Outcomes of Heated High Flow Nasal Cannula in Patients With Severe or Life-Threatening COVID-19 at a Military Treatment Facility—A Retrospective Cohort Study

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ABSTRACT

Introduction:

The coronavirus-19 (COVID-19) pandemic has forced radical changes in management of healthcare in military treatment facilities (MTFs). Military treatment facilities serve unique patients that have a service connection; thus, research and data on this population are relatively sparse. The purpose of this study was to provide descriptive data on characteristics and outcomes of MTF patients with COVID-19 who are treated with heated high-flow nasal cannula (HHFNC).

Materials and Methods:

We performed a single-center retrospective cohort study at the Wright-Patterson Medical Center, a 52-bed hospital in an urban setting. We received approval from our Institutional Review Board. The cohort included patients admitted from June 1, 2020, through May 15, 2021 with severe or life-threatening COVID-19 from a positive severe acute respiratory syndrome–related coronavirus 2 reverse transcription polymerase chain reaction test who were placed on HHFNC during their hospital stay. Severe disease was defined as dyspnea, respiratory rate $\geq$30/min, blood oxygen saturation $\leq$93% without supplemental oxygen, partial pressure of arterial oxygen to fraction of inspired oxygen ratio <300, or lung infiltrates involving >50% of lung fields within 24-48 hours. Life-threatening disease was defined as having septic shock or multiple organ dysfunction or requiring intubation. Patients meeting these criteria were retrieved from a quality improvement cohort that represents a consecutive group of patients with COVID-19 admitted to the Wright-Patterson Medical Center.

Results:

Our MTF managed 70 cases of severe or life-threatening COVID-19 from June 1, 2020, to May 15, 2021. Of the 70 cases, 19 (27%) were placed on HHFNC. After initiation of HHFNC, median SpO_2/FiO_2 was 281.8 and at 24 hours 145.4. Median respiratory rate oxygenation at these times were 10.7 and 9.4, respectively. Fifty percent required mechanical ventilation during hospitalization. Median intensive care unit length of stay was 11 days, with a maximum stay of 39 days. Median hospital length of stay was 12 days, with a maximum of 39 days.

Conclusion:

Our retrospective cohort study characterized and analyzed outcomes observed in a MTF population, with severe or life-threatening COVID-19, who were treated with HHFNC. While the study did not have the power to make concrete conclusions on the optimal form of respiratory support for COVID-19 patients, our data support HHFNC as a reasonable treatment modality despite some notable differences between our cohort and prior studied patient populations.

INTRODUCTION

The number of coronavirus-19 (COVID-19) cases in the United States is now over 33.3 million, with greater than 592,000 deaths (https://covid.cdc.gov/covid-data-tracker/). The scope and scale of this pandemic has forced radical changes in management of healthcare throughout the world with military treatment facilities (MTFs) being no exception. Military treatment facilities serve unique populations only caring for patients that have certain service connections, and thus research and data on this specific population are relatively sparse. Heated high-flow nasal cannula (HHFNC) has been extensively used in the COVID-19 pandemic because it provides non-invasive oxygenation with favorable outcomes in acute respiratory distress syndrome when compared to other modalities.[1] The purpose of this study was to provide data on characteristics and outcomes of MTF patients with COVID-19 who are treated with HHFNC.

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METHODS

We performed a single-center retrospective cohort study at the Wright-Patterson Medical Center, a 52-bed hospital in an urban setting. We received approval from our Institutional Review Board. The cohort included patients admitted from June 1, 2020, through May 15, 2021 with severe or life-threatening laboratory-confirmed COVID-19 who were placed on HHFNC during their hospital stay. Coronavirus-19 infection was confirmed with SARS-CoV-2 reverse transcription polymerase chain reaction test. Severe disease was defined as dyspnea, respiratory rate ≥30/min, blood oxygen saturation ≤93% without supplemental oxygen, partial pressure of arterial oxygen to fraction of inspired oxygen ratio <300, or lung infiltrates involving >50% of lung fields within 24-48 hours.[2] Life-threatening disease was defined as having septic shock or multiple organ dysfunction or requiring intubation.[2] Patients meeting these criteria were retrieved from a quality improvement cohort that represents a consecutive group of patients with COVID-19 admitted to the Wright-Patterson Medical Center. SpO_2/FiO_2 (S/F) was used to quantify oxygenation. Data were collected during the entirety of the patient's hospital stay. Clinical outcomes included intensive care unit (ICU) and hospital length of stay, mechanical ventilation during hospitalization, in-hospital mortality, supplemental oxygen requirement on discharge, S/F at 24 hours after initiation of HHFNC (a validated surrogate for PaO_2/FiO_2(P/F) ratios),[3] and change in S/F ($SPO_2/FiO_{224hrs} - SPO_2/FiO_{2on\ admission}$). Respiratory rate oxygenation (ROX) score was calculated: (SpO_2/FiO_2)/respiratory rate (breaths/minute) 24 hours after initiation of HHFNC. A ROX score of 3.85 is predictive of patient failure of HHFNC and need for intubation[4] and was further validated for use in COVID-19.[5]

TABLE I. Demographics and Clinical Characteristics of 19 Patients with Severe or Life-threatening COVID-19 Who Were Placed on High-flow Nasal Cannula between June 1, 2020, through May 15, 2021, at the Wright-Patterson Medical Center

	$n = 19$
Demographics	
Age (years)	71
Sex (% female)	26
BMI (kg/m^2, %)	28.9
Weight (kg)	90.3
Duty status (%)	
Active duty	5
Retired	79
Family of retired	16
Comorbidities (%)	
Pulmonary (Chronic Obstructive Pulmonary Disease (COPD), Interstitial Lung Disease (ILD), pulmonary hypertension)	16
Obstructive sleep apnea	21
Cardiac disease (Coronary Artery Disease (CAD), Chronic Heart Failure (CHF))	16
Hypertension	58
Chronic kidney disease III, IV, V, or End Stage Renal Disease (ESRD)	16
Diabetes mellitus II	32
Malignancy	11
Clinical data	
BMI < 30 (%)	53
BMI ≥ 30 (%)	47
SpO_2/FiO_2 initial	281.8
ROX initial	10.7
Treatment (%)	
Remdesivir	100
Dexamethasone	100

Continuous variables are reported as medians, and categorical variables are reported as percentages. ROX score (SpO_2/FiO_2)/respiratory rate.
Abbreviations: BMI, body mass index; ROX, respiratory rate oxygenation.

RESULTS

Our MTF managed 70 cases of severe or life-threatening COVID-19 from June 1, 2020, to May 15, 2021. Of the 70 cases, 19 (27%) were placed on HHFNC. Table I reports the demographics and clinical characteristics. The median age was 71 years; one patient was an active duty member, 16% were dependents, and 79% were retired military members (Table I). Sixteen percent had pulmonary disease (chronic obstructive pulmonary disease, diffuse parenchymal lung disease, and pulmonary hypertension), with no patients requiring oxygen at baseline. Twenty-one percent had obstructive sleep apnea, 16% had cardiac disease (coronary artery disease, heart failure), 58% hypertension, 16% chronic kidney disease, and 32% diabetes mellitus II. One patient had a known malignancy. Forty-seven percent were obese (body mass index (BMI) ≥30 kg/m^2). All 19 patients in our cohort received treatments of remdesivir and dexamethasone.

After initiation of HHFNC, median S/F was 281.8 and at 24 hours 145.4. Median ROX at these times were 10.7 and 9.4, respectively. Table II reports the clinical outcomes. Fifty percent required mechanical ventilation during hospitalization. Median ICU length of stay was 11 days, with a maximum stay of 39 days. Median hospital length of stay was 12 days, with a maximum of 39 days. Ninety percent required supplemental oxygen on discharge. Two patients were transferred for extracorporeal membrane oxygenation (ECMO). Four patients (20%) died in the hospital.

DISCUSSION

The purpose of our study was to characterize and study the outcomes of HHFNC use in a small COVID-19 MTF population. While HHFNC has been extensively used throughout the pandemic, its superiority compared with mechanical ventilation or non-invasive positive pressure ventilation (NIPPV) is still unclear, and there are no current published studies comparing these different types of respiratory support at MTFs. There is conflicting evidence in trials such as FLORALI[1] and HENIVOT[7] that HHFNC use in acute hypoxic respiratory failure is a superior modality. FLORALI showed a mortality benefit when compared to NIPPV and mechanical ventilation; however, this trial did not include COVID-19

TABLE II. Demographics and Clinical Characteristics of 19 Patients with Severe or Life-threatening COVID-19 Who Were Placed on High-flow Nasal Cannula between June 1, 2020, through May 15, 2021, at the Wright-Patterson Medical Center

	$n = 19$
Clinical outcomes	
SpO_2/FiO_2 24 hours	145.4
ROX 24 hours	9.4
Change in SpO_2/FiO_2 from initial	−136.5
Mechanical ventilation during hospitalization (%)	50
ICU length of stay (days)	11
Maximum ICU length of stay (days)	39
Hospital length of stay (days)	12
Maximum hospital length of stay (days)	39
In-hospital mortality (%)	20
Supplemental oxygen requirement on discharge (%)	90
Transferred for ECMO (%)	10

Continuous variables are reported as median values and categorical variables reported as percentages. Change in $SPO_2/FiO_2 = SPO_2/FiO_{224hrs} - SPO_2/FiO_{2on\ admission}$.

Abbreviations: ICU, intensive care unit; ECMO, extracorporeal membrane oxygenation; ROX, respiratory rate oxygenation; ROX score (SpO_2/FiO_2)/respiratory rate.

patients. HENIVOT included COVID-19 patients but demonstrated no difference in mortality or respiratory support days between modalities. Comparison to these trials is important, so appropriate evidence-based methodology can be utilized when implementing HHFNC in MTFs.

FLORALI[1] was a multicenter, open-label trial that randomized 310 patients with non-hypercapnic acute hypoxic respiratory failure into three arms, with 106 patients in the HHFNC group. Compared to our study, the median age was lower in FLORALI (61 vs. 71 years), the majority were male in both studies (74%), and median BMI was lower in FLORALI (26 vs. 28.9 kg/m^2). FLORALI had better outcomes than our study: 11% vs. 20% ICU mortality rate and 30% vs. 50% requiring mechanical ventilation. PaO_2/FiO_2 in FLORALI was 157 and S/F of our cohort was 145 after 24 hours (S/F < 235 correlates with a P/F < 200.[3]) These data suggest the two cohorts were similar in pulmonary disease severity. Another disease severity indicator was ROX score (referenced above). In our cohort, ROX change over the initial 24 hours was minimal and well above the 3.85, which predicts need for intubation[4]; despite a high ROX, 50% of our cohort still required intubation. This is likely because the majority of our cohort were intubated late in the hospitalization, likely making initial and 24-hour ROX scores less useful. FLORALI did not utilize ROX scores. FLORALI concluded that HHFNC did not decrease the rate of intubation but improved mortality rates both in ICU and at 90 days compared to standard oxygen therapy or NIPPV. While our cohort had worse outcomes than FLORALI with HHFNC, our study included only severe COVID-19 patients and did not separate patients into different treatment arms. FLORALI enrolled mostly community-acquired and hospital-acquired pneumonia. Current data suggest a high in-hospital mortality with severe COVID-19 patients, approximately twice that of critically ill patients with influenza, and thus, it is difficult to compare mortality differences between various critical illnesses.[6]

HENIVOT[7] was a multicenter, randomized, open label, two-group trial that compared HHFNC and NIPPV via helmet apparatus in patients with severe COVID-19. Fifty-five patients were randomized to HHFNC and 54 patients to NIPPV via helmet. For baseline characteristics compared to our study, HENIVOT had a younger sample (median age 63 vs. 71 years), and both studies were predominantly male (84% vs. 76%). Both studies had similar rates of hypertension (60% vs. 58%), but HENIVOT had a lower proportion with diabetes (18% vs. 32%). Outcomes between the trial and our study were notably similar, with HENIVOT having a negligibly higher intubation rate (51% vs. 50%), modestly higher ICU mortality rate (25% vs. 20%), and similar median ICU length of stay (10 vs. 11 days). Our cohort had a lower hospital stay (12 vs. 22 days) that was likely due to the need to transfer several patients for specific services; notably, two patients were transferred for venovenous ECMO and two patients were transferred for continuous renal replacement treatment. PaO_2/FiO_2 in HENIVOT was 102 and S/F of our cohort was 145 after 24 hours, which suggest a similar severity of pulmonary disease. HENIVOT also did not utilize ROX score. HENIVOT found no difference in days of respiratory support or mortality with HHFNC vs. NIPPV. Our study was the most similar to HENIVOT likely because both cohorts involved patients with COVID-19. While the results of HENIVOT suggest that there may be no difference between NIPPV via helmet and HHFNC, HHFNC is readily available at our MTF and requires less training for medical staff.

There are ongoing trials studying the difference between the three modalities in COVID-19. HELMET[8] is an ongoing randomized trial comparing helmet continuous positive airway pressure (CPAP) and HHFNC. The hypothesis is that helmet CPAP will reduce the need for invasive mechanical ventilation. RECOVERY[9] is an ongoing international effort aimed at studying treatments that may help in hospitalized patients with COVID-19 and currently has over 39,000 participants and over 180 active sites (https://www.recoverytrial.net/). RECOVERY-Respiratory Support is a parallel group, randomized controlled, open-label, multicenter, effectiveness trial studying CPAP from any device vs. HHFNC, with the primary outcome being requiring intubation within 30 days following initiation of CPAP or HHFNC.[9] These two trials will likely help elucidate the effectiveness of HHFNC vs. NIPPV for patients with severe COVID-19. If these studies prove the efficacy of one modality over the other, it will likely change the management of severe COVID-19 patients. This would have an impact across all MTFs and would justify the expense of purchasing and maintaining the appropriate respiratory equipment.

As discussed above, superiority of HHFNC vs. other respiratory modalities in the setting of acute hypoxemic respiratory failure secondary to severe COVID-19 remains controversial. While our study contributes to these data, an ideal study would recruit patients from multiple MTFs with COVID-19 into NIPPV, HHFNC, and mechanical ventilation study arms and directly compare these therapies on patient outcomes. If HHFNC can prevent intubation in patients with severe COVID-19, this therapy would improve important patient outcomes including possible in-hospital mortality. The American College of Physicians (ACP) recently released clinical recommendations supporting HHFNC as the initial therapy of hospitalized patients with acute hypoxemic respiratory failure; however, ACP did not specifically mention the COVID-19 population.[10]

Our study had several limitations. First, the study was conducted at a single MTF. Consequently, generalizability (external validity) to other settings should be done with caution. Second, while cited prior and ongoing studies are randomized controlled trials, ours was retrospective in design. Historically, retrospective studies are more susceptible to data inaccuracies and omissions than prospective investigations. However, in our study, missing data were virtually nil. Third, differences in sample size and patient type with previous studies should be considered. Our small sample size ($n = 19$ COVID-19 patients) compared to FLORALI ($n = 310$ non-COVID-19 patients) and HENIVOT ($n = 109$ COVID-19 patients) suggests caution for claims that a military population is similar to other MTFs and civilian populations on baseline characteristics and clinical outcome. For example, while our ICU mortality rate (20%) was midway between FLORALI (11%) and HENIVOT (25%) and our ICU length of stay (11 days) was nearly the same as HENIVOT (10 days), such similarities may be spurious. Fourth, our study analyzed a single treatment despite many different interventions being necessary to care for patients with severe COVID-19, which may introduce confounding variables. However, in our study, all patients received a similar COVID-19 treatment protocol.

CONCLUSIONS

Our retrospective cohort study characterized and analyzed outcomes observed in a MTF population, with severe or life-threatening COVID-19, who were treated with HHFNC. While the study did not have the power to make concrete conclusions on the optimal form of respiratory support for COVID-19 patients, our data support HHFNC as a reasonable treatment modality despite some notable differences between our cohort and prior studied patient populations.

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CONFLICT OF INTEREST STATEMENT

None declared.

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