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Original Article

qSOFA and Body Temperature: A Simple Strategy for Evaluate Cirrhotic Patients with Sepsis in Emergency Unit?

Di Micoli A*, Nizza D and Cavazza M

Department of Emergency Medicine, Sant'Orsola-Malpighi University Hospital, Via Massarenti 9, 40138 Bologna, Italy

Abstract

Background: Cirrhotic patients have a high risk of developing sepsis: an early diagnosis is essential for their management. The quick Sequential Organ Failure Assessment (qSOFA) is an accepted tool to identify patients with suspected infection at risk of negative evolution.This study aims to evaluate whether qSOFA can predict the risk of intra-hospital mortality in cirrhotic patients with suspected infection presenting in the Emergency Department; moreover this study aims to evaluated if a new score, T-qSOFA (that altered if qSOFA was ≥ 2 or body temperature >38°C), increases the accuracy of qSOFA.

Methods: qSOFA and T-qSOFA were calculated in 108 cirrhotic patients with suspected infection enrolled during 24 months.

Results: qSOFA was ≥ 2 in 9 patients whereas T-qSOFA was altered in 27.20 patients died (4 with qSOFA ≥2 and 7 with temperature >38°C). qSOFA had a high specificity to identifying patients with better prognosis but its sensitivity is low. "T-qSOFA" increases sensitivity and positive predictive value and became an independent predictor of mortality in the multivariate analysis.

Conclusion: qSOFA has good prognostic accuracy in patients with cirrhosis and suspected infection; T-qSOFA is an excellent, reproducible and quickly obtainable instrument to discriminate the risk of adverse prognosis in cirrhosis.

Keywords: Cirrhosis; Emergency care; Fever; Intensive care unit; qSOFA; Sepsis; T-qSOFA

***Corresponding author:** Di Micoli A, Department of Emergency Medicine, Sant'Orsola-Malpighi University Hospital, Via Massarenti 9, 40138 Bologna, Italy, Tel: +393403369979; E-mail: antonio.dimicoli@aosp.bo.it; antoniodimicoli@gmail.com

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Introduction

Cirrhotic patients have a high risk of developing bacterial infections, sepsis and septic shock, associated with greater mortality compared to general population: early diagnosis and risk stratification are essential for the correct management of these patients [1]. It is well known that the Systemic Inflammatory Response Syndrome (SIRS) criteria for the diagnosis of sepsis have poor accuracy in patients with cirrhosis and bacterial infections. In fact, patients with cirrhosis may have leucopenia due to hypersplenism, tachypnoea due to hepatic encephalopathy or ascites and bradycardia due to use of beta-blockers [2,3].

Following the new proposed criteria, sepsis is defined as a life-threatening organ dysfunction caused by a deregulated host response to infection. Thus, the role of systemic inflammation to organ dysfunction is central, and it is now defined as an acute change in Sequential Organ Failure Assessment (SOFA) score ≥ 2 points from baseline (Sepsis-3) [4].

The SOFA score is based on the following specific parameters: mean arterial blood pressure, platelet count, bilirubin blood levels, Glasgow Coma Scale (GCS), blood creatinine levels, ratio of oxygen partial pressure in arterial blood and inspirited fraction of oxygen. Septic shock is identified in patients in whom sepsis is associated with necessity of use of vasopressors to maintain Mean Arterial Pressure (MAP) ≥ 65 mmHg (circulatory failure) and levels of serum lactate ≥ 2 mmol/l (alteration of cellular metabolism). Considering the difficulty of calculating SOFA score outside the Intensive Care Unit (ICU), a simplified tool has been proposed to quickly identify patients with suspected infection at risk of negative evolution (death or prolonged hospitalization in ICU): the Quick SOFA (qSOFA). This score is calculated exclusively on parameters easily deductible in an emergency context: respiratory rate ≥ 2/min, altered state of consciousness and sistolic blood pressure ≤ 100 mmHg. It is positive if at least two of these parameters are altered. qSOFA is validated to quickly recognize potentially infected patients with a worse prognosis and a high risk of mortality [5].

These scores (SOFA and qSOFA) however have never been validated on cirrhotic patients with suspected infection presenting in the Emergency Department (ED). Firstly, this study aims to evaluate whether qSOFA can predict the risk of intra-hospital mortality in this population. Secondly, is evaluated if a new simply score, T-qSOFA that include body temperature > 38°C, increases the accuracy of qSOFA.

Material and Methods

In this observational retrospective study we consecutive enrolled adult patients with liver cirrhosis presenting to ED of Policlinico Sant'Orsola Malpighi in Bologna with suspected infection from January 2015 to December 2016. The diagnosis of cirrhosis was based of histological, clinical, biochemical, ultrasonographic and/or endoscopic findings. Inclusion criteria were diagnosis or suspected diagnosis of

bacterial and/or fungal infection in ED and age > 18 years old. The exclusion criteria were: severe extrahepatic disease (congestive heart failure New York Heart Association class ≥2, chronic obstructive pulmonary disease (GOLD) grade ≥ 2 and chronic kidney disease requiring renal replacement therapy); hepatocellular carcinoma beyond the Milan criteria [6]; HIV infection; use of immunosuppressive drugs and previous transplant.

If the same patient has made more visits in ED in the enrolment period, all visits were considered individually. Demographic, clinical, haemodynamic,neurological, hemogasanalytic, laboratory and ultrasound data (presence of ascites) were collected for each patient at ED. Based on these data, qSOFA, SOFA, Model for End-Stage Liver Disease (MELD) [7] and Child-Pugh [8] scores were calculated.

A new simply and dichotomous variable, named T-qSOFA, has been created: if body temperature is≥ 38°C or qSOFA ≥ 2 its value is 1, in other case its value is 0.Patients were followed until discharge or eventual death; the duration of hospitalization was also recorded and the site of infection reported, if identified. The protocol was approved by the local ethics committee of the Hospital, and all patients provided written informed consent.

The statistical variables were expressed as mean ± standard error or median and range, in the most appropriate way based on their distribution. The Pearson and Spearman tests were used to evaluate correlations between the analysed variables and mortality. A value of $p < 0.05$ was considered statistically significant. Univariate and multivariate Cox regression analyses of predictors of mortality were performed using a competiting risk approach with Fine and Gray method, and the result expressed as p value. Variables found to be associated with in-hospital mortality with a p value <0.1 in the univariate analysis were included in a multivariate analysis with stepwise backward elimination (entry $p < 0.05$, drop $p > 0.1$). The statistical analysis was performed using SPSS v 22.0 statistical package.

Results

108 patients with liver cirrhosis and suspected infection were enrolled. Their characteristics are described in table 1. The enrolled patients had mean values of MELD of 16, 0± 0,8. The Child-Pugh classes were divided in this way: 22 patients in class A, 53 patients in class B, 33 patients in class C as suggested in literature [8]. 55 patients had ascites and 20 shown an alterations of GCS (< 15). 73 patients had fever in ED (18 with TC >38°C) and 87 had an increase in C - reactive protein (PCR). There were 41 patients with both fever and increase in PCR. In 24 patients, the site of the infection was not identified during the hospitalization, while in 4 patients the sites were more than one (Table 2). qSOFA was ≥ 2 in 9 patients, whereas SOFA ≥ 2 in 89 patients (Figure 1), $p > 0.05$. T-qSOFA was 1 in 27 patients while 0 in the others (81).

During hospitalization 20 patients died (18.5%), of whom 4 with qSOFA ≥ 2 and 7 with temperature > 38°C. In the subgroup of patients with qSOFA ≥ 2, mortality was 44.4%, while among patients with qSOFA < 2 it was 16.1% ($p< 0.05$)(Figure 2). In the subgroup of patients with temperature >38°C mortality was 40.7 %. The death occurred on 17th±2 days of hospitalization for patients with a qSOFA ≥ 2 and on 23rd± 3 days for others. This time does not statistically significantly differ between the two subgroups.

Demographic Data	
Male	54 patients
Female	54 patients
Age	67 ± 0.8 years
Laboratoristic Data	
Total bilirubin (mg/dL)	3.6 ± 0.4
C Reactive- protein (mg/dL)	5.2 ± 0.6
Creatinine (mg/dL)	1.4 ± 0.7
INR	1.7 ± 0.9
Platelets (x 10^3/mmc)	115.2 ± 8.1
Leukocytes (x 10^3/mmc)	8.7 ± 6.5
Albumin (g/L)	3.1 ± 0.1
Hemodynamic Data	
Systolic blood pressure (mm Hg)	122.2 ± 10.1
Diastolic blood pressure (mm Hg)	70.4 ± 8.3
Heart rate (bpm)	85.2 ± 7.3
Breath frequency (acts per minutes)	14.0±2.1
Partial saturation of oxygen (%)	96.2 ±3.2
Clinical Data	
Ascitic decompensation	55 patients (50%)
Altered state of consciousness	20 patients (18%)
Fever	49 patients (45%)
Main Scores	
MELD	16.2 ± 0.8
Child - PughScore (A:B:C)	22:53:33

Table 1: Baseline characteristics of the sample.

Infection Site	**Cases**	**%**
Respiratory system	22	20
Urinary system	22	20
Skin	10	9
Cholangitis	6	6
Cholecystitis	6	6
Spontaneous bacterial peritonitis	6	6
Pancreatitis	4	4
Colitis from C. difficile	2	2
Gastroenteritis	2	2
Pericholecystic abscess	2	2
Acute appendicitis	1	1
Peritonitis	1	1
Rectal KPC	1	1
Media otitis	1	1
Visceral Leishmania	1	1
Endocarditis	1	1
Undefined site	24	22

Table 2: Sites of infections.

KPC: Klebsiella Pneumoniae Carbapenemase (KPC)-producing.

Sensitivity, specificity, positive and negative predictive value of qSOFA and T-qSOFA to predict mortality has benne calculated as indicated in table 3. In univariate analysis MELD, qSOFA, sistolic

blood pressure, body temperature, T-qSOFA, transfer to ICU, PCR, creatinine, INR, arterial blood, pH are statistically significant prognostic factors of mortality. Instead, considering the subgroup of patients with qSOFA<2, MELD and the variables that determine it, PCR and body temperature have been predictors of mortality in univariate analysis. Only T-qSOFA is predictors of mortality in multivariate analysis.Only 5 patients were transferred to ICU after evaluation in ED, including 4 with qSOFA ≥ 2 (p <0.00001) and all 5 with SOFA ≥ 2 and T-qSOFA = 1.

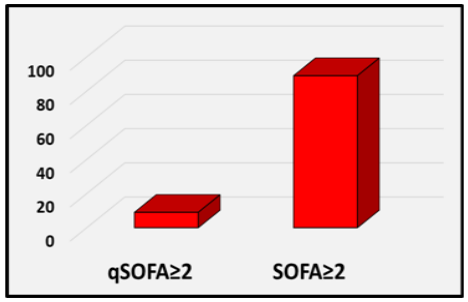

Figure 2: Distribution of scores in the population of the study.

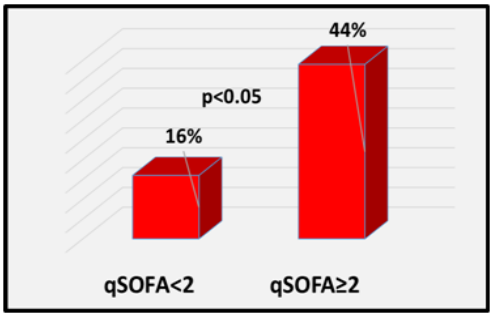

Figure 2: Mortality in the subgroups divided by qSOFA.

	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
qSOFA	20.00%	94.30%	44.40%	83.40%
T-qSOFA	55.00%	81.8.0 %	40.70%	88.90%
p value	0.01	ns	ns	0.01

Table 3: Accuracy of qSOFA and T-qSOFA.

KPC: Quick Sequential Organ Failure Assessment; T-qSOFA: Temperature Quick Sequential Organ Failure Assessment

Discussion

Patients with cirrhosis have a high risk of developing acute and severe bacterial infection and sepsis [1]. Moreover, sepsis represents one of the most causes of rapid death in this group of patients. Thus, for the clinician is essential to quickly identify this group of cirrhotic patients because early diagnosis and accurate stratification of adverse prognosis risk is required; indeed, these patients were often swiftly and empirically treated with antibiotics according to the available international recommendation [2] and local epidemiology as soon as the diagnosis of infection is suspected.

In other setting, SOFA score proved to fit to identify quickly septic patients in an emergency unit [9]. However, SOFA score requires the availability of a previous evaluation to the development of bacterial infection, in order to be able to calculate the deterioration. This represents a limit to the application of SOFA score in cirrhotic patients, who often have pre-existing conditions of organ failure: therefore it is necessary to have an instrument that does not depend on the previous clinical conditions and on the results of laboratory tests.

Unlike SOFA score, qSOFA does not require any previous evaluation. Moreover, in the context of ED, an easy instrument used at bedside, such as qSOFA, is necessary. This is the first study that evaluate, in a third level Hospital, the accuracy of this score in these group of patients. During the follow up we described a mortality (18%) comparable with other studies [10]. In our results, qSOFA shows high specificity to identifying patients with better prognosis, which only require conservative management approach. Instead, sensitivity of qSOFA is poor in identifying patients who later die and is only a predictor of mortality in univariate analysis. The low sensitivity of qSOFA to predict mortality in this study may be due to both factors; first, the limited number of patients included in the study; second, at the time of access to the ED the parameters of qSOFA could not be altered because most of these patients suddenly arrived at ED so strictly and frequently evaluated by the hepatologist physician: as soon as the first non-specific symptoms of the infection appear, they suggested to get to ED.

A qSOFA ≥ 2 has the role of directing physicians to perform further diagnostic tests for organ dysfunction, to start or enhance an adequate therapy and possibly decide to enhance patient's monitoring up to transfer to ICU. The addition of body temperature >38°C (objective and easily determinable parameter in an emergency context) to score in a new score "T-qSOFA" not only statistically increases both sensitivity (35%) and positive predictive value (58%) but also became an independent predictor of mortality to the multivariate analysis. Moreover, this new variable does not significantly decrease specificity and positive predictive value.

A simple and available action as the measurement of body temperature could significantly improve the management of cirrhotic patients with sepsis in the ED.This paper presents some limits. First, the study wad lead in a single centre that is a third level hospital for cirrhotic patients: so a selection bias is unavoidable; however, in our Hospital are often evaluated cirrhotic patients with a high MELD that most frequently develop sepsis. Second, the sample size is low so the results can be mainly influenced overall about the ICU access.Third the retrospective method does not permit any hope to deduce some data.

In conclusion, this study shows that, in a population of patients with liver cirrhosis and suspected infection presenting to ED of a third level centre, qSOFA has good specificity and good negative predictive value; in addition it is easily applicable, reproducible and it is quickly obtainable due to no need of diagnostic tests waiting that can slow down therapeutic decisions. Therefore, in addition to clinical judgment, a new score named qt-SOFA is an excellent instrument to discriminate the risk of adverse prognosis in cirrhotic patients.

Surely the failure to achieve two or more criteria of qSOFA should not delay the treatment of the infection in the cirrhotic patient. In this sense, both qSOFA and T-qSOFA cannot be considered a screening

test for sepsis.Other prospective and multicentre study are necessary in the future to evaluate better the validity of this scores.

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