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Supplementary Tables

Supplementary Table 1. Univariate analysis comparing culture negative to culture positive patients with change in SOFA score ≥ 2.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Negative Cultures** | **Positive Cultures** |  |
| **Characteristic** | **n = 5,875****mean + sd****frequency (%)** | **n = 697****mean + sd****frequency (%)** | **p-value** |
| Age, years  | 57 ± 17 | 59 ± 17 | 0.001 |
| Male sex  | 3,636 (62) | 391 (56) | <0.001 |
| Race |  |  | 0.445 |
|  African American | 605 (10) | 71 (10) |  |
|  Caucasian | 4,626 (78) | 563 (81) |  |
|  Other | 203 (4) | 18 (3) |  |
|  Unknown | 441 (8) | 45 (7) |  |
| *Physiological data and lab values on presentation* |   |   |   |
| Temperature maximum, °C (5,686; 674)  | 37.8 ± 0.9 | 37.9 ± 1.0 | 0.309 |
| Temperature minimum, °C (5,686; 674)  | 36.6 ± 0.8 | 36.5 ± 0.8 | 0.003 |
| Heart rate, min-1 (5,865; 695)  | 98 ± 18 | 101 ± 20 | <0.001 |
| Respiratory rate, min-1 (5,769; 686)  | 21 ± 6 | 21 ± 6 | 0.017 |
| Systolic blood pressure, mmHg (5,846; 693)  | 120 ± 23 | 117 ± 24 | <0.001 |
| Diastolic blood pressure, mmHg (5,842; 693)  | 62 ± 12 | 61 ± 12 | 0.114 |
| Oxygen saturation maximum, % (5,835; 692)  | 99 ± 2 | 99 ± 2 | 0.026 |
| Oxygen saturation minimum, % (5,835; 692)  | 90 ± 10 | 88 ± 12 | <0.001 |
| White blood cell count, K/uL (4,693; 576)  | 14.3 ± 14.2 | 14.3 ± 19.0 | 0.183 |
| Hematocrit, % (4,702; 578)  | 30.4 ± 6.2 | 30.5 ± 5.9 | 0.566 |
| Platelets, K/uL (4,702; 576)  | 179 ± 110 | 179 ± 126 | 0.339 |
| Bicarbonate, mmol/L (4,773; 580)  | 25.1 ± 5.0 | 24.6 ± 5.5 | 0.018 |
| Blood urea nitrogen, mg/dL (4,787; 582)  | 30 ± 22 | 32 ± 23 | 0.013 |
| Creatinine, mg/dL (4,822; 586)  | 1.54 ± 1.43 | 1.52 ± 1.36 | 0.764 |
| Glasgow Coma Scale maximum (3,870; 465)  | 12 ± 4 | 12 ± 4 | 0.210 |
| Glasgow Coma Scale minimum (3,870; 465)  | 10 ± 5 | 10 ± 5 | 0.293 |
| APACHE II score (5,875, 697)  | 15 ± 8 | 16 ± 8 | <0.001 |
| qSOFA score  | 2.3 ± 1  | 2.4 ± 1  | 0.461  |
| qSOFA score > 2 | 4,947 (87) | 607 (89) | 0.156 |
|  |   |   |   |
| *Antibiotic use* |  |   |   |
| None | 2,309 (39) | 414 (59) | <0.001 |
| Received on days 1, 2 & >2 before presentation | 1,182 (20) | 93 (13) | <0.001 |
| Received on days 1 & 2 before presentation  | 718 (12) | 24 (3) | <0.001 |
| Received only on day 1 before presentation | 1,099 (19) | 83 (12) | <0.001 |
|   |   |   |   |
| *Before presentation* |   |   |   |
| Mechanical ventilation | 1,806 (31) | 154 (22) | <0.001 |
| Renal replacement therapy | 136 (2) | 13 (2) | 0.536 |
| Plasma transfusion | 892 (15) | 121 (17) | 0.147 |
| Red blood cell transfusion | 907 (15) | 122 (18) | 0.173 |
| Platelet transfusion | 463 (8) | 54 (8) | 0.961 |
| Receiving vasopressors | 1,240 (21) | 156 (22) | 0.466 |
|   |   |   |   |
| *Therapies initiated within 24 hours of presentation* |   |   |   |
| Mechanical ventilation | 2,059 (35) | 236 (34) | 0.562 |
| Renal replacement therapy | 236 (4) | 36 (5) | 0.181 |
| Plasma transfusion | 276 (5) | 47 (7) | 0.023 |
| Red blood cell transfusion | 644 (11) | 71 (10) | 0.578 |
| Platelet transfusion | 309 (5) | 53 (8) | 0.013 |
|   |   |   |   |
| *Outcomes* |   |   |   |
| Hospital Survival | 4,840 (83) | 528 (76) | <0.001 |
| Post sepsis hospital length of stay, days (9,283; 1,105) | 3.6 ± 5.5 | 4.0 ± 5.7 | 0.335 |

Data are presented as mean + the standard deviation or frequency (percentage). \*If patients are missing values, the numbers of patients with values for that variable are shown in parentheses after the variable (n for negative cultures; n for positive cultures). Bonferroni adjusted p-value for statistical significance p<0.010.

Supplementary Table 2. Univariate analysis comparing in-hospital survival to mortality with change in SOFA score ≥ 2.

|  |  |  |  |
| --- | --- | --- | --- |
|   | **No Hospital Mortality** | **Hospital Mortality** |  |
| **Characteristic** | **n = 5,368** | **n = 1,204** | **p-value** |
| Age, years  | 56 ± 17 | 62 ± 16 | <0.001 |
| Male sex  | 3,302 (62) | 725 (60) | 0.423 |
| Race |  |  | <0.001 |
|  African American | 567 (11) | 109 (9) |  |
|  Caucasian | 4,261 (79) | 928 (77) |  |
|  Other race | 183 (3) | 38 (3) |  |
|  Unknown | 357 (7) | 129 (11) |  |
| *Physiological data and lab values on presentation* |   |   |   |
| Temperature maximum, °C (5,202; 1,158)  | 37.9 ± 0.9 | 37.7 ± 1.2 | <0.001 |
| Temperature minimum, °C (5,202; 1,158)  | 36.6 ± 0.6 | 36.3 ± 1.2 | <0.001 |
| Heart rate, min-1 (5,360; 1,200)  | 97 ± 18 | 100 ± 21 | <0.001 |
| Respiratory rate, min-1 (5,293; 1,162)  | 21 ± 6 | 23 ± 7 | <0.001 |
| Systolic blood pressure, mmHg (5,346; 1,193)  | 121 ± 22 | 114 ± 24 | <0.001 |
| Diastolic blood pressure, mmHg (5,345; 1,190)  | 63 ± 12 | 59 ± 13 | <0.001 |
| Oxygen saturation maximum, % (5,343; 1,184)  | 98 ± 2 | 99 ± 3 | 0.009 |
| Oxygen saturation minimum, % (5,343; 1,184) | 91 ± 8 | 84 ± 17 | <0.001 |
| White blood cell count, K/uL (4,202; 1,067)  | 13.4 ± 10.4 | 17.6 ± 25.2 | <0.001 |
| Hematocrit, % (4,210; 1,070)  | 30.4 ± 6.1 | 30.7 ± 6.5 | 0.220 |
| Platelets, K/uL (4,208; 1,070)  | 183 ± 111 | 163 ± 114 | <0.001 |
| Bicarbonate, mmol/L (4,302; 1,051)  | 25.6 ± 4.6 | 23.4 ± 6.2 | <0.001 |
| Blood urea nitrogen, mg/dL (4,300; 1,069)  | 28 ± 20 | 39 ± 25 | <0.001 |
| Creatinine, mg/dL (4,336; 1,072)  | 1.46 ± 1.44 | 1.83 ± 1.31 | <0.001 |
| Glasgow Coma Scale maximum (3,643; 692)  | 12 ± 3  | 9 ± 5 | <0.001 |
| Glasgow Coma Scale minimum (3,643; 692)  | 11 ± 4 | 7 ± 4 | <0.001 |
| APACHE II score (5,368, 1,204)  | 14 ± 7 | 21 ± 9 | <0.001 |
| qSOFA (5,198, 1,200)Positive Culture | 2.3 ± 0.8528 (10) | 2.4 ±0.7169 (14) | 0.004<0.001 |
|  |   |   |   |
| *Antibiotic use*  |  |   |   |
| None | 2,164 (40) | 559 (46) |  <0.001 |
| Received on days 1, 2 & >2 before presentation | 1,036 (19) | 239 (20) | <0.001 |
| Received on days 1 & 2 before presentation  | 644 (12) | 98 (8) | <0.001 |
| Received only on day 1 before presentation | 955 (18) | 227 (19) | <0.001 |
|   |   |   |   |
| *Before presentation* |   |   |   |
| Mechanical ventilation | 1,646 (31) | 314 (26) | 0.002 |
| Renal replacement therapy | 92 (2) | 57 (5) | <0.001 |
| Plasma transfusion | 676 (13) | 337 (28) | <0.001 |
| Red blood cell transfusion | 846 (16) | 183 (15) | 0.660 |
| Platelet transfusion | 405 (8) | 112 (9) | 0.047 |
| Receiving vasopressors | 879 (16) | 517 (43) | <0.001 |
|   |   |   |   |
| *Therapies initiated within 24 hours of presentation* |   |   |   |
| Mechanical ventilation | 1721 (32) | 574 (48) | <0.001 |
| Renal replacement therapy | 143 (3) | 129 (11) | <0.001 |
| Plasma transfusion | 181 (3) | 142 (12) | <0.001 |
| Red blood cell transfusion | 520 (10) | 195 (16) | <0.001 |
| Platelet transfusion | 221 (4) | 141 (12) | <0.001 |

Data are presented as mean + the standard deviation or frequency (percentage). \* If patients are missing values, the numbers of patients with values for that variable are shown in parentheses after the variable (n for negative cultures; n for positive cultures). Bonferroni adjusted p-value for statistical significance p<0.010.

Supplementary Table 3. Factors associated with mortality by multivariable logistic regression in patients with change in SOFA score ≥ 2.

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **odds ratio** | **95% CI** | **p-value** |
| Positive culture | 1.13 | (0.90, 1.43) | 0.303 |
| Age, 10 years | 1.40 | (1.32, 1.48) | <0.001 |
|  |  |  |  |
| *Physiological data and lab values on presentation* |   |   |   |
| Oxygen saturation maximum < 96% | 1.68 | (1.15, 2.44) | 0.007 |
| Oxygen saturation unknown | 4.82 | (1.92, 12.12) | 0.001 |
| Respiratory rate, min-1 | 1.03 | (1.02, 1.04) | <0.001 |
| Heart rate, min-1 | 1.01 | (1.00, 1.01) | 0.006 |
| Systolic blood pressure, mmHg | 0.99 | (0.99, 1.00) | 0.001 |
| Glasgow Coma Scale maximum, 8 - 10 | 1.75 | (1.15, 2.44) | 0.007 |
| Glasgow Coma Scale maximum, < 7 | 3.88 | (2.67, 5.60) | <0.001 |
| Glasgow Coma Scale, unknown | 3.44 | (2.42, 4.89) | <0.001 |
| APACHE II score | 1.09 | (1.07, 1.10) | <0.001 |
|   |   |   |   |
| *Before presentation* |   |   |   |
| Renal replacement therapy | 2.34 | (1.47, 3.71) | <0.001 |
| Plasma transfusion | 1.68 | (1.37, 2.07) | <0.001 |
| Red blood cell transfusion | 0.63 | (0.49, 0.82) | <0.001 |
| Receiving vasopressors | 1.77 | (1.47, 2.3) | <0.001 |

95% CI = 95% confidence interval. Bonferroni adjusted p-value for statistical significance p<0.010.

Supplementary Table 4. Factors associated with positive cultures by multivariable logistic regression in patients with change in SOFA score ≥ 2.

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **odds ratio** | **95% CI** | **p-value** |
| Age, 10 years | 1.12 | (1.06, 1.18) | <0.001 |
| Male sex | 0.77 | (0.65, 0.91) |  0.002 |
| Heart rate, min-1 | 1.01 | (1.00, 1.01) |  <0.001 |
| APACHE II score | 1.01 | (1.00, 1.02) |  0.034 |
|   |   |   |   |
| *Before presentation* |   |   |   |
| Red blood cell transfusion | 1.51 | (1.19, 1.91) | 0.001 |
|   |   |   |   |
| *Antibiotic use* |  |  |  |
| Received on days 1 before presentation | 0.45 | (0.36, 0.55) |  <0.001 |
| Received on days 1 & 2 before presentation | 0.58 | (0.44, 0.76) |  <0.001 |
|  |  |  |  |

95% CI = 95% confidence interval. Bonferroni adjusted p-value for statistical significance p<0.010.

Supplementary Table 5. Factors associated with mortality by multivariable logistic regression in culture negative versus culture positive patients with change in SOFA score ≥ 2.

|  |  |  |
| --- | --- | --- |
|   |  **Culture Negative (n = 5,875)** | **Culture Positive (n = 697)** |
| **Characteristic** | **odds ratio** | **95% CI** | **p-value** | **odds ratio** | **95% CI** | **p-value** |
| Age, 10 years | 1.41 | (1.33, 1.49) | <0.001 | 1.71 | (1.39, 2.10) | <0.001 |
|   |   |   |   |   |   |   |
| *Physiological data and lab values on presentation* |   |   |   |   |   |   |
| Oxygen saturation maximum, < 96% | 1.83 | (1.22, 2.74) | 0.003 | - | - | - |
| Oxygen saturation unknown | 5.10 | (1.97, 13.23) | 0.001 | - | - | - |
| Respiratory rate, min-1 | 1.03 | (1.02, 1.04) | <0.001 | 1.04 | (0.99, 1.08) | 0.105 |
| Heart rate, min-1 | 1.01 | (1.00, 1.01) | 0.005 | - | - | - |
| Glasgow Coma Scale maximum, 8 - 10 | 1.75 | (1.17, 2.61) | 0.007 | 1.81 | (0.50, 6.52) | 0.364 |
| Glasgow Coma Scale maximum, < 7 | 3.65 | (2.45, 5.43) | <0.001 | 7.18 | (1.95, 26.39) | 0.003 |
| Glasgow Coma Scale unknown | 3.78 | (2.58, 5.55) | <0.001 | 3.05 | (0.90, 10.26) | 0.072 |
| Platelets < 54 K/uL | - | - | - | 5.44 | (1.64, 18.03) | 0.006 |
| BUN 39 – 54 mg/dL | 2.54 | (1.57, 4.12) | < 0.001 | - | - | - |
| BUN > 54 mg/dL | 2.67 | (1.61, 4.43) | < 0.001 | - | - | - |
|   |   |   |   |   |   |   |
| APACHE II score | 1.09 | (1.08, 1.11) | <0.001 | 1.14 | (1.08, 1.19) | <0.001 |
|  |   |   |   |   |   |   |
| *Before presentation* |   |   |   |   |   |   |
| Renal replacement therapy | 2.39 | (1.43, 4.00) | 0.001 | - | - | - |
| Plasma transfusion | 1.73 | (1.38, 2.17) | <0.001 | - | - | - |
| Red blood cell transfusion | 0.61 | (0.46, 0.81) | 0.001 | - | - | - |
| Receiving vasopressors | 1.79 | (1.46, 2.19) | <0.001 | - | - | - |
|   |   |   |   |   |   |   |
| *Therapies initiated within 24 hours of presentation* |   |   |   |   |   |   |
| Renal replacement therapy on day of presentation | - | - | - | 6.12 | (1.86, 20.14) | 0.003 |

95% CI = 95% confidence interval. Bonferroni adjusted p-value for statistical significance p<0.010. If a covariate was not included in the final AIC model, this is denoted by “-“.

Supplementary Table 6. Univariate analysis comparing culture negative to culture positive patients with change in qSOFA score ≥ 2

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Negative Cultures** | **Positive Cultures** |  |
| **Characteristic** | **n = 6,024****mean + sd****frequency (%)** | **n = 746****mean + sd****frequency (%)** | **p-value** |
| Age, years  | 56 ± 17 | 59 ± 17 | 0.003 |
| Male sex  | 3,664 (61) | 419 (56) | 0.016 |
| Race |  |  | 0.980 |
|  African American | 620 (10) | 74 (10) |  |
|  Caucasian | 4,769 (79) | 594 (80) |  |
|  Other | 205 (3) | 24 (3) |  |
|  Unknown | 430 (7) | 54 (7) |  |
| *Physiological data and lab values on presentation* |   |   |   |
| Temperature maximum, °C (5,808; 726)  | 37.8 ± 0.9 | 37.9 ± 1.0 | 0.371 |
| Temperature minimum, °C (5,808; 726)  | 36.6 ± 0.8 | 36.5 ± 0.7 | 0.003 |
| Heart rate, min-1 (6,014; 745)  | 98 ± 18 | 102 ± 20 | <0.001 |
| Respiratory rate, min-1 (5,937; 738)  | 21 ± 6 | 21 ± 6 | 0.211 |
| Systolic blood pressure, mmHg (6,003; 744)  | 118 ± 22 | 115 ± 22 | <0.001 |
| Diastolic blood pressure, mmHg (5,997; 744)  | 62 ± 12 | 61 ± 12 | 0.178 |
| Oxygen saturation maximum, % (5,987; 743)  | 99 ± 2 | 99 ± 2 | 0.033 |
| Oxygen saturation minimum, % (5,987; 743)  | 90 ± 10 | 88 ± 12 | 0.002 |
| White blood cell count, K/uL (5,742; 699)  | 14.3 ± 13.4 | 14.7 ± 16.0 | 0.457 |
| Hematocrit, % (4,738; 614)  | 30.6 ± 6.2 | 30.7 ± 6.0 | 0.850 |
| Platelets, K/uL (4,737; 611)  | 190 ± 113 | 191 ± 130 | 0.515 |
| Bicarbonate, mmol/L (4,807; 621)  | 25.1 ± 5.0 | 24.6 ± 5.5 | 0.012 |
| Blood urea nitrogen, mg/dL (4,814; 619)  | 29 ± 21 | 31 ± 22 | 0.004 |
| Creatinine, mg/dL (4,852; 627)  | 1.47 ± 1.37 | 1.43 ± 1.19 | 0.912 |
| Glasgow Coma Scale maximum (4,089; 502)  | 12 ± 4 | 12 ± 4 | 0.452 |
| Glasgow Coma Scale minimum (4,089; 502)  | 11 ± 5 | 11 ± 5 | 0.665 |
| APACHE II score (6,024, 746)  | 14 ± 8 | 15 ± 8 | <0.001 |
| SOFA score (6,024, 746) | 6.0 ± 4  | 5.8 ± 4  | 0.319  |
| SOFA score ≥ 2 | 4,947 (82) | 607 (81) | 0.649 |
|  |   |   |   |
| *Antibiotic use* |  |   |   |
| None | 2,391 (40) | 430 (58) | <0.001 |
| Received on days 1, 2 & >2 before presentation | 1,126 (19) | 94 (13) | <0.001 |
| Received on days 1 & 2 before presentation  | 735 (12) | 25 (3) | <0.001 |
| Received only on day 1 before presentation | 1,148 (19) | 91 (12) | <0.001 |
|   |   |   |   |
| *Before presentation* |   |   |   |
| Mechanical ventilation | 1,806 (30) | 156 (21) | <0.001 |
| Renal replacement therapy | 132 (2) | 15 (2) | 0.853 |
| Plasma transfusion | 870 (14) | 130 (17) | 0.035 |
| Red blood cell transfusion | 866 (14) | 123 (17) | 0.137 |
| Platelet transfusion | 397 (7) | 57 (8) | 0.315 |
| Receiving vasopressors | 1,203 (20) | 151 (20) | 0.900 |
|   |   |   |   |
| *Therapies initiated within 24 hours of presentation* |   |   |   |
| Mechanical ventilation | 1,993 (33) | 231 (31) | 0.262 |
| Renal replacement therapy | 230 (4) | 37 (5) | 0.158 |
| Plasma transfusion | 270 (5) | 48 (6) | 0.022 |
| Red blood cell transfusion | 634 (11) | 80 (11) | 0.917 |
| Platelet transfusion | 262 (4) | 51 (7) | 0.003 |
|   |   |   |   |
| *Outcomes* |   |   |   |
| Hospital Survival | 5,025 (83) | 586 (79) | 0.001 |
| Post sepsis hospital length of stay, days (9,283; 1,105) | 3.5 ± 5.3 | 4.1 ± 5.7 | 0.024 |

Supplementary Table 7. Univariate analysis comparing in-hospital survival to mortality with change in qSOFA score ≥ 2

|  |  |  |  |
| --- | --- | --- | --- |
|   | **No Hospital Mortality** | **Hospital Mortality** |  |
| **Characteristic** | **n = 5,611** | **n = 1,159** | **p-value** |
| Age, years  | 56 ± 17 | 62 ± 16 | <0.001 |
| Male sex  | 3,394 (61) | 689 (59) | 0.531 |
| Race |  |  | <0.001 |
|  African American | 594 (11) | 100 (9) |  |
|  Caucasian | 4,453 (79) | 910 (79) |  |
|  Other race | 197 (4) | 32 (3) |  |
|  Unknown | 367 (7) | 117 (10) |  |
| *Physiological data and lab values on presentation* |   |   |   |
| Temperature maximum, °C (5,421; 1,113)  | 37.9 ± 0.9 | 37.7 ± 1.2 | <0.001 |
| Temperature minimum, °C (5,421; 1,113)  | 36.6 ± 0.6 | 36.3 ± 1.2 | <0.001 |
| Heart rate, min-1 (5,604; 1,155)  | 98 ± 18 | 101 ± 21 | <0.001 |
| Respiratory rate, min-1 (5,546; 1,129)  | 21 ± 6 | 23 ± 7 | <0.001 |
| Systolic blood pressure, mmHg (5,595; 1,152)  | 119 ± 22 | 112 ± 24 | <0.001 |
| Diastolic blood pressure, mmHg (5,592; 1,149)  | 62 ± 11 | 59 ± 12 | <0.001 |
| Oxygen saturation maximum, % (5,587; 1,143)  | 98 ± 2 | 99 ± 3 | 0.009 |
| Oxygen saturation minimum, % (5,587; 1,143) | 91 ± 8 | 84 ± 16 | <0.001 |
| White blood cell count, K/uL (4,321; 1,018)  | 13.5 ± 9.7 | 17.3 ± 24.1 | <0.001 |
| Hematocrit, % (4,330; 1,022)  | 30.6 ± 6.1 | 30.7 ± 6.5 | 0.962 |
| Platelets, K/uL (4,326; 1,022)  | 195 ± 114 | 168 ± 116 | <0.001 |
| Bicarbonate, mmol/L (4,424; 1,004)  | 25.5 ± 4.6 | 23.4 ± 6.2 | <0.001 |
| Blood urea nitrogen, mg/dL (4,409; 1,024)  | 26 ± 19 | 39 ± 25 | <0.001 |
| Creatinine, mg/dL (4,453; 1,026)  | 1.37 ± 1.34 | 1.86 ± 1.36 | <0.001 |
| Glasgow Coma Scale maximum (3,895; 696)  | 13 ± 3  | 9 ± 5 | <0.001 |
| Glasgow Coma Scale minimum (3,895; 696)  | 11 ± 4 | 7 ± 5 | <0.001 |
| APACHE II score (5,611, 1,159)  | 13 ± 7 | 21 ± 9 | <0.001 |
| SOFA Score (5,611, 1,159) | 5.5 ± 3.9 | 8.5 ± 4.2 | <0.001 |
| SOFA ≥ 2 Positive Culture | 4,460 (80)586 (10) | 1,094 (94)160 (14) | <0.0010.001 |
|  |   |   |   |
| *Antibiotic use*  |  |   |   |
| None | 2,287 (41) | 534 (46) |  <0.001 |
| Received on days 1, 2 & 3 before presentation | 991 (18) | 229 (20) | <0.001 |
| Received on days 1 & 2 before presentation  | 661 (12) | 99 (9) | <0.001 |
| Received only on day 1 before presentation | 1,020 (18) | 219 (19) | <0.001 |
|   |   |   |   |
| *Before presentation* |   |   |   |
| Mechanical ventilation | 1,660 (30) | 302 (26) | 0.018 |
| Renal replacement therapy | 92 (2) | 55 (5) | <0.001 |
| Plasma transfusion | 671 (12) | 329 (28) | <0.001 |
| Red blood cell transfusion | 820 (15) | 169 (15) | 1.000 |
| Platelet transfusion | 352 (6) | 102 (9) | 0.002 |
| Receiving vasopressors | 860 (15) | 494 (43) | <0.001 |
|   |   |   |   |
| *Therapies initiated within 24 hours of presentation* |   |   |   |
| Mechanical ventilation | 1,669 (30) | 555 (48) | <0.001 |
| Renal replacement therapy | 142 (3) | 125 (11) | <0.001 |
| Plasma transfusion | 179 (3) | 139 (12) | <0.001 |
| Red blood cell transfusion | 524 (9) | 190 (16) | <0.001 |
| Platelet transfusion | 182 (3) | 131 (11) | <0.001 |

Supplementary Table 8. Factors associated with mortality by multivariable logistic regression in patients with change in qSOFA score ≥ 2.

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **odds ratio** | **95% CI** | **p-value** |
| Positive culture | 1.05 | (0.83, 1.33) | 0.665 |
| Age, 10 years | 1.38 | (1.31, 1.46) | <0.001 |
|  |  |  |  |
| *Physiological data and lab values on presentation* |   |   |   |
| Oxygen saturation maximum < 96% | 1.78 | (1.23, 2.57) | 0.002 |
| Oxygen saturation unknown | 3.63 | (1.25, 10.61) | 0.018 |
| Respiratory rate, min-1 | 1.03 | (1.01, 1.04) | <0.001 |
| Heart rate, min-1 | 1.01 | (1.00, 1.01) | 0.001 |
| Systolic blood pressure, mmHg | 0.99 | (0.99, 1.00) | 0.002 |
| Glasgow Coma Scale maximum, 8 - 10 | 1.70 | (1.17, 2.47) | 0.005 |
| Glasgow Coma Scale maximum, < 7 | 3.72 | (2.57, 5.37) | <0.001 |
| Glasgow Coma Scale, unknown | 3.31 | (2.33, 4.71) | <0.001 |
| APACHE II score | 1.09 | (1.07, 1.10) | <0.001 |
|   |   |   |   |
| *Before presentation* |   |   |   |
| Renal replacement therapy | 2.16 | (1.36, 3.42) | 0.001 |
| Plasma transfusion | 1.70 | (1.38, 2.10) | <0.001 |
| Red blood cell transfusion | 0.60 | (0.47, 0.77) | <0.001 |
| Receiving vasopressors | 1.73 | (1.44, 2.10) | <0.001 |

95% CI = 95% confidence interval. Bonferroni adjusted p-value for statistical significance p<0.010.

Supplementary Table 9. Factors associated with positive cultures by multivariable logistic regression in patients with change in qSOFA score ≥ 2.

Supplementary Table 9. Factors associated with positive cultures by multivariable logistic regression in patients with change in qSOFA score ≥ 2.

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **odds ratio** | **95% CI** | **p-value** |
| Age, 10 years | 1.10 | (1.05, 1.10) | <0.001 |
| Male sex | 0.82 | (0.69, 0.96) |  0.012 |
| Heart rate, min-1 | 1.01 | (1.00, 1.01) |  <0.001 |
|   |   |   |   |
| *Antibiotic use* |  |  |  |
| Received on days 1 before presentation | 0.45 | (0.37, 0.56) |  <0.001 |
| Received on days 1 & 2 before presentation | 0.53 | (0.40, 0.68) |  <0.001 |
|  |  |  |  |

95% CI = 95% confidence interval. Bonferroni adjusted p-value for statistical significance p<0.010.

Supplementary Table 10. Factors associated with mortality by multivariable logistic regression in culture negative versus culture positive patients with change in qSOFA score ≥ 2.

|  |  |  |
| --- | --- | --- |
|   |  **Culture Negative (n = 5,875)** | **Culture Positive (n = 697)** |
| **Characteristic** | **odds ratio** | **95% CI** | **p-value** | **odds ratio** | **95% CI** | **p-value** |
| Age, 10 years | 1.39 | (1.31, 1.47) | <0.001 | 1.93 | (1.49, 2.50) | <0.001 |
|   |   |   |   |   |   |   |
| *Physiological data and lab values on presentation* |   |   |   |   |   |   |
| Oxygen saturation maximum, < 96% | 1.90 | (1.29, 2.80) | 0.001 | - | - | - |
| Oxygen saturation unknown | 4.50 | (1.54, 13.09) | 0.006 | - | - | - |
| Respiratory rate, min-1 | 1.03 | (1.00, 1.04) | <0.001 | 1.07 | (1.01, 1.13) | 0.16 |
| Heart rate, min-1 | 1.01 | (1.00, 1.01) |  0.001 | - | - | - |
| Systolic blood pressure, mmHg | 0.99 | (0.99, 1.00) |  0.01 | 0.97 | (0.95, 0.99) | 0.001 |
| Glasgow Coma Scale maximum, 8 - 10 | 1.72 | (1.16, 2.57) |  0.008 | 0.87 | (0.18, 4.32) | 0.863 |
| Glasgow Coma Scale maximum, < 7 | 3.61 | (2.43, 5.36) | <0.001 | 10.75 | (2.14, 54.00) | 0.004 |
| Glasgow Coma Scale unknown | 3.38 | (2.33, 4.91) | <0.001 | 2.50 | (0.57, 11.06) | 0.227 |
| Platelets < 54 K/uL | - | - | - | 17.95 | (2.76, 116.65) | 0.002 |
| BUN 39 – 54 mg/dL | 2.42 | (1.49, 3.93) | < 0.001 | - | - | - |
| BUN > 54 mg/dL | 2.75 | (1.61, 4.56) | < 0.001 | - | - | - |
|   |   |   |   |   |   |   |
| APACHE II score | 1.09 | (1.08, 1.11) | <0.001 | 1.17 | (1.10, 1.25) | <0.001 |
|  |   |   |   |   |   |   |
| *Before presentation* |   |   |   |   |   |   |
| Renal replacement therapy | 2.30 | (1.39, 3.80) | 0.001 | - | - | - |
| Plasma transfusion | 1.80 | (1.44, 2.25) | <0.001 | - | - | - |
| Red blood cell transfusion | 0.59 | (0.45, 0.77) | 0.001 | - | - | - |
| Receiving vasopressors | 1.77 | (1.44, 2.16) | <0.001 | - | - | - |

95% CI = 95% confidence interval. Bonferroni adjusted p-value for statistical significance p<0.010. If a covariate was not included in the final AIC model, this is denoted by “-“.

Supplementary Table 11. SIRS population: Univariate analysis comparing culture negative and culture positive patients with septic shock

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Negative Cultures** | **Positive Cultures** |  |
| **Characteristic** | **n = 1,242** | **n = 156** | **p-value** |
| Age, years  | 59 ± 16 | 61 ± 15 | 0.083 |
| Male sex  | 767 (62) | 95 (61) | 0.862 |
| African American | 150 (12) | 13 (8) | 0.187 |
| Caucasian | 924 (74) | 124 (79) | 0.202 |
| Other race | 30 (2) | 3 (2) | 0.999 |
|   |   |   |   |
| *Physiological data and lab values on presentation* |   |   |   |
| Temperature maximum, °C (1,221; 153)  | 37.9 ± 1.1 | 37.7 ± 1.1 | 0.151 |
| Temperature minimum, °C (1,221; 153)  | 36.5 ± 1.1 | 36.3 ± 1.1 | 0.282 |
| Heart rate, min-1 (1,242; 156)  | 99 ± 20 | 101 ± 23 | 0.136 |
| Respiratory rate, min-1 (1,237; 159)  | 22 ± 6 | 21 ± 6 | 0.124 |
| Systolic blood pressure, mmHg (1,231; 156)  | 108 ± 20 | 107 ± 21 | 0.472 |
| Diastolic blood pressure, mmHg (1,228; 156)  | 57 ± 11 | 56 ± 11 | 0.325 |
| Oxygen saturation maximum % (1,235; 155)  | 99 ± 2 | 99 ± 4 | 0.597 |
| Oxygen saturation minimum, % (1,235; 155)  | 88 ± 12 | 83 ± 18 | 0.001 |
| White blood cell count, K/uL (1,046; 146)  | 16.1 ± 11.0 | 15.6 ± 14.7 | 0.697 |
| Hematocrit, % (1,047; 146)  | 30.9 ± 6.2 | 30.7 ± 5.4 | 0.644 |
| Platelets, K/uL (1,048; 146)  | 168 ± 100 | 153 ± 105 | 0.105 |
| Bicarbonate, mmol/L (1,095; 147)  | 23.9 ± 5.5 | 23.0 ± 5.8 | 0.064 |
| Blood urea nitrogen, mg/dL (1,113; 148)  | 36.1 ± 22.6 | 37.1 ± 23.2 | 0.600 |
| Creatinine, mg/dL (1,121; 148)  | 1.9 ± 1.4 | 1.8 ± 1.2 | 0.432 |
| Glasgow Coma Scale maximum (936; 109)  | 10 ± 4 | 9 ± 4 | 0.213 |
| Glasgow Coma Scale minimum (936; 109)  | 8 ± 5 | 7 ± 4 | 0.165 |
| APACHE II score (1,242; 156)  | 20 ± 9 | 21 ± 8 | 0.035 |
|   |   |   |   |
| *Antibiotic use*  |   |   |
| None | 480 (39) | 99 (63) | <0.001 |
| Received on days 1, 2 & >2 before presentation | 221 (18) | 14 (9) | 0.007 |
| Received on days 1 & 2 before presentation  | 155 (12) | 6 (4) | <0.001 |
| Received only on day 1 before presentation | 292 (24) | 25 (16) | 0.045 |
|   |   |   |   |
| *Before presentation* |   |   |   |
| Mechanical ventilation | 492 (40) | 46 (30) | 0.015 |
| Renal replacement therapy | 70 (6) | 8 (5) | 0.999 |
| Plasma transfusion | 325 (26) | 47 (30) | 0.292 |
| Red blood cell transfusion | 223 (18) | 28 (18) | 0.999 |
| Platelet transfusion | 109 (9) | 11 (7) | 0.546 |
|   |   |   |   |
| *Therapies initiated in the first 24 hours of presentation* |   |   |
| Mechanical ventilation | 727 (59) | 92 (59) | 0.932 |
| Renal replacement therapy | 149 (12) | 27 (17) | 0.072 |
| Plasma transfusion | 105 (9) | 20 (13) | 0.075 |
| Red blood cell transfusion | 187 (15) | 24 (15) | 0.906 |
| Platelet transfusion | 94 (8) | 20 (13) | 0.030 |
|   |   |   |   |
| *Outcomes* |   |   |   |
| Hospital Survival | 797 (64) | 84 (54) | 0.014 |
| Post sepsis hospital length of stay, days (1,242; 156) | 4.0 ± 7.9 | 3.6 ± 7.5 | 0.574 |

Data are presented as mean + or frequency (percentage). \* If patients are missing values, the numbers of patients with values for that variable are shown in parentheses after the variable (n for negative cultures; n for positive cultures). Bonferroni adjusted p-value for statistical significance p<0.010.

Supplementary Table 12. SIRS population: Factors associated with positive culture in patients with septic shock

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **odds ratio** | **95% CI** | **p-value** |
| Age, 10 years | 1.149 | (1.020, 1.305) | 0.026 |
| Heart rate, min-1 | 1.008 | (0.999, 1.017) | 0.087 |
| Respiratory rate, min-1 | 0.97 | (0.942, 1) | 0.050 |
|   |   |   |   |
| *Received antibiotics during these times prior to presentation*None (reference) |   |  |
| Received only on day 1  | 0.436 | (0.28, 0.676) | 0.001 |
| Received only on day 1 & 2 | 0.482 | (0.272, 0.852) | 0.012 |
|   |   |   |   |
| Renal replacement therapy on day of presentation | 2.045 | (1.25, 3.345) | 0.004 |

95% CI = 95% confidence interval. Bonferroni adjusted p-value for statistical significance p<0.017.

Supplementary Table 13. SIRS population: Univariate analysis comparing in-hospital survival to mortality in patients with septic shock

|  |  |  |  |
| --- | --- | --- | --- |
|   | **No Hospital Mortality** | **Hospital Mortality** |  |
| **Characteristic** | **n = 881** | **n = 517** | **p-value** |
| Age, years  | 57 ± 15 | 61 ± 16 | <0.001 |
| Male sex  | 536 (61) | 326 (63) | 0.4254 |
| African American | 106 (12) | 57 (11) | 0.6051 |
| Caucasian | 675 (77) | 373 (72) | 0.064 |
| Other race | 19 (2) | 14 (3) | 0.5847 |
|   |   |   |   |
| *Physiological data and lab values on presentation* |   |   |   |
| Temperature maximum, °C (881; 517)  | 37.9 ± 0.9 | 37.7 ± 1.3 | <0.001 |
| Temperature minimum, °C (881; 517)  | 36.6 ± 0.8 | 36.1 ± 1.5 | <0.001 |
| Heart rate, min-1 (881; 517)  | 98 ± 20 | 101 ± 21 | 0.0252 |
| Respiratory rate, min-1 (865; 495)  | 21 ± 6 | 22 ± 7 | <0.001 |
| Systolic blood pressure, mmHg (872; 515)  | 110 ± 20 | 105 ± 19 | <0.001 |
| Diastolic blood pressure, mmHg (872; 512)  | 57 ± 10 | 56 ± 12 | 0.0044 |
| Oxygen saturation maximum,% (881; 509)  | 99 ± 1 | 99 ± 3 | 0.002 |
| Oxygen saturation minimum,% (881; 509)  | 90 ± 7 | 82 ± 18 | <0.001 |
| White blood cell count, K/uL (722; 470)  | 15.4 ± 10.2 | 17.0 ± 13.2 | 0.0254 |
| Hematocrit, % (722; 471)  | 30.8 ± 5.8 | 30.9 ± 6.5 | 0.9467 |
| Platelets, K/uL (722; 472)  | 178 ± 100 | 148 ± 99 | <0.001 |
| Bicarbonate, mmol/L (774; 468)  | 24.7 ± 4.9 | 22.3 ± 6.3 | <0.001 |
| Blood urea nitrogen, mg/dL (781; 480)  | 32.8 ± 21.2 | 41.8 ± 23.8 | <0.001 |
| Creatinine, mg/dL (788; 481)  | 1.69 ± 1.47 | 2.09 ± 1.24 | <0.001 |
| Glasgow Coma Scale maximum (712; 333)  | 11 ± 4 | 7 ± 4 | <0.001 |
| Glasgow Coma Scale minimum (712; 333)  |  9 ± 5 | 6 ± 4 | <0.001 |
| APACHE II score (881; 517) | 18 ± 8 | 24 ± 9 | <0.001 |
| Positive culture | 84 (10) | 72 (14) | 0.0137 |
|   |   |   |   |
| *Received antibiotics during these times prior to presentation* |   |   |
| *Antibiotic use*  | 364 (41) | 215 (42) | 0.9552 |
| None | 33 (4) | 20 (4) | 0.8859 |
| Received on days 1, 2 & >2 before presentation | 13 (1) | 10 (2) | 0.5201 |
| Received only on day 2 before presentation | 114 (13) | 47 (9) | 0.0302 |
| Received on days 1 & 2 before presentation  | 197 (22) | 120 (23) | 0.7409 |
|   |   |   |   |
| *Before presentation* |   |   |   |
| Mechanical ventilation | 497 (56) | 322 (62) | 0.0327 |
| Renal replacement therapy | 355 (40) | 183 (35) | 0.0775 |
| Plasma transfusion | 190 (22) | 182 (35) | <0.001 |
| Red blood cell transfusion | 155 (18) | 96 (19) | 0.6652 |
| Platelet transfusion | 68 (8) | 52 (10) | 0.1386 |
|   |   |   |   |
| *Therapies initiated in the first 24 hours of presentation* |   |   |
| Mechanical ventilation | 497 (56) | 322 (62) | 0.0327 |
| Renal replacement therapy | 65 (7) | 111 (21) | <0.001 |
| Plasma transfusion | 45 (5) | 80 (15) | <0.001 |
| Red blood cell transfusion | 96 (11) | 115 (22) | <0.001 |
| Platelet transfusion | 37 (4) | 77 (15) | <0.001 |

Data are presented as mean + or frequency (percentage). \* If patients are missing values, the numbers of patients with values for that variable are shown in parentheses after the variable (n for negative cultures; n for positive cultures). Bonferroni adjusted p-value for statistical significance p<0.017.

Supplementary Table 14. SIRS population: Factors associated with mortality in patients with septic shock by multivariable logistic regression

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **odds ratio** | **95% CI** | **p-value** |
| Age, 10 years | 1.40 | (1.27, 1.54) | < 0.001 |
|   |   |   |   |
| Systolic blood pressure, mmHg | 0.99 | (0.98, 1.00) | 0.011 |
| Oxygen saturation maximum, < 96% | 2.93 | (1.62, 5.32) | < 0.001 |
| Glasgow Coma Scale maximum, < 7 | 5.42 | (3.02, 9.72) | < 0.001 |
| Glasgow Coma Scale maximum, unknown | 7.61 | (4.24, 13.64) | < 0.001 |
| Bicarbonate ≤ 19 mmol/L | 1.75 | (1.04, 2.94) | 0.036 |
| APACHE II score | 1.09 | (1.07, 1.12) | < 0.001 |
| Positive culture | 1.36 | (0.88, 2.09) | 0.165 |
|   |   |   |   |
| *Before presentation* |   |   |   |
| Plasma transfusion | 1.66 | (1.20, 2.30) | 0.002 |
| Red blood cell transfusion | 0.60 | (0.39, 0.90) | 0.014 |
| Renal replacement therapy | 4.12 | (2.14, 7.93) | < 0.001 |

95% CI = 95% confidence interval. Bonferroni adjusted p-value for statistical significance p<0.017.

Supplementary Table 15. SOFA population. Univariate analysis comparing culture negative and culture positive patients with septic shock with change in SOFA score ≥ 2.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Negative Cultures** | **Positive Cultures** |  |
| **Characteristic** | **n = 1,240** | **n = 156** | **p-value** |
| Age, years  | 58 ± 16 | 61 ± 15 | 0.108 |
| Male sex  | 765 (62) | 95 (61) | 0.862 |
| Race |  |  | 0.492 |
|  African American | 150 (12) | 13 (8) |  |
|  Caucasian | 922 (74) | 124 (80) |  |
|  Other race | 30 (2) | 3 (2) |  |
|  Unkown | 138 (11) | 16 (10) |  |
|   |   |   |   |
| *Physiological data and lab values on presentation* |   |   |   |
| Temperature maximum, °C (1,219; 153)  | 37.9 ± 1.1 | 37.7 ± 1.1 | 0.118 |
| Temperature minimum, °C (1,219; 153)  | 36.4 ± 1.1 | 36.3 ± 1.1 | 0.091 |
| Heart rate, min-1 (1,240; 156)  | 99 ± 20 | 101 ± 23 | 0.150 |
| Respiratory rate, min-1 (1,205; 153)  | 22 ± 6 | 21 ± 6 | 0.082 |
| Systolic blood pressure, mmHg (1,229; 156)  | 108 ± 20 | 107 ± 21 | 0.153 |
| Diastolic blood pressure, mmHg (1,226; 156)  | 57 ± 11 | 56 ± 11 | 0.274 |
| Oxygen saturation maximum % (1,233; 155)  | 99 ± 2 | 99 ± 4 | 0.826 |
| Oxygen saturation minimum, % (1,233; 155)  | 88 ± 12 | 83 ± 18 | 0.002 |
| White blood cell count, K/uL (1,044; 146)  | 16.1 ± 11.0 | 15.6 ± 14.7 | 0.089 |
| Hematocrit, % (1,045; 146)  | 30.9 ± 6.2 | 30.7 ± 5.4 | 0.875 |
| Platelets, K/uL (1,046; 146)  | 168 ± 100 | 153 ± 105 | 0.036 |
| Bicarbonate, mmol/L (1,093; 147)  | 23.9 ± 5.5 | 23.0 ± 5.8 | 0.060 |
| Blood urea nitrogen, mg/dL (1,111; 148)  | 36.1 ± 22.6 | 37.1 ± 23.2 | 0.683 |
| Creatinine, mg/dL (1,119; 148)  | 1.9 ± 1.4 | 1.8 ± 1.2 | 0.614 |
| Glasgow Coma Scale maximum (934; 109)  | 10 ± 5 | 9 ± 4 | 0.108 |
| Glasgow Coma Scale minimum (934; 109)  | 8 ± 5 | 7 ± 4 | 0.221 |
| APACHE II score (1,240; 156)  | 20 ± 9 | 21 ± 8 | 0.063 |
|   |   |   |   |
| *Antibiotic use*  |   |   |
| None | 480 (39) | 99 (64) | <0.001 |
| Received on days 1, 2 & >2 before presentation | 220 (18) | 14 (9) | 0.008 |
| Received on days 1 & 2 before presentation  | 155 (13) | 6 (4) | 0.002 |
| Received only on day 1 before presentation | 292 (24) | 25 (16) | 0.044 |
|   |   |   |   |
| *Before presentation* |   |   |   |
| Mechanical ventilation | 491 (40) | 46 (30) | 0.018 |
| Renal replacement therapy | 70 (6) | 8 (5) | 0.936 |
| Plasma transfusion | 325 (26) | 47 (30) | 0.344 |
| Red blood cell transfusion | 223 (18) | 28 (18) | 1.000 |
| Platelet transfusion | 109 (9) | 11 (7) | 0.563 |
|   |   |   |   |
| *Therapies initiated in the first 24 hours of presentation* |   |   |
| Mechanical ventilation | 727 (59) | 92 (59) | 1.000 |
| Renal replacement therapy | 149 (12) | 27 (17) | 0.080 |
| Plasma transfusion | 105 (9) | 20 (13) | 0.100 |
| Red blood cell transfusion | 187 (15) | 24 (15) | 1.000 |
| Platelet transfusion | 94 (8) | 20 (13) | 0.036 |
|   |   |   |   |
| *Outcomes* |   |   |   |
| Hospital Survival | 797 (64) | 84 (54) | 0.016 |
| Post sepsis hospital length of stay, days (1,240; 156) | 4.0 ± 7.9 | 3.6 ± 7.5 | 0.031 |

Data are presented as mean + or frequency (percentage). \* If patients are missing values, the numbers of patients with values for that variable are shown in parentheses after the variable (n for negative cultures; n for positive cultures). Bonferroni adjusted p-value for statistical significance p<0.010.

Supplementary Table 16. SOFA population. Factors associated with positive culture in patients with septic shock and change in SOFA score ≥ 2.

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **odds ratio** | **95% CI** | **p-value** |
|  *Antibiotic use* |   |   |   |
| Received on day 1 prior to presentation | 0.441 | (0.284, 0.683) | <0.001 |
| Received on days 1 & 2 prior to presentation | 0.484 | (0.274, 0.856) | 0.013 |
| Renal replacement therapy on day of presentation | 2.00 | (1.23, 3.26) | 0.005 |

95% CI = 95% confidence interval. Bonferroni adjusted p-value for statistical significance p<0.010.

Supplementary Table 17. SOFA population Univariate analysis comparing in-hospital survival to mortality in patients with septic shock and change in SOFA score ≥ 2.

|  |  |  |  |
| --- | --- | --- | --- |
|   | **No Hospital Mortality** | **Hospital Mortality** |  |
| **Characteristic** | **n = 879** | **n = 517** | **p-value** |
| Age, years  | 57 ± 15 | 61 ± 16 | <0.001 |
| Male sex  | 536 (61) | 326 (63) | 0.425 |
| Race |  |  | 0.034 |
|  African American | 106 (12) | 57 (11) |  |
|  Caucasian | 673 (77) | 373 (72) |  |
|  Other race | 19 (2) | 14 (3) |  |
|  Unknown | 81 (9) | 73 (14) |  |
|   |   |   |   |
| *Physiological data and lab values on presentation* |   |   |   |
| Temperature maximum, °C (871; 501)  | 37.9 ± 0.9 | 37.7 ± 1.3 | <0.001 |
| Temperature minimum, °C (871; 501)  | 36.6 ± 0.8 | 36.1 ± 1.5 | <0.001 |
| Heart rate, min-1 (879; 517)  | 98 ± 20 | 101 ± 21 | 0.030 |
| Respiratory rate, min-1 (863; 495)  | 21 ± 6 | 22 ± 7 | <0.001 |
| Systolic blood pressure, mmHg (870; 515)  | 110 ± 20 | 105 ± 19 | <0.001 |
| Diastolic blood pressure, mmHg (870; 512)  | 57 ± 10 | 56 ± 12 | <0.001 |
| Oxygen saturation maximum,% (879; 501)  | 99 ± 1 | 99 ± 3 | <0.001 |
| Oxygen saturation minimum,% (879; 501)  | 90 ± 6 | 82 ± 18 | <0.001 |
| White blood cell count, K/uL (720; 470)  | 15.4 ± 10.2 | 17.0 ± 13.2 | 0.069 |
| Hematocrit, % (720; 471)  | 30.8 ± 5.8 | 30.9 ± 6.5 | 0.691 |
| Platelets, K/uL (720; 472)  | 178 ± 100 | 148 ± 99 | <0.001 |
| Bicarbonate, mmol/L (772; 468)  | 24.7 ± 4.9 | 22.3 ± 6.3 | <0.001 |
| Blood urea nitrogen, mg/dL (779; 480)  | 32.8 ± 21.2 | 41.8 ± 23.8 | <0.001 |
| Creatinine, mg/dL (786; 481)  | 1.69 ± 1.47 | 2.09 ± 1.24 | <0.001 |
| Glasgow Coma Scale maximum (710; 333)  | 11 ± 4 | 7 ± 4 | <0.001 |
| Glasgow Coma Scale minimum (710; 333)  |  9 ± 5 | 6 ± 4 | <0.001 |
| APACHE II score (879; 517) | 18 ± 8 | 24 ± 9 | <0.001 |
| Positive culture | 84 (10) | 72 (14) | 0.016 |
|   |   |   |   |
| *Antibiotic use*  |  |  |  |
| None | 634 (41) | 215 (42) | 0.994 |
| Received on days 1, 2 & >2 before presentation | 139 (16) | 95 (18) | 0.025 |
| Received only on day 2 before presentation | 114 (13) | 47 (9) | 0.035 |
| Received on days 1 & 2 before presentation  | 197 (22) | 120 (23) | 0.781 |
|   |   |   |   |
| *Before presentation* |   |   |   |
| Mechanical ventilation | 354 (40) | 183 (35) | 0.080 |
| Renal replacement therapy | 28 (3) | 50 (10) | <0.001 |
| Plasma transfusion | 190 (22) | 182 (35) | <0.001 |
| Red blood cell transfusion | 155 (18) | 96 (19) | 0.714 |
| Platelet transfusion | 68 (8) | 52 (10) | 0.163 |
|   |   |   |   |
| *Therapies initiated in the first 24 hours of presentation* |   |   |
| Mechanical ventilation | 497 (56) | 322 (62) | 0.041 |
| Renal replacement therapy | 65 (7) | 111 (22) | <0.001 |
| Plasma transfusion | 45 (5) | 80 (15) | <0.001 |
| Red blood cell transfusion | 96 (11) | 115 (22) | <0.001 |
| Platelet transfusion | 37 (4) | 77 (15) | <0.001 |

Data are presented as mean + or frequency (percentage). \* If patients are missing values, the numbers of patients with values for that variable are shown in parentheses after the variable (n for negative cultures; n for positive cultures). Bonferroni adjusted p-value for statistical significance p<0.010.

Supplementary Table 18. SOFA population. Factors associated with mortality in patients with septic shock and with change in SOFA score ≥ 2 by multivariable logistic regression

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **odds ratio** | **95% CI** | **p-value** |
| Age, 10 years | 1.41 | (1.28, 1.56) | < 0.001 |
|   |   |   |   |
| Systolic blood pressure, mmHg | 0.99 | (0.98, 1.00) | 0.007 |
| Glasgow Coma Scale maximum, < 7 | 5.44 | (3.05, 9.72) | < 0.001 |
| Glasgow Coma Scale maximum, unknown | 7.51 | (4.24, 13.29) | < 0.001 |
| APACHE II score | 1.09 | (1.07, 1.11) | < 0.001 |
| Positive culture | 1.25 | (0.82, 1.91) | 0.301 |
|   |   |   |   |
| *Before presentation* |   |   |   |
| Plasma transfusion | 1.62 | (1.17, 2.24) | 0.004 |
| Renal replacement therapy | 4.24 | (2.23, 8.07) | < 0.001 |

95% CI = 95% confidence interval. Bonferroni adjusted p-value for statistical significance p<0.010.

Supplementary Table 19. qSOFA population. Univariate analysis comparing culture negative and culture positive patients with septic shock with change in qSOFA score ≥ 2.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Negative Cultures** | **Positive Cultures** |  |
| **Characteristic** | **n = 1,203** | **n = 151** | **p-value** |
| Age, years  | 58 ± 16 | 61 ± 15 | 0.896 |
| Male sex  | 742 (62) | 93 (61) | 1.000 |
| Race |  |  | 0.601 |
|  African American | 144 (12) | 13 (9) |  |
|  Caucasian | 900 (75) | 120 (80) |  |
|  Other race | 26 (2) | 3 (2) |  |
|  Unkown | 133 (11) | 15 (10) |  |
|   |   |   |   |
| *Physiological data and lab values on presentation* |   |   |   |
| Temperature maximum, °C (1,219; 153)  | 37.9 ± 1.1 | 37.7 ± 1.1 | 0.511 |
| Temperature minimum, °C (1,219; 153)  | 36.5 ± 1.1 | 36.3 ± 1.1 | 0.054 |
| Heart rate, min-1 (1,240; 156)  | 99 ± 20 | 101 ± 23 | 0.161 |
| Respiratory rate, min-1 (1,205; 153)  | 22 ± 6 | 21 ± 6 | 0.080 |
| Systolic blood pressure, mmHg (1,229; 156)  | 108 ± 20 | 107 ± 21 | 0.175 |
| Diastolic blood pressure, mmHg (1,226; 156)  | 57 ± 11 | 56 ± 11 | 0.271 |
| Oxygen saturation maximum % (1,233; 155)  | 99 ± 2 | 99 ± 4 | 0.748 |
| Oxygen saturation minimum, % (1,233; 155)  | 88 ± 12 | 83 ± 19 | 0.002 |
| White blood cell count, K/uL (1,044; 146)  | 16.1 ± 11.0 | 15.8 ± 14.7 | 0.145 |
| Hematocrit, % (1,045; 146)  | 30.8 ± 6.2 | 30.7 ± 5.4 | 0.928 |
| Platelets, K/uL (1,046; 146)  | 168 ± 100 | 155 ± 104 | 0.069 |
| Bicarbonate, mmol/L (1,093; 147)  | 23.9 ± 5.5 | 22.8 ± 5.7 | 0.027 |
| Blood urea nitrogen, mg/dL (1,111; 148)  | 35.9 ± 22.3 | 37.0 ± 23.4 | 0.700 |
| Creatinine, mg/dL (1,119; 148)  | 1.9 ± 1.4 | 1.8 ± 1.2 | 0.652 |
| Glasgow Coma Scale maximum (934; 109)  | 10 ± 5 | 9 ± 4 | 0.092 |
| Glasgow Coma Scale minimum (934; 109)  | 8 ± 5 | 7 ± 4 | 0.195 |
| APACHE II score (1,240; 156)  | 20 ± 9 | 22 ± 8 | 0.073 |
|   |   |   |   |
| *Antibiotic use*  |   |   |
| None | 465 (39) | 96 (64) | <0.001 |
| Received on days 1, 2 & >2 before presentation | 213 (18) | 13 (9) | 0.007 |
| Received on days 1 & 2 before presentation  | 155 (13) | 6 (4) | 0.002 |
| Received only on day 1 before presentation | 280 (23) | 24 (16) | 0.052 |
|   |   |   |   |
| *Before presentation* |   |   |   |
| Mechanical ventilation | 479 (40) | 45 (30) | 0.022 |
| Renal replacement therapy | 68 (6) | 8 (5) | 1.000 |
| Plasma transfusion | 316 (26) | 47 (31) | 0.241 |
| Red blood cell transfusion | 218 (18) | 27 (18) | 1.000 |
| Platelet transfusion | 107 (9) | 11 (7) | 0.612 |
|   |   |   |   |
| *Therapies initiated in the first 24 hours of presentation* |   |   |
| Mechanical ventilation | 713 (59) | 89 (59) | 1.000 |
| Renal replacement therapy | 145 (12) | 27 (18) | 0.058 |
| Plasma transfusion | 102 (9) | 20 (13) | 0.076 |
| Red blood cell transfusion | 183 (15) | 24 (16) | 0.921 |
| Platelet transfusion | 91 (8) | 18 (12) | 0.090 |
|   |   |   |   |
| *Outcomes* |   |   |   |
| Hospital Survival | 778 (65) | 82 (54) | 0.016 |
| Post sepsis hospital length of stay, days (1,240; 156) | 4.0 ± 7.9 | 3.7 ± 7.6 | 0.051 |

Data are presented as mean + or frequency (percentage). \* If patients are missing values, the numbers of patients with values for that variable are shown in parentheses after the variable (n for negative cultures; n for positive cultures). Bonferroni adjusted p-value for statistical significance p<0.010.

Supplementary Table 20. qSOFA population. Factors associated with positive culture in patients with septic shock and change in qSOFA score ≥ 2.

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **odds ratio** | **95% CI** | **p-value** |
|  *Antibiotic use* |   |   |   |
| Received on day 1 prior to presentation | 0.414 | (0.264, 0.649) | <0.001 |
| Received on days 1 & 2 prior to presentation | 0.480 | (0.270, 0.856) | 0.013 |

95% CI = 95% confidence interval. Bonferroni adjusted p-value for statistical significance p<0.010.

Supplementary Table 21. qSOFA population Univariate analysis comparing in-hospital survival to mortality in patients with septic shock and change in qSOFA score ≥ 2.

|  |  |  |  |
| --- | --- | --- | --- |
|   | **No Hospital Mortality** | **Hospital Mortality** |  |
| **Characteristic** | **n = 860** | **n = 494** | **p-value** |
| Age, years  | 58 ± 16 | 61 ± 16 | <0.001 |
| Male sex  | 521 (61) | 314 (64) | 0.304 |
| Race |  |  | 0.034 |
|  African American | 104 (12) | 53 (11) |  |
|  Caucasian | 660 (77) | 360 (73) |  |
|  Other race | 17 (2) | 12 (2) |  |
|  Unknown | 79 (9) | 69 (14) |  |
|   |   |   |   |
| *Physiological data and lab values on presentation* |   |   |   |
| Temperature maximum, °C (871; 501)  | 37.9 ± 0.9 | 37.7 ± 1.3 | <0.001 |
| Temperature minimum, °C (871; 501)  | 36.6 ± 0.8 | 36.1 ± 1.4 | <0.001 |
| Heart rate, min-1 (879; 517)  | 98 ± 20 | 100 ± 21 | 0.039 |
| Respiratory rate, min-1 (863; 495)  | 21 ± 6 | 23 ± 7 | <0.001 |
| Systolic blood pressure, mmHg (870; 515)  | 110 ± 20 | 105 ± 19 | <0.001 |
| Diastolic blood pressure, mmHg (870; 512)  | 57 ± 10 | 56 ± 12 | <0.001 |
| Oxygen saturation maximum,% (879; 501)  | 99 ± 1 | 99 ± 3 | <0.001 |
| Oxygen saturation minimum,% (879; 501)  | 90 ± 7 | 82 ± 18 | <0.001 |
| White blood cell count, K/uL (720; 470)  | 15.3 ± 10.2 | 17.2 ± 13.2 | 0.069 |
| Hematocrit, % (720; 471)  | 30.8 ± 5.8 | 30.8 ± 6.4 | 0.691 |
| Platelets, K/uL (720; 472)  | 178 ± 100 | 149 ± 99 | <0.001 |
| Bicarbonate, mmol/L (772; 468)  | 24.7 ± 4.9 | 22.2 ± 6.3 | <0.001 |
| Blood urea nitrogen, mg/dL (779; 480)  | 32.6 ± 20.7 | 41.7 ± 24.0 | <0.001 |
| Creatinine, mg/dL (786; 481)  | 1.70± 1.48 | 2.10± 1.25 | <0.001 |
| Glasgow Coma Scale maximum (710; 333)  | 11 ± 4 | 7 ± 4 | <0.001 |
| Glasgow Coma Scale minimum (710; 333)  |  9 ± 5 | 6 ± 4 | <0.001 |
| APACHE II score (879; 517) | 18 ± 8 | 24 ± 9 | <0.001 |
| Positive culture | 82 (10) | 69 (14) | 0.016 |
|   |   |   |   |
| *Antibiotic use*  |  |  |  |
| None | 355 (41) | 206 (42) | 0.925 |
| Received on days 1, 2 & >2 before presentation | 136 (16) | 90 (18) | 0.286 |
| Received only on day 2 before presentation | 114 (13) | 47 (10) | 0.050 |
| Received on days 1 & 2 before presentation  | 190 (22) | 114 (23) | 0.726 |
|   |   |   |   |
| *Before presentation* |   |   |   |
| Mechanical ventilation | 350 (41) | 174 (35) | 0.053 |
| Renal replacement therapy | 28 (3) | 48 (10) | <0.001 |
| Plasma transfusion | 183 (21) | 180 (36) | <0.001 |
| Red blood cell transfusion | 151 (18) | 94 (19) | 0.546 |
| Platelet transfusion | 67 (8) | 51 (10) | 0.136 |
|   |   |   |   |
| *Therapies initiated in the first 24 hours of presentation* |   |   |
| Mechanical ventilation | 491 (57) | 311 (63) | 0.040 |
| Renal replacement therapy | 64 (7) | 108 (22) | <0.001 |
| Plasma transfusion | 43 (5) | 79 (16) | <0.001 |
| Red blood cell transfusion | 93 (11) | 114 (23) | <0.001 |
| Platelet transfusion | 36 (4) | 73 (15) | <0.001 |

Data are presented as mean + or frequency (percentage). \* If patients are missing values, the numbers of patients with values for that variable are shown in parentheses after the variable (n for negative cultures; n for positive cultures). Bonferroni adjusted p-value for statistical significance p<0.010.

Supplementary Table 22. qSOFA population. Factors associated with mortality in patients with septic shock and with change in qSOFA score ≥ 2 by multivariable logistic regression

|  |  |  |  |
| --- | --- | --- | --- |
| **Characteristic** | **odds ratio** | **95% CI** | **p-value** |
| Age, 10 years | 1.41 | (1.27, 1.55) | < 0.001 |
|   |   |   |   |
| Systolic blood pressure, mmHg | 0.99 | (0.98, 1.00) | 0.008 |
| Glasgow Coma Scale maximum, < 7 | 5.35 | (2.99, 9.58) | < 0.001 |
| Glasgow Coma Scale maximum, unknown | 7.04 | (3.95, 12.52) | < 0.001 |
| APACHE II score | 1.09 | (1.07, 1.11) | < 0.001 |
| Positive culture | 1.30 | (0.85, 2.00) | 0.231 |
|   |   |   |   |
| *Before presentation* |   |   |   |
| Plasma transfusion | 1.67 | (1.20, 2.32) | 0.002 |
| Renal replacement therapy | 4.22 | (2.22, 8.04) | < 0.001 |

95% CI = 95% confidence interval. Bonferroni adjusted p-value for statistical significance p<0.010.

Supplementary Table 23: Summary of analyses by sepsis definition

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|   | Total  | Culture Negative  | Culture Positive |   |   |
| Sepsis definition | sample population | N | % | N | % |   |   |
| SIRS  | 10,393 | 9,063 | 87 | 1,330 | 13 |   |   |
| SIRS + SOFA >=2 | 6,572 | 5,875 | 89 | 697 | 11 |   |   |
| SIRS + qSOFA >=2 | 6,770 | 6,024 | 89 | 746 | 11 |   |   |
|   |   |   |   |   |   |   |   |
| Septic shock only |   |   |   |   |   |   |   |
| SIRS  | 1,398 | 1,242 | 89 | 156 | 11 |   |   |
| SIRS + SOFA >=2 | 1,396 | 1,240 | 89 | 156 | 11 |   |   |
| SIRS + qSOFA >=2 | 1,354 | 1,203 | 89 | 151 | 11 |   |   |
|   |   |   |   |   |   |   |   |
|   |   |   |   |   |   |   |   |
| Hospital Mortality | Culture Negative  |   |   | Culture Positive |   | chisq test |
|   | N | Died | % | N | Died | % | p-value |
| SIRS  | 9,288 | 1,151 | 12.4 | 1,105 | 179 | 16.2 | 0.0004 |
| SIRS + SOFA >=2 | 5,875 | 1,035 | 17.6 | 697 | 169 | 24.2 | < 0.001 |
| SIRS + qSOFA >=2 | 6,024 | 999 | 16.6 | 746 | 160 | 21.4 | 0.0011 |
|   |   |   |   |   |   |   |   |
| Septic shock only |   |   |   |   |   |   |   |
| SIRS  | 1,242 | 445 | 36 | 156 | 72 | 46 | 0.0151 |
| SIRS + SOFA >=2 | 1,240 | 445 | 36 | 156 | 72 | 46 | 0.0157 |
| SIRS + qSOFA >=2 | 1,203 | 425 | 35 | 151 | 69 | 46 | 0.0162 |