSOFA). Further details of the results of each score can be found in Additional file 1: Supplementary Table 1. The decision curve analysis also revealed a better performance of mSOFA as compared to NEWS and qSOFA (Fig. 3), as could be observed by a greater net benefit throughout all threshold probabilities. In other words, when a new intervention is justified, as defined by the probability thresholds, the net benefit is always greater for the SOFA score which

Table 2
Demographic, clinical and hospital outcomes.

	2-day mortality			
Characteristic[a]	Total	Survivors	Non-survivors	*p-value*
No. (%) with data	1114 (100)	1048 (94.1)	66 (5.9)	
Sex, female	486 (43.6)	455 (43.4)	31 (47)	0.573
Age (years)	69 (52–81)	68 (52–80)	80 (68–89)	<0.001
Isochrones (min)[b]				
Arrival	11 (9–15)	11 (9–15)	12 (8–16)	0.49
Support	33 (26–41)	33 (25–41)	40 (30–50)	0.001
Transfer	11 (8–16)	11 (8–16)	10 (8–17)	0.57
Time zone				0.233
00:00–5:59	224 (20.1)	208 (19.8)	16 (24.2)	
6:00–11:59	283 (25.4)	264 (25.2)	19 (28.8)	
12:00–17:59	331 (29.7)	314 (30)	17 (25.8)	
18:00–23:59	276 (24.8)	262 (25)	14 (21.2)	
Basal evaluation				
RR (breaths/min)	18 (15–25)	18 (15–24)	28 (19–35)	<0.001
SpO2 (%)	96 (93–98)	96 (93–98)	87 (77–94)	<0.001
FiO2 (%)	0.21 (0.21–0.21)	0.21 (0.21–0.21)	0.21 (0.21–0.28)	0.001
SaFi	457 (433–467)	457 (438–467)	381 (286–430)	<0.001
SBP (mmHg)	134 (116–153)	1,358,118–153)	99 (84–148)	<0.001
DBP (mmHg)	79 (65–91)	80 (66–91)	60 (46–83)	<0.001
MBP (mmHg)	97 (88–111)	98 (85–111)	72 (58–103)	<0.001
Heart rate (beats/min)	87 (71–105)	87 (70–104)	97 (76–119)	0.078
Temperature (°C)	36 (35.7–36.6)	36 (35.7–36.6)	36.1 (35.1–36.7)	0.498
GCS (points)	15 (15–15)	15 (15–15)	7 (4–14)	<0.001
Glucose (mg/dl)	129 (107–167)	1,278,106–164)	173 (125–243)	0.001
Creatinine (mg/dl)	0.97 (0.78–1.31)	0.94 (0.77–1.22)	1.91 (1.04–2.87)	<0.001
Lactate (mmol/L)	2.17 (1.19–3.41)	2.09 (1.17–3.11)	7.32 (4.58–11.42)	<0.001
Hospital outcome				
CCI index (points)	2 (0–4)	2 (0–4)	5 (3–7)	<0.001
ICU inpatients	141 (12.7)	113 (10.8)	28 (42.4)	<0.001
Final diagnosis				0.334
Circulatory	365 (32.8)	339 (32.3)	26 (39.4)	
Neurology	163 (14.6)	157 (15)	6 (9.1)	
Trauma and injury	177 (15.9)	168 (16)	9 (13.6)	
Respiratory	57 (5.1)	53 (5.1)	4 (6.1)	
Infection	150 (13.5)	134 (12.8)	16 (24.2)	
Poisoning	83 (7.3)	82 (7.8)	1 (1.5)	
Digestive	58 (5.2)	55 (5.2)	3 (4.5)	
Others[c]	61 (5.5)	60 (5.7)	1 (1.5)	
Scoring systems				
mSOFA	1 (0–3)	1 (0–3)	8 (6–10)	<0.001
qSOFA	1 (1–2)	1 (1–2)	2 (2–3)	<0.001
NEWS	4 (2–7)	4 (2–7)	12 (8–15)	<0.001

RR: respiratory rate: SPO2: oxygen saturation; FIO2: fraction of inspired oxygen; SaFi: pulse oximetry saturation/fraction of inspired oxygen ratio; SBP: systolic blood pressure; DBP: diastolic blood pressure; MBP: mean blood pressure; GCS: Glasgow coma scale; CCI: Charlson comorbidity index; ICU: intensive care unit; mSOFA: modified Sequential Organ Failure Assessment; qSOFA: quick Sequential Organ Failure Assessment; NEWS: National Early Warning Score; SOFA: Sequential Organ Failure Assessment.

[a] Values expressed as total number (fraction) and medians [25th percentile-75th percentile] as appropriate.

[b] Arrival: time from ambulance activation to on-scene check-in. Support: time expended by EMS on scene. Transfer: time for transferring the patient from the scene to the hospital.

[c] Other pathology: endocrine, genitourinary, diseases of the blood and the immune system.

correctly identifies a greater percentage of patients at risk of short-term mortality.

4. Discussion

In this study, a modification of the SOFA score -mSOFA- that could be adapted to the prehospital needs and constraints has been developed, tested, and proposed in a prehospital setting with medical/nursing staff. When comparing with SOFA, the mSOFA retain the neurological, respiratory, and renal components with similar characteristics, but the mSOFA simplify the evaluation of cardiovascular function discarding the use of inotropes and adding the evaluation of the metabolic profile by using lactate. Our results showed that mSOFA can predict with great accuracy the risk of short-term mortality in patients with acute disease treated by EMS.

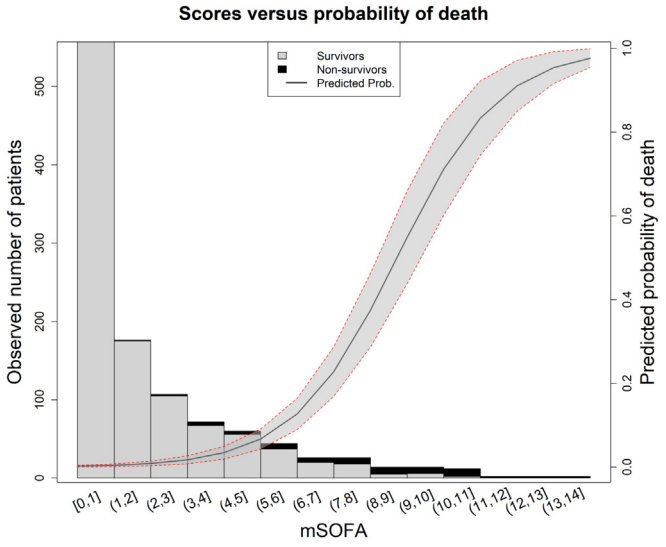

Fig. 1. mSOFA scores vs real and predicted probability of death. The grey area of the trend line corresponds to 95% confidence interval of the predicted probability of death (trend line). The bars correspond to the number of patients of the training cohort alive (grey) or death (black). mSOFA: modified Sequential Organ Failure Assessment.

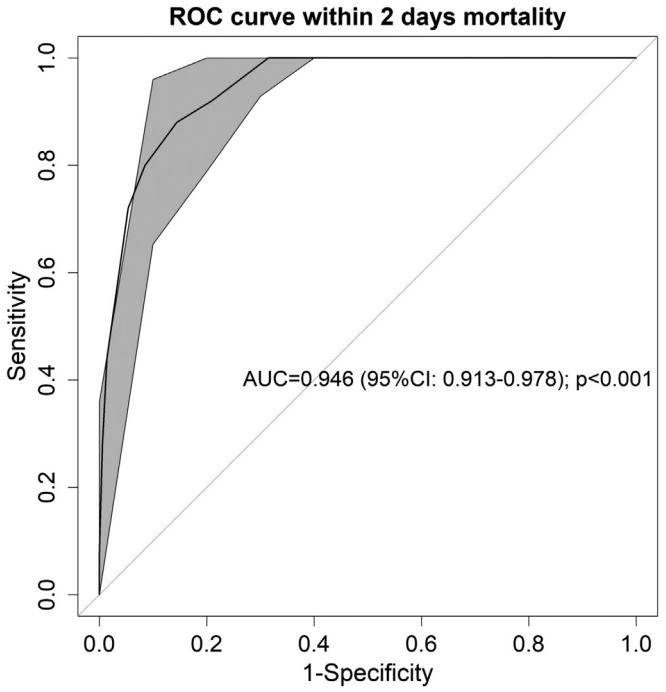

Fig. 2. Receiver operational curve (ROC) for the mSOFA score. The bold line shows the ROC curve value and the grey shading is the result of the validation coefficient. In the center of the graph is the area under the curve (AUC) and its 95% confidence interval and the p value of the hypothesis test (H0: AUC = 0.5).

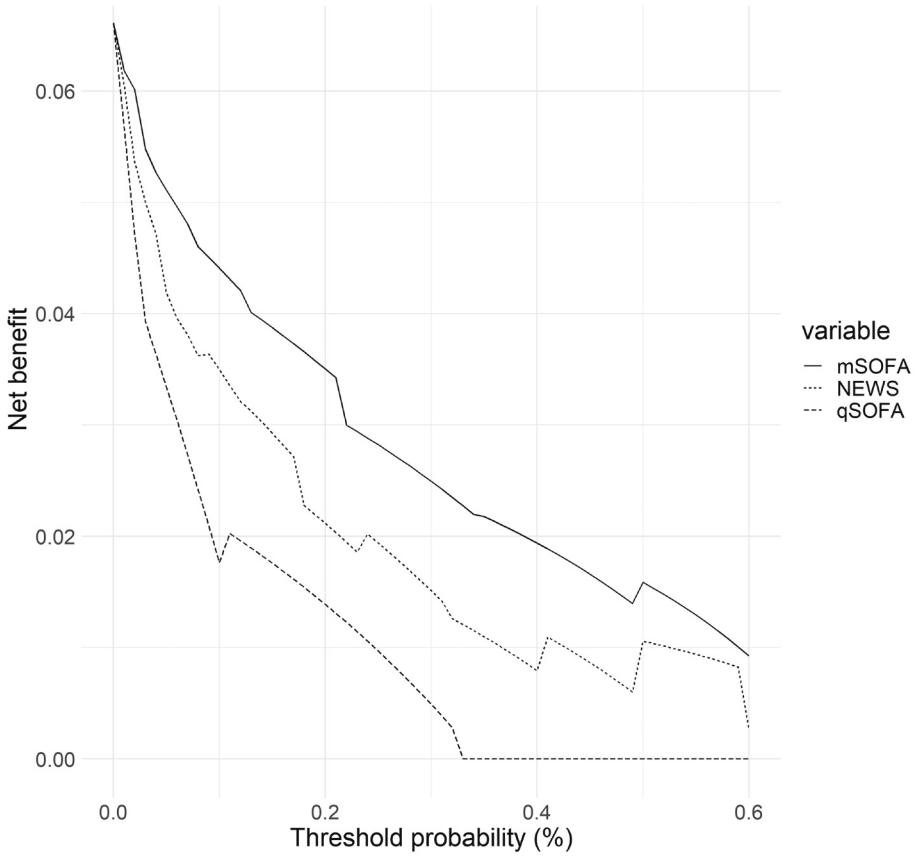

Fig. 3. Decision curve of the mSOFA (solid line), the NEWS (pointed line) and the qSOFA (dashed line) score. The threshold probability for the mortality is shown in x-axis and the y-axis indicates the net benefit. mSOFA: modified Sequential Organ Failure Assessment; qSOFA: quick Sequential Organ Failure Assessment; NEWS: National Early Warning Score; SOFA: Sequential Organ Failure Assessment.

The SOFA score has proven its clinical and prognostic utility, and is a tool commonly used in ICUs and more recently in non-ICU settings [19,27,28]. However, the implementation of this score in EMS is complex because the determination of platelets and bilirubin using a small-sized POCT in the ambulance is impossible, so despite of being an excellent score it is inappropriate to be used outside of the hospital environments.

Here, we have adapted the SOFA score to be used in prehospital care with the following modifications: (i) SaFi has been used to evaluate the respiratory function, because it presents an excellent correlation with the partial pressure of oxygen in arterial blood/fraction of inspired oxygen (PaFi), but adding a substantial advantage since it does not require an arterial blood extraction [29,30]. Therefore, the SaFi represents an effective alternative for a continuous monitoring of the respiratory function [31]. (ii) The evaluation of the cardiovascular function has been adapted, by discarding the use of inotropes, because the mSOFA is calculated with the patient's baseline parameters without any type of intervention by the EMS personnel, facilitating in this way a quick calculation at the scene [32]. (iii) Together with the evaluation of neurological, cardiovascular, respiratory, and renal function, a biomarker of anaerobic metabolism has been added through the use of lactate, a very specific predictor of poor short-term prognosis [33,34]. Lactate values lower than 2 mmol/L indicate a correct metabolic state, however, values higher than 4 mmol/L suggest a situation of hyperlactatemia, with a significant increase in mortality in the short-term [20,21,35].

In the prehospital care setting, the use of early warning scores has been promoted with the aim of effectively stratify patients at risk of short-term mortality, particularly in the case of time-dependent pathologies [36,37]. A notorious example is the NEWS, a score easy to calculate, widely implemented, and with proven effectiveness [38,39]. However, as we have shown here, the mSOFA demonstrated a better performance than the NEWS, because the first one takes advantage of both the organic and metabolic dysfunctions (although NEWS was originally developed to identify patients at risk of clinical deterioration). A mSOFA score above 6 points is associated with an early mortality rate of 10%. In this group of patients, advanced life support maneuvers and/or continuous monitoring should be implemented since the very first opportunity to do it.

The combined use of early warning scores with biomarkers (e.g., lactate, procalcitonin, MR-Proadrenomedullin) is beginning to be explored in various clinical settings, but predominantly for the case of early detection of sepsis [40-42]; composite scores like qSOFA-lactate or NEWS-lactate have shown a substantial improvement in the predictive capacity of mortality risk [43-45]. Our results with the mSOFA score show a better predictive capacity than all of the composite scores previously described [46,47]. It seems thus that the use of biomarkers that analyze metabolic damage in acute disease strengthens the predictive models in the initial assessment of the critically ill patient.

An early detection of patients likely to deteriorate quickly is certainly a challenge for the EMS [48,49]. The scoring systems represent tools of proven utility and easiness of use [17,50], which can help to identify real pluripathological patients with associated comorbidities and in complex clinical settings. In this sense, the present score could modify the prehospital management improving patients' management and, at the same time, optimizing resources, but at cost of requiring of qualified personnel trained to perform point-of-care testing.

5. Limitations

Our study has several limitations. Firstly, it was a convenience cohort taken over a specific period of time, which can be proven by the results obtained in the positive and negative likelihood ratios. Additionally, these results were not validated with an external sample. Consecutive patients who met the inclusion criteria and no exclusion criteria were included in the study, without any type of additional selection. Furthermore, to minimize potential bias, patients from both rural and urban areas, evacuated in ALS or BLS and during all time slots, all days of the week and during a full calendar year were included. Second, in the absence of a prehospital score "gold-standard" it has been decided to compare the mSOFA with the NEWS and the qSOFA as they the scores with the most reputation among the EMS, but it is a partial selection, nonetheless. Thirdly, although the number of patients is adequate to obtain preliminary results, prospective studies in different EMS are needed to verify the generalizability of our results; likewise, the limited number of patients means that the study of mSOFA by pathology groups requires further studies. Fourthly, point-of-care testing is not available in several health system, which limits the generalizability of the results to other regions. Finally, only cases of 2-day in-hospital mortality were included in the study, although it directly reflects the intensity of the acute disease that originated the demand for care, it may be interesting to explore the accuracy of the mSOFA in the longer term.

6. Conclusions

Scoring systems are now a reality in prehospital care, and the mSOFA score assesses multiorgan dysfunction in a simple and agile manner either bedside or *en route*. Patients with acute disease and a mSOFA score greater than 6 points transferred with high priority by EMS represent a high early mortality group.

The EMS needs tools adapted to prehospital care which can provide critical information to assist professionals in performing a rapid decision-making operation. Whether further prospective validation studies of this model will support our results, the application of the mSOFA certainly will help in these situations by providing a warning trigger in time-dependent pathologies.

Funding

This work was supported by the Gerencia Regional de Salud de Castilla y León (Spain) under Grant number [GRS 1678/A/18] and Grant number [GRS 1903/A/19].

Declaration of Competing Interest

The authors declare that they have no competing interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajem.2021.06.042.

References

[1] Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. Third international consensus definitions for Sepsis and septic shock (Sepsis-3). JAMA. 2016;315(8):801–10.
[2] de Grooth HJ, Geenen IL, Girbes AR, Vincent JL, Parienti JJ, Oudemans-van Straaten HM. SOFA and mortality endpoints in randomized controlled trials: a systematic review and meta-regression analysis. Crit Care. 2017;21(1):1–9.
[3] Kandori K, Okada Y, Matsuyama T, Morita S, Ehara N, Miyamae N, et al. Prognostic ability of the sequential organ failure assessment score in accidental hypothermia: a multi-institutional retrospective cohort study. Scand J Trauma Resusc Emerg Med. 2019;27(1):1–7.
[4] Vogel JA, Newgard CD, Holmes JF, Diercks DB, Arens AM, Boatright DH, et al. Validation of the Denver emergency department trauma organ failure score to predict post-injury multiple organ failure. J Am Coll Surg. 2016;222(1):73–82.
[5] Vasilevskis EE, Pandharipande PP, Graves AJ, Shintani A, Tsuruta R, Ely EW, et al. Validity of a modified sequential organ failure assessment score using the Richmond agitation-sedation scale. Crit Care Med. 2016;44(1):138–46.
[6] Guirgis FW, Puskarich MA, Smotherman C, Sterling SA, Gautam S, Moore FA, et al. Development of a simple sequential organ failure assessment score for risk assessment of emergency department patients with Sepsis. J Intensive Care Med. 2020;35(3):270–8.
[7] 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(4):489–97.
[8] Silcock DJ, Corfield AR, Gowens PA, Rooney KD. Validation of the National Early Warning Score in the prehospital setting. Resuscitation. 2015;89:31–5.
[9] Hoikka M, Silfvast T, Ala-Kokko TI. Does the prehospital National Early Warning Score predict the short-term mortality of unselected emergency patients? Scand J Trauma Resusc Emerg Med. 2018;26(1):1–7.
[10] Endo T, Yoshida T, Shinozaki T, Motohashi T, Hsu HC, Fukuda S, et al. Efficacy of prehospital National Early Warning Score to predict outpatient disposition at an emergency department of a Japanese tertiary hospital: a retrospective study. BMJ Open. 2020;10(6):e034602.
[11] Galvagno SM, Sikorski RA, Floccare DJ, Rock P, Mazzeffi MA, DuBose JJ, et al. Prehospital point of care testing for the early detection of shock and prediction of lifesaving interventions. Shock. 2020;54(6):710–6.
[12] Brant EB, Martin-Gill C, Callaway CW, Angus DC, Seymour CW. Prehospital identification of community sepsis using biomarkers of host response. Intensive Care Med. 2020;46(4):823–4.
[13] van den Nouland DPA, Brouwers MCGJ, Stassen PM. Prognostic value of plasma lactate levels in a retrospective cohort presenting at a university hospital emergency department. BMJ Open. 2017;7(1):e011450.
[14] Schewe JC, Kappler J, Dovermann K, Graeff I, Ehrentraut SF, Heister U, et al. Diagnostic accuracy of physician-staffed emergency medical teams: a retrospective observational cohort study of prehospital versus hospital diagnosis in a 10-year interval. Scand J Trauma Resusc Emerg Med. 2019;27(1):36.
[15] Fladt J, Meier N, Thilemann S, Polymeris A, Traenka C, Seiffge DJ, et al. Reasons for prehospital delay in acute ischemic stroke. J Am Heart Assoc. 2019;8(20):e013101.
[16] Pirneskoski J, Kuisma M, Olkkola KT, Nurmi J. Prehospital National Early Warning Score predicts early mortality. Acta Anaesthesiol Scand. 2019;63(5):676–83.
[17] Williams TA, Tohira H, Finn J, Perkins GD, Ho KM. The ability of early warning scores (EWS) to detect critical illness in the prehospital setting: a systematic review. Resuscitation. 2016;102:35–43.
[18] Hargreaves DS, de Carvalho JLJ, Smith L, Picton G, Venn R, Hodgson LE. Persistently elevated early warning scores and lactate identifies patients at high risk of mortality in suspected sepsis. Eur J Emerg Med. 2020;27(2):125–31.
[19] 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(8):762–74.
[20] Swan KL, Avard BJ, Keene T. The relationship between elevated prehospital point-of-care lactate measurements, intensive care unit admission, and mortality: a retrospective review of adult patients. Aust Crit Care. 2019;32(2):100–5.
[21] Martín-Rodríguez F, López-Izquierdo R, Medina-Lozano E, Ortega Rabbione G, Del Pozo Vegas C, Carbajosa Rodríguez V, et al. Accuracy of prehospital point-of-care lactate in early in-hospital mortality. Eur J Clin Investig. 2020;50(12):e13341.
[22] Morris E, McCartney D, Lasserson D, Van den Bruel A, Fisher R, Hayward G. Point-of-care lactate testing for sepsis at presentation to health care: a systematic review of patient outcomes. Br J Gen Pract. 2017;67(665):e859–70.
[23] Swan KL, Keene T, Avard BJ. A 12-month clinical audit comparing point-of-care lactate measurements tested by paramedics with in-hospital serum lactate measurements. Prehosp Disaster Med. 2018;33(1):36–42.
[24] Ko BS, Kim K, Choi SH, Kang GH, Shin TG, Jo YH, et al. Prognosis of patients excluded by the definition of septic shock based on their lactate levels after initial fluid resuscitation: a prospective multi-center observational study. Crit Care. 2018;22(1):1–7.
[25] Gattinoni L, Vasques F, Camporota L, Meessen J, Romitti F, Pasticci I, et al. Understanding lactatemia in human Sepsis. Potential impact for early management. Am J Respir Crit Care Med. 2019;200(5):582–9.
[26] von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Lancet. 2007;370(9596):1453–7.
[27] Lambden S, Laterre PF, Levy MM, Francois B. The SOFA score-development, utility and challenges of accurate assessment in clinical trials. Crit Care. 2019;23(1):1–9.
[28] Karakike E, Kyriazopoulou E, Tsangaris I, Routsi C, Vincent JL, Giamarellos-Bourboulis EJ. The early change of SOFA score as a prognostic marker of 28-day sepsis mortality: analysis through a derivation and a validation cohort. Crit Care. 2019;23(1):1–8.
[29] Brown SM, Grissom CK, Moss M, Rice TW, Schoenfeld D, Hou PC, et al. Nonlinear imputation of Pao2/Fio2 from Spo2/Fio2 among patients with acute respiratory distress syndrome. Chest. 2016;150(2):307–13.
[30] Brown SM, Duggal A, Hou PC, Tidswell M, Khan A, Exline M, et al. Nonlinear imputation of PaO2/FIO2 from SpO2/FIO2 among mechanically ventilated patients in the ICU: a prospective. Observ Study Crit Care Med. 2017;45(8):1317–24.
[31] Martín-Rodríguez F, López-Izquierdo R, Del Pozo Vegas C, Delgado-Benito JF, Ortega GJ, Castro Villamor MA, et al. Association of prehospital oxygen saturation to inspired oxygen ratio with 1-, 2-, and 7-day mortality. JAMA Netw Open. 2021;4(4):e215700.

[32] Nawrocki PS, Poremba M, Lawner BJ. Push dose epinephrine use in the management of hypotension during critical care transport. Prehosp Emerg Care. 2020;24(2):188–95.
[33] Lane DJ, Wunsch H, Saskin R, Cheskes S, Lin S, Morrison LJ, et al. Epidemiology and patient predictors of infection and sepsis in the prehospital setting. Intensive Care Med. 2020;46(7):1394–403.
[34] Boland LL, Hokanson JS, Fernstrom KM, Kinzy TG, Lick CJ, Satterlee PA, et al. Prehospital lactate measurement by emergency medical services in patients meeting sepsis criteria. West J Emerg Med. 2016;17(5):648–55.
[35] Pedersen M, Brandt VS, Holler JG, Lassen AT. Lactate level, aetiology and mortality of adult patients in an emergency department: a cohort study. Emerg Med J. 2015;32(9):678–84.
[36] Lane DJ, Wunsch H, Saskin R, Cheskes S, Lin S, Morrison LJ, et al. Assessing severity of illness in patients transported to hospital by paramedics: external validation of 3 prognostic scores. Prehosp Emerg Care. 2020;24(2):273–81.
[37] Patel R, Nugawela MD, Edwards HB, Richards A, Le Roux H, Pullyblank A, et al. Can early warning scores identify deteriorating patients in pre-hospital settings? A systematic review. Resuscitation. 2018;132:101–11.
[38] Abbott TEF, Cron N, Vaid N, Ip D, Torrance HDT, Emmanuel J. Pre-hospital National Early Warning Score (NEWS) is associated with in-hospital mortality and critical care unit admission: a cohort study. Ann Med Surg (Lond). 2018;27:17–21.
[39] Shaw J, Fothergill RT, Clark S, Moore F. Can the prehospital National Early Warning Score identify patients most at risk from subsequent deterioration? Emerg Med J. 2017;34(8):533–7.
[40] Baumann BM, Greenwood JC, Lewis K, Nuckton TJ, Darger B, Shofer FS, et al. Combining qSOFA criteria with initial lactate levels: improved screening of septic patients for critical illness. Am J Emerg Med. 2020;38(5):883–9.
[41] Liu S, He C, He W, Jiang T. Lactate-enhanced-qSOFA (LqSOFA) score is superior to the other four rapid scoring tools in predicting in-hospital mortality rate of the sepsis patients. Ann Transl Med. 2020;8(16):1013.
[42] Yu H, Nie L, Liu A, Wu K, Hsein YC, Yen DW, et al. Combining procalcitonin with the qSOFA and sepsis mortality prediction. Medicine (Baltimore). 2019;98(23):e15981.
[43] Ho KM, Lan NSH. Combining quick sequential organ failure assessment with plasma lactate concentration is comparable to standard sequential organ failure assessment score in predicting mortality of patients with and without suspected infection. J Crit Care. 2017;38:1–5.
[44] Jo S, Yoon J, Lee JB, Jin Y, Jeong T, Park B. Early warning score-lactate for mortality and the need for critical care among general emergency department patients. J Crit Care. 2016;36:60–8.
[45] Martín-Rodríguez F, López-Izquierdo R, Del Pozo Vegas C, Delgado Benito JF, Del Brio Ibáñez P, Moro Mangas I, et al. Predictive value of the prehospital NEWS2-L —National Early Warning Score 2 lactate— for detecting early death after an emergency. Emergencias. 2019;31(3):173–9.
[46] Jung YT, Jeon J, Park JY, Kim MJ, Lee SH, Lee JG. Addition of lactic acid levels improves the accuracy of quick sequential organ failure assessment in predicting mortality in surgical patients with complicated intra-abdominal infections: a retrospective study. World J Emerg Surg. 2018;13:1–7.
[47] Dundar ZD, Kocak S, Girisgin AS. Lactate and NEWS-L are fair predictors of mortality in critically ill geriatric emergency department patients. Am J Emerg Med. 2020;38(2):217–21.
[48] Carroll G, Levy K, Pescatore R, Hong R. Examination of EMS decision making in determining suitability of patient diversion to urgent care centers. Healthcare (Basel). 2019;7(1):24.
[49] Bijani M, Abedi S, Karimi S, Tehranineshat B. Major challenges and barriers in clinical decision-making as perceived by emergency medical services personnel: a qualitative content analysis. BMC Emerg Med. 2021;21(1):1–12.
[50] Scott LJ, Redmond NM, Garrett J, Whiting P, Northstone K, Pullyblank A. Distributions of the National Early Warning Score (NEWS) across a healthcare system following a large-scale roll-out. Emerg Med J. 2019;36(5):287–92.