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Predictors of mortality of bloodstream infections among internal medicine patients in a Swiss Hospital: Role of quick Sequential Organ Failure Assessment

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ABSTRACT

Background: Sepsis has been associated with high morbidity and mortality. The aims were to determine predictors of mortality among patients with bloodstream infections (BSIs) and to ascertain the role of quick Sequential Organ Failure Assessment (qSOFA) in predicting poor outcomes.

Methods: All internal medicine patients with BSIs at the Hospital of Jura, Switzerland during a three year period (July 2014 to June 2017) were included.

Results: Among 404 BSIs, *Escherichia coli* represented the most common species isolated (156 episodes; 38.6%), followed by *Staphylococcus aureus* (68; 16.8%). The most common site of infection was urinary tract accounting for 39.6% of BSIs (160 episodes). Thirty-day mortality was 18.1%. Multivariate analysis revealed BSI due to staphylococci, malignancy (haematologic or solid organ), qSOFA ≥ 2 points, Pitt bacteraemia score as independent predictors of mortality, while appropriate empiric antibiotic therapy and administration of antibiotic therapy within three hours from infection's recognition were identified as a predictor of good prognosis. qSOFA showed the highest sensitivity (87.7%), negative predictive value (96.6%) and accuracy (0.83) as compared to other scores. Mortality among 141 septic patients was 45.4%. Malignancy (haematologic or solid organ), primary BSI, Pitt bacteraemia score, were independently associated with mortality, while appropriate empiric antibiotic therapy and administration of antibiotic therapy within the first hour from infection's recognition were associated with better prognosis.

Conclusion: qSOFA as compared to other severity scores showed an excellent negative predictive value. Better prognosis was associated with administration of appropriate empiric antibiotic therapy and its timely initiation.

1. Introduction

Sepsis remains a major public health issue which is characterized by a dysregulated host response to infection and leads to increased morbidity and mortality [1–3]. Since the first definition, sepsis was characterized as an infection with presence of at least two criteria of Systemic Inflammatory Response Syndrome (SIRS) [3]. Their applicability has been criticized as a sepsis screening tool because of inadequate specificity and sensitivity [4]. A new definition for sepsis and septic shock was released the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3), which introduced a bedside criterion, known as the quick Sequential Organ Failure Assessment (qSOFA) score, to facilitate the identification of patients with suspected infection who are likely to have poor outcome [1].

Since its publication, many studies, retrospective and prospective ones were conducted in order to assess its accuracy in predicting mortality among patients with suspected infection with controversial results probably due to high heterogeneity concerning types of infections or severity [5–7]. There is scarcity of data assessing qSOFA in predicting mortality among bacteraemic patients [8,9].

The primary aim of this study was to identify predictors of mortality among internal medicine patients with bloodstream infection and the

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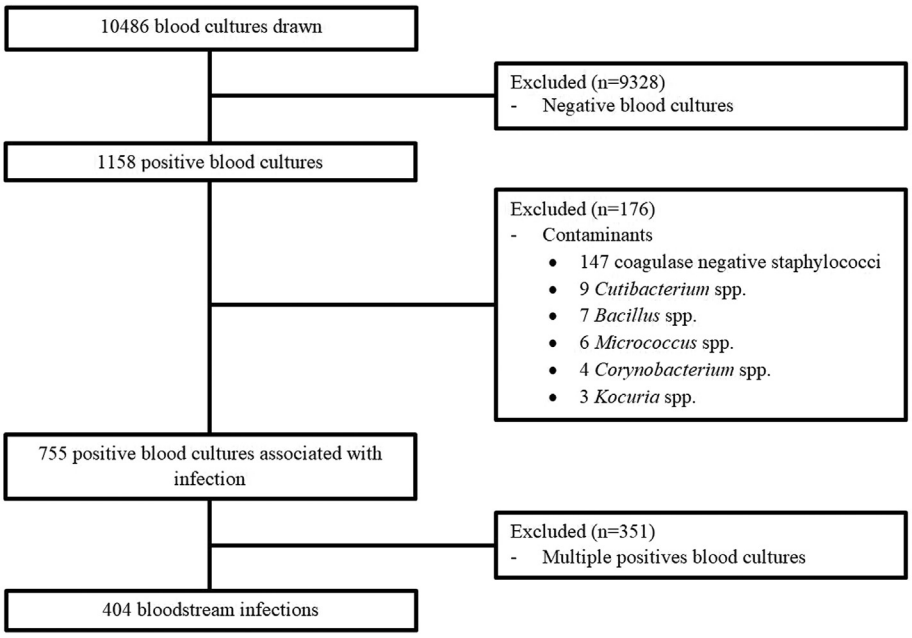

Fig. 1. Flowchart of study patients.

subgroup of sepsis. The secondary aim was to assess the value of qSOFA in predicting mortality compared to SIRS and other severity scores.

2. Materials and methods

This was a retrospective study conducted at the Internal Medicine of the Hospital of Jura a secondary care hospital in north-west Switzerland during a three year period (July 2014 to June 2017). The Internal Medicine branch of the Emergency Department treated 9′800 patients per year. The Internal medicine Department had 54 beds with roughly 2′500 admissions per year. The general Intensive Care Unit (ICU) had 6 beds with approximately 450 admissions per year. The study was approved by the Ethics Committee of Northwest and Central Switzerland (No 2018-02321).

All adult patients (≥18 years old) with a positive blood culture were eligible. Patients hospitalized in the Department of Surgery were excluded. Blood cultures were routinely drawn from patients with signs or symptoms of systemic infection and sent to the Department of Microbiology and incubated the BacT/ALERT System (bioMerieux, Marcy l'Etoile, France). Isolates recovered from positive blood cultures were identified by Gram stain and by the Vitek 2 Advanced Expert System (bioMerieux). Antibiotic susceptibility was interpreted according to EUCAST guidelines [10]. Isolation of a common commensal organism from blood cultures, such as *Bacillus* spp., coagulase-negative staphylococci (CNS), *Corynebacterium* spp., *Micrococcus* spp., and *Cutibacterium* spp., was characterized as true BSI if the pathogen was isolated from at least two blood culture sets, as described by US Centers for Disease Control and Prevention (CDC) guidelines; for all other pathogens, only one positive blood culture associated with clinical signs of infection were needed in order to be defined as BSI [11]. Primary or secondary BSI (urinary, respiratory, catheter-related, abdominal, skin and soft tissue infections, endocarditis) was determined in accordance to the CDC definition [11]. Infection was categorized as sepsis or septic shock according to new sepsis definition [1]. Multidrug-resistance (MDR) was characterized according to published definitions [12]. The date of collection of the first positive blood culture was defined as infection onset. The worst values during first 3 h of emergency department stay for community onset infections and of the first 12 h from infection recognition for hospital onset were used to calculate qSOFA. For community onset infections, time to antibiotic administration was defined as the period between emergency department triage and administration of antimicrobials, while for hospitalized patients was measured since recognition of infection.

Primary outcome was 30-day mortality. The hospital's computerized database (Carefolio Acute; Tecost SA, Fribourg, Switzerland) was used in order to collect clinical data and laboratory results. Parameters assessed included demographic characteristics (age, sex), co-morbidities [13–16], severity scores of illness upon onset of infection [Simplified Acute Physiology Score II (SAPS II), SOFA, qSOFA [1], SIRS, Pitt bacteraemia score [17]], laboratory results (leucocyte count, C-reactive protein, procalcitonin, lactates), previous hospitalization (during last six months), previous operation (during last month), admission at ICU, mechanical ventilation (invasive or not invasive) and complications (acute kidney injury, atrial fibrillation, deep venous thrombosis or pulmonary embolism, acute heart failure, myocardial infarction).

Data analyses were performed by SPSS version 23.0 (SPSS, Chicago, IL) software. Categorical variables were analyzed by using the Fisher exact test and continuous variables with Mann–Whitney *U* test. Multiple logistic regression analysis was used. Factors contributing to multicolinearity were excluded from the multivariate analysis. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated to evaluate the strength of any association. All statistic tests were 2-tailed and $P < .05$ was considered statistically significant. Area under the receiver operating characteristic (AUROC) curves for 30-day mortality were generated for hypotension, fever, SIRS ≥2, qSOFA ≥2, SAPS II, SOFA score, Pitt bacteraemia score.

3. Results

Among 10′486 blood cultures drawn during the study period, 931 positive blood cultures were from internal medicine patients; 176 were characterized as contaminants and the remaining 755 positive blood cultures were attributed to 404 BSI (Fig. 1). Among BSI, *Escherichia coli* represented the most common species isolated (156 episodes; 38.6%), followed by *Staphylococcus aureus* (68; 16.8%), other Enterobacteriaceae (68 episodes; 16.8%), and streptococci (66; 16.3%) (Table 1). Twenty-four polymicrobial BSI were documented. The most common sites of infection were urinary tract accounting for 39.6% of BSIs (160 episodes), lower respiratory tract (62; 15.3%), primary BSI (54; 13.4%) and intra-abdominal (44; 10.9%) (Table 1). The majority of

Table 1
Distribution of isolated pathogens according to site of infection.

Isolates	Primary (54)	Urinary tract (160)	Lower respiratory tract (62)	Intra-abdominal (44)	Skin and soft tissue (23)	Bone or joint (23)	Central venous catheter-related (15)	Other (23)	All (404)
Gram-positive	25 (46.3%)	16 (10.0%)	43 (69.4%)	9 (20.5%)	20 (87.0%)	21 (91.3%)	12 (80.0%)	18 (78.3%)	164 (40.6%)
Staphylococci	13 (24.1%)	5 (3.1%)	15 (24.2%)	2 (4.5%)	10 (43.5%)	16 (69.6%)	11 (73.3%)	6 (26.1%)	78 (19.3)
S. aureus	12 (22.2%)	4 (2.5%)	15 (24.2%)	2 (4.5%)	10 (43.5%)	15 (65.2%)	6 (40.0%)	4 (17.4%)	68 (16.8%)
CNS	1 (1.9%)	1 (0.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (4.3%)	5 (33.3%)	2 (8.7%)	10 (2.5%)
Enterococci	2 (3.7%)	5 (3.1%)	2 (3.2%)	3 (6.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (17.4%)	16 (4.0%)
Streptococci	9 (16.7%)	4 (2.5%)	25 (40.3%)	3 (6.8%)	11 (47.8%)	5 (21.7%)	1 (6.7%)	8 (34.8%)	66 (16.3%)
Other	1 (1.9%)	1 (0.6%)	1 (1.6%)	1 (2.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (1.0%)
Gram-negative	25 (46.3%)	150 (93.8%)	19 (30.6%)	34 (77.3%)	3 (13.0%)	3 (13.0%)	3 (20.0%)	5 (21.7%)	242 (59.9%)
E. coli	10 (18.5%)	117 (73.1%)	7 (11.3%)	18 (40.9%)	2 (8.7%)	2 (8.7%)	0 (0.0%)	0 (0.0%)	156 (38.6%)
Enterobacteriaceae *(excluding E. coli)*	10 (18.5%)	33 (20.6%)	8 (12.9%)	14 (31.8%)	0 (0.0%)	1 (4.3%)	1 (6.7%)	1 (4.3%)	68 (16.8%)
P. aeruginosa	5 (9.3%)	2 (1.2%)	2 (3.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	9 (2.2%)
Other	0 (0.0%)	1 (0.6%)	4 (6.5%)	3 (6.8%)	1 (4.3%)	0 (0.0%)	2 (13.3%)	4 (17.4%)	15 (3.7%)
Anaerobes	1 (1.9%)	0 (0.0%)	2 (3.2%)	5 (11.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	8 (2.0%)
Candida	3 (5.6%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (13.3%)	0 (0.0%)	5 (1.2%)
Polymicrobial	2 (3.7%)	9 (5.6%)	4 (6.5%)	5 (11.4%)	1 (4.3%)	1 (4.3%)	2 (13.3%)	0 (0.0%)	24 (5.9%)

CNS, coagulase negative staphylococci; BSI, bloodstream infections.

infections were community onset (316; 78.2%).

Thirty-day mortality was 18.1%. Table 2 shows the univariate and multivariate analyses for predictors of mortality of BSI. Multivariate analysis revealed BSI due to staphylococci (OR 2.5; 95% CI 1.1–5.9), malignancy (haematologic or solid organ) (OR 3.2; 95% CI 1.6–6.6), qSOFA ≥ 2 points (OR 11.4; 95% CI 4.3–30.5), Pitt bacteraemia score (OR 1.6; 95% CI 1.2–2.1) as independent predictors of mortality, while appropriate empiric antibiotic therapy (OR 0.152; 95% CI 0.046–0.502) and administration of antibiotic therapy within 3 h from infection recognition (OR 0.416; 95% CI 0.192–0.902) were identified as predictors of good prognosis.

According to the new definitions [1], 141 patients developed sepsis or septic shock with a mortality of 45.4%. Univariate and multivariate analyses of predictors of mortality among patients with sepsis or septic shock is depicted in Table 3. Multivariate analysis identified malignancy (haematologic or solid organ) (OR 3.6; 95% CI 1.5–8.6), primary BSI (OR 3.4; 95% CI 1.0–11.1), Pitt bacteraemia score (OR 1.8; 95% CI 1.3–2.5), as predictors of mortality among septic patients, while; appropriate empiric antibiotic therapy (OR 0.076; 95% CI 0.013–0.431) and administration of antibiotic therapy within the first hour from infection recognition (OR 0.294; 95% CI 0.092–0.942) were associated with better prognosis. Only 29 patients (20.6%) received antibiotics within 1 h from presentation. Patients with primary bacteraemia received antibiotic treatment later than those with secondary (11.8 ± 9.5 *vs* 5.8 ± 6.5 h; $P < .001$),

The performance of severity scores, including qSOFA, and vital signs to predict 30-day mortality among patents with BSI is shown in Table 4. qSOFA showed the highest sensitivity (87.7%), negative predictive value (96.6%) and accuracy (0.83) as compared to other scores. The second best variable was the Pitt bacteraemia score that showed comparable negative predictive value (94.5%), but a lower sensitivity (79.5%) and accuracy (0.79).

4. Discussion

BSIs have been associated with high morbidity and mortality rates and for most sources of infection, with the notable exception of urinary tract ones, patients with BSI had higher risk of mortality as compared to those with infection without BSI [18–21]. In the present study 30-day mortality among all patients was 18.1%, rising to 45.4% among septic ones, which are comparable to that previously reported [18–20].

Since the first definition of sepsis and for over two decades, the SIRS criteria have been used to identify sepsis [3]. However, the SIRS criteria are poor indicator of prognosis, therefore, in 2016, a new definition of sepsis was established and the qSOFA score was introduced [1]. In line with this concept, in the present study, the majority of patients had at least two SIRS criteria (356 patients; 88.1%), which failed to predict mortality (accuracy of 0.51). The advantage of qSOFA score is its reliance solely on three clinical variables and it doesn't depend on laboratory values, leading to earlier recognition of sepsis which is indispensable to improving outcomes and decreasing sepsis-related mortality [1]. qSOFA was independently associated with mortality in the multivariate analysis. It has also outperformed all other variables and scores in the prediction of 30-day mortality. These results underline its importance in predicting patients that are in increased risk for morbidity and mortality.

Our results are comparable to that reported in a meta-analysis of 23 studies, with a sensitivity, specificity and accuracy of qSOFA in predicting mortality of 51%, 83% and 0.74, respectively [5]. Sensitivity, specificity and accuracy of SIRS criteria were 86%, 29% and 0.71, respectively [5]. There was a high variation of aforementioned variables among included studies which could be explained by the difference in timing of qSOFA measurement or the infection's severity or even the source of infection [5]. Our study population consists of patients with bloodstream infection and as previously shown in studies with confirmed infection, qSOFA showed better sensitivity and specificity as compared to studies with suspected infections [5]. To the best of our knowledge this is one of the few studies to ascertain and prove the efficacy of qSOFA in prediction of mortality among patients with bloodstream infections.

The two most consistent predictors of survival in the literature were administration of appropriate antibiotic therapy and its timely initiation [18,19]. Their importance was highlighted in the Surviving Sepsis Campaign guidelines that proposed antibiotic administration among septic patients within the first hour, a goal attained in our cohort only in 20.6% of septic patients [2]. A possible explanation could be that the new definition for sepsis recognition, based only in clinical criteria, was published in 2016 and until then the SIRS criteria were implemented based on clinical and laboratory results, with the latter being a cause of retarding sepsis identification [1]. This low percentage should incite a rigorous educational campaign among medical and nursing personnel for the timely identification and treatment of septic patients.

Comorbidities were a well described predictor associated with worst outcome among infected patients. In our study, in accordance to literature [20,22], malignancy was associated with higher mortality among all patients and the subgroup of septic ones. Malignancy increases the risk of infection by impairing immune system's capacity, while chemotherapy directly affects bone marrow hematopoietic

Table 2
Univariate and multivariate analyses for predictors of mortality of patients with bloodstream infection.

Characteristics	Univariate analysis			Multivariate analysis
	Survivors (n = 331)	Non-survivors (n = 73)	P	OR (95% CI)
Demographics				
Age (years)	73.5 ± 14.1	75.1 ± 12.0	0.668	
Male gender	190 (57.4%)	90 (69.9%)	0.064	
Comorbidities				
Coronary disease	62 (18.7%)	15 (20.5%)	0.743	
Chronic Heart Failure	28 (8.5%)	7 (9.6%)	0.818	
Diabetes Mellitus	85 (25.7%)	20 (27.4%)	0.769	
Chronic Obstructive Pulmonary Disease	34 (10.3%)	6 (8.2%)	0.828	
Chronic Renal Insufficiency (moderate to severe)	94 (28.4%)	17 (23.3%)	0.469	
Malignancy	76 (23.0%)	39 (53.4%)	< 0.001	3.2 (1.6–6.6)
Haematologic	6 (1.8%)	6 (8.2%)	0.011	
Solid organ	71 (21.5%)	33 (45.2%)	< 0.001	
Chemotherapy (during last month)	42 (12.7%)	38 (38.4%)	< 0.001	
Cirrhosis	15 (4.5%)	13 (17.8%)	< 0.001	
Obesity	25 (7.6%)	6 (8.2%)	0.810	
Parkinson's disease	8 (2.4%)	4 (5.5%)	0.242	
Dementia	35 (10.6%)	16 (21.9%)	0.012	
Malnutrition	62 (18.7%)	27 (37.0%)	0.002	
Immunosuppression	37 (11.2%)	21 (28.8%)	< 0.001	
Charlson Comorbidity Index	5.8 ± 2.9	7.5 ± 2.7	< 0.001	
Infection data				
Hospital-acquired	58 (17.5%)	30 (41.1%)	< 0.001	–
Septic shock	25 (7.6%)	17 (23.3%)	< 0.001	–
Neutropenia (neutrophils $< 1\times 10^9$/l)	7 (2.1%)	5 (6.8%)	0.047	
CRP (mg/l) (among 399 patients)	193.5 ± 120.6	204.9 ± 150.4	0.950	
Procalcitonin (ng/ml) (among 279 patients)	23.9 ± 63.0	22.9 ± 53.0	0.403	
Lactates (mmol/l) (among 139 patients)	3.0 ± 1.9	4.9 ± 3.7	0.004	
Time of antibiotic administration (hours)	6.6 ± 7.2	9.6 ± 8.4	0.001	
Administration of antibiotic therapy within three hours	162 (48.9%)	21 (28.8%)	0.002	0.416 (0.192–0.902)
Appropriate empiric antibiotic therapy	313 (94.6%)	57 (78.1%)	< 0.001	0.152 (0.046–0.502)
Severity scores upon infection onset				
SIRS (≥2 criteria)	291 (87.9%)	65 (89.0%)	1.000	
qSOFA (≥2 criteria)	72 (21.8%)	64 (87.7%)	< 0.001	11.4 (4.3–30.5)
SOFA score	2.7 ± 2.1	5.3 ± 2.9	< 0.001	
SAPS II score	28.7 ± 8.3	37.6 ± 8.2	< 0.001	
Pitt Bacteremia Score	0.9 ± 1.1	2.5 ± 1.5	< 0.001	1.6 (1.2–2.1)[a]
Hospitalization data				
Previous hospitalization (during last six months)	141 (42.6%)	49 (67.1%)	< 0.001	
Previous operation (during last month)	10 (3.0%)	2 (2.7%)	1.000	
Admission at Intensive Care Unit	43 (13.0%)	15 (20.5%)	0.100	
Mechanical ventilation (invasive or noninvasive)	18 (5.4%)	7 (9.6%)	0.184	
Central venous catheter	61 (18.4%)	26 (35.6%)	0.002	
Complications				
Acute kidney injury	101 (30.5%)	43 (58.9%)	< 0.001	
Atrial fibrillation	15 (4.5%)	2 (2.7%)	0.748	
Deep venous thrombosis/pulmonary embolism	5 (1.5%)	1 (1.4%)	1.000	
Blood transfusion	25 (7.6%)	17 (23.3%)	< 0.001	
Acute heart failure	21 (6.3%)	11 (15.1%)	0.028	
Myocardial infarction	14 (4.2%)	6 (8.2%)	0.227	
Type of infection				
Primary	34 (10.3%)	20 (27.4%)	< 0.001	–
Urinary tract	147 (44.4%)	13 (17.8%)	< 0.001	
Lower respiratory tract	45 (13.6%)	17 (23.3%)	0.048	
Intra-abdominal	35 (10.6%)	9 (12.3%)	0.679	
Skin and soft tissue	18 (5.4%)	5 (6.8%)	0.584	
Bone or joint	20 (6.0%)	3 (4.1%)	0.780	
Central venous catheter-related	11 (3.3%)	4 (5.5%)	0.490	
Other	21 (6.3%)	1 (1.7%)	0.399	
Microbiologic data				
Gram-positive	126 (38.1%)	38 (52.1%)	0.035	
Streptococci	54 (16.3%)	11 (15.1%)	0.862	
Staphylococci	56 (16.9%)	22 (30.1%)	0.014	2.5 (1.1–5.9)
Gram-negative	208 (62.8%)	34 (46.6%)	0.012	
E. coli	142 (42.9%)	14 (19.2%)	0.001	–
Enterobacteriaceae (excluding *E. coli*)	51 (15.4%)	17 (23.3%)	0.120	
Multidrug-resistant pathogen	29 (8.8%)	12 (16.4%)	0.056	–
Polymicrobial	18 (5.4%)	6 (8.2%)	0.409	

Data are number (%) of patients or mean ± standard deviation.
OR: odds ratio; CI: confidence interval; CRP: C-reactive protein; SIRS: Systemic Inflammatory Response Syndrome; qSOFA: quick Sequential Organ Failure Assessment; SAPS II: Simplified Acute Physiology Score II.
[a] For each point of the score.

Table 3
Univariate and multivariate analyses for predictors of mortality of 141 patients with sepsis or septic shock due to bloodstream infection.

Characteristics	Univariate analysis			Multivariate analysis
	Survivors (n = 77)	Non-survivors (n = 64)	P	OR (95% CI)
Demographics				
Age (years)	74.6 ± 11.7	75.1 ± 12.0	0.754	
Male gender	46 (59.7%)	45 (70.3%)	0.218	
Comorbidities				
Coronary disease	18 (23.4%)	14 (21.9%)	1.000	
Chronic Heart Failure	11 (14.3%)	7 (10.9%)	0.619	
Diabetes Mellitus	21 (27.3%)	18 (28.1%)	1.000	
Chronic Obstructive Pulmonary Disease	11 (14.3%)	6 (9.4%)	0.443	
Chronic Renal Insufficiency (moderate to severe)	23 (29.9%)	14 (21.9%)	0.338	
Malignancy	21 (27.3%)	36 (56.3%)	0.001	3.6 (1.5–8.6)
Haematologic	1 (1.3%)	6 (9.4%)	0.047	
Solid organ	20 (26.0%)	30 (46.9%)	0.013	
Chemotherapy (during last month)	13 (16.9%)	25 (39.1%)	0.004	
Cirrhosis	5 (6.5%)	13 (20.3%)	0.021	–
Obesity	1 (1.3%)	6 (9.4%)	0.047	
Parkinson's disease	2 (2.6%)	3 (4.7%)	0.659	
Dementia	15 (19.5%)	16 (25.0%)	0.541	
Malnutrition	16 (20.8%)	23 (35.9%)	0.059	
Immunosuppression	12 (15.6%)	19 (29.7%)	0.065	
Charlson Comorbidity Index	6.6 ± 2.7	7.7 ± 2.7	0.015	
Infection data				
Hospital-acquired	18 (23.4%)	28 (43.8%)	0.012	
Septic shock	25 (32.5%)	17 (26.6%)	0.466	
Neutropenia (neutrophils $< 1\times 10^9$/l)	3 (3.9%)	5 (7.8%)	0.468	
CRP (mg/l) (among 139 patients)	213.7 ± 117.9	190.9 ± 149.3	0.099	
Procalcitonin (ng/ml) (among 111 patients)	44.4 ± 97.5	18.5 ± 41.9	0.034	
Lactates (mmol/l) (among 75 patients)	3.5 ± 2.0	5.3 ± 3.9	0.053	
Time of antibiotic administration (hours)	4.2 ± 4.9	10.1 ± 8.8	< 0.001	
Administration of antibiotic therapy within first hour	21 (27.3%)	8 (12.5%)	0.037	0.294 (0.092–0.942)
Appropriate empiric antibiotic therapy	77 (100%)	49 (76.6%)	< 0.001	0.076 (0.013–0.431)
Severity scores upon infection onset				
SIRS (≥2 criteria)	75 (97.4%)	58 (90.6%)	0.141	
SOFA score	4.5 ± 2.5	5.7 ± 2.8	0.015	
SAPS II score	34.4 ± 8.4	38.7 ± 7.8	0.004	
Pitt Bacteremia Score	2.1 ± 1.4	2.8 ± 1.2	0.002	1.8 (1.3–2.5)[a]
Hospitalization data				
Previous hospitalization (during last six months)	40 (51.9%)	44 (68.8%)	0.058	
Previous operation (during last month)	2 (2.6%)	2 (3.1%)	1.000	
Admission at Intensive Care Unit	43 (13.0%)	15 (20.5%)	0.100	
Mechanical ventilation (invasive or noninvasive)	10 (13.0%)	7 (10.9%)	0.798	
Central venous catheter	23 (29.9%)	23 (35.9%)	0.475	
Complications				
Acute kidney injury	34 (44.2%)	38 (59.4%)	0.091	
Atrial fibrillation	7 (9.1%)	1 (1.6%)	0.072	
Deep venous thrombosis/pulmonary embolism	2 (2.6%)	1 (1.6%)	1.000	
Blood transfusion	6 (7.8%)	14 (21.9%)	0.027	
Acute heart failure	8 (10.4%)	9 (14.1%)	0.606	
Myocardial infarction	5 (6.5%)	6 (9.4%)	0.546	
Type of infection				
Primary	7 (9.1%)	19 (29.7%)	0.002	3.4 (1.0–11.1)
Urinary tract	27 (35.1%)	11 (17.2%)	0.002	–
Lower respiratory tract	17 (22.1%)	14 (21.9%)	1.000	
Intra-abdominal	10 (13.0%)	9 (14.1%)	1.000	
Skin and soft tissue	3 (3.9%)	3 (4.7%)	1.000	
Bone or joint	5 (6.5%)	3 (4.7%)	0.728	
Central venous catheter-related	6 (7.8%)	3 (4.7%)	0.511	
Other	2 (2.6%)	2 (3.1%)	1.000	
Microbiologic data				
Gram-positive	34 (44.2%)	32 (50.0%)	0.503	
Streptococci	17 (22.1%)	9 (14.1%)	0.278	
Staphylococci	12 (15.6%)	18 (28.1%)	0.098	
Gram-negative	49 (63.6%)	29 (45.3%)	0.041	
E. coli	29 (37.7%)	12 (18.8%)	0.016	–
Enterobacteriaceae (excluding *E. coli*)	15 (19.5%)	14 (21.9%)	0.835	
Multidrug-resistant pathogen	8 (9.1%)	10 (15.6%)	0.301	
Multimicrobial	9 (11.7%)	4 (6.3%)	0.383	

Data are number (%) of patients or mean ± standard deviation.
OR: odds ratio; CI: confidence interval; CRP: C-reactive protein; SIRS: Systemic Inflammatory Response Syndrome; SOFA: Sequential Organ Failure Assessment; SAPS II: Simplified Acute Physiology Score II.
[a] For each point of the score.

Table 4
Performance of different scores and vital signs in predicting 30-day mortality of bloodstream infections.

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy
Hypotension	38.4	89.4	44.4	86.8	0.64
Fever	61.6	18.7	14.3	68.9	0.60
SIRS ≥2	89.4	12.1	18.3	83.3	0.51
qSOFA ≥2	87.7	78.3	47.1	96.6	0.83
SAPS II	–	–	–	–	0.78
SOFA	–	–	–	–	0.77
Pitt bacteraemia score	–	–	–	–	0.80

PPV: positive predictive value; NPV: negative predictive value; SIRS: Systemic Inflammatory Response Syndrome; qSOFA: quick Sequential Organ Failure Assessment; SAPS II: Simplified Acute Physiology Score II.

function and nutritional status [23]. In our cohort, 80 out of 115 patients (69.6%) with malignancy had received chemotherapy during the last month prior to BSI. Even though these patients were prone to develop neutropenia, only a small percentage among our cohort was neutropenic (12; 3.0%).

As previously shown in a European cohort [24], as well as, in a cohort from Switzerland [25], *E. coli* is the predominant cause of bacteraemia followed by *S. aureus*. Isolation of MDR pathogens was extremely low (10.1%), showing only a trend towards higher mortality (8.8% non-MDR *vs* 16.4% MDR; *P* 0.056). Multivariate analysis among all patients with bloodstream infection, as previously shown [26], revealed that staphylococcal infections were associated with worst outcome as compared to other pathogens, but no difference among age, comorbidities, severity scores and appropriateness and time of initiation of antibiotic therapy was detected between staphylococcal and non-staphylococcal infections, indicating that staphylococci, and especially *S. aureus*, harbor an armamentarium of virulence factors that amplify immune evasion and host cell injury leading to higher mortality [4]. On the other hand, BSI due to *E. coli*, which was mainly due to urinary tract infections, was associated with better survival among, as previously observed [18].

The most common site of infection identified in the present study was urinary tract followed by lower respiratory tract and primary BSI with the latter been independently associated with worst prognosis, in accordance to the literature [18,19]. The absence of identified infectious source has been previously shown to be associated with higher mortality, as also observed in the present study among septic patients [18,19]. This non-identification of a source of infection was responsible for an important delay of antibiotic administration (5.8 ± 6.5 h in secondary bloodstream infection *vs* 11.8 ± 9.5 in primary; $P < .001$), even among septic patients, probably attributing to the worst outcome of these patients.

The study had several limitations, including the fact that it is a single center one. The study was conducted in a community hospital, thus our population had fewer comorbidities as compared hospitalized in large university centers. Even though it was a retrospective one, all BSIs in internal medicine department were included, which offers a more comprehensive understanding of BSIs, while, on the other hand it increases heterogenicity by including different pathogens and sources of infection. A low percentage of multidrug resistance was observed, so our findings may not be generalizable to countries with high percentages of multidrug-resistant pathogens [24]. Furthermore, only bloodstream infections were included, thus caution is needed when extrapolating these results in non bacteraemic infections.

5. Conclusions

In conclusion, qSOFA as compared to SIRS and other severity scores showed better performance in predicting mortality among internal medicine patients in a secondary hospital with BSIs. Pathogen species and anatomic site of infection influenced mortality with staphylococci and primary BSIs being associated with worse prognosis. Better prognosis was associated with administration of appropriate empiric antibiotic therapy and its timely initiation.

Declarations of interest

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