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Respiratory Distress in Hospitalized Non-Mechanically Ventilated COVID-19 Adults: A Retrospective Multicenter Cohort Study

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Abstract

Background: COVID-19 typically presents with respiratory symptoms which may progress with severe disease. There are standard guidelines for managing respiratory distress (e.g. opioids, anxiolytics) and palliative care teams are well versed in managing these symptoms. **Aim:** Determine the extent to which hospitalized COVID-19 patients with moderate respiratory distress received medications or palliative consultation for symptom management and if these interventions had any association with outcomes. **Design:** Retrospective chart review for hospitalized COVID-19+ patients from March 2-April 30, 2020. **Setting:** Large integrated health system in the New York Metropolitan area. **Patients:** 312 adult patients hospitalized with COVID-19 with an order for a non-rebreather mask and meeting criteria for moderate respiratory distress on the Respiratory Distress Observation Scale: concurrent respiratory rate $\geq$30 and heart rate $\geq$110 at any point during hospitalization. Patients receiving mechanical ventilation or intensive care were excluded. **Results:** Most COVID-19 patients experiencing moderate respiratory distress did not receive medications or palliative consultation for symptom management. Patients who received medications were predominantly white, older, and had a Do-Not-Resuscitate order. Patients who received a palliative consultation were more likely to be older, female, and white, with a Do-Not-Resuscitate order. Mortality was similar between those receiving medication and those who did not. **Conclusion:** Medications and palliative expertise for symptom management were underused for patients with moderate respiratory distress due to COVID-19. Education and triggers may help providers to identify moderate respiratory distress and consider symptomatic treatment and palliative consultation when appropriate.

Keywords

coronavirus, COVID-19, palliative care, dyspnea, symptom management

Background

The novel coronavirus (COVID-19) was first detected in late 2019 and quickly escalated to a global pandemic causing devastating morbidity and mortality.[1-3] Since the beginning of 2021, over 500,000 people have died from COVID-19 in the United States alone, overwhelming hospitals and health systems across the country.[4]

Throughout the first wave of the pandemic, many articles described the symptomatic needs and course of disease for patients diagnosed with COVID-19.[5,6] Dyspnea is one of the most common presenting symptoms, along with cough and fever. Some studies reported dyspnea in up to 71% of all COVID-19 cases, and in 88-91% of cases requiring mechanical ventilation.[6,7] The proportion of COVID-19 patients experiencing dyspnea may be even higher due to underreporting with patient sedation, delirium, agitation, altered mental status, or innate cognitive changes associated with the end of life.[7-9] While no specific tools have been recommended to assess dyspnea burden in patients hospitalized with COVID-19, the Respiratory Distress Observation Scale (RDOS) is a validated tool commonly used by palliative care experts. This instrument can be easily used to objectively assess dyspnea in all patients, even those with impaired communication.[9,10]

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Respiratory symptoms of patients hospitalized with COVID-19 can for the most part be managed conservatively. Standard of care includes oxygen supplementation and hydration. Some experts have recommended a symptom-driven approach, such as antipyretics, anxiolytics, antipsychotics, and opioids as additional treatments.[7,11] In general, opioids are a common and effective treatment to relieve dyspnea in patients with advanced respiratory illness regardless of underlying etiology.[12,13] Despite concern over the perceived potential to hasten death in patients with advanced illness, and observations that orders for opioids are a marker of end-of-life,[14,15] the use of opioids for management of dyspnea has not been associated with a significant decrease in time to death.[16,17] Additionally, prescribing practices remain uneven and there are notable disparities for Black and Hispanic patients in the face of solid evidence that use of opioids in the context of advanced illness is effective.[18,19]

Even prior to the COVID-19 pandemic, dyspnea was under diagnosed and undertreated among patients hospitalized in the intensive care unit (ICU).[20] The COVID-19 pandemic has dramatically increased the number of patients experiencing dyspnea while simultaneously hindering the ability of physicians to appropriately assess and treat it, due to both sheer numbers of cases admitted over a short time span and reduced clinician-patient interactions related to isolation precautions and need for personal protective equipment. This study seeks to examine the extent to which moderate respiratory distress in patients hospitalized with COVID-19 was treated with opioids and/or anxiolytics or palliative care input.

Methods

Assessment Tool

The RDOS incorporates 8 variables including heart and respiratory rate, restlessness, paradoxical breathing pattern, use of accessory muscles, grunting at the end expiration, nasal flaring, and look of fear. Each variable is scored from 0 to 2 with added values ranging from 0 to 16. Respiratory distress is rated as follows: $\leq$3 mild, 4 to 6 moderate, and $\geq$7 severe distress.[9] Understanding the retrospective nature of our study and the need to rely on data gathering through electronic medical records only objective data related to heart and respiratory rate were collected. However, in order to increase the accuracy of our assessment tool, we only included those patients with moderate respiratory distress that had and order for a non-rebreather mask (NRM), which we used as a factor for high oxygen requirements and at risk for dyspnea.

Study Sample

Adult ($\geq$18 years old) patients admitted to one of 14 hospitals in a large integrated health system in the New York Metropolitan area with COVID-19 between March 2 and April 30, 2020 meeting criteria for moderate respiratory distress and who were prescribed for an NRM. Moderate respiratory distress was defined by the Respiratory Distress Observation Scale of concurrent respiratory rate (RR) $\geq$30 and heart rate (HR) $\geq$110.[8] When the timestamps for RR $\geq$30 and HR $\geq$110 did not develop at the same time, the timestamp of the second metric developed was used as the timestamp for onset of respiratory distress. Those who received mechanical ventilation during the course of hospitalization were excluded. The study was approved by the institutional IRB and the COVID-19 Research Consortium.

Data Elements

Demographic characteristics included gender, age, race (White, African American/Black, Asian, Other/ Multiracial), Hispanic/Latino ethnicity). Medication variables included orders for at least one medication typically used for respiratory distress management: hydromorphone, morphine, oxycodone, or lorazepam. Orders for fentanyl and midazolam were not included as these are commonly used for sedation in the ICU setting. Orders for a palliative care consult were noted, and reasons for consult categorized as need for symptom management, goals of care (GOC) conversation, or both. Other study variables included documented do-not-resuscitate (DNR) orders, timing of DNR order (e.g. early DNR indicates DNR order in ER or within 24 hours of admission), and discharge disposition (deceased, discharged).

Timestamps were pulled for variables and outcomes of interest, including first concurrent RR 30 and HR $\geq$110, first dose of any medication for symptom management, and palliative care consult. Among patients that received any medication for symptom management, time difference from respiratory distress to first medication was computed by subtracting respiratory distress timestamp from first medication timestamp. For patients that received their first medication after palliative care consult, time from palliative care consult to first medication was computed by subtracting palliative care consult timestamp from first medication timestamp. Among patients that received a medication and later died, time from first medication to death was computed by subtracting first medication timestamp from death timestamp.

Statistical Analysis

Descriptive statistics were performed to assess the bivariate association between orders for medications for symptom management and/or palliative care consult with demographic and medical variables, e.g. gender, age, race, ethnicity, DNR status, and discharge disposition. Continuous variables were compared across groups using the two-sample t-test, and transformations were applied as needed to meet the assumptions for the validity of the two-sample t-test. Age as an ordinal variable was compared across groups using the Mann Whitney U test, and all other categorical variables were compared across groups using the Chi-Square test or Fisher's Exact test, as appropriate. All analyses were conducted using SAS Studio Version 3.8 (SAS

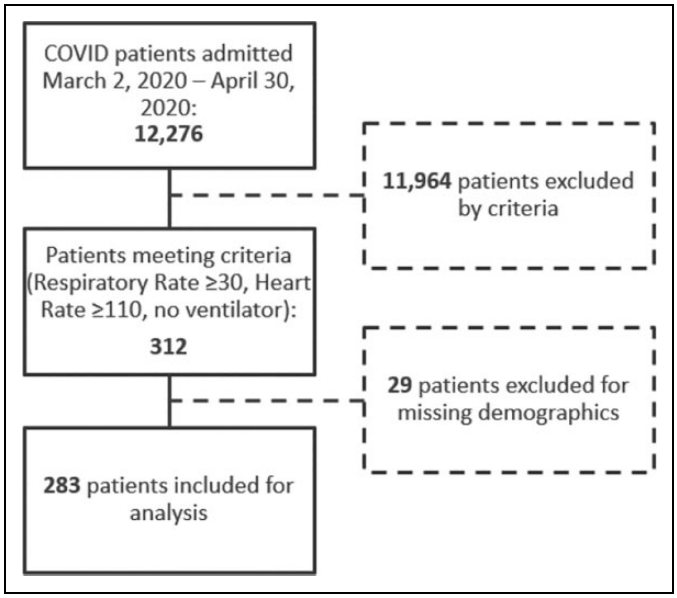

Figure 1. Flow diagram of COVID patients included for analysis.

Institute Inc., Cary, NC, USA), and a p-value < 0.05 was considered statistically significant.

Results

Of the 12,276 adults admitted with COVID-19 from March 2-April 30, 2020, 2.5% (312) with moderate respiratory distress were included for analysis. 29 patients were excluded for missing demographic information (unknown race or ethnicity) for a total of 283 patients in the final sample (Figure 1). The majority were male (61%), white (46%), and non-Hispanic/ Latino (82%) (Table 1). The median age was 74 years old (IQR: 60, 85). 109 (38.5%) received one or more medications used to manage respiratory distress (e.g. hydromorphone, lorazepam, morphine, oxycodone). For the 73 patients (26%) that received a palliative care consult, GOC conversation was the most common reason for consultation (64%). Just under 16% of total patients (N = 45) had both a palliative consult and received medication for respiratory distress. 102 patients had an early DNR status ordered (36%) and 149 expired (53%).

Tables 1 and 2 outline the results of the bivariate analyses that were conducted to examine association between receiving medications/palliative consult and demographic and medical characteristics. Older age ($p < 0.0001$), white race ($p = 0.0005$), having an early DNR status ($p < 0.0001$), and dying prior to discharge ($p < 0.0001$) were each significantly associated with having any medication prescribed. Female gender ($p = 0.0277$), older age ($p < 0.0001$), white race ($p = 0.0014$), non-Hispanic/Latino ethnicity ($p = 0.0356$), having an early DNR status ($p = 0.0025$) and dying prior to discharge ($p < 0.0001$) were each associated with having a palliative care consult (Table 3). Those patients seen in palliative consultation were more likely to receive medication to manage respiratory distress ($p < 0.0001$).

Table 3 describes hospital disposition of the (109) patients that received any medication for symptom management, palliative consultation, or both. The median time from moderate respiratory distress to first medication (for any patient receiving medication after consult) was 9 hours (IQR: 2, 20). Of 45 patients that received both medication and a palliative care consult, 19 (42%) received medication before palliative care consult and 26 (58%) received medication after palliative care consult. Time from moderate respiratory distress documentation to first medication did not differ significantly by palliative care consult vs. none. Of those that received a medication and expired during their hospitalization, the median time from first medication to death was 26 hours (IQR: 14, 88). Time from first medication to death did not differ significantly by whether the patient had a palliative care consult: 24 hours (IQR: 14.5, 85.5) for those that received a palliative care consult vs.33 hours (IQR: 14, 91) for those that did not receive a palliative care consult ($p = 0.38$).

Discussion

Main Findings

This study provides an overview on use of pharmacologic management and palliative consultation for moderate respiratory distress in hospitalized COVID-19 patients during the first surge of the pandemic. All patients included for analysis met the Respiratory Distress Observation Scale criteria for moderate respiratory distress of concurrent heart rate $\geq$110 and respiratory rate $\geq$30. Medications for routinely managing such symptoms (e.g. hydromorphone, lorazepam, morphine, oxycodone) were only ordered for 38.5% of cases. Palliative care expertise, though able to help with managing this distressful symptom, was requested for only 25% of cases.

Although all 283 patients included for analysis were experiencing moderate respiratory distress, 61% did not receive any symptom management. Those who did were more likely to be white, older, and had a DNR order in place. Of the 174 patients who did not receive medication for symptom management, 34% died during their hospitalization. Though it can be argued that survivors may have had their respiratory distress addressed by means other than opioids or benzodiazepines, it may be more difficult to support that hypothesis for those that died and did not received any of these medications.

Patients that did receive a palliative care consult were more likely to be older, female, white patients with a DNR order in place. Palliative consultations were more likely to be called for goals of care discussions, particularly for patients who already had advanced directives in place. Although patients were more likely to have their respiratory symptoms addressed when the palliative team was involved, patients who were consulted for GOC conversations were still experiencing moderate respiratory distress. The results suggest that the primary medical teams were either not recognizing and/or not addressing respiratory distress. It could be that providers were concerned that pharmacologic treatment of symptoms might tip the

Table 1. Association Between Demographic/Clinical Characteristics and Any Medication Use.

Variable	Overall (N = 283)	Any medication use (n = 109)	No medication use (n = 174)	*P*-value
Gender, n (%)				0.7984
Female	109 (38.5)	43 (39.5)	66 (37.9)	
Male	174 (61.5)	66 (60.6)	108 (62.1)	
Age, median (IQR)	74.0 (60.0, 85.0)	81.0 (72.0, 89.0)	68.0 (53.0, 80.0)	<0.0001
Age category, n (%)				<0.0001
18-34	11 (3.9)	3 (2.8)	8 (4.6)	
35-49	27 (9.5)	5 (4.6)	22 (12.6)	
50-64	49 (17.3)	8 (7.3)	41 (23.6)	
65-79	87 (30.7)	32 (29.4)	55 (31.6)	
80+	109 (38.5)	61 (56.0)	48 (27.6)	
Race, n (%)				0.0005
White	130 (45.9)	67 (61.5)	63 (36.2)	
African American/ Black	55 (19.4)	14 (12.8)	41 (23.6)	
Asian	32 (11.3)	8 (7.3)	24 (13.8)	
Other/ Multiracial	66 (23.3)	20 (18.4)	46 (26.4)	
Ethnicity, n (%)				0.2967
Hispanic/ Latino	50 (17.7)	16 (14.7)	34 (19.5)	
Non-Hispanic/ Latino	233 (82.3)	93 (85.3)	140 (80.5)	
DNR order, n (%)				<0.0001
Yes	161 (56.9)	94 (86.2)	67 (38.5)	
No	122 (43.1)	15 (13.8)	107 (61.5)	
Early DNR order, n (%)				<0.0001
Yes	102 (36.0)	63 (57.8)	39 (38.2, 22.4)	
No	181 (64.0)	46 (42.2)	135 (74.6, 77.6)	
Hydromorphone, n (%)		—	—	—
Yes	39 (13.8)			
No	244 (86.2)			
Lorazepam, n (%)		—	—	—
Yes	35 (12.4)			
No	248 (87.6)			
Morphine, n (%)		—	—	—
Yes	68 (24.0)			
No	215 (76.0)			
Oxycodone, n (%)		—	—	—
Yes	3 (1.1)			
No	280 (98.9)			
Discharge disposition, n (%)				<0.0001
Discharged	134 (47.4)	19 (17.4)	115 (66.1)	
Deceased	149 (52.7)	90 (82.6)	59 (33.9)	
Palliative care consult, n (%)				<0.0001
Yes	73 (25.8)	45 (41.3)	28 (16.1)	
No	210 (74.2)	64 (58.7)	146 (83.9)	
Reason for palliative care consult (N = 73), n (%)				0.0439
GOC/ACP	47 (64.4)	24 (53.3)	23 (82.1)	
Symptoms	16 (21.9)	13 (28.9)	3 (10.7)	
GOC and symptoms	10 (13.7)	8 (17.8)	2 (7.1)	

Abbreviations: IQR: Interquartile Range; DNR: Do Not Resuscitate; GOC: Goals of Care; ACP: Advance Care Planning.

balance toward mortality and so were reluctant to administer these treatments. Although patients prescribed medications with no palliative consult did not have a statistically significant longer time to mortality than those who received a palliative care consult, this may have been due to the relatively low numbers of patients (36 hours vs. 24 hours, p = 0.33). The primary managing team may have recognized an end-of-life scenario in some cases and so were more likely to provide pharmacologic comfort, and this is support by a similar time interval between first documentation of respiratory distress and medication administration. Palliative care consults typically occurred late in the patient's hospital course, suggesting that some of these patients may have experienced more prolonged respiratory distress with the same final outcome.

The results of this study suggest opportunities for health systems to provide education and consistently identify and manage moderate respiratory distress in patients, both within and outside the context of COVID-19. The lack of symptom management for the majority of patients with respiratory distress and the time lag between onset of respiratory distress and first medication

Table 2. Association Between Demographic/Clinical Characteristics and Palliative Care Consult.

Variable	Palliative care consult (n = 73)	No palliative care consult (n = 210)	*P*-value
Gender, n (%)			0.0277
Female	36 (49.3)	73 (34.8)	
Male	37 (50.7)	137 (65.2)	
Age, median (IQR)	82.0 (73.0, 88.0)	70.5 (56.0, 81.0)	<0.0001
Age category, n (%)			<0.0001
18-34	0 (0.0)	11 (5.2)	
35-49	1 (1.4)	26 (12.4)	
50-64	7 (9.6)	42 (20.0)	
65-79	22 (30.1)	65 (31.0)	
80+	43 (58.9)	66 (31.4)	
Race, n (%)			0.0014
White	48 (65.8)	82 (39.1)	
African American/ Black	9 (12.3)	46 (21.9)	
Asian	5 (6.9)	27 (12.9)	
Other/ Multiracial	11 (15.1)	55 (26.2)	
Ethnicity, n (%)			0.0356
Hispanic/ Latino	7 (9.6)	43 (20.5)	
Non-Hispanic/ Latino	66 (90.4)	167 (79.5)	
DNR order, n (%)			<0.0001
Yes	66 (90.4)	95 (45.2)	
No	7 (9.6)	115 (54.8)	
Early DNR order, n (%)			0.0025
Yes	37 (50.7)	65 (31.0)	
No	36 (49.3)	145 (69.1)	
Hydromorphone, n (%)			<0.0001
Yes	22 (30.1)	17 (8.1)	
No	51 (69.9)	193 (91.9)	
Lorazepam, n (%)			0.0002
Yes	18 (24.7)	17 (8.1)	
No	55 (75.3)	193 (91.9)	
Morphine, n (%)			0.0177
Yes	25 (34.3)	43 (20.5)	
No	48 (65.8)	167 (79.5)	
Oxycodone, n (%)			0.5714
Yes	0 (0.0)	3 (1.4)	
No	73 (100.0)	207 (98.6)	
Discharge disposition, n (%)			<0.0001
Discharged	18 (24.7)	116 (55.2)	
Deceased	55 (75.3)	94 (44.8)	

provides a window of opportunity for improving patient care. As healthcare becomes more automated and technology-oriented, a respiratory distress trigger may be an effective tool to alert healthcare providers to patient needs, especially if a patient is unable to communicate directly or patient-provider interactions are limited by a highly infectious condition such as COVID-19. The goal is to highlight "blind spots," address biases and reduce disparities in provision of symptom management medication. These triggers may be particularly important in the context of COVID-19 or similar crises where the healthcare system is stretched far beyond usual capacity.

Limitations

There were a number of study limitations. First, due to the exponential increase in patient admissions during this time period, traditional medical floors were transitioned into makeshift ICUs. Despite extensive checking and cleaning of data, we cannot entirely rule out the possibility that some patients in this dataset received ICU level care during the course of their hospitalization. Additionally, this analysis could only use data indicating that medications were ordered but cannot confirm at what point they were actually administered or the reason for administration. For example, while we believe that all opioids prescribed were for management of respiratory distress, there is the possibility that some may have been prescribed for pain management. Similarly, we are unable to incorporate the prescription of bronchodilators for respiratory distress, as the use of these medications was reduced in the first stages of the COVID-19 pandemic over concerns of aerosolization.[21] Second, the rapid surge of patients requiring hospitalization led health systems to bring in redeployed physicians who may not

Table 3. Supplemental Data Summary: Medication Timing (Time From RDOS to First Medication, Time From PC Consult to First Medication, and Time From First Medication To Death).

Variable		*P*-value
Any medication and palliative care (PC) consult (N = 283), n (%)		—
Yes	45 (15.9)	
No	238 (84.1)	
Any medication and PC consult timing (N = 45), n (%)		—
First medication before PC consult	19 (42.2)	
First medication same time/ after PC consult	26 (57.8)	
Any medication and deceased (N = 283), n (%)		—
Yes	90 (31.8)	
No	193 (68.2)	
Time from RDOS to first medication (hours), median (IQR)*		0.4581
Overall (N = 101)	9.0 (2.0, 20.0)	
PC consult (n = 41)	6.00 (1.00, 17.00)	
No PC consult (n = 60)	9.00 (3.00, 20.00)	
Time from PC consult to first medication (hours), median (IQR)**		—
Overall (N = 25)	20.00 (2.00, 70.00)	
Time from first medication to death (hours), median (IQR)***		0.3817
Overall (N = 89)	26.0 (14.0, 88.0)	
PC consult (n = 40)	24.0 (14.5, 85.5)	
No PC consult (n = 49)	33.00 (14.0, 91.0)	

*8 outliers excluded (4 with PC consult and 4 without PC consult).

**Only among patients with first medication after PC consult, 1 outlier excluded.

***1 outlier excluded (0 with PC consult and 1 without PC consult).

have been familiar with current standards of respiratory distress symptom management and/or knowledge to consult palliative care. The overwhelming surge of admissions and severity of illness that occurred in the spring of 2020 resulted in an unparalleled increase in palliative care consultation requests. The demand for palliative services was so out of proportion to the usual consult load that the existing teams were unable to see every patient for whom a consult was requested.[22] This mismatch could have affected the results. Finally, we were unable to determine to what extent symptom management may have been affected by limitations of staffing and patient contact precautions. In the early days of the pandemic, assessment and monitoring of dyspnea in this population may have been limited by the need for protective equipment and shortened physical contact between patients and providers in order to protect clinical staff from exposure.

Conclusion

This study examined symptom management for moderate respiratory distress associated with COVID-19 in hospitalized patients and the outcomes for these patients. The COVID-19 pandemic has caused overwhelming morbidity and mortality in the United States and around the world. In the beginning of the pandemic, while the disease course and effective therapies were still somewhat unknown, common symptoms would still have been treatable according to best practices. While overall symptom management was underprovided, it did not require additional palliative medicine intervention to be effective. Quality improvement initiatives to rectify such under-treatment might include the use of medical record triggers for respiratory distress, interprofessional education for inpatient care teams, and/or use of validated protocols for addressing respiratory symptoms (e.g. pharmacologic management, option for palliative care consultation).

Authors' Note

Tara Liberman, Santiago Lopez, and Edith Burns designed the study. Sima Parikh performed initial chart review. Stephanie Izard analyzed and interpreted the data. Regina Roofeh wrote the first draft of the manuscript. All authors made a substantial contribution to the concept or design of the work, revised it critically for important intellectual content and take public responsibility for appropriate portions of the content. All authors approved the final version of the manuscript to be published.

Declaration of Conflicting Interests

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