Cogitare Enfermagem

ORIGINAL ARTICLE

PERSISTENT SYMPTOMS, SELF-REPORTED HEALTH AND QUALITY OF LIFE OF COVID-19 SURVIVORS: A COHORT STUDY*

HIGHLIGHTS

1. COVID-19 symptoms persisted for 180 days, fatigue more commonly.
2. Mild dyspnea and myalgia also have been reported.
3. Despite persistent symptoms, the general quality of life was "good".
4. COVID-19 survivors were satisfied with their health state.

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ABSTRACT

Objective: This study investigates persistent symptoms, health satisfaction, and general quality of life of COVID-19 survivors at 30, 90, and 180 days after Intensive Care Unit discharge. **Method:** A multicentric prospective cohort study of COVID-19 survivors discharged from eight hospitals in Curitiba – Paraná (Brazil) between September 2020 and January 2022. Eligible COVID-19 survivors were interviewed by phone. A descriptive analysis was performed, and data were compared using Cochran's Q test and Friedman's nonparametric test. **Results:** Sixty-two COVID-19 survivors responded to the three interview moments. The most persistent symptoms were fatigue, mild dyspnea, and myalgia. At 30, 90, and 180 follow-up days, most patients reported "good" general quality of life (59.7%, 62.9%, 51.6%, respectively) and a "satisfactory" health state (43.5%, 48.4%, 46.8%, respectively). **Conclusion:** This study revealed the persistence of symptoms after COVID-19 infection; understanding these consequences is the first step towards developing medical treatments and management strategies for these patients.

KEYWORDS: Coronavirus Infections; Intensive Care Unit; Health Status; Quality of life.

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INTRODUCTION

According to the World Health Organization (WHO), two years after the first case of COVID-19 was confirmed in Wuhan, China, more than 500 million people have been contaminated and over 6 million people died due to the infection[1]. Some post-infection consequences were noticed with the many recovered patients but are still uncertain[2].

Post-COVID-19 syndrome occurs in patients infected by SARS-CoV-2 and still present symptoms, even after two months, that cannot be explained by other diagnosis[3]. Several studies showed that most patients present the illness's sequelae even after the infection's acute phase, the most common symptoms being fatigue/ muscle weakness, dyspnea, cognitive dysfunctions, sensorimotor symptoms, and headaches[4-5]. A cohort study done at Jin Yin-tan Hospital (Wuhan, China) with 736 patients revealed that 76% of survivors reported at least one symptom after six months of COVID-19 infection, the most common being fatigue, muscle weakness, and sleep difficulties[6-7]. The same study followed the patients until 12 months after the acute infection, demonstrating that fatigue was the most reported sequelae, followed by sleep difficulties and hair loss. Furthermore, some symptoms were most frequently found after 12 months rather than six months, such as dyspnea, anxiety, and depression[8-9].

The persistence of symptoms after COVID-19 infection is associated with increased disability and negatively impacts physical function and quality of life[10]. Some studies have reported that post-COVID-19 syndrome may lead to poor quality of life, revealing that patients with at least one symptom had significantly lower physical and mental life quality than those who were asymptomatic[11-12]. Furthermore, patients requiring intensive care reported lower quality of life than those inward admission[13-14].

Considering that, after COVID-19 infection, the number of persistent symptoms remains high even in patients who were not hospitalized[15], the greater number of persistent symptoms may be associated with worse health outcomes, including quality of life. However, despite increasing evidence of the potential long-term impacts of COVID-19 on health, this is not clear.

The primary aim of this study was to investigate persistent symptoms in patients hospitalized due to COVID-19 infection at 30-, 90- and 180 days post-ICU discharge. Secondarily, we assess the patient's health satisfaction and general quality of life.

METHOD

This is a multicentric prospective cohort study of COVID-19 survivors discharged from eight intensive care units (ICUs) from hospitals in Curitiba – Brazil. During the study period between September 2020 and January 2022, these ICUs reached a maximum capacity of 225 exclusive beds for COVID-19. Of these, 124 were public beds, 71 were private, and health insurance beds, and 30 received both public and private patients.

Patients aged > 18 years, hospitalized for COVID-19 treatment, with laboratory confirmation (RT-PCR test obtained from nasopharyngeal swab before or immediately after hospitalization), and discharged from ICU were eligible for follow-up. Patients were excluded if they had negative or inconclusive PCR results for SARS-CoV-2, language, and cognition disorders and could not provide consent and respond to the telephone survey. The criteria established for discontinuing the follow-up were refusal expressed by the participant at any time, manifestation of discomfort, inability to understand or answer the questions throughout the research, and hospital readmissions.

Eligible COVID-19 survivors were contacted by phone by trained researchers and invited to answer telephone surveys at 30, 90, and 180 days after ICU discharge. Data were acquired and stored on a password-protected digital platform provided by REDCap® (Research Electronic Data Capture, REDCap 8.11.6 - © 2021 Vanderbilt University). This secure, web-based application is designed to support data capture for research studies.

We designed a questionnaire to collect post-discharge clinical symptoms, usually investigated in other studies, including fever, cough, sore throat, chest pain, myalgia, arthralgia, fatigue, dyspnea, headache, dizziness, fainting, gastrointestinal disorders (vomiting, diarrhea, and abdominal pain), anosmia, hyposmia, hypogeusia, vision change/loss, paresthesia, paresis, and other symptoms. More than one symptom could be reported. Furthermore, the medical records were accessed to build the patient's clinical profile during the ICU stay.

Patients were also asked to rate their health status based on health satisfaction (very dissatisfied; dissatisfied; neither satisfied nor dissatisfied; satisfied; very satisfied) and general quality of life (poor; poor; neither poor nor good; good; very good).

Categorical variables were described as absolute frequency and percentage values. According to the Kolmogorov-Smirnov normality test, the patient's age had a normal distribution and was described as mean and standard deviation values. The length of ICU stays and the number of symptoms with non-normal distributions in the same normality test was described as mean, median, minimum, and maximum values.

Considering the sample of participants who responded to the interview at the three moments (30, 90, and 180 days after ICU discharge), the proportion of the presence of each of the symptoms (dichotomous variables) was compared between the three moments using the Q Cochran test followed by post hoc paired comparison with Bonferroni corrections. The levels of quality of life, health satisfaction, and dyspnea were compared between the three moments using the Friedman nonparametric test, followed by post hoc paired comparison with Bonferroni corrections.

The statistical significance level was set at 5%, and data were analyzed using the statistical software IBM SPSS Statistics, version 28.0 (IBM SPSS Inc., Chicago, IL, USA). Missing data were not imputed.

The study was approved by the Research Ethics Committee of the Pontifical Catholic University of Paraná (PUC-PR) (Reference number 4.293).

RESULTS

Between September 2020 and January 2022, 1.686 patients diagnosed with COVID-19 were discharged from the ICU of the hospitals included in this research. However, we analyzed telephone survey data from 164 patients 30, 90, and 180 days after ICU discharge (Figure 1).

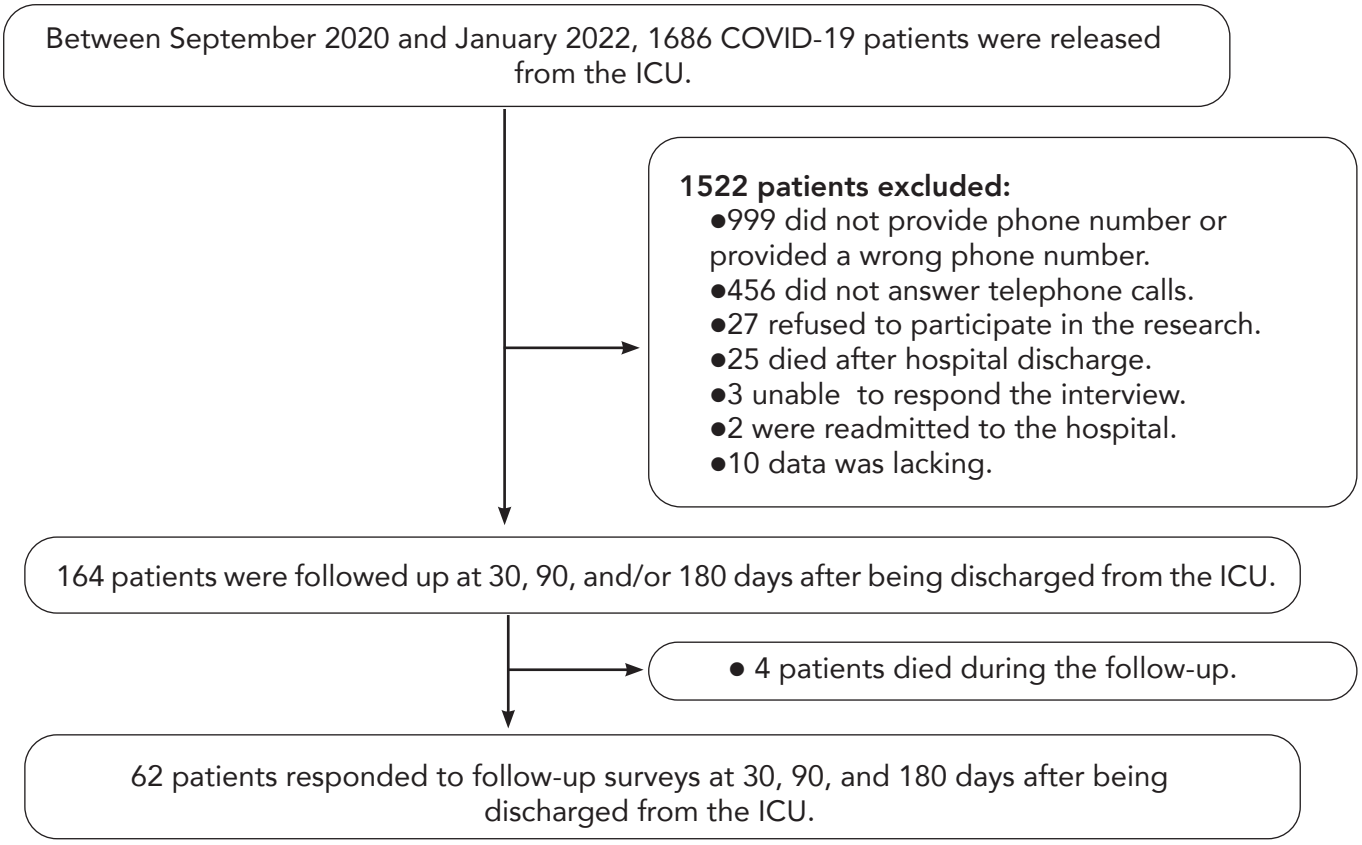

Figure 1 - Flow chart of the sample process selection. Curitiba, PR, Brazil, 2022
Fonte: The authors (2022).

Sample characteristics, clinical condition and severity scores at ICU admission, outcomes, and level of functional dependence at ICU discharge are summarized in Table 1.

Table 1 - Characteristics of the participants during the period of ICU stay. Curitiba, PR, Brazil, 2022

Characteristics	**Total (n = 164)**
Age (years) – mean ± SD	52.4 ± 15.6
Female sex – n (%)	87 (53)
Clinical condition at ICU admission	
Level of hemodynamic support – n (%)	
No support	106 (67.9)
Volume support (5mL/kg/hour)	28 (17.9)
Support with volume and vasoactive drugs	22 (14.1)
Level of ventilatory support – n (%)	
Ambient air	2 (1.3)
Oxygen therapy (nasal catheter or O_2 mask)	96 (61.5)
Non-invasive ventilation	24 (15.4)

Invasive ventilation	34 (21.8)
Severity scores at ICU admission	
APACHE II score – mean; median (IQR)	11.5; 11 (1 – 31)
Glasgow score - mean; median (IQR)	14.2; 15 (15 – 15)
Outcomes	
Length of ICU stay (days) – mean; median (IQR)	17.7; 11 (7 – 23)
Glasgow scores at ICU discharge – mean, median (IQR)	14.9; 15 (15 – 15)
Level of functional dependence at ICU discharge [a]– n (%)	
Able to live independently	69 (44.2)
Needing assistance in elaborate activities (e.g., driving)	48 (30.8)
Needing help with basic activities (e.g., personal care)	33 (21.2)
Dependent in all activities (e.g., locomotion, personal care)	6 (3.8)

Abbreviations: n: frequency; %: percentage; SD: standard deviation; IQR: interquartile range; O_2:oxygen.

[a]: 8 missing data.

Fonte: Authors (2022).

Among the 164 respondents, only 62 (37.8%) participated in the three moments; 30 (18.3%) responded to telephone survey 30 and 90 days after ICU discharge; 15 (9.1%) responded to telephone survey 30 and 180 days after ICU discharge; 12 (7.3%) responded to telephone survey 90 and 180 days after ICU discharge; 31 (18.9%) on day 30 only; nine (5.5%) on day 90 only; and five (3%) on day 180 after ICU discharge. Therefore, 138 responses about persistent symptoms, general quality of life, and health satisfaction were obtained 30 days after ICU discharge, 113 responses 90 days after ICU discharge, and 94 responses 180 days after ICU discharge (Table 2).

The most prevalent symptoms at 30, 90 and 180 days after ICU discharge were fatigue (65.9%, 51.3%, and 44.7%, respectively), mild dyspnea (42.0%, 31.0%, and 29.8%, respectively) and myalgia (29.0%, 22.1%, and 17.0%, respectively). However, most patients reported "good" general quality of life (57.2%, 63.1%, and 50.5%, respectively), and patients that reported "very good" general quality of life increased from 11.6% in 30 days to 19.4% in 180 days. Regarding health satisfaction, "satisfied" was reported by 51.1%, 48.6 and 47.3% of patients, respectively, and we also observed an increase in "very satisfied" patients (10.2%, 12.6%, and 17.2%, respectively) (Table 2).

Table 2 - Persistent symptoms, general quality of life, and health satisfaction reported 30, 90, and 180 days after ICU discharge. Curitiba, PR, Brazil, 2022

Variables	30 days after ICU discharge (n = 138)	90 days after ICU discharge (n = 113)	180 days after ICU discharge (n = 94)
Quality of life[a]n(%)			
Very poor	2 (1.4)	1 (0.9)	0 (0)
Poor	9 (6.5)	4 (3.6)	6 (6.5)
Neither poor nor good	32 (23.2)	24 (21.6)	22 (23.7)

Good	79 (57.2)	70 (63.1)	47 (50.5)
Very good	16 (11.6)	12 (10.8)	18 (19.4)
Health satisfaction n (%)			
Very dissatisfied	1 (0.7)	2 (1.8)	0 (0)
Dissatisfied	17 (12.4)	15 (13.5)	10 (10.8)
I am neither satisfied nor dissatisfied	35 (25.5)	26 (23.4)	23 (24.7)
Satisfied	70 (51.1)	54 (48.6)	44 (47.3)
Very satisfied	14 (10.2)	14 (12.6)	16 (17.2)
Symptoms n (%)			
Fatigue	91 (65.9)	58 (51.3)	42 (44.7)
Dyspnea			
No	67 (48.6)	75 (66.4)	62 (66.0)
Mild	58 (42.0)	35 (31.0)	28 (29.8)
Moderate	13 (9.4)	3 (2.7)	4 (4.3)
Myalgia	40 (29.0)	25 (22.1)	16 (17.0)
Arthralgia	20 (14.5)	18 (15.9)	12 (12.8)
Cough	22 (15.9)	10 (8.8)	5 (5.3)
Headache	14 (10.1)	8 (7.1)	5 (5.3)
Dizziness, fainting	10 (7.2)	1 (0.9)	0 (0)
Chest pain	8 (5.8)	3 (2.7)	1 (1.1)
Paresis, paresthesia	7 (5.1)	3 (2.7)	3 (3.2)
Gastrointestinal disorders	5 (3.6)	1 (0.9)	0 (0)
Anosmia, hyposmia, hypogeusia	5 (3.6)	1 (0.9)	0 (0)
Sore throat	5 (3.6)	3 (2.7)	1 (1.1)
Vision loss/change	4 (2.9)	2 (1.8)	2 (2.2)
Others n (%)	16 (11.6)	6 (5.3)	4 (4.3)
Number of Symptoms mean; median (IQR)	2.3; 2 (1-3)	1.6; 1 (0-3)	1.3; 1 (0-2)

Abbreviations: n: frequency; %: percentage; IQR: interquartile range.

[a]2 missing data at 90 days after ICU discharge, and one missing data at 180 days after ICU discharge.

[b] 1 missing data at 30 days after ICU discharge, two at 90 days after ICU discharge, and one at 180 days after ICU discharge.

Fonte: Authors (2022).

We also compared the presence of symptoms, quality of life, and health satisfaction of 62 patients who participated in the three interview moments (Table 3). The majority (51.6%) were males, with a mean age of 50.3 ± 13.9 years median length of ICU stays of 13 days (range, 2-128 days).

Table 3- Comparison between symptoms, general quality of life, and health satisfaction at 30, 90, and 180 days after ICU discharge. Curitiba, PR, Brazil, 2022

Variables	30 days after ICU discharge (n = 62)	90 days after ICU discharge (n = 62)	180 days after ICU discharge (n = 62)	p-value
Quality of life n (%)				
Very poor	1 (1.6)	1 (1.6)	0 (0)	
Poor	1 (1.6)	0 (0)	4 (6.5)	**0.864**
Neither poor nor good	15 (24.2)	14 (22.6)	14 (22.6)	
Good	37 (59.7)	39 (62.9)	32 (51.6)	
Very Good	8 (12.9)	8 (12.9)	12 (19.4)	
Health satisfaction n (%)				
Very dissatisfied	1 (1.6)	1 (1.6)	0 (0)	
Dissatisfied	4 (6.5)	7 (11.3)	8 (12.9)	0.715
I am neither satisfied nor dissatisfied	20 (32.3)	16 (25.8)	14 (22.6)	
Satisfied	27 (43.5)	30 (48.4)	29 (46.8)	
Very satisfied	10 (16.1)	8 (12.9)	11 (17.7)	
Symptoms n(%)				
Fatigue	35 (56.5)	27 (43.5)	28 (45.2)	0.187
Dyspnea				
No	34 (54.8)	39 (62.9)	41 (66.1)	0.200
Mild	25 (40.3)	22 (35.5)	18 (29)	
Moderate	3 (4.8)	1 (1.6)	3 (4.8)	
Myalgia	16 (25.8)	14 (22.6)	8 (12.9)	0.031[#] 30 vs.90: 1 30 vs. 180: 0.034[##] 90 vs. 180:0 .173
Arthralgia	8 (12.9)	9 (14.5)	8 (12.9)	0.939
Cough	7 (11.3)	5 (8.1)	2 (3.2)	0.121
Headache	7 (11.3)	3 (4.8)	2 (3.2)	0.122
Dizziness, fainting	6 (9.7)	1 (1.6)	0 (0)	0.006[#] 30 vs 90: 0.037[##] 30 vs 180: 0.008[##] 90 vs. 180:1
Gastrointestinal disorders	4 (6.5)	1 (1.6)	0 (0)	0.039[#] 30 vs 90: 0.199 30 vs. 180: 0.043[##] 90 vs 180: 1
Paresis, paresthesia	2 (3.2)	1 (1.6)	1 (1.6)	0.779
Chest pain	2 (3.2)	2 (3.2)	1 (1.6)	0.819
Anosmia, hyposmia, hypogeusia	2 (3.2)	0 (0)	0 (0)	0.135
Vision loss/change	2 (3.2)	0 (0)	1 (1.6)	0.368
Sore throat	1 (1.6)	2 (3.2)	1 (1.6)	0.717

Others n(%)	7 (11.3)	2 (3.2)	2 (3.2)	0.062
Number of symptoms, mean; median (IQR)	2.1; 2 (1-3)	1.4; 1 (0-2)	1.2; 1 (0-2)	<0.001# 30 vs 90: 0.018## 30 vs. 180: 0.001## 90 vs. 180:1

Abbreviations: n: frequency; %: percentage; IQR: interquartile range.

Q Cochran significance.

Significance of the two comparisons corrected with Bonferroni post-Q Cochran test.

Fonte: Authors (2022).

We observed a statistically significant difference in the proportion of patients with myalgia (p = 0.031), dizziness and fainting (p = 0.006), and gastrointestinal disorders (p = 0.039). The two-by-two comparison showed a significant reduction in myalgia and gastrointestinal disorders from 30 days to 180 days (p = 0.034 and p = 0.043, respectively); there was no difference from 90 days to 30 and 180 days. Regarding dizziness and fainting, 90 and 180 days significantly reduced compared to 30 days (p = 0.037 and p = 0.008, respectively).

During the follow-up, the number of symptoms reduced significantly (p < 0.001). The difference in median change was observed from 30 to 90 days (p = 0.018) and from 30 to 180 days (p = 0.001).

DISCUSSION

This cohort study analyzed the health outcomes of COVID-19 survivors after ICU discharge at 30, 90, and 180 days. The most reported symptoms were fatigue, mild dyspnea, and myalgia, which persisted for 180 days. Despite that, most patients were generally satisfied with their health and reported good quality of life.

The most common symptom reported during follow-up was fatigue. Consistent with the present study, other studies also found a high prevalence of fatigue in the early stages post-infection, 27.7-71%[2,16-17], persisting in 31% of patients throughout two years after the COVID-19 infection[18].

In addition, previous studies have shown that fatigue is commonly observed in patients who recovered from severe acute respiratory syndrome (SARS) and can persist for four years, specifically during COVID-19; some studies suggest that multiple factors and mechanisms are responsible for fatigue development, such as a combination of central, peripheral and psychological factors[19-20]. Systemic inflammation and cell-mediated immune mechanisms are believed to influence the central nervous system, which can contribute to post-COVID-19 fatigue more than direct neuroinvasion[20]. Infection of skeletal muscle, viral-induced myositis, cytokine disturbance, muscle wasting and deconditioning, corticosteroids myopathy and inflammation to muscle fibers and neuromuscular junctions, or a combination of these factors, could have contributed to post-COVID-19 fatigue[21]. Lastly, psychological and social factors due to the COVID-19 pandemic also contribute to the symptoms[22].

After 180 days, dyspnea remained the second most reported symptom among patients. Although this study did not assess chest image or pulmonary function test, previous studies have shown that fibrotic abnormalities and persistent lung diffusion impairment might last for months, which can explain the presence of this symptom[8,23]. Due to COVID-19 being mainly a respiratory disease, some patients suffer from endothelial damage and

intense lung immune inflammatory reactions in the acute phase of the infection. Those who overcome the infection can develop long-term dyspnea, with or without signs of fibrotic abnormalities in chest images[19].

Myalgia, reported by 25.8% at 30 days after ICU discharge, decreased to 12.9% at 180 days. These findings concord with a previous study, which found a decrease in patients reporting myalgia from 40% in 3 months to 15% in 6 months[24]. Other studies have shown an increase from 3% in 6 months to 8% in 2 years post-infection[6,18]. SARS-CoV-2 infects the cell by the interaction between its spike domain with angiotensin-converting enzyme-2 (Ace2). Skeletal muscle tissue exhibits a lot of ACE2, making it susceptible to the COVID-19 infection. This mechanism might explain myalgia and muscle weakness in patients during the acute and post-acute phases of the disease[21].

During our follow-up, we observed a reduction in the median number of symptoms reported, suggesting a partial recovery in symptoms for about 180 days. Indeed, the persistence of post-COVID-19 symptoms is widely explored in the literature. Studies show that six months after illness onset, 76% of the patients reported at least one persistent symptom, and after one year, the absence of symptoms is not possible for some patients[8]. Also, patients with at least one persistent symptom had a significantly reduced physical and mental health status and quality of life compared to patients without symptoms[25].

Poor quality of life has been frequently observed in COVID-19 survivors. The meta-analysis found that 58% of post-COVID-19 patients had reported poor quality of life[26]. Moreover, studies have shown that ICU admission is associated with worse quality of life than ward admission[12].

Controversially, most patients were satisfied with their health and reported good general quality of life throughout the follow-up. At 180 days after ICU discharge, 47.3% of patients considered themselves satisfied with their health. Furthermore, 62.8% of patients also reported a good general quality of life. These findings agree with previous studies showing that COVID-19's impact on quality of life after hospital discharge persists with partial improvement after months[27]. In contrast, other studies found that patients who had COVID-19 had a higher likelihood of depression and lower quality of life than those who did not have COVID-19[28], and some patients were still improving their health-related quality of life (HRQoL) two years after hospital discharge[18].

A possible explanation for these results lies in the WHO´s concept of health, which defines health as more than the absence of disease or infirmity, considering it a complete physical, mental, and social well-being[29]. Rather than restricting health to an absence of illness, health was conceptualized more in terms of the presence of absolute and positive qualities[30]. During the interviews, the patients demonstrated that they consider health far beyond the physical state after COVID-19 infection, which was noticed in their reports. In this study, we also did not use any instrument to assess, through scores, quality of life; we let patients openly rate it. This may explain the results obtained regarding health satisfaction and general quality of life.

The greatest limitation of the study was the severe sample loss. Many patients were eligible for our follow-up, but several could not be contacted; almost 60% of patients did not provide phone numbers or wrong phone numbers, and more than 25% did not answer telephone calls. We also had a large sample loss during follow-up, which has also been reported by other studies that used telephone surveys. Less severe patients may have been included in this cohort. The authors emphasize that readers must be cautious with the external validity of the current findings, especially about general quality of life and health satisfaction. Whereas patients may have based their answers about health status obtained during the interview on the health status at ICU discharge, which could be better at this time since it was very bad at ICU discharge, this was not evaluated in this study.

CONCLUSION

In conclusion, several months after COVID-19 infection, many patients report persistent symptoms. Although, in this study, most participants were satisfied with their health and reported good quality of life, the persistence of symptoms harms health outcomes, as already observed in other cohort studies. Understanding these consequences is the first step towards developing medical treatments and management strategies that best meet patients' needs and help minimize this disease's health impacts.

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