Supplementary material

Supplementary Table 1. Statistical comparison of the clinical characteristics of the patients who developed or had a worsened organ injury during the hospital stay, compared to controls.

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| --- | --- | --- | --- | --- | --- | --- |
|  | | New Organ Injury  (n. 166) | No Organ Injury  (n. 191) | *p* | Odds Ratio  (95% CI) | *p* |
| Anamnestic data: | | | | | | |
| Age (yr) | | 79 (71–86) | 78 (67–84) | 0.159 |  |  |
| Sex (male) | | 91 (54.8%) | 94 (49.2%) | 0.290 |  |  |
| NEWS score | | | | | | |
|  | >5 | 47 (28.3%) | 21 (11.0%) |  |  |  |
| 3–5 | 60 (36.1%) | 55 (28.8%) | <0.001 | 3.58 (1.88–6.82) | <0.001 |
| <3 | 59 (35.5%) | 115 (60.2%) |  | 1.59 (0.93–2.70) | 0.086 |
| Symptom duration (d) | | 2 (1–3) | 2 (1–3) | 0.670 |  |  |
| Symptom duration >7 days (yes) | | 7 (4.2%) | 18 (9.4%) | 0.054 |  |  |
| Lenght of stay (d) | | 12.47 (7.13–22.09) | 10.45 (6.41–17.28) | 0.032 |  |  |
| Chronic immunosuppressive therapy (yes) | | 21 (12.7%) | 17 (8.9%) | 0.252 |  |  |
| Chronic anticoagulant therapy (yes) | | 49 (29.7%) | 51 (26.8%) | 0.551 |  |  |
| Chronic antiplatelet therapy (yes) | | 31 (18.7%) | 39 (20.4%) | 0.679 |  |  |
| COVID-19 (yes) | | 7 (4.2%) | 5 (2.6%) | 0.403 |  |  |
| Comorbidities: | | | | | | |
|  | Ischemic cardiomyopathy | 31 (18.7%) | 43 (22.5%) | 0.372 |  |  |
| Heart failure | 57 (34.3%) | 50 (26.2%) | 0.093 |  |  |
| TIA/stroke | 33 (19.9%) | 36 (18.8%) | 0.806 |  |  |
| Dementia | 68 (41%) | 71 (37.2%) | 0.464 |  |  |
| COPD | 18 (10.8%) | 17 (8.9%) | 0.538 |  |  |
| Cirrhosis | 2 (1.2%) | 7 (3.7%) | 0.139 |  |  |
| Diabetes | 42 (25.3%) | 46 (24.1%) | 0.790 |  |  |
| CKD | 42 (25.3%) | 29 (15.2%) | 0.017 |  |  |
| Sepsis focus: | | | | | | |
|  | Unknown | 26 (15.7%) | 29 (15.2%) | 0.036 |  |  |
| Pulmonary | 33 (19.9%) | 16 (8.4%) |  |  |
| Urinary | 76 (45.8%) | 98 (51.3%) |  |  |
| Abdomen | 14 (8.4%) | 17 (8.9%) |  |  |
| Bloodstream infection | 3 (1.8%) | 8 (4.2%) |  |  |
| Other | 14 (8.4%) | 23 (12.0%) |  |  |
| Positive cultural exam | 109 (65.7%) | 128 (67.0%) | 0.552 |  |  |
| Laboratory parameters: | | | | | | |
|  | Hemoglobin (g/dL) | 11.1 (9.7–12.6) | 11.3 (9.8–13) | 0.377 |  |  |
| WBC (×109/L) | 15.07 (10.06–21.28) | 12.43 (8.1–18.34) | 0.002 | 1.02 (0.99–1.04) | 0.860 |
| Platelets (×109/L) | 193 (123–299) | 208 (155–297) | 0.162 |  |  |
| Creatinine (mg/dL) | 1.84 (1.21–2.73) | 1.17 (0.84–1.73) | <0.001 | 1.08 (0.96–1.20) | 0.170 |
| PT (sec) | 12.8 (11.9–15) | 11.9 (11.3–12.9) | <0.001 |  |  |
| aPTT (sec) | 37.4 (33.1–43.1) | 34 (30.8–38.5) | <0.001 |  |  |
| INR | 1.25 (1.13–1.45) | 1.12 (1.07–1.22) | <0.001 |  |  |
| Fibrinogen (mg/dL) | 599 (437–742) | 536 (418–724) | 0.112 |  |  |
| D-Dimer (ng/mL) | 4321 (2714–15,121) | 3221 (1535–10,914) | 0.077 |  |  |
| CRP (mg/dL) | 185 (124–264) | 131 (69–206) | <0.001 |  |  |
| Procalcitonin (ng/mL) | 10.99 (1.97–38.95) | 3.78 (0.49–15.63) | <0.001 | 1.01 (1.00–1.02) | 0.014 |
| SCORE | | | | | | |
|  | Positive SIC score at ED admission | 46 (27.7%) | 9 (4.7%) | <0.001 | 6.33 (2.90–13.83) | <0.001 |

aPTT: activated partial thromboplastin time; CI: confidence interval; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; CRP: c-reactive protein; ED: emergency department; INR: international normalized ratio; NEWS: national early warning score; SIC: sepsis induced coagulopathy; PT: prothrombin time; WBC: white blood cell.

Supplementary Table 2. Statistical comparison of the clinical characteristics of the patients who developed a thrombotic event during the hospital stay, compared to controls.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | | Any Thrombotic event  (n. 14) | No Thrombosis  (n. 343) | *p* | Odds Ratio  (95% CI) | *p* |
| Anamnestic data: | | | | | | |
| Age (yr) | | 79 (68.5–84) | 79 (70–85) | 0.741 |  |  |
| Sex (male) | | 4 (28.6%) | 181 (52.8%) | 0.102 |  |  |
| NEWS score | | | | | | |
|  | >5 | 4 (28.6%) | 64 (18.7%) |  |  |  |
| 3–5 | 6 (42.9%) | 109 (31.8%) | 0.298 |  |  |
| <3 | 4 (28.6%) | 170 (49.6%) |  |  |  |
| Symptom duration (d) | | 2 (1–4) | 2 (1–3) | 0.514 |  |  |
| Symptom duration >7 days (yes) | | 3 (21.4%) | 22 (6.4%) | 0.066 |  |  |
| Length of stay (d) | | 11.22 (5.4–25.4) | 11.6 (6.7–19.4) | 0.960 |  |  |
| Chronic immunosuppressive therapy (yes) | | 0 (0.0%) | 38 (11.1%) | 0.378 |  |  |
| Chronic anticoagulant therapy (yes) | | 7 (50.0%) | 93 (27.3%) | 0.064 |  |  |
| Chronic antiplatelet therapy (yes) | | 0 (0.0%) | 70 (20.4%) | 0.081 |  |  |
| COVID-19 (yes) | | 2 (14.3%) | 10 (2.9%) | 0.075 |  |  |
| Comorbidities: | | | | | | |
|  | Ischemic cardiomyopathy | 2 (14.3%) | 72 (21.0%) | 0.743 |  |  |
| Heart failure | 9 (64.3%) | 98 (28.6%) | 0.007 | 5.63 (1.70–18.68) | 0.005 |
| TIA/stroke | 3 (21.4%) | 66 (19.2%) | 0.739 |  |  |
| Dementia | 7 (50.0%) | 132 (38.5%) | 0.386 |  |  |
| COPD | 3 (21.4%) | 32 (9.3%) | 0.148 |  |  |
| Cirrhosis | 1 (7.1%) | 8 (2.3%) | 0.305 |  |  |
| Diabetes | 2 (14.3%) | 86 (25.1%) | 0.531 |  |  |
| CKD | 4 (28.6%) | 67 (19.5%) | 0.491 |  |  |
| Sepsis focus: | | | | | | |
|  | Unknown | 3 (21.4%) | 52 (15.2%) | 0.212 |  |  |
| Pulmonary | 4 (28.6%) | 45 (13.1%) |  |  |
| Urinary | 3 (21.4%) | 171 (49.9%) |  |  |
| Abdomen | 1 (7.1%) | 30 (8.7%) |  |  |
| Bloodstream infection | 0 (0.0%) | 11 (3.2%) |  |  |
| Other | 3 (21.4%) | 34 (9.9%) |  |  |
| Positive cultural exam | 11 (78.6%) | 226 (65.9%) | 0.611 |  |  |
| Laboratory parameters: | | | | | | |
|  | Hemoglobin (g/dL) | 11.4 (9.5–13.3) | 11.2 (9.8–12.8) | 0.905 |  |  |
| WBC (×109/L) | 11.74 (7.38–14.92) | 13.54 (8.68–19.31) | 0.181 |  |  |
| Platelets (×109/L) | 128 (98–179) | 208 (138–300) | 0.005 |  |  |
| Creatinine (mg/dL) | 1.4 (0.83–1.9) | 1.47 (0.97–2.28) | 0.523 |  |  |
| PT (sec) | 13.5 (11.7–19.1) | 12.3 (11.4–13.67) | 0.073 |  |  |
| aPTT (sec) | 34.95 (33.2–56.8) | 35.65 (32.1–40.9) | 0.440 |  |  |
| INR | 1.38 (1.13–1.91) | 1.16 (1.08–1.31) | 0.046 |  |  |
| Fibrinogen (mg/dL) | 404 (317–621) | 570 (434–737) | 0.035 | 0.99 (0.99–1.00) | 0.050 |
| D-Dimer (ng/mL) | 9413 (7081–28,807) | 3695 (2005–10,945) | 0.028 |  |  |
| CRP (mg/dL) | 162.4 (83.4–246.9) | 159.9 (88.1–234.1) | 0.842 |  |  |
| Procalcitonin (ng/mL) | 4.03 (1.65–27.52) | 5.83 (1.04–26.08) | 0.988 |  |  |
| SCORE | | | | | | |
| Positive SIC score at ED admission | | 8 (57.1%) | 47 (13.7%) | <0.001 | 9.48 (2.95–30.40) | <0.001 |

aPTT: activated partial thromboplastin time; CI: confidence interval; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; CRP: c-reactive protein; ED: emergency department; INR: international normalized ratio; NEWS: national early warning score; SIC: sepsis induced coagulopathy; PT: prothrombin time; WBC: white blood cell.

Supplementary Table 3. Statistical comparison of the clinical characteristics of the patients who developed a major bleeding during the hospital stay, compared to controls.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | | Any Bleeding  (n. 36) | No Bleeding  (n. 321) | *p* | Odds Ratio  (95% CI) | *p* |
| Anamnestic data: | | | | | | |
| Age (yr) | | 78.5 (63.5–84) | 79 (69.5–85) | 0.954 |  |  |
| Sex (male) | | 20 (55.6%) | 165 (51.4%) | 0.636 |  |  |
| NEWS score | | | | | | |
|  | >5 | 6 (16.7%) | 62 (19.3%) |  |  |  |
| 3–5 | 14 (38.9%) | 101 (31.5%) | 0.662 |  |  |
| <3 | 16 (44.4%) | 158 (49.2%) |  |  |  |
| Symptom duration (d) | | 1 (1–3) | 2 (1–3) | 0.115 |  |  |
| Symptom duration >7 days (yes) | | 2 (5.6%) | 23 (7.2%) | 0.720 |  |  |
| Length of stay (d) | | 16.4 (10.8–27) | 11.1 (6.3–19.3) | 0.003 |  |  |
| Chronic immunosuppressive therapy (yes) | | 2 (5.6%) | 36 (11.2%) | 0.401 |  |  |
| Chronic anticoagulant therapy (yes) | | 12 (34.3%) | 88 (27.5%) | 0.397 |  |  |
| Chronic antiplatelet therapy (yes) | | 5 (13.9%) | 65 (20.2%) | 0.362 |  |  |
| COVID-19 (yes) | | 4 (11.1%) | 8 (2.5%) | 0.024 | 3.53 (0.88–14.16) | 0.075 |
| Comorbidities: | | | | | | |
|  | Ischemic cardiomyopathy | 5 (13.9%) | 69 (21.5%) | 0.286 |  |  |
| Heart failure | 13 (36.1%) | 94 (29.3%) | 0.396 |  |  |
| TIA/stroke | 9 (25%) | 60 (18.7%) | 0.363 |  |  |
| Dementia | 14 (38.9%) | 125 (38.9%) | 0.995 |  |  |
| COPD | 2 (5.6%) | 33 (10.3%) | 0.366 |  |  |
| Cirrhosis | 1 (2.8%) | 8 (2.5%) | 0.917 |  |  |
| Diabetes | 8 (22.2%) | 90 (24.9%) | 0.722 |  |  |
| CKD | 10 (27.8%) | 61 (19%) | 0.211 |  |  |
| Sepsis focus: | | | | | | |
|  | Unknown | 5 (13.9%) | 50 (15.6%) | 0.752 |  |  |
| Pulmonary | 5 (13.9%) | 44 (13.7%) |  |  |
| Urinary | 21 (58.3%) | 153 (47.7%) |  |  |
| Abdomen | 2 (5.6%) | 29 (9%) |  |  |
| Bloodstream infection | 0 (0.0%) | 11 (3.4%) |  |  |
| Other | 3 (8.3%) | 34 (10.6%) |  |  |
| Positive cultural exam | 24 (66.7%) | 213 (66.4%) | 0.096 |  |  |
| Laboratory parameters: | | | | | | |
|  | Hemoglobin (g/dL) | 10.5 (9.1–13) | 11.2 (9.8–12.7) | 0.441 |  |  |
| WBC (×109/L) | 14.25 (8.5–20.19) | 13.34 (8.67–19.01) | 0.913 |  |  |
| Platelets (×109/L) | 131 (93–290) | 208 (145–300) | 0.007 |  |  |
| Creatinine (mg/dL) | 2.02 (1.33–4.12) | 1.41 (0.94–2.07) | 0.001 | 1.26 (1.10–1.44) | 0.001 |
| PT (sec) | 13.2 (11.9–15.07) | 12.25 (11.4–13.5) | 0.008 |  |  |
| aPTT (sec) | 37.65 (32.9–45) | 35.1 (31.9–40.42) | 0.132 |  |  |
| INR | 1.31 (1.13–1.48) | 1.16 (1.08–1.30) | 0.005 |  |  |
| Fibrinogen (mg/dL) | 492 (367–673) | 581 (431–748) | 0.031 | 0.99 (0.99–1.00) | 0.022 |
| D-Dimer (ng/mL) | 4964 (2523–22,786) | 3739 (2011–10,914) | 0.298 |  |  |
| CRP (mg/dL) | 159.35 (86.37–232) | 159.9 (88.7–236.4) | 0.822 |  |  |
| Procalcitonin (ng/mL) | 10.47 (2.18–42.40) | 5.69 (0.87–23.96) | 0.060 |  |  |
| SCORE | | | | | | |
|  | Positive SIC score at ED admission | 16 (44.4%) | 39 (12.1%) | <0.001 | 4.83 (2.22–10.50) | <0.001 |

aPTT: activated partial thromboplastin time; CI: confidence interval; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; CRP: c-reactive protein; ED: emergency department; INR: international normalized ratio; NEWS: national early warning score; SIC: sepsis induced coagulopathy; PT: prothrombin time; WBC: white blood cell.

Supplementary Table 4. Statistical comparison of the clinical characteristics of the patients who had the need for a blood component transfusion (red cells, platelet pools, and fresh frozen plasma) during the hospital stay, compared to controls.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | | Need for Blood Component tranfusion  (n. 57) | No need for transfusion  (n. 300) | *p* | Odds Ratio  (95% CI) | *p* |
| Anamnestic data: | | | | | | |
| Age (yr) | | 78 (69.5–84) | 79 (69.2–85) | 0.380 |  |  |
| Sex (male) | | 28 (49.1%) | 157 (52.3%) | 0.657 |  |  |
| NEWS score | | | | | | |
|  | >5 | 16 (28.1%) | 52 (17.3%) |  |  |  |
| 3–5 | 22 (38.6%) | 93 (31.0%) | 0.029 | 1.59 (0.68–3.75) | 0.281 |
| <3 | 19 (33.3%) | 155 (51.7%) |  | 1.12 (0.51–2.44) | 0.768 |
| Symptom duration (d) | | 1 (1–3) | 2 (1–3) | 0.441 |  |  |
| Symptom duration >7 days (yes) | | 3 (5.3%) | 22 (7.3%) | 0.575 |  |  |
| Length of stay (d) | | 18.6 (12.4–25.6) | 10.4 (6.3–17.4) | <0.001 |  |  |
| Chronic immunosuppressive therapy (yes) | | 7 (12.3%) | 31 (10.3%) | 0.662 |  |  |
| Chronic anticoagulant therapy (yes) | | 16 (28.1%) | 84 (28.2%) | 0.986 |  |  |
| Chronic antiplatelet therapy (yes) | | 7 (12.3%) | 63 (21.0%) | 0.129 |  |  |
| COVID-19 (yes) | | 5 (8.8%) | 7 (2.3%) | 0.028 | 7.74 (1.71–35.02) | 0.008 |
| Comorbidities: | | | | | | |
|  | Ischemic cardiomyopathy | 13 (22.8%) | 61 (20.3%) | 0.673 |  |  |
| Heart failure | 17 (29.8%) | 90 (30.0%) | 0.979 |  |  |
| TIA/stroke | 9 (15.8%) | 60 (20.0%) | 0.461 |  |  |
| Dementia | 23 (40.4%) | 116 (38.7%) | 0.811 |  |  |
| COPD | 8 (14.0%) | 27 (9.0%) | 0.241 |  |  |
| Cirrhosis | 1 (1.8%) | 8 (2.7%) | 1.000 |  |  |
| Diabetes | 12 (21.1%) | 76 (25.3%) | 0.492 |  |  |
| CKD | 12 (21.1%) | 59 (19.7%) | 0.810 |  |  |
| Sepsis focus: | | | | | | |
|  | Unknown | 11 (19.3%) | 44 (14.7%) | 0.339 |  |  |
| Pulmonary | 10 (17.5%) | 39 (13.0%) |  |  |
| Urinary | 21 (36.8%) | 153 (51.0%) |  |  |
| Abdomen | 5 (8.8%) | 26 (8.7%) |  |  |
| Bloodstream infection | 1 (1.8%) | 10 (3.3%) |  |  |
| Other | 9 (15.8%) | 28 (9.3%) |  |  |
| Positive cultural exam | 40 (70.2%) | 197 (65.7%) | 0.050 |  |  |
| Laboratory parameters: | | | | | | |
|  | Hemoglobin (g/dL) | 9.2 (8.2–10.75) | 11.4 (10.1–12.9) | <0.001 | 0.58 (0.48–0.70) | <0.001 |
| WBC (×109/L) | 15.71 (7.69–22.14) | 13.20 (8.82–18.76) | 0.191 |  |  |
| Platelets (×109/L) | 138 (75–297) | 208 (148–298) | 0.012 |  |  |
| Creatinine (mg/dL) | 1.7 (1.05–2.86) | 1.42 (0.93–2.19) | 0.098 |  |  |
| PT (sec) | 12.3 (11.5–14.7) | 12.3 (11.4–13.6) | 0.340 |  |  |
| aPTT (sec) | 37.5 (32.9–49.2) | 34.9 (31.9–39.9) | 0.013 |  |  |
| INR | 1.19 (1.09–1.40) | 1.16 (1.08–1.30) | 0.196 |  |  |
| Fibrinogen (mg/dL) | 570 (438–696) | 566 (422–745) | 0.749 |  |  |
| D-Dimer (ng/mL) | 6167 (2611–14,861) | 3700 (1865–11,029) | 0.226 |  |  |
| CRP (mg/dL) | 183.2 (118.2–233.9) | 152.2 (83.5–236.4) | 0.095 |  |  |
| Procalcitonin (ng/mL) | 10.16 (1.95–49.36) | 5.78 (0.83–23.61) | 0.038 | 1.007 (0.99–1.01) | 0.228 |
| SCORE | | | | | | |
|  | Positive SIC score at ED admission | 20 (35.1%) | 35 (11.7%) | <0.001 | 5.28 (2.35–11.83) | <0.001 |

aPTT: activated partial thromboplastin time; CI: confidence interval; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; CRP: c-reactive protein; ED: emergency department; INR: international normalized ratio; NEWS: national early warning score; SIC: sepsis induced coagulopathy; PT: prothrombin time; WBC: white blood cell.