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Research Article

Two-Years after Hospital Discharge, How is COVID-19 Patients' Health Perceived?

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Abstract

Objectives: The aim of this study was to describe COVID-19 hospitalized patients' health 24 months after discharge. **Patients and methods:** Patients from a French prospective cohort who were hospitalized for COVID-19 were clinically assessed at 12 (M12) and 24 months (M24) post-discharge. Multiple scores were used: the modified Medical Research Council score (mMRC), the Fatigue Severity Scale (FSS) and the Short Form 12 (SF12). We compared scores at M12 versus M24 and SF12 scores at M24 versus population norms. **Results:** Ninety patients completed both M12 and M24 follow-ups. About 30% presented dyspnea at M24 versus 47% at M12. No difference was found between mMRC, FSS and SF12 scores between M12 and M24. The total number of symptoms experienced at M24 was significantly lower than at M12. **Conclusions:** Even after 24 months after SARS-CoV2 infection onset, patients still experience physical symptoms (i.e. dyspnea, fatigue), and an altered quality of life compared to the general population.

Keywords: COVID-19; Fatigue; QOL; SF12; Two-years

Introduction

The long-term effects of SARS-CoV2 infection have been the topic of a lot of medical research recently and many studies explored the physical, neurological and psychiatric impacts of COVID-19 on patients [1-3]. Fatigue and quality of life were majorly studied in the first year following infection. Persistent fatigue and a lower Quality Of Life (QOL) were reported [4-6]. The idea of long term COVID has slowly settled down in the medical field as an important consequence of the SARS-CoV2 infection.

We had already assessed patients' fatigue and QOL 6 and 12 months after infection onset, and found a persistence of fatigue and a lower quality of life (both in the physical and mental aspect) at the 12 months follow-up [7].To our knowledge few studies have evaluated the fatigue and QOL among patients two years after the infection [8-10].

The aim of this study was to assess the clinical state (fatigue, dyspnea and quality of life) of patients who had been hospitalized for COVID-19 24 months after discharge. Additionally, we compared health states at 12 months (M12) and 24 months (M24) and depending on initial severity. We also compared QOL at M24 to the general population norms [11].

Patients and Methods

A prospective cohort study was set up at Reims University Hospital. The population of this study has already been described in a previous article [7]. Follow-up consultations at 12 and 24 months were carried out by clinicians, during which a clinical exam was realized alongside a series of scores: Modified Medical Research

Council (mMRC), Fatigue Severity Scale (FSS) and Short Form 12 (SF12). The mMRC score is based on a 5 levels assessment going from 0 "no dyspnea except in the case of sustained effort" to 4 "dyspnea preventing the patient from leaving the house or occurring when dressing and undressing" [12]. The FSS scale used to assess fatigue was composed of 9 items, going from 1 "does not correspond to me at all", to 7 "corresponds to me perfectly" [13]. QOL was assessed using the SF12 scale version 2, divided into two subscores (Physical Component Summary score (PCS12) and Mental Component Summary score (MCS12)) and compared to the general population norms [11].

Patient's health states were compared between M12 and M24. Moreover, to evaluate the impact of the initial severity of COVID-19 on the evaluated outcomes at M24, patients were divided into 2 groups depending on their initial clinical status (i.e. severe and non-severe). Severe SARS-CoV-2 infection was defined as severe initial pneumonia (i.e. fever and SpO2<90% or respiratory rate > 30/min or acute respiratory failure needing respiratory support and/or admission in ICU and/or acute circulatory failure due to sepsis or septic shock) or Acute Respiratory Distress Syndrome (ARDS).

Qualitative variables were described as numbers and percentages, and quantitative variables were described via means and standard deviations, or as medians and Interquartile Ranges (IQR), depending on the variable distribution.

For comparisons of scores between M12 and M24, Wilcoxon and McNemar's test for paired series were used. Chi-2 tests (or Fisher tests when necessary) were used for the comparison of severe vs non-severe groups. Student t-tests, or Mann-Whitney when adequate, were used for quantitative variables comparisons.

A p value < 0.05 was considered significant. All analyses were conducted using R studio® Version 4.0.5. This study was approved by the Ethics Committee (CPP Ile de France III) under the number CPP 3838-RM. The study was registered on the database https://clinicaltrials.gov/ct2/home under N° NCT04553575.

All patients who agreed to take part in the study received full information and signed informed consent. Due to the nature of the research, supporting data is not available.

Results

After hospital discharge, 90 patients completed both follow-ups at 12 and 24 months (Table 1). Only 30.3% of patients at the M24 assessment declared perceived dyspnea when asked, compared to 46.7% at M12 (p-value 0.01). When summed, the total number of symptoms experienced (sum of "dyspnea, palpitations, cough, headache, chest pains, arthromyalgia, diarrhea and asthenia for each patient) at M24 was significantly lower than at M12 (p-value <0.0001) (Table 2). Dyspnea was also assessed using the mMRC and at M12 60% of patients had a score ≥1 versus 62% at M24. mMRC results were not significantly different between the two assessments (p-value 0.59) unlike the perceived dyspnea at questioning (Table 2). Rehospitalization seemed to be more important at M24 compared to M12 (p-value 0.04). No other significant difference was found between the two assessments.

Variables	Number (%)	Median [IQR]
Socio-demographic characteristics		
Age		60.50 [56.00-68.75]
>70 years old	17 (18.89)	
Men	50 (55.56)	
Live at home	90 (100.00)	
Symptoms		
Fever	70 (77.78)	
Cough	68 (75.56)	
Dyspnea	38 (42.22)	
Headache	22 (24.44)	
Diarrhea	31 (34.44)	
Anorexia	11 (12.22)	
Ageusia	8 (8.89)	
Anosmia	11 (12.22)	

Muscle pains	28 (31.11)	
Abdominal pains	8 (8.89)	
Clinical situation		
Severe clinical profile[1]	34 (37.78)	
Heart rate (beat/min)		90.00 [82.00-100.00]
>45 and ≤120	88 (97.78)	
>120	1 (1.12)	
Respiratory rate (/min)		20.00 [18.00-26.50]
>30	10 (11.11)	
Systolic blood pressure (mmHg)		130.00 [121.00-140.00]
>140	22 (24.44)	
Glasgow score		15.00 [15.00-15.00]
<15	2 (2.22)	
Early Warning Score+		5.00 [3.00-8.00]
≤4	37 (44.04)	
>4 and ≤6	15 (17.86)	
>6	32 (38.10)	
Biology		
Creatinine (µmol/L)		76.00 [61.00-89.00]
>120	10 (11.11)	
CRP (mg/L)+		87.35 [32.05-147.00]
<40	26 (28.89)	
≥40 and <150	39 (43.33)	
≥150	21 (23.33)	
Lymphocytes (G/L)		0.90 [0.70-1.20]
<1.5	75 (83.33)	
Neutrophils (G/L)		5.00 [3.10-6.33]
<2	4 (4.44)	
Bacterial co-infection	3 (3.33)	
Therapeutics		
Antivirals[2]	81 (90.00)	
Hydroxychloroquine	23 (25.56)	
Antibiotic therapy	86 (95.56)	
Corticoids	61 (67.78)	
Anticoagulants	83 (92.22)	
Evolution		
Resuscitation[3]	28 (31.11)	
Oxygen therapy	65 (72.11)	
Pulmonary embolism	8 (8.89)	

Home visits	69 (76.67)	
Follow-up care and rehabilitation	20 (22.22)	
Re-hospitalisation	3 (3.33)	

[1] Includes severe initial pneumonia and acute respiratory distress syndrome (ARDS). Criteria for severe pneumonia were: fever and SpO2<90% or respiratory rate >30/min or acute respiratory failure needing respiratory support (invasive or not) and/or admission in ICU and/or acute circulatory failure (sepsis or septic shock)

[2] Includes: Lopinavir/Ritonavir or Darunavir/Ritonavir or Remdesivir

[3]Transfer in ICU or usage of resuscitation techniques.

+ Presence of NA.

Table 1: Initial characteristics of patients.

At 12 months, the mean FSS score was 3.6 (95% CI 3.2-4.0) and at 24 months the mean score was 3.5 (95% CI 3.1-3.9) (p-value 0.32).

	M12 n=90	**M24 n= 90**	**p-value**
Re-hospitalization Yes (%)	5 (5.56)	14 (15.56)	0.04
Experienced dyspnea Yes (%)	42 (46.67)	27 (30.31)	0.01
Experienced palpitations Yes (%)	16 (17.78)	12 (13.48)	0.45
Chest pains Yes (%)	15 (16.67)	10 (11.24)	0.27
Cough Yes (%)	20 (22.22)	15 (16.85)	0.36
Headaches Yes (%)	20 (22.22)	21 (23.86)	1
Arthromyalgia Yes(%)	41 (45.56)	35 (39.33)	0.36
Diarrhea Yes (%)	15 (16.67)	14 (15.91)	1
Other symptoms* Yes (%)	46 (51.11)	39 (43.33)	0.32
Systolic blood pressure Median [Q1-Q3] > 140 mmHg (%) (high blood pressure)	131.00 [120.00-149.00] 31 (35.63)	130.00 [120.00-142.50] 24 (26.67)	0.21
Heart rate (bpm) Median [Q1-Q3]	77.50 [66.75-85.25]	75.00 [70.00-82.00]	0.46

mMRC rating 0 (%) 1 (%) 2 (%) 3 (%) 4 (%)	 35 (39,33) 26 (29.21) 14 (15.74) 9 (10.11) 5 (5.62)	 33 (37.93) 27 (31.03) 16 (18.39) 9 (10.35) 2 (2.30)	0.59+
Anxiolytics Yes (%)	9 (10.00)	8 (8.89)	1
BMI Median [Q1-Q3] ≥ 40 kg/m² (%)	28.00 [25.00-32.00] 5 (5.56)	28.00 [25.00-32.75] 6 (6.67)	0.55
SpO2 Median [Q1-Q3] < 94% (%)	97.00 [96.00-98.00] 4 (4.71)	98.00 [96.00-99.00] 7 (8.24)	0.23
Hypnotics Yes (%)	11 (12.22)	7 (7.78)	0.29
Antidepressants Yes (%)	10 (11.11)	8 (8.89)	0.72
Anticoagulants Yes (%)	10 (11.11)	10 (11.11)	1
Asthenia Yes (%)	53 (58.89)	42 (47.73)	0.08
Sum of symptoms[§] Median [Q1-Q3]	2 [1-4]	1 [0-2]	<0.0001
FSS mean score: > 4 (%) < 4 (%) Mean ± SD	 38 (43.68) 49 (56.32) 3.56 ± 1.96	 33 (41.25) 47 (58.75) 3.50 ± 1.91	0.32
SF12 score **PCS12 :** mean ± SD **MCS12 :** mean ± SD	 42.92 ± 9.09 47.43± 5.90	 42.66 ± 10.47 46.82 ± 5.80	 0.28 0.35

[*]Anxiety, problems of concentration, decreased visual acuity, panic attacks, rhinorrhea, fatigue, insomnia, cognitive decline, dyspnoea upon effort, hair loss vertigo, headaches, diarrhoea, constipation, dysgeusia. [§]Sum of dyspnea, palpitations, cough, headache, chest pains, arthromyalgia, diarrhea and asthenia for each patient. + p-value of the test done after dividing the variable in two: those with an mMRC score > or = 1 and those with a score <1. **Abbreviations**: BMI: Body Mass Index, SpO2: peripheral oxygen saturation.

Table 2: Comparison of states of health in assessments at M12 and M24.

Regarding the QOL, at 12 months, the mean score of PCS12 was 42.9 (95% CI, 41.0-44.8) and the mean score of MCS12 was 47.4 (95% CI, 46.2-48.6). At 24 months the mean score of PCS12 was 42.7 (95% CI, 40.5-44.9) and the mean score of MCS12 was 46.8 (95% CI, 45.6-48.0). No significant difference was found between the two PCS12 scores and the two MCS12 scores at M12 and M24 (p-values 0.28 and 0.35 respectively). At M24, a lower score was observed for PCS12 with a significant difference (p-value<0.0001) when compared to the general French population, however MCS12 mean score was not significantly different in patients compared to the general population (p-value 0.11).

Furthermore, the only significant differences between groups found at the 24 months assessment based on severity were: heart rate results (p-value 0.02) and the total number of symptoms which was significantly higher in patients with a severe initial disease (p-value < 0.0001) (Table 3).

	SEVERE (n=34)[1]	**NOT SEVERE (n=56)**	**p-value**
Re hospitalization			
Yes (%)	4 (11.76)	10 (17.86)	0.44
Dyspnea			
Yes (%)	10 (29.41)	17 (30.36)	0.73
Palpitations			
Yes (%)	6 (17.65)	6 (10.71)	0.70
Chest pains			
Yes (%)	0	10 (17.86)	0.01
Cough			
Yes (%)	5 (14.71)	10 (17.86)	0.67
Headaches			
Yes (%)	11 (32.35)	10 (17.86)	0.26
Arthromyalgia			
Yes (%)	17 (50.00)	18 (32.14)	0.20
Diarrhoa			
Yes (%)	8 (23.53)	6 (10.71)	0.16
Other symptoms[2]			
Yes (%)	16 (47.06)	23 (41.07)	0.56
Systolic blood pressure			
Median [Q1-Q3]	130 (116.2-142.5]	130 [120-141.2]	0.65
>140 mmHg (%)	10 (25.00)	14 (129.41)	
Heart rate (bpm)			
Median [Q1-Q3]	79.00 [74.00-85.50]	72.50 [68.00-81.00]	0.02

MMRC			
0 (%)	11 (33.33)	22 (40.74)	0.95+
1 (%)	11 (33.33)	16 (29.63)	
2 (%)	6 (18.18)	10 (18.52)	
3 (%)	4 (12.13)	5 (9.26)	
4 (%)	1 (3.03)	1 (1.85)	
Anxiolytics			
Yes (%)	5 (14.71)	3 (5.36)	0.15
BMI			
Median [Q1-Q3]	28.50 [26.00-32.80]	27 [24.00-32.200]	0.19
≥ 40 kg/m² (%)	1 (2.94)	5 (8.93)	
SpO2			
Median [Q1-Q3]	98.00 [96.00-99.00]	98.00 [96.25-99.00]	0.42
< 94 %	2 (93.55)	5 (90.74)	
Hypnotics			
Yes (%)	4 (11.76)	3 (5.36)	0.42
Antidepressants			
Yes (%)	4 (11.76)	4 (7.14)	0.47
Anticoagulants			
Yes (%)	2 (5.88)	8 (14.29)	0.31
Asthenia			
Yes (%)	16 (47.06)	26 (46.43)	0.53
Sum of symptoms[3] Mean ± SD	1.65±1.52	1.52±1.67	<0.0001
FSS Mean ± SD	3.89 ± 1.94	3.23 ± 1.85	0.09
PCS12 mean ±SD	42.41± 10.21	42.80 ± 10.70	0.82
MCS12 mean ± SD	47.09± 4.53	46.66 ± 6.45	0.70

[1]Includes severe initial pneumonia and acute respiratory distress syndrome (ARDS). Criteria for severe pneumonia were: fever and SpO2<90% or respiratory rate > 30/min or acute respiratory failure needing respiratory support (invasive or not) and/or admission in ICU and/or acute circulatory failure (sepsis or septic shock); [2]Anxiety, problems of concentration, decreased visual acuity, panic attacks, rhinorrhea, fatigue, insomnia, cognitive decline, dyspnoea upon effort, hair loss vertigo, headaches, diarrhoea, constipation, dysgeusia ; [3]Sum of dyspnea, palpitations, cough, headache, chest pains, arthromyalgia, diarrhea and asthenia for each patient (statistical test done on medians); + p-value of the test done after dividing the variable in two : those with an mMRC score > or = 1 and those with a score<1. **Abbreviations:** BMI: Body Mass Index, SpO2: peripheral oxygen saturation.

Table 3: Comparison of the state of health at M24 of patients with a severe versus not severe initial COVID19 diagnosis.

Discussion

This study is one of the first, to our knowledge, to assess patients two years after hospitalization for COVID-19 in France. We found out that dyspnea, fatigue and a lower physical quality of life still persisted even two years after infection onset.

These findings, along the ones found in our previous study [7], highly suggest the persistence of physical symptoms, especially fatigue, and a lower quality of life in these patients.

One study showed that, two years after discharge, the most common symptoms included fatigue and dyspnea [9] while another found some recovery in symptomatology without a complete return to normality [10]. However, the persistence of fatigue has been demonstrated in other studies and has been shown to recover very slowly compared to perceived dyspnea which seemed to decline quicker [14]. Fatigue, although being subjective, has been a global human experience, known to impact patients in every aspect of their lives. This idea led to post-COVID19 fatigue being compared to the "chronic fatigue syndrome" and even associated with some similar endothelial damage [15].

Like shown in our results, perceived dyspnea was incoherent with the mMRC scale. This result can stress the subjective nature of symptoms coupled with the personal experience of patients. It can also relate back to neurological and psychological affections of post-COVID19, influencing the overall experience and symptom assessment [16]. Likewise, the results for perceived asthenia and FSS score tended to slightly differ, perceived asthenia seems to be on the track to get better while FSS remained stable.

Concerning quality of life, our study showed a lower PCS12 score compared to the French population norms [11] at both assessments. On the contrary, the MCS12 score in patients was not significantly different from the French norm. One study found a lower QOL in patients even two years after infection onset [8] and psychological alterations lasting in time. Due to the limited number of enrolled patients, generalization of these results is delicate and a lack of statistical power might explain the absence of difference found between severe patients and non-severe patients contrary to other studies claims [9].

Compared to the previously mentioned studies, our results have shown a persistence in symptoms at 24 months after discharge, although a small recovery in some was noticed. Our study found that dyspnea and fatigue are still present in patients, with more than half still presenting an mMRC score greater than 1 and an unchanged FSS score.

Consequently, these findings coupled with the other studies' results highly suggest a long-lasting effect of COVID-19 on physical and psychological health. They seem to accentuate the idea of a long form of COVID-19, especially marked by fatigue, dyspnea and general lower quality of life.

Conclusion

Even 24 months after SARS-CoV2 infection onset, patients still experience physical symptoms (i.e. dyspnea, fatigue), and an altered quality of life compared to the general population. Our results combined with others studies support the claims of long term COVID and help develop a better understanding of the infection's natural evolution; they also tend to show long-term, slow and sometimes futile, improvement of clinical state in patients.

These findings all converge into one major global concern being the long-lasting effect of infectious diseases on patients' health and how it is dealt with in our medical society and in our hospitals. More studies need to be done to further understand the long-term effects of SARS-CoV2 and other infections on general long-term health.

Ethics Approval and Consent to Participate

This study was performed in line with the principles of the Declaration of Helsinki, received ethics committee approval (number 3838-RM) and informed consent was obtained for each patient.

Competing Interests

The authors have no competing interests to declare

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Authors' Contributions

Study concept and design: Peter-Joe Noujaim, Claire Coutureau, Lukshe Kanagaratnam, Damien Jolly

Acquisition of data: Peter-Joe Noujaim, Damien Jolly and Lukshe Kanagaratnam

Analysis and interpretation of data: Peter-Joe Noujaim, Lukshe Kanagaratnam, Arwa Ben Salah and Damien Jolly

Drafting of the manuscript: Peter-Joe Noujaim

Critical revision of the manuscript for important intellectual content: all authors

All authors read and approved the final manuscript.

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