



Letter to the Editor

Post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19

Dear editor,

In this journal, we recently reported a series of 279 hospitalized patients with novel coronavirus 2019 disease (COVID-19) and their short-term outcome.¹ However, only a few studies have assessed post-discharge persistent symptoms and health-related quality of life (HRQoL) after hospitalization for COVID-19.^{2,3}

Here, we describe a single-centre study assessing post-discharge persistent symptoms and HRQoL of patients hospitalized in our COVID-19 ward unit more than 100 days after their admission. COVID-19 diagnosis was based on positive SARS-CoV-2 real-time reverse transcriptase-polymerase chain reaction on nasal swabs, and/or typical abnormalities on chest computed tomography. Patients who were directly admitted to the ICU without being hospitalized in our COVID-19 unit were excluded. Demographic and clinical data at admission were extracted from electronic medical records.

We designed a short phone questionnaire to collect post-discharge clinical symptoms, modified Medical Research Council (mMRC) dyspnoea scale scores, professional and physical activities, and attention, memory and/or sleep disorders. HRQoL was assessed using the EQ-5D-5 L questionnaire, a widely used, validated European questionnaire⁴. Patients are asked to rate their health state from 1 to 5 in five domains (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and on a scale ranging from 0 (“the worst possible health”) to 100 (“the best possible health”) on a visual analogue scale (EQ-VAS). Based on the answers, an EQ-5D- index can be calculated, ranging from states worse than dead (<0) to 1 (full health).⁵

All eligible patients were contacted by phone by trained physicians and were asked to answer to the questionnaire. Deceased, unreachable, demented, bedridden and non-French speaking patients were excluded. We compared patients managed in hospital ward without needing intensive care (“ward group”) with those who were transferred in intensive care units (ICU) for artificial ventilation, including non-invasive ventilation, high flow nasal cannula and/or mechanical ventilation (ICU group), with t-tests for quantitative variables and Chi-square tests for qualitative variables. All tests were two-sided, and a *P*-value < 0.05 was considered statistically significant. All analyses were performed with R version 3.6.1. (R Foundation for Statistical Computing, Vienna, Austria). The study was approved by the local institutional review board (IRB 00006477).

Of the 279 hospitalized patients between March 15th and April 14th, 2020 in our COVID-19 unit, 48 were admitted to ICU, and 57 patients died within the three months following admission

(43 in the ward group and 14 in the ICU group) (Supplementary figure 1). After having excluded demented or bedridden (*n* = 18), unreachable (*n* = 69), non-French speaking patients (*n* = 12), and those declining participation (*n* = 2), 120 patients answered the phone questionnaire after a mean (±SD) of 110.9 (±11.1) days following admission: 96 in the ward group and 24 in the ICU group for artificial ventilation (mechanical ventilation for 14, CPAP for 10 and high flow nasal cannula for 7).

After a mean of 110.9 days, the most frequently reported persistent symptoms were fatigue (55%), dyspnoea (42%), loss of memory (34%), concentration and sleep disorders (28% and 30.8%, respectively) (Table 1). Loss of hair was reported by 24 (20%) patients, including 20 women and 4 men. Comparisons between ward- and ICU patients led to no statistically significant differences regarding those symptoms. Thirty-five (29%) patients had a mMRC grade ≥2 (“Walks slower than people of the same age because of dyspnoea or has to stop for breath when walking at own pace”).

Before COVID-19 infection, 56 (46.7%) were active workers, amongst them, 38 (69.1%) had gone back to work at the time of the phone interview, amongst the 39 patients who had regular sports activity before their hospitalization for COVID-19, 28 (71.8%) have been able to resume physical activity, but at a lower level for 18 (46%). There was no statistically significant difference between ward and ICU groups, but there was a non-significant trend towards a reduced proportion of patients returning to work amongst ICU patients (46.7% versus 77.5%, *P* = 0.061).

In both group, dimensions of the EQ-5D (mobility, self-care, pain, anxiety or depression, usual activity) were altered with a slight difference in pain in the ICU group, but no statistically significant difference in the other groups (Fig. 1). Mean EQ-VAS was 70.3% and mean EQ-5D index 0.86, with no difference between ICU and ward patients (Table 1).

The present study shows that most patients requiring hospitalization for COVID-19 still have persistent symptoms, even 110 days after being discharged, especially fatigue and dyspnoea. These results highlight the need for a long-term follow-up of those patients and rehabilitation programs. Surprisingly, many patients (mainly women) spontaneously reported significant hair loss, which may correspond to a *telogen effluvium*, secondary to viral infection and/or a stress generated by the hospitalization and the disease.⁶ Nevertheless, HRQoL was quite satisfactory, as most patients who had a professional activity before the infection went back to work.

Except pain or discomfort, we found no significant difference regarding persistent symptoms and HRQoL between ward patients versus ICU patients. This clearly supports the interest of a full resuscitation for COVID patients despite heaviness of cares. However, patients from our “ICU group” were relatively non-severe, as those who were directly admitted to ICU (thus corresponding to the most severe forms) were not included in our study.

Table 1

Post-discharge persistent symptoms and health-related quality of life of 120 patients after a mean of 110.9 days after their admission for COVID-19.

	Overall	Ward patients	ICU patients	P value
	N = 120	N = 96	N = 24	
Age, years	63.2 (15.7)	64.1 (16.1)	59.6 (13.7)	0.208
Sex, male	75 (62.5)	56 (58.3)	19 (79.2)	0.099
Comorbidities				
Diabetes	26 (21.7)	22 (22.9)	4 (16.7)	0.698
Hypertension	56 (46.7)	45 (46.9)	11 (45.8)	1.000
Body mass index (kg/m ²)				<0.001
<25, n (%)	35 (29.2)	32 (33.3)	3 (12.5)	
≥25, n (%)	57 (47.5)	37 (38.5)	20 (83.3)	
Missing, n (%)	28 (23.3)	27 (28.1)	1 (4.2)	
Clinical features at admission				
Confusion	7 (5.8)	6 (6.2)	1 (4.2)	1.000
Cough	87 (72.5)	69 (71.9)	18 (75.0)	0.959
Dyspnoea	88 (73.3)	68 (70.8)	20 (83.3)	0.327
Myalgia	19 (15.8)	16 (16.7)	3 (12.5)	0.851
Diarrhoea	29 (24.2)	25 (26.0)	4 (16.7)	0.488
Admission data				
Length of stay in hospital, days	11.2 (13.4)	7.4 (5.4)	26.5 (22.3)	<0.001
Length of stay in ICU, days	–	–	17.1 (15.7)	–
Persistent symptoms				
Cough	20 (16.7)	14 (14.6)	6 (25.0)	0.358
Chest pain	13 (10.8)	11 (11.5)	2 (8.3)	0.941
Fatigue	66 (55.0)	52 (54.2)	14 (58.3)	0.891
Dyspnoea	50 (41.7)	38 (39.6)	12 (50.0)	0.487
Ageusia	13 (10.8)	9 (9.4)	4 (16.7)	0.509
Anosmia	16 (13.3)	14 (14.6)	2 (8.3)	0.638
Hair loss	24 (20.0)	18 (18.8)	6 (25.0)	0.690
Attention disorder	32 (26.7)	28 (29.2)	4 (16.7)	0.327
Memory loss	41 (34.2)	36 (37.5)	5 (20.8)	0.194
Sleep disorder	37 (30.8)	29 (30.2)	8 (33.3)	0.535
mMRC dyspnoea scale				0.438
Grade 0	56 (46.7)	47 (49.0)	9 (37.5)	
Grade 1	29 (24.2)	22 (22.9)	7 (29.2)	
Grade 2 or more	35 (29.2)	27 (28.1)	8 (33.3)	
Professional and physical activities				
Returned to work/worked before hospitalization	38/56 (67.9)	31/41 (75.6)	7/15 (46.7)	0.061
Resumed sport/practiced sport regularly before hospitalization	28/39 (71.8)	23/31 (74.2)	5/8 (62.5)	0.937
EQ-5D-5L				
EQ-VAS (%)	70.3 (21.5)	69.9 (21.4)	71.7 (22.2)	0.711
EQ-5D index	0.86 (0.20)	0.86 (0.19)	0.82 (0.21)	0.306

Results are expressed as count (%) for categorical variables and as mean (standard deviation) for quantitative variables. ICU: intensive care unit; mMRC: modified Medical Research Council.

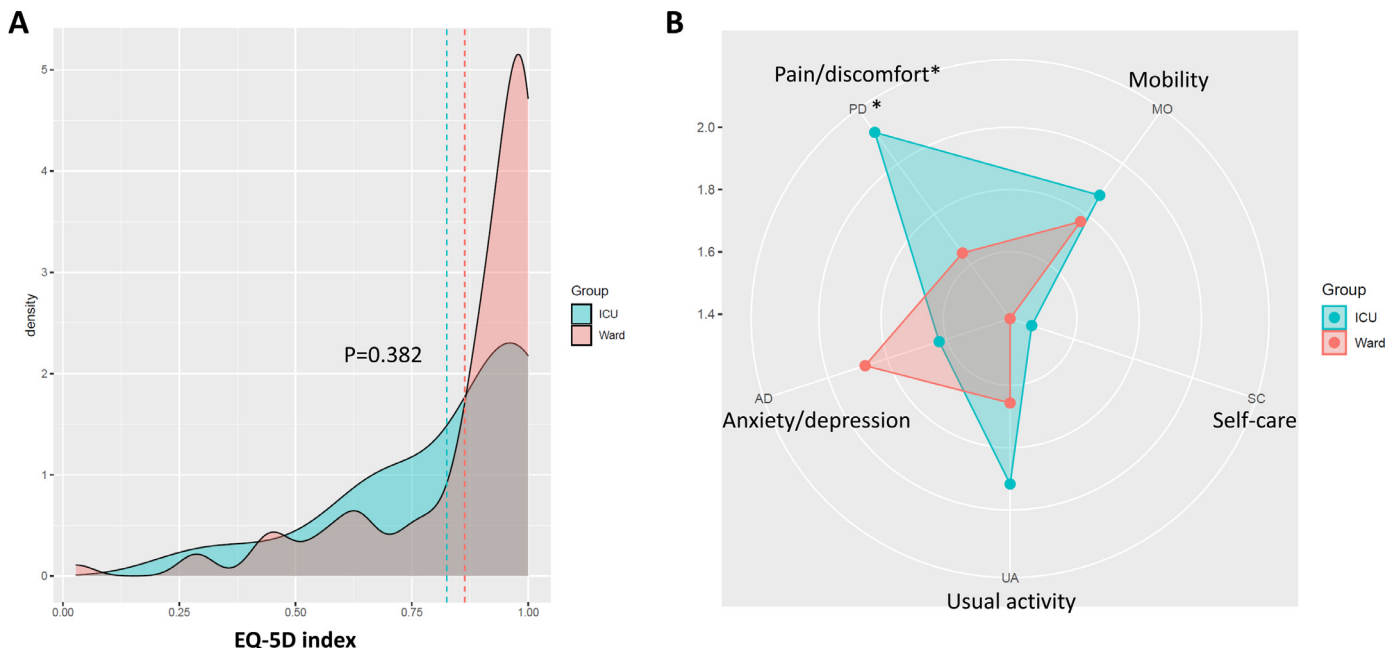


Fig. 1. Health-related quality of life after hospitalization for COVID-19 assessed by the EQ-5D 5L in the ward and the ICU groups. 1A: Distribution of the EQ-5D index (0: death to 1: full health). 1B: EQ-5D 5L scores in the ward and in the ICU groups on each domain. Each domain is scored on a 5-point scale: 1 no problem, 2 slight problem, 3 moderate problem, 4 severe problem, 5 unable to do. *: $P=0.032$.

Other limitations of our study include the limited number of patients, the single-centre nature of our series, and the high rate of unreachable patients, which could lead to differential bias.

In conclusion, many symptoms persist several months after hospitalization for COVID-19. While there were few differences between HRQoL between ward and ICU patients, our findings must be confirmed in larger cohorts, including more severe ICU patients.

Author Contributions

All authors have made substantial contributions to this work and have approved the final version of the manuscript. Concept and design: EG, BF, YN. Acquisition of data: all authors. Statistical analysis: YN. Interpretation of data: EG, BF, YN. Writing original draft: EG, YN. Writing review and editing: all authors.

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Declaration of Competing Interest

None of the authors declared any competing interest in link with the present study.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.jinf.2020.08.029](https://doi.org/10.1016/j.jinf.2020.08.029).

References

1. Nguyen Y, Corre F, Honsel V, Curac S, Zarrouk V, Fantin B, et al. Applicability of the CURB-65 pneumonia severity score for outpatient treatment of COVID-19. *J Infect* 2020;**81**(3):e96–8.

2. Carfi A, Bernabei R, Landi F, Gemelli Against COVID-19 Post-Acute Care Study Group. Persistent Symptoms in Patients After Acute COVID-19. *JAMA* 2020.
3. Halpin SJ, McIvor C, Whyatt G, Adams A, Harvey O, McLean L, et al. Post-discharge symptoms and rehabilitation needs in survivors of COVID-19 infection: a cross-sectional evaluation. *J Med Virol* 2020.
4. Herdman M, Gudex C, Lloyd A, M Janssen, Kind P, Parkin D, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res Int J Qual Life Asp Treat Care Rehabil* 2011;**20**(10):1727–36.
5. Andrade LF, Ludwig K, Goni JMR, Oppe M, de Pouvourville G. A French Value Set for the EQ-5D-5L. *Pharmacoeconomics* 2020;**38**(4):413–25.
6. Turkmen D, Altunisik N, Sener S, Colak C. Evaluation of the effects of COVID-19 pandemic on hair diseases through a web-based questionnaire. *Dermatol Ther* 2020:e13923.

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