Electronic Supplementary Material

# Predictive accuracy of the Quick Sepsis-related Organ Failure Assessment score in Brazil: a prospective multicenter study

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METHODS

**Data collection**

The case manager of each institution prospectively entered all data into the study database. The managers were instructed to register the worst Glasgow coma score, the highest respiratory rate and the lowest systolic blood pressure for each patient. The details for data collection are available online data supplement. As a strategy to minimize partial missing data, the case managers could include qSOFA data in the database only when all 3 variables were available. As our main objective was to pragmatically assess the sensitivity of qSOFA in mortality prediction as if it was used as a screening tool, we considered only the values available at the moment the healthcare team raised the suspicion of sepsis and started diagnostic and treatment measures such as laboratory samples, blood cultures and antibiotic administration. For patients enrolled in the ED, we collected the worst values for each component from hospital admission until the moment the healthcare team suspected sepsis. For patients in wards, we collected data from the 24 hours immediately prior to the suspicion of sepsis. We also collected the severity scores of the Sequential Organ Failure Assessment (SOFA) with the

worst values on the day of sepsis diagnosis and the Simplified Acute Physiology Score 3 (SAPS 3) for those admitted to the ICU. We assessed transfer to the ICU only in the first 24 hours after sepsis diagnosis. We obtained data on ICU length of stay for those admitted to the ICU in the first 24 hours of sepsis and on hospital length of stay for all patients. All patients were followed until hospital discharge.

**Definitions**

Life-threatening organ dysfunction was defined as the presence of any of the following: systolic blood pressure <90 mmHg or mean arterial pressure <65 mmHg or reduction in systolic blood pressure >40 mmHg; creatinine >2.0 mg/dL or diuresis less than 0.5 mL/kg/h in the last 2 hours; bilirubin >2 mg/dL; platelet count <100,000 cells/mm3; lactate >2 mmol/L (or above the reference value); coagulopathy (international normalized ratio >1.5 or activated partial thromboplastin time >60 sec); PaO2/FiO2 ratio <300 or a recent or increased O2 need to maintain SpO2 >90%.

Vasopressor-dependent sepsis was defined as the need of vasopressors for sepsis-induced hypotension, despite adequate fluid resuscitation (20).

Public institutions were those whose major income came from the Sistema Unico de Saude (the universal public health care system in Brazil) and private institutions were those whose main source of income was private healthcare companies.

**RESULTS**

**Table E1. General characteristics of the participating institutions.**

| Variable | All institutions (n = 74) |
|---|---|
| Hospital location | |
| State capitals | 47 (63%) |
| Countryside | 27 (37%) |
| Hospital geographic region | |
| Southeast | 58 (78%) |
| South | 6 (9%) |
| Middle West | 5 (7%) |
| Northeast | 3 (4%) |
| North | 2 (2%) |
| Main source of income | |
| Public system | 27 (36%) |
| Private health system | 47 (64%) |
| Emergency services | 66 (89%) |
| Teaching status | |
| Academic | 41 (55%) |
| Non-academic | 33 (45%) |
| Hospital size | |
| ≤ 100 beds | 15 (20%) |
| 101 to 500 beds | 55 (74%) |
| ≥ 500 beds | 4 (5%) |
| Intensive care unit size | |
| ≤10 beds | 15 (20%) |
| 11 to 50 beds | 51 (69%) |
| > 50 beds | 8 (11%) |

**Table E2. Main characteristic for patients with missing values for qSOFA and the study population – cohort 1 and 2**

| Variable | Cohort 1 | | | Cohort 2 | | |
|---|---|---|---|---|---|---|
| | Patients with missing qSOFA values (n = 123) | Patients with available qSOFA values (n = 5460) | P-value | Patients with missing qSOFA values (n=573) | Patients with available qSOFA values (n = 4711) | P-value |
| Age (years) | 63 (45.5 - 80) | 64 (41 – 80) | 0.89 | 69 (56 - 81) | 65 (48 - 78) | <0,001 |
| Male sex | 61 (49.6) | 2519 (46.1) | 0.50 | 332 (57.9) | 2432 (51.6) | 0.005 |
| SAPS 3 score (points)[a] | 45 (38 - 50) (n=10) | 54 (43 - 64) (n=2023) | 0.03 | 68 (54 - 84) (n=74) | 58 (48 - 68) (n=2441) | <0,001 |
| SOFA score (points) | 1 (0 - 3) (n=58) | 1 (0 - 4) (n=5189) | 0.44 | 4 (1 - 7) (n=306) | 3 (2 - 6) (n=4354) | 0.09 |
| Severity of illness | | | | | | |
| Infection without organ dysfunction | 59 (48.0) | 2477 (45.4) | 0.56 | 0 (0) | 0 (0) | - |
| Sepsis | 55 (44.7) | 2427 (44.5) | | 370 (64.6) | 3480 (73.9) | |
| Vasopressor-dependent sepsis | 9 (7.3) | 556 (10.2) | | 203 (35.4) | 1231 (26.1) | |
| Number of organ dysfunction | 1 (0 - 1) | 1 (0 - 2) | 0.42 | 1 (1 - 2) | 2 (1 - 2) | 0.05 |
| Mechanical ventilation | 23 (18.7) | 589 (10.8) | 0.008 | 202 (35.3) | 1185 (25.2) | <0,001 |
| ICU length of stay (days) | 6 (3 - 12.3) (n=39) | 4.4 (2.1 - 9.3) (n=2137) | 0.12 | 5.3 (2.7 - 11.7) (n=172) | 4.7 (2.4 - 10.3) (n=2491) | 0.29 |
| Hospital length of stay [a] (days) | 9.6 (4.1 - 19.9) | 5.9 (2.0– 12.0) | <0.001 | 11.7 (5.1-23.7) | 8.8 (4.1 – 19.1) | 0.06 |
| Hospital mortality | 28 (22.8) | 766 (14.0) | 0.009 | 224 (39.1) | 1338 (28.4) | <0.001 |

Data are expressed as n (%) or median (interquartile range).

[a] hospital length of stay calculated from the diagnosis of sepsis until hospital discharge.

qSOFA = Quick Sequential Organ Failure Assessment. COPD = chronic obstructive pulmonary disease. SAPS = Simplified Acute Physiologic Score. SOFA = Sequential organ-failure assessment. ICU= intensive care unit.

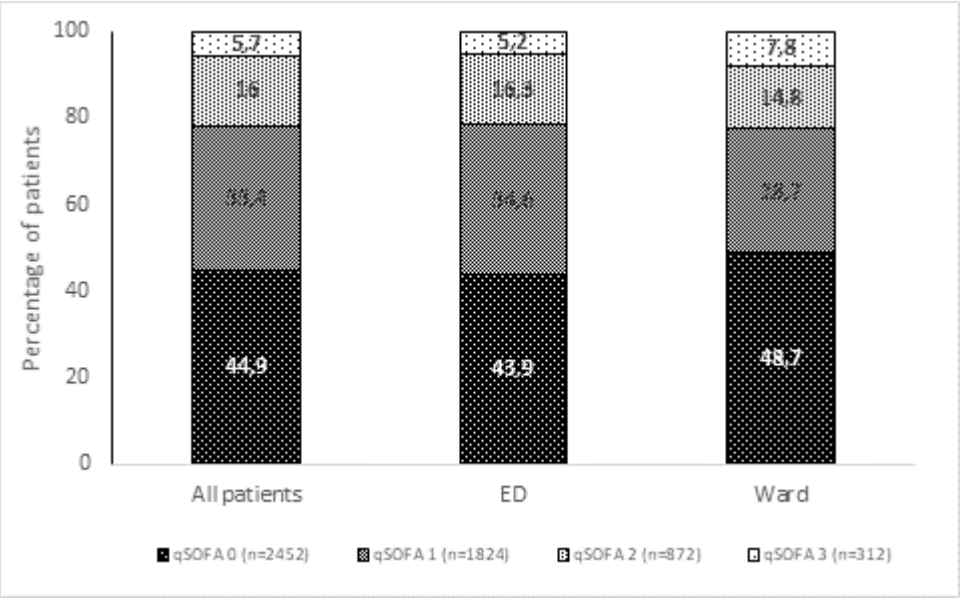


Figure E1 – Frequency of positive qSOFA components among emergency and ward patients with infection without organ dysfunction or sepsis in cohort 1 according to the location of sepsis diagnosis. ED – emergency department.

**Table E3. Performance of qSOFA≥ 2 to predict mortality in cohort 1 considering only cases with available qSOFA (main analysis), and imputing all missing values of qSOFA ≥2 or all missing values ≤ 1**

| Variable | Main analysis (only cases with available qSOFA values) | All missing qSOFA imputed as ≥ 2 | All missing qSOFA imputed as ≤ 1 |
|---|---|---|---|
| Mortality | | | |
| N | 5460 | 5583 | 5583 |
| Sensitivity | 53.9 [50.3 – 57.5] | 55.5 [52.0 – 59.0] | 52.0 [48.5 – 55.5] |
| Specificity | 83.6 [82.5 – 84.6] | 81.9 [80.8 – 83.0] | 83.9 [82.8 – 84.9] |
| PPV | 34.9 [32.2 – 37.7] | 33.7 [31.2 – 36.4] | 34.9 [32.2 – 37.7] |
| NPV | 91.7 [90.9 – 92.5] | 91.7 [90.9 – 92.5] | 91.3 [90.5 – 92.1] |
| Positive LR | 3.28 [2.99 – 3.60] | 3.07 [2.82 – 3.35] | 3.23 [2.94 – 3.55] |
| Negative LR | 0.55 [0.51 – 0.60] | 0.54 [0.50 – 0.59] | 0.57 [0.53 – 0.62] |
| AUROC | 75 [73.2 – 76.9] | 74.6 [72.8 – 76.4] | 73.6 [71.5 – 75.5] |

qSOFA = quick Sequential Organ Failure Assessment. SIRS = Systemic Inflammatory Response Syndrome. SOFA = Sequential Organ Failure Assessment. PPV = positive predictive value. NPV = negative predictive value. LR = likelihood ratio. AUROC = Area under the ROC curve.

**Table E4 Performances for the prediction of ICU admission within 24 hours and the composite endpoint of ICU admission within 24 hours plus ICU length of stay greater than 48 hs among patients with suspected infection in cohort 1.**

| Variable | qSOFA ≥ 2 | qSOFA ≥ 1 | qSOFA ≥ 1 or lactate > 2mmol/L | SIRS criteria ≥ 2 | Organ dysfunction ≥ 1 | SIRS ≥ 2 + organ dysfunction ≥ 1 | SOFA ≥ 2 |
|---|---|---|---|---|---|---|---|
| ICU admission within 24h | | | | | | | |
| N | 5460 | 5460 | 5319 | 5460 | 5460 | 5460 | 5189 |
| Sensitivity | 39.7 [37.7- 41.9] | 78.3 [76.5- 80.0] | 88.2 [86.7- 89.5] | 76.4 [74.5- 78.2] | 79.6 [77.8- 81.3] | 60.4 [58.3- 62.5] | 69.7 [67.6- 71.6] |
| Specificity | 90.1 [89.0- 91.0] | 60.0 [58.3- 61.7] | 45.6 [43.9- 47.4] | 25.2 [23.7- 26.7] | 61.6 [59.9- 63.2] | 72.3 [70.7- 73.8] | 67.0 [65.3- 68.6] |
| PPV | 72.2 [69.5- 74.7] | 56.0 [54.2- 57.8] | 52.0 [50.3- 53.6] | 39.9 [38.4- 41.4] | 57.4 [55.6- 59.2] | 58.6 [56.5- 60.6] | 57.8 [55.8- 59.8] |
| NPV | 69.7 [68.3- 71.1] | 81.0 [79.3- 82.5] | 85.2 [83.5- 86.9] | 62.1 [59.5- 64.7] | 82.3 [80.7- 83.7] | 73.7 [72.2- 75.2] | 77.3 [75.6- 78.8] |
| Positive LR | 4.00 [3.56- 4.49] | 1.96 [1.87- 2.05] | 1.62 [1.57- 1.68] | 1.02 [0.99- 1.05] | 2.07 [1.97- 2.17] | 2.18 [2.04- 2.32] | 2.11 [1.99- 2.23] |
| Negative LR | 0.67 [0.65- 0.69] | 0.36 [0.33- 0.39] | 0.26 [0.23- 0.29] | 0.94 [0.85- 1.03] | 0.33 [0.30- 0.36] | 0.55 [0.52- 0.58] | 0.45 [0.42- 0.49] |
| ICU admission within 24h + ICU length of stay > 48h | | | | | | | |
| N | 5446 | 5446 | 5305 | 5446 | 5446 | 5446 | 5175 |
| Sensitivity | 41.9 [39.5- 44.3] | 79.5 [77.5- 81.4] | 89.3 [87.6- 90.7] | 76.3 [74.2- 78.4] | 82.5 [80.6- 84.3] | 63.0 [60.6- 65.3] | 73.0 [70.7- 75.2] |
| Specificity | 87.1 [86.0- 88.2] | 55.6 [54.0- 57.2] | 41.7 [40.1- 43.3] | 25.0 [23.6- 26.4] | 57.5 [55.9- 59.1] | 69.2 [67.7- 70.6] | 63.6 [62.0- 65.2] |
| PPV | 58.4 [55.6- 61.3] | 43.6 [41.9- 45.4] | 40.4 [38.8- 42.0] | 30.6 [29.2- 32.0] | 45.7 [43.9- 47.5] | 46.9 [44.8- 49.0] | 46.5 [44.5- 48.5] |
| NPV | 77.6 [76.3- 78.9] | 86.3 [84.8- 87.6] | 89.7 [88.2- 91.1] | 70.9 [68.4- 73.4] | 88.4 [87.1- 89.6] | 81.2 [79.8- 82.5] | 84.5 [83.0- 85.8] |
| Positive LR | 3.25 [2.94- 3.60] | 1.79 [1.71- 1.87] | 1.53 [1.48- 1.58] | 1.02 [0.99- 1.05] | 1.94 [1.86- 2.03] | 2.04 [1.92- 2.17] | 2.01 [1.90- 2.11] |
| Negative LR | 0.67 [0.64- 0.70] | 0.37 [0.33- 0.41] | 0.26 [0.22- 0.30] | 0.95 [0.85- 1.05] | 0.30 [0.27- 0.34] | 0.53 [0.50- 0.57] | 0.42 [0.39- 0.46] |

qSOFA = Quick Sequential Organ Failure Assessment. SIRS = Systemic Inflammatory Response Syndrome. SOFA = Sequential Organ Failure Assessment. PPV = positive predictive value. NPV = negative predictive value. LR = likelihood ratio. ICU = intensive care unit.

**Table E5. Main characteristics of patients in Cohort 2 (patients presenting outside of the ICU with sepsis), both for all patients and for survivors compared to non-survivors.**

| Variable | All patients (n = 4711) | Hospital survivors (n = 3373) | Hospital non-survivors (n = 1338) | P value |
|---|---|---|---|---|
| Type of institution | | | | <0.0001 |
| Public | 1451 (30.8) | 721 (21.4) | 730 (54.6) | |
| Private | 3260 (69.2) | 2652 (78.6) | 608 (45.4) | |
| Age (years) | 65 (48 – 78) | 63 (44 – 77) | 69 (56 – 80) | <0.0001 |
| Male sex | 2432 (51.6) | 1687 (50.0) | 745 (55.7) | <0.0001 |
| Comorbidities | | | | |
| Cancer | 824 (17.5) | 497 (14.7) | 327 (24.4) | <0.0001 |
| Diabetes | 1160 (24.6) | 840 (24.9) | 320 (23.9) | 0.48 |
| Chronic heart failure | 462 (9.8) | 285 (8.4) | 177 (13.2) | <0.0001 |
| COPD | 413 (8.8) | 284 (8.4) | 129 (9.6) | 0.18 |
| Chronic renal failure | 574 (12.2) | 372 (11.0) | 202 (15.1) | <0.0001 |
| Arterial hypertension | 2037 (43.2) | 1424 (42.2) | 613 (45.8) | 0.03 |
| Immunossupression | 726 (15.4) | 454 (13.5) | 272 (20.3) | <0.0001 |
| SAPS 3 score (points)[a] | 58 (48 – 68) | 54 (44 – 62) | 70 (60 – 82) | <0.0001 |
| Source of infection | | | | <.0001 |
| Lung | 2208 (46.9) | 1516 (44.9) | 692 (51.7) | |
| UTI | 881 (18.7) | 721 (21.4) | 160 (12.0) | |
| Abdominal | 626 (13.3) | 421 (12.5) | 205 (15.3) | |
| Others | 996 (21.1) | 715 (21.2) | 281 (21.0) | |
| Type of infection | | | | <.0001 |
| Community acquired | 3514 (74.6) | 2702 (80.1) | 812 (60.7) | |
| Healthcare associated [a] | 1197 (25.4) | 671 (19.9) | 526 (39.3) | |
| Severity of illness | | | | <0.0001 |
| Sepsis | 3480 (73.9) | 2813 (83.4) | 667 (49.9) | |
| Vasopressor-dependent sepsis | 1231 (26.1) | 560 (16.6) | 671 (50.1) | |
| Location at sepsis presentation | | | | <0.0001 |
| Emergency department | 3509 (74.5) | 2673 (79.2) | 836 (62.5) | |
| Wards | 1202 (25.5) | 700 (20.8) | 502 (37.5) | |
| ICU admission in 24 hours[b] | | | | |
| From ED | 1813 (51.7) | 1342 (50.2) | 471 (56.3) | 0.002 |
| From wards | 744 (61.9) | 409 (58.4) | 335 (66.7) | 0.003 |
| Time to sepsis diagnosis (h) | 0.15 (0.0 – 1.0) | 0.1 (0.0 – 0.7) | 0.3 (0.0 – 2.4) | <0.0001 |
| Mechanical ventilation | 1185 (25.2) | 429 (12.7) | 756 (56.5) | <0.0001 |
| ICU length of stay (days) | 4.7 (2.4 – 10.3) | 4.1 (2.4 – 8.7) | 6.5 (2.3 – 14.5) | <0.0001 |
| Hospital length of stay [c] (days) | 8.8 (4.1 – 19.1) | 8.9 (4.8 – 17.6) | 8.2 (2.4 – 19.3) | <0.0001 |

Data are expressed as n (%) or median (interquartile range). Percentages are column percents when given for the entire population and row percents when given for the population categorized by hospital outcomes.

[a]Healthcare-associated infections include those infections acquired by out-clinic, hospice and homecare patients as well as those not present at hospital admission and started after 48 hours of hospital stay.

[b]percentages for survivors and non-survivors calculated for the total number of ED patients (n = 3509) or ward patients (n = 1202)

[c] hospital length of stay calculated from the diagnosis of sepsis until hospital discharge.

COPD = chronic obstructive pulmonary disease. SAPS = Simplified Acute Physiologic Score. SOFA = Sequential organ-failure assessment. UTI = urinary tract infection. ED = emergency department. ICU= intensive care unit.

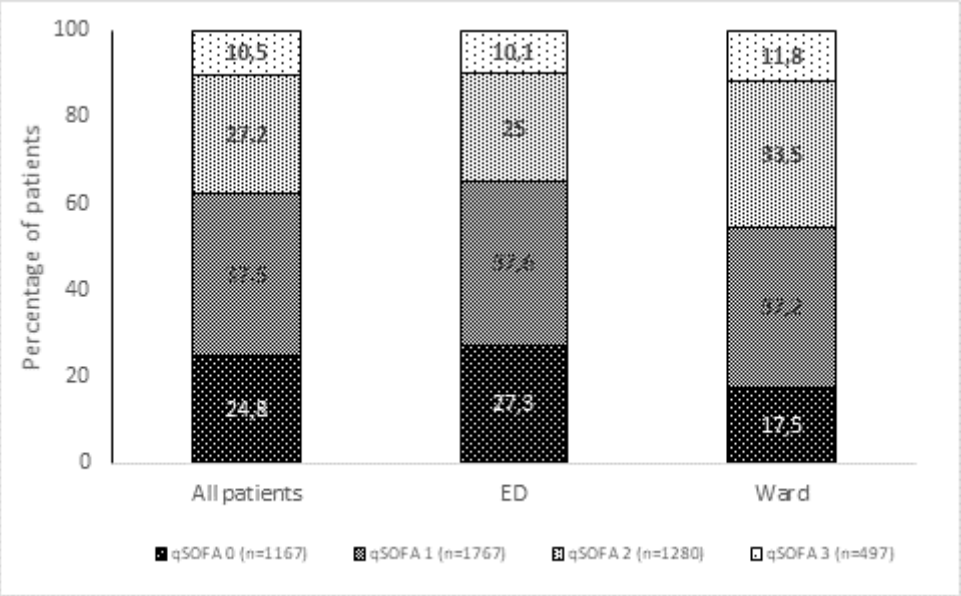


Figure E2. – Frequency of positive qSOFA components among emergency and ward patients with sepsis in cohort 2 according to the location. ED = emergency department.

**Table E6. Screening tools among patients with sepsis in Cohort 2, both for all patients and for survivors compared to non-survivors.**

| Variable | All patients (n = 4711) | Hospital survivors (n = 3373) | Hospital non-survivors (n = 1338) | P value |
|---|---|---|---|---|
| qSOFA ≥ 2 | | | | <0.0001 |
| No | 2934 (62.3) | 2427 (82.7) | 507 (17.3) | |
| Yes | 1777 (37.7) | 946 (53.2) | 831 (46.8) | |
| qSOFA criteria | | | | |
| Respiratory rate ≥ 22 | | | | <0.0001 |
| No | 2615 (55.5) | 2066 (79.0) | 549 (21.0) | |
| Yes | 2096 (44.5) | 1307 (62.4) | 789 (37.6) | |
| Glasgow < 15 | | | | <0.0001 |
| No | 3315 (70.4) | 2640 (79.6) | 675 (20.4) | |
| Yes | 1396 (29.6) | 733 (52.5) | 663 (47.5) | |
| SBP ≤ 100 | | | | <0.0001 |
| No | 2385 (50.6) | 1930 (80.9) | 455 (19.1) | |
| Yes | 2326 (49.4) | 1443 (62.0) | 883 (38.0) | |
| qSOFA | | | | <0.0001 |
| 0 | 1167 (24.8) | 1046 (89.6) | 121 (10.4) | |
| 1 | 1767 (37.5) | 1381 (78.2) | 386 (21.8) | |
| 2 | 1280 (27.2) | 736 (57.5) | 544 (42.5) | |
| 3 | 497 (10.5) | 210 (42.3) | 287 (57.7) | |
| Organ dysfunctions | 2 (1 – 2) | 1 (1 – 2) | 2 (1 – 3) | <0.0001 |
| Number of organ dysfunction | | | | <0.0001 |
| 1 | 2347 (49.8) | 1950 (83.1) | 397 (16.9) | |
| 2 | 1370 (29.1) | 968 (70.7) | 402 (29.3) | |
| 3 | 659 (14.0) | 350 (53.1) | 309 (46.9) | |
| 4 or more | 335 (7.1) | 105 (31.3) | 230 (68.7) | |
| Lactate > 2 mmol/L | 2474 (62.9) | 1781 (62.3) | 693 (64.3) | |
| qSOFA ≥ 1 or lactate > 2mmol/L[a] | | | | <0.0001 |
| No | 373/4585 (8.1) | 338 (90.6) | 35 (9.4) | |
| Yes | 4212/4585 (91.9) | 2941 (69.8) | 1271 (30.2) | |
| SIRS ≥ 2 + organ dysfunction ≥ 1 | | | | <0.0001 |
| No | 2578 (54.7) | 2159 (83.7) | 419 (16.2) | |
| Yes | 2133 (45.3) | 1214 (56.9) | 919 (43.1) | |
| SOFA score (points) | 3 (2 – 6) | 3 (1 – 5) | 7 (4 – 10) | <0.0001 |
| SOFA points | | | | <0.0001 |
| 0 | 490/4354 (11.3) | 476 (97.1) | 14 (2.9) | |
| 1 | 556/4354 (12.8) | 488 (87.8) | 68 (12.2) | |
| 2 | 625/4354 (14.4) | 547 (87.5) | 78 (12.5) | |
| 3 | 538/4354 (12.4) | 448 (83.3) | 90 (16.7) | |
| 4 | 464/4354 (10.7) | 355 (76.5) | 109 (23.5) | |
| 5 or more | 1681/4354 (38.6) | 843 (50.1) | 838 (49.9) | |
| SOFA ≥ 2 points | | | | <0.0001 |
| No | 1046/4354 (22.2) | 964 (92.2) | 82 (7.8) | |
| Yes | 3308/4354 (76.0) | 2193 (66.3) | 1115 (33.7) | |
| SIRS criteria | | | | 0.003 |
| 0 | 106 (2.3) | 80 (75.5) | 26 (24.5) | |
| 1 | 955 (20.3) | 669 (70.1) | 286 (29.9) | |
| 2 | 2130 (45.2) | 1567 (73.6) | 563 (26.4) | |
| 3 | 1262 (26.8) | 895 (70.9) | 367 (29.1) | |
| 4 | 258 (5.5) | 162 (62.8) | 96 (37.2) | |
| SIRS ≥ 2 | | | | 0.411 |

| | | | |
|---|---|---|---|
| No | 1061 (22.5) | 749 (70.6) | 312 (29.4) |
| Yes | 3650 (77.5) | 2624 (71.9) | 1026 (28.1) |

Data are expressed as n (%) or median (interquartile range). Percentages are column percents when given for the entire population and row percents when given for the population categorized by hospital outcomes.

[a] lactate is available for 4585 patients and SOFA score for 4354.

qSOFA = Quick Sequential Organ Failure Assessment. SBP = systolic blood pressure. SIRS = Systemic Inflammatory Response Syndrome. SOFA = Sequential Organ Failure Assessment.