**Supplementary Material**

Prone positioning in awake COVID-19 patients: a systematic review and meta-analysis

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**Pubmed Search Strategy**

((COVID[tiab] OR Coronavirus[tiab] OR SARS-CoV\*[tiab])) AND ((pronation[tiab] OR prone[tiab])) NOT ((animal[mh], NOT human[mh])) NOT ((comment[pt] OR editorial[pt] OR practice-guideline[pt] OR review[pt]))

**Supplementary Table 1. Characteristics of included studies.**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Author | Journal | Year | Country | Study design | Nr pronated patients | Exclusion criteria | Highest respiratory support during pronation | Adverse events | Longest follow-up |
| Alsharif H [1] | Crit Care Med | 2021 | Saudi Arabia | Prospective | 31 | ND | CPAP | ND | ICU stay |
| Altinay M [2] | Braz J Anesthesiol | 2021 | Turkey | Retrospective | 25 | Patients supported with NIV, HFNC or invasive mechanical ventilation, GCS <12 or hemodynamic instability;  primary pulmonary pathologies,  awake PP <12 hours in 1 day | Non rebreathe facemask | ND | ICU stay |
| Bahloul M [3] | Acute Crit Care | 2021 | Tunisia | Prospective | 21 | Patients in cardiac arrest, those who required NIV and/or in­vasive mechanical ventilation, with hemodynamic instability, agitation and/or coma | HFNC | ND | ICU stay |
| Barker J [4] | Postgrad Med J | 2021 | UK | Retrospective | 10 | Patients intubated prior to or immediately on arrival to ICU and those who underwent APP on the ward | NIV | ND | 28-day |
| Bastoni D [5] | BMJ | 2020 | Italy | Case series | 10 | Needed rapid intubation and ICU admission; receiving helmet NIV CPAP with sufficient improvement of arterial gas exchanges; altered mental status or uncollaborative; end-stage comorbidity | CPAP | ND | ND |
| Brunin Y [6] | Am J Respir Crit Care Med | 2021 | France | Case report | 1 | ND | Non rebreath facemask | ND | ICU stay |
| Burton-Papp HC [7] | F1000Research | 2020 | UK | Retrospective | 20 | ND | NIV | None | Hospital discharge |
| Cammarota G [8] | Critical Care | 2021 | Italy | Prospective | 20 | Contraindications to NIV or prone position, dyspnea, diagnosis of diaphragmatic palsy, history of neuromuscular disease, pregnancy, impossibility to obtain a diaphragmatic and pulmonary ultrasound assessment, poor tolerance and/or severe worsening of clinical conditions during study phases necessitating NIV/prone position discontinuation, and previous intubation during the same hospitalization period. | NIV |  |  |
| Caputo N [9] | Acad Emerg Med | 2020 | USA | Prospective cohort study | 50 | DNR/DNI code status, in cardiac arrest, receiving NIV or those who were intubated in the prehospital setting | Non rebreathe facemask | None | 72-hours |
| Cherian SV [10] | Respiratory Medicine | 2021 | USA | Retrospective | 59 | Patients unable to prone for at least 3 h in a day | HFNC/NIV | ND | Hospital discharge |
| Chiumello D [11] | Annals of Intensive Care | 2021 | Italy | Prospective | 40 | Patients needing immediate endotracheal intubation, presented unstable hemodynamics or had a GCS<15 | Helmet CPAP | ND | 28-days |
| Cohen D [12] | Internal Medicne Journal | 2020 | Israel | Case report | 2 | ND | HFNC | None | Hospital discharge |
| Coppo A [13] | Lancet Respir Med | 2020 | Italy | Prospective cohort study | 56 | Pregnant, uncollaborative, altered mental status, HYHA class below II, increased pro-B-type natriuretic peptide concentrations (more than twice the upper normal limit), chronic obstructive pulmonary disease requiring home non-invasive ventilation or oxygen therapy, contraindications (as decided by the attending physician), impending intubation | Helmet CPAP | None | Hospital discharge |
| Cruz Salcedo EM [14] | Cureus | 2020 | USA | Case report | 1 | ND | HFNC/NIV | None | Hospital discharge |
| Damarla M [15] | Am J Respir Crit Care Med | 2020 | USA | Retrospective | 10 | Patients requiring urgent mechanical intubation | HFNC | None | 28-days |
| Despres C [16] | Critical Care | 2020 | France | Case series | 6 | Patients requiring urgent mechanical intubation | HFNC | ND | ND |
| Dubosh NM [17] | Am J Emerg Med. | 2021 | USA | Prospective | 22 | Needed immediate intubation, unable to safely change position with minimal assistance | non-rebreather mask | ND | Hospital discharge |
| Dueñas-Castell C [18] | Journal of Intensive Care Medicine | 2021 | Colombia | Prospective | 212 | Patients who were referred  to another institution or whose hospital stay was less than 24 h. | Face mask with reservoir | ND | Hospital discharge |
| Ehrman S [19] | Lancet Respir Med | 2021 | USA | RCT | 564 | Haemodynamically unstable, BMI >40 kg/m², pregnancy, contraindication to awake prone positioning | HFNC | Vomiting, central line dislodgment | 28-days |
| Elharrar X [20] | JAMA | 2020 | France | Prospective cohort study | 24 | Patients requiring urgent mechanical intubation and impaired consciousness | HFNC | Back pain | ND |
| Elkattawi S [21] | Respiratory Medicine Case Report | 2020 | USA | Case report | 1 | ND | NC | None |  |
| Esperatti M [22] | Critical Care | 2022 | Argentina | Prospective | 187 | decreased level of consciousness, presence of shock requiring vasopressors, immediate need for  intubation, use of positive pressure ventilation prior to HFNO, and with do-not-intubate orders | HFNC | syncope requiring intubation, cardiorespiratory arrest, arterial line displacement with bleeding and  hypotension | Hospital discharge |
| Fazzini B [23] | Journal of the Intensive Care Society | 2021 | UK | Prospective | 46 | ND | CPAP | None | 90-days |
| Ferrando C [24] | Critical Care | 2020 | Spain and Andorra | Prospective, multicenter | 55 | Previous mechanical ventilation or non-invasive mechanical ventilation before starting HFNC; SpO2 >93% | HFNC | ND | ICU discharge |
| Golestani-Eraghi M [25] | Journal of Clinical Anesthesia | 2020 | Iran | Case series | 10 | ND | NIV | None | ICU stay |
| Hallifax RJ [26] | BMC Open Respiratory Research | 2020 | UK | Retrospective | 11 | ND | HFNC/CPAP | ND | Hospital Discharge |
| Hashemian SM [27] | Tanaffos | 2021 | Iran | RCT | 45 | BMI <18 or >30, emergent intubation or already intubated | CPAP | ND | Hospital discharge |
| Jagan N [28] | Crit Care Expl | 2020 | USA | Retrospective | 40 | Pregnancy, intubation at the time of admission | ND | ND | Hospital discharge |
| Jayakumar D [29] | J Intensive care medicine | 2021 | India | RCT | 30 | Pregnancy, hemodynamic shock, GCS<15,immediate intubation, contraindications to prone positioning | NIV | None | Hospital discharge |
| Jha A [30] | ERJ Open Res | 2022 | UK | Prospective | 25 | Respiratory distress; haemodynamic instability; unstable spinal injury or recent abdominal surgery; pregnancy; morbid obesity; neurological issues; facial injury; gastrointestinal issues such as vomiting | non-rebreather mask | Discomfort | Hospital discharge |
| Johnson SA [31] | Ann Am Thorac Soc. | 2021 | USA | RCT | 15 | Unable to change position without assistance, pregnant, incarcerated, admitted to an ICU or transfer was  imminent, mechanically ventilated, or receiving hospice | NC | ND | Hospital discharge |
| Jouffroy R [32] | J Critical Care | 2021 | France | Retrospective | 40 | ND | NIV | ND | 28-days |
| Kelly NL [33] | J Intensive Care Soc. | 2021 | UK | Retrospective | 17 | Immediate intubation, cardiovascular instability, altered  consciousness | non-rebreather mask | ND | Hospital discharge |
| Khanna A [34] | Lung India | 2021 | India | Retrospective | 12 | ND | Non rebreathe mask | ND | Hospital discharge |
| Khanum I [35] | Monaldi Archives for Chest Disease | 2021 | Pakistan | Retrospective | 23 | Invasive mechanical ventilation, mild COVID-19, proning for 24 hours or less | NIV | Discomfort | Hospital discharge |
| Kharat A [36] | ERJ | 2021 | Switzerland | Cluster RCT | 10 | Oxygen needs >6 L·min−1 using a nasal cannula or with >40% FiO2 using a Venturi mask to obtain a SpO2 level of 90–92%; pregnant women; terminally ill patients; and those unable to self-prone | NC | Discomfort | Hospital discharge |
| Liu X [37] | Med Clin | 2021 | China | Retrospective | 29 | Unable to tolerate prone position due to diseases and other factors,  such as heart failure and heart diseases | ND | ND | Hospital discharge |
| Loureiro-Amigo J [38] | Archivos de Bronconeumología | 2021 | Spain | Retrospective | 60 | ICU admission, NIV, HFNC, moderate or severe dependence for activities of daily living, solid or hematologic cancer, chronic dialysis, neurodegenerative disease or hemiplegia. | Non rebreathe mask | ND | Hospital discharge |
| Moghadam VD [39] | Brazilian Journal of Anesthesiology | 2020 | Iran | Prospective | 10 | ND | ND | ND | ND |
| Nauka PC [40] | Critical Care Explorations | 2021 | USA | Retrospective | 41 | ND | HFNC | ND | Hospital discharge |
| NG Z [41] | European Respiratory Journal | 2020 | Singapore | Prospective | 10 | Patients who were drowsy or uncooperative, or those with ophthalmic, cervical or abdominal pathologies (including pregnancy) | HFNC | ND | Hospital discharge |
| Numata K [42] | Disaster Med Public Health Prep | 2021 | Japan | Retrospective |  | pregnancy, immunocompromisation  or starting intubation or palliative care within 1 day after admission. | HFNC | ND | Hospital discharge |
| Nunn K [43] | Case Rep Crit Care | 2021 | UK | Case report | 1 | ND | HFNC | ND | Hospital discharge |
| Oliveira VM [44] | Respiratory care | 2022 | Brazil | Prospective | 66 | ND | ND | ND | Hospital discharge |
| Padrão EMH [45] | Acad Emerg Med  . | 2020 | Brazil | Retrospective | 57 | Patients intubated in other hospitals; hemodynamic instability; recent abdominal surgery; acute hypercapnic respiratory failure; unstable fractures; pregnancy; other contraindication to the prone position, as judged by the treating physician; DNR/DNI patients | Non rebreathe mask | Accidental removal of peripheral IV lines; back pain | 14-days |
| Paternoster G [46] | Medicina Intensiva | 2020 | Italy | Case series | 11 | Excessive cough, hypotension, morbid obesity or patient refusal | Helmet CPAP | ND | 28-days |
| Paul V [47] | Journal of Intensive Care Medicine | 2020 | USA | Case report | 1 | ND | HFNC | Discomfort, anxiety | Hospital Discharge |
| Perez-Nieto OR [48] | Eur Respir J | 2021 | Mexico | Retrospective | 505 | voluntarily discharged; referred to another hospital prior to outcome ascertainment, incomplete clinical records | HFNC | ND | Hospital discharge |
| Pierucci P [49] | Frontiers in Medicine | 2021 | Italy | Prospective | 16 | ND | CPAP | ND | Hospital discharge |
| Prud’homme E [50] | Chest | 2021 | France | Retrospective | 48 | Patients not requiring oxygen supplementation | HFNC | ND | 14-days |
| Ramirez GA [51] | Minerva Medica | 2020 | Italy | Case series | 36 | Non-eligible to intubation for age and/or comorbidities; chronically receiving CPAP for obstructive sleep apnea; previously intubated and requiring ICU during the same admission; enrolled in a concomitant randomized trial on the use of early CPAP; severe contraindications to CPAP (e.g. coma or hemodynamic instability). | CPAP | Emesis | 20-days |
| Retucci M [52] | Chest | 2020 | Italy | Prospective | 12 | Need for immediate  intubation, Glasgow Coma Scale <15, systolic BP (SBP) <90 mm Hg, and SpO2 <90% at FIO2 >0.8 | Helmet CPAP | None | Hospital discharge |
| Ripoll-Gallardo A [53] | Disaster Med Public Health Prep. | 2020 | Italy | Case series | 13 | ND | CPAP | None | Hospital discharge |
| Rosen J [54] | Crit Care | 2021 | Sweden | RCT | 36 | Oxygen supplementation with a device other than HFNO or NIV; inability to assume prone position; immediate need for endotracheal intubation; severe hemodynamic instability; previous intubation for COVID-19 pneumonia; pregnancy; terminal illness; do-not-intubate order | NIV | Pressure sore, vomiting, central line dislodgment | 30-day |
| Sanz-Moncusì M [55] | Intensive and Critical Care Nursing | 2021 | Spain | Case report | 1 | ND | HFNC | None | Hospital discharge |
| Sartini C [56] | JAMA | 2020 | Italy | Cross sectional survey | 15 | ND | CPAP | None | 14-days |
| Sellmann T [57] | Anaesthesist | 2021 | Germany | Case reports | 2 | ND | CPAP | None | Hospital discharge |
| Simioli F [58] | Turk Thorac J | 2021 | Italy | Retrospective | 18 | ND | HFNC/CPAP | Interface displacement, oxygen desaturation, worsening of dyspnea, chest tightness, neck pain, and agitation | Hospital discharge |
| Singh P [59] | Indian J Crit Care Med | 2020 | India | Retrospective | 15 | ND | NIV | Patients hemodynamically unstable, drowsy, or uncooperative | ICU discharge |
| Slessarev M [60] | Can J Anesth | 2020 | Canada | Case report | 1 | ND | HFNC | ND | Hospital discharge |
| Solverson K [61] | Can J Anesth | 2020 | Canada | Case series | 17 | ND | NC/HFNC | Discomfort | Hospital discharge |
| Sryma PB [62] | Lung India | 2021 | India | Prospective | 30 | Hypercapnic respiratory failure, hemodynamic instability, altered sensorium; patients requiring immediate tracheal intubation; with duration of hypoxia or hospitalization for more than 12 h; BMI >30 kg/m2; PaO2/FiO2 <100 on NIV or HFNC; intolerance to pronation | HFNC/CPAP | Backache and bloating sensation | Hospital discharge |
| Sztajnbok J [63] | Respiratory Medicine Case Report | 2020 | Brazil | Case series | 2 | ND | Non rebreathe facemask | None | ND |
| Taboada M [64] | Journal of Clinical Anesthesia | 2020 | Spain | Prospective | 50 | Inability to collaborate or refusal, unstable hemodynamic status, patients with moderate or severe ARDS needing intubation, and mechanical ventilation | ND | ND | 45-days |
| Tatlow C [65] | Physioterapy | 2021 | Australia | Retrospective | 13 | ND | ND | ND | Hospital discharge |
| Taylor SP [66] | Ann Am Thorac Soc | 2020 | USA | Cluster RCT | 28 | Unable to self-turn, spinal instability, facial or pelvic fractures, open chest or abdomen, altered  mental status, anticipated difficult airway, signs of respiratory fatigue, or receiving end-of-life care | CPAP | Loss of an intravenous catheter | Hospital discharge |
| Testani E [67] | Case Reports in Women’s Health | 2021 | USA | Case report | 1 | ND | NC/non rebreather mask | None | Hospital discharge |
| Thompson AE [68] | JAMA Internal Medicine | 2020 | USA | Prospective | 25 | Altered mental status with inability to turn in bed  without assistance, extreme respiratory distress requiring  immediate intubation or oxygen requirements  less than those specified in the inclusion criteria | Facemask | ND | 45-days |
| Tonelli R [69] | Pulmonology | 2021 | Italy | Retrospective | 38 | Patients with endotracheal intubation performed within the first 24-h from admission, ceiling of escalation, do not intubate decision | NIV | ND | 30-days |
| Tu GW [70] | Annals of Translational Medicine | 2020 | China | Prospective | 9 | ND | HFNC | None | ND |
| Vianello A [71] | J Clinical Medicine | 2021 | Italy | Prospective | 93 | ND | NIV | ND | Hospital discharge |
| Vibert F [72] | European Journal of Obstetrics & Gynecology and Reproductive Biology | 2020 | France | Case report | 1 | ND | HFNC | None | Hospital discharge |
| Villarreal-Fernandez E [73] | Critical Care | 2020 | USA | Case series | 6 | Preexisting chronic respiratory failure, morbid obesity, concurrent clinical signs of respiratory distress, hypercapnia, alteration in hemodynamics, or lactic acidosis | HFNC/NIV | Emesis | ND |
| Wendt C [74] | Journal of Emergency Nursing | 2021 | USA | Retrospective | 31 | ND | NC/non rebreather mask | ND | ND |
| Winearls S [75] | BMJ Open Resp Res | 2020 | UK | Retrospective | 24 | Imminent intubation, reduced conscious level, significant immobility or current pressure areas | CPAP | Discomfort | 28-days |
| Whittemore P [76] | BMJ Case Rep | 2020 | UK | Case report | 1 | ND | Non rebreathe facemask | None | Hospital discharge |
| Wormser J [77] | Irish Journal of Medical Science | 2021 | France | Prospective | 27 | Less than 4 L/min oxygen flow | Low flow oxygen | Discomfort, pain, anxiety | Hospital discharge |
| Xu DW [78] | WJCC | 2021 | China | Case report | 1 | ND | HFNC | ND | Hospital discharge |
| Xu Q [79] | Critical Care | 2020 | China | Retrospective multicenter | 10 | ND | HFNC | Discomfort, anxiety | Hospital discharge |
| Zang X 80] | Intensive Care Med | 2020 | China | Retrospective | 23 | ND | ND | ND | 90-days |

Abbreviations: CPAP: continuous positive airway pressure; DNR: do not resuscitate; HFNC: high flow nasal cannula; NC: nasal cannula; ND: no data; NIV: non-invasive ventilation; RCT: randomized clinical trial.

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**Supplementary Fig. 1. Funnel plots for differences in peripheral capillary oxygen saturation (SpO2) and ratio of arterial oxygen partial pressure (PaO2) to fractional inspired oxygen (FiO2) and respiratory rate before and after pronation.**