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Prolonged Symptoms After COVID-19 Infection in Outpatients

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We review 127 encounters for polymerase chain reaction–confirmed coronavirus disease 2019 (COVID-19) infection at a multidisciplinary outpatient clinic. We describe the symptomatology, time course, exam, and radiographic findings in this population. Patients with COVID-19 can experience persistent symptoms, primarily respiratory in nature, which can be severe enough to warrant hospitalization.

Keywords. COVID-19; ambulatory care; prolonged symptoms.

Despite reports of prolonged symptoms resulting from coronavirus disease 2019 (COVID-19), the literature describing its natural history is limited, particularly among outpatients [1]. Studies of persistent symptoms have focused on discharged hospitalized patients [2] or have relied on surveys [3, 4], rather than formal medical evaluations. Data suggest that 10% of patients can experience symptoms, such as dyspnea and fatigue, 3 weeks after acute illness [4]. We describe patients evaluated at an outpatient clinic during various stages of illness after diagnosis with COVID-19.

METHODS

The Emory Acute Respiratory Clinic (ARC) was initiated in April 2020 by the Divisions of General Internal Medicine and Infectious Diseases for patients with confirmed or suspected COVID-19. The ARC was created following recognition that local case rates in the Atlanta metropolitan area were rapidly increasing and an outpatient facility was urgently needed to decompress the demand on emergency departments (EDs) to

evaluate persons with known or suspected COVID-19. A primary care suite, temporarily idled due to the shutdown of in-person visits, was selected as the initial ARC site. The site was selected for specific qualities that would facilitate infection control and patient disposition, including an isolated location away from other patient care areas, direct patient access from a parking lot away from common areas, and a location adjacent to the hospital campus with wheelchair access to the ED. Providers were recruited from primary care and infectious diseases staff, and nursing staff were provided by numerous departments across the health system experiencing decreased clinical volume due to reduction in clinical services during this period. All staff were trained in operating procedures adapted for COVID-19 from those originally developed for evaluation of persons under investigation for Ebola virus disease in the outpatient setting [5]. Patients calling our health system for COVID-19 testing or care for symptoms related to confirmed or suspected illness were triaged to the ARC if they were determined by nursing staff to have symptoms requiring an in-person evaluation (including dyspnea, chest tightness, wheezing, or weakness) but without severity requiring ED-level care. Patients evaluated at the ARC who were determined by their provider to need ED- or inpatient-level care were immediately transferred to the ED or hospital.

A retrospective chart review was performed of patients seen from April 3 through May 16, 2020, with confirmed COVID-19, defined as a positive reverse transcription polymerase chain reaction (RT-PCR) assay for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) conducted before the encounter or on a specimen collected during the visit. Encounters without RT-PCR confirmation of infection were excluded from the analysis. Encounters were classified as acute, subacute, or convalescent depending on the duration since symptom onset (<1, 1–4, or >4 weeks). Demographic and clinical data were analyzed with standard descriptive statistics. For symptoms, examination findings, disposition, and other encounter-specific data, the analysis considered multiple encounters with the same patient to be separate encounters.

RESULTS

Among 404 consecutive patient encounters between April 3 and May 16, 127 (31.4%) had confirmed disease (107 unique patients with 1–4 visits) (Table 1). One in 5 patients was a health care worker, and nearly half were Black. Ten patients were known to be previously hospitalized. Patients presented up to 96 days from symptom onset and during acute, subacute, and convalescent stages (15.7%, 58.3%, and 26.0%, respectively) (Table 2). In most convalescent encounters, symptoms were characterized as worse or persistent.

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Table 1. Characteristics of Confirmed COVID-19 Patients Seen at the Emory Acute Respiratory Clinic, April 3–May 16, 2020 (n = 107)

Characteristic	No. (%)
Sex	
Female	81 (75.7)
Male	26 (24.3)
Age	
Median, y	55
Range, y	24–89
Race	
Black	52 (48.6)
White non-Hispanic	27 (25.2)
Hispanic	5 (4.7)
Other	23 (21.5)
Health care worker	42 (21.2)
Comorbid conditions	
Hypertension	42 (39.3)
Obesity	29 (27.1)
Diabetes	22 (20.6)
Asthma	23 (21.5)
Tobacco use	3 (2.8)
Days from onset ^a	
Median, d	14
Range	1 – 96

Abbreviation: COVID-19, coronavirus disease 2019.

^aAmong 127 total encounters.

Though measured or subjective fever was reported in 60% of acute encounters, it was less common in subacute and convalescent stages. Cough was reported in nearly 75% of encounters across all stages, while dyspnea on exertion was more common during subacute and convalescent stages. Smell or taste alteration was present in approximately half of acute and subacute visits, but only in a quarter of convalescent encounters. Lung auscultation was largely normal during all stages. When measured, resting pulse oximetry was <95% oxygen saturation in 11% of cases. Infiltrates were reported in less than one-third of 64 chest radiographs performed. Electrocardiography was performed in 15 (11.8%) encounters, with only 2 studies illustrating acute changes with tachycardia.

About half of encounters had 1 or more secondary diagnoses, including a variety of respiratory and other conditions (Table 2). A diagnosis of secondary bacterial pneumonia was made in 8.7% of encounters. Although most patients were discharged home, direct transfers from the ARC to the ED or inpatient ward occurred in 17.3% of all encounters and were most prevalent among subacute visits. Reasons for transfers to the ED or hospital included hypoxia (68.2%), dyspnea without hypoxia (22.7%), chest pain (4.5%), and asthma exacerbation (4.5%).

DISCUSSION

Following acute illness, patients with COVID-19 can experience significant prolonged symptoms. Increasing awareness of

chronic symptoms has led to new terminology such as “post-acute COVID-19” and “long haulers” [1, 6]. Although respiratory symptoms were common in our patients across all stages of illness, we found abnormalities in lung auscultation, pulse oximetry, and chest radiography in only a minority of patients. However, illness in >17% of encounters was concerning enough to warrant transfer to the ED or hospital. Furthermore, in over half of the encounters, there were 1 or more secondary diagnoses, including numerous respiratory and cardiovascular conditions that may have resulted from COVID-19 or exacerbated the symptoms.

Because the typical course can vary among patients of different ages and medical backgrounds, our experience may differ from clinics caring for other populations. As our study is also limited to the outpatient encounter, we cannot assess complications diagnosed after the visit. Although RT-PCR is considered the most sensitive test for diagnosing acute illness, it is also likely that some patients with COVID-19 infection were excluded from our analysis due to false-negative results or clearance of viral shedding in patients tested after the acute period.

While this study cannot determine the prevalence of persistent symptoms among patients recovering from COVID-19, our experience highlights the need for urgent care resources for patients. Clinics following COVID-19 patients should be prepared to manage prolonged symptoms and direct patients, if necessary, to higher levels of care or appropriate subspecialists. Following the recent Emergency Use Authorization (EUA) of monoclonal antibody treatments (bamlanivimab and the cocktail casirivimab plus imdevimab) by the Food and Drug Administration [7, 8], ambulatory clinics in the United States now must consider whether and how to offer these treatments. Many of the patients in this study would have likely met the criteria for high risk of progression to severe COVID-19 outlined in the EUAs [7, 8], as half of the patients were 55 years old or older and comorbid conditions including hypertension and obesity were prevalent. However, the majority of our patients presented after 1 week of illness, and most would not have qualified at the time of the encounter for treatments that must be given within 10 days of symptom onset. Although we have seen an increase in the ability and willingness of other clinics to manage ambulatory COVID-19 patients who are outside their isolation period, demand for ARC appointments remains high due to the post-holiday surge of cases [9] and implementation of infusion therapy for monoclonal antibody treatments. Since the period of the study, we have also faced challenges maintaining staffing levels and relocating the clinic since our health system reopened routine care.

Further study of the prevalence, pathophysiology, and treatment of persistent symptoms in COVID-19 is needed. Although the second wave of the US pandemic affected many younger patients, typically with mild illness, the potential for prolonged

Table 2. Symptoms and Examination Findings in Confirmed COVID-19 Encounters by Illness Stage

	Illness Stage			
	All Encounters (n = 127)	Acute	Subacute	Convalescent
		(<7 d) (n = 20)	(7–28 d) (n = 74)	(>28 d) (n = 33)
Symptom reported, No. (%)				
Fever	42 (33.1)	12 (60.0)	20 (27.0)	10 (30.3)
Chills	31 (24.4)	8 (40.0)	17 (23.0)	6 (18.2)
Body aches	44 (34.6)	12 (60.0)	24 (32.4)	8 (24.2)
Headache	46 (36.2)	9 (45.0)	29 (39.2)	8 (24.2)
Sore throat	24 (18.9)	5 (25.0)	13 (17.6)	6 (18.2)
Rhinorrhea	9 (7.1)	5 (25.0)	3 (4.1)	1 (3.0)
Sinus congestion	43 (33.9)	8 (40.0)	25 (33.8)	10 (30.3)
Cough	95 (74.8)	14 (70.0)	59 (79.7)	22 (66.7)
Dyspnea	51 (40.2)	4 (20.0)	33 (44.6)	14 (42.4)
Dyspnea on exertion	83 (65.4)	9 (45.0)	52 (70.3)	22 (66.7)
Chest tightness	58 (45.7)	8 (40.0)	30 (40.5)	20 (60.6)
Wheezing	18 (14.2)	3 (15.0)	13 (17.6)	2 (6.1)
Altered taste or smell	50 (39.4)	9 (45.0)	33 (44.6)	8 (24.2)
Diarrhea	28 (22.0)	6 (30.0)	18 (24.3)	4 (12.1)
Symptom character, No. (%) (n = 119) ^a				
New	23 (19.3)	9 (60.0)	10 (14.1)	4 (12.1)
Worse	51 (42.9)	5 (33.3)	37 (52.1)	9 (27.3)
Persistent	45 (37.8)	1 (6.7)	24 (33.8)	20 (60.6)
Lung auscultation, No. (%) (n = 116) ^a				
Normal	101 (87.1)	18 (100.0)	57 (83.8)	26 (86.7)
Abnormal ^b	15 (12.9)	0 (0.0)	11 (16.2)	4 (13.3)
Resting pulse oximetry, No. (%) (n = 109) ^a				
<92	4 (3.7)	1 (6.7)	3 (4.6)	0 (0.0)
92–94	8 (7.3)	0 (0.0)	5 (7.7)	3 (10.3)
95–99	97 (89.0)	14 (93.3)	57 (87.7)	26 (89.7)
Chest radiograph, No. (%) (n = 64) ^a				
Normal	44 (68.8)	3 (42.9)	28 (71.8)	13 (72.2)
Infiltrates ^c	20 (31.2)	4 (57.1)	11 (28.2)	5 (27.8)
Secondary diagnoses, No. (%) ^d				
None	67 (52.8)	12 (60.0)	43 (58.1)	12 (36.4)
Asthma, COPD, reactive airway disease	12 (9.4)	0 (0)	5 (6.8)	7 (21.2)
Seasonal allergies	7 (5.5)	1 (5.0)	2 (2.7)	4 (12.1)
Sinusitis	5 (3.9)	0 (0)	4 (5.4)	1 (3.0)
Pneumonia (non-COVID-19)	11 (8.7)	2 (10.0)	4 (5.4)	5 (15.2)
Cardiac (heart failure or arrhythmia)	4 (3.1)	1 (5.0)	2 (2.7)	1 (3.0)
Hypovolemia	4 (3.1)	1 (5.0)	3 (4.1)	0 (0)
Rash or urticaria	2 (1.6)	0 (0)	1 (1.4)	1 (3.0)
Anxiety	8 (6.3)	1 (5.0)	4 (5.4)	3 (9.1)
Other ^e	12 (9.4)	2 (10.0)	6 (8.1)	4 (12.1)
Encounter disposition, No. (%)				
Discharge home	105 (82.7)	17 (85.0)	58 (78.4)	30 (90.9)
Discharge to ER	15 (11.8)	3 (15.0)	10 (13.5)	2 (6.1)
Direct hospital admission	7 (5.5)	0 (0.0)	6 (8.1)	1 (3.0)

Abbreviations: COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; ER, emergency room.

^aPercentages are of the patient encounters with known information.

^bAbnormal findings included rales, rhonchi, and decreased air movement.

^cIncludes 1 chest radiograph demonstrating pulmonary edema.

^dEncounters may have more than 1 secondary diagnosis.

^eOther diagnoses included gastrointestinal reflux disease (n = 2), medication side effects (n = 2), urinary tract infection, hiccups, pleurisy, bronchiectasis, otalgia, hepatitis, migraine, diabetes mellitus.

and debilitating symptoms is concerning [6, 10]. As the United States is in the midst of the third wave, health systems must creatively adapt existing resources to manage the increasing numbers of patients in all stages of illness.

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