**Corticosteroids for hospitalized patients with mild to critically-ill COVID-19: A multicenter, retrospective, propensity score–matched study**

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**SUPPLEMENTAL MATERIALS**

**Supplemental Table 1. Baseline Characteristics of the Overall Study Population**

|  |  |  |
| --- | --- | --- |
|  |  | **(N = 1092)** |
| **Gender** - no. (%) |  |
|  | female | 381 (34.9) |
|  | male | 711 (65.1) |
| **Age** - no. (%) |  |
|  | < 40 yr | 271 (24.8) |
|  | 40 - 59 yr | 357 (32.7) |
|  | 60 - 79 yr | 362 (33.2) |
|  | ≥ 80 yr | 102 (9.3) |
| **Height** - cm | 166.3±9.8 |
| **Body weight** - kg | 67.0±16.0 |
| **Body Mass Index** - no. (%) |  |
|  | < 18.5 | 62 (6.9) |
|  | ≥ 18.5, < 25 | 514 (56.9) |
|  | ≥ 25 | 327 (36.2) |
| **Race/region** - no. (%) |  |
|  | Japanese | 1008 (92.3) |
|  | East Asians outside of Japan (China, Korea) | 20 (1.8) |
|  | South-East Asians | 30 (2.7) |
|  | Westerners - Caucasians | 31 (2.8) |
|  | Westerners - Blacks | 1 (0.1) |
|  | Others | 2 (0.2) |
| **Smoking history** - no. (%) |  |
|  | Never | 571 (57.9) |
|  | Former or Current | 416 (42.1) |
| **Comorbidities** - no. (%) |  |
|  | Hypertension | 299 (27.4) |
|  | Diabetes mellitus | 194 (17.8) |
| **Time from symptom onset to admission** - days | 8.1±4.7 |
| **Score of 7-point ordinal scale on Day 1** - no. (%) |  |
|  | 2 or 3 | 62 (5.7) |
|  | 4 | 278 (25.5) |
|  | 5 | 385 (35.3) |
|  | 6 | 367 (33.6) |
| **SpO2 / FiO2 on Day1** | 416.4±92.6 |
| **Symptoms due to COVID-19** |  |
|  | Fever ≥ 37℃ - no. (%) | 714 (65.4) |
|  | Dyspnea - no. (%) | 378 (34.6) |
|  | Taste and/or smell disorder - no. (%) | 227 (20.8) |
| **Pneumonia on initial Xp/CT** - no. (%) | 827 (75.7) |
| **Laboratory data** |  |
|  | C-reactive protein - mg/dL | 5.5±6.4 |
|  | Lymphocyte count - /µL | 1135.7±651.3 |
| **Treatment for COVID-19** |
|  | Favipiravir - no. (%) | 421 (38.6) |
|  | Macrolide - no. (%) | 367 (33.6) |
|  | Ciclesonide - no. (%) | 264 (24.2) |
|  | Corticosteroid - no. (%) | 235 (21.5) |
|  | Chloroquine - no. (%) | 161 (14.7) |
|  | Lopinavir/ritonavir - no. (%) | 70 (6.4) |
|  | Immunoglobulin - no. (%) | 32 (2.9) |
|  | Tocilizumab - no. (%) | 19 (1.7) |
| 　 | Others - no. (%) | 306 (28.0) |

Because only a few patients had a baseline 7-point ordinal score of 3, the patients with a baseline score of 2 and 3 were combined for the analysis. Categorical variables were presented as numbers (%), and compared using the chi square test. Normally distributed continuous variables were presented as mean and standard deviation (SD), and compared using the *t* test. A *p* value of <0.05 was considered statistically significant. COVID-19, coronavirus disease 2019; CT, computed tomography.

**Supplemental Table 2. Outcomes for the Overall Study Population**

|  |  |  |
| --- | --- | --- |
| 　 | 　 | (N=1092) |
| Score of 7-point ordinal scale on Day 15 - no. (%) |  |
|  | 1 (death) | 23 (2.1) |
|  | 2 (hospitalized, on invasive mechanical ventilation or Extra-Corporeal Membrane Oxygenation) | 96 (8.8) |
|  | 3 (hospitalized, on Non-invasive Positive Pressure Ventilation or High-Flow Nasal Cannula) | 10 (0.9) |
|  | 4 (hospitalized, requiring low flow supplemental oxygen) | 116 (10.6) |
|  | 5 (hospitalized, not requiring supplemental oxygen, requiring ongoing medical care) | 140 (12.8) |
|  | 6 (hospitalized, not requiring supplemental oxygen, no longer required ongoing medical care) | 287 (26.3) |
|  | 7 (discharged/not hospitalized) | 401 (36.7) |
|  | unknown | 19 (1.7) |
| Time to PCR negativity of the swab solution - days | 15 [10, 23] |
| Duration of fever - days | 7 [4, 13] |
| Oxygen supplementation - no. (%) | 472 (43.3) |
| Non-invasive Positive Pressure Ventilation or High-Flow Nasal Cannula - no. (%) | 39 (3.6) |
| Invasive mechanical ventilation with tracheal intubation - no. (%) | 172 (15.8) |
| Extra-Corporeal Membrane Oxygenation - no. (%) | 38 (3.5) |
| Hospitalization period - days | 18 [12, 27] |
| Mortality - no. (%) |  |
|  | on Day 14 | 23 (2.1) |
|  | on Day 28 | 41 (3.8) |
| 　 | during the entire observation period | 59 (5.4) |

Categorical variables were presented as numbers (%). Continuous variables related to time were presented as median [interquartile ranges]. PCR, polymerase chain reaction.

**Supplemental Table 3. Baseline Characteristics of the Patients who Received Corticosteroids**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | **All patients receiving corticosteroids (N=235)** | **Within 3 days after admission (N = 163)** | **≥ 4 days after admission (N = 72)** | *p*-value |
| **Gender** - no. (%) |  |  |  |  |
|  | female | 59 (25.1) | 44 (27.0) | 15 (20.8) | 0.315 |
|  | male | 176 (74.9) | 119 (73.0) | 57 (79.2) |  |
| **Age** - no. (%) |  |  |  |  |
|  | < 40 yr | 18 (7.7) | 16 (9.8) | 2 (2.8) | 0.186 |
|  | 40 - 59 yr | 82 (34.9) | 59 (36.2) | 23 (31.9) |  |
|  | 60 - 79 yr | 98 (41.7) | 65 (39.9) | 33 (45.8) |  |
|  | ≥ 80 yr | 37 (15.7) | 23 (14.1) | 14 (19.4) |  |
| **Height** - cm | 167.0±9.6 | 166.5±9.6 | 168.2±9.5 | 0.247 |
| **Body weight** - kg | 70.4±17.1 | 69.9±18.3 | 71.5±14.2 | 0.524 |
| **Body Mass Index** - no. (%) |  |  |  |  |
|  | < 18.5 | 7 (3.4) | 4 (2.8) | 3 (4.8) | 0.082 |
|  | ≥ 18.5, < 25 | 110 (53.7) | 84 (58.7) | 26 (41.9) |  |
|  | ≥ 25 | 88 (42.9) | 55 (38.5) | 33 (53.2) |  |
| **Race/region** - no. (%) |  |  |  |  |
|  | Japanese | 226 (96.2) | 158 (96.9) | 68 (94.4) | 0.473 |
|  | East Asians outside of Japan (China, Korea) | 5 (2.1) | 3 (1.8) | 2 (2.8) |  |
|  | South-East Asians | 3 (1.3) | 2 (1.2) | 1 (1.4) |  |
|  | Westerners - Caucasians | 1 (0.4) | 0 (0.0) | 1 (1.4) |  |
| **Smoking history** - no. (%) |  |  |  |  |
|  | Never | 115 (53.5) | 91 (59.9) | 24 (38.1) | 0.004 |
|  | Former or Current | 100 (46.5) | 61 (40.1) | 39 (61.9) |  |
| **Comorbidities** - no. (%) |  |  |  |  |
|  | Hypertension | 99 (42.1) | 64 (39.3) | 35 (48.6) | 0.181 |
|  | Diabetes mellitus | 76 (32.3) | 50 (30.7) | 26 (36.1) | 0.412 |
| **Time from symptom onset to admission** - days | 8.0±4.1 | 8.4±4.3 | 7.0±3.6 | 0.018 |
| **Score of 7-point ordinal scale on day 1** - no. (%) |  |  |  |  |
|  | 2 or 3 | 41 (17.4) | 32 (19.6) | 9 (12.5) | 0.060 |
|  | 4 | 110 (46.8) | 74 (45.4) | 36 (50.0) |  |
|  | 5 | 75 (31.9) | 54 (33.1) | 21 (29.2) |  |
|  | 6 | 9 (3.8) | 3 (1.8) | 6 (8.3) |  |
| **SpO2 / FiO2** |  |  |  |  |
|  | at day 1 | 349.0±125.4 | 342.1±130.5 | 364.8±112.2 | 0.204 |
|  | just before corticosteroid initiation | 273.6±134.7 | 292.8±139.1 | 230.4±113.6 | 0.001 |
| **Symptoms due to COVID-19** |  |  |  |  |
|  | Fever ≥ 37℃ - no. (%) | 189 (80.4) | 126 (77.3) | 63 (87.5) | 0.069 |
|  | Dyspnea - no. (%) | 129 (54.9) | 92 (56.4) | 37 (51.4) | 0.473 |
|  | Taste and/or smell disorder - no. (%) | 29 (12.4) | 19 (11.7) | 10 (14.1) | 0.604 |
| **Pneumonia on initial Xp/CT** - no. (%) | 227 (96.6) | 159 (97.5) | 68 (94.4) | 0.227 |
| **Laboratory data** |  |  |  |  |
|  | C-reactive protein - mg/dL |  |  |  |  |
|  |  at day 1 | 9.6±7.1 | 9.7±7.1 | 9.4±7.1 | 0.803 |
|  |  just before corticosteroid initiation | 11.8±8.3 | 10.2±7.5 | 15.3±9.1 | <0.001 |
|  | Lymphocyte count - /µL | 919.4±811.5 | 861.8±592.2 | 1048.6±1157.9 | 0.120 |
| **Treatment for COVID-19** |
|  | Favipiravir - no. (%) | 146 (62.1) | 98 (60.1) | 48 (66.7) | 0.340 |
|  | Macrolide - no. (%) | 152 (64.7) | 114 (69.9) | 38 (52.8) | 0.011 |
|  | Ciclesonide - no. (%) | 63 (26.8) | 35 (21.5) | 28 (38.9) | 0.006 |
|  | Chloroquine - no. (%) | 53 (22.6) | 33 (20.2) | 20 (27.8) | 0.203 |
|  | Lopinavir/ritonavir - no. (%) | 22 (9.4) | 6 (3.7) | 16 (22.2) | <0.001 |
|  | Immunoglobulin - no. (%) | 18 (7.7) | 9 (5.5) | 9 (12.5) | 0.064 |
|  | Tocilizumab - no. (%) | 11 (4.7) | 6 (3.7) | 5 (6.9) | 0.275 |
| 　 | Others - no. (%) | 140 (59.6) | 102 (62.6) | 38 (52.8) | 0.158 |

Because only a few patients had a baseline 7-point ordinal score of 3, the patients with a baseline score of 2 and 3 were combined for the analysis. Categorical variables were presented as numbers (%), and compared using the chi square test. Normally distributed continuous variables were presented as mean and standard deviation (SD), and compared using the *t* test. A *p* value of <0.05 was considered statistically significant. COVID-19, coronavirus disease 2019; CT, computed tomography.

**Supplemental Table 4. Outcome of the Patients who Received Corticosteroids**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| 　 | 　 | Within 3 days after admission (N = 163) | ≥ 4 days after admission (N = 72) | Odds ratio or Hazard ratio (95%CI) | *p*-value |
| Score of 7-point ordinal scale on Day 15 - no. (%) |  |  |  |  |
|  | 1 | 10 (6.1) | 5 (6.9) | 0.597 (0.363-0.982) | 0.042 |
|  | 2 | 28 (17.2) | 17 (23.6) |  |  |
|  | 3 | 5 (3.1) | 3 (4.2) |  |  |
|  | 4 | 39 (23.9) | 20 (27.8) |  |  |
|  | 5 | 25 (15.3) | 12 (16.7) |  |  |
|  | 6 | 26 (16.0) | 9 (12.5) |  |  |
|  | 7 | 28 (17.2) | 5 (6.9) |  |  |
|  | unknown | 2 (1.2) | 1 (1.4) |  |  |
| Time to PCR negativity of the swab solution - days | 20 [13, 25] | 21 [16, 30] | 1.479 (1.073-2.039) | 0.017 |
| Duration of fever - days | 10 [4, 19] | 11 [7, 16] | 0.949 (0.702-1.285) | 0.737 |
| Invasive mechanical ventilation - no. (%) | 62 (38.0) | 32 (44.4) | - | 0.355 |
| Duration of invasive mechanical ventilation - days | 10.5 [8, 26] | 14.5 [8.5, 26] | 1.007 (0.648-1.565) | 0.975 |
| Hospitalization period - days | 26 [16, 37] | 27 [19, 36] | 1.057 (0.785-1.424) | 0.715 |
| Mortality - no. (%) |  |  |  |  |
|  | on Day 14 | 10 (6.1) | 5 (6.9) | - | 0.779 |
|  | on Day 28 | 18 (11.0) | 10 (13.9) | - | 0.520 |
| 　 | during the entire observation period | 23 (14.1) | 14 (19.4) | - | 0.333 |

Categorical variables were presented as numbers (%). Continuous variables related to time were presented as median [interquartile ranges]. Ordinal variables were compared between groups using a proportional odds model. Cox proportional hazards model was used to calculate the hazard ratio and its 95% confidence interval for the treatment effect between groups. A *p* value of <0.05 was considered statistically significant. CI, confidence interval; PCR, polymerase chain reaction.

**Supplemental Figure 1. Time from Admission to Tracheal Intubation**

Kaplan–Meier curves for the time from admission to tracheal intubation. IQR, interquartile ranges.

**Supplemental Figure 2. Survival Curve**

Kaplan–Meier curves for survival in the overall population (A), baseline 7-point ordinal score of 2 or 3 (B), baseline score of 4 (C), and baseline score of 5 (D). Because only a few patients had a baseline score of 3, the patients with a baseline score of 2 and 3 were combined for the analysis.