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Research Article

Cognitive Impairment and Fatigue in Intensive Care Patients Three Months after the Acute Phase of COVID-19 Infection: Follow-Up with Focus on Differences between the First and Later Waves of the Pandemic

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Background. Cognitive symptoms and fatigue may persist after intensive care unit (ICU) care. It remains unclear whether post-COVID-19 symptoms are related to ICU care itself or the infection. *Objective*. The primary aim was to investigate the prevalence of residual cognitive impairment and fatigue after ICU care for COVID-19 and to evaluate the importance of demographic factors. A secondary aim was to investigate whether differences in ICU treatment between the first wave (March 2020 to July 2020) and later waves (August 2020 to January 2021) of COVID-19 were associated with differences in cognitive outcomes. *Design*. Prospective follow-up study. *Subjects/Patients*. Swedish cohort of COVID-19 patients referred from ICU. *Methods*. Montreal Cognitive Assessment (MoCA), Multidimensional Fatigue Inventory-20 (MFI-20), Hospital Anxiety and Depression Scale, Insomnia Severity Scale, and RAND-36 were administered approximately three months after admission to ICU. Mann–Whitney tests were used to investigate group differences, and multiple linear regression was used to investigate the relationship between fatigue and covarying factors. *Results*. 71 patients completed follow-up, and 60 patients underwent a cognitive screening of which 30% had MoCA scores indicative of cognitive impairment (<26 points). Higher age was related to poorer cognitive performance. Patients scored above the normal range on all subscales on the MFI-20. There was a significant difference in length of ICU stay between wave one and following waves, but no statistically significant differences emerged on cognitive screening. Intubated patients' fatigue ratings were lower compared to those not intubated—despite longer ICU stay. No difference in MoCA scores emerged between patients who were, or were not, intubated. *Conclusion*. Cognitive impairment and fatigue were evident in patients three months after a severe COVID-19 infection, but global cognitive functioning was not related to ICU length of stay. Less fatigue among patients who had been intubated merits further investigation.

1. Introduction

Cognitive symptoms and fatigue are particularly frequent after COVID-19 infection of all severities [1]. The severity of the acute infection does not seem to affect the likelihood of long-term fatigue, while a history of depression, on the other hand, is correlated with post-COVID-19 fatigue [1]. Metabolic and structural brain abnormalities have been found to correlate with late neurological and cognitive impairment and have been suggested as underlying substrates for persisting cognitive symptoms after COVID-19 infection [2]. Delirium is common in severe cases during the acute phase of COVID-19 infection and is a strong predictor for long-lasting post-COVID-19 impairments [3].

Persisting inflammation might lead to an autoimmune response, which could also lead to cognitive disabilities [4].

Intensive care treatment for COVID-19 infection in Sweden was modified during the pandemic in pace with increasing understanding of the disease. Differences in the length of intensive care unit (ICU) stay at different stages of the pandemic are probably related to the changes in treatment protocols. Regular discussions with ICU colleagues throughout the pandemic and local hospital data (unpublished) noted that more patients were intubated during the first wave of the disease and that routine treatment with steroids started in the summer of 2020 and thereafter was used for most ICU patients. Both the need for intubation and the need for corticosteroid treatment have been shown to be negatively related to cognitive functioning over time [5]. Glucocorticoid treatment during the acute phase has been reported to have both beneficial and harmful effects on long-term cognitive function after COVID-19 [6].

Persisting impairments after ICU, postintensive care syndrome (PICS), can include both physical and cognitive symptoms such as muscle weakness, polyneuropathy, memory loss, and impaired language and executive functions [7]. Psychological sequelae in terms of depression, post-traumatic stress disorder (PTSD), and anxiety are also common. Delirium during an ICU stay due to any diagnosis seems to give an increased risk of long-term cognitive disabilities, but other acute physiological stressors such as hypo- and hyperglycaemia during hospitalisation may also increase risk of long-term cognitive impairments [8].

The objective of the present study was to investigate residual cognitive impairment and fatigue after an ICU stay due to a COVID-19 infection and to evaluate any possible demographic-related factors. A secondary aim was to investigate if differences in acute treatment regimes, with resulting shorter length of ICU treatment in the later waves of COVID-19, were associated with better outcomes regarding cognitive function and fatigue.

2. Methods and Material

This is a follow-up study of a consecutive cohort of patients who received intensive care for COVID-19 infection and underwent a follow-up assessment at the Department of Rehabilitation Medicine at Danderyd University Hospital. This is a large district general hospital serving the north of Stockholm.

During the pandemic, the Department of Rehabilitation Medicine collaborated with the ICU in providing routine follow-up to patients who required ICU care for COVID-19. On discharge from the ICU, all patients were referred to the rehabilitation department for a planned clinical follow-up post-ICU within 4-12 weeks after discharge, approximately 3 months from their admission to hospital. For convenience, date of admission to hospital was used to represent the date of onset of COVID-19 for each patient. Some referrals to the rehabilitation department (11%) came from ICUs at other hospitals, and these patients were offered the same clinical follow-up. In parallel, a research protocol was developed for the study, closely related to the clinical follow-up routines, and patients were invited to give consent to participation in the follow-up research study including use of their pseudoanonymised clinical data.

To investigate whether there were any differences in outcome related to the time of disease onset and ICU treatment, the total cohort was divided into two subsamples: the first wave (wave 1) admitted between March 2020 and July 2020 and the later waves (wave 2+) admitted between August 2020 and January 2021. These time periods represent waves of ICU admissions of new COVID-19 in Stockholm (Figure 1).

Inclusion criteria were confirmed COVID-19 infection requiring ICU care and age of 18 years or older. Informed consent was obtained.

2.1. Data Collection. To investigate residual cognitive symptoms and fatigue, screening tools for cognitive dysfunction (the Montreal Cognitive Assessment (MoCA©) [9] and self-reported questionnaires for fatigue (the Multidimensional Fatigue Inventory (MFI-20) [10, 11], anxiety and depression (the Hospital Anxiety and Depression Scale (HADS) [12], insomnia (the Insomnia Severity Index (ISI) [13], and health-related quality of life (RAND-36) [14] were used. The MoCA was used with copyright permission from the MoCA Test Inc. Detailed information about the assessment instruments is found in Table 1 in the Supplementary information. Data was collected on demographics (age, gender, education level, occupation status at follow-up, and language) and clinical variables (time of admission, preexisting medical conditions, and smoking habits). Length of stay in the ICU, intubation, treatment with corticosteroids, and remdesivir were retrospectively collected from the patients' medical records.

2.2. Statistics. Statistical analysis was carried out in SPSS version 29. Histograms were constructed for numeric variables. Kurtosis and skewness were assessed for continuous variables to assess for normality before running the analysis. Nonparametric tests were used where the data were not normally distributed and when the data were on interval levels (questionnaires). Categorical, nonparametric, or not normally distributed data are presented as frequency, median, and range and normally distributed data as mean and standard deviation (SD). Nonparametric tests (chi-square and Mann–Whitney U-test) were used for comparisons between the first and subsequent waves of COVID-19 infection, except for age and length of ICU stay, where independent samples t-test was used for comparison between subsamples. The chi-square test was used for gender, language, smoking habits, preconditions, days at ICU, and treatment at ICU.

Spearman's nonparametric correlation tests were used to investigate correlations.

Multiple linear regression was used to investigate the relationship between fatigue and intubation, depression, and insomnia. Assumptions were checked with plots and descriptives and Durbin–Watson statistic to detect the presence of autocorrelation. Multicollinearity was not found between the explanatory variables (variance inflation factor, $VIF < 2$).

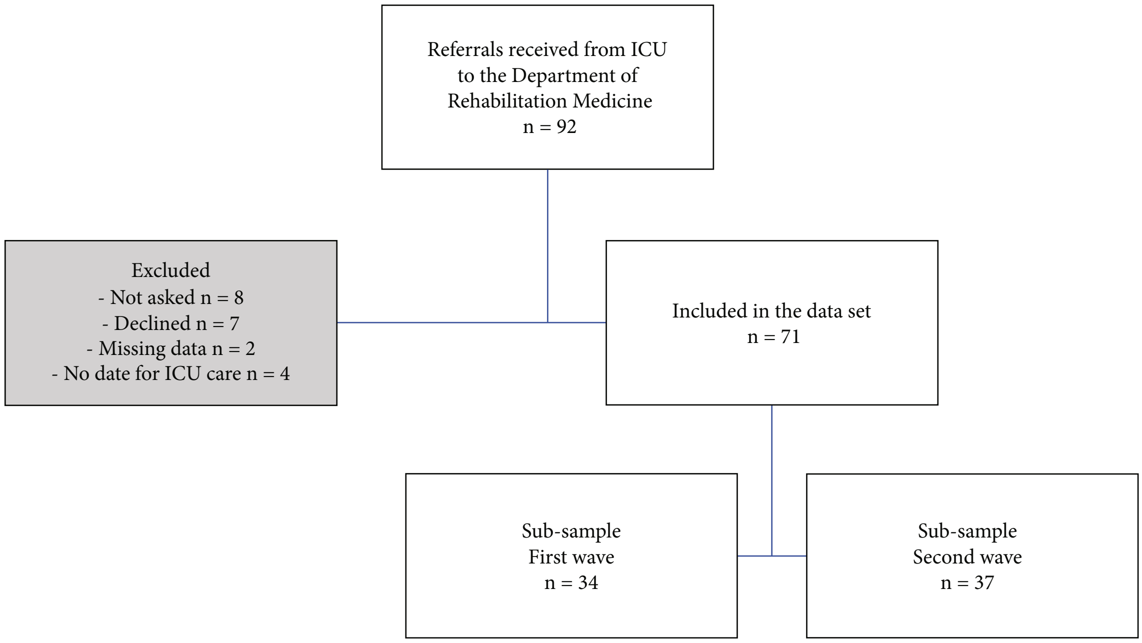

Figure 1: Flow chart for participants in the dataset.

The P value was set to $P < 0.05$. For variables with large numerical differences between the groups where P values were over 0.05, the effect size $(Z/\text{sqrt}(n) = r)$ was calculated.

2.3. Ethics. The study was approved by the Swedish Ethical Review Authority (D-nr 2020-02997).

3. Results

3.1. Characteristics. Of the 71 patients included in the study, 63 (89%) were referred from the ICU at Danderyd University Hospital, and 8 (11%) were referred from other hospitals in Stockholm. The demographic characteristics of the patients are presented in Table 1. Most patients in the cohort were males of working age. The most common coexisting medical conditions were hypertension and diabetes mellitus. Only a minority of patients were working at the time of the follow-up visit, with a large proportion of the cohort on sick leave. Before the onset of COVID-19 infection, about two-thirds of the total cohort was working (not shown in Table 1).

3.2. Cohort Characteristics. Demographics and clinical characteristics for patients from the first and subsequent waves are shown in Table 2 (demographic and clinical characteristics) and Table 3 (assessment). No demographic differences were identified between the two subsamples. However, patients treated during the first wave had significantly longer ICU stays (Table 2). Intubated patients ($n = 49$) had a longer stay at the ICU compared to nonintubated patients ($n = 21$) (21.8 days, SD = 18.4, vs. 7.0 days, SD = 10.6, $P = 0.001$).

3.3. Cognitive Impairment. For the total cohort, the MoCA score was within normal limits (Table 3). Nonetheless, 18 (30%) of the patients performed below the cut-off score of 26, thus suggesting cognitive impairment (wave 1: 10 patients (38%) below cut-off; wave 2+: 7 patients (23%), data for wave missing: for one patient). The difference was not statistically significant. Of the 60 patients with results on MoCA, 48 (80%) were aged <65 years, and 12 were ≥65 years. For patients ≥ 65 years of age, half of the patients had a MoCA score ≤ 25 points. For patients younger than 65 years of age, only one-fourth had a MoCA score ≤ 25 points.

3.4. Self-Rated Measurements. The patients scored general fatigue, physical fatigue, reduced activity, reduced motivation, and mental fatigue above normal, indicating that they suffered from different dimensions of fatigue. However, there was a large range within the group, from substantially lower rates of fatigue compared to the general population to maximum scores indicating extreme fatigue (Table 3). The patients also scored low for vitality and general health compared to a healthy Swedish population [15]. Results from the HADS indicated no clinically significant symptoms of depression or anxiety in most patients. However, the range of scores was substantial (Table 3), indicating large interindividual differences. There was no statistically significant difference between the waves on any of the self-rated measurements, but a trend towards higher general fatigue among patients in wave 2+.

There were no gender differences for variables presented in Tables 2 and 3.

3.5. Associations. The MoCA score correlated negatively with age ($r = -0.38$, $P = 0.003$, $n = 60$). No relations were found between the MoCA score and length of ICU stay and intubation, nor between MoCA score and any of the self-ratings.

We found no correlations between age, educational level, and length of ICU stay, with any of self-ratings. However, anxiety, depression, and insomnia correlated highly with

Table 1: Sociodemographic data of the studied cohort.

Sociodemographic data	Total ($n = 71$)
Age, mean (SD)	56 (11)
Gender	
Female	13 (18%)
Male	52 (82%)
Language ($n = 66$)	
Fluent in Swedish	57 (80%)
Not fluent	9 (13%)
Education ($n = 47$)	
≤12 years	28 (60%)
>12 years	19 (40%)
Smoking ($n = 70$)	
Smokers	2 (3%)
Former smokers	27 (38%)
Nonsmokers	41 (60%)
Occupation at follow-up	
In work	11 (16%)
Pensioner	15 (21%)
Full-time sick leave	32 (45%)
Part-time sick leave	8 (11%)
Other	5 (1%)
Medical preconditions	
Hypertension	36 (51%)
Diabetes	16 (23%)
Lung disease	7 (10%)
Heart/vascular disease	6 (9%)
Treatment at ICU	
Intubation	50 (71%)
Cortisone	43 (61%)
Remdesivir	26 (37%)

Values are presented as frequencies and percentages, except for age, which is displayed as mean and standard deviation (SD).

Table 2: Comparison of sociodemographics and treatment at ICU between the time periods wave 1 and 2, respectively.

	Wave 1 ($n = 34$)	Wave 2+ ($n = 37$)	P value
Age mean (SD)	57 (9)	56 (13)	0.706
Gender			
Female	7 (20.5%)	8 (21%)	0.634
Male	27 (79.5%)	33 (89%)	
Fluent in Swedish	31 (91%)	26 (81%)	0.240
Not fluent	3 (9%)	6 (19%)	
Missing	0 (0%)	5 (16%)	
Level of education			
≤12 years	14 (61%)	14 (58%)	0.859
>12 years	9 (39%)	10 (42%)	
Smoking	1 (3%)	1 (3%)	0.434
Former smoker	12 (35%)	15 (41%)	
Not smoking	21 (61%)	20 (56%)	
Missing	0	1 (3%)	
Preconditions			
Hypertension	14 (41%)	22 (59%)	0.124
Diabetes	6 (18%)	10 (27%)	0.345
Lung disease	4 (12%)	3 (8%)	0.606
Heart/vascular disease	4 (12%)	2 (5%)	0.336
Days at ICU mean (SD)	26 (21)	9 (10)	<0.001
Treatment ICU			
Intubation	33 (97%)	17 (46%)	<0.001
Cortisone	7 (21%)	36 (97%)	<0.001
Remdesivir	0 (0%)	26 (70%)	<0.001

Values are displayed as frequencies and percentages except for age and days at ICU, which are displayed as mean and standard deviation (SD). P values for differences between the waves are presented. Chi-square test was used for discrepancy analyses except for age and days at ICU, where independent samples t-test was used.

all the fatigue measures (see Table 2 in the Supplementary information).

Patients who were intubated (fatigue data on n41/50) scored lower than those who were not (n21/21) on MFI-20 *general fatigue*(median = 14, range = 2 – 20 vs. median = 16, range = 8 – 20, $P = 0.042$), *physical fatigue* (median = 14, range = 6 – 20 vs. median = 18, range = 9 – 20, $p = 0.006$), and *reduced activity* (median = 12, range = 5 – 20 vs. median = 16, range = 5 – 20, $P = 0.010$) but no other self-ratings. No significant differences were found between intubation on the MoCA score or age.

3.6. Post Hoc Analyses. As we found a significant difference on three MFI-20 fatigue measurements (i.e., general fatigue, physical fatigue, and reduced activity), we decided to investigate further the relationship between intubation and these fatigue measurements with regression analyses. The three fatigue measurements were the independent variables in three different analyses with intubation as a categorical variable. As there were significant correlations with all the fatigue measures and HADS depression, HADS anxiety, and ISI, these were included in the initial model. However, due to a strong correlation between HADS anxiety and HADS depression, we decided to not include HADS anxiety in the model. Comparing models with and without HADS anxiety showed a better model fit when HADS anxiety was removed from the model. For both, MFI-20 general fatigue and reduced activity, insomnia and depression were associated with greater fatigue, while depression and insomnia were not associated with physical fatigue. In all models, intubation was related to lower fatigue scores. Results from the regression analyses are presented in Tables 4–6.

4. Discussion

This study found that approximately one-third of the patients had a MoCA score below the normal range (≤25), indicating cognitive impairment three months post-ICU

Table 3: Cognitive functioning, fatigue, depression, anxiety, sleep disorder, and vitality in comparison to time periods.

		Total	Wave 1	Wave 2+	P value
MoCA total score, $n = 57$	Mean (SD) Median (range)	26.2 (3.1) 27 (18-31)	25.9 (3.3) 26 (20-30)	26.5 (3.0) 27 (18-31)	0.550
MoCA ≤ 25 points	N (%)	18 (30%)	10 (38%)	7 (23%)	0.192
General fatigue (MFI-20)	Mean (SD) Median (range) N	14.1 (4.2) 15 (2-20) ($n = 62$)	13.1 (4.2) 13.5 (5-20) ($n = 28$)	15.0 (4.0) 15.5 (2-20) ($n = 34$)	0.062
Physical fatigue (MFI-20)	Mean (SD) Median (range) N	14.9 (3.8) 15 (6-20) ($n = 62$)	14.0 (3.9) 15 (6-20) ($n = 28$)	15.6 (3.1) 16 (9-20) ($n = 34$)	0.107
Reduced activity (MFI-20)	Mean (SD) Median (range) N	13.2 (4.3) 13 (5-20) ($n = 62$)	12.2 (4.3) 12 (5-20) ($n = 28$)	13.9 (4.2) 14 (5-20) ($n = 34$)	0.105
Reduced motivation (MFI-20)	Mean (SD) Median (range) N	9.3 (3.9) 8 (4-19) ($n = 62$)	9.2 (3.9) 9 (4-19) ($n = 28$)	9.3 (4.0) 8 (4-19) ($n = 34$)	0.949
Mental fatigue (MFI-20)	Mean (SD) Median (range) N	10.2 (4.0) 10 (4-20) ($n = 62$)	9.8 (4.0) 10 (4-20) ($n = 28$)	10.6 (4.0) 10.5 (4-20) ($n = 34$)	0.349
Depression (HADS)	Mean (SD) Median (range) N	4.2 (4.2) 3 (0-18) ($n = 64$)	4.0 (4.6) 2 (0-20) ($n = 28$)	4.4 (4.0) 3 (0-18) ($n = 36$)	0.398
Anxiety (HADS)	Mean (SD) Median (range) N	4.2 (4.7) 3 (0-17) ($n = 64$)	4.9 (5.4) 2 (0-17) ($n = 28$)	4.6 (4.1) 4 (0-13) ($n = 34$)	0.859
Sleep disorder (ISI)	Mean (SD) Median (range) N	10.1 (7.2) 8 (0-28) ($n = 66$)	10.4 (7.1) 8 (0-24) ($n = 30$)	9.9 (7.3) 8 (0-27) ($n = 36$)	0.638
General health (RAND-36)	Mean (SD) Median (range) N	47.5 (19.2) 45 (5-80) ($n = 58$)	44.1 (22.4) 45 (5-80) ($n = 27$)	50.5 (17.0) 50 (15-80) ($n = 31$)	0.266
Vitality (RAND-36)	Mean (SD) Median (range) N	47.9 (22.4) 50 (5-100) ($n = 57$)	51.0 (25.3) 55 (5-100) ($n = 26$)	45.4 (19.2) 40 (5-85) ($n = 31$)	0.312

Values are displayed as mean, standard deviation (SD), median, and range. P values for differences between waves 1 and 2+ are presented. Mann–Whitney U-test was used for discrepancy analysis. Confidence interval was set at 95% for all variables.

Table 4: Multiple linear regression investigating the relationship of MFI-20 general fatigue (dependent variable) with intubation, Hospital Anxiety and Depression Scale (HADS) depression, and Insomnia Severity Index (ISI).

MFI general fatigue	Unstand. coeff.		Stand. coeff.	Sig.	95% confidence interval for B		Collinearity statistics	
Independent variables	B	SE			Lower bound	Upper bound	Tolerance	VIF
(Constant)	12.244	0.985	—	<0.001	10.271	14.218	—	—
Intubation	-2.299	0.922	-0.260	0.016	-4.147	-0.451	1.000	1.000
HADS depression	0.334	0.125	0.313	0.010	0.084	0.584	0.795	1.258
ISI total	0.202	0.068	0.350	0.004	0.067	0.338	0.795	1.258

R^2 adjusted, 0.390; R^2 change, 0.390; Sig F change, <0.001.

treatment for COVID-19. No difference in MoCA score was found when comparing patients treated in the ICU during wave 1 (i.e., March 2020 and July 2020) with patients treated during wave 2+ (i.e., August 2020 and January 2021). Patients included in the study reported high level of fatigue exceeding normal levels according to Swedish normative

Table 5: Multiple linear regression investigating the relationship of MFI-20 physical fatigue (dependent variable) with intubation, Hospital Anxiety and Depression Scale (HADS) depression, and Insomnia Severity Index (ISI).

MFI physical fatigue Independent variables	Unstand. coeff. *B*	 SE	Stand. coeff.	Sig.	95% confidence interval for *B* Lower bound	 Upper bound	Collinearity statistics Tolerance	 VIF
(Constant)	14.613	1.010	—	<0.001	12.591	16.635	—	—
Intubation	-2.618	0.945	-0.322	0.008	-4.511	-0.724	1.000	1.000
HADS depression	0.226	0.128	0.330	0.083	-0.030	0.482	0.795	1.258
ISI total	0.111	0.069	0.209	0.114	-0.028	0.250	0.795	1.258

R^2 adjusted, 0.205; R^2 change, 0.245; Sig F change, <0.001.

Table 6: Multiple linear regression investigating the relationship of MFI-20 reduced activity (dependent variable) with intubation, Hospital Anxiety and Depression Scale (HADS) depression, and Insomnia Severity Index (ISI).

MFI physical fatigue Independent variables	Unstand. coeff. *B*	 SE	Stand. coeff.	Sig.	95% confidence interval for *B* Lower bound	 Upper bound	Collinearity statistics Tolerance	 VIF
(Constant)	12.080	1.022	—	<0.001	10.033	14.127	—	—
Intubation	-2.733	0.957	-0.309	0.006	-4.650	-0.817	1.000	1.000
HADS depression	0.353	0.129	0.331	0.009	0.094	0.612	0.795	1.258
ISI Total	0.146	0.070	0.252	0.114	0.005	0.286	0.795	1.258

R^2 adjusted, 0.346; R^2 change, 0.311; Sig F change, <0.001.

values [11]. However, we found no significant differences in fatigue between the waves even though the length of ICU stay was significantly longer in the first wave with a mean of 26 days compared to 9 days in the successive waves. The treatment strategies offered in the ICU differed significantly between the waves, with more intubations in the first wave and a more routine use of cortisone and increasing use of remdesivir in the wave 2+. Intubated patients were treated for a longer time at the ICU and reported significantly less fatigue after 3 months, as compared to nonintubated patients. Treatment strategy (using COVID-19 wave as a proxy) was, however, not related to cognitive performance, as measured with the total MoCA score.

Premorbid cognitive levels should be considered when evaluating cognitive performance. In the current study, we did not evaluate premorbid cognitive functioning per se, nor did we collect data on the frequency of subjective complaints. However, the percentage of patients in this cohort performing at a level indicative of cognitive impairment is higher than in healthy subjects [9]. Furthermore, cognitive impairment as detected by MoCA is associated with worse functional and medical status for a number of medical conditions [16]. Whether this is due to nonspecific PICS, COVID-19 infection, or a combination requires further study, although length of ICU stay does not appear to be a significant contributor.

In a previous Swedish study involving 211 participants, the median MoCA score at hospital discharge was 25 points. In our study, conducted about three months posthospital discharge, the median MoCA score was slightly higher, at 27 points. This could suggest slow improvement in the cognitive impairments that follow severe COVID-19 infection, although factors such as age, education, and language difficulties may influence the results. Similarly, a French study found that about half of ICU-treated post-COVID-19 patients reported one or more symptoms six months postinfection, with no change in the prevalence of postintensive care syndrome despite improved ICU management [17]. In our study, half of the patients over 65 had a MoCA score below 26, compared to one-fourth in those under 65, although the small sample size (only 12 patients over 65) makes comparisons uncertain. A cross-sectional study involving 1,539 patients aged 60 and above found that 36% exhibited cognitive impairment six months post-COVID-19 infection, as measured by the TICS-40 screening instrument [18], indicating that patients over 65 years of age might need targeted attention after ICU care.

All MFI-20 fatigue subscales were scored less favourably by the participants compared to a Swedish norm population [15]. Fatigue is one of the most common risk factors for not returning to work after illnesses such as stroke and traumatic brain injury and in some studies is the independent determinant of not being able to return to work [19]. Post-COVID-19 fatigue has been shown in several studies [20]. A study analysing the prevalence of fatigue approximately 10 weeks after the acute infection (ranging from mild to severe acute infection) using the Cognitive Failures Questionnaire (CFQ-11) found that half of the patients met the criteria for fatigue. One-third had not been able to return to employment 10 weeks after the acute infection [1]. Data from our study showed that 15% of patients were working three months after the acute infection, compared with 65% before the infection. However, data is lacking regarding causes of not being able to return to work and whether work adaptations were available for those working at the time of the follow-up. It is too early to comment on long-term estimates of fatigue as a residual condition; however, if the pattern mimics the long-term effects of SARS and MERS infection, patients might be expected to suffer from fatigue even four years after the acute disease [21, 22].

Unexpectedly, patients who had been intubated had scores representing less general and physical fatigue as well as reduced activity levels three months after COVID-19, despite a longer ICU stay. This contradicts earlier findings with less favourable outcomes in intubated patients with longer ICU stays [23, 24]. Various factors might influence performance on different fatigue measures. Physical fatigue was unaffected by depression or insomnia. However, depression negatively affected results for reduced activity, and both insomnia and depression had a negative impact on general fatigue, aligning with findings from previous studies on self-rated fatigue [25]. Interpreting these results remains speculative, possibly indicating a psychological basis. Intubated patients may have evaluated their current fatigue relative to high physical fatigue experienced during earlier stages of rehabilitation due to prolonged immobility during ICU stay. These findings are noteworthy, emphasizing the importance of including psychological factors in future studies on long-term outcomes after COVID-19. However, it is important to acknowledge that other medical factors not addressed in this study may also play a role.

The risk of poor long-term outcomes after ICU care has been reported to be higher in men than in women [26]. There were significantly more men than women in our study, which is consistent with a Swedish nationwide cohort study on the gender distribution in ICU units during the COVID-19 pandemic. In the present study, there was no difference between men and women in any of the tested variables. However, only 15 females participated.

4.1. Strengths and Limitations. The main outcome of the present study was cognitive impairment according to MoCA. A strength is that patients were invited to participate solely on the basis of ICU-treated COVID-19 and not related to later symptoms or rehabilitation needs. MoCA scores were also available for a large proportion (80%) of the cohort, although the missing 20% could affect the findings. There were 92 referrals from the ICU to the Department of Rehabilitation Medicine, of which 71 were included in the study. Data on nonparticipants is not available, so it is unknown in which direction results may have been affected: people with a lower level of cognitive functioning may have chosen not to participate in the follow-up to a greater extent, such that actual cognitive function could have been worse than presented in our study. Alternatively, it could also have been that nonparticipants had fewer cognitive problems and may not have seen a reason to participate or could have been too busy if they were back at work. Most of the participants were men (80%), reflecting the distribution of males and females treated at the ICU for severe COVID-19 infection in Sweden 2020-2021. As the proportion of women in this study was low, the study lacked sufficient power to show whether there were gender differences in the outcome.

5. Clinical Applications

Both cognitive impairments and fatigue make it difficult to cope with the challenges of everyday life, as well as affecting employment status. This study supports a need for outpatient follow-up after ICU care for COVID-19 infection with individualised rehabilitation targeted to findings. The development of evidence-based rehabilitation methods for this patient group is important.

6. Conclusion

Cognitive impairment and fatigue were evident in patients three months after a severe COVID-19 infection. Global cognitive functioning, as measured with MoCA, was not associated with differences in ICU treatment regimens or ICU length of stay but was negatively associated with age. Unexpectedly, patients who had been intubated had less self-rated fatigue. The reason for this needs to be investigated further as there may be both psychological and physiological explanations. Our findings suggest that older patients, in particular, should be followed up due to the greater frequency of post-COVID-19 cognitive impairment. Psychological factors should be considered when interpreting study results in future studies.

Data Availability

The anonymized datasets generated during the current study are available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare no competing interests.

Authors' Contributions

M. Löfgren and C. Nygren Deboussard shared last authorship.

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Supplementary Materials

This section provides a description of the assessment instruments for general cognitive function (MoCA), fatigue (MFI-20), mood (HADS), insomnia (ISI), and health-related quality of life (RAND-36) as well as rank correlation analysis with Spearman's rho between self-rating assessment measures. *(Supplementary Materials)*

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