RESEARCH ARTICLE

Long-term follow-up and health-related quality of life in COVID-19 patients treated in hospital

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Abstract

Objective: To evaluate the persistence of symptoms and health-related quality of life of coronavirus disease-2019 patients.

Method: The cross-sectional study was conducted from April to September 2020 at Health Sciences University, Yedikule Chest Diseases Hospital, Istanbul, Turkey, and comprised patients of either gender who had to be hospitalised and treated for coronavirus disease-2019. Those who had spent ≤3 months (46-90 days) post-discharge formed Group 1, those having spent 3-6 were in Group 2, while those with >6 months post-discharge were in Group 3. Data was collected over the telephone Using the EuroQol's quality of life scale with 5 dimensions and 5 levels. The variables likely to affect the persistence of symptoms and the quality of life questionnaire scores were analysed using SPSS 16.

Results: Of the 225 subjects, 135(60%) were male and 90(40%) were female. The overall mean age was 55.7±19.91 years. There were 85(37.8%) participants in Group 1, 83(36.9%) in Group 2, and 57(25.3%) in Group 3. The age (p=0.09) and gender (p=0.23) distribution across the groups had no significant difference. Patients were called on an average 131.72±58.9 days after discharge (range: 46-279 days). Only 52 (23.1%) patients continued to show symptoms. Anxiety was the domain in which most patients 64(28.4%) reported deterioration.

Conclusion: Most patients who have had coronavirus disease-2019COVID-19 after a long follow-up period did not show any symptoms or had any significant deterioration in their quality of life.

Keywords: COVID 19, Post-discharge symptoms, Quality of life.

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Introduction

A great deal of information has been obtained over the past year regarding the management of the acute phase of coronavirus disease-2019 (COVID-19). The first publications on the subject reported that in a significant portion of COVID-19 patients, various symptoms persist for a long time after discharge from the hospital.[1-3] Oscar et al. reported that half of their COVID-19 patients had symptoms, such as fatigue, dyspnoea, or anosmia, after completing their treatment.[4] COVID-19 can have a persisting impact on patients' physical and psychosocial health and can significantly impair quality of life (QoL).[5] There is a growing body of literature focussing on this issue.[6,7] A study showed that QoL of patients was worse even three months after the treatment.[8] The current study was planned to evaluate the long-term persistence of symptoms and health-related QoL (HRQoL) of COVID-19 patients post-treatment.

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Materials and Methods

The cross-sectional study was conducted from April to September 2020 Health Sciences University, Yedikule Chest Diseases Hospital, Istanbul, Türkiye. After approval from the institutional ethics review committee, records of patients who had been hospitalised with a diagnosis of COVID-19 were evaluated. Medical information of the patients was obtained from their electronic files. Patient information was converted to standardized variables and recorded in an electronic listing programme. The patients were then called by phone to collect information about HRQoL.

The case definition was based on the World Health Organisation (WHO) COVID-19 case definition sheet.[9] Accordingly, a positive nucleic acid amplification test, reverse transcription polymerase chain reaction (RT-PCR), along with appropriate clinical and imaging findings, was used to confirm the diagnosis (proven cases). If the clinical picture and computed tomography (CT) findings were strongly suggestive of COVID-19, even if the RT-PCR test was negative, the patient was classified as a "highly probable case" and was included in the study. Patients who did not fit the WHO case definition were excluded.

Patients were treated in line with the National COVID-19 Treatment Guidelines of Turkey's Ministry of Health.[10] The patients who did not have fever and did not require oxygen in the preceding 48-72 hours were discharged to complete the isolation period at home, regardless of the RT-PCR test result.

The severity of disease was graded clinically and was classified as "mild" in patients who did not require oxygen support (haemoglobin [Hb] oxygen saturation >93% while breathing room air) at the time of hospitalisation or as "moderate-severe" in patients with a Hb oxygen saturation ≤93% while breathing room air at the time of hospitalisation. The radiological extent of the pulmonary involvement of the disease was classified by examining chest radiographs. The right and left lung areas were divided into the upper, middle and lower regions. The involvement level was graded as follows: 0 = no findings of pneumonia on the chest radiography; 1 = involvement of a single zone in one lung; 2 = multi-region involvement in one lung; and 3 = bilateral involvement. The level of oxygen support was also recorded as an indicator of disease severity: 0 = no oxygen support required; 1 = oxygen support with nasal cannula; 2 = oxygen support with reservoir mask; and 3 = oxygen support with a high-flow nasal cannula or non-invasive mechanical ventilation device.

Patients who died in the hospital were excluded, and so were those who could not speak the Turkish language or whose contact information was not available.

The doctors called the patients enrolled who were categorised into three groups. Those who had spent <3 months (46-90 days) post-discharge formed Group 1, those having spent 3-6 were in Group 2, while those with >6 months post-discharge were in Group 3.

Data was collected using the EuroQol's Five-Dimensional Five-Level Questionnaire (EQ-5D-5L) to assess generic HRQoL.[11] The questionnaire consisted of 5 questions eliciting information about 5 domains of life: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each domain of the EQ-5D-5L is scored on a 5-point Likert scale: 0 -no problem; 1 = slight problem; 2 = moderate problem; 3 = severe problem; and 4 = unable to do. The original questions of the questionnaire were translated into Turkish.

In terms of statistics, the sample size was calculated with post-hoc power analysis using G*power software[12] with 80% power and 0.05 alpha level. The number of samples required to show that the rate of patients with symptom permanence regressed from 20% to 5% is statistically significant, and the number of samples required to show that the symptom-free rate increased from 70% to 88% for QoL variables were both calculated.

The gathered data ws analysed using SPSS 16. One-way analysis of variance (ANOVA) was used to compare the mean values, and chi-square or Fisher's Exact tests were used to compare the frequencies. The relations between QoL questionnaire scores and other variables likely to affect these scores, like age, gender, comorbidities, smoking status, disease severity indicators, symptoms during hospitalisation, medications used, and time post-discharge, were analysed using Spearman's correlation test. Variables showing $p<0.1$ were carried forward to linear regression and multivariable analysis. In all analyses, $p<0.05$ indicated statistical significance.

Results

Of the 450 patients who had been hospitalised with a COVID-19 diagnosis, 225(50%) subjects formed the study

Table-1: Symptoms of patients at the time of hospitalisation.

Symptoms	n (%)				p value
	Total	Group 1	Group 2	Group 3	
Any	222	85 (100)	81 (97.6)	56 (98.2)	0.38
Non-specific symptoms	169 (75.1)	66 (77.6)	56 (67.5)	47 (82.4)	0.11
Fatigue	114 (%50.7)	53 (62.3)	36 (43.4)	25 (43.8)	0.03
Fever	81 (36)	24 (28.2)	29 (34.9)	28 (49.1)	0.04
Joint pain	53 (%23.6)	21 (24.7)	19 (22.9)	13 (22.8)	0.95
Respiratory symptoms	173 (%76.9)	66 (77.6)	65 (78.3)	42 (73.7)	0.80
Shortness of breath	119 (%52.9)	49 (57.6)	41 (49.4)	29 (50.9)	0.54
Cough	109 (%48.4)	41 (48.2)	41 (49.4)	27 (47.4)	0.98
Chest pain	20 (%8.9)	8 (9.4)	8 (9.6)	4 (7.0)	0.85
URT symptoms	20 (8.9)	6 (7.1)	8 (9.6)	6 (10.5)	0.74
CNS symptoms	20 (8.9)	7 (8.2)	7 (8.4)	6 (10.5)	0.88
GIS symptoms	36 (16)	20 (23.5)	11 (13.2)	5 (8.8)	0.04

URT: Upper respiratory tractus, CNS: Central nervous system, GIS: Gastrointestinal system.

Table-2: Frequency of symptoms reported by patients during the follow-up period.

Symptoms	n (%)				Correlation coefficient (rho)	p value
	Total	Group 1	Group 2	Group 3		
Non-specific symptoms	17 (7.6)	10 (11.8)	6 (7.2)	1 (1.75)	-0.15	0.03
Fatigue	12 (5.3)	7 (8.2)	5 (6.0)	Nil	-0.14	0.04
Fever	2 (0.9)	2 (2.3)	Nil	Nil	-0.11	0.10
Joint pain	4 (1.8)	1 (1.2)	3 (3.6)	Nil	-0.01	0.82
Respiratory symptoms	34 (15.1)	17 (20)	14 (16.9)	3 (5.3)	-0.15	0.02
Shortness of breath	23 (10.2)	13 (15.3)	7 (8.4)	3 (5.3)	-0.13	0.04
Cough	9 (4.0)	3 (3.5)	6 (7.2)	Nil	-0.05	0.48
Chest pain	6 (2.7)	3 (3.5)	3 (3.6)	Nil	-0.07	0.26
URT symptoms	2 (0.9)	1 (1.2)	1 (1.2)	Nil	-0.04	0.52
Anosmia	Nil	Nil	Nil	Nil	-	-
Sore throat/ Hoarseness	2 (0.9)	1 (1.2)	1 (1.2)	Nil	-0.04	0.52
CNS symptoms	5 (2.2)	1 (1.2)	4 (4.8)	Nil	-0.007	0.92
Headache	2 (0.9)	1 (1.2)	1 (1.2)	Nil	-0.04	0.52
Vertigo	Nil	Nil	Nil	Nil	-	-
Amnesia	3 (1.3)	Nil	3 (3.6)	Nil	0.09	0.17
GIS symptoms	2 (0.9)	Nil	2 (2.4)	Nil	0.02	0.74
Anorexia/Weight loss	1 (0.4)	Nil	1 (1.2)	Nil	0.01	0.82
Diarrhea	1 (0.4)	Nil	1 (1.2)	Nil	0.01	0.82

URT: Upper respiratory tract, CNS: Central nervous system, GIS: Gastrointestinal system.

Table-3: Quality-of-Life (QoL) questionnaire scores reported by the patients during follow-up.

QoL questionnaire domain	Scores, n (%, in the group)					Correlation coefficient (rho)	p value
	0	1	2	3	4		
Mobility							
Total (n=225)	174 (77.3)	31 (13.8)	18 (8.0)	2 (0.9)	Nil		
Group 1	59 (69.4)	17 (20.0)	8 (9.4)	1 (1.2)	Nil	-0.17	0.01
Group 2	65 (78.3)	8 (9.6)	9 (10.8)	1 (1.2)	Nil		
Group 3	50 (87.7)	6 (10.5)	1 (1.8)	Nil	Nil		
Self-care							
Total (n=225)	212 (94.2)	6 (2.7)	6 (2.7)	1 (0.4)	Nil		
Group 1	79 (92.9)	2 (2.4)	4 (4.7)	Nil	Nil	-0.10	0.13
Group 2	76 (91.6)	4 (4.8)	2 (2.4)	1 (1.2)	Nil		
Group 3	57 (100)	Nil	Nil	Nil	Nil		
Usual activities							
Total (n=225)	202 (89.8)	13 (5.8)	8 (3.6)	2 (0.9)	Nil		
Group 1	73 (85.9)	7 (8.2)	4 (4.7)	1 (1.2)	Nil	-0.12	0.08
Group 2	75 (90.4)	3 (3.6)	4 (4.8)	1 (1.2)	Nil		
Group 3	54 (94.7)	3 (5.3)	Nil	Nil	Nil		
Pain/discomfort							
Total (n=225)	207 (92.0)	14 (6.2)	4 (1.8)	Nil	Nil		
Group 1	79 (92.9)	5 (5.9)	1 (1.2)	Nil	Nil	0.007	0.92
Group 2	75 (90.4)	5 (6.0)	3 (3.6)	Nil	Nil		
Group 3	53 (93.0)	4 (7.0)	Nil	Nil	Nil		
Anxiety/depression							
Total (n=225)	161 (71.6)	64 (28.4)	Nil	Nil	Nil		
Group 1	64 (75.3)	21 (24.7)	Nil	Nil	Nil	-0.02	0.79
Group 2	54 (65.1)	29 (34.9)	Nil	Nil	Nil		
Group 3	43 (75.4)	14 (24.6)	Nil	Nil	Nil		

sample (Figure); 135(60%) male and 90(40%) female. The overall mean age was 55.7±19-91 years. There were 85(37.8%) participants in Group 1, 83(36.9%) in Group 2, and 57(25.3%) in Group 3. The age (p=0.09) and gender (p=0.23) distribution across the groups had no significant difference.

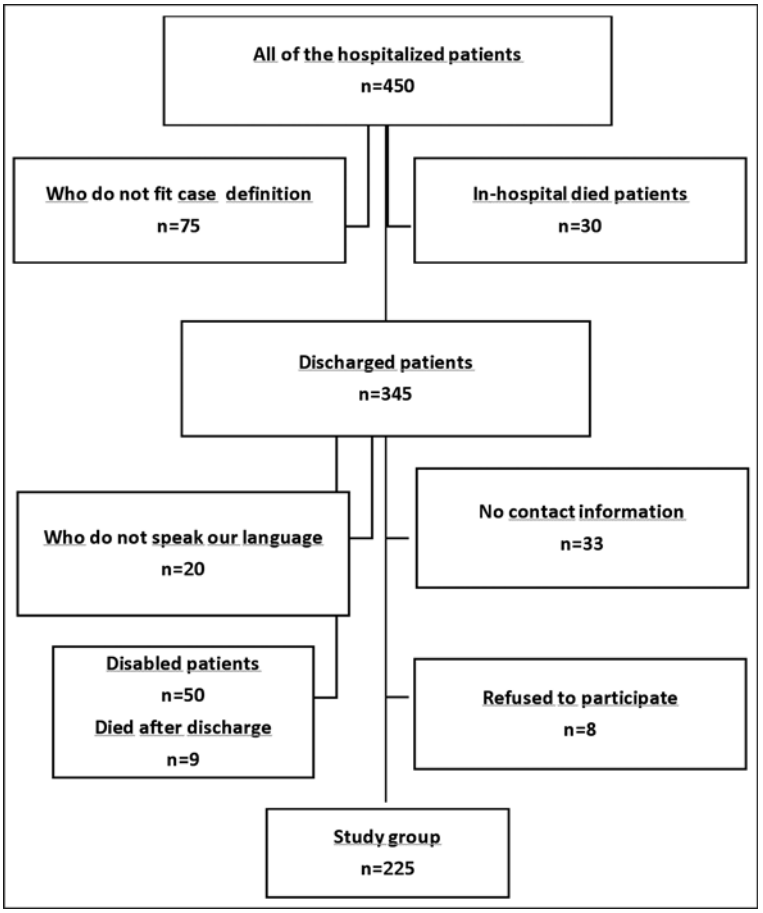

Figure: Enrollement flowchart.

The most common symptom during hospitalisation had been fatigue, and the most common respiratory symptom was shortness of breath (Table-1).

Patients were called on an average 131±58.9 days post-discharge (range: 46-279 days). The median duration was 128 days (interquartile range [IQR]: 77-181 days). Only 52 patients (23.1%) continued to show symptoms. Shortness of breath was the most frequently reported respiratory symptom post discharge 23(10.2%) (Table-2).

The scores of the QoL questionnaire were noted separately and the domain in which the fewest patients reported having problems was personal care 13(5.8%), while anxiety was the domain in which most patients 64(28.4%) reported deterioration (Table-3).

Personal care scores increased with age (rho=0.17, p=0.01), but age did not affect the scores in other domains. The scores were mildly but significantly higher in women for self-care (rho=0.43, p=0.0001), daily activity (rho=0.0.2, p=0.003), pain/discomfort (rho=0.0.16, p=0.01), and anxiety/depression (rho=0.15, p=0.02).

The presence of a comorbidity significantly affected the QoL scale results. Congestive heart failure (CHF) showed the strongest association as its presence was associated with an increasing of scores in all questionnaire domains: pain/discomfort, rho=0.23, p=0.001; anxiety/depression, rho=0.18, p=0.008; mobility, rho=0.15, p=0.003; personal care, rho=0.30, p=0.0001; usual activity, rho=0.33, p=0.0001). The presence of asthma was only associated with an increase in the daily activity domain score (rho=0.15, p=0.03), the presence of chronic obstructive lung disease (COPD) was associated with higher scores in mobility (rho=0.16, p=0.02), personal care (rho=0.15, p=0.02), and usual activity (rho=0.14, p=0.04) domains.

Based on the variables during the hospitalisation period, the clinical severity of the disease, the degree of oxygen

Table-4: Variables that affected the quality-of-life (QoL) domains based on multivariable analysis.

Variables	QoL domains, p values				
	Mobility	Self-care	Usual activities	Pain/discomfort	Anxiety/depression
Sex	NS	0.01	0.048	0.003	NS
Comorbidities					
CHF	0.04	0.003	0.001	0.01	0.08
COPD	0.02	NS	NS	NS	NS
Malignancy	NS	0.004	NS	0.0001	NS
Admission symptoms					
Non-specific symptoms	NS	0.02	NS	NS	NS
SoB	0.03	0.04	0.01	0.007	NS
Severity indicators					
Radiological extent	0.01	NS	0.04	NS	0.03
Time from discharge	0.04	NS	NS	NS	NS

CHF; Congestive heart failure, SoB: Shortness of breath, COPD: Chronic obstructive lung disease, NS: Mot significant.

support given to patients, and the radiological extent of the disease did not affect the QoL scores significantly (p>0.05). In addition, the presence of upper respiratory tract (URT), central nervous system (CNS), or gastrointestinal system (GIS) symptoms did not affect the survey scores (p>0.05). Of the respiratory symptoms, only shortness of breath was associated with higher questionnaire scores: pain/discomfort, rho=0.18, p=0.006; mobility, rho=0.20, p=0.003; personal care, rho=0.16, p=0.02; and usual activity, rho=0.26, p=0.0001).

When the effect of time post-discharge on the QoL scores was analysed, it was found that despite the prolonged period after discharge, the proportion of patients with anxiety/depression and of patients with pain/discomfort did not change significantly over time (p>0.05). Contrarily, with increased time, significant decreases were observed in both the number and the questionnaire scores of patients with problems with mobility (p<0.05). For the personal care and usual activity domains, the number of sufferers and the scores of these patients decreased over time, but this decrease was not statistically significant (p>0.05).

Based on the multivariable analysis, female gender, having CHF, and the existence of shortness of breath at the time of admission had a negative effect on most of the domain scores of the QoL questionnaire, while the time from discharge was a significant variable but only for some domain scores (Table-4).

Discussion

Most community-acquired pneumonia patients treated as inpatients continue to complain of cough and dyspnoea one month after treatment.[13-15] Similar studies in patients recovering from COVID-19 showed that more such patients suffer from some symptoms over a long period post-treatment.[4] A study in China reported that 76% of recovered COVID-19 patients showed at least one symptom during the follow-up period.[16] In contrast, this rate was only 23.1% in the present study. One reason for this discrepancy may have been related to the length of the follow-up period, which was relatively short in most previous studies, and high rates indicate early follow-up results. The findings of the present study showed that the rate of treated COVID-19 patients who continued to show symptoms after discharge from hospital decreased in the first three months at almost the same rate as reported for community-acquired pneumonia patients.[17] Furthermore, the proportion of patients who continued to show symptoms in the patient group with a longer follow-up period decreased even further. These results alleviate concerns that people with COVID-19 will continue to exhibit symptoms for a long period of time. In a study of COVID-19 patients followed up for an average of 100-153 days, the proportion of symptomatic patients was high.[16] This high rate reported in the current and other studies may be related to the addition of some symptoms not directly associated with the disease in the analysis. For example, although anxiety and depression are not primary symptoms of the disease, patients may complain of these symptoms after discharge.[2]

Fatigue is the most frequently reported symptom that persists during follow-up after recovery in patients with COVID-19.[5,16] As fatigue is the most frequent first admission symptom,[18] it is reasonable to argue that it is the most frequent symptom during follow-up. In the present study, only 5.2% patients complained of fatigue post-recovery, even within the first three months after discharge, and no patients complained of this symptom at six months or more after discharge. In contrast with other studies,[6,7] in the current series, shortness of breath was the most frequently observed post-discharge symptom. This may be because this was the most common symptom at the time of diagnosis in the current patients.

Impairments in QoL have also been reported in patients who have had COVID-19;[6,7] but in the present study, 70% patients reported no persistent problems in all QoL questionnaire domains. A deterioration of QoL is expected to improve over time following an illness. The current study showed that over time, people who have had COVID-19 achieved a significantly better QoL in terms of mobility, one of the domains of the QoL questionnaire, and tended to show significant improvements in terms of usual activity and personal care domains. On the other hand, patients did not have better QoL levels in terms of anxiety/depression and pain/discomfort even six months after hospital discharge. Anxiety/depression has been reported as the most common problem that persists a long time after treatment for COVID-19.[5,8] In one study, the rate of depression in newly recovered patients was 29.2%.[19] In the current study, about 30% patients had problems with anxiety, but the absence of a decrease in the rate of those who have problems over time indicates that a significant portion of patients who have had COVID-19 and recover will have a long-lasting tendency towards anxiety. Post-treatment anxiety may not be simply related to having had COVID-19 as it is known that many uninfected people in society also show anxiety related to the disease.[20] During the COVID-19 pandemic, restrictions imposed by the authorities, such as quarantine and social distancing, placed pressure on society. In some studies, the rate of anxiety/depression for

those without the disease was reported to be similar to that for affected individuals who had recovered.[21,22]

In the current study, worsening personal care scores after recovery were more pronounced in older patients. This result was not unexpected, but it was surprising that age did not affect the scores in the other survey domains. It was also surprising that women had worse QoL scores than men. The deterioration of QoL scores in women was consistently detected in almost all questionnaire domains. Similar results have not been reported in a previous study[6]. This finding suggests that women are more vulnerable to the effects of COVID-19 after recovery than men.

The current study has limitations due to the small number of patients and the administration of the questionnaire over the telephone. As this was a retrospective study, it was not possible to evaluate the baseline QoL scores of the patients. To determine whether this affected the results, the three patient groups were compared according to all the variables. As there was no significant difference, this kind of evaluation may yield acceptable results.

Conclusions

The number of patients reporting symptoms after recovery from COVID-19 continued to decline over time, and the rate of those showing symptoms more than six months after treatment was very low. Although deterioration in QoL tended to improve over time, there may be no significant improvement in anxiety/depression and pain/discomfort domains even with more than a six-month follow-up.

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