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**New domiciliary supplemental oxygen therapy after hospitalization for COVID-19
in metropolitan Chicago**

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Abstract

Background: A knowledge gap exists in understanding the beneficial use and duration of domiciliary supplemental oxygen (DSO) therapy among survivors of COVID-19 hospitalizations with persistent hypoxemia upon discharge. The purpose of this single center study was to begin to address this issue.

Methods: In this retrospective study we report features of U.S. military veterans residing in metropolitan Chicago with no prior DSO therapy who survived COVID-19 hospitalization, were discharged on DSO, and were followed for 6 months.

Results: We found that the majority of the 65 elderly patients (median age, 70 years), predominantly obese Black males, who survived COVID-19 hospitalizations at the Jesse Brown VA Medical Center and discharged on DSO did not undergo a formal 6-minute walk test (6MWT) to re-assess ongoing ambulatory supplemental oxygen requirements (46 patients or 71%). Nonetheless, DSO therapy was discontinued in most patients predominantly within 8 weeks of hospital discharge (34 patients, 52%). In addition, a large proportion of patients, obese Blacks in particular, who survived COVID-19 hospitalizations and were treated with DSO for at least 8 weeks thereafter developed post-acute sequelae of COVID-19 infection (PASC) (30 patients, 46%).

Conclusions: Given these findings, we recommend that healthcare providers be appraised about proper monitoring and evaluation, including timely performance of 6MWT, of patients who survived COVID-19 hospitalizations and treated with DSO for persistent hypoxemia upon discharge. Whether obese Black males who survived COVID-19 hospitalizations and are treated with DSO thereafter have an elevated risk in developing PASC remains to be determined in larger, prospective studies.

Introduction

It is well-established that long-term, domiciliary supplemental oxygen therapy is beneficial in some patients with distinct lung diseases (1-5). To that end, a knowledge gap exists in understanding the attributes of domiciliary supplemental oxygen therapy among survivors of COVID-19 hospitalizations who were discharged with domiciliary supplemental oxygen therapy due to persistent hypoxemia (6-9).

For instance, Chopra et al (10) reported that only 32 out of 1,250 survivors of COVID-19 hospitalizations in the State of Michigan (2.6%) required new domiciliary supplemental oxygen 60 days after discharge. Banerjee et al (11) found low 30-day all-cause mortality (1.3%) and hospital re-admission rate (8.5%) among 621 patients with acute COVID-19 illness in the U.S. who were discharged from the hospital with supplemental oxygen. However, the median follow-up of these patients was only 26 days thereby precluding assessment of long-term, domiciliary supplemental oxygen therapy. Moreover, whether these patients had new supplemental oxygen requirements upon hospital discharge was not addressed in this study. Finally, Shah et al (7) did not report new supplemental oxygen requirements among 60 patients prospectively followed for 12 weeks for respiratory outcomes after COVID-19 hospitalizations in Vancouver, Canada.

Given the paucity of studies addressing clinical management of new domiciliary supplemental oxygen therapy among survivors of COVID-19 hospitalizations with persistent hypoxemia, the purpose of this single center, retrospective study was to begin to address this knowledge gap. Here we report features of U.S. military veterans residing in metropolitan Chicago with no prior domiciliary supplemental oxygen therapy who survived COVID-19 hospitalizations, were discharged with domiciliary supplemental oxygen therapy due to persistent hypoxemia and were followed for 6 months.

Methods

A retrospective review of VA Computerized Patient Record System (CPRS) of 285 veterans hospitalized at and discharged from the Jesse Brown VA Medical Center (JBVAMC) in Chicago, Illinois, between March 2020 and February 2021 for RT-PCR-positive, acute COVID-19 illness was performed. These patients were identified using the JBVAMC registry of all patients tested at the JBVAMC for COVID-19 during this period. Jesse Brown VAMC is a tertiary academic health care center located in the near West Side neighborhood of Chicago. It consists of a 220-bed facility (158 acute care beds) and 4 community-based outpatient clinics. The medical center provides care to approximately 49,000 veterans who reside in the City of Chicago and Cook County, Illinois, and in 6 counties in northwestern Indiana. It is a major teaching affiliate of Feinberg School of Medicine of Northwestern University and University of Illinois College of Medicine at Chicago. The study was approved by JBVAMC Institutional Review Board.

Patient data abstracted from CPRS comprised of demographics, co-morbidities, and hospital course. After hospital discharge, data collected from CPRS included flow rate and duration of domiciliary supplemental oxygen therapy, follow-up virtual and/or face-to-face clinic visits with healthcare providers, unscheduled visits to the emergency department, hospitalizations, and documentation of post-acute sequelae of SARS-CoV-2 infection (PASC) symptoms (defined below) by health care providers at day 30, week 8, and from 8 weeks to 6 months thereafter. In each patient, the need for domiciliary supplemental oxygen upon hospital discharge was assessed by detailed medical history, clinical examination, and pulse oximetry $<88\%$ at rest or during ambulation. Domiciliary supplemental oxygen, ancillary equipment, technical support, education, educational resources, and regular home visits were provided to eligible patients by a single commercial vendor contracted by JBVAMC in accordance with Veterans Health Administration Directive 1173.13. Post-acute sequelae of SARS-CoV-2 infection was defined as symptoms and/or abnormalities associated with SARS-CoV-2 infection (e.g., “brain fog” and shortness of breath) that persisted beyond 4 weeks of hospital discharge that were not present prior to the onset of SARS-CoV-2 and were not attributable to alternative diagnoses (12-16).

Descriptive statistics were used for primary analysis and are reported as means and standard deviation, median with interquartile range (IQR) and percent where appropriate.

Results

Clinical course after hospital discharge

We found that 65 of 285 patients (23%) with acute COVID-19 illness were discharged from JBVAMC with new domiciliary supplemental oxygen therapy during the study period. None had domiciliary supplemental oxygen therapy prescribed before contracting COVID-19 infection. Patient characteristics are depicted in Table 1. They were elderly (median age, 70), obese, predominantly Black (69%) men (94%) (Table 1). Sixty-eight per cent had a history of smoking and 19% reported smoking tobacco at the time of hospital admission. The predominant underlying co-morbidities among this cohort were hypertension (83%), hyperlipidemia (62%), diabetes mellitus type-2 (49%), obstructive sleep apnea (40%), chronic obstructive pulmonary disease (COPD) (29%), and gastroesophageal reflux disease (25%) (Table 1).

During hospitalization, 2 patients (3%) required invasive mechanical ventilation, 7 (10%) non-invasive ventilation, and 19 (29%) high-flow supplemental oxygen delivered with nasal cannulae. The remaining 37 patients required supplemental oxygen at flow rates ≤ 5 L/min or none. Mean length of hospital stay was 11 ± 10 days. All 65 patients were discharged from JBVAMC with a median supplement oxygen flow rate of 2 L/min (IQR, 2-2 L/min) either continually or during exertion (Table 1).

All 65 patients were followed for 6 months after hospital discharge. Within 30 days of hospital discharge, 50 patients (77%) had at least one follow-up clinic virtual or face-to-face visit with a primary care physician (PCP) at JBVAMC. Eighteen patients (28%) had at least one unscheduled visit to the emergency department and 9 (14%) had at least one all-cause readmission to JBVAMC. No deaths were reported during this time frame (Table 2).

Eight weeks after hospital discharge, 60 patients (92%) had at least one follow-up virtual or face-to-face clinic visit with a PCP at JBVAMC. Twenty-three patients

(35%) had at least one unscheduled visit to the emergency department and 13 (20%) had at least one all-cause hospitalization at JBVAMC during this time frame. Importantly, 43 patients (66%) reported PASC (Table 2). No deaths were reported during this observation period.

From 8 weeks to 6 months after hospital discharge, 51 patients (79%) had at least one follow-up virtual or face-to-face clinic visit with PCP, 31 (48%) had at least one unscheduled visit to the emergency department and 9 (14%) had at least one all-cause hospitalization at JBVAMC. At this time point, 17 patients (26%) had PASC-related visits to the emergency department or readmission at JBVAMC, and 29 (45%) had PASC reported to their PCPs (Table 2). Two patients (3%) died during follow-up, both did not require high flow nasal cannula or non-invasive or invasive ventilation during their index hospitalization. (Table 2).

New domiciliary supplemental oxygen therapy

A six-minute walk test (6MWT) to assess ongoing requirement for domiciliary supplemental oxygen therapy was only performed in 4 patients prior to 8 weeks and 15 patients (23%) after 8 weeks from hospital discharge. Nonetheless, domiciliary supplemental oxygen therapy was discontinued in 34 patients (52%) within 8 weeks of hospital discharge (Table 2), 6 of which had discontinuation of supplemental oxygen within 4 weeks of discharge. The number of patient referrals to the pulmonary clinic at JBVAMC during the 6-month observation period was less than 50% during each study period. (Table 2).

Thirty patients (46%), predominantly obese Black males with hypertension and hyperlipidemia, who were discharge with domiciliary supplemental oxygen therapy reported PASC for at least 8 weeks after hospital discharge reported PASC (Table 3). Out of these only 10 patients (33%) had documented supplemental oxygen discontinued by self or provider during the study period (from 4 weeks to 6 months of index COVID-19 hospitalization). None required invasive mechanical ventilation during hospitalization. Thirteen patients required supplemental high-flow oxygen therapy through nasal cannula or noninvasive ventilation. Nine patients (30%) were re-admitted to JBVAMC within 30 days of hospital discharge while 10 (33%) were re-admitted within

8 weeks. Two patients who were treated with domiciliary supplemental oxygen and subsequently diagnosed with PASC died during follow-up (Table 3).

Discussion

There are three new findings of this study. We found that the majority of elderly patients, predominantly obese Black males, residing in metropolitan Chicago who survived COVID-19 hospitalizations at JBVAMC, discharged on domiciliary supplemental oxygen due to persistent hypoxemia, and followed for 6 months did not undergo 6MWT to re-assess the need for domiciliary supplemental oxygen. Nonetheless, oxygen therapy was discontinued in most patients predominantly within 8 weeks of hospital discharge. During this time frame, 92% of patients had at least one follow-up virtual or face-to-face clinic visit with a PCP. In addition, a large proportion of patients, obese Black in particular, who survived COVID-19 hospitalizations and were treated with domiciliary supplemental oxygen for at least 8 weeks thereafter developed PASC. Given these data, we recommend that healthcare providers be appraised about proper monitoring and evaluation, including timely performance of 6MWT, of patients who survived COVID-19 hospitalizations and treated with domiciliary supplemental oxygen for persistent hypoxemia upon discharge. Whether obese Black males who survived COVID-19 hospitalizations and treated with domiciliary supplemental oxygen thereafter are more prone to develop PASC remains to be determined in larger, prospective studies.

A recent, large cohort study of U.S. military veterans who survived COVID-19 hospitalizations found higher risk of persistent hypoxemia four months after hospital discharge in comparison to veterans who survived influenza hospitalizations (14). Because COVID-19 is a new disease entity dedicated practice guidelines for managing domiciliary supplemental oxygen therapy in survivors of COVID-19 hospitalizations with persistent hypoxemia have not been published as of yet (8, 17). For instance, Ayoubkhani et al (16) recently reported on 47,780 patients with COVID-19 who were discharged from hospitals in the UK and followed for a mean of 140 days. Although the investigators found an increase rate of respiratory dysfunction in these patients compared with a matched control group, they did not address new domiciliary

supplemental oxygen therapy among them. Similar omissions are noted in recent large cohort studies of patients with COVID-19 conducted in China and Switzerland (9, 18).

A prospective, single site observational cohort study of 152 patients who survived COVID-19 hospitalization in New York City, NY and were followed for a median of 37 days found that 52 (34%) had a new supplemental oxygen requirement at discharge (19). Twenty patients still required 1-2 L/min supplemental oxygen during the ensuing short follow-up. These figures are similar to those reported in the current study. Finally, Loerinc et al (20) reported new domiciliary oxygen therapy in 41 out of 310 patients (13.2%) hospitalized for COVID-19 in an academic medical center in Atlanta, GA within 30 days of discharge. However, no additional details about ongoing need for supplemental oxygen after this time point were provided. Taken together, these studies highlight the urgent need to establish a practice guideline for domiciliary supplemental oxygen therapy in survivors of COVID-19 hospitalizations with persistent hypoxemia after discharge.

The limitations of our retrospective study are obvious, including single medical center in metropolitan Chicago, small sample size, male predominance, and no matched control group. This limits the generalizability of our observations and limit our ability to elucidate the possible roles of comorbid conditions and tobacco smoking as risk factors for developing PASC. We also recognize that most outpatient encounters reported in this study occurred remotely using telehealth-enabled technology due to the ongoing COVID-19 pandemic in metropolitan Chicago. This may have limited formal health assessment, including ongoing need for supplemental oxygen, of our patients. Nonetheless, we have addressed this issue, in part, by extending the study period to 6 months after hospital discharge thereby facilitating patient access to primary care providers at JBVAMC. In addition, interrogation of CPRS, JBVAMC-specific robust electronic health record, enabled us to capture all post-discharge clinic and virtual visits of our patients along with complications observed during this time frame. Moreover, the commercial vendor contracted by JBVAMC provided regular delivery of oxygen tanks or concentrators and supplies along with home visits to patients' residences thereby promoting adherence with prescribed supplemental oxygen therapy.

Finally, the results of this study underscore the need to develop, implement and disseminate cost-effective, wireless, telehealth-enabled technologies to monitor patients who survived COVID-19 hospitalizations with limited access to clinic visits after discharge for actual need for domiciliary supplemental oxygen therapy.

In summary, we recommend that healthcare providers be appraised about proper monitoring and evaluation, including timely performance of 6MWT, of patients who survived COVID-19 hospitalizations and treated with domiciliary supplemental oxygen for persistent hypoxemia upon discharge. Whether obese Black males who survived COVID-19 hospitalizations and treated with domiciliary supplemental oxygen thereafter are more prone to develop PASC and if use of DSO is associated with development or persistence of PASC remains to be determined in larger, prospective studies.

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Table 1. Characteristics of patients discharged on new supplemental oxygen therapy.

Baseline characteristics (n=65)	N (%)
Age (median [IQR]), yrs.	70 (62-74)
Sex	
Male	61 (94)
Female	4 (6)
Race	
African American	45 (69)
Caucasian	16 (25)
Others	4 (6)
Smoking history	
Current smoker	12 (19)
Previous smokers	32 (49)
Unknown	21 (32)
Underlying co-morbidities	
Hypertension	54 (83)
Hyperlipidemia	40 (62)
Obesity (BMI ≥ 30 kg/m ²)	38 (59)
Diabetes mellitus, type 2	32 (49)
Obstructive sleep apnea	26 (40)
Chronic obstructive pulmonary disease	19 (29)
Coronary artery disease	10 (15)
Gastroesophageal reflux disease	16 (25)
Chronic kidney disease	15 (23)
Non-lung cancer	9 (14)
Asthma	5 (8)
HFpEF	4 (6)
History of venous thromboembolism	4 (6)
HFrEF	3 (5)
Cirrhosis	3 (5)
Interstitial lung disease	2 (3)
Lung cancer	1 (2)
Solid organ transplant	1 (2)
Sarcoidosis	1 (2)

Connective tissue disease	1 (2)
Index hospitalization	
Invasive mechanical ventilation	2 (3)
Non-invasive ventilation	7(10)
High flow nasal cannula	19 (29)
Mean length of stay ($\pm$ SD), day	11 ($\pm$ 10)
Median supplemental oxygen on discharge	2 liters/minute (IQR, 2-2)

IQR, interquartile range; SD, standard deviation; BMI, body mass index; HFrEF, heart failure with reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction

Table 2. Patient outcomes after hospital discharge.

Outcome (n=65)	At 8 weeks N (%)		8 weeks to 6 months N (%)
	Within 30 days	30 days to 8 weeks	
Health care utilization and mortality			
Primary care provider visits	50 (77)	60 (92)	51 (79)
Emergency department visits	18 (28)	23 (35)	31 (48)
Readmissions (all causes)	9 (14)	13 (20)	9 (14)
Mortality (all causes)	0 (0)	0 (0)	2 (3)
Supplemental oxygen reassessment and utilization			
Six-minute walk test	4 (6)		15 (23)
Pulmonary clinic visit	26 (40)		15 (23)
Supplemental oxygen discontinued	34 (52)		10 (15)
Insufficient documentation	0		6 (9)
PASC			
Total with PASC (reported at PCP or ED visit	NN (%%)		30 (46)
Reported during ED visits/readmissions	43 (66)		17 (26)
Reported to primary care provider	39 (60)		29 (45)

PASC, post-acute sequelae of COVID-19 infection; ED, emergency department

Table 3. Characteristics of patients who reported PASC ≥ 8 weeks after hospital discharge.

Characteristics of patients with PASC (N=30)	N (%)
Age (median [IQR]), yrs.	70 (63-76)
Sex	
Male	30 (100)
Race	
African American	21 (70)
Caucasian	6 (20)
Others	3 (10)
Smoking history	
Current smoker	8 (26)
Previous smokers	17 (56)
Unknown	5 (18)
Co-morbid conditions	
Hypertension	25 (83)
Hyperlipidemia	20 (66)
Obesity (BMI ≥ 30 kg/m ²)	18 (60)
Diabetes mellitus, type 2	14 (46)
Obstructive sleep apnea	12 (40)
Chronic obstructive pulmonary disease	10 (33)
Gastroesophageal reflux disease	10 (33)
Coronary artery disease	6 (20)
Chronic kidney disease	5 (16)
Non-lung cancer	4 (13)
HFpEF	3 (10)
Cirrhosis	3 (10)
Asthma	2 (6)
History of venous thromboembolism	2 (6)
HFrEF	2 (6)
Interstitial lung disease	1 (3)
Lung cancer	1 (3)
Solid organ transplant	1 (3)

Sarcoidosis	1 (3)
Connective tissue disease	1 (3)
Index hospitalization	
Mean length of stay ($\pm$ SD), day	11 ($\pm$ 10)
Supplemental oxygen therapy	
In-hospital	
Non-invasive ventilation	3 (10)
High-flow nasal canula	10 (33)
Invasive mechanical ventilation	0
At hospital discharge	
N (%)	NN (%%)
Median flow rate, L/min (IQR)	2 (2-3)
Readmission and mortality outcomes	
Readmission within	
30 days (all cause)	9 (30)
30 days to 8 weeks (all cause)	10 (33)
8 weeks to 6 months (all cause)	5 (16)
Mortality (all cause) #	2 (6)

#Median time to death: 130 days

PASC, post-acute sequelae of COVID-19 infection; IQR, interquartile range; BMI, body mass index; HFrEF, heart failure with reduced ejection fraction; HFpEF, heart failure with preserved ejection fraction; SD, standard deviation