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High Flow Nasal Cannula Versus Noninvasive Positive Pressure Ventilation as Initial Respiratory Support in Patients with Chronic Obstructive Pulmonary Disease and Covid-19: Exploratory Analysis in Two Intensive Care Units

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Abstract

Objective. To identify the type of the non-invasive ventilatory treatment for patients diagnosed with chronic obstructive pulmonary disease (COPD), with respiratory status deteriorated by COVID-19 pneumonia, and in need of treatment in the Intensive Care Unit (ICU). **Materials and Methods.** This cross-sectional study was conducted over a one-year period in the medical intensive care units of two hospitals. As the patients' clinical condition deteriorated and the parameters of the arterial blood gas (ABG) analysis worsened, oxygen support was applied via a high flow nasal cannula (HFNC) or by non-invasive positive pressure ventilation (NPPV). According to the control values of the arterial oxygen saturation (SaO_2) and the parameters of ABG, the patients were enabled to be transferred between the two types of non-invasive ventilatory support. The primary outcome was the length of hospital stay, while secondary outcomes were the rate of intubation, the mortality rate, and respiratory support-free days. **Results.** Out of 21 critical patients with COPD and COVID-19, 11 (52.4%) were initially treated with NPPV and 10 (47.6%) with HFNC. The ages (67±9.79 in NPPV group vs. 70.10±10.25 in HFNC group) and severity of illness (SOFA score 5 (3.5) in NPPV group vs. 5 (2.8) in HFNC group) were similar between the two groups. Switching the mode of respiratory support was more common in NPPV (58.3% in survivor group vs. 41.7% in non-survivor group). Patients treated with NPPV compared to HFNC had a nominally longer length of stay (15 (11) vs. 11.5 (4.25)), and higher risk of intubation (66.7% vs. 33.3%) and mortality (66.7% vs. 33.3%), but the comparisons did not reach statistical significance. Survivors had significantly longer Medical Intensive Care Unit and hospital stays, but significantly lower FiO_2 (0.60 vs.1) and higher values of PaO_2/FiO_2 (78(32.4) vs. 56.3(17.8)) than non-survivors. All patients were treated with corticosteroids, and the duration of treatment was similar between groups. **Conclusion.** In critically ill patients with COPD and COVID-19, both HFNC and NPPV were commonly used as the initial mode of ventilation. Switching to a different mode and adverse patient outcomes were more frequent in patients initially treated with NPPV. Survivors had higher values of PaO_2/FiO_2 than non-survivors.

Key Words: COPD ▪ HFNC ▪ NPPV ▪ COVID-19 Pneumonia.

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Introduction

The SARS CoV2 virus usually infects the respiratory system, causing severe pneumonia. Patients with acute respiratory failure (ARF) require intensive care treatment, with a subsequent need for ventilators (1-3). High-flow nasal cannula oxygen therapy (HFNC) and non-invasive positive pressure ventilation (NPPV) are widely used in patients experiencing ARF as alternatives to standard oxygen therapy, to avoid invasive mechanical ventilation (IMV) (4). In addition, awake prone positioning in spontaneously breathing patients is a therapeutic intervention for COVID-19 respiratory failure, and is expected to reduce the treatment failure when combined with HFNC or NPPV (5).

The infection with SARS CoV2 appears to be more severe in patients with chronic obstructive pulmonary disease (COPD), and in smokers, due to tobacco exposure that leads to an alteration in the regulation of an angiotensin-converting enzyme 2 (ACE-2) and its overexpression. The levels of ACE-2 are inversely related to the forced expiratory volume in the first second (FEV1) (6). Preexisting COPD often leads to severe deterioration of symptoms, and a 4–5.9-fold greater risk of developing a severe form of COVID-19, compared to patients without it (7, 8).

Patients who develop a moderate or severe form of COVID-19 requiring hospitalization should be treated with the current pharmacotherapeutic agents, including treatment with corticosteroids (9). HFNC should be preferred over NPPV in acute hypoxemic respiratory failure, noted in severe COPD cases, despite conventional, low-flow oxygen therapy, due to the lower failure rate (10, 11). NPPV can potentially worsen lung injury due to the high transpulmonary pressure and tidal volume (12). The patients on HFNC or NPPV should be monitored closely for deterioration of their clinical status and early intubation, leading to IMV (13, 14). Understanding COPD's pathophysiology leads to the hypothesis that NPPV will reduce the number of ICU days compared to HFNC. The data regarding COPD treatment with severe COVID-19 is insufficient for low- and middle-income countries due, in the first instance, to limitations in the available oxygen resources and apparatus providing high flow oxygenation treatment and noninvasive ventilatory support (15).

Methods

This cross-sectional study, including 21 patients, was conducted in the period from June 2020-December 2021 in two hospital facilities' Medical Intensive Care Units (MICU) in the Western Balkans: the University Clinical Center of Republika Srpska, Banja Luka, and Prim. Dr. Abdulah Nakaš General Hospital, Sarajevo.

The study population comprised patients diagnosed with COVID-19 pneumonia and COPD, without respiratory acidosis, identified on the day of hospital admission according to arterial blood gas analysis ($7.35 \leq pH \leq 7.45$). As their clinical condition deteriorated and the parameters of the arterial blood gas (ABG) analysis worsened, determined by a decrease in the partial arterial pressure of oxygen (PaO_2) ≤60 mmHg (milimeters of mercury), there was an increase in the partial arterial pressure of carbon dioxide ($PaCO_2$) ≥50 mmHg, or arterial oxygen saturation decreased (SaO_2) ≤92%, despite the oxygen support delivery via an oronasal mask with 15l/min flow, patients were admitted to the Intensive Care Unit (ICU). Chest X-ray analysis or computed tomography (CT) chest scan (due to technical limitations) was performed on the day of hospital admission to confirm the diagnosis of pneumonia, and repeatedly with the deterioration of the patient's clinical and respiratory status. According to the parameters of SaO_2 and the parameters of ABG, oxygen support via HFNC or NPPV was applied. Once the HFNC was initiated, the fraction of inspired oxygen (FiO_2) as a percentage (%) and the oxygen flow rate (l/min) were recorded.

Two methods of NPPV were applied: continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP) with recordings of the values of NPPV. However, the therapeutic effectiveness of these non-invasive modes was not further evaluated individually through the results of the study due to the small sample size.

HFNC treatment was initiated for patients with SpO_2 <88% under oxygen supply (O_2) at 15 L/min and/or PaO_2/FiO_2 <150. HFNC treatment was applied with a properly fitted nasal cannula, and the application was initiated and titrated according to the following: oxygen flow raised from 30 L/min until 60 L/min to accustom the patient; FiO_2 to maintain peripheral oxygen saturation (SpO_2 90-92%); temperature 31–37°C, according to the patient's comfort level.

CPAP ventilatory support was initiated in patients if PaO_2/FiO_2 <200 or PaO_2 <60 mmHg (while on oxygen or HFNC) or if PaO_2/FiO_2 <300 or SpO_2 <88% on O_2 >15 L/min and the patient had BMI >30. BiPAP was initiated in patients if PaO_2/FiO_2 <100 or with respiratory distress under CPAP. The FiO_2 initial value in both centers was 100% with a gradual decrease in value according to the peripheral SpO_2 and the parameters of arterial ABG. Suggested parameters for BiPAP initiation include PEEP 10-12 cmH_20 and a pressure support (PS) set, with the aim of tidal volume (VT) 4–6 ml/kg and FiO_2 aimed at a target of SpO_2 90-92%. In the case of clinical deterioration and respiratory distress, BiPAP was assigned as the first treatment option in patients with hypercapnic respiratory failure (pH<7.3, $PaCO_2$ ≥50mmHg). The criteria for endotracheal intubation were: respiratory arrest, respiratory pause with unconsciousness, severe hemodynamic instability (i.e., systolic blood pressure (SBP) <90 mmHg instead of adequate volume resuscitation), and intolerance to CPAP leading to discontinuation of the device, if after 4 hours of CPAP, PaO_2/FiO_2 was decreasing, with a respiratory rate (RR) ≥30, and PaO_2 <60 mmHg. Once invasive mechanical ventilation was initiated, the most commonly used ventilation mode was synchronized intermittent mandatory ventilation (SIMV). The parameters for the invasive mechanical ventilation should be set up in concordance with a "lung protective" ventilation strategy, but they are not currently under consideration within the framework of this study.

According to the control values of SaO_2, the parameters of ABG and clinical follow-up aimed at improvement of ventilatory status, the patients were enabled to transfer between two types of non-invasive ventilatory support (HFNC and NPPV). The ratio of oxygen saturation (ROX index) was calculated within every 24 hours. Accordingly, HFNC failure was determined if ROX was below 2.85 at 2 hours, below 3.47 at 4 hours; or below 3.85 at 12 hours. CPAP failure was determined if PaO_2/FiO_2 <100 or there was a 20% increase in $PaCO_2$. BiPAP failure was determined by the criteria reached for endotracheal intubation. The termination of the non-invasive ventilatory support by HFNC/NPPV was determined by the improvement in the patient's clinical condition (SpO_2 ≥92%), and by an increase in the values of ABG (PaO_2 ≥60 mmHg or SaO_2 ≥92%), with a gradual decrease in peripheral oxygen supply. Awake proning was performed for the patients on HFNC once ventilatory support was initiated, and in certain cases of invasive mechanical ventilation, according to clinical case-by case decisions.

The following laboratory tests were conducted on the day of admission to the ICU: complete blood cell count (CBC), differential blood cell count, including neutrophil granulocytes (Neu), lymphocytes (Lym), monocytes (Mon), and eosinophil granulocytes (Eos), C reactive protein (CRP), D-dimer, parameters of ABG: partial arterial pressure of oxygen and carbon dioxide (PaO_2, $PaCO_2$ respectively), pH value, bicarbonate level (HCO_3) and base excess (BE) according to the reference range values.

All patients, on the day of admission to the hospital, were assigned the following descriptive parameters: gender, age, smoking status (smoker, non-smoker), and comorbidities (chronic heart failure, arterial hypertension, acute coronary syndrome, obesity, diabetes mellitus type II, and chronic renal insufficiency). The following parameters were calculated on the day of admission to the ICU: body mass index (BMI) and Sequential Organ Failure Assessment (SOFA) score. The SOFA score was calculated for all patients admitted to the ICU to determine the level of organ dysfunction (based on the dysfunction of six organ systems) and mortality risk. Arterial blood gas analysis (ABG) was taken on the day of admission to the hospital and the day of admission to the ICU.

On admission to the ICU, some patients underwent prone positioning. The therapeutic procedures consisted of using corticosteroids in various doses, and duration of treatment. After serious clinical, diagnostic, and laboratory parameter evaluation, some patients were treated with monoclonal antibody-tocilizumab. The primary outcome was the length of hospital stay. The secondary outcomes were: the rate of intubation, the death rate (survivor, non-survivor), and respiratory support-free days.

Statistical Analysis

The data are expressed as the mean and standard deviation for normally distributed, or as the median and interquartile range for not normally distributed continuous variables and counts with percentages for categorical variables. The normality of data distribution was tested using the Kolmogorov-Smirnov test. A comparison of measures for continuous variables was performed by using the Mann– Whitney U and Student's t-tests. As appropriate, a proportion comparison was calculated using the Pearson Chi-square test and Fisher's exact test. The Kaplan Meier test was used for survival analysis. The analyses were performed using IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp. A P value <0.05 was considered significant. We calculated the odds ratio (OR) for intubation between the groups of patients treated with different ventilatory modes.

Results

A total of 21 confirmed COVID-19 pneumonia and COPD patients, of which 13 were men (61.9%), with a mean age of 67.9±9.7 years, were included in the study. Thirteen (61.9%) of the evaluated patients were current smokers. Chronic heart failure (CHF) was identified as the most common comorbidity in 10 patients (47.6%). Once transferred to the MICU, in 11 patients (52.4%), NPPV was the preferred mode of non-invasive ventilatory support. A ventilation mode switch, regardless of the deterioration or improvement of respiratory distress and clinical status, was identified in 12 (57.1%) patients (Table 1). Patients treated with NPPV had higher intubation and mortality rates compared to the patients treated with HFNC, but the difference did not reach statistical significance (Table 2). Moreover, patients on NPPV were switched to another ventilation mode significantly more often than patients on HFNC, as shown in Table 3.

Table 1. Demographic and Clinical Characteristics of COPD* Patients with COVID-19 Treated with NPPV†/HFNC‡

Demographic and clinical characteristics	All patients (N=21)	NPPV† (N=11)	HFNC‡ (N=10)	P value
Age (years) (mean±SD)	67.9±9.7	67±9.79	70.10±10.25	0.516§
Male sex (N; %)	13 (61.9)	8 (61.5)	5 (38.5)	0.201‖
SOFA** (median, IQR)	5 (3)	5 (3.5)	5 (2.8)	0.91 ¶
BMI†† (mean±SD)	27.3±5.4	27.62±6.01	26.33±3.77	0.635§
CHF‡‡ (N; %)	10 (47.6)	7 (70)	3 (30)	0.890‖
Smoker (N; %)	13 (61.9)	10 (76.9)	3 (23.1)	0.477‖
Ventilation mode switch (N; %)	12 (57.1)	11 (91.7)	1 (8.3)	0.018‖
Prone position (N; %)	11 (52.4)	8 (72.7)	3 (27.3)	0.890‖
Vasopressors (N; %)	2 (9.5)	1 (50)	1 (50)	0.481‖
Corticosteroids (N; %)	21 (100)	15 (71.4)	6 (28.6)	-
Tocilizumab (N; %)	5 (23.8)	3 (60)	2 (40)	0.517‖

*Chronic obstructive pulmonary disease; †Non-invasive positive pressure ventilation/‡High flow nasal cannula; §Student's t-test; ‖Pearson's Chi-square test; ¶Mann-Whitney U test; **Sequential Organ Failure Assessment; ††Body Mass Index; ‡‡Chronic Heart Failure

Table 2. Comparison of Intubation and Mortality Rates Between COPD* Patients with COVID-19 Treated with NPPV†/HFNC‡

Comparison of intubation and mortality rates	All patients (N=21)	NPPV† (N=11)	HFNC‡ (N=10)	P value
Hospital stay, days (median, IQR)	14 (8.5)	15 (11)	11.5 (4.25)	0.256§
Intubation (N; %)	12 (57.1)	8 (66.7)	4 (33.3)	0.577‖
Mortality (N; %)	12 (57.1)	8 (66.7)	4 (33.3)	0.577‖

*Chronic obstructive pulmonary disease; †Non-invasive positive pressure ventilation/‡High flow nasal cannula; §Mann-Whitney U test; ‖Pearson's Chi-square test.

Table 3. Clinical Characteristics Between Survivor and Non-survivor COPD* Patients with COVID-19 Treated with NPPV†/HFNC‡

Clinical characteristics between survivor and non-survivor	Survivor (N=9)	Non-survivor (N=12)	P value
Age (years) (mean±SD)	63.6±8.9	71.17±9.4	0.07§
Male sex (N; %)	6 (46.2)	7 (53.8)	0.70‖
Hospital stay, days (median, IQR)	20 (24)	11 (5)	0.01¶
ICU** stay days (mean±SD)	12.3±7.7	6.7±2.6	0.03§
Respiratory support free days (median, IQR)	1 (2)	0	0.004¶
Smoker (N; %)	5 (38.5)	8 (61.5)	0.60‖
††CHF (N; %)	6 (60)	4 (40)	0.13‖
Ejection fraction (%) (mean±SD)	55±9.1	47.3±11	0.28§
Arterial hypertension (N; %)	5 (33.3)	10 (66.7)	0.16‖
Acute coronary syndrome (N; %)	3 (50)	3 (50)	0.67‖
Diabetes mellitus type 2 (N; %)	3 (50)	3 (50)	0.67‖
‡‡BMI (mean±SD)	26.3±3.6	27.9±6.5	0.51§
SaO_2 (%) (mean±SD)	74.3±12.2	80.5±10.5	0.23§
Initial setting Prone position (N; %)	7 (63.6)	4 (36.4)	0.04‖
Initial setting NPPV (N; %)	7 (46.7)	8 (53.3)	0.58‖
Duration of initial setting, days (median, IQR)	5 (6)	3.5 (3.75)	0.08¶
Switch to different setting (N; %)	7 (58.3)	5 (41.7)	0.09‖
Duration of secondary setting, days (median, IQR)	3 (7.5)	0 (1.75)	0.07¶
PaO_2 (mmHg) (median, IQR)	49.3 (19.9)	53.5 (17.2)	0.34¶
FiO_2 (decimal) (median, IQR)	0.60 (0.35)	1 (0.08)	0.01¶
PaO_2/FiO_2 (mmHg/decimal) (median, IQR)	78 (32.4)	56.3 (17.8)	0.03¶
Platelets ($x10^9$ /L) (mean±SD)	253.9±69.5	204.67±96.2	0.21§
Glasgow comma score – reduced consciousness (N; %)	1 (20)	4 (80)	0.24‖
Billirubin (umol/L) (median, IQR)	7.8 (8)	12.2 (6.7)	0.57¶
Mean arterial pressure (mmHg) (mean±SD)	101.4±12.3	87.7±16.1	0.04§
Vasopressor (N; %)	1 (50)	1 (50)	0.83‖
Creatinine (umol/L) (median, IQR)	86 (14)	91 (36.2)	0.32¶
§§SOFA score (median, IQR)	5 (3.5)	5 (2.8)	0.91¶
Leukocytes ($x10^9$ /L) (median, IQR)	8.8 (5.8)	12.3 (9.2)	0.20¶
Hemoglobin (g/L) (mean±SD)	133.7±17.7	144±19.5	0.23§
Hematocrit (1) (mean±SD)	0.41±0.07	0.43±0.05	0.37§
Neutrophils (%) (mean±SD)	79.8±12.2	87.8±9.5	0.11§
Lymphocytes (%) (median, IQR)	13 (21.8)	4.7 (11.8)	0.19¶

Table 3 (Continued)

Clinical characteristics between survivor and non-survivor	Survivor (N=9)	Non-survivor (N=12)	P value
C-reactive protein (mg/L) (median, IQR)	44.7 (69.7)	60.7 (140.1)	0.12¶
D-dimer (g/L) (median, IQR)	1.5 (9.3)	2.4 (8.2)	0.48¶
$PaCO_2$ (mmHg) (median, IQR)	32.03(45.75)	42.0 (23.25)	0.32¶
HCO_3 (mmol/L) (mean±SD)	24.6±7.4	27.5±5.5	0.37§
pH (median, IQR)	7.45 (0.05)	7.42 (0.08)	0.47¶
BE (mmol/L) (median, IQR)	1 (6.5)	2.9 (5.8)	0.39¶
Duration of corticosteroid therapy, days (median, IQR)	14 (4.5)	11.5 (5)	0.11¶
Tocilizumab (N; %)	3 (60)	2 (40)	0.38‖

*Chronic obstructive pulmonary disease; †Non-invasive positive pressure ventilation/‡High flow nasal cannula; §Student's t-test; ‖Pearson's Chi-square test; ¶Mann-Whitney U test; **Intensive care unit, ††Chronic heart failure, ‡‡Body mass indeks, §§Sequential Organ Failure Assessment.

We calculated the odds ratio (OR) for intubation between the groups of patients treated with different ventilatory modes, and found that it was 1.75 times more likely in patients on NPPV compared to HFNC (OR=1.75, 95% CI 0.242–12.642). The relative risk (RR) for intubation in patients on NPPV was 1.4 (95% CI 0.399–4.907). Table 3 compares the clinical characteristics of survivors and non-survivors, showing that survivors had significantly longer MICU and hospital stay compared to non-survivors. In addition, a considerably higher number of patients in the survival group were placed in the prone position, and these patients had significantly lower FiO_2 and higher values of PaO_2/FiO_2 compared to non-survivors. PaO_2/FiO_2 and FiO_2 values in Table 3 refer to mean calculations from initiation of the specific noninvasive ventilation mode up to half an hour of measurement. All patients were treated with corticosteroids, and the duration of treatment was similar between the groups. Tocilizumab was used somewhat more often in the survivors' group.

Although arterial hypertension was more frequent in the non-survivor group (66.7%), with a decrease in the mean value of the ejection fraction (47.3±11), it did not reach statistical significance in comparison to survivors. Diabetes mellitus type II showed the same occurrence rate (50%) between survivors and non-survivors.

Survival analysis was presented using a Kaplan-Meier curve. The survival rate in patients on HFNC was slightly higher, but the difference between the groups did not reach statistical significance. In the curve, a slightly higher intubation rate is seen in patients on NPPV, but this difference also did not reach statistical significance (Figure 1).

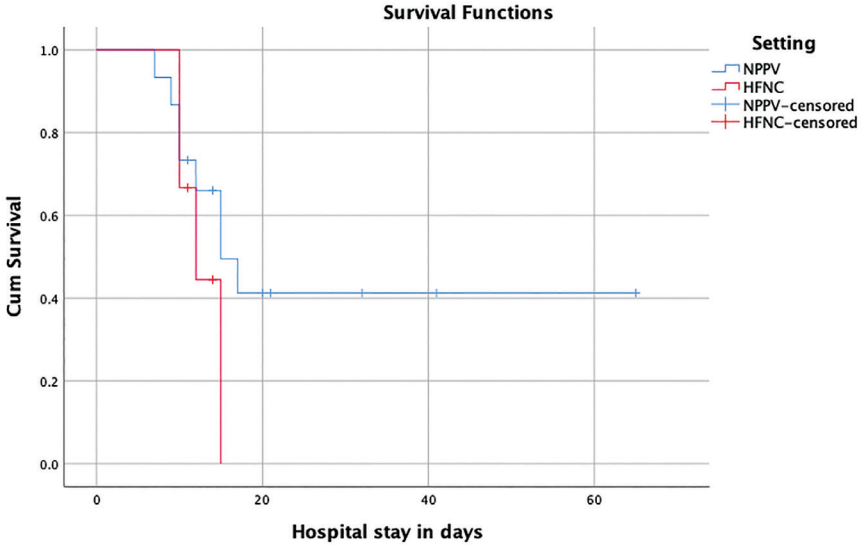

Figure 1. Kaplan Meier curve: test of equality of survival distribution in Chronic obstructive pulmonary disease of patients with COVID -19 treated with *Non-invasive positive pressure ventilation and †High flow nasal cannula.

Discussion

According to the results of our study, even though NPPV was the preferred mode of non-invasive ventilatory support, patients on NPPV were switched to another ventilation mode significantly more often than patients on HFNC. A significantly higher number of COPD patients in the survival group had significantly higher values of PaO_2/FiO_2 ratio and lower FiO_2 values compared to non-survivors, which is in concordance with the favorable clinical outcome. Our results correlate with the study by Grasseli et al., who evaluated risk factors associated with mortality among patients with COVID-19 in intensive care units in Lombardy, Italy. They identified several independent risk factors associated with mortality, including: older age, male sex, a high fraction of inspired oxygen (FiO_2) and low PaO_2/FiO_2 ratio on ICU admission, and a history of chronic obstructive pulmonary disease (16). Patients treated with NPPV in our study had prolonged overall hospital stay due to the more severe clinical course of the disease. The duration of ICU stay days was also prolonged for survivors in our study compared to non-survivors. The switch to another mode of ventilatory setting in our study occurred more frequently in the survivor group, most probably due to the successful treatment.

In half of the patients in our study, treatment was initiated with NPPV due to their deteriorated clinical condition, resulting in survival for 46.7% of them. In contrast, the results of the study by Sun J. et al., accounting for 82 COPD patients, identified treatment failure in 39.5% of patients treated with NIV (17). No significant differences were found for 28-day mortality in the same study (15.4% in the HFNC group and 14% in the NIV group, P=0.824). However, in our study, mortality and intubation rates were twice as high for NPPV than HFNC (66.7% and 33.3%, respectively), but the difference did not reach statistical significance. According to the previous findings it is indicative that patients with NPPV were in a worse condition than patients with HFNC at the time of the treatment initiation, as well as that the patients with BIPAP were in worse condition than those with CPAP.

The values of $PaCO_2$ in our study were lower in the survivor group compared to the non-survivors, but the difference did not reach statistical significance. Moreover, meta-analyses involving 525 COPD patients with hypercapnic respiratory failure indicated that HFNC could significantly reduce $PaCO_2$ levels and the length of hospital stay, without greatly influencing PaO_2 level, the incidence of tracheal intubation, and mortality rate compared to NIV (18). A randomized, controlled trial by Li et al. evaluated COPD patients with acute compensated hypercapnic respiratory failure, and identified that HFNC improved the prognosis compared to conventional oxygen therapy, with a reduction in $PaCO_2$, but also identified the value of $PaCO_2$ higher than 59 mmHg as an independent risk factor for treatment failure after 24 hours (19). The pH value in arterial blood gas analysis was decreased in non-survivors compared to the survivor group, yet it did not reach the level of acidosis or statistical significance. However, a randomized controlled trial by Cortegiani et al. assessed the potential of HFNC compared to non-invasive ventilatory support (NIV) in the reduction of $PaCO_2$ in patients with hypercapnic ARF with mild-to-moderate respiratory acidosis, and determined the benefit of treatment with HFNC, especially in cases of COPD exacerbations, as an alternative to NIV (20).

Acute coronary syndrome was equal in appearance (a total of three cases in survivors as well as in the non-survivor group) without reaching statistical significance between the groups in our study, but arterial hypertension was more common among non-survivors. The study by Sheikh et al. associated patients with COVID-19 pneumonia suffering from COPD with more cardiovascular events and extended hospital stays (21). According to their results, the presence of COPD was associated with 1.74 higher odds of ICU admission and 1.47 higher odds of death.

The study of Chen et al. evaluated the predictors of the severity of COVID-19 in patients suffering from underlying chronic airway disease, and

identified: elevated neutrophil counts (P=0.001), decreased lymphocyte counts (P<0.001), eosinopenia (P<0.001), elevated D-dimer levels (P=0.001), increased LDH (P<0.001), elevated blood urea nitrogen (P<0.001), and increased inflammation markers, including CRP (P<0.001) as potential indicators of disease progression and treatment effectiveness (22). These results correlate with the findings of our study, where in the non-survivor group neutrophil count, D-dimer values, and C reactive protein levels were much higher compared to the survivor group, along with the decrease in lymphocyte count, but that difference did not reach statistical significance.

Limitations of the Study

The main limitations of our study are related to the small number of subjects. Another limitation relates to the finding that patients with NPPV were in a worse condition than patients with HFNC when choosing the initial treatment. There are also possible confounding factors that might have affected the observed small differences between the study arms, such as baseline lung function and severity of preexisting COPD, treatment adherence among patients before onset of COVID-19, the time between symptom onset and medical care, that have not been evaluated in this study. Moreover, further investigations, implying more accurate results and proper treatment directions, should be conducted in the future.

Conclusion

In this exploratory study, noninvasive ventilation and high flow oxygen were commonly used as initial respiratory support for COVID-19 respiratory failure in patients with COPD. Switching between the modes was common. Patients initially treated with high flow oxygen had overall better outcomes but the comparisons did not reach statistical significance.

What Is Already Known on This Topic:

Patients diagnosed with COPD and COVID-19 can be evaluated for several ventilatory support strategies, depending on the type of respiratory failure (hypoxaemic or hypercapnic or acute on chronic respiratory failure) including oxygen supplementation, HFNC or noninvasive ventilatory support (CPAP, BiPAP) (23). Insufficiently controlled hypoxaemia in such patients demands application of noninvasive ventilatory support, with HFNC as the first line of treatment in patients with COVID-19 and acute hypoxaemic respiratory failure (11). The benefits of HFNC in COPD and COVID-19 patients are related to the reduction in hypercapnia and the work of breathing (24). However according to the available data, in patients with COPD with acute (or chronic) hypercapnic respiratory failure, NPPV is determined as the first line of treatment, regardless of the previously stated benefits of HFNC (25). COPD and COVID-19 burden in developing countries has been recently questioned. According to the available data COVID-19 case-fatality rates are relatively higher in countries with higher COPD prevalence (26). The strong correlation between COPD prevalence and COVID-19-related mortality in developing nations could be related to differences in level of comorbidities among patients, or to inequalities in distribution of healthcare resources (15).

What This Study Adds:

Since this study accounted for a significantly small number of COPD patients with severe hypoxaemic respiratory failure due to COVID-19, no optimal treatment strategy using either NPPV or HFNC was identified. However, since the survival rate in our study was higher on HFNC and the intubation rate was higher on NPPV, it led us to undertake a further obligation to identify the optimal timing for HFNC application to prevent further clinical deterioration and pending intubation. This study was conducted in the lack of oxygen resources and noninvasive positive pressure ventilators within the environment of the middle-income country, providing the insight in the most appropriate approach to COPD patients with COVID-19 requiring the intensive care treatment.

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