

**Table S1. Demographics and clinical parameters profile of HFNC survivors and CPAP failure.**

|                                      | HFNC survivors<br>(n=64) | CPAP failure<br>(n=41) | <i>p</i>     |
|--------------------------------------|--------------------------|------------------------|--------------|
| <i>Demographics</i>                  |                          |                        |              |
| Age                                  | 69 (59 - 75)             | 74 (70 - 79)           | <b>0.001</b> |
| BMI                                  | 27.4 (24.2 - 29.4)       | 27.3 (24.5 - 29.3)     | 0.892        |
| Gender, male                         | 40 (62.5)                | 21 (51.2)              | 0.254        |
| Hospital stay (days)                 | 21.5 (14.25 - 31.5)      | 13 (9 - 17.75)         | <b>0.001</b> |
| ICU admission (28 days)              | 3 (4.62)                 | 25 (60.9)              | <b>0.001</b> |
| COVID-19 Vaccination                 | 13 (20.3)                | 7 (17.5)               | 0.762        |
| <i>Comorbidities</i>                 |                          |                        |              |
|                                      | 3 (2 - 5)                | 4 (3 - 6)              | 0.101        |
| Charlson Comorbidity Index           | 3 (2 - 5)                | 5 (4 - 6)              | 0.007        |
| Diabetes                             | 33 (51.1)                | 18 (43.9)              | 0.473        |
| Coronary artery disease              | 18 (28.1)                | 13 (31.7)              | 0.694        |
| COPD                                 | 14 (20.3)                | 6 (14.6)               | 0.461        |
| Heart failure                        | 15 (23.4)                | 15 (36.5)              | 0.148        |
| Hypertension                         | 37 (57.8)                | 32 (78)                | 0.081        |
| Chronic kidney disease               | 7 (10.9)                 | 9 (21.9)               | 0.261        |
| Atrial fibrillation                  | 5 (7.8)                  | 8 (19.5)               | 0.077        |
| Cerebrovascular disease              | 2 (6.4)                  | 3 (7.3)                | 0.335        |
| Respiratory failure                  | 0 (0)                    | 0 (0)                  | -            |
| <i>Vital and clinical parameters</i> |                          |                        |              |
| Heart rate                           | 80 (70 - 95)             | 82 (76 - 92)           | 0.338        |
| DBP mmHg                             | 80 (65 - 85)             | 75 (70 - 83.75)        | 0.732        |
| SBP mmHg                             | 132.5 (120 - 148)        | 135 (130 - 150)        | 0.213        |
| MBP mmHg                             | 94 (83 - 106)            | 95 (88 - 101)          | 0.626        |
| Fever                                | 28 (43.7)                | 22 (53.6)              | 0.324        |
| Glasgow Coma Scale                   | 15 (15 - 15)             | 15 (15 - 15)           | 0.665        |
| <i>Therapy</i>                       |                          |                        |              |
| Corticosteroids                      | 64 (100)                 | 41 (100)               | 1            |
| Anti-IL6                             | 8 (12.5)                 | 7 (17)                 | 0.522        |
| Remdesivir                           | 1 (1.5)                  | 1 (2.4)                | 0.739        |
| Anti-SARS-CoV-2                      | 1 (1.5)                  | 3 (7.3)                | 0.129        |

Data are n (%) and median (IQR). N is the total number of patients with available data.

BMI: Body mass index; ICU: Intensive care Unit; COPD: Chronic Obstructive pulmonary disease; COVID-19: coronavirus disease 2019; DBP: diastolic blood pressure; IL-6: interleukin 6; SBP: systolic blood pressure; MBP: mean blood pressure; IL-6: interleukin 6 ICU: Intensive care Unit; MBP: mean blood pressure; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; SBP: systolic blood pressure

**Table S2. Laboratory findings profile according to the respiratory support .**

|   | HFNC survivors<br>(n=64) | CPAP failure<br>(n=41) | <i>p</i>     |
|---|--------------------------|------------------------|--------------|
| <i>Laboratory findings</i>              |                          |                        |              |
| Albumin, g/dL                           | 3.14 (2.9 – 3.3)         | 2.9 (2.7 – 3.28)       | <b>0.024</b> |
| ALT, U/L                                | 25 (15 - 42)             | 30 (20 - 47)           | 0.257        |
| AST, U/L                                | 29 (21 - 40)             | 30 (23 - 66)           | 0.449        |
| CK, U/L                                 | 100 (51 - 210)           | 103 (57 - 266)         | 0.537        |
| Creatinine, mg/dL                       | 1 (1 - 1)                | 1 (1 - 2)              | 0.264        |
| D-dimer, mcg/mL                         | 3 (3 - 4)                | 4 (4 - 4)              | 0.320        |
| Fibrinogen, mg/dL                       | 640 (462 – 761)          | 607 (533 - 682)        | 0.182        |
| Hb, gr/dL                               | 14 (12 - 14)             | 14 (11 - 15)           | 0.884        |
| IL-6, pg/mL                             | 28 (10 – 66.8)           | 63.9 (40 - 113)        | <b>0.001</b> |
| LDH, U/L                                | 351 (281 - 436)          | 438 (343 - 608)        | <b>0.011</b> |
| Bilirubin, total, mg/dl                 | 0,65 (0,44 – 0,84)       | 0,64 (0,5 – 1)         | 0.151        |
| NT-proBNP, pg/mL                        | 497 (183 - 1625)         | 641 (229 - 2518)       | 0.510        |
| CRP, mg/dL                              | 6.3 (3.3 – 14.3)         | 10.3 (5.2 - 12.9)      | 0.293        |
| PCT, ng/mL                              | 0.14 (0.08 – 0.46)       | 0.15 (0.08 – 0.44)     | 0.956        |
| Ferritin, mg/dl                         | 652 (254 – 2170)         | 743 (471 – 1358)       | 0.509        |
| Platelet count, cells x 10 <sup>4</sup> | 223 (166 - 289)          | 198 (150 - 246)        | 0.216        |
| Troponin, pg/mL                         | 30.3 (16 - 85)           | 54 (14.6 – 116.1)      | <b>0.006</b> |
| Urea, mg/dL                             | 56 (41 – 84.5)           | 55 (39 - 82)           | 0.774        |
| WBC, cells                              | 7245 (4900 - 12300)      | 9100 (6200 - 12100)    | 0.169        |
| Lymphocyte count, cells                 | 803 (599 - 1219)         | 815 (560 - 1090)       | 0.351        |
| Neutrophil count, cells                 | 5748 (3425 – 9477)       | 7280 (4836 – 10164)    | 0.299        |
| Neutrophil/lymphocyte ratio             | 7.4 (4.1 – 10)           | 8.5 (5.7 – 14)         | <b>0.049</b> |

Data are n (%) and median (IQR). N is the total number of patients with available data.

ALT: Alanine transaminase; AST: aspartate transaminase; CK: creatine kinase; CRP: C-reactive protein; Hb: hemoglobin; IL-6: interleukin 6; LDH: lactate dehydrogenase; NT-proBNP: N-terminal pro-brain natriuretic peptide; PCT: procalcitonin; WBC: white blood cells

**Table S3. Comparison of respiratory parameters between HFNC survivors and c-PAP failure.**

|  | <b>HFNC survivors<br/>(n=64)</b> | <b>c-PAP failure<br/>(n=41)</b> | <b><i>p</i></b> |
|--|----------------------------------|---------------------------------|-----------------|
| Respiratory Rate, T0                     | 20 (20 - 25)                     | 25 (21 - 30)                    | <b>0.004</b>    |
| SpO <sub>2</sub> /FiO <sub>2</sub> , T0  | 158.3 (153.3 - 187)              | 153.3 (147 - 201.2)             | 0.243           |
| ROX, T0                                  | 7.5 (6.8 - 8.7)                  | 6.2 (4.9 - 8.5)                 | 0.075           |
| PaO <sub>2</sub> /FiO <sub>2</sub> , T0  | 113.5 (97.8 - 133.33)            | 99.1 (90.4 - 136.2)             | 0.152           |
| Respiratory Rate, T6                     | 20 (20 - 22)                     | 24 (21 - 27)                    | <b>0.001</b>    |
| SpO <sub>2</sub> /FiO <sub>2</sub> , T6  | 163 (160 - 171)                  | 158.3 (153 - 163)               | <b>0.008</b>    |
| ROX, T6                                  | 8 (7.1 - 8.7)                    | 6.4 (5.3 - 7.7)                 | <b>0.001</b>    |
| PaO <sub>2</sub> /FiO <sub>2</sub> , T6  | 138.6 (128.3 - 166)              | 128.3 (110 - 184)               | 0.098           |
| Respiratory Rate, T24                    | 20 (18 - 22)                     | 22 (20 - 26)                    | <b>0.005</b>    |
| SpO <sub>2</sub> /FiO <sub>2</sub> , T24 | 174 (160 - 196)                  | 157 (135 - 163)                 | <b>0.001</b>    |
| ROX, T24                                 | 8.9 (7.7 - 10.5)                 | 7.2 (5.8 - 8.8)                 | <b>0.001</b>    |
| PaO <sub>2</sub> /FiO <sub>2</sub> , T24 | 151 (120 - 176)                  | 116 (85 - 156)                  | <b>0.005</b>    |
| Respiratory Rate, T48                    | 20 (18 - 22)                     | 21 (20 - 24)                    | <b>0.047</b>    |
| SpO <sub>2</sub> /FiO <sub>2</sub> , T48 | 165 (161.6 - 206.6)              | 160.6 (156.6 - 180)             | 0.071           |
| ROX, T48                                 | 8.9 (7.9 - 10.4)                 | 7.6 (6.4 - 9)                   | <b>0.007</b>    |
| PaO <sub>2</sub> /FiO <sub>2</sub> , T48 | 148 (129 - 168)                  | 116 (103 - 130)                 | <b>0.001</b>    |

Data are n (%) and median (IQR). N is the total number of patients with available data.

FiO<sub>2</sub>: fraction of inspired oxygen; PaCO<sub>2</sub>: partial pressure of carbon dioxide; PaO<sub>2</sub>: partial pressure of oxygen; ROX: respiratory rate oxygenation; SO<sub>2</sub>: oxygen saturation