Turk J Intensive Care 2022;20(Suppl 1):91-8
DOI: 10.4274/tybd.galenos.2022.52244

Ayşe Müge Karcıoğlu,
Hatice Zeynep Atlı,
Oğuz Karcıoğlu,
Işıl Özkoçak Turan

The Evaluation of COVID-19 Patients Treated with HFNC in Intensive Care Unit

Yoğun Bakımda HFNO ile Tedavi Edilen COVİD-19 Hastalarının Değerlendirilmesi

Received/Geliş Tarihi : 06.04.2022
Accepted/Kabul Tarihi : 14.06.2022

©Copyright 2022 by Turkish Society of Intensive Care Turkish Journal of Intensive Care published by Galenos Publishing House.

Ayşe Müge Karcıoğlu
University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Intensive Care, Ankara, Turkey

Hatice Zeynep Atlı, Işıl Özkoçak Turan
Ankara City Hospital, Clinic of Intensive Care, Ankara, Turkey

Oğuz Karcıoğlu
Hacettepe University Faculty of Medicine, Department of Chest Diseases, Ankara, Turkey

Ayşe Müge Karcıoğlu MD (✉),
University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Intensive Care, Ankara, Turkey

E-mail : aysemugeturker@gmail.com
Phone : +90 507 755 59 88
ORCID ID : orcid.org/0000-0002-2154-7975

ABSTRACT *Objective:* Since the coronavirus disease-2019 (COVID-19) pandemic caused respiratory failure in many patients, oxygen delivery methods had to be diversified, and their numbers increased. High flow nasal cannula (HFNC), which has been shown beneficial in acute respiratory failure previously, also came to the fore. We investigated the efficacy of HFNC on patients hospitalized in intensive care units due to COVID-19.
Materials and Methods: We retrospectively screened the patients followed up in the intensive care unit due to COVID-19. Patients treated with HFNC performed the study group. We analyzed the relationships among demographics, laboratory results, treatment modalities, complications, and outcomes.
Results: Among the 330 patients including mean ventilation duration with HFNC was 7.84 days. One hundred seventy (51.5%) patients were intubated during HFNC treatment. Only 5 of them were extubated. Intubated patients had higher mean HFNC duration [9.74 days - minimum (min): 2 , maximum (max): 49] compared to non-intubated patients (6.05 days - min: 1, max: 30). There was a significant relationship between mortality and age [Odds ratio (OR): 1.04], Acute Physiology and Chronic Health Evaluation-II score (OR: 1.35), having cancer (OR: 3.89), receiving non-invasive ventilation (OR: 5.94), and presence of secondary bacterial infection (OR: 44.6).
Conclusion: HFNC, whose benefit in acute respiratory failure has been proven, is also widely and successfully used in COVID-19 patients. Comprehensive randomized studies are required to demonstrate the effect of HFNC use on intubation requirement and mortality.
Keywords: Ventilation, mortality, COVID-19, respiratory failure, pneumonia, oxygen therapy

ÖZ *Amaç:* Koronavirüs hastalığı-2019 (COVİD-19) pandemisi nedeniyle solunum yetmezliği gelişen hastalarda oksijen desteği için farklı cihazlar ve yöntemler kullanılmıştır. Bu yöntemlerden birisi de daha önce akut solunum yetmezliğinde faydalı olduğu gösterilen yüksek akımlı nazal kanüldür (HFNO). Bu çalışmada, COVİD-19 nedeniyle yoğun bakım ünitelerinde yatan hastalarda HFNO'nun etkinliğinin araştırılması amaçlanmıştır.
Gereç ve Yöntem: COVİD-19 nedeniyle yoğun bakımda takip edilen hastalar geriye dönük olarak tarandılar. Yoğun bakım yatışı sırasında HFNO ile tedavi edilen hastalar çalışma grubunu oluşturdu. Demografik veriler, laboratuvar sonuçları, tedavi modaliteleri, komplikasyonlar ve klinik sonuçlar arasındaki ilişki incelendi.
Bulgular: Dahil edilen 330 hasta arasında HFNO ile ortalama ventilasyon süresi 7,84 gündü. Yüz yetmiş (%51,5) hasta HFNO tedavisi sırasında entübe edilmişti. Bunlardan sadece 5'i ekstübe olabilmişti. Entübe edilen hastaların ortalama HFNO alma süresi [9,74 gün - minimum (min): 2, maksimum (maks): 49] entübe olmayan hastalara (6,05 gün - min: 1, maks: 30) göre daha yüksekti. Mortalite ile yaş [olasılık oranı (OR): 1,04], Akut Fizyoloji ve Kronik Sağlık Değerlendirmesi-II skoru (OR: 1,35), kanser öyküsü (OR: 3,89), non-invaziv ventilasyon uygulanması (OR: 5,94) ve sekonder bakteriyel enfeksiyon varlığı (OR: 44,6) arasında anlamlı bir ilişki vardı.
Sonuç: Akut solunum yetmezliğinde faydası kanıtlanmış olan HFNO'nun, COVİD-19 hastalarında da yaygın ve başarılı bir şekilde kullanıldığı görülmüştür. HFNC kullanımının entübasyon gereksinimi ve mortalite üzerindeki etkisini göstermek için kapsamlı randomize çalışmalara ihtiyaç vardır.
Anahtar Kelimeler: Ventilasyon, mortalite, COVİD-2019, solunum yetmezliği, pnömoni, oksijen tedavisi

Introduction

High flow nasal cannula oxygen therapy (HFNC) is a relatively new oxygen delivery system for adults. It allows the delivery of oxygen at the desired level reliably. It also provides heated and humidified gas, enhancing patients' comfort, decreasing breathing work, and preventing airway epithelium injury. Nasal usage and its soft and flexible prongs allow a more tolerable procedure for patients. An easy-adjust and straightforward interface makes it -user-friendly- for doctors.

The positive impact of HFNC in acute respiratory failure patients was shown previously in various studies (1-3). Severe acute respiratory syndrome coronavirus-2 pandemic [coronavirus disease-2019 (COVID-19)], as a disease causing acute respiratory failure, resulted in increased need for intensive care units (ICU) and depletion of medical supplies such as mechanic ventilators, ventilation sets, and oxygen masks. Although early intubation was preferred at first, this approach was abandoned, and higher intubation thresholds were used (4). So HFNC became a vital tool for oxygen delivery. Despite previous studies reporting usage rates up to 65 percent, the benefits of HFNC in preventing intubation were not shown (5-7). Nevertheless, higher intubation thresholds and high usage rates of HFNC in the literature suggest it may decrease the intubation rates in case of appropriate use.

In this study, we aimed to investigate the clinical features, and outcomes of COVID-19 patients treated with HFNC in ICUs. The primary outcome of the study is the determine the clinical, laboratory, and radiological findings and outcomes of COVID-19 patients treated with HFNC. The secondary outcome was to identify factors associated with death.

Materials and Methods

We included the adult patients followed in the COVID-19 ICUs of the tertiary health center between 01.08.2020 and 01.01.2021. We gathered the medical information of the patients retrospectively by evaluating their records. We collected the basal demographic data, comorbidities, previous history of long-term oxygen therapy, and continuous positive airway pressure, Acute Physiology and Chronic Health Evaluation-II (APACHE-II) scores, length of hospitalization, polymerase chain reaction test results, computerized thorax tomography findings, and laboratory results. Complications including secondary bacterial pneumonia, pneumothorax, pulmonary thromboembolism (PTE) were recorded. Concomitant non-invasive ventilation (NIV) use, intubation, and extubation information data were collected. We obtained the data from the computerized database of the hospital.

HFNC was performed with Fisher & Paykel HealthCare, Airvo™ 2, and Inspired O2FLO™. GE Healthcare Carescape R860 mechanic ventilator was used for non-invasive and invasive mechanical ventilation.

The study protocol was approved by the Institutional Ethical Committee of Ankara City Hospital (decision no: E1/1463/2021, date: 20.01.2021).

Statistical Analysis

SPSS software version 23.0 was used for statistical analysis. Descriptive analyses were presented using mean ± standard deviation for normally distributed variables and median and minimum (min)-maximum (max) values for skew distributed variables. Categorical variables were expressed as numbers and percentages (%). For comparison between groups, Mann-Whitney U test and t-test were used for continuous variables, and the chi-square test was used for categorical variables. Logistic regression analysis will be used to evaluate the relationship between independent variables.

Selection of Patients

We retrospectively reviewed 987 patients followed in the ICU between 01.08.2020 and 01.01.2021. We excluded 115 patients because they stayed in ICU lower than 48 hours. Two hundred sixty six patients received nasal or mask oxygen. One hundred twenty seven patients were admitted as intubated and 5 patients with tracheostomy to the ICU. One hundred forty four patients were intubated in ICU while they were receiving nasal or mask oxygen. The remaining 330 patients treated with HFNC constituted the study group (Figure 1).

Results

We included 330 patients with a mean age of 66,7 (min 27 - max: 95). Two hundred twenty seven (68.8%) patients were male 103 (31.2%) were female. The mean APACHE-II score was 11.6 (min: 3, max: 28). The most common comorbidities were hypertension (HT) and diabetes mellitus (DM), and coronary artery diseases (CAD) (55.2%, 34.8%, and 20.9%) respectively). Median PaO_2/FiO_2 was 101.6 (40-223). Baseline characteristics of patients are depicted in Table 1.

Table 1. Baseline characteristics				
		HFNC (106)	**HFNC + NIV (224)**	**Total (330)**
Age	Median, min-max	68.0 (31-88)	66.6 (27-95)	66.7 (27-95)
Sex	Female/male (F/M)	39/67	64/160	103/227
Comorbidities (n, perc)				
Hypertension		55 (51.9%)	127 (56.7%)	182 (55.2%)
Diabetes mellitus		37 (34.9%)	78 (34.8%)	115 (34.8%)
CAD		27 (25.5%)	42 (18.8%)	69 (20.9%)
COPD		12 (11.3%)	17 (7.6%)	29 (8.8%)
Cancer		10 (9.4%)	18 (8.0%)	28 (8.5%)
Heart failure		7 (6.6%)	20 (8.9%)	27 (8.2%)
Asthma		7 (6.6%)	13 (5.8%)	20 (6.1%)
CKD		7 (6.6%)	10 (4.5%)	17 (5.2%)
CVD		2 (1.9%)	11 (4.9%)	13 (3.9%)
Demans		6 (5.7%)	4 (1.8%)	10 (3%)
PaO_2/FiO_2 median, min-max*		116 (44-223)	92.5 (40-217)	101.7 (40-223)

HFNC: High flow nasal cannula, NIV: non-invasive ventilation, min: minimum, max: maximum, CAD: coronary artery disease, COPD: chronic obstructive pulmonary disease, CKD: chronic kidney disease, CVD: cerebrovascular disease, n: number, perc: percentage, *PaO_2/FiO_2 was calculated at the beginning of HFNC

The primary laboratory abnormalities were lactate dehydrogenase (LDH), interleukin-6 (IL-6), and C-reactive protein (CRP) levels were increased in 330 (100%), 324 (97.3%), and 319 (97.3%) individuals, respectively. Two hundred eighty four (86.1%) had lymphopenia. Laboratory results are summarized in Table 2.

Computed thorax tomography revealed multilobar ground-glass infiltration consistent with COVID-19 in 327 (99.1%) patients. Two patients had simultaneous PTE at first admission. During follow-up, 3 more patients developed PTE, and 6 patients developed pneumothorax. There may be more concomitant PTE underdiagnosed due to non-contrast computed tomographies.

All patients received favipiravir, 18 patients received remdesivir, and 2 patients received ritonavir-lopinavir as antiviral treatment. We observed that most patients received immunosuppressant therapy due to severe disease. Treatment modalities are presented in Table 3.

The mean ventilation duration with HFNC was 7.84 days. Two hundred twenty-four of 330 (67.9%) patients were applied non-invasive mechanic ventilation concomitantly. Intubation was performed in 170 (51.5%) patients during

Table 2. Laboratory results			
Lab (med, min-max)	**HFNC (106)**	**HFNC + NIV (224)**	**Total (330)**
WBC ($x10^9$/L)	9.13 (2.83-108.7)	9.19 (0.12-22.94)	9.17 (0.12-108.7)
Neutrophile ($x10^9$/L)	7.64 (0.82-17.09)	8.03 (0.04-21.27)	7.90 (0.04-21.27)
Lymphocyte ($x10^9$/L)	0.57 (0.05-82.74)	0.54 (0.02-36.0)	0.55
Sedimentation* (mm/h)	47.5 (5.0-140.0)	38 (3-123)	42 (3-140)
CRP (g/L)	0.13 (0.001-0.360)	0.136 (0.001-0.54)	0.134 (0.001-0.540)
Procalcitonin (mcg/L)	0.19 (0.03-78.83)	0.23 (0.02-35.04)	(0.02-78.8)
IL-6 (pg/mL)	51.4 (2.0-2020)	44.15 (1.30-1703.0)	44.95 (1.3-2020)
LDH (u/L)	516 (159-2058)	552 (179-1396)	(159-2058)
Ferritin (mcg/L)	624 (22-33743)	702 (23-10795)	676 (22-33743)

*199 patients had sedimentation results. CRP: C-reactive protein, min: minimum, max: maximum, WBC: white blood cell, IL-6: interleukin-6, LDH: lactate dehydrogenase, HFNC: high flow nasal cannula, NIV: non-invasive ventilation, min: minimum, max: maximum, med: median

Table 3. Treatment modalities			
Drugs	**HFNC (106)**	**HFNC + NIV (224)**	**Total (330)**
Antivirals			
Favipiravir	106 (100%)	220 (100%)	330 (100%)
Remdesivir	2 (1.9%)	16 (7.1%)	18 (5.5%)
Ritonavir-lopinavir	1 (0.9%)	1 (0.4%)	2(0.2%)
Immun-modulators			
Tocilizumab	23 (21.7%)	28 (12.5%)	51 (15.5%)
Anakinra	7 (6.6%)	23 (10.3%)	30 (9.1%)
Steroid	95 (89.6%)	221 (98.7%)	316 (95.8%)
Pulse	42 (39.6%)	120 (53.6%)	162 (49.1%)
Maintenance*	98 (92.5%)	220 (98.2%)	318 (96.4%)
Others			
Hydroxychloroquine	47 (44.3%)	81 (36.2%)	126 (38.2%)
Colchicine	14 (13.2%)	124 (55.4%)	114 (34.5%)
Convalescent plasma	19 (17.9%)	37 (16.5%)	56 (17%)
Cytokine filter	1 (0.9%)	27 (12.1%)	28 (8.5%)
Immune-globulin	1 (0.9%)	3 (1.3%)	4 (1.2%)

*58% of the patients received maintenance steroid treatment as methylprednisolone and 42% as dexamethasone. Pulse steroid has been administered in different dosages (250 mg, 500 mg, 1 gr). HFNC: High flow nasal cannula, NIV: non-invasive ventilation

HFNC treatment. Only 5 of them were extubated. Intubated patients had higher mean HFNC duration (9.74 days - min: 2, max: 49) compared to non-intubated patients (6.05 days - min: 1, max: 30) (Figure 2).

The mean length of stay in ICU was 13.9 days for all study group. Patients who received NIV stayed in ICU (14.4 days) longer than those who did not receive NIV (12.7 days) (p=0.019). Similarly, the non-NIV group has a lower intubation rate (36.8%) than the NIV received group (58.5%).

There was documented secondary bacterial pneumonia in 71 (41.7%) intubated patients. The most seen agents are *Acinetobacter* spp. (40), *Clostridium striatum, Staphylococcus aureus* (8), and *Klebsiella* spp. (8). We couldn't obtain a respiratory specimen from non-intubated individuals.

Of the 155 patients who transferred to the COVID general ward, 7 were transferred to another ICU for further follow-up, and 5 were discharged home. During ICU stay, 163 patients (49.4%) died. Examination of the relationship between comorbidities and mortality revealed that there was a statistically significant relationship between the presence of heart failure (p=0.007), HT (p=0.04), cerebrovascular disease (p=0.04), and cancer (p=0.01) and mortality. The only treatment modality with a statistically significant relationship

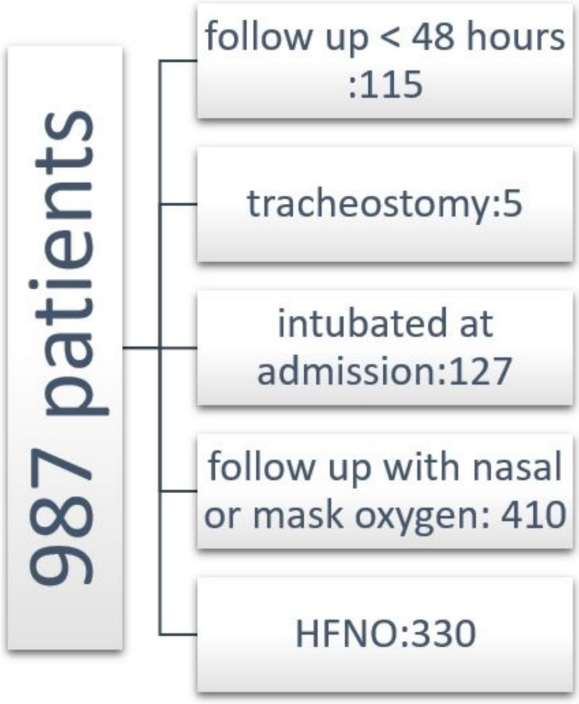


Figure 1. Study design

Table 4. APACHE-II scores							
		HFNC (106)		HFNC+ NIV (224)		Total (330)	
APACHE-II (med, min-max)		10.0 (3-28)		11.0 (3-26)		11.0 (3-28)	
Point	Expected mortality	n	Observed mortality	n	Observed mortality	n	Observed mortality
0-4 point (n, perc)	4%	8 (7.5%)	0%	5 (2.2%)	20%	13 (3.9%)	7.7%
5-9 point (n, perc)	8%	35 (33.0%)	2.9%	66 (29.5%)	16.7%	101 (30.6%)	11.9%
10-14 point (n, perc)	15%	38 (35.8%)	44.7%	95 (42.4%)	66.3%	133 (40.3%)	79.2%
15-19 point (n, perc)	24%	16 (15.1%)	68.8%	40 (17.9%)	90%	56 (17.0%)	83.9%
20-24 point (n, perc)	40%	9 (8.5%)	88.9%	18 (8.0%)	83.3%	27 (8.2%)	85.2%

APACHE-II: Acute Physiology and Chronic Health Evaluation-II, HFNC: High flow nasal cannula, NIV: non-invasive ventilation, med: median, n: number, min: minimum, max: maximum, perc: percentage

with mortality was cytokine filter (p=0.001). Among laboratory results, increased CRP (p=0.004) and procalcitonin (p=0.001) levels were associated with mortality. The range of observed mortality was higher than expected mortality in whole group (7.7%-85.2%, 4%-40%, respectively). While mortality observed in patients with an APACHE-II score below 10 was lower than expected in the HFNC group and slightly higher than expected in the HFNC + NIV group, the mortality rates in patients with an APACHE-II score of 10 and above were much higher than expected in both groups (Table 4). We made logistic regression analysis to determine independent factors associated with mortality. We found that mortality was increasing with age (OR: 1.04), APACHE-II score (OR: 1.35), having cancer (OR: 3.89), receiving NIV (OR: 5.94), and presence of secondary bacterial infection (OR: 44.6).

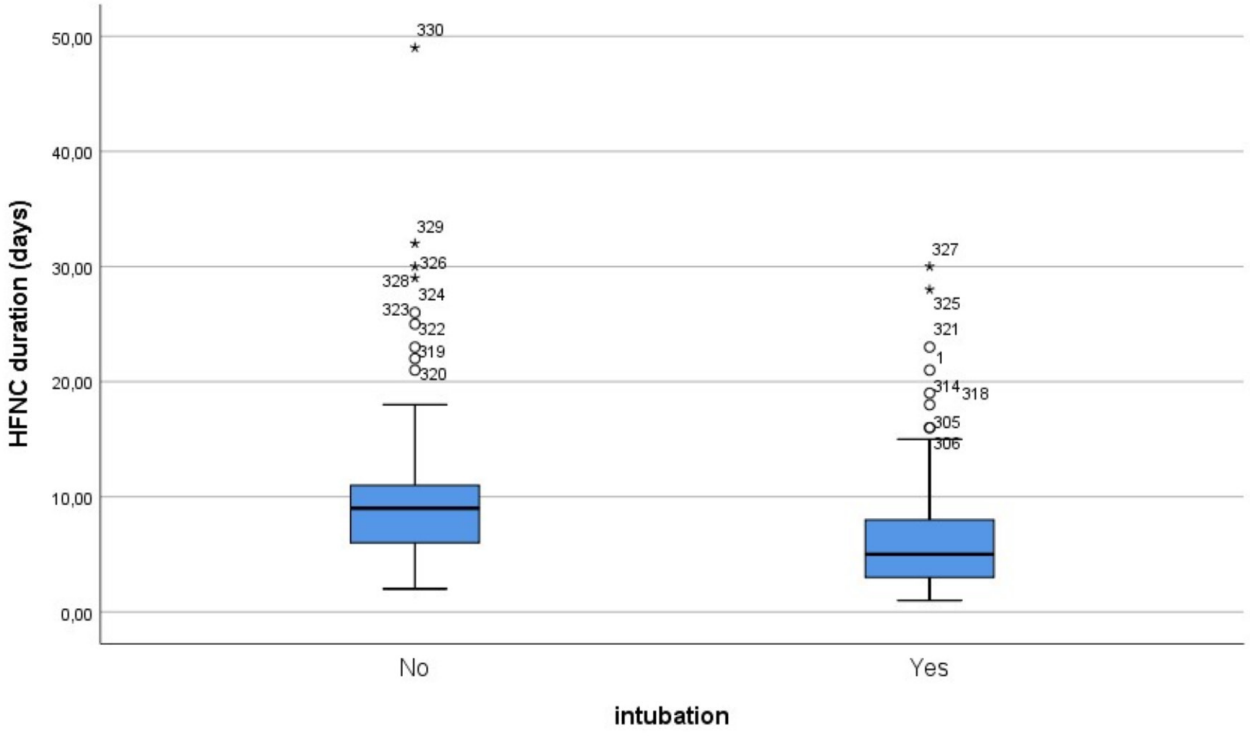


Figure 2. Comparison of HFNC durations between intubated and non-intubated patients
HFNC: High flow nasal cannula

Discussion

In this retrospectively designed study, we investigated clinical, laboratory, and radiological characteristics of COVID-19 patients treated with HFNC hospitalized in the ICU for the primary outcome, and we found that most of the patients were elderly (med: 66.7) and the most common comorbidities were HT, DM, and CAD. LDH, IL-6, and CRP were increased in almost all patients, and the most common radiologic finding was multilobar ground-glass infiltration. While the mean ICU stay of the patients was 13.9 days, HFNC was applied for a mean of 7.8 days; approximately two-thirds of patients received NIV concomitantly and half of them were intubated. During ICU stay, 163 patients (49.4%) died, and logistics regression showed that advanced age, higher APACHE-II score, cancer, receiving NIV, and secondary bacterial infection were significantly associated with mortality as the secondary outcome.

Most of our patients were elderly and had comorbidities consistent with the literature. In a study on the use of HNFC in severe COVID-19 patients, the median age of the patients was 61, and the most common diseases were HT, DM and CAD (8) A meta-analysis investigating ICU admissions of COVID-19 patients also showed that 85% of patients were >70 age years old (9). HT, DM, and CAD were listed as most common comorbidities in several studies (10,11). These findings seem to reflect intensive care patients' general characteristics rather than the use of HFNC. Considering that our patients were also treated with HFNC in the ICU, it is not surprising that the findings were similar.

Though its use is viewed with suspicion as it may cause increased aerosol production initially, NIV has been used in many centers during the COVID-19 period. We also used NIV in many patients with acute respiratory failure due to COVID-19. We found that NIV plus HFNC group had shorter HFNC duration and longer hospitalization time than those receiving HFNC alone. Duan et al. (12) compared HFNC and NIV as first-line therapy. They chose one of these and used the latter as rescue treatment. They stated no difference between groups regarding total HFNC + NIV duration, intubation rate, and mortality (12). In another study, Wang et al. (13) investigated the sufficiency of HFNC in critically ill COVID-19 patients and used NIV as a rescue therapy as well. They reported HFNC failure at 41% and intubation rate at 29% (13). A multicenter study examining the mortality rate of patients who underwent intubation after NIV failure also reported a mortality rate of 43% (14). HFNC and NIV have been applied together or consecutively in various countries. However, this was determined not by evidence or guidelines but by countries' availability to access devices.

We found that 48.5% of patients survived the disease without intubation. Only 2.9% of intubated patients could be extubated, and 49.4% of the patients died in total. In the study mentioned above, Celejewska-Wojcik et al. (8) investigated mortality and intubation rate of COVID patients in ICU receiving HFNC prospectively. They reported that 44% of patients required intubation during follow-up and the overall mortality was 30.2% (8). The intubation rate is similar to our study, but the mortality rate is lower than ours. It may be because our patients are more severe. Although we know that these results cannot conclude that HFNC avoids or delays intubation, we can say that it is used effectively in a severe patient group in this period. In addition, considering the positive results of the HFNC in non-COVID patients in terms of intubation in literature, we can deduce that it will be beneficial in this group as well (1,15,16).

There is a long list of risk factors associated with high mortality, including older age (≥65 years), having obesity, HT, diabetes, chronic heart failure, chronic renal disease, chronic liver disease cancer, high D-dimer, high troponin, lymphopenia, neutrophilia, immunosuppression, acute respiratory distress syndrome, male sex obtained from multiple studies (5,17,18). In terms of risk factors associated with mortality, the results of our study are compatible with the literature. We found that concurrent heart failure, cerebrovascular disease, HT, cancer, increased CRP, increased procalcitonin level, and secondary bacterial pneumonia are associated with mortality have been corrected via logistic regression analysis revealed higher age (OR: 1.04), APACHE-II score (OR: 1.35), cancer (OR: 3.89), receiving NIV (OR: 5.94), and secondary bacterial infection (OR: 44.6) independently increased the mortality. Although the APACHE-II score, which has been used to predict ICU mortality for many years (19), also reflects COVID-19 mortality in low scores; mortality was much higher than expected in patients with a high APACHE-II score of 10 or higher. In two separate studies, it was emphasized that the APACHE-II score underestimated mortality in patients hospitalized in ICU due to COVID-19, supporting our findings (20,21). This may be related to the more severe and fatal course of COVID-19 in the elderly and the fact that the majority of patients hospitalized in ICUs are elderly.

Secondary bacterial infections are a relatively less-investigated topic in the literature. Grasselli et al. (22) had

stated that Gram-negative bacteria and *Staphylococcus aureus* were the most common microorganisms cause ventilator-associated pneumonia and doubled the risk of death. Similarly, Gram-negative bacteria (especially *Acinetobacter* spp., *Klebsiella*) and *S. aureus* were the most common isolated bacteria. Albeit it seems that there was a greater risk for culture-positive patients in terms of mortality ($p<0.001$, OR: 44.7), there may not be a direct relationship since we could collect respiratory samples only in intubated patients.

The high number of patients is one of the strengths of our study. Including the NIV and intubation rates, comorbidities, and treatment data improves the power of reflecting real life. The most important limitation of the study is that it does not include data comparing patients with and without HFNC. However, it should be taken into account that the necessity of providing maximum support to all possible patients during the intensive care patient load is excessive may create an ethical problem in this type of study.

Conclusion

Oxygen support and the delivery route were two of the critical issues of the COVID-19 era. This study showed that HFNC is an essential option for oxygen support as it was used nearly in half of the patients without the need for intubation. Although we couldn't conclude that it decreases the intubation and mortality rates, we believe that further prospectively designed studies may help to determine its contributions.

Ethics

Ethics Committee Approval: The study protocol was approved by the Institutional Ethical Committee of Ankara City Hospital (decision no: E1/1463/2021, date: 20.01.2021).

Informed Consent: Retrospective study.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: I.Ö.T., H.Z.A., Design: A.M.K., O.K., Data Collection and Process: O.K., Analysis or Interpretation: O.K., A.M.K., I.Ö.T., Literature Search: H.Z.A., Writing: A.M.K., O.K., H.Z.A., I.Ö.T.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Rochwerg B, Granton D, Wang DX, Helviz Y, Einav S, Frat JP, et al. High flow nasal cannula compared with conventional oxygen therapy for acute hypoxemic respiratory failure: a systematic review and meta-analysis. Intensive Care Med 2019;45:563-72.
2. Sztrymf B, Messika J, Mayot T, Lenglet H, Dreyfuss D, Ricard JD. Impact of high-flow nasal cannula oxygen therapy on intensive care unit patients with acute respiratory failure: a prospective observational study. J Crit Care 2012;27:324.e9-13.
3. Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. N Engl J Med 2015;372:2185-96.
4. Anesi GL, Jablonski J, Harhay MO, Atkins JH, Bajaj J, Baston C, et al. Characteristics, Outcomes, and Trends of Patients With COVID-19-Related Critical Illness at a Learning Health System in the United States. Ann Intern Med 2021;174:613-21.
5. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China. JAMA Intern Med 2020;180:934-43.
6. Myers LC, Parodi SM, Escobar GJ, Liu VX. Characteristics of Hospitalized Adults With COVID-19 in an Integrated Health Care System in California. JAMA 2020;323:2195-8.
7. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. JAMA 2020;323:1574-81.
8. Celejewska-Wójcik N, Polok K, Górka K, Stachura T, Kania A, Nastałek P, et al. High-flow nasal oxygen therapy in the treatment of acute respiratory failure in severe COVID-19 pneumonia: a prospective observational study. Pol Arch Intern Med 2021;131:658-65.
9. Cohen JF, Korevaar DA, Matczak S, Chalumeau M, Allali S, Toubiana J. COVID-19-Related Fatalities and Intensive-Care-Unit Admissions by Age Groups in Europe: A Meta-Analysis. Front Med (Lausanne) 2021;7:560685.
10. Ñamendys-Silva SA, Alvarado-Ávila PE, Domínguez-Cherit G, Rivero-Sigarroa E, Sánchez-Hurtado LA, Gutiérrez-Villaseñor A, et al. Outcomes of patients with COVID-19 in the intensive care unit in Mexico: A multicenter observational study. Heart Lung 2021;50:28-32.
11. Grasselli G, Greco M, Zanella A, Albano G, Antonelli M, Bellani G, et al. Risk Factors Associated With Mortality Among Patients With COVID-19 in Intensive Care Units in Lombardy, Italy. JAMA Intern Med 2020;180:1345-55.
12. Duan J, Chen B, Liu X, Shu W, Zhao W, Li J, et al. Use of high-flow nasal cannula and noninvasive ventilation in patients with COVID-19: A multicenter observational study. Am J Emerg Med 2021;46:276-81.
13. Wang K, Zhao W, Li J, Shu W, Duan J. The experience of high-flow nasal cannula in hospitalized patients with 2019 novel coronavirus-infected pneumonia in two hospitals of Chongqing, China. Ann Intensive Care 2020;10:37.
14. Boscolo A, Pasin L, Sella N, Pretto C, Tocco M, Tamburini E, et al. Outcomes of COVID-19 patients intubated after failure of non-invasive ventilation: a multicenter observational study. Sci Rep 2021;11:17730.
15. Bell N, Hutchinson CL, Green TC, Rogan E, Bein KJ, Dinh MM. Randomised control trial of humidified high flow nasal cannulae versus standard oxygen in the emergency department. Emerg Med Australas 2015;27:537-41.
16. Sayan İ, Altınay M, Çınar AS, Türk HŞ, Peker N, Şahin K, et al. Impact of HFNC application on mortality and intensive care length of stay in acute respiratory failure secondary to COVID-19 pneumonia. Heart Lung 2021;50:425-9.
17. COVID-ICU Group on behalf of the REVA Network and the COVID-ICU Investigators. Clinical characteristics and day-90 outcomes of 4244 critically ill adults with COVID-19: a prospective cohort study. Intensive Care Med 2021;47:60-73.
18. Gupta S, Hayek SS, Wang W, Chan L, Mathews KS, Melamed ML, et al. Factors Associated With Death in Critically Ill Patients With Coronavirus Disease 2019 in the US. JAMA Intern Med 2020;180:1436-47.
19. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med 1985;13:818-29.
20. Beigmohammadi MT, Amoozadeh L, Rezaei Motlagh F, Rahimi M, Maghsoudloo M, Jafarnejad B, et al. Mortality Predictive Value of APACHE II and SOFA Scores in COVID-19 Patients in the Intensive Care Unit. Can Respir J 2022;2022:5129314.
21. Stephens JR, Stümpfle R, Patel P, Brett S, Broomhead R, Baharlo B, et al. Analysis of Critical Care Severity of Illness Scoring Systems in Patients With Coronavirus Disease 2019: A Retrospective Analysis of Three U.K. ICUs. Crit Care Med 2021;49:e105-7.
22. Grasselli G, Scaravilli V, Mangioni D, Scudeller L, Alagna L, Bartoletti M, et al. Hospital-Acquired Infections in Critically Ill Patients With COVID-19. Chest 2021;160:454-5.