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TITRE

Evaluation of the performance of qSOFA, NEWS2 and MEDS scores for predicting in-hospital mortality in elderly patients with sepsis in the emergency departments.

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SERMENT D'HIPPOCRATE

En présence des Maîtres de cette Faculté, de mes chers condisciples et selon la tradition d'Hippocrate,

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Résumé

Titre: Evaluation des indicateurs de performance des scores qSOFA, MEDS et NEWS2 sur la mortalité intra-hospitalière du patient âgé admis aux urgences pour une infection, un sepsis ou un choc septique.

Contexte: Le sepsis est un enjeu majeur de santé publique car son incidence annuelle est croissante et sa mortalité élevée. Il se définit actuellement comme une défaillance d'organe secondaire à une infection pouvant entrainer le décès du patient. Une reconnaissance précoce des patients à risque d'évoluer défavorablement est recommandée à l'aide de scores tel que le qSOFA, le MEDS et le NEWS2. Les personnes âgées présentent une population particulièrement fragile avec des particularités physiologiques il est nécessaire de valider ces scores pronostiques dans cette tranche de population.

Méthode : Notre étude était une étude monocentrique, prospective et non interventionnelle réalisée sur une période d'inclusion de 2 mois (du 15 février au 15 avril 2021) avec un suivi jusque J-28. Les patients recrutés étaient les patients chez qui l'urgentiste en charge suspectait une infection après examen clinique ou à l'aide d'examens complémentaires. Le diagnostic d'infection a été réévalué par 2 experts une fois la phase de suivi terminée. Les données démographiques, le diagnostic retenu après le passage aux urgences, les valeurs biologiques et les paramètres permettant le calcul des scores qSOFA, MEDS et NEWS2 ont été relevés. L'objectif principal de notre étude était d'évaluer la performance pronostique de ces trois scores sur la mortalité intra-hospitalière chez les patients âgés de plus de 65 ans se présentant aux urgences avec un diagnostic d'infection posé par le médecin urgentiste en charge.

Résultats : Parmi nos 620 patients, la mortalité intra-hospitalière était de 11.6% chez les patients âgés de plus de 65 ans et de 5.8% chez les patients de moins de 65 ans avec une mortalité globale de 9.5%. Pour prédire la mortalité à J28, le score MEDS avait la meilleure sensibilité dans la population âgée comparativement aux scores qSOFA et NEWS2. Contrairement à la littérature, le qSOFA avait une mauvaise sensibilité. L'impact de la deuxième vague COVID est à prendre en compte dans l'interprétation de nos résultat par l'attention nécessaire que nous avons portée aux patients potentiellement et septiques se présentant dans notre structure.

Conclusion : Le score MEDS semble le plus sensible pour dépister un patient âgé à risque d'évoluer défavorablement dans un contexte d'infection. Une nouvelle étude est nécessaire après la crise COVID-19 pour déterminer quel score est le plus performant pour détecter précocement les patients âgés à risque de développer une infection sévère.

Mots Clés : Patients âgés ; Sepsis ; qSOFA ; NEWS2 ; MEDS ; Urgences.

Abstract

Title: Evaluation of the performance indicators of the qSOFA, MEDS and NEWS2 scores on in-hospital mortality of elderly patients admitted to the emergency department for infection, sepsis or septic shock.

Context: Sepsis is a major public health issue because its annual incidence is increasing and its high mortality. It is currently defined as organ failure secondary to an infection that can lead to the death of the patient. Early recognition of patients at risk of adverse outcomes is recommended using scores such as qSOFA, MEDS and NEWS2. The elderly is a particularly fragile population with physiological characteristics and it is necessary to confirm these prognostic scores in this population.

Method: Our study was a monocentric, prospective and non-interventional study carried out over an inclusion period of 2 months (from 15 February to 15 April 2021) with a follow-up until D-28. The patients recruited were those in whom the emergency physician in charge suspected an infection after clinical examination or with the help of complementary examinations. The diagnosis of infection was reassessed by 2 experts once the follow-up phase was over. Demographic data, the diagnosis retained after the emergency room visit, biological values and parameters allowing the calculation of qSOFA, MEDS and NEWS2 scores were recorded. The main objective of our study was to evaluate the prognostic performance of these three scores on in-hospital mortality in patients over 65 years of age presenting to the emergency department with a diagnosis of infection made by the emergency physician in charge.

Results: Among our 620 patients, the in-hospital mortality was 11.6% in patients aged over 65 years old and 5.8% in patients aged under 65 years old with an overall mortality of 9.5%. To predict mortality at D-28, the MEDS score had the best sensitivity in the elderly population compared to qSOFA and NEWS2 scores. Contrary to the literature, qSOFA had a poor sensitivity. The impact of the second wave of COVID needs to be integrated in the interpretation of our results by the necessary focus we put on potentially and septic patients presenting in our structure.

Conclusion: The MEDS score seemed to be the most sensitive to screen infected elderly patients at risk of deterioration. A new study is required after the COVID-19 crisis to determine which score is the most accurate to early detect elderly patients at risk of developing severe infection.

Key words: Elderly patients; Sepsis; qSOFA; NEWS2; MEDS; Emergency

TABLE OF CONTENTS

ABBREVIATIONS

- **qSOFA:** quick Sequential (sepsis-related) Organ Failure Assessment
- **NEWS2 :** National Early Warning Score 2
- **MEDS :** Mortality in Emergency Department Sepsis
- **SIRS :** Systemic Inflammatory Response Syndrome
- **COPD :** Chronic Obstructive Pulmonary Disease
- **65yo :** 65 Years-old
- **ICU :** Intensive Care Unit
- **ED :** Emergency Department
- **SS/SC :** Severe Sepsis and Septic Shock

INTRODUCTION

Epidemiology

Sepsis is a major public health issue because its annual incidence is increasing[1] and its mortality high. In 2001, the French cohort study EPISEPSIS[2] conducted in 205 intensive care units demonstrated that it represents 15% of patients admitted to intensive care. In another study published in 2020 in the Lancet, Rudd et al. reported an estimate of 48.9 million cases of sepsis in the world responsible for 11 million deaths during 2017[3]. This figure represents 19% of all causes of death combined that year. Finally, in-hospital mortality from sepsis increases with age, ranging from 10 to 20% in people under 65 years of age and up to 40% in people over 85 years of age[1].

Definition

In 2016, the Surviving Sepsis Campaign redefined sepsis during the 3rd International Consensus (Sepsis-3, revised 2018)[4]. In its new definition, the infectious pathology is now classified into three stages: infection, sepsis and septic shock. Sepsis is now defined as the combination of infection, host response and organ dysfunction. Any organ dysfunction should therefore prompt-us to search an underlying septic etiology. The presence of organ dysfunction should be investigated using the "SOFA" (Sequential Organ Failure Assessment) score. After an infection, an increase of at least two points compared to the baseline score identifies a patient with a risk of mortality by sepsis ≥ 10% and who will therefore require adapted and rapid management.

Septic shock is defined as sepsis with profound circulatory, cellular and metabolic abnormalities, which corresponds to:

- The need to introduce vasopressors to achieve Mean Arterial Pressure ≥ 65 mmHg
- Serum lactates above 2 mmHg in the absence of hypovolemia.

Septic shock is associated with an in-hospital mortality of 40%.

Screening tools

The incidence of sepsis is constantly increasing with the ageing population, but intra-hospital mortality has been decreasing[2] since the use of screening tools and the use of management protocols recommended by the Surviving Sepsis Campaign in 2012, namely: the early

introduction of antibiotic therapy, filling and hemodynamic support when necessary. The key to management therefore lies in the early identification of patients who are "at risk" of developing sepsis and septic shock. It is to enable this rapid identification that we use scores such as qSOFA, MEDS and NEWS2

The qSOFA (quick sequential (sepsis-related) organ failure assessment) score is the most widely used score since sepsis-3. Its superiority compared to the old definition (SIRS) was validated in the emergency department by the study of Y. Freund et al in 2017[5]. The qSOFA is a score that can be used quickly because it does not require waiting for laboratory results. It identifies patients at risk of developing sepsis in presumed infected patients and considers three criteria: respiratory rate ≥ 22/min; blood pressure ≤ 100 mmHg; a Glasgow score ≤ 14. (Figure 1)

The MEDS (Mortality in Emergency Department Sepsis) score was first described by the team of Shapiro et al in 2003[6]. It is used to estimate the in-hospital mortality at D-28 of septic patients admitted to the emergency department. It is composed of 9 risk factors such as age > 65 years, consciousness disorders or the presence of a lower respiratory infection. This score can vary from 0 to 27. Patients are then classified into 5 groups, each group being associated with a different risk of mortality. We find a mortality of <5% for a score <7, a mortality of 7% to 10% for a score between 8 and 12, a mortality of 15% to 20% for a score between 12 and 15 and finally a mortality of 40% to 50% for scores >15. The calculation of this score can be done in the emergency room but it requires biological parameters.

Finally, the NEWS2 score is the latest version of the National Early Warning Score (NEWS) first produced in 2012 and updated in December 2017. It's a scoring system widely used throughout the UK to monitor physiological parameters in order to enable the early detection of clinical deterioration (Figure 2). This alert score is based on the monitoring of 7 parameters: blood pressure, heart rate, consciousness, temperature, respiratory rate, saturation and the need for oxygen supplementation. The particularity of NEWS2 compared to the old NEWS score is that it also considers the notion of COPD in the patient.

Objective

Early recognition of patients with potentially severe sepsis will allow identification and acceleration of patient management as soon as they are assessed by the emergency room reception and orientation nurse. Thus, these patients can be integrated into a dedicated

network allowing early antibiotic therapy, vascular filling and support by vasopressors if necessary. The elderly is a particularly fragile population with physiological characteristics. It is necessary to confirm these prognostic scores in this population.

The main objective of the research was to evaluate the prognostic performance of the qSOFA, NEWS2 and MEDS scores in patients over 65 years of age presenting to the emergency department with a diagnosis of infection made by the emergency physician in charge.

MATERIALS AND METHODS

Outline of the study

Our study was a monocentric, prospective, non-interventional study. The study was conducted in the emergency department of an academic hospital between the 15th February 2021 and the 15th April 2021. Recruited patients were those for whom emergency physician in charge suspected an infection, either through clinical examination or complementary examinations (radiological, microbiological). The diagnosis of infection was re-evaluated remotely by 2 experts once the follow-up phase was completed. In case of discrepancies, a consensus was reached between the 2 experts. Patients with no confirmed infection were excluded from the study. We also excluded pregnant women, minors, patients under legal protection, or patients refusing to participate, prisoners and patients with localized infections without general repercussions (abscess, cystitis, angina etc.). For each included patient, the reception and orientation nurse assisted by the emergency physician had to fill in the parameters needed to calculate qSOFA score, the NEWS score and the MEDS score on admission.

Objective and evaluation criteria

The main judgment criterion was in-hospital mortality at 28 days. Hospitalized patients at D28 were considered alive. Secondary endpoints were admission to intensive care (resuscitation/continuous monitoring) unit, length of hospital stay, length of stay in intensive care, length of stay in resuscitation, length of time before antibiotic therapy and a composite endpoint of mortality or admission to intensive care for more than 72 hours.

A comparison of the performance of the scores was made between the population aged 65 years and over and the rest of the population.

Statistical analyses

Numerical variables were expressed as average and 95% confidence intervals, and categorical variables were expressed as number and percentage. In the case of missing variables for scores, we assumed that the values were within normal values. To achieve the performance of the qSOFA, NEWS and MEDS scores in predicting the main judgement criterion, we calculated the diagnostic performance (sensitivity, specificity, positive and negative predictive values) for a qSOFA greater than or equal to 2, a NEWS2 $\geq$ 7 and a MEDS greater than or equal to 5. The scores were compared with each other in the population over 65 years old. Each score was also compared between the population over 65 and the population 18-64 years old. A p value of less than 0.05 was considered significant. The analyses were performed using GraphPad Prism v6.0 (GraphPad Software, San Diego, California, USA). The study was approved by our institutional ethical board (2020_118) and registered on Clinical Trials (NCT04721275). Included patients were informed of their participation to a study and can decided to refuse to participate.

RESULTS

Population characteristics:

The demographic and clinical characteristics of the population are presented in Table 1.

Our population was homogeneous in terms of sex ratio with respectively 48.7% women and 51.3% men but more disparate in terms of age. 225 (36.3%) patients were under-65 years-old and 395 (63.7%) were in the elderly category. The median age was 46.66 [CI95% 66.49-69.59] in the under-65yo group and 80.88 [CI95% 79.35-81.08] in the over-65yo group.

Among the 620 patients, 72 (11.62%) had a positive qSOFA score greater than or equal to 2; 519 patients (83.7%) had a positive MEDS score greater than or equal to 5 and 176 patients (28.4%) had a positive NEWS2 score greater than or equal to 7.
The positivity of these 3 scores was statistically more often found in the population over 65 years old. (60/72 patients for the qSOFA. 392/519 for the MEDS and 138/176 for the NEWS2). Out of a total of 620 patients admitted for suspected infection, 59 patients died before the 28th day post-admission, including 46 in the over-65 population. 52 patients were admitted to ICU with an equal distribution of admissions in our two populations (26 and 26). Finally, 26 patients progressed to septic shock, including 19 in the "elderly" category.

	Overall (n=620)	18-64 years old (n=225)	65 years old and older (n=395)	P value
Age (years old)	68.04 [66.49-69.59]	46.66 [44.73-48.59]	80.22 [79.35-81.08]	<0.0001
Heart rate (/min)	92.36 [90.79-93.94]	98.77 [96.21-101.3]	88.72 [86.80-90.63]	<0.0001
Systolic blood pressure (mmHg)	134.5 [132.4-136.6]	131.4 [128.6-134.3]	136.3 [133.5-139.1]	0.017
Diastolic blood pressure (mmHg)	74.12 [72.79-75.45]	76.55 [74.51-78.58]	72.74 [71.01-74.47]	0.0007
Respiratory rate (/min)	23.71 [23.05-24.38]	24.16 [23.05-325.26]	24.14 [23.31-24.97]	0.752
Oxygen saturation (%)	95.23 [94.88-95.58]	96.38 [95.95-96.82]	94.58 [94.10-95.06]	<0.0001
Glasgow Coma Scale	14.81 [14.55-15.08]	14.91 [14.82-14.99]	14.56 [14.43-14.69]	<0.0001
Temperature (°C)	37.41 [37.27-37.56]	37.49 [37.35-37.64]	37.37 [37.15-37.59]	0.844
Leukocytis (G/l)	11.26 [10.57-11.95]	11.81 [10.46-13.15]	10.95 [10.19-11.71]	0.617
Platelets (G/l)	249.3 [239.6-259.1]	259.2 [242.6-275.7]	243.7 [231.6-255.8]	0.041
Emergency department Lenght of stay (hours)	13.84 [13.10-14.58]	12.78 [11.53-14.02]	14.45 [13.53-15.37]	0.004
In-hospital LoS (days)	10.41 [9.33-11.48]	7.92 [6.46-9.38]	11.73 [10.30-13.16]	<0.0001
Delay before antibiotics (hours)	7.82 [7.29-8.36]	7.34 [6.50-8.18]	8.08 [7.39-8.77]	0.334
qSOFA score 0 1 2 3	 273 (44.0%) 275 (44.4%) 63 (10.2%) 9 (1.4%)	 129 (57.3%) 84(37.3%) 10 (4.4%) 2 (0.9%)	 144 (36.4%) 191(48.4%) 53(13.4%) 7 (1.8%)	<0.0001
MEDS score 0-4 5-7 8-12 13-15 >=16	 101 (16.3%) 96 (15.5%) 341 (55.0%) 65 (10.5%) 17 (2.7%)	 98 (43.6%) 43(19.1%) 83(36.9%) 0 1 (0.4%)	 3 (0.8%) 53 (13.4%) 258 (65.3%) 65 (16.5%) 16 (4.0%)	<0.0001
NEWS2 score 0 1-4 5-6 >= 7	 57 (9.2%) 275 (44.3%) 112 (18.1%) 176 (28.4%)	 26(11.6%) 124(55.1%) 37 (16.4%) 38 (16.9%)	 31 (7.8%) 151 (38.2%) 75 (19.0%) 138 (34.9%)	<0.0001
Sex ratio F/M	302/318	114/111	188/207	0.504
COPD	47 (7.6%)	9 (4%)	38(9.6%)	0.011
Septic shock	26 (4.2%)	7 (3.1%)	19 (4.8%)	0.406
In-hospital mortality at D28	59 (9.5%)	13 (5.8%)	46 (11.6%)	0.016
COVID-19	201 (32.4%)	71 (31.6%)	130 (32.9%)	0.729
Admitted in ICU	52 (8.4%)	26 (11.6%)	26 (6.6%)	0.032

Tableau 1: Demographic and clinical characteristics of patients. Data are presented as mean with 95% confidence intervals, or as number (percentage).

Finally, our study was carried out during a period marked by the COVID-19 crisis. In our cohort, 201 patients out of 620 were diagnosed with COVID-19. It represented 32.4% of our cohort, with a homogeneous distribution of patients with COVID-19 in our two populations (31.6% in the under-65yo group and 32.9% in the over-65yo group).

Table 2 shows the results of our study concerning the 3 scores after exclusion of patients with a positive diagnosis for COVID-19.

	Overall (n=376)	18-64 yo (n=111)	Older than 65yo (=265)	P value
qSOFA score				<0.0001
0	181 (48.1%)	78 (70.3%)	103 (38.9%)	
1	145 (38.6%)	25 (22.5%)	120 (45.2%)	
2	44 (11.7%)	7 (6.3%)	37 (14.0%)	
3	6 (1.6%)	1 (0.9%)	5 (1.9%)	
MEDS score				<0.0001
0-4	70 (18.6%)	67 (60.4%)	3 (1.1%)	
5-7	71 (18.9%)	20 (18.0%)	51 (19.2%)	
8-12	188 (50%)	24 (21.6%)	164 (61.9%)	
13-15	37 (9.8%)	0	37 (14.0%)	
>=16	10 (2.7%)	0	10 (3.8%)	
NEWS2 score				<0.0001
0	41 (10.9%)	17 (15.3%)	24 (9.1%)	
1-4	180 (47.9%)	71 (64.0%)	109 (41.1%)	
5-6	53 (14.1%)	9 (8.1%)	44 (16.6%)	
>= 7	102 (27.1%)	14 (12.6%)	88 (33.2%)	
In-hospital mortality at D28	29 (7.7%)	6 (5.4%)	23 (8.7%)	0.394
Admitted in ICU	17 (4.5%)	6 (5.4%)	11 (4.2%)	0.593

Tableau 2: Prognostic scores excluding COVID-19 patients.

Primary endpoint:

The overall mortality of patients in our cohort on day 28 was 9.5%. It was statistically different between our two populations with respectively 11.6% in elderly patients and 5.8% in patients under 65 years old. (p= 0,016). After exclusion of "COVID" patients, the mortality at D-28 was 7.7% with respectively 8.7% mortality in patients over 65 yo. and 5.4% in patients under 65 yo. (p= 0,394).

The performance of the three studied scores on mortality at D-28 was reported in Table 3 for patients over 65 yo. and in Table 4 for patients under 65 yo.

	qSOFA		MEDS		NEWS2	
Number of patients	<2 335	≥2 60	<5 3	≥5 392	<7 257	≥7 138
In-hospital mortality	32	14	0	46	21	25
Sensitivity	30.43 [95%CI 17.74-45.75]		100 [92.29-100]		54.35 [39.01-69.10]	
Specificity	86.82 [95%CI 82.81-90.19]		0.86 [0.18-2.49]		67.62 [62.44-72.51]	
Positive Predictive Value	23.33 [13.38-36.04]		11.73 [8.72-15.34]		18.12 [12.08-25.57]	
Negative Predictive Value	90.45 [86.78-93.37]		100 [29.24-100]		91.83 [87.78-94.87]	
Likelihood ratio	2.309		1.009		1.679	
Number of patients excluding COVID	<2 222	≥2 42	<5 3	≥5 261	<7 176	≥7 88
In-hospital mortality	14	9	0	23	9	14
Sensitivity	39.13 [19.71-61.46]		100 [85.18-100]		60.87 [38.54-80.29]	
Specificity	86.31 [81.31-90.38]		1.25 [0.26-3.60]		69.29 [63.05-75.06]	
Positive Predictive Value	21.43 [10.30-36.81]		8.81 [5.67-12.93]		15.91 [8.98-25.25]	
Negative Predictive Value	93.69 [89.65-96.51]		100 [29.24-100]		94.89 [90.52-97.64]	
Likelihood ratio	2.858		1.013		1.982	

Tableau 3: Diagnostic performances for the prediction of in-hospital mortality in the elderly population with and without COVID's patients.

	qSOFA		MEDS		NEWS2	
Number of patients	<2 213	≥2 12	<5 98	≥5 127	<7 187	≥7 38
In-hospital mortality	10	3	1	12	7	6
Sensitivity	23.08 [5.04-53.81]		92.31 [63.97-99.81]		46.15 [19.22-74.87]	
Specificity	95.75 [92.09-98.04]		45.75 [38.91-52.72]		84.91 [79.36-89.44]	
Positive Predictive Value	25.00 [5.49-57.19]		9.45 [4.98-15.92]		15.79 [6.02-31.25]	
Negative Predictive Value	95.31 [91.54-97.73]		98.98 [94.45-99.97]		96.26 [92.44-98.48]	
Likelihood ratio	5.436		1.702		3.058	
Number of patients excluding COVID	<2 145	≥2 9	<5 98	≥5 56	<7 139	≥7 15
In-hospital mortality	5	2	1	6	4	3
Sensitivity	28.57 [3.67-70.96]		85.71 [42.13-99.64]		42.86 [9.90-81.59]	
Specificity	95.25 [90.43-98.06]		65.99 [57.72-73.59]		91.84 [86.17-95.71]	
Positive Predictive Value	22.22 [2.82-60.01]		10.71 [4.04-21.88]		20.00 [4.33-48.09]	
Negative Predictive Value	96.55 [92.14-98.87]		98.98 [94.45-99.97]		97.12 [92.80-99.21]	
Likelihood ratio	6.0		2.520		5.250	

Tableau 4: Diagnostic performances for the prediction of in-hospital mortality in the 18-64 years old population with and without COVID's patients.

The sensitivity of the three scores was higher in the elderly population than in the young population, and the MEDS had the best sensitivity of the three scores. The qSOFA had the

best specificity in both populations whereas the MEDS had a poor specificity especially in the elderly population.

After exclusion of patients admitted for a diagnosis of COVID-19, the qSOFA and NEWS2 scores had a better sensitivity, specificity and a better likelihood ratio especially in the young population. The best sensitivity was obtained using the MEDS score in both populations but the likelihood ratio remained poor.

Secondary endpoints:

A. Admission to intensive care unit (ICU):

8.4% of the patients in our cohort required admission to an intensive care unit, with a statistically significant difference between our two populations, i.e. 11.6% of admissions in the under-65 age group and 6.6% in the over-65 age group (p=0.032). This difference between the two populations was no longer significant after excluding COVID patients (5.4% of admissions in the under-65yo and 4.2% in the over-65yo).

	qSOFA		MEDS		NEWS2	
Number of patients	<2 335	≥2 60	<5 3	≥5 392	<7 257	≥7 138
Admitted in ICU	21	5	0	26	6	20
Sensitivity	19.23 [6.55-39.35]		100 [86.77-100]		76.92 [56.35-91.03]	
Specificity	85.09 [81.04-88.57]		0.81 [0.17-2.36]		68.02 [63.00-72.75]	
Positive Predictive Value	8.33 [2.76-18.39]		6.63 [4.38-9.57]		14.49 [9.08-21.49]	
Negative Predictive Value	93.73 [90.58-96.08]		100 [29.24-100]		97.67 [94.99-99.14]	
Likelihood ratio	1.290		1.008		2.405	
Number of patients excluding COVID	<2 222	≥2 42	<5 3	≥5 261	<7 176	≥7 88
Admitted in ICU	9	2	0	11	2	9
Sensitivity	18.18 [2.28-51.78]		100 [71.51-100]		81.82 [48.22-97.72]	
Specificity	84.19 [79.10-88.46]		1.19 [0.25-3.42]		68.77 [62.67-74.43]	
Positive Predictive Value	4.76 [0.06-16.16]		4.22 [2.12-7.42]		10.23 [4.78-18.53]	
Negative Predictive Value	95.95 [92.44-98.13]		100 [29.24-100]		98.86 [95.96-99.86]	
Likelihood ratio	1.150		1.012		2.620	

Tableau 5: Diagnostic performances for the prediction of admission in the ICU in the elderly population, with and without COVID19's patients.

	qSOFA		MEDS		NEWS2	
Number of patients	<2 213	≥2 12	<5 98	≥5 127	<7 187	≥7 38
Admitted in ICU	26	0	2	24	16	10
Sensitivity	0 [0-13.23]		92.31 [74.87-99.05]		38.46 [20.23-59.43]	
Specificity	93.97 [89.70-96.85]		45.93 [39.04-52.94]		85.93 [80.31-90.44]	
Positive Predictive Value	0 [0-26.46]		17.52 [11.56-24.93]		26.32 [13.40-43.10]	
Negative Predictive Value	87.79 [82.63-91.87]		97.96 [92.82-99.75]		91.44 [86.48-95.03]	
Likelihood ratio	0		1.707		2.734	
Number of patients excluding COVID	<2 145	≥2 9	<5 98	≥5 56	<7 139	≥7 15
Admitted in ICU	8	0	2	6	7	1
Sensitivity	0 [0-36.94]		75.00 [34.91-96.81]		12.50 [0.32-52.65]	
Specificity	93.84 [88.62-97.14]		65.75 [57.45-73.40]		90.41 [84.43-94.66]	
Positive Predictive Value	0 [0-33.63]		10.71 [4.04-21.88]		6.67 [0.17-31.95]	
Negative Predictive Value	94.48 [89.42-97.59]		97.96 [92.82-99.75]		94.96 [89.90-97.95]	
Likelihood ratio	0		2.190		1.304	

Tableau 6: Diagnostic performances for the prediction of admission in the ICU in the 18-64 years old population, with and without COVID19's patients.

The sensitivity of the MEDS to predict ICU admission was better than NEWS2 and qSOFA in both populations. The specificity of the qSOFA was the best in both populations. The likelihood ratio of the NEWS2 was the best in the elderly and the young populations.

After exclusion of patients admitted for a diagnosis of COVID-19, the sensitivity of the MEDS was better in both populations. The specificity of the qSOFA and the NEWS2 scores remained approximately the same for our two populations. In the elderly population, the NEWS score had the best likelihood ratio (2.62) whereas the MEDS had the best likelihood ratio (2.19) in the young population.

B. Concerning the length of hospital stay and the length of stay in the emergency room

In terms of length of stay in the emergency department, the median was 13.84 hours [95% CI 13.10-14.58] for our entire population, with a median of 12.78 for the "young" population and a median of 14.45 for the "elderly" population. The median length of stay was 10.41 days [95% CI 9.33-11.48] for our entire population with a median of 7.92 for the "young" population and a median of 11.73 for the "elderly" population. The elderly population had a significant longer stay in the emergency department (p=0.004) and in the hospital (p=0.0001).

C. Time to antibiotic therapy.

The median time to antibiotic administration was 7.82 hours [IC95% 7.29-8.36] for our entire population with a median of 7.34 for the "young" population and a median of 8.08 for the "old" population. There was therefore no significant difference between our two populations on this criterion (p=0.334).

Etiologies of infections diagnosed in the emergency room

COVID-19 pneumonia represented the majority of our inclusions with 32.42% of our population. The most representative infections were then lower respiratory tract infections (18.23%), uro-genital infections (15.97%), gastro-intestinal infections (14.52%) and cutaneous infections (7.10%). (Figure 4)

DISCUSSION

The main objective of our study was to compare the performance of the qSOFA, NEWS2 and MEDS scores on in-hospital mortality by comparing their performance in young and elderly patients. In the elderly population, the MEDS score seemed to be the most sensitive to predict sepsis and ICU admission and the qSOFA had the best likelihood ratio to predict mortality. The NEWS2 had the best likelihood ratio to predict admission to ICU. These results were similar in the young population. After exclusion of COVID-19 patients, our results were the same except that the MEDS score had the best likelihood ratio in the young population.

The elderly population can have an atypical presentation of sepsis. Indeed, the elderly can be asymptomatic or pauci-symptomatic until a brutally unfavorable evolution, making it more difficult to detect patients said to be "at risk". They do not present the same symptomatology as younger patients. For example, they do not always present a fever as a symptom of infection. Interpreting biological markers can also be more complicated in these patients, who often already have other comorbidities[7].

Our results were discordant with the literature. The MEDS score had a good sensitivity as reported by Zhang et al. (2020 Emergency Med J) who reported in a meta-analysis a moderate accuracy of the MEDS score to predict mortality among ED patients with suspected infection[8]. Their sensitivity was 79% with a specificity of 77% on in-hospital mortality at D-28. The disparity of these results may be associated with age of the studied populations since age is a criterion of the MEDS score.

On the other hand, the qSOFA had a very bad sensitivity in our study both in the elderly and in the young population. These results were in opposition with the results of Freund et al. (JAMA 2017) who reported a very good accuracy of the qSOFA in the ED to predict in-hospital mortality[5]. They reported that the use of qSOFA resulted in greater prognostic accuracy for in-hospital mortality than did either SIRS or severe sepsis, with a sensitivity of 70% and a specificity of 79%. Other studies have reported more mixed results. The meta-analysis of Song J et al. reported a sensitivity of 51% and a specificity of 83% for in-hospital mortality[9].

Other studies looked for comparison between qSOFA and NEWS score. In 2017 Churpek et al. conducted a retrospective study over 8 years with a cohort of 30 000 patients and reported

that early warning scores such as NEWS were more accurate and provided an earlier response than qSOFA and SIRS for predicting mortality for patients outside the ICU with suspected infection[10]. The study by Usman et al. in 2019 was a single-center, 2-year retrospective study. On this cohort of 115 000 patients they reviewed the viability of NEWS as an early predictor of severe sepsis and septic shock (SS/SC) [11]. For the detection of SS/SC they reported a sensitivity of 43.3% and a specificity of 97.6% for the NEWS score. The NEWS score was more accurate when compared with qSOFA and SIRS for the early detection of adverse outcomes. In accordance with these two recent studies, our study shows a better sensitivity for the NEWS2 than for the qSOFA score.

In 2015, the team of Shapiro et al conducted a prospective, observational study on a cohort of 3000 patients. They reported that in-hospital mortality of infected patients was related to the number of organ failures and that it would increase by 15% per organ failure[12]. Therefore, although the qSOFA is a useful score for rapid and early screening at the patient's bedside, it would seem necessary to complement it with the SOFA, thus allowing the evaluation of all organ failures.

Our study was conducted over a period of two months in an academic hospital and had several limitations. First, it was a monocentric study. Secondly, we must take into account the lack of power of our study due to the small number of patients diagnosed with “Septic Shock” (26 patients). And finally, our study took place during a period strongly marked by the COVID-19 crisis. That can explain the difference between our results and other studies. Indeed, the diagnosis of SARS-CoV-2 infection was retained in 30% of our population. The COVID-19 crisis had intrinsically changed our management. During this period, we focused more on triage of patients. We used a dedicated channel, in a dedicated care sector with sufficient number of staff to allow optimal monitoring of any patient suspected of COVID-19 infection (at any age : fever, cough, dyspnea, rhinitis, anosmia or agueusia) and for any patient over 75 years of age with “extended criteria” (Idem but also sudden confusion or decompensation of chronic pathology). Moreover, the use of masks and barrier measures may reduce the incidence of severe infections. This could explain our low mortality rate (5-8%) after excluding COVID-19 patients comparing to the literature (20-40%). This low mortality impacted the diagnostic performance of all our three scores. Nevertheless, after excluding COVID-19 patients, the diagnostic performance of our scores was quite similar. It is in accordance with Ferreira et al. (2020 Annals of Intensive Care)[13]. They reported that qSOFA did not stratified as sepsis critical ill SARS-CoV-2 infected patients. We also reported a

different proportion of patients admitted in ICU after excluding COVID-19 patients. That may have had an impact on other infected patients. Finally, the mean delay before the antibiotic treatment was very long. That was another proof that our population was not represented critically ill patients. A new study conducted after the COVID-19 pandemic will be more informative.

CONCLUSION

The MEDS score seemed to be the most sensitive score to detect elderly patients at risk of developing a severe infection. Nevertheless, our study was carried out in the middle of the COVID-19 crisis and a new study conducted after the pandemic will be more informative. Moreover, the MEDS score required biological exam and emergency physicians need a quick tool to early detect elderly patients at risk of developing a severe infection.

ANNEXES

Box 4. qSOFA (Quick SOFA) Criteria

Respiratory rate ≥22/min

Altered mentation

Systolic blood pressure ≥100 mm Hg

Figure 1: qSOFA. From the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Characteristic	Points Assigned
Predisposition	
Age > 65 year	3
Nursing home resident	2
Rapidly terminal comorbid illness	6
Infection	
Lower respiratory infection	2
Response	
Bands > 5%	3
Organ dysfunction	
Tachypnea or hypoxemia	3
Septic shock	3
Platelet count <150,000/mm^3	3
Altered mental status	2

Point Range	MEDS Group	Original 28-day Predicted Mortality Rate
0 - 4	Very low	1.1%
5 - 7	Low	4.4%
8 - 12	Moderate	9.3%
13 - 15	High	16.1%
> 15	Very high	39.0%

Figure 2: Components and calculation of Mortality in Emergency Department Sepsis score (MEDS)

Physiological parameter	Score 3	2	1	0	1	2	3
Respiration rate (per minute)	≤8		9–11	12–20		21–24	≥25
SpO_2 Scale 1 (%)	≤91	92–93	94–95	≥96			
SpO_2 Scale 2 (%)	≤83	84–85	86–87	88–92 ≥93 on air	93–94 on oxygen	95–96 on oxygen	≥97 on oxygen
Air or oxygen?		Oxygen		Air			
Systolic blood pressure (mmHg)	≤90	91–100	101–110	111–219			≥220
Pulse (per minute)	≤40		41–50	51–90	91–110	111–130	≥131
Consciousness				Alert			CVPU
Temperature (°C)	≤35.0		35.1–36.0	36.1–38.0	38.1–39.0	≥39.1	

Figure 3: NEWS2 scoring system with a dedicated section (SpO2 Scale 2) for use in patients with hypercapnic respiratory failure (usually due to COPD)

Respiratory system (n=321; 51.77%)	COVID	201	32,42%
	Pneumonia	113	18,23%
	Other respiratory infections	7	1,13%
Uro-genital system (n=99; 15.97%)	Pyelonephritis	48	7,74%
	Urinary tract infection	23	3,71%
	Urinary sepsis	21	3,39%
	PID	4	0,65%
	Other urogenital infections	3	0,48%
Digestive system (n=90; 14.52%)	Appendicitis	25	4,03%
	Cholecystitis	22	3,55%
	Colitis	18	2,90%
	Diverticulitis	7	1,13%
	Other digestive infections	18	2,90%
Other (n=51; 8.22%)	IBS with no clinically identified source	19	3,06%
	Bacteremia	9	1,45%
	Febrile neutropenia	6	0,97%
	Other infectious diseases	17	2,74%
Skin System (n=44 ; 7.10%)	Erysipelas	35	5,65%
	Other skin infection	9	1,45%
Osteoarticular system (n=8 ; 1.29%)	Septic arthritis	4	0,65%
	Other	4	0,65%
Neurological system (n=7 ; 1.13%)	Meningitis	3	0,48%
	Febrile confusion	3	0,48%
	Encephalitis	1	0,16%

Figure 4: Etiologies of infections diagnosed in the emergency department between the 15th of February to the 15th of April.

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Résumé

Titre: Evaluation des indicateurs de performance des scores qSOFA, MEDS et NEWS2 sur la mortalité intra-hospitalière du patient âgé admis aux urgences pour une infection, un sepsis ou un choc septique.

Contexte: Le sepsis est un enjeu majeur de santé publique car son incidence annuelle est croissante et sa mortalité élevée. Il se définit actuellement comme une défaillance d'organe secondaire à une infection pouvant entrainer le décès du patient. Une reconnaissance précoce des patients à risque d'évoluer défavorablement est recommandée à l'aide de scores tel que le qSOFA, le MEDS et le NEWS2. Les personnes âgées présentent une population particulièrement fragile avec des particularités physiologiques il est nécessaire de valider ces scores pronostiques dans cette tranche de population.

Méthode : Notre étude était une étude monocentrique, prospective et non interventionnelle réalisée sur une période d'inclusion de 2 mois (du 15 février au 15 avril 2021) avec un suivi jusque J-28. Les patients recrutés étaient les patients chez qui l'urgentiste en charge suspectait une infection après examen clinique ou à l'aide d'examens complémentaires.

Résultats : Pour prédire la mortalité à J28, le score MEDS avait la meilleure sensibilité dans la population âgée comparativement aux scores qSOFA et NEWS2. Contrairement à la littérature, le qSOFA avait une mauvaise sensibilité. Nos résultats ont été impactés par la crise du COVID-19 et ont plusieurs biais : mortalité faible, forte population COVID avec un retentissement sur nos organisations.

Conclusion : Le score MEDS semble le plus sensible pour dépister un patient âgé à risque d'évoluer défavorablement dans un contexte d'infection. Une nouvelle étude est nécessaire après la crise COVID-19 pour déterminer quel score est le plus performant pour détecter précocement les patients âgés à risque de développer une infection sévère.

Mots clés : Patients âgés ; Sepsis ; qSOFA ; NEWS2 ; MEDS ; Urgences.

JURY

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