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Golden hour of sepsis: Can we do more?

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Abstract: *Introduction: Sepsis is a life-threatening organ dysfunction due to a dysregulated host response to an infection1 and also an important worldwide health problem. Recent progresses in understanding pathogenesis are reflected in increasing emphasis put on time (Sepsis Update 2018 decreased the time for diagnosis and treatment from 3- 6 hs Sepsis-2 to 1 hour). The aim of the study was to combine an early warning score (increased sensitivity- NEWS2) and a biomarker (increased specificity- presepsin) in order to detect earlier an acute illness (infection) before becoming life-threatening.*

Materials and methods: It was a retrospective, single-center observational cohort study of 125 consecutive patients who were diagnosed with systemic inflammatory response syndrome between July 2016 and July 2018 at Emergency Department of "Dr. Carol Davila" Central Military Emergency University Hospital, Bucharest, Romania in order to determine sooner, which patient will further develop a sepsis. We used the area under receiver–operator characteristic curves (AUC) to assess the overall discriminatory power of NEWS2, MEDS and presepsin in detecting sepsis, septic shock and the probability of death on admission and compared them with combined scores between NEWS2 and presepsin.

Results: Using a combined score and a simple algorithm, the NEWS2 score had changed (12,8%) for 16 patients. For 10 out of 95 (10,52%) without sepsis and 6 out of 30 (20%) of septic patients, more points were added to NEWS2 meaning that more septic patients were diagnosed before an infection become life-threatening

Conclusions: In the present study, we have tried to assess the impact of a monitoring score and a rapid POCT biomarker, in a condition when time is of critical importance. Using a verified early warning score, NEWS2, with increased sensibility and low specificity and presepsin, POCT biomarker with increased specificity, we diagnosed sepsis earlier in a number of cases.

Keywords: *sepsis, early warning score, NEWS2, combined score, presepsin*

INTRODUCTION

Sepsis is a life-threatening organ dysfunction due to a dysregulated host response to an infection [1] and also an important worldwide health problem. Nowadays the global sepsis estimates are more than double than previous calculations, with 11 million sepsis deaths and 48.9 million incident sepsis cases in 2017 with a global trend of decreasing sepsis [2]. Although Sepsis-3 definition is designed to put a diagnosis in prehospital settings, battlefield and Emergency Department (ED) on arrival there is much to be done to further improve diagnostic of patients with sepsis. The specificity of the Sepsis-3 criteria is great, but sometimes the sepsis diagnostic is put too late for a specific patient.

Rapid clinical evaluation on arrival in ED and as soon as possible paraclinical evaluation are realized with POCT (point of care testing) devices which allow a more rapid targeted response (complete blood count, acid-base analysis, targeted biomarkers, etc.) to gain time for the patient and to prevent and fight against further deterioration of a patient in a not an optimal state. Sepsis-2 [3] emphasized the fact

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that time management is of critical importance. Early targeted therapy and management bundle put an algorithm at hand for doctors and 2018 Sepsis update [4] indirectly stressed out that rapid medical intervention is paramount because what it should have been done in the first 3-6 hours, from that moment on, it must be done in one hour. For greater accuracy and tailored treatment more exhaustive laboratory analysis usually arrive in at least 30-40 minutes.

By 2015 over 36 Early Warning Scores were used and evaluated for accurately forecast the prognosis [5]. Developed as specific tools, in different environments (different wards, ED, ICU), some scores are nowadays obsolete or of limited use [5, 6] but some are still used and revised (NEWS2).

A possible research direction in sepsis might be to combine an early warning sign/score with increased sensibility, low specificity and a specific biomarker which will increase the specificity to buy time for the patient and ultimately to save more lives with increased cost-results efficiency.

Conceived in 2012, verified on different wards for several years and revised in 2017, National Early Warning Score 2 is nowadays used in United Kingdom with great success [7].

Used in different environments, presepsin is one of the biomarkers which passed the proof the time, as a valuable tool in POCT, being used for more than a decade now [8, 9, 10, 11, 12, 13]. Presepsin increases in patients developing infections in a severity-dependent manner [14, 15, 16]. Previous studies showed that presepsin levels performed when used for early diagnosis, risk stratification and prognosis [17, 18].

The aim of the study was to find new ways in which to combine these recently developed tools, an early warning score (NEWS2) and a specific biomarker (presepsin) in order to diagnose more cases of severe infections, before developing sepsis, preventing further deterioration of an already altered patient with multiple comorbidities. The proposed score is easy to calculate, rapidly available and allowed us to markedly decrease the time for intervention for patients with altered medical status before becoming life-threatening.

MATERIAL AND METHODS

Study design

This was a retrospective, single-center observational cohort study of 125 consecutive patients who were diagnosed with systemic inflammatory response syndrome between July 2016 and July 2018 at Emergency Department of "Dr. Carol Davila" Central Military Emergency University Hospital, Bucharest, Romania in order to determine sooner, which patient will further develop a sepsis. We developed a simple algorithm for earlier diagnose of sepsis and compared the results with Sepsis-3 criteria, NEWS2 and MEDS scores. All patients were above 18 years old and have agreed to sign the informed consent. The study was approved by the ethical committee at "Dr. Carol Davila" Central Military Emergency University Hospital, Bucharest, Romania.

Blood sample analysis

Presepsin concentrations were measured using a chemiluminescent enzyme immunoassay (PATHFAST™ Presepsin), performed on the PATHFAST point-of-care analyzer (Mitsubishi Chemical Medience Corporation, Tokyo, Japan). Measuring range is 20–20,000 ng/L; manufacturer's URL (95th percentile) is 320 ng/L. Correlation between heparinized and EDTA plasma was Y = 1.00× + 1.53 (r=0.999, n=23) [19].

Developing a tool for earlier diagnosis of sepsis

National Early Warning Score (NEWS) 2 is recommended by the NHS (National Health System) UK to determine the degree of illness of a patient, to prompt critical care intervention and recommends the NEWS 2 in the following settings: Emergency (for initial assessment, serial monitoring and assessment for triage), ward (for initial inpatient assessment and serial monitoring), prehospital (for communication of illness severity to receiving hospitals). Respiratory rate, hypercapnic respiratory failure/room or supplemental O_2, temperature, systolic BP (mmHg), pulse (beats per minute) and consciousness are assessed.

In order to try other combination of NEWS2 and PSP we have obtained other scorings to better predict the prognosis and earlier detection of sepsis.

We have created a new score NEWS2PSP: for PSP between 0-1000 pg/ml we granted 1 point; between 1000-2000 points=2 points, and so on. Adding those values to NEWS2 score lead us to the new score NEWS2 PSP.

Another compounded score was tested: for PSP<200 pg/ml we have given 1 point, 2 points for PSP=200- 300 pg/ml, 3 points for PSP=300-500 pg/ml, 4 points for PSP=500-1000 pg/ml and 5 points for PSP>1000 pg/ml. The new score was NEWS2PSP2.

NEWS2PSP3 resulted from granting 1 point if PSP>1000 and 0 points if PSP<1000.

Granting 0 points for PSP<5000 pg/ml, 1 point for PSP=5000-10000 pg/ml and 2 points for PSP>10000 and adding these points to NEWS2 lead us to NEWS2PSP4.

Statistical analysis

Descriptive statistics was used to summarize the study population. Baseline and follow-up characteristics were described by means and standard deviations (SD) or by median and interquartile range (IQR) for continuous variables, as appropriate, and by percentages for categorical variables. We performed Chi2 statistics or Fisher's exact tests when appropriate for qualitative variables, and the Wilcoxon/Mann–Whitney test for continuous variables with skewed distributions to compare baseline patient characteristics and study outcomes. Categorical variables are presented as counts and percentages. We used the area under receiver–operator characteristic curves (AUC) to assess the overall discriminatory power of NEWS2, MEDS and presepsin in detecting sepsis, septic shock of the probability of death on admission. The IBM SPSS version 20.0 software (IBM Corp., Armonk, NY, USA) was used for statistical analysis.

RESULTS

There were 125 consecutive patients which were considered to have SIRS (systemic inflammatory response syndrome) and included in the study. When 2 or more SIRS criteria were found, presepsin (PSP) was assessed. From these 30 were diagnosed as having sepsis (Sepsis-3 definition, with 2 or more qSOFA criteria) and 11 were diagnosed as having septic shock. During the study 27 patients have died from different causes, some of them being sepsis or septic shock. The mean age was of 70.88 years with standard deviation of 15.74 years; they ranged from 18 to 96 years. Of the total study population, 79 (63.2%) were men. Table 1 provides the baseline characteristics demographic data, the calculated scores, selected comorbidities and the site of infection.

Table 1: Baseline characteristics, used scores, selected comorbidities and the site of infection

Demographics	All patients (n=125)	Sepsis (n=30)	Septic shock (n=11)	Exitus (n=27)
Age (mean, SD)	70.888 (15.74406)	73.4666 (15.3139)	72.2727 (15.3391)	75.6296 (14.4277)
Sex (male, %)	79 (63.2)	23 (29.11)	10 (12.65)	20 (74.07)
Weight (mean, SD)	71.472 (12.6835)	70.7333 (9.2805)	72.2727 (9.3525)	70.5185 (15.8637)
GCS (mean, SD)	14.264 (2.1841)	12.8666 (2.9970)	12.4545 (2.6064)	13.8148 (2.4651)
QSOFA (mean, SD)	0.672 (0.9779)	2.2666 (0.4422)	2.5454 (0.4979)	1.1481 (1.1123)
NEWS2 (mean, SD)	4.768 (3.6532)	9.7333 (2.8511)	12 (2.3741)	6.5925 (4.0208)
MEDS (mean, SD)	9.568 (4.3512)	14.0333 (2.9606)	15.8181 (2.5873)	12.9259 (4.2681)
PSP (mean, SD)	2594.608 (3063.226)	3582.8 (4306.524)	2961.545 (2163.594)	3272.593 (4373.756)
Selected comorbidities				
Malignancy (%)	35 (28)	10 (28.57)	2 (5.71)	8 (22.85)
Diabetes melitus (%)	27 (21.6)	9 (33.33)	4 (14.81)	6 (22.22)
Cardiac failure (%)	49 (39.2)	9(18.36)	4 (8.16)	13 (26.53)
Kidney failure (%)	36 (28.8)	7 (19.44)	3 (8.33)	11 (30.55)
Respiratory failure (%)	20 (16)	8 (40)	3 (15)	8 (40)
Institutionalized patient (%)	7 (5.6)	3 (42.85)	1 (14.28)	6 (85.71)
Site of infection				
Abdominal (%)	26 (20.8)	6 (23.07)	3 (11.53)	8 (30.76)
Cutaneous (%)	15 (12)	1 (6.66)	0	3 (20)
Endocard (%)	1 (0.83)	0	0	1 (100)
Pulmonary (%)	20 (16)	6 (0.3)	2 (10)	5 (25)
Kidney (%)	28 (22.4)	11 (39.28)	5 (17.85)	5 (17.85)
Unspecified (%)	35 (28)	6 (17.14)	1 (2.85)	5 (14.28)

GCS= Glasgow Coma Scale, qSOFA= quick Sequential Organ Failure Assessment, NEWS2= National Early Warning Score 2, MEDS= Mortality in Emergency Department Score, PSP= presepsin

Patients who met the Sepsis-3 criteria (2 or more qSOFA points) were treated accordingly to the current guidelines for sepsis. Only 30 patients were diagnosed with sepsis and 11 with septic shock.

Table 2 shows the Area Under the Receiver Operating Characteristics and confidence intervals for the different scores and compound scores.

NEWS2 9.7±2.9, MEDS 14.0±3.0 and PSP (presepsin) 3582.8±4380.1 showed increased values for sepsis with statistical significance for NEWS2 p<0.001 MEDS p<0.001; of note the statistical significance for PSP was p=0.043. For sepsis NEWS2 has the best AUROC (Area under ROC) 0.962

(95%CI 5.54-7.51), MEDS 0.875 (95%CI 4.39-7.36), PSP 0.603(95%CI 41.32-2559.17) according to Sepsis-3 criteria as depicted in Figure 2. ROC curves are the same for septic shock NEWS2 0.974 (95%CI 6.11-9.74), MEDS 0.913(95%CI 4.39-9.3) and respectively for PSP 0.626 (95%CI 1526.19-2330.88) (Figure 3).

Table 2: AUROC and 95%CI calculated for different combined scores in sepsis, septic shock and mortality

	Sepsis		Septic shock		Mortality	
	AUROC	**95%CI**	**AUROC**	**95%CI**	**AUROC**	**95%CI**
NEWS2	0,962	5,54- 7,51	0,974	6,11- 9,74	0,670	0,79- 3,85
MEDS	0,875	4,39- 7,36	0,913	4,39- 9,3	**0,762**	2,55- 6,01
PSP	0,603	41,32- 2559,17	0,626	-1526,19- 2330,88	0,561	-454,79- 2184,34
NEWS2PSP	0,z924	6,36- 9,45	0,949	5,66- 11,20	0,656	1,21- 5,39
NEWS2PSP2	0,953	5,69- 7,84	**0,975**	6,31- 10,19	0,676	0,94- 4,17
NEWS2PSP3	0,956	5,95- 7,65	**0,975**	6,22- 9,96	0,672	0,90- 4,03
NEWS2PSP4	**0,971**	5,69- 7,65	0,972	6,07- 9,76	0,670	0,82- 3,91

Figure 1: Receiver-operating characteristics (ROC) curves for NEWS2, MEDS, PSP and for derived scores (NEWS2PSP, NEWS2PSP2, NEWS2PSP3, NEWS2PSP4) in sepsis (AUROC 0,971 %95 CI 5,69- 7,65 for NEWS2PSP4)

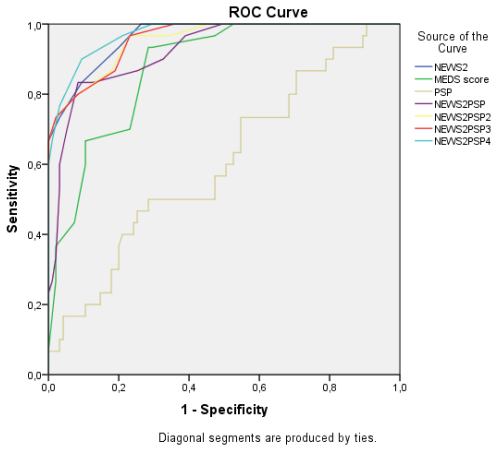


Figure 2: Receiver-operating characteristics (ROC) curves for NEWS2, MEDS, PSP and for derived scores (NEWS2PSP, NEWS2PSP2, NEWS2PSP3, NEWS2PSP4) in septic shock (AUROC 0,975 %95 CI 6,31- 10,19 for NEWS2PSP2 respectively AUROC 0,975 %95 CI 6,22- 9,96 for NEWS2PSP3)

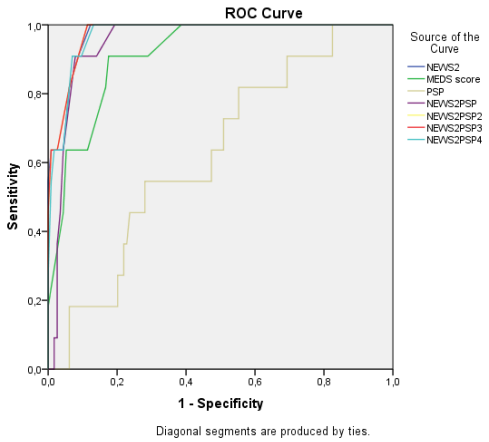
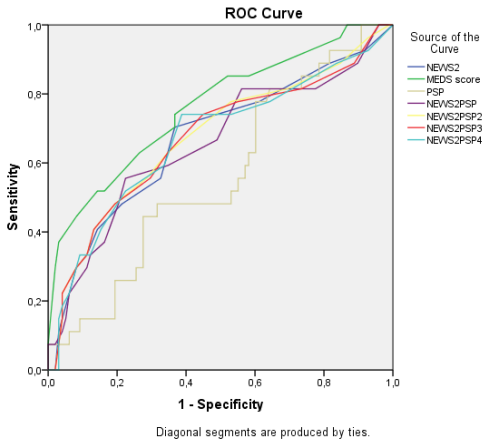


Figure 3: Receiver-operating characteristics (ROC) curves for NEWS2, MEDS, PSP and for derived scores (NEWS2PSP, NEWS2PSP2, NEWS2PSP3, NEWS2PSP4) in mortality (AUROC 0,762 %95 CI 2,55- 6,01 for MEDS score)



We created a new score, NEWS2PSP, transforming PSP values as follows: between 0-1000 pg/ml = 1 point; 1000-2000 pg/ml = 2 poits, and so on; adding these points to NEWS2 score resulted the new score NEWS2PSP; AUROC for

sepsis and septic shock were not superior to NEWS2: AUROC NEWS2PSP in sepsis 0.924 (95%CI 6.36- 9.45), in septic shock 0.949 (95%CI 5.66-11.20), compared to AUROC NEWS2 in sepsis 0.962 (95%CI 5.54-7.51) or in septic shock 0.974 (95%CI 6.11-9.74). MEDS, a specific designed score was superior to NEWS2PSP in predicting mortality AUROC MEDS 0.762 (95%CI 2.55-6.01), AUROC NEWS2PSP 0.656 (95%CI 1.21-5.39).

Another compounded score was tested: for PSP<200 pg/ml we have given 1 point, 2 points for PSP=200- 300 pg/ml, 3 points for PSP=300-500 pg/ml, 4 points for PSP=500-1000 pg/ml and 5 points for PSP>1000 pg/ml. Those values were added to NEWS2 and formed NEWS2PSP2 which has no more added value to NEWS2 for predicting sepsis (AUROC NEWS2 0.962 (95%CI 5.54-7.51), AUROC NEWS2PSP2 0.953 (95%CI 5.69-7.84), minimal in septic shock (AUROC NEWS2 0.974 (95%CI 6.11-9.74), AUROC NEWS2PSP2 0.975 (95%CI 6.31-10.19). MEDS kept an advantage in predicting death over NEWS2PSP2 (AUROC MEDS 0.762 (95%CI 2.55-6.01), AUROC NEWS2PSP2 0.676 (95%CI 0.94-4.17).

NEWS2PSP3 resulted from granting 1 point if PSP>1000 and 0 points if PSP<1000- with no better prognostic value over NEWS2 for predicting sepsis ((AUROC NEWS2 0.962 (95%CI 5.54-7.51), AUROC NEWS2PSP3 0.956 (95%CI 5.95-7.65) and kept a slightly advantage over NEWS2 in septic shock AUROC NEWS2 0.974 (95%CI 6.11-9.74), AUROC NEWS2PSP3 0.975 (95%CI 6.22-9.96). MEDS kept an advantage in predicting death over NEWS2PSP3 (AUROC MEDS 0.762 (95%CI 2.55-6.01), AUROC NEWS2PSP3 0.672 (95%CI 0.90-4.03).

Granting 0 points for PSP<5000 pg/ml, 1 point for PSP=5000-10000 pg/ml and 2 points for PSP>10000 and adding these points to NEWS2 lead us to NEWS2PSP4 which is superior to NEWS2 (AUROC NEWS2PSP4 0.971 (95%CI 5.69-7.65) compared to AUROC NEWS2 0.962 (95%CI 5.54-7.51). Using a cut-off value of 9.5 for NEWS2PSP4 we can diagnosis of sepsis with a sensitivity of 60%. (for a NEWS2PSP4 compound score >6.5 sepsis is diagnosed with a sensitivity of 90% and 90.5% specificity).

Using this simple algorithm, for 16 patients the NEWS2 score had changed (12.8%). For 10 out of 95 (10.52%) without sepsis and 6 out of 30 (20%) of septic patients, more points were added to NEWS2 meaning that more septic patients were diagnosed before an infection become life-threatening.

For septic shock NEWS2PSP4 was a reliable score; AUROC values were as follows: AUROC NEWS2 0.974 (95%CI 6.11-9.74), and NEWS2PSP4 0.972 (95%CI 6.07-9.76) (very close), while MEDS kept the advantage in predicting mortality (similar AUROC for NEWS2 and NEWS2PSP4) (AUROC NEWS2 0.670 (95%CI 0.79-3.85), MEDS 0.762 (95%CI 2.55-6.01), NEWS2PSP4 0.670 (95%CI 0.82-3.91). Figures 1, 2 and 3 represent receiver-operating characteristics (ROC) curves for NEWS2, MEDS, PSP and the derived scores for sepsis/ septic shock/mortality as above.

DISCUSSION

In our study we proved that adding a specific biomarker, presepsin, to NEWS2 we can put a sepsis diagnosis earlier, reliable, with increased accuracy, avoiding further deterioration. Studies have proved that clinical deterioration is often forecasted by changes in vital signs up to 6 to 24 hours [20, 21]. This can buy time for a specific patient, but in fact also for the system to recover.

To be remembered, although an increased specificity sign, ST elevation, did not decrease mortality per se. Only after angina pectoris was combined with a specific biomarker, troponin, combined with proactive actions, coronary stenting, markedly decreased the mortality.

Immunity against a microorganism relies primarily on the activity of monocytes, macrophages and granulocytes that recognize pathogen-associated molecular patterns that activate downstream pathways and participate to bacteria clearance. This is partly done through a cluster-of-differentiation marker protein 14 (CD14), which has an immediate response against lipopolysaccharides (LPS) [14, 22]. After binding of LPS to CD14 through the LPS-binding protein (LBP), a subtype of soluble CD14 (sCD14-ST, or presepsin, a 13 kDa protein that is a truncated N-terminal fragment of CD14 [15, 16] is released to the blood flow.

Different scores were used as specific tools in specific circumstances. The more versatile ones are the ones that can be used in as many as possible situations, with minimum of resources, as fast as possible. National Early Warning Score 2 (NEWS2) is released after 5 years of trials after the first version of evaluation in hospitals in UK. This score advocates a system to standardize the assessment and response to acute illness and its efficacy was proven in time. Using six simple physiological parameters already recorded in routine practice, NEWS2 is a pragmatic approach with a key emphasis on system-wide standardization

Rapid diagnostic on ED saves lives. Acute myocardial infarction, stroke and sepsis are medical conditions when short time to diagnosis is of paramount importance, that cannot be overemphasized.

NEWS2 can be used as a point of departure for assessing an acute medical illness, but to accurately diagnose a patient a specific tool is needed (ST elevation for acute myocardial

infarction on EKG, CT scan for stroke and nowadays qSOFA criteria for sepsis).

As Sepsis-3 stated, a sepsis is declared when an infection becomes life-threatening. This puts a rapid diagnose with minimal resources. Having some preliminary results can gain time to earlier diagnose a life-threatening condition and to prevent further deterioration. When we have the Sepsis-3 criteria, the diagnosis is obvious.

We proved that with minimal resources, monitoring vital parameters and assessing a score and when suitable a POCT biomarker, in 15 minutes we raised the suspicion of sepsis, before becoming manifest, with increased accuracy, gaining at least 45 minutes. We found that a biomarker, presepsin, can accurately earlier diagnose sepsis used in correlation with a verified score, NEWS2 which is used for a patient to access the appropriate level of care at a certain moment. We also took into account MEDS as a level of reference, for its power to predict the prognosis due to sepsis (Mortality in Emergency Department Score).

Of note is that the presepsin values were used to help diagnose sepsis after Sepsis-2 definition, but in our study, we tried to use the presepsin for earlier detection of sepsis, after Sepsis-3 definition, before the clinical life-threatening criteria to become manifest (SBP≤100 mmHg, ≥22 breaths per min, GCS<15).

With an altered mental state, incomplete anamnesis to be taken from relatives or the lack of proper documents, increasing number of patients on admission and too often not enough personnel, an accurate, proper assessment on admission is mandatory. After the initial evaluation, vital functions monitoring and blood samples are taken, before more complete laboratory analysis to be available – with a median of one hour, the Point-Of-Care-Testing devices can give you a more comprehensive understanding of the actual medical state in approximatively 15 minutes. POCT biomarkers, arterial gases analysis and complete blood count with multiple scores applied, offer a more comprehensive assessment of a patient and sometimes prioritize the subsequent investigations. While a MEDS score needs not so easy to get information (rapid terminal comorbid illness, neutrophil bands, lower respiratory infection or nursing home resident) NEWS2 is a reliable, verified score intended to be used for monitoring, with increased sensitivity. Based on initial evaluation, taking presepsin (available in 17 minutes) only to patients with SIRS and NEWS2 assessment, taken together increased the number of the patients to be earlier diagnosed with sepsis with 10%. Presepsin was the ideal biomarker due to the fact that it has earlier response compared with procalcitonin after the onset of an infection (peak level<2 h) plus a short half-time (0,5-1 h) compared with those of procalcitonin (2-3 h and 20-24 h, respectively) and CRP (6 h and 4-6 h, respectively) lead us to use this biomarker. The lack of specificity as procalcitonin increases also in surgical interventions, cardiogenic shock, thermal shock, graft-versus-host disease, immunotherapy, burns, acute pancreatitis lead us to consider using presepsin as specific biomarker [21, 23, 24].

To our knowledge this was the first report of PSP and NEWS2 score used in combination for sepsis diagnosis. Nevertheless, although this association is better for earlier detection of sepsis, there no added advantages in predicting septic shock or mortality.

Sepsis is not a completely understood pathology. Surviving Sepsis Campaign with the periodic reevaluation (even the Sepsis, Sepsis-2, Sepsis-3 definition suggests the dynamics and the major concern involved) still leaves room for refinement and improvement. Our study reflects our approach for earlier diagnose of sepsis. Having a patient with clear criteria for sepsis accordingly to qSOFA leaves no room for doubts and the nowadays guidelines stress the importance of earlier diagnosis and rapid measurements to be taken (2018 Sepsis Uptated) in the first hour.

Sepsis defined as life-threatening organ dysfunction caused by a dysregulated host response to infection does not shed light over the dysregulation. Is it due to the increased aggressivity of the pathogen, to the amount of the pathogen, to the particularities of the injured organ/system, of the comorbidities which decrease the defense mechanisms, of the defense of the defense mechanisms itself? In order to achieve timely treatment for a possible lethal condition, a sensitive screening tool is more important than a specific one [25, 26] and identifying the poor prognostic factors may have a role [27].

Although qSOFA has an increased specificity and minimal resources to be used, lacks the sensibility and consequently the diagnosis of sepsis is often put too late. Even one point granted on initial evaluation does not imply that subsequent evolution is not going to be worse, to further deteriorate without becoming life-threatening. So, more refined approach is sometimes necessary.

Study limitations and strengths.

The present study has some limitation. First, being a single center retrospective, observational study we may not have a comprehensive view of this complex pathology. Second, being a tertiary hospital, may have had more complex patients which may have biased in generalizing the

conclusions. Future studies should include more patients from different sites. Third, sepsis defined as life-threatening condition, may alter the health status by itself- an out-control infection might bias the renal function by itself or by aggravation of an already altered renal function as a comorbidity in a more general health status. Fourth, the limited number of patients studied, although significant, are a mere part of the patients with sepsis, so the drawn conclusions should be further verified. Fifth, the size of the cohort might have not enough power requested to draw final conclusions. Finally, although already described in literature, the correlation between presepsin/ biomarker with renal clearance levels and kidney function in patients with life-threatening condition should be studied further.

As strengths in our study we assessed the impact of an earlier intervention over a life-threatening condition in which time is of critical importance. Although widely used, the scores are sometimes inadequately applied. Making distinction between the goals and the moment to be applied to, a score is not a goal in itself. Using a monitoring, verified score as NEWS2, high sensitivity, low specificity combined with a specific biomarker with short time until peak values are attained, lead us to suggest that before becoming dysregulated and life threatening, the sepsis might have an earlier, more optimized approach.

CONCLUSIONS

In the present study, we have tried to assess the impact of a monitoring score and a rapid POCT biomarker, in a condition where time is of critical importance. We acknowledged that in a not completely understood lethal pathology as sepsis, different approaches might be tried in order to earlier detect a life-threatening condition. Using a verified monitoring score, NEWS2, with increased sensibility and low specificity and presepsin, POCT biomarker result within 17 minutes, we diagnosed sepsis earlier.

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