


# Long-Term Follow up of Renal and Other Acute Organ Failure in Survivors of Critical Illness Due to Covid-19

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## Abstract

**Background:** Little is known about the long-term health sequelae and outcomes of various organ failures in ICU survivors of Covid-19. The aim of our research was to study the characteristics of 120-day ICU survivors of the initial pandemic surge and report their long term (>6 months) outcomes.

**Methods:** We conducted a telephone questionnaire-based follow up study of 120- day survivors of Covid-19 admitted to ICUs at Montefiore Medical Center, Bronx, NY from 3/10/2020 to 4/11/2020. The study period was 2 months (11/1/2020-12/31/2020).

**Results:** 126 out of 300 (42%) survived to 120-days post-hospital discharge. The median age of survivors was 54 (47-61) years. Seventy-eight (62%) patients developed acute kidney injury (AKI); thirty-five (44.9%) of them required renal replacement therapy (RRT). One hundred-five (83.3%) required invasive mechanical ventilation; ten of them required tracheotomy. 103 (81.7%) completed the telephone questionnaire-based study, at a median (IQR) of 216.5 (200-234.5) days after hospital discharge. 29 (28.2%) patients reported persistent shortness of breath, 24, (23.3%) complained of persistent cough, and persistent anosmia in 9 (8.8%). AKI resolved completely in 58 (74.4%) patients. Of 35 AKI patients who required initiation of RRT during hospitalization, 27 (77%) were liberated from RRT and 20 (57%) had resolution of AKI. Of 20 patients without AKI resolution, 12 developed chronic kidney disease, whereas 8 still require RRT. Thirty-three (32.4%) patients developed post-traumatic stress disorder (PTSD) and 10 (11.8%) reported major depression. Many of the patients (68%) regained baseline functional status. Readmissions occurred in 22.3% patients within first 6 months after discharge.

**Conclusion:** Persistent symptoms of long Covid have been reported in ICU survivors of Covid-19 for extended durations. Outcomes of Covid-19 associated acute kidney injury are excellent. There is a high incidence of PTSD and depression in COVID-19 ICU survivors. Functional outcomes are good, but these patients remain at increased risk of hospital readmission.

## Keywords

covid-19, acute kidney injury, renal replacement therapy, ICU, organ failure

## Introduction

Coronavirus-19 induced disease (Covid-19) has affected more than 31 million Americans and caused over 570 000 deaths in the United States as of April 7, 2021.<sup>1</sup> Patients admitted to intensive care units (ICUs) are reported to have higher morbidity and mortality and usually develop multi system organ failures like acute respiratory failure, shock, acute renal failure, thromboembolic complications, need for prolonged ventilatory support with tracheostomy, acute stroke etc.<sup>2-6</sup> Little is known about the long-term health sequelae and outcomes of various organ failures in ICU survivors of Covid-19.

Although more than 22 million people are reported to have “recovered” from the disease, many of them continue to experience severe persistent symptoms which has been termed, “Long Covid” or “Post-acute Covid-19 syndrome”.<sup>7</sup>

Post-acute Covid-19 syndrome is a multisystem condition which can affect patients with mild to severe Covid-19 disease.<sup>8</sup> The commonly reported symptoms range from

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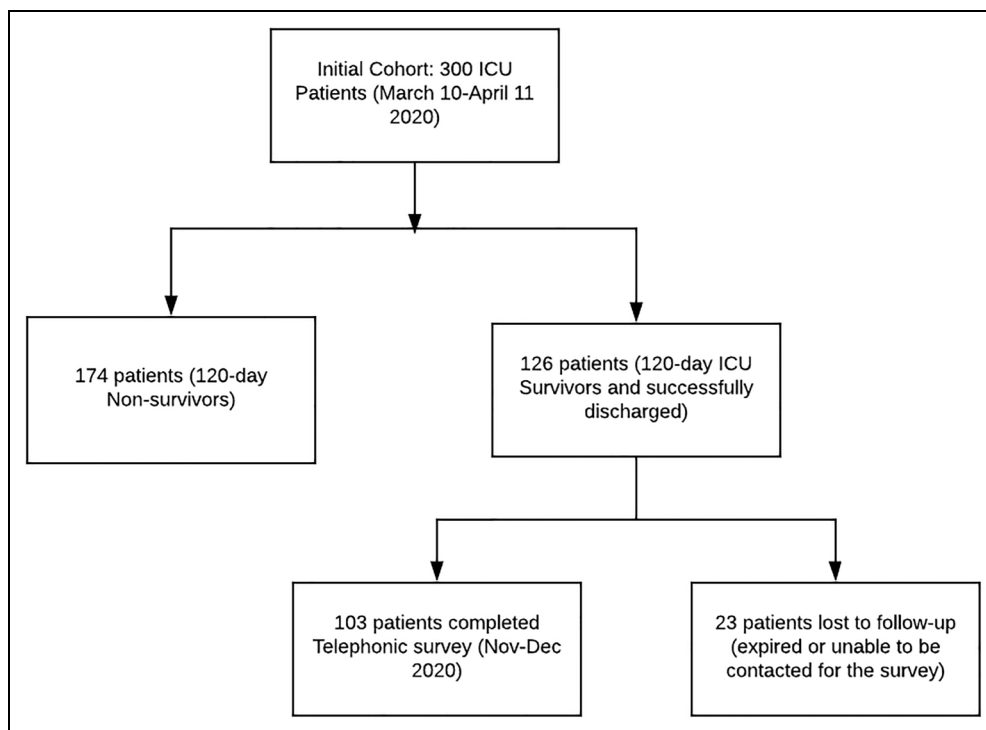
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**Figure 1.** Flow diagram of patients.

nonspecific fatigue, dyspnea, cough, chest pain, arthralgia, anosmia, to manifestations related to persistent organ dysfunction involving lungs, heart, kidneys, neuropsychiatric symptoms and rash.<sup>8,9</sup> Pathophysiology of late sequelae of Covid-19 could be related to direct organ damage by the virus, persistent hyperinflammatory state, hypercoagulable state or poor host immune response.<sup>7</sup> As healthcare systems still remain overwhelmed with management of hospitalized Covid-19 patients, the management of long term Covid-19 sequelae has been relatively neglected.

Few studies have reported the characteristics of patients with Post-acute Covid-19 syndrome, follow up and outcomes of organ failures of Covid-19 patients, ranging from 2 to 6 months after acute illness.<sup>10–20</sup> None of these studies specifically reported long term follow up and outcomes (more than 6 months) of critically ill patients admitted to the ICU. The aim of our research was to study the epidemiology and characteristics of 120-day ICU survivors of the initial surge of the pandemic and report their persistent symptoms, long term outcomes (more than 6-month follow up) of major organ failures (renal, respiratory), functional outcomes and readmissions.

## Methods

### Study Design

We conducted a telephone questionnaire-based follow up study of Covid-19 patients who had been admitted to ICUs at our institution from March 10 to April 11, 2020. Respondents completed a 10 to 15-min standard questionnaire created by the

research team. Previously, our group published outcomes of the first 300 adult Covid-19 patients admitted to Intensive care units of our hospital system during the initial surge of the pandemic.<sup>21</sup> Of this initial cohort of 300 patients, those who were alive for 120 days and were either discharged home or to a skilled nursing facility met the inclusion criteria for the telephonic questionnaire (Figure 1). The study period spanned 2 months (11/1/2020-12/31/2020). Our study was approved by the Institutional Review Board of the Albert Einstein College of Medicine (IRB# 2020-11358) and informed consent was obtained by telephone. We collected data regarding patient demographics, baseline characteristics and comorbidities, ICU course, complications (respiratory failure, renal failure, shock, acute stroke, thromboembolic complications) and outcomes for the 120-day survivors. Data on outcome of acute organ failures (renal, respiratory), persistent symptoms (cough, shortness of breath, anosmia), pressure ulcers, readmissions and functional outcomes (depression, post-traumatic stress disorder, functional outcome and ability to return to work) were collected from respondents by telephonic survey and, in addition, were manually extracted from our institution's electronic health record (EPIC) by the research team where applicable. Validated objective scales were used to screen for depression (PHQ-2/9), post-traumatic stress disorder (Primary care PTSD Screen for DSM-5) and functional outcome (The Post Covid-19 Functional Status Scale) during the telephonic survey.<sup>22–24</sup> Acute Kidney Injury (AKI) resolution was defined as return of the serum creatinine to baseline value. Baseline creatinine was defined using the last creatinine value in the electronic medical record between 7 days to 365 days

prior to the current admission.<sup>25</sup> If no baseline creatinine value was available, we defined baseline creatinine as the lowest serum creatinine value during the current hospitalization.

### Statistical Analysis

Descriptive statistics were obtained. Continuous variables were reported as median and interquartile range (IQR), whereas categorical variables were reported as counts and percentages. All

**Table 1.** Baseline Characteristics of Study Patients.

	Total cohort (n = 126)	Cohort with follow-up Interview (n = 103)
Age- years- median (IQR)	54 (47-61)	54 (46-61)
BMI- kg/m <sup>2</sup> - median (IQR)	30.5 (26.4-35.4)	30.6 (26.4-35.4)
# days before ICU admit- median (IQR)	5 (3-7)	5 (3-7)
White- n (%)	12 (9.5%)	11 (10.7%)
Black- n (%)	29 (23%)	22 (21.4%)
Hispanic- n (%)	57 (45.2%)	48 (46.6%)
Other- n (%)	25 (19.8%)	18 (17.5%)
Male gender- n (%)	65 (51.6%)	51 (49.5%)
Known COVID exposure- n (%)	22 (17.5%)	17 (16.5%)
Sick family members- n (%)	37 (29.4%)	37 (35.9%)
<b>Presenting symptoms- n (%)</b>		
Fever	87 (69%)	73 (70.9%)
SOB	104 (82.5%)	82 (79.6%)
Cough	96 (76.2%)	77 (74.8%)
Diarrhea	26 (20.6%)	24 (23.3%)
<b>Patient Comorbidities- n (%)</b>		
DM	55 (43.7%)	48 (46.6%)
HTN	73 (57.9%)	58 (56.3%)
CAD	13 (10.3%)	11 (10.7%)
Asthma	20 (15.9%)	19 (18.4%)
COPD	4 (3.2%)	4 (3.9%)
ESRD on HD	2 (1.6%)	2 (1.9%)
CKD	13 (10.3%)	10 (9.7%)
HIV +	2 (1.6%)	2 (1.9%)
HFrEF	3 (2.4%)	2 (1.9%)
Cirrhosis	1 (0.8%)	1 (1%)
Cancer	2 (1.6%)	2 (1.9%)
Smoker	20 (15.9%)	17 (16.5%)
ETOH use	14 (11.1%)	14 (13.6%)
Drug abuse	1 (0.8%)	1 (1%)

Data are summarized as median (IQR) or n (%), where n = available sample size. \*Percentages may not total 100 because of rounding. Abbreviations; ICU: intensive care unit; BMI: Body mass index; Kg: Kilogram; COPD: chronic obstructive pulmonary disease; CAD: coronary artery disease; ESRD on HD: End-stage renal disease on hemodialysis; CKD: Chronic kidney disease; HIV: human immunodeficiency virus; HFrEF: heart failure with reduced ejection fraction; HFpEF: heart failure with preserved ejection fraction; DM: Diabetes Mellitus; HTN: Hypertension; ETOH: Alcohol.

analyses were performed using SAS software, version 9.4 (SAS Institute Inc., Cary, NC USA).

## Results

### Characteristics, Renal and Other Outcomes of 120-day Survivors

Out of the initial cohort of 300 patients, 126 (42%) survived to 120-days (post-hospital discharge), of whom 59 (46.8%) were discharged home and the rest (n=67, 53.2%) to skilled nursing or rehabilitation facilities (Figure 1). The median (IQR) age of our 120-day survivors was 54 (47-61) years, 51.6% were males and median (IQR) body mass index was 30.5 (26.4-35.4) kg/m<sup>2</sup>. The majority of our population consisted of Hispanic (n=57, 45.2%) and Black (n=29, 23%) patients. Hypertension (n=73, 57.9%) and diabetes mellitus (n=55, 43.7%) were the most common comorbid conditions associated with our cohort of Covid-19 patients. Table 1 lists baseline characteristics of our 120-day survivors and patients who completed the follow-up telephonic survey.

Seventy-eight (62%) patients had developed acute kidney injury (AKI); 33 presented with AKI on admission, and 45 developed AKI during the hospital course.

Thirty-five (44.9%) patients with AKI required renal replacement therapy (RRT). Table 2 provides AKI outcomes of 120-day ICU survivors. One hundred-five (83.3%) of our 120-day survivors required invasive mechanical ventilation; median number of days on a ventilator was 7.5 (3-14). Ten patients required tracheotomy for long term ventilator support and weaning. Septic shock requiring vasopressor support developed in 17 (13.5%) patients. Thrombotic complications developed in many patients including deep venous thrombosis (n=22, 21.4%), acute pulmonary embolism (n=5, 4.9%), and acute ischemic stroke (n=16, 15.5%). Median ICU and hospital length of stay was 11 (6-17) and 23 (14-33) days, respectively. Table 3 provides major ICU outcomes of our 120-day survivors.

**Table 2.** AKI Outcomes (n = 78) at Follow Up.

No. of patients with AKI- n(%)	78 (61.9%)
AKI on admission	33(42.3%)
AKI during hospitalization	45 (57.7%)
<b>AKI resolution- n (%)</b>	58/78 (74.4%)
<b>Without AKI Resolution- n (%)</b>	20/78 (25.6%)
Developed CKD	12/20 (60%)
Still require RRT	8/20 (40%)
<b>RRT Outcomes- n (%)</b>	
AKI required RRT	35/78 (44.9%)
Came off RRT	27/35 (77.1%)
<b>Most recent serum Creatinine (median [IQR])</b>	
Patients with AKI resolution	0.90 (0.68-1.20)
Patients without AKI resolution	3.20 (1.28-4.60)

Data are summarized as median (IQR) or n (%), where n = available sample size. Abbreviations; AKI: Acute kidney injury; CKD: Chronic kidney disease; RRT: Renal replacement therapy.

**Table 3.** ICU Outcomes for 120-day Covid-19 Survivors (n = 126).

MV- n (%)	105 (83.3%)
No. of days on MV- median (IQR)	7.5 (3-14)
Vasopressors- n (%)	17 (13.5%)
VV ECMO- n (%)	2 (1.6%)
LOS in ICU, days -median (IQR)	11 (6-17)
Total LOS in hospital, days- median (IQR)	23 (14-33)
Tracheostomy – n (%)	10 (7.9%)
<b>Disposition at discharge- n (%)</b>	
Home	59 (46.8%)
Acute Rehabilitation	31 (24.6%)
SNF	35 (27.8%)
LTACH	1 (0.8%)

Data are summarized as median (IQR) or n (%), where n = available sample size. Abbreviations; MV: Mechanical ventilation; VV ECMO Venovenous Extracorporeal. Membrane Oxygenation; LOS: length of stay; SNF: skilled nursing facility. LTACH: long term acute care hospital.

### Long Term Outcomes in Surveyed Covid-19 Patients

Of 126 Covid-19 patients discharged alive to home or skilled nursing facilities, and who remained alive at 120 days post-hospital-discharge, our research team was able to contact and interview 103 (81.7%) members of this cohort (Figure 1). Our telephone survey was performed at a median (IQR) of 216.5 (200-234.5) days after hospital discharge. The median (IQR) age of surveyed Covid-19 patients was 54 (46-61) years and 49.5% were males. A significant percentage of patients complained of persistent symptoms including shortness of breath (n = 29, 28.2%), persistent cough (n = 24, 23.3%) and anosmia (n = 9, 8.8%).

AKI resolved completely in 58 (74.4%) of the 78 patients who had developed this organ injury with return of serum creatinine to baseline level. Of the 35 AKI patients who required initiation of RRT during hospitalization, 27 (77%) were liberated from RRT and 20 (57%) had resolution of AKI. In 43 AKI patients who did not require RRT, 38 (88.3%) had complete resolution of AKI. Of 20 patients without AKI resolution, 12 developed chronic kidney disease (CKD), whereas 8 still require RRT.

None of the 10 patients who required tracheotomy for long term ventilator support were able to be decannulated; all of these individuals continued to require ventilatory support and were residing in nursing homes. Seven (6.8%) patients had persistent supplemental oxygen requirements (provided by nasal cannula). Thirty-three (32.4%) patients reported development of post-traumatic stress disorder and 10 (11.8%) reported major depressive symptoms. Only 40 (38.8%) patients were able to return to work at the time of the phone survey due to ongoing health issues. Most of the patients (68%) regained their baseline functional status with no or negligible limitations and only 16% developed moderate to severe functional limitations in their everyday life. Table 4 presents the long-term outcomes of Covid-19 patients studied in the telephonic survey and readmissions data. Twenty-three (22.3%) patients were

readmitted subsequent to their initial hospitalization; 17 admitted in the Montefiore Health System and the rest to other hospitals. None of the comorbidities had a statistically significant association with post-acute sequela of Covid-19 (PASC) except for asthma with more asthmatics developing PASC (persistent shortness of breath, cough, anosmia, depression, post-traumatic stress disorder) (Table 5).

**Table 4.** Outcomes Reported at Follow-Up Survey (n = 103).

Persistent O2 requirement- n (%)	7 (6.8%)
Tracheostomy and not decannulated - n (%)	10 (9.7%)
<b>Persistent symptoms- n (%)</b>	
Cough	24 (23.3%)
SOB	29 (28.2%)
Anosmia	9 (8.8%)
<b>Thromboembolic complications- n (%)</b>	
Stroke	16 (15.5%)
PE	5 (4.9%)
DVT	22 (21.4%)
Internal Jugular Vein	3(13.6%)
Upper extremity Vein	2(9%)
Lower extremity	10(45.4%)
Proximal/Distal	5/5
Unknown site	7(31.8%)
<b>Functional outcomes</b>	
PTSD	33 (32.4%)
Depression	10 (11.8%)
Return to work	40 (38.8%)
<b>Post Covid-19 Functional Status scale</b>	
0	34 (33%)
1	34 (33%)
2	18 (17.5%)
3	9 (8.7%)
4	8 (7.8%)
Pressure ulcer	28 (27.2%)
Total Readmissions- n (%)	23 (22.3%)
Readmissions at Montefiore- n (%)	17 (73.9%)
<b>Reason for admission- n (%)</b>	
Gangrene	3(17.6%)
Sepsis	2 (11.7%)
Upper extremity ulcer	1(5.8%)
Acute Pulmonary Embolism	1(5.8%)
Tachyarrhythmia	1(5.8%)
Acute respiratory failure	1(5.8%)
Gastrointestinal bleeding	1(5.8%)
Asthma exacerbation	1(5.8%)
Dislodged tracheostomy	1(5.8%)
Hysteroscopy	1(5.8%)
Small bowel obstruction	1(5.8%)
Syncope	1(5.8%)
Abscess	1(5.8%)
Acute cholecystitis	1(5.8%)
Readmission at outside hospital- n (%)	6
<b>Reason for readmission</b>	
Gangrene	2(33.3%)
Chest pain	1(5.8%)
Unknown	3(50%)

Data are summarized as median (IQR) or n (%), where n = available sample size. Abbreviations; SOB: shortness of breath; PE: Pulmonary embolism; DVT: Deep venous thrombosis; PTSD: Post Traumatic Stress disorder.

**Table 5.** Comorbidity Status and PASC<sup>8</sup> Reported at Follow-Up Survey (n = 103).

Comorbidity – n(%)	PASC reported (n = 51)	PASC not reported (n = 52)	p-value*
DM	22 (43.1)	26 (50.0)	0.56
HTN	33 (64.7)	25 (48.1)	0.11
CAD	4 (7.8)	7 (13.5)	0.53
Asthma	14 (27.5)	5 (9.6)	0.02
COPD	1 (2.0)	3 (5.8)	0.62
ESRD on HD	1 (2.0)	1 (2.0)	1.00
CKD	4 (7.8)	6 (11.5)	0.74
HIV +	2 (3.9)	0 (0.0)	0.24
HFrEF	1 (2.0)	1 (2.0)	1.00
Cirrhosis	0 (0.0)	1 (2.0)	1.00
Cancer	1 (2.0)	1 (2.0)	1.00
Smoker	9 (17.7)	8 (15.4)	0.80
ETOH use	10 (19.6)	4 (7.7)	0.09
Drug abuse	0 (0.0)	1 (2.0)	1.00

<sup>8</sup>defined as persistent SOB, cough, anosmia, depression, or PTSD.

\*corresponds to Fisher's exact test for association.

Data are summarized as median (IQR) or n (%), where n = available sample size. Abbreviations; DM: Diabetes Mellitus; HTN: Hypertension; CAD: coronary artery disease; COPD: chronic obstructive pulmonary; ESRD on HD: End-stage renal disease on hemodialysis; CKD: Chronic kidney disease; HIV: human immunodeficiency virus; HFrEF: heart failure with reduced ejection fraction; ETOH: Alcohol.

## Discussion

Our study reports long term follow up and outcomes (more than 6 months) of major organ failures (renal, respiratory), persistent symptoms of long Covid and functional outcomes (Post Traumatic Stress Disorder [PTSD], major depression) in 120-day ICU survivors of Covid-19.

AKI has been reported in up to 24%-57% of hospitalized Covid-19 patients and in 61%-78% of those requiring ICU admissions and has been associated with poor prognosis.<sup>26-31</sup> The long-term renal outcomes of survivors of Covid-19 associated AKI remain unknown due to a paucity of published data. In a recent editorial by Stockmann et al. long term renal outcomes of ICU patients with Covid-19 associated AKI requiring RRT were described.<sup>32</sup> Their retrospective study included 74 patients with median follow up of 151 days post initiation of RRT. At the conclusion of follow-up period, thirty-six (46.8%) patients expired, 1(1.4%) was still hospitalized and 37 (50%) were successfully discharged from the hospital. 34 out of 37 (91.9%) were able to come off RRT completely, with 23 (62.2%) achieving full recovery. The median (IQR) duration of RRT in survivors was 27 days (11-50 days). These findings support our observations as AKI resolved completely in 74.4% of our survivors. AKI-RRT outcomes were better in the Stockmann study compared to ours since 91.9% of their patients were able to be liberated from RRT completely compared to 77% of our patients. This difference might be explained by the greater severity of AKI in our high-risk Black and Hispanic populations who comprised a larger percentage of our study population.<sup>33,34</sup> Another study from France reported 3-month

follow up of Covid-19 associated AKI from the initial surge of the pandemic.<sup>35</sup> Of 27 patients with AKI, renal recovery was achieved in 23 (85%) patients, none of them requiring RRT at 90 days. New onset CKD developed in 4 of their patients. Overall, the long-term renal outcomes of ICU survivors of Covid-19 illness are encouraging, both in patients with and without the need for RRT. Nugent et al. did notice a greater rate of eGFR decrease after discharge and slower renal recovery in patients with Covid-19 associated AKI compared to AKI without Covid-19, emphasizing the need for closer monitoring of renal function in Covid-19 associated AKI patients in the outpatient setting.<sup>36</sup>

Our study reports presence of persistent symptoms of long Covid in up to one-third of the ICU survivors of Covid-19 completing the questionnaire- based survey. These findings are similar to the prior published reports.<sup>10,11,14,15</sup> The most common reported symptoms in these prior studies included dyspnea, cough, chest pain, fatigue, muscle weakness and persistent loss of taste or smell.<sup>10,11,14,15</sup> But the evidence regarding long term consequences in critically ill ICU patients is scant from these studies as only 4 to 12.6% of their patients were admitted to an ICU. The authors did find that ICU patients had worse pulmonary diffusion abnormalities and chest imaging findings.<sup>10</sup> It is reasonable to postulate that critically ill ICU patients suffer more severe residual damage to major organs such as the lungs and kidneys, thereby explaining the presence of persistent symptoms such as chest tightness, dyspnea and cough in this cohort of patients.

Our 120-day Covid-19 ICU survivor population represents a younger cohort of patients, with the median age of 54 years and similar to a large multi-center study by Gupta and colleagues where mean age of patients alive at 28 days was 57.4 years.<sup>37</sup> About 90% of our 120-day survivors were also able to be extubated by first 4 months. Gupta et al. reported extubation rate of 44.9% by day 28. Our higher extubation rate can be explained by the longer duration of follow up of 4 months compared to 28 days in Gupta study.

Outcomes of patients discharged with tracheotomy have been encouraging per published reports, with decannulation achieved in 60 to 81% of patients in long term care facilities.<sup>38-40</sup> None of our 10 patients with tracheotomy were able to be decannulated or liberated from mechanical ventilation by the time of the performance of our follow-up study. This may reflect more severe respiratory illness in our patients and possibly more aggressive ventilator liberation attempts among patients reported in prior studies.

About 32.4% of our patients developed PTSD symptoms, which is in line with previously reported prevalence of 30% in Covid-19 patients.<sup>41</sup> Functional outcomes of the majority of our patients were good, likely because of aggressive acute and subacute rehabilitation services which have been associated with improved motor, respiratory and functional outcomes.

Covid-19 has been associated with a higher risk of hospital readmissions, ranging from 4.4% to as high as 19.9% within the first 2 months after discharge.<sup>42,43</sup> Our study showed a readmission rate of 22.3% during the first 6 months after discharge.

Our study has several major strengths. First, we included only critically ill patients who had been admitted to an ICU. Second, the study population represents the very initial surge of the pandemic when healthcare systems first encountered Covid-19 and did not have experience managing such patients. Third, our follow up survey was done more than six months after hospital discharge, providing longer follow up. Fourth, we had good follow-up and completion rate of the telephone survey, capturing 81% of the targeted cohort.

We also acknowledge a few limitations of our study, including it being a single center study, and that data were unavailable for 23 (19%) patients. We also did not perform comprehensive follow up physical exams, laboratory tests, pulmonary function tests and imaging studies. We did not collect data on whether our patients were at home or skilled nursing or rehabilitation facility at the time of phone interview. Lastly, we relied on patients' responses via a telephone survey, which can lead to recall bias.

## Conclusion

The burden of care for ICU survivors of Covid-19 is extensive and likely will continue to grow. These patients report persistent symptoms of long Covid for extended durations (more than 6 months). Outcomes of organ failures including acute kidney injury are excellent and the majority of initially afflicted patients are able to be liberated from RRT. There is a high incidence of post-traumatic stress disorder and depression in COVID-19 survivors. Functional outcomes are good, but these patients remain at increased risk of hospital readmissions in the months following the index hospitalization.

## Author Contributions

SC and PD conceptualized the study; SC, AN, VD, DCL and DO contributed in telephonic survey and data collection; MJF contributed in data analysis; SK contributed in writing and editing the manuscript; JT contributed in editing the manuscript; SK and PD provided overall supervision.

## Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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## Ethical Approval

Not applicable, because this article does not contain any studies with human or animal subjects.

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## Supplemental Material

Supplemental material for this article is available online.

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