THERAPEUTIC ADVANCES in
Pulmonary and Critical Care Medicine

Original Research Article

Predictors of Functional Impairment in Severe COVID-19 Patients Two Months After Discharge

Ther Adv Pulm Crit Care Med

Volume 19: 1–15

DOI: 10.1177/29768675241305102

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Abstract

Background: The Post-COVID-19 Functional Status (PCFS) scale is a validated tool used to measure the functional status of patients discharged from the hospital.

Objectives: To describe the functional limitations of hospitalized COVID-19 patients at the time of discharge and two months afterward, and to identify risk factors associated with functional impairment.

Design: Retrospective study.

Methods: A total of 540 patients were included in this monocentric study. The functional status assessment using the PCFS scale and ventilatory needs were recorded at discharge and two months later. Univariate and multivariate analyses were performed in order to identify the risk factors of a high PCFS score.

Results: Two months after discharge, the PCFS grade was 0 in 60,6% of the survivors, 1 in 24.5%, 2 in 6.9%, 3 in 2.8%, and 4 in 5.3%. The identified risk factors of a high PCFS scale were: age, arterial hypertension, diabetes mellitus, immunosuppression, cardiovascular disease, high need for oxygen and high News2 score at admission, a high percentage of ground glass at chest CT scan performed at admission or during follow-up, elevated leukocytes, neutrophils, LDH, D-dimers, procalcitonin, and serum creatinine levels. During the hospital stay, treatment with steroids, tocilizumab, longer duration of hospitalization, ICU admission and prolonged stay, and the occurrence of thromboembolic or hemorrhagic events were also significantly associated with a higher PCFS. Multivariate analysis identified that only age and a high News2 score at admission were independent risk factors of a low PCFS score.

Conclusion: Multiple risk factors for a higher PCFS score were identified, but only age and a high News2 score at admission were found to be independent risk factors.

Plain Language Summary

Study aiming to identify the risk factors for functional impairment in patients recovering from Severe COVID-19 infection

Why was the study done? COVID-19 survivors can experience persistent symptoms during the recovery phase, affecting their physical, cognitive, or mental health and limiting their ability to engage in regular physical activities. The study aims to identify the factors that best predict the functional impairment in these patients.

What did the researchers do? The study included 540 patients. Their functional status was assessed at discharge and again two months later using a specific scale. Statistical analyses were conducted to identify the risk factors for functional impairment.

What did the researchers find? Two months after hospitalization for COVID-19, 4 out of 10 patients still exhibited mild to severe functional impairment. The study identified several risk factors, with age and the severity of COVID-19 infection emerging as the most significant predictors of functional impairment after severe COVID-19.

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What do the findings mean? Clinicians and physicians taking care of COVID-19 hospitalized patients can use the identified risk factors to predict early on which patients may require rehabilitation or home help following their recovery.

Keywords: Post-COVID-19, functional limitations, PCFS scale

Received: 2 May 2024; revised manuscript accepted: 19 November 2024.

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Introduction

COVID-19, caused by the SARS-CoV-2 virus, has been spreading since December 2019, leading to a new pandemic.[1] The medical and social responses to the COVID-19 pandemic have been unprecedented.[2]

During the acute phase, COVID-19 is known to induce a wide range of symptoms and complications other than respiratory including cardiovascular, gastrointestinal, renal, neurological, naso-oropharyngeal, and musculoskeletal.[3]

These symptoms may persist during the post-acute phase, affecting the physical, cognitive, or mental health of COVID-19 survivors and limiting their regular physical activities.[4–6] The most common symptom is fatigue, with other symptoms reported in the literature including dyspnea, chest discomfort, chest pain, breathlessness, cough, dizziness, myalgia, joint pain, and loss of smell and taste.[4–6] Data show that 87% of COVID-19 survivors had at least 1 of these symptoms 60 days after hospital discharge.[4]

The functional limitations of COVID-19 survivors can be measured and monitored by the Post-COVID-19 Functional Scale (PCFS), introduced by Klok and colleagues in March 2020.[7,8] This ordinal scale can be used at discharge and afterward to monitor the evolution of functional impairment over time and to identify patients who could benefit from rehabilitation and monitor their response to therapy.[8,9] The scale has been validated and translated into several languages.[9–12] To date, only a few studies have investigated the risk factors for functional impairment in the post-acute phase of COVID-19 (< 3 months) using this scale.[2,13,14]

In this study, we aimed to assess the functional status of hospitalized COVID-19 patients at discharge and two months later. We also investigated the risk factors for functional impairment in the post-acute phase of COVID-19.

Materials and Methods

Study Design and Participants

All patients with COVID-19, confirmed by a positive PCR test (n = 556; age range: 12-96 years), who were admitted to the adult wards or ICU of the Hôtel-Dieu de France University Medical Center in Beirut, Lebanon, between March 1, 2020, and March 1, 2021, were included in the study. Duplicate records for the same patient (administrative error), patients admitted as COVID-19 cases who were initially placed in isolation while awaiting PCR test results, which later turned out to be negative and patients who did not respond to phone calls after 3 follow-up attempts were all excluded. Patients over 15 years old and with a weight exceeding 50 kg were admitted to the adult wards or ICU and were included in the study.

The reporting of this study conforms to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement[15] (Supplemental material, Table S1).

Procedure

The patients were contacted by phone by the authors and trained medical students/residents, who conducted interviews to collect data on the functional and the ventilatory statuses of the patients at discharge (M0) and two months later (M2). During these interviews, the functional status of each patient was assessed using the PCFS scale. This scale consists of 5 grades numbered from 0 to 4, based on the patients' functional limitations.[7,8] Patients are graded 0 when they don't have any functional limitation, 1 for negligible functional limitation, 2 for slight functional limitation, 3 for moderate functional limitation without a need for daily assistance and 4 for severe functional limitation with a need for daily assistance.[7,8] The ventilatory status was categorized into the following groups: no need for oxygen, need for oxygen, noninvasive ventilation, and tracheostomy.

Additional information was obtained from the patients' database. The demographic characteristics were collected, including age, weight, gender, and blood type. The past medical history was also collected, including arterial hypertension, diabetes mellitus, immunosuppression, cardiovascular disease, and chronic renal failure. The latter was defined as the presence of a glomerular filtration rate < 60 mL/min, estimated by the CKD-EPI equation. Immunosuppression was defined as any condition that could compromise immunity, including treatment by immunosuppressants or oral glucocorticoids for more than a month, chemotherapy within 2 weeks of hospital admission, immunodeficiency disorders, and HIV. Cardiovascular disease was defined as any disease involving the heart or blood vessels, including coronary artery disease, previous myocardial infarction, heart failure, cardiomyopathy, previous abnormal heart rhythms, valvular heart disease, congenital heart disease, aortic aneurysm, stroke, peripheral artery disease, and thromboembolic disease.

The clinical characteristics at admission were recorded, including oxygen needs, the News2 score, and the viral load (PCR Ct value). The oxygen needs at admission were categorized into the following groups: no oxygen needed, nasal canula: < 4 L/min, nasal canula: 4 to 8 L/min, non-rebreather mask or high-flow nasal oxygen (HFNO), and intubation. The News2 score was calculated according to the Royal College of Physicians[16] at admission by interns or residents based on the vital signs measured by the nurses. All cases were tested using RT-PCR at the Rodolphe Mérieux Laboratory within the Faculty of Pharmacy of the Saint Joseph University of Beirut. Viral RNA was extracted from 140 µL of nasopharyngeal and oropharyngeal swab fluid (stored in a viral transport medium) using the QIAmp® Viral RNA Mini Kit from Qiagen®, following the manufacturer's guidelines. RT-PCR for SARS-CoV-2 was conducted on these RNA extracts, targeting the genes encoding the envelope protein (E) and the RNA-dependent RNA polymerase (RdRp), as described by Corman et al.[17] The method utilized a synthetic RNA positive control, provided by the Charité Virology Institute in Berlin, Germany, via the European Virus Archive (EVAg).

Additionally, chest imaging findings at admission and during follow-up were recorded, including the percentage of ground glass, lobar condensation (LC), pulmonary embolism (PE), and pneumomediastinum (PM). The laboratory results at admission were also collected, including the number of leucocytes (/µL), neutrophils (/µL), lymphocytes (/µL), ferritin (ng/mL), LDH (U/L), D-dimers (µg/mL), CRP (mg/L), procalcitonin (µg/L), triglycerides (mmol/L), LDL (mmol/L), HDL (mmol/L), and serum creatinine (µmol/L).

The hospital follow-up was documented, including the day symptoms started, length of stay, admission to the ICU, the day the patient was transferred to the ICU, ICU length of stay, hospitalization unit, intubation day, extubation day, and occurrence of a thromboembolic or hemorrhagic event. The day of hospital admission was designated as day 0, with the onset of symptoms, ICU transfer, intubation, and extubation days referenced accordingly.

Finally, information on the treatment received was recorded, including glucocorticoids, hydroxychloroquine, azithromycin, ivermectin, remdesivir, tocilizumab, and baricitinib, as well as the use of the prone position.

Outcomes

The primary outcome is the functional status assessed by the PCFS scale at M2. Secondary outcomes include the functional status at M0 and the ventilatory statuses at both M0 and M2. Clinical characteristics (oxygen needs, News2 score, and viral load), chest imaging findings, and laboratory results at admission were used to assess the severity of patients' illness during the acute phase of COVID-19.

Statistical Analysis

Data were analyzed using the Statistical Package for the Social Sciences (IBM SPSS Statistics for Windows) version 26.

Qualitative variables were presented as percentages, including the PCFS scale, gender, blood type, Rhesus antigen, presence of comorbidities, presence of LC, PE, or PM, oxygen needs at admission, treatments received, prone positioning, admission to ICU, and occurrence of thromboembolic or hemorrhagic event. Quantitative variables that met normality assumptions were presented as means ± standard deviations, including age, weight, ground glass estimation at CT scan, day symptoms

started, and PCR Ct value. Quantitative variables that did not meet normality assumptions were presented as medians (quartile 1-quartile 3), including the News2 score, laboratory results, length of stay, ICU transfer day, intubation, and extubation days.

The Mann-Whitney test was used to determine the risk factors for a high PCFS by examining associations between these qualitative variables and the PCFS scale: gender, rhesus blood type, presence of arterial hypertension, presence of diabetes mellitus, presence of immunosuppression, presence of cardiovascular disease, presence of chronic renal failure, presence of pulmonary embolism at admission and during follow-up, presence of pneumomediastinum at admission and during follow-up, admission to ICU during hospital stay, occurrence of a thromboembolic or hemorrhagic event, treatment with glucocorticoids, hydroxychloroquine, azithromycin, ivermectin, remdesivir, tocilizumab or baricitinib, as well as use of prone position.

The Kruskal–Wallis test was used to determine the risk factors for a high PCFS by examining associations between these qualitative variables and the PCFS scale: blood type and the oxygen needs at admission.

Spearman's correlation was used to identify risk factors for a high PCFS by examining associations between these quantitative variables and the PCFS scale: age, weight, News2 score at admission, viral load at admission, percentage of ground glass at admission and during follow-up, laboratory results at admission (number of leucocytes, neutrophils, lymphocytes, ferritin, LDH, D-dimers, CRP, procalcitonin, triglycerides, LDL, HDL, and serum creatinine), day symptoms started, length of hospital stay, day the patient was transferred to ICU, ICU length of stay, intubation day and extubation day. A value of $P < .05$ was considered significant.

A multinomial logistic regression and a likelihood ratio test were performed, including all variables present or assessed at admission that were identified as confounders or mediators in a Directed Acyclic Graph (DAG) combined with the univariate analysis (Supplemental Material, Figure S1): age, weight, arterial hypertension, diabetes mellitus, immunosuppression, cardiovascular disease, chronic renal failure, D-dimers, LDH, leucocytes, neutrophils, CRP, procalcitonin, serum creatinine, day symptoms started, News2 score, ground glass percentage at admission, and hospitalization unit. PCFS grade 4 was chosen as the reference category in the multinomial logistic regression.

Missing data were addressed using listwise deletion for the univariate analysis. The multivariate analysis was conducted only on valid cases, that is, cases without missing data.

Results

Of the 556 patients, 16 were removed from the study due to either duplicate records for the same patient (administrative error) or patients admitted as COVID-19 cases who were initially placed in isolation while awaiting PCR test results, which later turned out to be negative. 70 (13.0%) died during hospitalization. Two months after discharge, 101 (18.8%) patients died, and 3 were lost to follow-up; however, all 104 were included in the PCFS study at discharge. Thus, 470 patients were included in the PCFS study at discharge and 436 were included 2 months after discharge (Figure 1).

The mean age of the 470 patients was 61 ± 16. Of these, 312 (66.4%) were male. 149 (31.7%) patients did not require oxygen upon admission. A total of 40 (8.5%) patients were admitted to the ICU. Patient characteristics are detailed in Table 1.

At discharge, among the 470 patients, 128 (27.2%) had a PCFS grade of 0, 114 (24.3%) had a grade of 1, 106 (22.6%) had a grade of 2, 64 (13.6%) had a grade of 3, and 58 (12.3%) had a grade of 4. Two months after discharge, among the 436 patients, 264 (60.6%) had a PCFS grade of 0, 107 (24.5%) had a grade of 1, 30 (6.9%) had a grade of 2, 12 (2.8%) had a grade of 3, and 23 (5.3%) had a grade of 4 (Figure 2).

At discharge, 337 (73.6%) patients were oxygen-independent, 111 (24.2%) needed oxygen, 4 (0.9%) needed non-invasive ventilation, and 6 (1.3%) had a tracheostomy. Two months later, 401 (91.8%) were oxygen-independent, 30 (6.8%) needed oxygen, 3 (0.7%) required noninvasive ventilation, and 4 (0.9%) had a tracheostomy (Supplemental material, Figure S2).

Univariate Analysis at M0 and M2

Among the demographic characteristics, only age was positively correlated with a high PCFS score

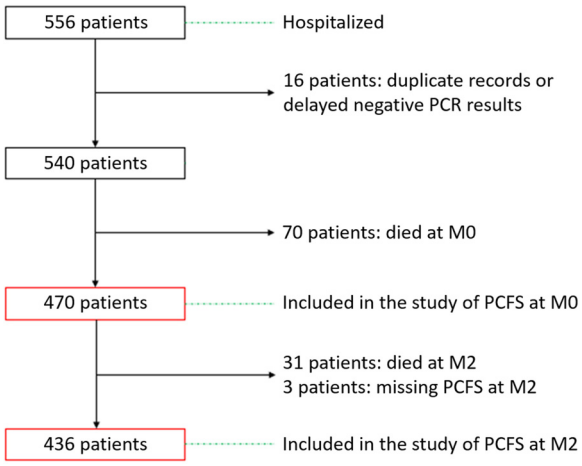

Figure 1. Selection of study population.

both at discharge ($r=.158$; $P=.001$) and after 2 months ($r=.222$; $P<.001$).

Arterial hypertension and diabetes mellitus were associated with a high PCFS score at discharge ($P=.005$ and $P=.026$, respectively) and at 2 months ($P<.001$ and $P=.017$, respectively). Immunosuppression and cardiovascular disease were associated with a high PCFS score only at M2 ($P=.033$ and $P=.020$, respectively).

At admission, higher oxygen needs (need for a non-rebreather mask or high-flow nasal oxygen) were strongly associated with a high PCFS score both at discharge ($P<.001$) and 2 months later ($P<.001$). The News2 score was positively correlated with a high PCFS score at discharge ($r=.357$; $P<.001$ and at 2 months ($r=.280$; $P<.001$). The CT value of the first PCR was negatively correlated with a high PCFS score at discharge ($r=-.156$; $P=.014$) but not at 2 months ($P=.823$).

A high percentage of ground glass on CT scans performed at admission was correlated to a high PCFS score both at M0 and at M2 ($r=.173$; $P=.001$ and $r=.137$; $P=.009$, respectively). This correlation was also observed when CT scans were performed during follow-up ($r=.247$; $P=.001$ and $r=.386$; $P<.001$, respectively).

The following laboratory tests at admission were correlated with a high PCFS score both at discharge and 2 months later: leukocytosis ($r=.105$; $P=.023$ and $r=.103$; $P=.031$, respectively), high neutrophils count ($r=.126$; $P=.006$ and $r=.121$; $P=.012$, respectively), elevated LDH ($r=.195$; $P<.001$ and $r=.135$; $P=.006$, respectively), high D-dimers ($r=.141$; $P=.003$ and $r=.177$; $P<.001$, respectively), and high procalcitonin ($r=.179$; $P<.001$ and $r=.108$; $P=.035$, respectively). High CRP and lymphopenia were correlated with a high PCFS score only at M0 ($r=.122$; $P=.009$ and $r=-.118$; $P=.011$, respectively).

Patients treated with glucocorticoids or tocilizumab had higher PCFS scores at M0 and at M2 ($P<.001$). Those treated with remdesivir or who used prone positioning had higher PCFS score only at M0 ($P=.011$ and $P=.003$, respectively).

A longer hospital stay, admission to ICU, and the occurrence of a thromboembolic event were associated with a high PCFS score both at M0 and at M2 ($r=.338$; $P<.001$; $P<.001$; $P=.027$ and $r=.350$; $P<.001$; $P<.001$; $P=.037$, respectively). Early intubation was associated with a high PCFS score at M0 ($r=-.319$; $P=.037$), while a longer ICU stay and the occurrence of a hemorrhagic event were associated with a high PCFS score at M2 ($r=.320$; $P=.006$ and $P=.003$, respectively). Delayed extubation appeared to be associated with a high PCFS score at M2 ($r=.366$; $P=.051$).

Tables S2 and S3 in the supplemental material provide additional associations with a high PCFS score at discharge and at two months.

Multivariate Analysis at M2

The multivariate analysis was conducted on 299 cases (ie, cases without missing data).

Table 1. Characteristics of the patients studied at discharge (M0) and 2 months later (M2).

	At discharge		2 months later	
	N		N	
Age (years)	468	61 ± 16	434	60 ± 16
Weight (kg)	441	80.9 ± 16.4	416	81 ± 16.5
Gender				
Male	312	66.4	291	66.7
Female	158	33.6	145	33.3
Blood type				
A	187	45.9	179	46.1
B	48	11.8	45	11.6
AB	23	5.7	22	5.7
0	149	36.6	142	36.6
Rhesus antigen				
Negative	38	9.3	35	9.0
Positive	369	90.7	353	91.0
Presence of arterial hypertension (yes)	244	51.9	220	50.5
Presence of diabetes mellitus (yes)	124	26.4	107	24.5
Presence of immunosuppression (yes)	42	8.9	37	8.5
Presence of cardiovascular disease (yes)	102	21.7	83	19.0
Presence of Chronic renal failure (yes)	60	12.8	49	11.2
Ground glass estimation at admission CT scan (%)	398	25 ± 18	367	24 ± 17
Ground glass estimation at follow-up CT scan (%)	171	38 ± 25	159	36 ± 23
Presence of LC at admission CT scan (yes)	30	7.5	23	6.3
Presence of LC at follow-up CT scan (yes)	21	11.7	16	9.5
Presence of PE at admission CT scan (yes)	3	0.8	3	0.8
Presence of PE at follow-up CT scan (yes)	6	3.3	5	3.0
Presence of PM at admission CT scan (yes)	2	0.5	2	0.5
Presence of PM at follow-up CT scan (yes)	8	4.4	5	3.0
Need of oxygen at admission				
No oxygen needed	149	31.7	147	33.7
Nasal canula: < 4 L/min	124	26.4	115	26.4

(Continued)

Table 1. Continued.

	At discharge		2 months later	
	N		N	
Nasal canula: 4 to 8 L/min	127	27.0	114	26.1
Non-rebreather mask or HFNO	70	14.9	60	13.8
Intubation	0	0.0	0	0.0
News 2 score	469	5 (2-6)	435	4 (2-6)
First Ct value	249	22.7 ± 5.8	229	22.6 ± 5.8
Leucocytes (/µL)	470	7100 (5200-10 000)	436	7000 (5200-9900)
Neutrophiles (/µL)	470	5380 (3700-8050)	436	5255 (3585-7760)
Lymphocytes (/µL)	470	850 (570-1310)	436	875 (570-1350)
Ferritin (ng/mL)	445	735 (357-1279)	412	733 (352-1256)
LDH (U/L)	443	325 (249-425)	412	321 (248-423)
D-dimers (µg/mL)	444	0.79 (0.45-1.59)	412	0.76 (0.43-1.5)
CRP (mg/L)	462	79.35 (31.3-144)	428	78 (30-142)
Procalcitonin (µg/L)	414	0.15 (0.07-0.37)	384	0.14 (0.07-0.3)
HDL (mmol/L)	101	1.15 (0.99-1.42)	98	1.18 (1.01-1.42)
LDL (mmol/L)	102	2.86 (2.19-3.53)	99	2.87 (2.21-3.53)
Triglycerides (mmol/L)	306	1.79 (1.34-2.48)	289	1.8 (1.34-2.49)
Serum creatinine (µmol/L)	459	74 (60-100)	425	73 (58-95)
Treatment with glucocorticoids (yes)	379	80.6	346	79.4
Treatment with hydroxychloroquine (yes)	103	21.9	99	22.7
Treatment with azithromycin (yes)	166	35.3	155	35.6
Treatment with ivermectin (yes)	98	20.9	88	20.2
Treatment with remdesivir (yes)	27	5.7	27	6.2
Treatment with tocilizumab (yes)	67	14.3	59	13.5
Treatment with baricitinib (yes)	25	5.3	22	5.0
Prone positioning	125	27.1	119	27.7
Day symptoms started (days)	448	−7 ± 6	418	−7 ± 6
Length of stay (days)	470	8 (5-15)	436	8 (5-14)
Admission to ICU (yes)	40	8.5	34	7.8
ICU transfer day (days)	87	3 (1-6)	71	2 (1-5)
ICU length of stay (days)	88	11 (7-19)	73	11 (7-17)

(Continued)

Table 1. Continued.

	At discharge		2 months later	
	N		N	
Intubation day (days)	43	4 (2-10)	31	4 (2-8)
Extubation day (days)	31	13 (11-20)	29	13 (11-20)
Occurrence of a thromboembolic event (yes)	20	4.3	17	3.9
Occurrence of a hemorrhagic event (yes)	29	6.2	22	5.1

When applying the Wald test and controlling for the covariates (Table 2), each 1-year increase in age decreased the odds of having a PCFS grade of 0 (OR = 0.897; $P = .004$) and the odds of having a PCFS grade of 1 by 10.3% (OR = 0.897; $P = .004$) compared to a PCFS grade of 4. Each 1-kilogram increase in weight increased the odds of having a PCFS grade of 0 by 6.3% (OR = 1.063; $P = .020$) and increased the odds of having a PCFS grade of 1 by 6.1% (OR = 1.063; $P = .029$) compared to a PCFS grade of 4. Each 1-unit increase in CRP (1 mg/L) decreased the odds of having a PCFS grade of 1 by 1.2% (OR = 0.988; $P = .046$) compared to a PCFS grade of 4.

When controlling for the covariates, the odds of having a PCFS grade of 0 (compared to 4) were 485.6% higher for patients without diabetes mellitus (OR = 5.856; $P = .033$), 814.3% higher for immunocompetent compared to immunocompromised patients (OR = 9.143; $P = .024$), and 866.8% higher for patients admitted to a regular ward compared to those admitted to ICU (OR = 9.668; $P = .016$). The odds of having a PCFS grade of 2 (compared to 4) were 858.1% higher for patients without diabetes mellitus compared to those without diabetes mellitus (OR = 9.581; $P = .024$).

Except for weight (PCFS 0 vs 4 and PCFS 1 vs 4) and CRP (PCFS 1 vs 4), the multivariate analysis indicates that comorbidities lead to lower functional outcomes. Although we observe a paradoxically significant association for weight and CRP, it is important to note that the odds ratios are very close to 1 (OR = 1.063, OR = 1.061, and OR = 0.988, respectively), which significantly reduces their clinical relevance.

The likelihood ratio test (Table 3) identified age ($P < .001$) and a high News2 score at admission ($P = .042$) as independent risk factors for a high PCFS score.

Discussion

This study described the functional limitations of COVID-19 hospitalized patients at discharge and two months later using the PCFS scale. It also identified two independent risk factors for functional impairment two months after discharge: age and a high News2 score at admission.

Previous studies have assessed functional limitations in COVID-19 patients using tests such as the 1-min sit-to-stand test, the Short Physical Performance Battery, and the Barthel index.[18] Unlike these tests, the PCFS is COVID-19-specific.[8] Moreover, this scale does not target a single organ, or specify the etiology of functional impairment, making it helpful in a disease that affects several organs, such as COVID-19.[10] In fact, many symptoms like fatigue, dyspnea, chest discomfort, chest pain, breathlessness, myalgia, or joint pain can contribute to poor functional status following recovery from COVID-19.[4–6] Additionally, the PCFS score has been shown to correlate with symptom presence and severity, decreased quality of life, reduced work productivity, and impaired daily activities.[10,11]

In our study, the distribution of PCFS at discharge aligns with existing literature.[2,13,14,19] Banic et al reported that 1 to 2 months after discharge, 21.5% of patients had a PCFS grade of 0, 29.1% had a grade of 1, 27.6% had a grade of 2, 19.9% had a grade of 3, and 1.9% had a grade of 4.[13] Notably, Taboada et al observed improvements in PCFS scores at 6 months post-discharge: 44.3% of patients had a grade of 0, 31.1% had a grade of 1, 14.8% had a grade of 2, 6.6% had a grade of 3, and 3.3% had a grade of

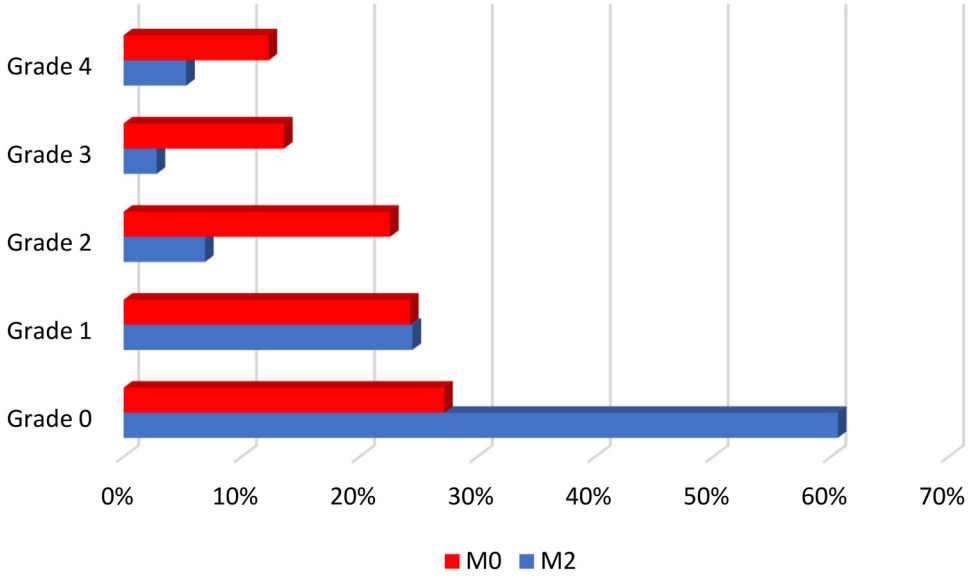

Figure 2. PCFS score at discharge (M0) and 2 months later (M2).

4.[20] This improvement was confirmed in others studies.[21–23]

Our results identified advanced age, arterial hypertension, diabetes mellitus, immunosuppression, and cardiovascular disease as risk factors for a high PCFS score. The literature has already identified advanced age and comorbidities as risk factors for functional impairments.[2,13,14] However, unlike previous studies that identified female gender as a risk factor,[2,13,14] our findings did not show a significant association between sex and functional impairment.

Our study identified several clinical and paraclinical factors recorded upon admission that correlate with a high PCFS score. These include a high ground glass percentage at chest CT scan, elevated oxygen requirements, a high News2 score, low first PCR CT value, leukocytosis, elevated neutrophil count, lymphopenia, high LDH, high D-dimers, high CRP, high procalcitonin, and elevated serum creatinine. The need for oxygen supplementation at admission has been previously documented as a risk factor in the literature.[2,13] These findings suggest that functional impairment can be predicted very early, as these parameters are measured upon hospital admission and are indicative of disease severity from its onset.

In our study, a longer hospital stay, ICU admission, a longer ICU stay, early intubation, and the occurrence of hemorrhagic or thromboembolic events were all correlated with a high PCFS score. An ICU admission and a longer hospital and ICU length of stay have all been described as risk factors for high PCFS scores,[2,14] underscoring the heightened risk of functional impairment in patients with severe diseases. These associations may be explained by muscle weakness, loss of muscle mass and function secondary to extended hospitalization, critical illness polyneuropathy, critical illness myopathy, and post-intensive care syndrome.[24–28]

Our results indicated that high D-dimers and the occurrence of a thromboembolic event were associated with a high PCFS score, while the presence of pulmonary embolism on a chest CT scan was not. The association of high D-dimers and the occurrence of a thromboembolic event with a high PCFS score might be attributed to the fact that the PCFS score is derived from the Post-VTE Functional Status (PVFS) scale. Both the PCFS and PVFS scales share similar items, as the PVFS scale was previously developed in 2019 to evaluate functional limitations following venous thromboembolism.[29,30] It is therefore understandable that a COVID-19 patient who experienced a thromboembolic event may have a higher

Table 2. Risk factors of a high PCFS score 2 months after discharge (M2)—multinominal logistic regression.

	PCFS 0		PCFS 1		PCFS 2		PCFS 3	
	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
Age (years)	0.897 (0.834-0.966)	.004	0.897 (0.833-0.966)	.004	0.952 (0.876-1.035)	.250	0.986 (0.886-1.098)	.800
Weight (kg)	1.063 (1.010-1.120)	.020	1.061 (1.006-1.119)	.029	1.044 (0.983-1.109)	.160	1.036 (0.957-1.121)	.385
Hypertension								
No	0.935 (0.163-5.360)	.940	0.785 (0.131-4.704)	.791	0.711 (0.091-5.553)	.745	1.586 (0.115-21.89)	.731
Yes (ref.)	1		1		1		1	
Diabetes mellitus								
No	5.856 (1.153-29 752)	.033	4.498 (0.848-23 869)	.077	9.581 (1.342-68 413)	.024	14 550 (0.817-258 971)	.068
Yes (ref.)	1		1		1		1	
Immunosuppression								
No	9.143 (1.344-62 174)	.024	4.642 (0.662-32 538)	.122	6.696 (0.434-103 294)	.173	0.474 (0.025-9.017)	.620
Yes (ref.)	1		1		1		1	
Cardiovascular disease								
No	0.407 (0.091-1.815)	.239	0.533 (0.112-2.523)	.427	0.788 (0.118-5.29)	.807	0.220 (0.020-2.443)	.218
Yes (ref.)	1		1		1		1	
Chronic renal failure								
No	1.069 (0.115-9.965)	.953	4.055 (0.318-51 678)	.281	3.167 (0.118-85 181)	.493	1.442 (0.051-40 753)	.830
Yes (ref.)	1		1		1		1	
Ground glass estimation at admission CT scan (%)	0.993 (0.949-1.039)	.753	1.010 (0.965-1.057)	.683	0.998 (0.947-1.052)	.952	0.966 (0.884-1.056)	.446
News 2 score	0.94 (0.666-1.327)	.725	1.090 (0.768-1.548)	.629	1.266 (0.844-1.9)	.254	1.286 (0.754-2.193)	.355

(Continued)

Table 2. Continued.

	PCFS 0		PCFS 1		PCFS 2		PCFS 3	
	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
Leucocytes (/µL)	1 (1-1)	.793	1 (1-1)	.672	1 (1-1)	.925	1 (1-1)	.858
Neutrophiles (/µL)	1 (0.999-1)	.313	1 (1-1)	.764	1 (0.999-1)	0.678	1 (1-1)	.892
LDH (U/L)	1.001 (0.995-1.006)	.757	1.002 (0.996-1.007)	.545	1.002 (0.996-1.009)	.473	1.002 (0.992-1.011)	.754
D-dimers (µg/mL)	1.141 (0.860-1.513)	.360	1.149 (0.866-1.523)	.335	1.138 (0.858-1.510)	.369	1.129 (0.845-1.507)	.412
CRP (mg/L)	0.992 (0.980-1.003)	.142	0.988 (0.977-1)	.046	0.992 (0.979-1.004)	.194	0.994 (0.977-1.010)	.438
Procalcitonin (µg/L)	2.464 (0.572-10 625)	.226	2.584 (0.599-11 145)	.203	2.558 (0.592-11 066)	.209	2.483 (0.554-11 137)	.235
Serum creatinine (µmol/L)	0 .997 (0.983-1.011)	.686	1.002 (0.987-1.016)	.815	1.002 (0.988-1.017)	.752	1.004 (0.989-1.020)	.587
Day symptoms started	0.902 (0.811-1.002)	.055	0.929 (0.832-1.037)	.189	0.968 (0.845-1.108)	.636	0.888 (0.738-1.069)	.209

likelihood of scoring poorly on the PCFS scale due to the overlap in criteria between the 2 scales and to the functional limitations directly attributed to the thromboembolic event.[29,30] The presence of pulmonary embolism on a chest CT scan was not correlated with the PCFS score in our study, probably because of the relatively low prevalence of pulmonary embolism among the study population.

Among the treatments administered, glucocorticoids, tocilizumab, remdesivir, and prone position were associated with a high PCFS score. This correlation can be explained by the disease severity: patients with more severe COVID-19 are more likely to receive 1 of these treatments. Additionally, the association may also be due to treatment-related factors. For instance, glucocorticoids can induce muscle weakness and the prone position may limit patient mobility, potentially accelerating muscle loss and contributing to functional impairment.[31]

Among all the variables in our study, older age, and a high News2 score were the only independent risk factors for high PCFS scores. A previous study had identified age and length of hospital stay and ICU stay as independent risk factors for high PCFS scores.[14] Length of hospital and ICU stays often reflects the severity of the disease, indicating that it may act more as a mediator of the disease's impact, similarly to the New2 score.

Most of the risk factors identified in our study have been previously reported as mortality factors in COVID-19, including arterial hypertension, diabetes mellitus, cardiovascular disease, high oxygen needs at admission, high News2 scores, lymphopenia, elevated D-dimers, ICU admission, and the occurrence of thromboembolic or hemorrhagic events.[1,32–37] Age, in particular, has also been described as an independent risk factor for mortality.[32] It is noteworthy that the mortality rate observed in our study was consistent with findings reported in the literature following hospital discharge.[1] Similarly, the risk factors identified in our study have also been associated with long COVID when assessed over extended periods after hospital discharge (> 3 months) in several studies.[20–23]

One can note that other viruses of the same family have already been associated with functional impairment after recovery. For instance, survivors of the Middle East respiratory syndrome (MERS)

Table 3. Risk factors of a high PCFS score 2 months after discharge (M2)—likelihood ratio test.

	−2 Log likelihood of reduced model	*P*-value
Age (years)	547.215	<.001
Weight (kg)	532.104	.144
Hypertension	525.948	.952
Diabetes mellitus	532.778	.111
Immunosuppression	534.391	.058
Cardiovascular disease	527.998	.602
Chronic renal failure	528.762	.477
Ground glass estimation at admission CT scan (%)	528.924	.453
News 2 score	535.191	.042
Leucocytes (/µL)	527.693	.656
Neutrophiles (/µL)	529.629	.358
LDH (U/L)	526.299	.903
D-dimers (µg/mL)	529.676	.352
CRP (mg/L)	531.661	.171
Procalcitonin (µg/L)	531.584	.176
Serum creatinine (µmol/L)	533.046	.100
Day symptoms started	530.719	.243
Admission to ICU	534.309	.060

experienced a lower quality of life even 14 months after recovery.[38]

This study has several limitations. First, it involved a relatively small number of patients from a single center, which may not be representative of other hospital populations. Second, there was a significant drop in the number of patients assessed between discharge and 2 months later, leading to a less representative sample and a potential selection bias towards less severe cases at M2. Third, some variables studied, such as treatments with glucocorticoids or tocilizumab, were typically used for more severe patients, and follow-up CT scans were only performed for patients who did not improve, which may affect the results. Fourth, the functional impairment of the patients prior to their COVID-19 infection was not assessed, making it difficult to evaluate the progression of their limitation. Fifth, data on symptoms limiting functional status were not collected. It is possible that recall bias may have also occurred. Although response bias was minimized because patients were contacted by phone exclusively by the authors or trained medical students/residents, it remains a potential issue. Finally, while the PCFS score has been validated for use in COVID-19 patients, it is inherently a subjective measure and may be subject to biases related to self-reporting and recall.

Conclusion

The PCFS scale is a validated tool for assessing functional impairment in COVID-19 patients. While this retrospective monocentric study identified multiple risk factors associated with high PCFS scores, several confounding factors must be considered. Our results indicate that only advanced

age and a high News2 score upon admission are independent risk factors for a high PCFS score. However, further studies with larger patient populations are necessary to confirm the utility of the PCFS scale in identifying patients who may benefit from rehabilitation and in monitoring their response to therapy.

Acknowledgments
The authors would like to thank Science PRO sarl for conducting critical review and editing of the article.

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Availability of Data and Materials
The data supporting the conclusions of this article will be made available by the authors on request.

Declaration of Conflicting Interests
The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Disclosure Statement
A small part of the data presented in this study was previously published as abstracts for the European Respiratory Society International Congress (Eur Respir J 2021; 58: Suppl. 65, PA1993—*Eur Respir J* 2022; 60: Suppl. 66, 2766—*Eur Respir J* 2022; 60: Suppl. 66, 2778). This manuscript was also the topic of a not published dissertation in 2024 at the Faculty of Medicine of the Saint Joseph University of Beirut. This article has been reviewed for academic writing standards by Science PRO SARL. We also acknowledge the use of ChatGPT for assistance in grammar correction and English syntax enhancement.

Funding
The authors received no financial support for the research, authorship, and/or publication of this article.

Ethics Approval and Consent to Participate
The Ethical Committee of the Saint-Joseph University of Beirut (Lebanon) approved this study (approval numbers CEHDF #1631 and CE #1642). The study protocols were conducted in line with the principles of "Good Clinical Practice" outlined in the "Declaration of Helsinki" (October 2013) and adhered to the "International Ethical Guidelines for Biomedical Research Involving Human Subjects" established by the Council for International Organizations of Medical Sciences (CIOMS) in collaboration with the World Health Organization (WHO). Verbal informed consent was obtained from the patients, as the interviews were conducted by telephone; for participants under 18 years old, consent was obtained from a parent or legal guardian. The consent is documented in the general hospital consent form.

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Supplemental Material
Supplemental material for this article is available online.

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