Acta Clin Croat (Suppl. 1) 2023; 62:125-131
doi: 10.20471/acc.2023.62.s1.16

Review

NONINVASIVE MECHANICAL VENTILATION IN COVID-19 RELATED ACUTE RESPIRATORY FAILURE

Gordana Pavliša[1,2], Kristina Gašparović[3], Hrvoje Puretić[1], Lidija Ljubičić[1], Andrija Nekić[2], Vlasta Vuković[2], Katarina Vukančić[2] and Andrea Vukić Dugac[1,2]

[1]Jordanovac Department of Respiratory Diseases, Zagreb University Hospital Center, Zagreb, Croatia;
[2]School of Medicine, University of Zagreb, Zagreb, Croatia;
[3]Department of Cardiovascular Diseases, Zagreb University Hospital Center, Zagreb, Croatia

SUMMARY – Coronavirus disease 2019 (COVID-19) is presented with a wide range of symptoms, from asymptomatic disease to severe and progressive interstitial pneumonia. As part of interstitial pneumonia, respiratory failure is typically presented as hypoxia and is the most common cause of hospitalization. When oxygen therapy fails, continuous positive airway pressure (CPAP) or noninvasive mechanical ventilation (NIV) are used as respiratory support measures of first choice. Noninvasive respiratory support (NIRS) is applied in order to save intensive care unit resources and to avoid complications related to invasive mechanical ventilation. Emerging evidence has shown that the use of CPAP or NIV in the management of acute hypoxemic respiratory failure in COVID-19 reduces the need for intubation and mortality. The advantage of NIRS is the feasibility of its application on wards. NIV could be administered *via* a face mask or helmet interface. Helmet adheres better than mask and therefore leakage is reduced, a delivery of positive end-expiratory pressure is more accurate, and the risk of nosocomial transmission of infections is lowered. Patients on NIRS must be carefully monitored so that further respiratory deterioration is not overlooked and additional measures of care including timely intubation and invasive mechanical ventilation could be performed if needed.

Key words: *Coronavirus disease 2019; Respiratory failure; Continuous positive airway pressure; Noninvasive mechanical ventilation; Noninvasive respiratory support*

Introduction

The virus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) causes a disease called coronavirus disease 2019 (COVID-19), which has spread rapidly throughout the world. In March 2020, the World Health Organization declared the COVID-19 pandemic outbreak. The disease has a wide spectrum of symptoms, from asymptomatic disease to severe and progressive interstitial pneumonia and *multiple-organ failure*. Up to 20% of patients develop severe or critical illness characterized by acute respiratory failure[1]. As part of interstitial pneumonia, respiratory failure is typically presented by hypoxia, without carbon dioxide retention, defined as type 1 respiratory failure. Due to the rapid spread of the disease and involvement of a large number of patients, medical resources have been in short supply, with especially great pressure on the intensive care unit (ICU). Data suggest that approximately 20% of infected cases require hospitalization, out of which around one-fourth (5%) require intensive care management[2]. This further

Correspondence to: *Assoc. Prof. Gordana Pavliša, MD, PhD*, Jordanovac Department of Respiratory Diseases, Zagreb University Hospital Center, Jordanovac 104, HR-10000 Zagreb, Croatia
E-mail: gordana.pavlisa11@gmail.com

emphasized the need for maximum understanding and utilization of noninvasive measures of respiratory support in order to save ICU resources but also to avoid complications related to intubation and invasive mechanical ventilation. Conventional oxygen therapy, high-flow *oxygen* therapy (HFOT), continuous positive airway pressure (CPAP) or noninvasive mechanical ventilation (NIV) are used as noninvasive respiratory support (NIRS) measures to treat respiratory failure. There is evidence that the use of NIV in *acute hypoxemic* respiratory failure (AHRF) doubled during this pandemic. It is estimated that about 30% of patients with AHRF were treated with NIV[3].

Evidence Supporting NIV in COVID-19 Related Acute Hypoxemic Respiratory Failure

In patients with COVID-19 with AHRF in whom the need for oxygen exceeds the possibilities of low-flow oxygen therapy, it is recommended to prioritize the use of other modalities of NIRS over endotracheal intubation (ETI) and invasive mechanical ventilation. The first step of support is HFOT. In case of HFOT failure, the use of CPAP and NIV is advised[4]. It has been shown that the use of HFOT, CPAP or NIV in the management of AHRF in COVID-19 patients reduces the need for intubation and mortality[5-7]. A recent systematic review and meta-analysis of 25 randomized clinical trials (3804 patients) summarized evidence on the clinical effectiveness of NIV and HFOT compared with conventional oxygen therapy in patients with acute respiratory failure. Both HFOT and NIV reduced the need for endotracheal intubation. Also, NIV was significantly associated with a lower risk of mortality and tracheal intubation[5]. The RECOVERY-RS Randomized Clinical Trial compared CPAP with conventional oxygen therapy in COVID-19 patients. The composite primary outcome of tracheal intubation or mortality within 30 days was significantly lower with CPAP (36.3%; 137 of 377 participants) *versus* conventional oxygen therapy (44.4%; 158 of 356 participants)[6]. Franco *et al. conducted an* observational study that included 670 COVID-19 patients in whom HFNC, CPAP or NIV were applied outside ICU. The arterial oxygen tension/inspiratory oxygen fraction ratio (PaO_2/FiO_2) at baseline was 152±79. The overall unadjusted 30-day mortality rate was 26.9%, with 16%, 30% and 30% for HFOT, CPAP and NIV, respectively. A total ETI rate was 27%, with 29%, 25% and 28%, respectively. After adjustment for confounders, the relative probability of death, ETI and length of stay were not different among the groups[7]. Bellani *et al*. also showed that NIV could be successful outside ICU. The study included over 900 COVID-19 patients receiving NIV outside ICU, and 62.4% of patients were discharged alive without intubation[8]. A special feature of these studies[7,8] was that all subjects were treated outside ICUs and high dependency units (HDUs). It reflects the reality of patient care during the pandemic when medical professionals were forced to apply advanced respiratory support methods on wards because ICU beds were almost completely reserved for intubated patients. During the peak of the COVID-19 pandemic, the prevalence of NIV use outside ICUs was high, involving approximately 12% of hospitalized patients with COVID-19[8]. An additional aggravating circumstance was that health workers with less experience in the field of respiratory support were often involved in the treatment process on the wards and patient monitoring was at a lower level than average in the non-pandemic time. Such real-life studies show that the implementation of advanced methods of respiratory support are also feasible on the wards. Severe respiratory failure with arterial oxygen pressure PaO_2/FiO_2 <150 mm Hg was a significant predictor of failure[8]. Considering this finding, special attention should be paid to these patients and they should be transferred to the ICU in order to be under more vigilant supervision. Decision on the modality of preference primarily depends on the patient's comorbidities, availability of the device, patient's preferences, comfort, and tolerance of the device. In principle, when the application of low-flow oxygen therapy does not achieve adequate oxygenation, clinicians primarily apply HFOT. CPAP and NIV are mainly used when it is estimated that the application of positive pressure could have an additional beneficial effect.

Mask *versus* Helmet Interface

In patients with acute respiratory failure, NIV is primarily administered *via* face mask or helmet interface. Some authors prefer helmet interface over face mask. The advantages of the helmet may be better adhesion of the interface and thus reduced leakage and more accurate delivery of positive end-expiratory

pressure. According to some studies, patients tolerate the helmet better and its use results in greater reduction in respiratory work[9]. A meta-analysis conducted by Ferreyro *et al*. included randomized clinical trials comparing face mask noninvasive ventilation, helmet noninvasive ventilation with standard oxygen therapy in the treatment of adult patients with AHRF. It showed that, when compared with standard oxygen therapy, helmet NIV was associated with a lower risk of intubation than face mask NIV (helmet NIV: risk ratio [RR] 0.26 [95% credible interval {CrI} 0.14-0.46]; face mask NIV: RR 0.76 [95% CrI 0.62-0.90]) and lower mortality (helmet NIV: RR 0.40 [95% CrI 0.24-0.63]; face mask NIV: RR 0.83 [95% CrI 0.68 -0.99])[5]. The HENIVOT was a multicenter randomized clinical study in which the effects of HFOT and helmet NIV were directly compared in patients with COVID-19. A total of 109 patients with moderate to severe hypoxemia (PaO_2/FiO_2 ≤200) were included in the study. Subjects were randomized into HFOT and helmet NIV groups. A significantly lower incidence of intubation in the helmet NIV group than in the HFOT group (30% *vs*. 51%; difference, -21% [95% CI -38% to -3%]; p=0.03) and a higher number of invasive mechanical ventilation-free days at 28 days in the helmet NIV than in the high-flow nasal oxygen group (28 [IQR, 13-28] *vs*. 25 [IQR 4-28]; mean difference, 3 days [95% CI 0-7]; p=0.04) was observed[10]. Aliberti *et al*. investigated the effect of helmet CPAP and COVID-19 in patients with AHRF (median (IQR) PaO_2/FiO_2 ratio 142.9 (96.7-203.2)). Median FiO_2 of 0.6 (0.5-0.6) and mean ± SD *positive end-expiratory pressure (*PEEP) of 10.8±2.3 cm H_2O were initially applied. When CPAP treatment was initiated, the PaO_2/FiO_2 ratio significantly improved (205.6 (140.0-271.1), p<0.0001). Median duration of helmet CPAP treatment was 6 (3-10) days. Only four patients discontinued helmet CPAP because of intolerance; 55.4% of patients improved during the HDU stay, were weaned to oxygen therapy and transferred to the general ward[11]. The advantage of helmet interface is that it enables delivery of a constant and stable amount of PEEP with free-flow systems and a PEEP valve, with no need for a ventilator. This is particularly useful in the time of the pandemic and lack of ventilators in certain centers. Also, these systems are simple and require shorter staff training in relation to the handling and maintenance of ventilators[12,13]. An additional advantage of the helmet is that it fits better, with less leakage than face mask, so it has a lower risk of environmental contamination and nosocomial transmission of infections[14]. Moreover, high-efficiency particulate air filters can be positioned on the exhalation port of the device, thus further reducing the risk of viral spread[15].

Settings of Noninvasive Mechanical Ventilation

Studies of invasive mechanically ventilated patients with ARDS have shown that ventilation with high tidal volumes and elevated driving pressures can cause ventilator induced lung injury. We can expect similar consequences in patients who breathe spontaneously, if large driving pressures and large tidal volumes are applied. Accordingly, the concept of patient-self-inflicted lung injury (P-SILI) was developed[16]. The goal of respiratory support is to improve oxygenation and avoid intubation but also to reduce shortness of breath and work of breathing. There is evidence that NIV can reduce inspiratory effort only if sufficient pressure support is applied[17]. Of course, the application of substantial inspiratory pressures results in an increase in tidal volumes[18]. There is concern that if ventilation using high transpulmonary pressures and large tidal volumes continues for a long time, it will further induce progression of lung injury[19]. This is particularly sensitive with NIV because tidal volume and minute ventilation could not be precisely monitored. Goligher *et al*. showed that the benefit of reducing tidal volume on mortality in ARDS patients on mechanical ventilation depends on elastance, which suggests that lung protective ventilation primarily depends on driving pressure rather than tidal volumes[20].

With the onset of the pandemic, numerous societies issued guidelines on the management of respiratory failure in COVID-19 patients[4,21,22]. They generally agree that in hypoxic COVID-19 patients in whom conventional oxygen therapy is not sufficient, the next step of treatment should be HFOT. In cases HFOT is not available or HFOT fails and there is no urgent indication for endotracheal intubation, noninvasive pressure support is suggested. Winck and Scala suggest that the primary type of noninvasive pressure support should be CPAP modality. It is recommended to start CPAP if PaO_2/FiO_2 <200 or PaO_2 <60 mm Hg or respiratory rate (RR) >30 with the use of oxygen

or HFOT. Considering previously well-known beneficial effect of CPAP in patients with obesity hypoventilation syndrome, the use of CPAP is recommended even earlier in patients with body mass index (BMI) of 30 kg/m^2, already when PaO_2/FiO_2 <300 or oxygen saturation (SpO_2) <93% with the use of oxygen in a flow rate greater than 5L/min. CPAP should be administered with an initial pressure of 10 cm H_2O. The authors advise not to apply inspiratory pressures higher than 12-13 cm H_2O in order to avoid barotrauma, P-SILI or negative hemodynamic effect[23]. In contrast, the Guidelines of the Italian Thoracic Society allow the application of pressures during CPAP therapy up to 15-20 cm H_2O[21]. Target SpO_2 values are at least 93% and PaO_2 of 60 mm Hg or higher. In the study by Aliberti *et al.*, lung *recruitability* was defined as an increase of PaO_2/FiO_2 ratio of at least 30% six hours after initiation of CPAP therapy[11]. If CPAP therapy fails, the step-up therapy is NIV. The principles of NIV therapy are similar to those in non-COVID-19 patients. The criteria for starting NIV are PaO_2/FiO_2 <100 and RR ≥30/min or signs of respiratory distress with CPAP. It is suggested to use PEEP 12-16 cm H_2O and set inspiratory positive airway pressure (IPAP) to target *tidal* volume (TV) 4-6 mL/kg. Fraction of inspired oxygen should be applied to achieve SpO_2 of 90%-95%. The lowest effective IPAP and EPAP should be applied in order to avoid further induction of lung injury, as well as *aerosolization*. NIV is the first choice therapy in patients with hypercapnic respiratory failure[23]. Whenever possible, it is recommended to use high performance ventilators because home ventilators usually do not reach an adequate FiO_2[21]. In the acute and subacute phase, continuous monitoring of the electrocardiogram, SpO_2 and systemic blood pressure is needed[21]. It is necessary to check the arterial blood gas analysis an hour after therapy initiation[4]. During the period of discontinuation of the mask in order to rest from CPAP/NIV, to eat or drink, it is important to maintain adequate oxygenation. In these periods, it is recommended to apply HFOT at a flow rate of 50 L/min and FiO_2 to achieve SpO_2 of at least 92%[23]. In patients who require 24-hour CPAP or NIV support, fluid and food intake may be insufficient. It is necessary to take this into account and, if needed, provide parenteral nutrition and fluid replacement[21]. If NIV failure occurs, an experienced team capable of performing intubation should be available. In patients with *hemodynamic* instability, multi-organ failure, abnormal mental status, intolerance of the interface, NIV is not the method of choice. Other options such as invasive ventilation should be primarily considered[24].

Indications for Intubation

Another concern related to the use of noninvasive respiratory support is that it will expose the patient to the risk of delayed intubation and increased mortality[23]. Postponing intubation to the point when it is performed in a condition of emergency may increase the likelihood of complications related to the procedure itself[25]. Also, intubation in emergency conditions presents the risk of incomplete implementation of protective protocols and increases the risk of transmission of infection to *medical staff* involved in the procedure.

The criteria for intubation are not standardized and require judgment of an experienced clinician and individualized approach[26]. Certainly, high-risk patients are those in whom respiratory failure progresses over hours, patients with a permanent need for high pressure support and high FiO_2. Also, a factor independently associated with NIV failure is the previously mentioned PaO_2/FiO_2 <150. It reflects severe respiratory failure and it could probably be used as a simple criterion to decide which patients should undergo early intubation. It is consistent with the risk factors previously reported for other forms of acute hypoxemic respiratory failure[8]. There are other risk factors more specific of COVID-19, such as elevated serum concentrations of C-reactive protein or thrombocytopenia, which are probably a reflection of an hyperinflammatory status or progression towards multiple organ failure[27,28].

In the algorithm proposed by Winck and Scala, the indications for intubation included the presence of either at least 1 major criterion or at least two minor criteria lasting for ≥1 h. Major criteria included respiratory arrest; respiratory pause with unconsciousness; severe hemodynamic instability (i.e., *systolic blood pressure* <90 mm Hg instead of adequate volume resuscitation); and intolerance of the interface that results in discontinuation of the device. Minor criteria included reduction of ≥30% of basal PaO_2/FiO_2 ratio; PaO_2/FiO_2 ratio <100; 20% increase of arterial carbon dioxide tension if basal arterial carbon dioxide tension

was ≥40 mm Hg; worsening of alertness; new onset or persistent respiratory distress; SpO2 <90%; and exhaustion[23]. The same criteria were used in the work of Alberti *et al*.[11].

Self-Pronation

Prone position (PP) has been used for many years in patients with acute respiratory distress syndrome (ARDS) receiving invasive mechanical ventilation with sedation and paralysis. Numerous trials demonstrated the effectiveness of PP in improving oxygenation[29,30]. An important element of the overall success and outcome is the duration of PP application. In 2013, Guérin *et al*. found that prone ventilation should be employed for at least 16 h/day in order to reduce mortality[31]. Pronation can improve lung mechanics and facilitate ventilation. PP results in partially reduced cardiac and abdominal compression on the lung parenchyma and consequently increases recruitment of the dorsal lung regions. By decompression of the dorsal parts of the lungs, which are larger in volume than the frontal ones, a greater percentage of alveoli are open. This enables ventilation at a lower pressure and achievement of targeted oxygenation by applying a smaller fraction of oxygen. This reduces the likelihood of lung injury caused by mechanical ventilation. Also, since pulmonary perfusion is distributed better to the dorsal lung regions, the overall alveolar ventilation perfusion ratio improves[32]. Additionally, this position facilitates drainage of the dorsal parts of the lungs and removal of secretions[33]. PP has been studied in awake COVID-19 patients in whom noninvasive respiratory support was applied. Ding *et al*. evaluated the efficacy of early PP combined with either HFOT or NIV in preventing intubation in patients with moderate to severe ARDS. There is evidence that early prone in combination with either NIV or HFOT may reduce the intubation rate in patients with moderate ARDS. The largest increase in PaO_2/FiO_2 was recorded in the group in which NIV was combined with PP[34]. Sartini *et al*. evaluated the effect of PP in COVID-19 patients using NIV. It was shown that PP was associated with improved oxygenation, increased PaO_2/FiO_2 ratio, and decreased respiratory rate[35]. However, the results of studies are not uniform. In a randomized open-label trial on COVID-19 patients who were on oxygen therapy or NIV, awake proning did not significantly reduce the rate of intubation, mortality, ventilator-free days, or ICU-free days[36]. Considering the lack of clinical evidence, in recently published recommendations for the care of COVID-19 patients, the Society of Critical Care Medicine (SCCM) provided no recommendation for PP in nonintubated patients[37]. Nevertheless, clinicians recognized the potential of PP in improving oxygenation and possibly preventing intubation. Awake proning has some peculiarities. Given that patients on NIV are awake, the duration of the prone trial significantly depends on the patient's tolerance of the position. Many patients find this position uncomfortable; the equipment puts pressure on their face or neck or they cannot sleep in PP. Unfortunately, the improvement in gas exchange obtained in PP may be lost once they return to the supine position[38]. Thus, it is recommended that patients stay in PP as long as possible. If an improvement in oxygenation is noticed after the first hour, the patient should be stimulated to stay in that position as long as possible, at least 6-8 hours a day[23].

Conclusion

Noninvasive respiratory support is an effective method of treating respiratory failure in COVID-19 patients. If performed by an experienced team, it can significantly reduce the need for invasive mechanical ventilation, and save ICU resources. Although COVID-19 is caused by a single pathogen, the heterogeneity of clinical presentation has been recognized, so there is no single strategy that fits all patients. This is why individualized approach and careful monitoring of each patient is extremely important. Although since the beginning of the pandemic, research has been significantly accelerated and knowledge gathered, additional research is needed to further define the role and principles of management of acute hypoxemic respiratory failure in COVID-19 patients.

References

1. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, *et al*. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020 Mar 17;323(11):1061-9. doi: 10.1001/jama.2020.1585.
2. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020 Apr 7;323(13):1239-42. doi: 10.1001/jama.2020.2648.

3. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, *et al*. clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020 Apr 30;382(18):1708-20. doi: 10.1056/NEJMoa2002032.
4. Alhazzani W, Møller MH, Arabi YM, Loeb M, Gong MN, Fan E, *et al*. Surviving sepsis campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). Intensive Care Med. 2020 May;46(5):854-87. doi: 10.1007/s00134-020-06022-5.
5. Ferreyro BL, Angriman F, Munshi L, Del Sorbo L, Ferguson ND, Rochwerg B, *et al*. Association of noninvasive oxygenation strategies with all-cause mortality in adults with acute hypoxemic respiratory failure: a systematic review and meta-analysis. JAMA. 2020 Jul 7;324(1):57-67. doi: 10.1001/jama.2020.9524.
6. Perkins GD, Ji C, Connolly BA, Couper K, Lall R, Baillie JK, *et al*. Effect of noninvasive respiratory strategies on intubation or mortality among patients with acute hypoxemic respiratory failure and COVID-19: the RECOVERY-RS Randomized Clinical Trial. JAMA. 2022 Feb 8;327(6):546-58. doi: 10.1001/jama.2022.0028.
7. Franco C, Facciolongo N, Tonelli R, Dongilli R, Vianello A, Pisani L, *et al*. Feasibility and clinical impact of out-of-ICU noninvasive respiratory support in patients with COVID-19-related pneumonia. Eur Respir J. 2020 Nov 5;56(5):2002130. doi: 10.1183/13993003.02130-2020.
8. Bellani G, Grasselli G, Cecconi M, Antolini L, Borelli M, De Giacomi F, *et al*. Noninvasive ventilatory support of patients with COVID-19 outside the intensive care units (WARd-COVID). Ann Am Thorac Soc. 2021 Jun;18(6):1020-6. doi: 10.1513/AnnalsATS.202008-1080OC.
9. Amirfarzan H, Cereda M, Gaulton TG, Leissner KB, Cortegiani A, Schumann R, *et al*. Use of helmet CPAP in COVID-19 – a practical review. Pulmonology. 2021 Sep-Oct;27(5):413-22. doi: 10.1016/j.pulmoe.2021.01.008.
10. Grieco DL, Menga LS, Cesarano M, Rosà T, Spadaro S, Bitondo MM, *et al*. Effect of helmet noninvasive ventilation *vs* high-flow nasal oxygen on days free of respiratory support in patients with COVID-19 and moderate to severe hypoxemic respiratory failure: the HENIVOT randomized clinical trial. JAMA. 2021 May 4;325(17):1731-43. doi: 10.1001/jama.2021.4682.
11. Aliberti S, Radovanovic D, Billi F, Sotgiu G, Costanzo M, Pilocane T, *et al*. Helmet CPAP treatment in patients with COVID-19 pneumonia: a multicentre cohort study. Eur Respir J. 2020 Oct 15;56(4):2001935. doi: 10.1183/13993003.01935-2020.
12. Bellani G, Patroniti N, Greco M, Foti G, Pesenti A. The use of helmets to deliver non-invasive continuous positive airway pressure in hypoxemic acute respiratory failure. Minerva Anestesiol. 2008 Nov;74(11):651-6.
13. Foti G, Sangalli F, Berra L, Sironi S, Cazzaniga M, Rossi GP, *et al*. Is helmet CPAP first line pre-hospital treatment of presumed severe acute pulmonary edema? Intensive Care Med. 2009 Apr;35(4):56-62. doi: 10.1007/s00134-008-1354-7.
14. Pisani L, Mega C, Vaschetto R, Bellone A, Scala R, Cosentini R, *et al*. Oronasal mask *versus* helmet in acute hypercapnic respiratory failure. Eur Respir J. 2015 Mar;45(3):691-9. doi: 10.1183/09031936.00053814.
15. Lucchini A, Giani M, Isgró S, Rona R, Foti G. The "helmet bundle" in COVID-19 patients undergoing noninvasive ventilation. Intensive Crit Care Nurs. 2020 Jun;58:102859. doi: 10.1016/j.iccn.2020.102859.
16. Sullivan ZP, Zazzeron L, Berra L, Hess DR, Bittner EA, Chang MG. Noninvasive respiratory support for COVID-19 patients: when, for whom, and how? J Intensive Care. 2022 Jan 15;10(1):3. doi: 10.1186/s40560-021-00593-1.
17. L'Her E, Deye N, Lellouche F, Taille S, Demoule A, Fraticelli A, *et al*. Physiologic effects of noninvasive ventilation during acute lung injury. Am J Respir Crit Care Med. 2005 Nov 1;172(9):1112-8. doi: 10.1164/rccm.200402-226OC.
18. Kallet RH, Diaz JV. The physiologic effects of noninvasive ventilation. Respir Care. 2009 Jan;54(1):102-15.
19. Rochwerg B, Brochard L, Elliott MW, Hess D, Hill NS, Nava S, *et al*. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. Eur Respir J. 2017 Aug 31;50(2):1602426. doi: 10.1183/13993003.02426-2016.
20. Goligher EC, Costa ELV, Yarnell CJ, Brochard LJ, Stewart TE, Tomlinson G, *et al*. Effect of lowering vt on mortality in acute respiratory distress syndrome varies with respiratory system elastance. Am J Respir Crit Care Med. 2021 Jun 1;203(11):1378-85. doi: 10.1164/rccm.202009-3536OC.
21. Italian Thoracic Society (ITS-AIPO) and Italian Respiratory Society (IRS-SIP). Managing the respiratory care of patients with COVID-19. [cited 2022 Jul 30]. Available from: http://www.aiponet.it/
22. BTS/ICS Guidance: Respiratory care in patients with acute hypoxaemic respiratory failure associated with COVID-19. [cited 2022 Jul 30]. Available from: http://www.brit-thoracic.org.uk
23. Winck JC, Scala R. Non-invasive respiratory support paths in hospitalized patients with COVID-19: proposal of an algorithm. Pulmonology. 2021 Jul-Aug;27(4):305-12. doi: 10.1016/j.pulmoe.2020.12.005.
24. World Health Organization. Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected. Interim guidance – 13 March 2020. [cited 2022 Jul 30]. Available from: http://www.who.int
25. McKown AC, Casey JD, Russell DW, Joffe AM, Janz DR, Rice TW, *et al*. Risk factors for and prediction of hypoxemia during tracheal intubation of critically ill adults. Ann Am Thorac Soc. 2018 Nov;15(11):1320-7. doi: 10.1513/AnnalsATS.201802-118OC.
26. Azoulay E, de Waele J, Ferrer R, Staudinger T, Borkowska M, Povoa P, *et al*. International variation in the management of severe COVID-19 patients. Crit Care. 2020 Aug 5;24(1):486. doi: 10.1186/s13054-020-03194-w.
27. Yamada T, Wakabayashi M, Yamaji T, Chopra N, Mikami T, Miyashita H, *et al*. Value of leukocytosis and elevated C-reactive protein in predicting severe coronavirus 2019 (COVID-19): a systematic review and meta-analysis. Clin Chim Acta. 2020 Oct;509:235-43. doi: 10.1016/j.cca.2020.06.008.
28. Chen W, Li Z, Yang B, Wang P, Zhou Q, Zhang Z, *et al*. Delayed-phase thrombocytopenia in patients of coronavirus disease 2019 (COVID-19). Br J Haematol. 2020 Jul;190(2):179-84. doi: 10.1111/bjh.16885.

29. Abroug F, Ouanes-Besbes L, Elatrous S, Brochard L. The effect of prone positioning in acute respiratory distress syndrome or acute lung injury: a meta-analysis: areas of uncertainty and recommendations for research. Intensive Care Med. 2008 Jun;34(6):1002-11. doi: 10.1007/s00134-008-1062-3.
30. Alsaghir AH, Martin CM. Effect of prone positioning in patients with acute respiratory distress syndrome: a meta-analysis. Crit Care Med. 2008 Feb;36(2):603-9. doi: 10.1097/01.CCM.0000299739.98236.05.
31. Guérin C, Reignier J, Richard JC, Beuret P, Gacouin A, Boulain T, *et al*. Prone positioning in severe acute respiratory distress syndrome. N Engl J Med. 2013 Jun 6;368(23):2159-68. doi: 10.1056/NEJMoa1214103.
32. Koulouras V, Papathanakos G, Papathanasiou A, Nakos G. Efficacy of prone position in acute respiratory distress syndrome patients: a pathophysiology-based review. World J Crit Care Med. 2016 May 4;5(2):121-36. doi: 10.5492/wjccm.v5.i2.121.
33. Zanella A, Cressoni M, Epp M, Hoffmann V, Stylianou M, Kolobow T. Effects of tracheal orientation on development of ventilator-associated pneumonia: an experimental study. Intensive Care Med. 2012 Apr;38(4):677-85. doi: 10.1007/s00134-012-2495-2.
34. Ding L, Wang L, Ma W, He H. Efficacy and safety of early prone positioning combined with HFNC or NIV in moderate to severe ARDS: a multi-center prospective cohort study. Crit Care. 2020 Jan 30;24(1):28. doi: 10.1186/s13054-020-2738-5.
35. Sartini C, Tresoldi M, Scarpellini P, Tettamanti A, Carco F, Landoni G, *et al*. Respiratory parameters in patients with COVID-19 after using noninvasive ventilation in the prone position outside the intensive care unit. JAMA. 2020 Jun 9;323(22):2338-40. doi: 10.1001/jama.2020.7861.
36. Ibarra-Estrada MÁ, Marín-Rosales M, García-Salcido R, Aguirre-Díaz SA, Vargas-Obieta A, Chávez-Peña Q, *et al*. Prone positioning in non-intubated patients with COVID-19 associated acute respiratory failure, the PRO-CARF trial: a structured summary of a study protocol for a randomised controlled trial. Trials. 2020 Nov 23;21(1):940. doi: 10.1186/s13063-020-04882-2.
37. Alhazzani W, Evans L, Alshamsi F, Moller MH, Ostermann M, Prescott HC, *et al*. Surviving sepsis campaign guidelines on the management of adults with coronavirus disease 2019 (COVID-19) in the ICU: first update. Crit Care Med. 2021 Mar 1;49(3):e219-e234. doi: 10.1097/CCM.0000000000004899.
38. Retucci M, Aliberti S, Ceruti C, Santambrogio M, Tammaro S, Cuccarini F, *et al*. Prone and lateral positioning in spontaneously breathing patients with COVID-19 pneumonia undergoing noninvasive helmet CPAP treatment. Chest. 2020 Dec;158(6):2431-5. doi: 10.1016/j.chest.2020.07.006.

Sažetak

NEINVAZIVNA MEHANIČKA VENTILACIJA U AKUTNOJ RESPIRACIJSKOJ INSUFICIJENCIJI ZBOG COVID-19

G. Pavliša, K. Gašparović, H. Puretić, L. Ljubičić, A. Nekić, V. Vuković, K.Vukančić i A. Vukić Dugac

*Bolest uzrokovana novim koronavirusom 2019 (*COVID-19) prezentira se širokim rasponom simptoma, od asimptomatske bolesti do teške i progresivne intersticijske upale pluća. Kao dio intersticijske pneumonije respiracijska insuficijencija tipično je obilježena hipoksijom i najčešći je uzrok hospitalizacije. Kada terapija kisikom ne uspije, kontinuirani pozitivni tlak u dišnim putovima (CPAP) ili neinvazivna mehanička ventilacija (NIV) mjere su respiracijske potpore prvog izbora. Neinvazivna respiracijska potpora (NIRS) primjenjuje se kako bi se uštedjeli resursi jedinica intenzivnog liječenja i izbjegle komplikacije povezane s invazivnom mehaničkom ventilacijom. Uporaba CPAP-a ili NIV-a u liječenju akutne hipoksemične respiracijske insuficijencije kod COVID-19 smanjuje potrebu za intubacijom i smrtnost. Prednost NIRS-a je da se može provoditi na odjelima. NIV se može primijeniti preko maske ili kacige. Kaciga bolje prianja u odnosu na masku i stoga je smanjen gubitak zraka, isporuka pozitivnog tlaka na kraju izdisaja je točnija, a rizik od nozokomijalnog prijenosa infekcija je manji. Bolesnici na NIRS-u moraju se pažljivo nadzirati kako se ne bi previdjelo daljnje respiracijsko pogoršanje i kako bi se mogle provesti dodatne mjere skrbi uključujući pravodobnu intubaciju i invazivnu mehaničku ventilaciju.

Ključne riječi: *Bolest uzrokovana novim koronavirusom 2019; Respiracijska insuficijencija; Kontinuirani pozitivni tlak u dišnim putovima; Neinvazivna mehanička ventilacija; Neinvazivna respiracijska potpora*