Postintensive Care Syndrome in Survivors of Critical Illness Related to Coronavirus Disease 2019: Cohort Study From a New York City Critical Care Recovery Clinic*

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OBJECTIVE: Determine the characteristics of postintensive care syndrome in the cognitive, physical, and psychiatric domains in coronavirus disease 2019 ICU survivors.

DESIGN: Single-center descriptive cohort study from April 21, to July 7, 2020.

SETTING: Critical care recovery clinic at The Mount Sinai Hospital in New York City.

PATIENTS: Adults who had critical illness due to coronavirus disease 2019 requiring an ICU stay of 7 days or more and who agreed to a telehealth follow-up in the critical care recovery clinic 1-month post hospital discharge.

INTERVENTIONS: None.

MEASURES AND MAIN RESULTS: Patient-reported outcome measures assessing physical and psychiatric domains were collected electronically, a cognitive test was performed by a clinician, and clinical data were obtained through electronic medical records. Outcome measures assessed postintensive care syndrome symptoms in the physical (Modified Rankin Scale, Dalhousie Clinical Frailty Scale, Neuro-Quality of Life Upper Extremity and Lower Extremity Function, Neuro-Quality of Life Fatigue), psychiatric (Insomnia Severity Scale; Patient Health Questionnaire-9; and Posttraumatic Stress Disorder Checklist for *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition), and cognitive (Telephone Montreal Cognitive Assessment) domains. The 3-Level Version of EuroQoL-5D was used to assess the physical and psychiatric domains. A diagnosis of postintensive care syndrome was made in cases with evidence of impairment in at least one postintensive care syndrome domain. We included 45 patients with a mean (SD) age of 54 (13) years, and 73% were male. Ninety-one percent of coronavirus disease 2019 ICU survivors fit diagnostic criteria for postintensive care syndrome. 86.7 % had impairments in the physical domain, 22 (48%) reported impairments in the psychiatric domain, and four (8%) had impairments on cognitive screening. We found that 58% had some degree of mobility impairment. In the psychiatric domain, 38% exhibited at least mild depression, and 18 % moderate to severe depression. Eighteen percent presented Posttraumatic Stress Disorder Checklist for *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition, scores suggestive of posttraumatic stress syndrome diagnosis. In the Telephone Montreal Cognitive Assessment, 9% had impaired cognition.

***See also p. 1569.**

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CONCLUSIONS: Survivors of critical illness related to coronavirus disease 2019 are at high risk of developing postintensive care syndrome. These findings highlight the importance of planning for appropriate post-ICU care to diagnose and treat this population.

KEY WORDS: coronavirus disease 2019; critical illness; depression; frailty; postintensive care syndrome; posttraumatic stress syndrome

As of January 16, 2020, the total number of confirmed cases of coronavirus disease 2019 (COVID-19) is over 94 million worldwide (1). Approximately 10–16% of these patients have required ICU admissions (2–4). Critical illness related to severe COVID-19 is associated with a high mortality rate ranging between 49% and 75%, especially in patients requiring mechanical ventilation (2–6). In the United States, a large cohort study of patients with COVID-19–related critical illness reported a 33% mortality rate among those patients who received mechanical ventilation (78 %) (5).

Rightfully, the initial focus of COVID-19 research was on acute treatment and mortality (7–9). Health systems across the world rapidly ramped up resources to meet the needs of the rapid surge in critically ill COVID-19 patients (4). However, months into this global pandemic, we are beginning to see a growing number of COVID-19 ICU survivors. Long-term complications of critical illness, including postintensive care syndrome (PICS), need to be addressed urgently in this population. PICS is defined as the presence of any impairment affecting the physical, psychiatric, or cognitive domains as a result of critical illness (10–12). The exact prevalence of PICS is unknown; however, Marra et al (12) followed 406 ICU survivors at 3 and 12 months and found at least one deficit in a PICS domain in 64% and 56% of patients, respectively.

Preventative measures that are often effective in non-COVID ICU patients may unfeasible in this patient population. Several strategies from the ICU liberation bundle Awakening, Breathing trials, Coordination with daily sedation interruption and ventilator liberation practices (13), Delirium monitoring and management (14), Early Mobility (15–17), and Family empowerment and engagement (ABCDEF) have been associated with improved outcomes in critically ill patients (18). Patients with critical illness related to COVID-19 may be at high risk for developing PICS due to the constraints on social support (isolation precautions), presence of severe acute lung injury that requires prolonged mechanical ventilation with exposure to high doses of sedatives, and limited implementation of early mobilization. In addition, imposed service limitation due to exposure restrictions and risk of transmission are likely contributing factors to developing PICS and need further investigation.

Emerging evidence suggests that individuals who are hospitalized for COVID-19 are at risk for muscle weakness, fatigue, and mood symptoms 6 months following discharge and those who were more severely ill during hospital care are at greater risk for enduring health problems (19). However, little is known about the prevalence or characteristics of PICS in patients who survive critical illness related to COVID-19. The high number of COVID-19–related critical illness survivors will create a significant burden on healthcare resources across the care continuum, and comprehensive description of these patients is needed to inform the design and implementation of rehabilitation interventions and long-term care management for individuals with PICS secondary to COVID-19. As such, we used data collected at an academic quaternary-care hospital in New York City to describe the physical, psychiatric, and cognitive impairments of COVID-19 ICU survivors.

METHODS

Study Design and Participants

This is a descriptive single-center cohort study, conducted in the critical care recovery clinic (CCRC) at The Mount Sinai Hospital in New York City between April 21, 2020, and July 7, 2020.

Prolonged ICU stay has been recognized as a risk factor for developing PICS in survivors of acute respiratory distress syndrome and sepsis (20, 21). A referral to the CCRC was triggered for patients with a minimum 7-day ICU length of stay. Patients who were included in the present study had critical illness related to COVID-19, were referred to the CCRC, received telehealth care through the CCRC, and agreed to a telehealth follow-up encounter 1-month post hospital discharge. There is no consensus within PICS literature on when PICS can or should be diagnosed. The time frame of 1-month

follow-up was chosen in order to assess for patients who had deficits requiring interventions and maximize early identification and treatment of these persons in need. We defined a confirmed COVID-19 case by a positive result on the reverse-transcriptase polymerase chain reaction assay of a specimen collected on a nasopharyngeal swab. Critical illness due to severe COVID-19 was defined as respiratory failure, shock, or multiple organ dysfunction (6, 22). Participants who did not complete the self-report portion of the follow-up were excluded from the study. The Institutional Review Board approved all study procedures.

Data Collection and Outcome Measures

Self-reported demographic data collected included age, gender, race, ethnicity, education level, employment status, marital status, smoking status, and history of substance abuse. Data regarding medical comorbidities (Charlson comorbidity index), psychiatric history, and hospitalization, including hospital and ICU length of stay, Sequential Organ Failure Assessment (SOFA) score, clinical documentation of delirium, maximal respiratory support, and COVID-19 treatment, were collected from the patient's electronic medical record (Epic System Corporation). As part of the clinical care, surveys containing patient-reported outcome (PRO) measures to assess PICS symptoms were collected within a month post hospital discharge, through a secure questionnaire form in Research Electronic Data Capture Software (REDCap, Vanderbilt University).

Outcome measures were selected to evaluate symptoms affecting the three core domains of PICS. Psychometric tools were used given the need to administer them over telehealth. PRO measures were used to assess the physical and psychiatric domains. To assess the physical domain, the scales used included the mobility, pain, self-care, and usual activities dimensions of the 3-Level Version of Euro-QoL-5D (EQ-5D-3L) (23). Additionally, this domain was assessed with the Modified Rankin Scale (mRS) (24), the Dalhousie Clinical Frailty Scale (DCFS) (25), the Quality of Life in Neurologic Disorders (Neuro-QoL) CAT v1.0 upper extremity function and Neuro-QoL lower extremity function CAT v1.0 (26–28), and the Neuro-QoL short form v1.0 to assess fatigue (26–28). For the psychiatric domain, we used the Insomnia Severity Index (29), Patient Health Questionnaire-9 (PHQ-9) (30), the anxiety/depression dimension of the EQ-5D-3L (23), and the Posttraumatic Stress Syndrome Checklist for *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition (PCL-5) (31). Last, for the cognitive domain, the Telephone Montreal Cognitive Assessment (T-MoCA) was administered by a CCRC clinician (32). The diagnosis of PICS was determined by a dysfunction in at least one PICS domain. For a full description of outcome measures, including domains assessed, scale details, and interpretation, see **Table 1**.

Data Analysis

Study data were exported from Research Electronic Data Capture (REDCap, a secure, web-based software platform hosted at the Icahn School of Medicine at Mount Sinai) to SPSS v.26 (IBM SPSS Statistics for Windows, Version 26.0; IBM Corp., Armonk, NY) for cleaning and scoring. Measures were scored according to published manuals. Missing items were handled according to recommendations of the scale's authors; otherwise, no summary score was computed. Descriptive statistics were calculated as mean, SD, median, interquartile range (IQR), minimum and maximum for continuous measures, and as count and percentage for categorical measures. For measures with cut points provided in the test manual, we report both the summary score and clinical category. Data from the PRO Measurement Information System (PROMIS)/Neuro-QoL test banks were submitted to the National Institute of Neurological Disorders and Stroke Health Measures Scoring Service for scoring based on their CAT algorithms and standardization based on normative samples (28). The resulting T-scores were used to create high and low functioning categories based on the PROMIS/NeuroQOL recommended cut off points corresponding to Moderate Symptoms or Impairment (28) (Table 1).

RESULTS

Patient Demographic and Clinical Characteristics

From April 21 and July 07, 2020, 121 patients with critical illness related to COVID-19 met the criteria for a referral to the CCRC. Of these, 72 patients were not seen in the clinic: 28 could not be reached, six were in an acute rehabilitation facility, 13 were in a subacute rehabilitation facility, 11 in long-term acute care hospitals (LTACHs), one missed the clinic appointment, and nine expired. A total of 49 patients were seen in the

TABLE 1.
Outcome Measures

Scale	Postintensive Care Syndrome Domain	Construct	Scale (Range)	Cut Off/Interpretation
Modified Rankin Scale	Physical	Neurologic disability	0–5	≥2 indicates disability
Patient-Reported Outcome Measurement Information System Short Form v1.0 Fatigue	Physical	Fatigue	T-score range[a]	Higher T-scores (> 60) indicate high levels of fatigue
Neuro-QoL UE Function v1.0	Physical	UE (fine motor skills, activities of daily living)	T-score range[a]	Lower T-scores (< 40) indicate poor UE function
Neuro-QoL LE Function v1.0	Physical	LE (mobility)	T-score range[a]	Lower T-scores (< 40) indicate poor LE function
Dalhousie Clinical Frailty Scale Clinical Frailty Score	Physical	Frailty	1–9	Clinical Frailty Scale > 4 indicates frailty
Insomnia Severity Index	Psychiatric	Insomnia	0–28	> 15 indicate clinical insomnia
Telephone Montreal Cognitive Assessment	Cognitive	Cognition	0–22	< 19 indicates cognitive impairment
3-Level Version of Euro-QoL-5D	Physical psychiatric	Mobility, self-care usual activities, pain/discomfort, anxiety/depression	1–3	Items interpreted separately ≥ 2 indicates disfunction
Patient Health Questionnaire-9	Psychiatric	Depressive symptoms	0–27	1–4: minimal depression; 5–9: mild depression; 10–14: moderate depression; 15–19: moderately severe depression; 20–27: severe depression
PTSD Checklist for *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition	Psychiatric	PTSD symptoms	0–80	≥ 31 indicates probable PTSD

LE = lower extremity, Neuro-QoL = Quality of Life in Neurologic Disorders, QoL = quality of life, PTSD = posttraumatic stress disorder, UE = upper extremity.
[a]Refer to *Data Analysis* section.

CCRC. Forty-five patients were included in the study analysis, and four were excluded because of incomplete PROs (**Fig. 1**).

The mean (SD) age was 53.9 (12.9) years, and 73.3% of patients were male. The most common preexistent comorbidities identified were hypertension (44.4%) and diabetes mellitus type 2 (20.0%). The calculated Charlson Comorbidity Index was 1.8 (1.9). Seven patients (15.2 %) had a history of smoking, one (2.2%) of alcohol dependence, and no patients reported illicit

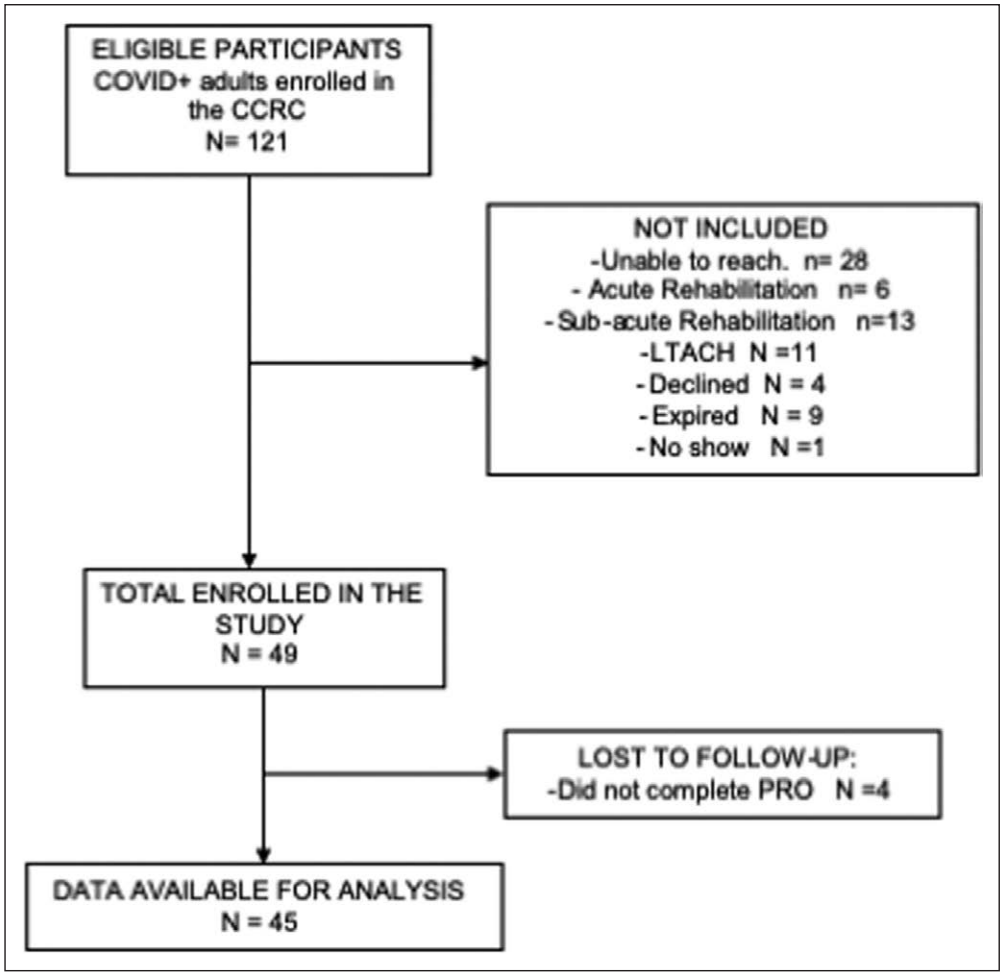

Figure 1. Flow chart diagram. CCRC = clinical care recovery clinic, COVID = coronavirus disease, LTACH = long-term acute care hospitals, PRO = patient-reported outcome.

drug use. Five patients (11.1%) and four patients (8.9%) had a history of anxiety and depression, respectively. The characteristics of the study participants are presented in **Table 2**.

Hospitalization Characteristics

The median (IQR) hospital length of stay was 18 d (12.5–27 d), whereas the median ICU length of stay was 10 day (7–15 d). The median SOFA score on ICU admission was 4.5 (3–6). Thirty-six patients (80.0%) required mechanical ventilation, one (2.2%) bilevel positive airway pressure, and two (4.4%) high-flow nasal cannula. Of the patients who required mechanical ventilation, 15 (33.3%) were sedated with propofol, 24 (53.3%) with benzodiazepines, 20 (44.4%) with opioids, and 21 (46.7%) required paralytics. Fourteen patients (31.1%) required prone ventilation, and eight (17.8%) had a tracheostomy. The median duration of mechanical ventilation was 8.0 days (IQR, 6–14 d) and ranged from 1 to 30 days. Last, delirium was documented in 19 patients (42.2%). A summary of hospitalization data is presented in **Table 3**.

Physical Domain

Thirty-nine participants (86.7%) reported at least one physical impairment, the majority presenting with problems in mobility and pain. The EQ-5D-3L showed that 30 patients (66.7%) had difficulties in mobility: 29 reported "some problems in walking about," and one reported being "confined to bed." Sixteen patients (35.6%) reported problems with self-care, and 30 patients (66.6%) reported problems with usual activities. Twenty-seven patients (60%) reported moderate or extreme pain or discomfort. The mRS showed 26 patients (57.7%) had some degree of disability: 14 (31.1%) had scores indicating "moderate disability; requiring some external help but able to walk without the assistance of another individual"; six (13.3%) scored "moderately severe disability; unable to walk or attend to bodily functions without the assistance of another individual"; and 6 (13.3%) scored "severe disability; bedridden, incontinent, requires continuous care."

Overall, eight patients (17.8%) were considered frail according to the DCFS (score > 4), 13 (28.9%) patients reported poor upper extremity function (Neuro-QoL Upper Extremity Function T-score < 40), and six patients (13.3%) reported poor lower extremity function (Neuro-QoL Lower Extremity Function T-score < 40). Last, 10 patients (22.2%) had elevated levels of fatigue (P-Fatigue T-score > 60).

Twenty-one of 45 patients (46%) received neuromuscular blockade. The EQ-5D-3L evidenced that

TABLE 2.
Patient Demographics

Demographic Variables	*n*	Mean (SD)/%
Age (yr)	44	53.9 (12.9)
Gender		
Male	33	73.3
Female	10	22.2
Race		
Asian	7	15.6
Black or African American	7	15.6
White	12	26.7
Other	15	33.3
Ethnicity		
Hispanic or Latino	17	37.8
Not Hispanic or Latino	24	53.3
Highest level of education ($n = 38$)		
Less than high school	6	13.3
High school diploma or equivalent	9	20.0
Some college, no degree	11	24/4
Associate's degree	2	4.4
Bachelor's degree	6	13.3
Master's degree	4	8.9
Employment status ($n = 45$)		
Self-employed	5	11.1
Full time	15	33.3
Part time	3	6.7
Unemployed	8	17.8
Disabled	4	8.9
Retired	6	12.2
Marital status ($n = 35$)		
Married/domestic partnership	22	61.1
Divorced/separated	8	22.2
Single (never married)	3	8.3
Widowed	2	5.6
Body mass index ($n = 45$)		
Normal (18.5–24.9)	9	20.0
Overweight (25–29.9)	17	37.8
Obese class I (30–34.9)	10	22.2
Obese class II (35–39.9)	5	11.1
Obese class III (> 40)	4	8.9
Smoking, alcohol, substance abuse		
History of smoking	5	11.1
Current smoker	2	4.4
History of alcohol dependence or abuse	1	2.2
History of illicit drug use	0	0
Comorbidities		
Hypertension	20	44.4
Myocardial infarction	3	6.7
Congestive heart failure	1	2.2
Peripheral vascular disease	1	2.2
Cerebrovascular accident or transient ischemic attack	4	8.9
Dementia	2	4.4
Chronic obstructive pulmonary disease	1	2.2
Peptic ulcer disease	1	2.2
Liver disease	2	4.4
Diabetes mellitus	9	20.0
Moderate to severe chronic kidney disease	2	4.4
Solid tumor	2	4.4
Charlson comorbidity index	45	2 (2)
Psychiatric history		
Anxiety	5	11.1
Depression	4	8.9
Posttraumatic stress disorder	0	0

TABLE 3.
Hospitalization Summary

Variables	*n*	Median (IQR)/%
Hospitalization		
Hospital length of stay (d)	45	18 (12–27)
ICU length of stay (d)	42	10 (7–15)
Sequential Organ Failure Assessment score at admission	38	4.5 (3–6)
Delirium	19	42.2
Coronavirus disease-19 treatment		
Corticosteroids	25	55.6
Azithromycin	21	46.7
Hydroxychloroquine	34	75.6
Remdesivir	5	11.1
Tocilizumab	14	31.1
Sarilumab	7	15.6
Therapeutic anticoagulation	23	51.1
Convalescent plasma	1	2.2
Stem cell transplant	5	11.1
ICU treatment		
Antibiotics (not azithromycin)	28	62.2
Renal replacement therapy	2	4.4
Maximal respiratory support		
Invasive MV	36	80.0
MV duration (d)	35	8 (6–14)
Proning	14	31.1
Paralysis	21	46.7
Selective pulmonary vasodilator	2	4.4
Tracheostomy	8	17.8
Opioids	20	44.4
Benzodiazepines	24	53.3
Propofol	15	33.3
Bilevel positive airway pressure	1	2.2
High-flow nasal cannula	2	4.4
Nonrebreather mask	1	2.2

IQR = interquartile range, MV = mechanical ventilation.

those patients who received paralytics had more problems performing usual activities compared with those who were not paralyzed (66.7% vs 29.2%).

Psychiatric Domain

A total of 22 patients (48.9%) presented with psychiatric impairment, with depression endorsed most commonly, followed by insomnia. On the EQ-5D-3L, 17 patients (37.8%) reported feeling "moderately anxious or depressed," and two patients (4.4%) reported feeling "extremely anxious or depressed." On the PHQ-9, 17 patients (37.8%) had scores in the range of at least mild depression (score > 4), with eight (17.8 %) scoring in the range of moderate to severe (score > 9). We also found that eight patients (17.8%) reported PCL-5 symptoms suggestive of PTSD (score ≥ 31). Clinical insomnia was also a common concern, with 11 patients (24.4%) scoring at subthreshold, and another six (13.3%) scoring at the moderate or severe cutoff.

Cognitive Domain

Of the 45 patients in this cohort, only 30 patients (66.7%) were administered a cognitive screening using the T-MoCA test due to staff shortages during the pandemic. Twenty-four of 30 patients (80%) scored 19 and above, suggesting no cognitive impairment, whereas six of 30 patients (20%) scored less than 19 which reflects impaired cognition; one of them had preexisting dementia.

PICS Diagnosis

Nearly all patients (41; 91.1%) met the criteria for PICS. Of these, 22 (53.6%) had impairments in two domains, and two (4.9%) had impairments in all three. The outcome measures indicating dysfunction in PICS domains (physical, psychiatric, and cognitive) are described in **Table 4**.

DISCUSSION

To our knowledge, this is the first study illustrating the prevalence and characteristics of PICS in COVID-19 patients. As such, direct comparison of our results with published studies is not yet possible. Approximately, 91% of those COVID-19 ICU survivors in this study met criteria for PICS symptoms, whereas prior literature suggests a rate of 64%

TABLE 4.
Outcome Measures Indicating Dysfunction in Postintensive Care Syndrome Domains (Cognitive, Physical, and Psychiatric)

Outcome Measures (Cut Off Value)	Full Sample		Impairment	
	n	Mean (SD)	*n*	%
Cognitive				
Telephone Montreal Cognitive Assessment	30	20.0 (3.0)	6	13.3
Physical				
EQ-5D-3L: mobility	45	1.7 (0.5)	30	66.7
EQ-5D-3L: pain/discomfort	44	1.7 (0.6)	27	60.0
EQ-5D-3L: self-care	45	1.4 (0.6)	16	35.6
EQ-5D-3L: usual activities	45	1.9 (0.7)	30	66.7
Modified Rankin Scale	45	2.6 (1.6)	26	57.8
Dalhousie Clinical Frailty Scale	43	3.3 (1.4)	8	17.8
Neuro-QoL Upper Extremity Function	42	44.7 (10.1)	13	28.9
Neuro-QoL Lower Extremity Function	42	51.1 (8.7)	6	13.3
Patient-Reported Outcome Measurement Information System Fatigue Item Bank	39	53.5 (11.7)	10	22.2
Psychiatric				
EQ-5D-3L: Anxiety/Depression	44	1.5 (0.6)	19	42.2
Patient Health Questionnaire-9	42	5.7 (6.9)		
Minimal depression			25	55.6
Mild depression			9	20.0
Moderate depression			2	4.4
Moderately severe depression			3	6.7
Severe depression			3	6.7
Posttraumatic Stress Disorder Checklist for *Diagnostic and Statistical Manual of Mental Disorders*, Fifth Edition	42	18.0 (21.2)	8	17.8
Insomnia Severity Index	43	7.1 (6.8)	6	13.3

EQ-5D-3L = 3-level version of Euro-QoL-5D, Neuro-QoL = Quality of Life in Neurologic Disorders Short Form v1.0, QoL = quality of life. Physical and psychiatric domains were assessed using patient-reported outcome measures.

in non–COVID-19 ICU survivors (albeit at a 3-mo follow-up) (12), and prevalence of deficits specific to PICS domains ranging between 25% and 80% (33). The higher prevalence of PICS reported here is likely due to multiple factors, including shorter follow-up period, the limited use of preventative measures such as the ABCDEF bundle due to isolation precautions, and the severity of the disease.

We found that 90% of patients referred to our CCRC received prolonged mechanical ventilation, and almost half were prescribed neuromuscular blocking agents, known predisposing factors for the development of ICU

acquired weakness (34–39). Expectedly, approximately 87% of our cohort exhibited an impairment in the physical domain. This is in contrast to prior evidence showing that 25–44% of ICU survivors developed some degree of physical impairment (39, 40). Our findings suggest that persons with severe COVID-19, particularly those who required neuromuscular blockade, may be more likely to develop at least some physical impairment.

A systematic review and meta-analysis showed that 25% of ICU survivors had PTSD at 3 months post ICU discharge. In comparison, 20% had persistent or new PTSD symptoms, 1-year post ICU discharge (41). Similarly, in survivors from the Bringing to light the Risk Factors And Incidence of Neuropsychological dysfunction in ICU survivors (BRAIN-ICU) study, 37% of patients experienced symptoms of depression at three months (42). Similar prevalences of self-reported PTSD and depression were found in our cohort, as compared to those reported in non–COVID-19 ICU survivors with PICS (35, 43–46). For non–COVID-19 ICU survivors, impairments in psychiatric domains such as anxiety, depression, and PTSD have been shown to have a negative impact on long-term quality of life (41). The same considerations in the treatment of and planning for negative effects on quality of life should be extended to ICU survivors of COVID-19.

Cognitive impairment after critical illness is known to be multifactorial and complex. Prior studies implemented a battery of comprehensive cognitive performance tests, assessing executive function, memory, information processing speed, language, attention, and concentration and found that 25–71% had cognitive impairment at a 12-month follow-up (47, 48). More sensitive comprehensive neurocognitive batteries than the T-MoCA likely would have yielded higher rates of cognitive impairment in our sample. We identified gross cognitive impairment in only a small portion of the sample based on a brief screening tool. Future research on this population should incorporate more comprehensive cognitive assessments that are more sensitive to detecting clinically significant cognitive deficits.

The results of this study illustrate the extensive multidomain symptoms experienced by COVID ICU survivors and can help other hospitals prepare for the long-term postdischarge health management priorities of patients who survive critical illness related to COVID-19. Our findings highlight the importance of addressing the need for appropriate follow-up and resources for these patients to assess and treat the cognitive, physical, and psychiatric sequelae of critical illness. Diagnosis of PICS alone will not improve outcomes; the management, treatment, and education of patients and their families are essential in mitigating the long-term effects of critical care.

Limitations of the Study

There are limitations to this study that warrant consideration. First, the data reported here were collected as part of a clinical service that was not initially designed to serve as a research study. As such, referral criteria for the CCRC were chosen to identify those most in need of follow-up care (20, 21) and therefore limited our investigation of PICS incidence to those with ICU stays of at least 7 days. However, since previous studies of critical illness survivors have found that length of stay is not a strong predictor of PICS, reported rates of PICS symptoms in our sample may underestimate PICS in COVID-19 critical care survivors (33). Clinical services were provided via telehealth during the pandemic, which limited our assessment battery to tools that could be administered remotely. Consequently, physical examinations (i.e., pulmonary function testing, 6-min walk test) and more thorough cognitive examinations impossible. T-MoCA scores were only available for 67% of our subjects, limiting our ability to comment on the types of cognitive impairments that survivors of severe COVID-19 might experience in the short term. Although we collected information about preexisting history of anxiety, depression, education, and employment status, data were not available on pre-COVID physical dysfunction. Additionally, patient contact restrictions during the height of the pandemic in New York City made it unfeasible to conduct telehealth follow-up with 30 patients who met enrollment criteria to the CCRC but were not seen because they were admitted in rehabilitation and LTACH facilities. Given patients admitted to rehabilitation or LTACH often have long-lasting deficits, the exclusion of these patients who required additional inpatient care likely resulted in underestimation of the prevalence of PICS in our cohort.

Future Directions

Future studies in larger multicenter samples should strive to use standardized, validated outcome measures that

extend generalizability of results across different cohorts of COVID-19 ICU survivors. Such studies should consider including diagnostic interviews by mental health professionals to accurately identify psychiatric disorders, as well as structured multimodal evaluation of cognitive functioning. Additionally, studies that directly compare the characteristics of PICS in COVID-19 ICU survivors with non–COVID-19 ICU survivors are an important direction for future research. Evaluation of the effects of potentially modifiable factors, such as social isolation, survivor's guilt, emotional support, and resilience, will identify treatment targets to improve outcomes of persons with severe COVID-19 infection.

CONCLUSIONS

To our knowledge, this study represents the most comprehensive clinical report of COVID-19 ICU survivors. We found that approximately 90% of ICU survivors reported symptoms affecting at least one PICS domain. Our findings highlight the importance of planning for appropriate post-ICU care for patients who survived critical illness related to COVID-19. The high prevalence of PICS seen in our sample suggests a need for rehabilitation interventions such as physical and occupational therapy, neuropsychologic assessment, and long-term monitoring for symptoms related to PICS. COVID-19 should be recognized as a chronic disease, so that appropriate resources are allocated to address the long-term impact of PICS in COVID-19 ICU survivors.

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Drs. Martillo and Dangayach contributed equally to the study's conception, study design, data acquisition, interpretation of data, and drafting of the article, and they are accountable for the accuracy and integrity of the results. Dr.Tabacof contributed to the article drafting and tables and figures design. Dr. Spielman contributed to the statistical analysis and drafted the data analysis section in the article. Dr. Dams-O'Connor contributed to the interpretation of the results, drafting of the article, and edited the tables. Dr. Chan contributed with data collection and edited the article. Dr. Kohli-Seth assisted in the supervision of the study. Drs. Cortes and Escalon contributed equally to the study design, data interpretation, article drafting, and supervision of the study. All authors performed a critical revision of the article for relevant intellectual content and approved this version for publication.

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