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Research Article

The Impact of COVID-19 on Parkinson's Disease: A Case-Controlled Registry and Questionnaire Study on Clinical Markers and Patients' Perceptions

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Introduction. Parkinson's disease (PD) is a neurodegenerative disease with motor and nonmotor symptoms. Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). *Objectives*. To explore how COVID-19 affects motor, nonmotor, and general health aspects of PD and to map how PD patients perceive their change in symptoms since falling ill with COVID-19. *Method*. The study was descriptive, case-controlled, and based on both registry and questionnaire data. At baseline, the controls were matched on age, sex, and disease severity. Information on the severity of the disease, nonmotor symptoms, motor symptoms, and general health was retrieved from the Swedish Registry for PD. Registry data from a COVID-19 group ($n = 45$) and a control group ($n = 73$), as well as questionnaires from a COVID-19 group ($n = 24$) and a control group ($n = 42$), were compared. *Results*. We did not find that SARS-CoV-2 infection affects any major aspect of nonmotor symptoms, motor symptoms, general health, and perception of change in PD patients' post-COVID-19. Compared to controls, the COVID-19 group reported a more positive subjective experience of pain and quality of life and a perception of change post-COVID-19 regarding general motor function, sleep quality, and mood (all $p < 0.05$). *Conclusion*. Although SARS-CoV-2 infection does not seem to affect PD symptoms in any major respect, the subjective experience of several aspects of life in PD patients might be slightly improved post-COVID-19 compared to a control group. The findings warrant further investigations due to the small sample size and possible survivorship bias.

1. Introduction

Parkinson's disease (PD) is a neurodegenerative disease with both motor and nonmotor symptoms. PD results in various symptoms, including autonomic dysfunction, cognitive impairment, and mood disorders. The cardinal signs of PD are tremors, bradykinesia, rigidity, and postural instability. The coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Multiple authors have examined the general aspects of the relationship between COVID-19, the pandemic, PD, healthcare, and patient care [1–5]. Victorino et al. and Bhidayasiri et al. agree that healthcare professionals should be vigilant for complications when treating PD patients with COVID-19 and that keeping accurate medical records of these effects is crucial [1, 2]. Helmich and Bloem and Tipton and Wszolek argue that patients with PD are under increased risk to suffer more negative consequences of the effects of the pandemic, such as social isolation, reduced physical exercise, and increased stress, thus worsening motor and nonmotor symptoms [4, 5]. Others have investigated the prevalence, impact, and predictors of COVID-19 in PD [6, 7]. These studies have been exploratory but with the general implication that PD patients could be more susceptible to SARS-CoV-2 infection and run an increased mortality risk due to COVID-19 [6, 7].

However, few studies have focused on COVID-19 and its potential effects on clinical PD features. In a study by Cilia et al., COVID-19 was found to worsen both motor and nonmotor symptoms of PD [8]. Furthermore, Brown et al. observed that although PD patients who have suffered through COVID-19 reported worse nonmotor and motor function, PD patients not diagnosed with SARS-CoV-2 infection also reported this, be it a lower, yet still alarming, frequency [3]. While a few minor studies have been conducted, the changes in medication, nonmotor and motor symptoms, and general health in PD patients during and after COVID-19 are not yet thoroughly understood [9]. Furthermore, the studies investigating these aspects have presented somewhat conflicting results [9].

Apart from the normally expected pathological effects of COVID-19 on patients with PD, several other observations have connected certain aspects of COVID-19 more specifically to PD [10]. Hyposmia is one of the key prodromal symptoms of PD [11] but is also observed when SARS-CoV-2 results in the downregulation of olfactory receptors [12]. COVID-19 has previously been reported to worsen PD symptoms and lead to an increased need for dopaminergic medication [10, 13]. To enter human cells, the virus binds to angiotensin-converting enzyme 2 (ACE2) receptors [14, 15]. Dopaminergic neurons express high levels of ACE2 receptors, and as the neurons degenerate, the amount of ACE2 receptors decreases [10, 16, 17]. Some studies have suggested that SARS-CoV-2 might use SARS-CoV-2 spike protein to bind to toll-like receptor 4 (TLR4), increasing ACE2 expression and causing hyperinflammation [18, 19]. This inflammation may subsequently lead to alpha-synuclein buildup and neuronal death, leading some to speculate that SARS-CoV-2-associated TLR4 binding could increase the rate of PD progression [20]. These links, combined with the general pathological mechanisms of COVID-19, justify investigating the effects of COVID-19 on PD and whether PD could be a risk factor for SARS-CoV-2-associated morbidity and mortality.

This study is aimed at exploring how COVID-19 affects the various aspects of PD symptomatology. Our primary study objective was to map the possible effects of COVID-19 on PD patients, specifically regarding the motor, nonmotor, and general health impacts. We also wanted to gather the patients' opinions regarding their view on different aspects of PD post-COVID-19 and their perception of these changes. Therefore, our secondary study objective was to assess possible subjective changes in general health and nonmotor and motor symptoms in PD patients.

2. Method

2.1. Study Design and Data Sources. This was an investigator-initiated, descriptive, and case-controlled study. The study has two parts—a registry study and a questionnaire study—with the questionnaire study including the patients in the registry study and an additional cohort. Both study parts were based on comparing a group that had COVID-19 with a similar group that had not been infected with COVID-19. The registry study was based on the Swedish Registry for PD (ParkReg). ParkReg was initiated in 2011 and consists of data from 10,600 Swedish PD patients, including data on treatment, diagnosis, and disease symptomatology. It has national coverage of around 40%. Information is entered for the registered patients approximately once yearly. Data in the questionnaire study was collected by sending out physical paper surveys to PD patients nationwide in Sweden (see Table 1 for an overview of included instruments). Patients who had COVID-19 were identified via ParkReg. Skåne University Hospital was the coordinating site.

2.2. Inclusion and Exclusion Criteria. Participants had to be 18 years old or older and diagnosed with idiopathic PD to be included in the study. It was also required that all participants had a minimum of one previous registry data point in ParkReg. Patients in the COVID-19 groups also had confirmed infection with SARS-CoV-2, as reported by healthcare professionals inserting information into the registry. Additionally, all study participants were asked if they had suffered from test-confirmed COVID-19 as part of the study questionnaire. Patients with nonidiopathic PD and those unable to give informed consent were excluded.

2.3. Cases and Controls. The COVID-19 cases of both the registry and questionnaire studies were matched individually with controls, striving towards a 2 : 1 control : COVID-19 ratio. The controls were matched on disease severity as measured by the total score of the Clinical Impression of Severity Index for Parkinson's Disease (CISI-PD) score ± 3, by sex, and by age in years ± 3. A minority of the patients in the registry study case group were matched 1 : 1 with their registry control group due to a lack of suitable controls. Some of the participants included in the questionnaire study had no

Table 1: Overview of the instruments included in the registry and questionnaire studies. This study utilized several validated instruments to assess different aspects of PD nonmotor and motor symptomatology and general health aspects.

	Abbreviation	Field of application	Categorization	Reference
Clinical Impression of Severity Index for Parkinson's Disease	CISI-PD	Clinical judgment (by a medical professional) on Parkinson's disease severity based on motor symptoms and complications, cognitive status, and disability.	C, V	Martínez-Martín et al. [21]
EuroQol-5 Dimension European Quality of Life Five Dimension Five Level	EQ-5D-5L	Patient-reported quality of life across 5 domains: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.	Q, R, V	Schrag et al. [35]
Non-Motor Symptoms Questionnaire	NMSQ	Patient-reported nonmotor symptoms across 9 domains: gastrointestinal, urinary tract, sexual function, cardiovascular, attention, delusions, depression/anxiety, fatigue, and pain.	Q, R, V	Romenets et al. [36]
Post-COVID-19 Functional Status	PCFS/aFS	Patient-reported functional status and limitations related to persistent symptoms of COVID-19.	Q, V	Klok et al. [22]
Perception of change post-COVID-19	PCPC	Patient-reported perception of change after COVID-19 across 8 domains: general health, motor function, fatigue, attention, delusions, depression/anxiety, memory, and ability to smell and taste.	Q, A	A
8-item Parkinson's Disease Questionnaire	PDQ8	Patient-reported health-related quality of life across 8 domains: mobility, activities of daily living, emotional well-being, stigma, social support, cognitions, communication, and bodily discomfort	Q, R, V	Tan et al. [37]

A short explanation of what each scale assesses and reference for more in-depth details, as well as categorization of the scales and how they served this study, is presented. Q (used in the questionnaire study), R (used in the registry study), C (used in the matching of cases to controls), V (validated), and A (synthesized by authors, not validated).

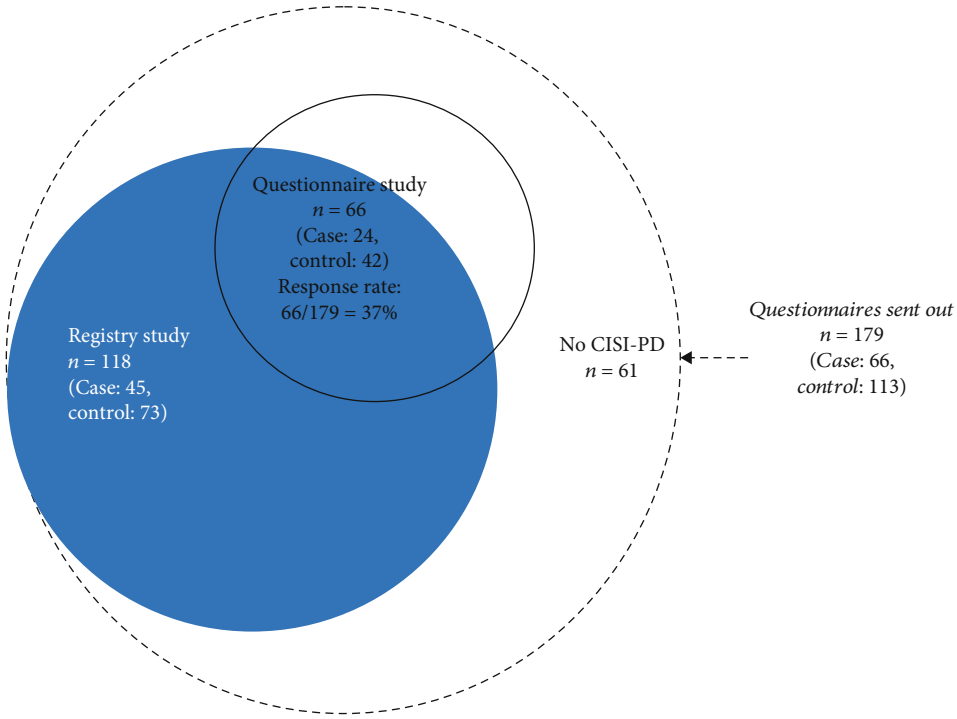

Figure 1: Venn diagram of the study population and sample size of the questionnaire and registry study groups. The questionnaire study included both the registry and no CISI-PD groups. In total, 179 questionnaires were sent out to potential participants, whereof 66 were filled out completely and included in the questionnaire study, resulting in a response rate of 37%. The no CISI-PD group had the same inclusion and exclusion criteria as the registry study group, apart from lacking the disease severity matching by the Clinical Impression of Severity Index for Parkinson's Disease (CISI-PD). The data from the group inside the blue circle were analyzed in the registry study.

previous CISI-PD data point in ParkReg and could not be matched on CISI-PD score, hence the "no CISI-PD" group (Figure 1).

2.4. Registry Study. An analysis of the data collected in ParkReg on the involved patients was performed. One data point before COVID-19 and one data point postinfection were analyzed. The dates of these data points had to be within 1 year before or following the SARS-CoV-2 infection. The data points in ParkReg regarding the control groups were also within these 2 years from the SARS-CoV-2 infection of their respective COVID-19 case. The following instruments have been analyzed both post- and pre-COVID-19 in the registry study case and control groups: CISI-PD (clinical impression of disease severity) [21], On-Off score (time spent in on/off and the limitations of fluctuations on everyday life, similar to the MDS-UPDRS items 4.1–4.4), the 8-item Parkinson's Disease Questionnaire (PDQ-8), the EuroQol-5 Dimension European Quality of Life Five Dimension Five Level (EQ-5D-5L), and the Non-Motor Symptoms Questionnaire (NMSQ).

2.5. Questionnaire Study. The questionnaire was conducted by sending questionnaires to the patients selected from ParkReg. On-Off score, PDQ-8, EQ-5D-5L, and NMSQ were all included in the questionnaire, together with the Post-COVID-19 Functional Status (PCFS) [22] (see Table 1 for an overview of included instruments). Questions regarding the patient's perception of change regarding various nonmotor and motor symptoms post-COVID-19 (PCPC) were added. The average date for the SARS-CoV-2 infection was calculated and was used to adapt the PCPC to suit the control group. Similarly, the PCFS was modified to suit the control group (adapted functional scale (aFS)). Each study subject in the questionnaire study received a phone call from one of the researchers, where the participants had an opportunity to ask questions about the study.

2.6. Ethics. The study was conducted following the principles of the Declaration of Helsinki and according to GCP (Good Clinical Practice) rules and GDPR (General Data Protection Regulation). All personal data was pseudonymized in the study. An ethical application was filed to the Swedish Ethical Review Authority (EPM), and the application was approved before initiating the study (diary number: 2021-04202). An application for registry data retrieval was made to and approved by the Swedish Neuro Registries (http://www.neuroreg.se). Informed consent was obtained from questionnaire study subjects. Study subjects received no compensation for their participation.

2.7. Statistical Analysis. IBM SPSS Statistics version 27 was used for the statistical analyses. Results were compiled and presented with descriptive statistics using medians and lower and upper quartiles. The nonmotor, motor, and general health parameters from cases and controls in the questionnaire study, as well as both pre- and post-COVID-19 data from the registry study, were compared using the nonparametric Mann–Whitney *U*-test. The significance level was

Table 2: Registry study cases and controls before and after COVID-19. To be considered pre- or post-COVID-19, the data point had to be the closest to a confirmed SARS-CoV-2 infection and no longer than 1 year from the date of infection. For the control group, the data points are matched to the date when SARS-CoV-2 infection was confirmed. Data is shown as the median (first quartile, third quartile) unless otherwise noted.

	COVID-19		Control		Total		$^*p$
n	45		73		118		
Sex (M/F)	31/14		48/25		79/39		
Age (years)	67 (59.5, 76.5)		71 (62, 78.5)		70 (62, 78)		
	Pre	Post	Pre	Post	Pre	Post	
CISI-PD	8 (4, 12)	8 (4, 12.5)	7 (4, 11)	9 (4.75, 13)	7 (4, 11)	9 (4, 13)	0.552
NMSQ	10 (9, 11)	11 (6, 15)	8 (5.5, 13.5)	11 (6, 16.5)	9 (6, 13)	11 (6, 15.75)	0.813
PDQ-8	8 (2, 11)	10 (4, 16)	8.5 (3.25, 14)	9 (4, 15)	8 (3, 13)	9.5 (4, 15)	0.794
EQ-5D-5L$_{index}$	0.77 (0.56, 0.86)	0.73 (0.40, 0.86)	0.69 (0.52, 0.83)	0.60 (0.40, 0.82)	0.72 (0.54, 0.84)	0.64 (0.40, 0.83)	0.898

CISI-PD: Clinical Impression of Severity Index for Parkinson's Disease; NMSQ: Non-Motor Symptoms Questionnaire; PDQ-8: 8-item Parkinson's Disease Questionnaire; EQ-5D-5L: EuroQol-5 Dimension European Quality of Life Five Dimension Five Level. $^*p$ (statistical significance) in the Mann–Whitney *U*-test testing differences between the RS case and control group post-COVID-19.

defined as $p < 0.05$. The effect size (r) was calculated according to Cohen's (1988) criteria.

3. Results

The registry study group consisted of 45 patients with COVID-19 and 73 matched controls. Similarly, the QS included 66 COVID-19 patients and 113 matched controls.

A total of 179 participants were enrolled in the questionnaire study, and of these, 118 that had at least one CISI-PD data point in ParkReg were also included in the registry study. At baseline, the registry case and control group had similar total scores in CISI-PD, NMSQ, PDQ8, and EQ-5D-5L. A Mann–Whitney *U*-test revealed no significant difference in CISI-PD, NMSQ, PDQ8, and EQ-5D-5L total scores post-COVID-19 between the registry study COVID-19 case and control groups (Table 2).

Of the 179 patients selected for the questionnaire study, 66 returned a completed questionnaire, resulting in a 37% response rate (Figure 2). The median (Q1–Q3) time between infection and questionnaire response was 11.8 (9.7–17.9) months. 17% of COVID-19 cases were vaccinated at the date when their SARS-CoV-2 infection was confirmed. At the time of the questionnaire study, vaccination coverage was 88% for cases and 98% for controls (Table 3). Repeated Mann–Whitney *U*-tests showed no significant difference between questionnaire cases and controls regarding NMSQ, PDQ8, PCFS/aFS, and PCPC total scores post-COVID-19 (Table 3). See Table 1 for an overview of included instruments. Using a Mann–Whitney *U*-test, no significant differences were detected between questionnaire cases and controls regarding the item EQ-5D-5L health in the EQ-5D-5L scale ($p = 0.164$) (Table 3).

3.1. Quality of Life. The questionnaire control group (median (Md) = 0.70, $n = 41$) experienced a lower quality of life (EQ-5D-5L$_{index}$) than the questionnaire COVID-19 case group (Md = 0.81, $n = 23$) ($p = 0.022$, $r = 0.29$). Of the five subitems included in the EQ-5D-5L instrument, the only significant difference was that the control group experienced more pain than the case group ($p = 0.022$, $r = 0.29$).

3.2. Motor Symptoms. The questionnaire control group (Md = −1.00, $n = 41$) perceived a more negative change in general motor function (PCPC item 2) than the questionnaire COVID-19 case group (Md = 0.00, $n = 22$) since the approximate COVID-19 date ($p = 0.005$, $r = 0.36$).

3.3. Nonmotor Symptoms. These controls also perceived a more negative change in mood (PCPC item 10) ($p = 0.050$, $r = 0.25$) and sleep quality (PCPC item 14) ($p = 0.037$, $r = 0.27$) than the COVID-19 case group (Table 3 and Figure 3).

4. Discussion

The primary finding of this study is that PD patients who have survived COVID-19 do not seem to be affected in any major way regarding nonmotor symptoms, motor symptoms, and general health. However, we found indications that participants that had not experienced COVID-19 reported a higher degree of pain and a lower quality of life than those who had. We found the controls to report a slight reduction in general motor ability, mood, and sleep quality compared to the COVID-19 case group. These findings were made on average 1 year after SARS-CoV-2 infection, thus solely reflecting the state of the study subjects at that single time of disease progression. Hence, one cannot draw further conclusions about patient symptomatology at previous or later stages.

To our knowledge, no previous studies have investigated patient-perceived change post-COVID-19, but some studies have explored motor and nonmotor symptomatology after a SARS-CoV-2 infection. The largest study that explored similar changes found that both nonmotor and motor symptoms had worsened significantly in the COVID-19 group compared to the control group [8]. Fatigue and urinary issues were the most affected nonmotor issues, while cognitive function was mildly reduced. It should be noted that that study had a smaller population but used similar outcome measures as the present study. Nonetheless, our findings are somewhat contradictory. Most notably, while the previous study found that COVID-19 seems to be a risk factor for worsening nonmotor and motor function in PD

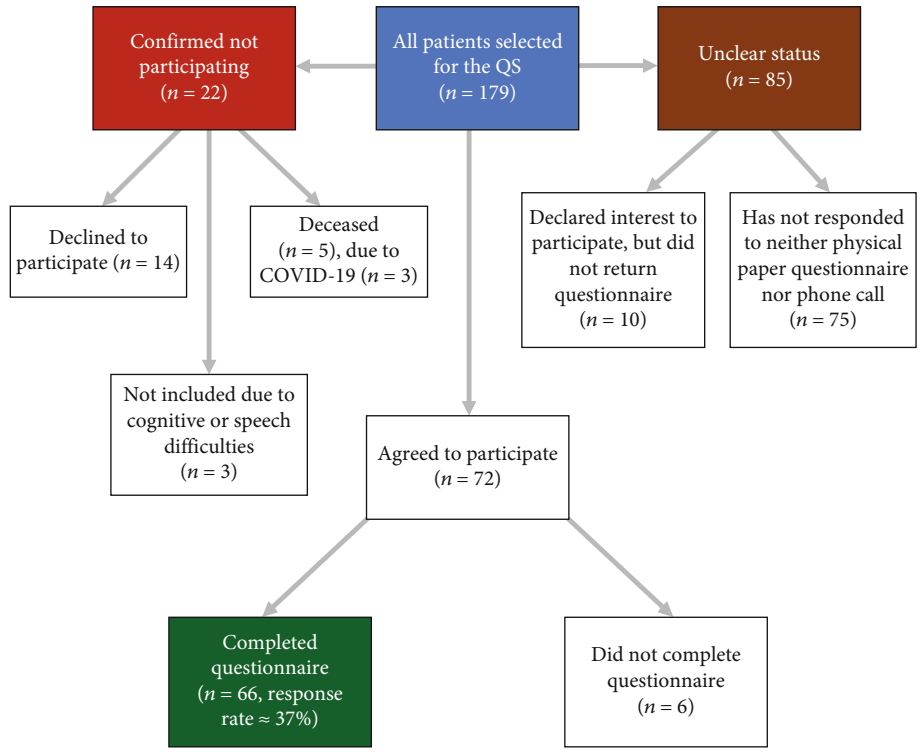

Figure 2: Flowchart of participants in the questionnaire study (QS). A total of 66 questionnaires were completed. The response rate was 37%. Participants who did not initially respond to the questionnaire were contacted via telephone to discuss the study and their participation.

Table 3: Questionnaire study of cases and controls after COVID-19.

	COVID-19	Control	Total	*p, r
n	24	42	66	
Sex (M/F)	17/7	26/16	43/23	
Age (years)	69 (60, 75.25)	70 (62, 77.5)	70 (62, 77)	
NMSQ	9 (3, 15)	11 (7.5, 14.75)	11 (6, 15)	0.251
PDQ-8	8 (4, 11)	9 (6, 13.5)	8 (5, 12)	0.265
EQ-5D-5L health	70 (60, 85)	62.5 (42.5, 78.75)	68 (50, 80)	0.094
PCFS/aFS	1 (0, 2)	2 (1, 3)	2 (0, 3)	0.287
PCPC	-2 (-6, 0)	-5.5 (-13.25, -1.25)	-4 (-9, -1)	0.093
EQ-5D-5L$_{index}$	0.81 (0.70, 0.89)	0.70 (0.54, 0.80)	0.72 (0.57, 0.83)	0.022, 0.29
EQ-5D-5L item 4	1 (0, 2)	2 (1, 2)	1 (1, 2)	0.022, 0.29
PCPC item 2	0 (-1, 0)	-1 (-1, 0)	-1 (-1, 0)	0.005, 0.36
PCPC item 10	0 (0, 0)	0 (-1, 0)	0 (-1, 0)	0.050, 0.25
PCPC item 14	0 (0, 0)	-1 (-1, 0)	0 (-1, 0)	0.037, 0.27
Infect. Vac.	4, 17%			
Quest. Vac.	21, 88%	41, 98%	62, 94%	

CISI-PD: Clinical Impression of Severity Index for Parkinson's Disease; NMSQ: Non-Motor Symptoms Questionnaire; PDQ-8: 8-item Parkinson's Disease Questionnaire; PCFS: Post-COVID-19 Functional Status; aFS: adapted Functional Status; EQ-5D-5L$_{index}$: EuroQol-5 Dimension European Quality of Life Five Dimension Five Level$_{index}$; PCPC: perception of change questionnaire. Five individual items from the questionnaires are also presented: EQ-5D-5L health (patient perceived general health on a scale 0-100), EQ-5D-5L item 4 (perceived pain on an ordinal scale), PCPC item 2 (perception of change in general motor function), PCPC item 10 (perception of change in mood and sadness), and PCPC item 14 (perception of change in sleep quality). Frequency and coverage presented for positive vaccination status at the date of confirmed SARS-CoV-2 infection (Infect. Vac.) and time of filling out the questionnaire study (Quest. Vac.). *p (statistical significance) in the Mann–Whitney U-test testing differences between QS case and control group post COVID-19. r = effect size in the Mann–Whitney U-test on differences between the COVID-19 case and control groups.

patients, our study found no significant difference in these aspects of PD. In line with the previous study, a narrative review article concluded that COVID-19 greatly impacts PD patients, exacerbating motor and nonmotor symptoms [23]. The results of our study indicate minor differences in the opposite direction, i.e., that PD patients surviving

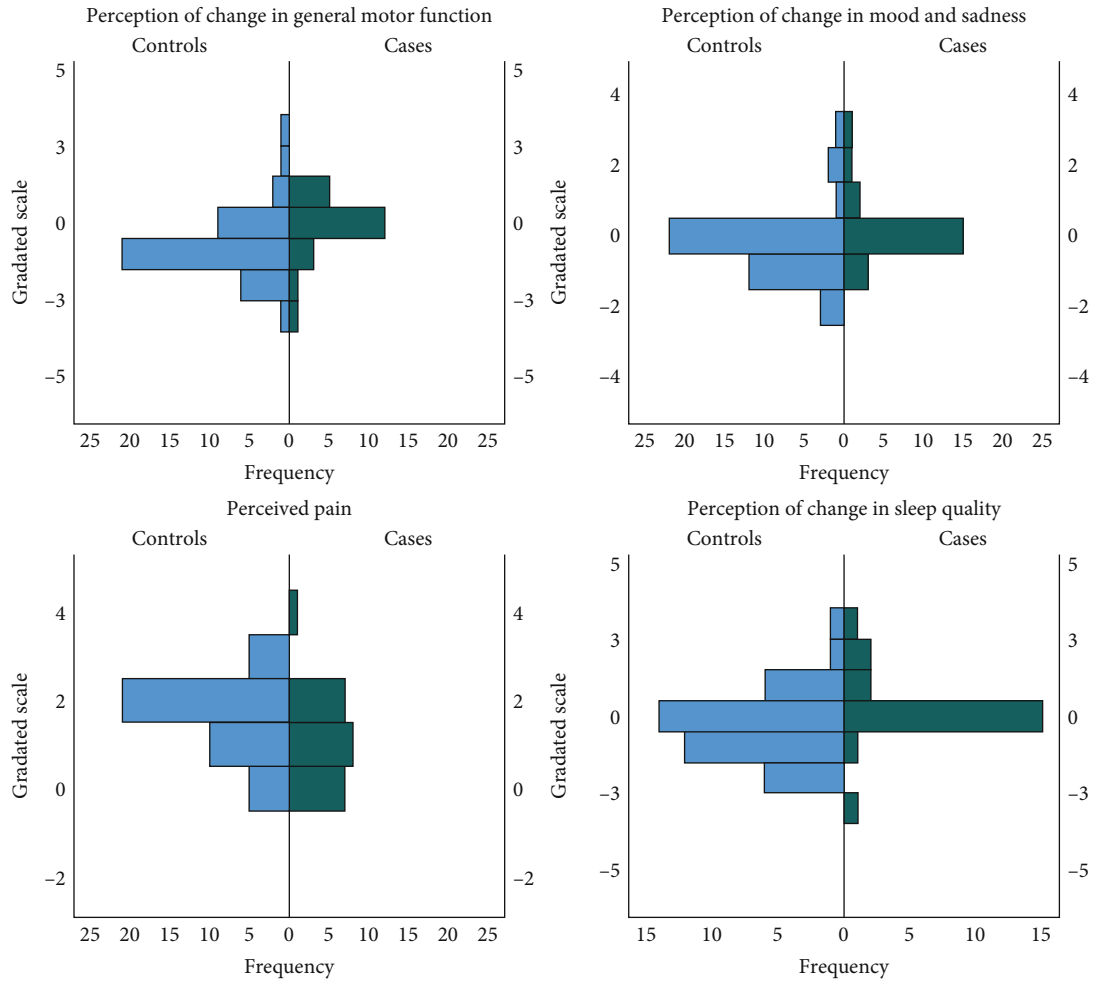

FIGURE 3: Response distribution on individual items consisting of ordinal variables where difference between control and cases was statistically significant in the questionnaire study. EQ-5D-5L item 4 (perceived pain on an ordinal scale), PCPC item 2 (perception of change in general motor function), PCPC item 10 (perception of change in mood and sadness), and PCPC item 14 (perception of change in sleep quality). For perceived pain, 0—I have no pain or discomfort, 1—I have slight pain or discomfort, 2—I have moderate pain or discomfort, 4—I have severe pain or discomfort, and 5—I have extreme pain or discomfort. For perception of change, 0—no perceived change after confirmed COVID-19, -3—maximal worsening perceived after COVID-19 confirmation, and 3—maximal improvement perceived after COVID-19 confirmation. For statistical analysis, see Table 3.

SARS-CoV-2 infection might improve their general motor function, or at least the perception of it, compared to a control group. Interestingly, a similar improvement in tremor, rigidity, balance disturbances, off-time, and some nonmotor aspects was reported in a recent uncontrolled American PD cohort post-COVID-19 [24].

Several factors could contribute to these findings. Patients surviving COVID-19 might be positively biased in their reporting of symptoms. Since patients probably feel happy about overcoming a major health crisis, it is plausible that such feelings might confuse the interpretation of current symptomatology concerning COVID-19. This phenomenon has been reported particularly in older individuals, strengthening the applicability of this theoretical bias in the cohorts of this study [25]. Another aspect to consider is the increased contact with healthcare providers that COVID-19 likely led to. This additional communication with and utilization of healthcare in the treatment of COVID-19 could lead to increased care, awareness, and treatment optimization of other underlying health conditions such as PD, thus potentially confounding outcomes. Because the control group had limited access to routine and specialized healthcare due to the pandemic, this might have further fostered potential disparities in follow-up time and treatment control, possibly resulting in differences in PD symptomatology outcomes [26, 27].

Yet another explanation supported by prior research on attitude alterations post-COVID-19 is that the health crisis associated with SARS-CoV-2 infection could inspire patients to focus on future self-care and a healthier lifestyle [28], leading to long-term improvement of both objective health parameters and subjective experience of health and disease symptomatology. Although cases and controls were matched on age, gender, and disease severity, the relatively low response rate of 37% (Figure 2) limits the extent of the intended case-control effect in the questionnaire study.

At the date of infection, the case group had a vaccination coverage of only 17%, rising to 88% at the time of participating in the questionnaire study. The control group was 98% covered by the time of the questionnaire study (Table 3). As vaccination reduces the risk of severe COVID-19 [29], it is likely that the cases had a relatively high risk of severe COVID-19. Other relevant studies that observed worsening of nonmotor and motor symptoms reported similar vaccination rates [8]. Thus, the vaccination rate is unlikely to be an explanatory factor to the differing results on change of nonmotor and motor function. Data about vaccination coverage in the registry group is insufficient.

The major limitation of this study is a selection bias known as survivorship bias, which is best defined as an error that arises when one only analyzes data from study subjects who have made it past a certain selection or elimination process [30]. Although the groups were matched pre-COVID-19, this survivorship bias might be part of why the COVID-19 group had more positive results regarding the experience of life and pain and perception of change than the control group. The frailest patients might have died due to SARS-CoV-2 infection [31], which could have resulted in healthier cases compared to controls. Furthermore, there is a knowledge gap regarding what proportion of PD patients in Sweden died from COVID-19, limiting the possibility of taking survivorship bias into account in the statistical analysis. Another limitation is that the representability of the PD patients in ParkReg in relationship to the entire PD population is not well mapped. The national coverage of PD patients in ParkReg is about 40% [32]. A higher coverage would have enabled a better assessment of the impact of SARS-CoV-2 infection on PD, regarding prevalence and changes in symptomatology over time. Other methodological limitations include the relatively short follow-up time of around 1 year (long-term effects of COVID-19 on PD could manifest later), somewhat indistinct measures, many outcomes, small sample size, and low response rate in the questionnaire study. On the other hand, the detailed real-life follow-up in the questionnaire study, the inclusion of control groups, and the longitudinal evaluation are strengths of this study.

Study subjects were matched to controls in the ParkReg based on CISI-PD, age, and sex, and as visualized in Table 2, they were similar in CISI-PD, NMSQ, PDQ-8, and EQ-5D-5L scores at baseline. As for medication and socioeconomic factors, the authors do not have sufficient patient data to consider these possible confounders and acknowledge that this lack of information is a limiting factor when interpreting the results.

The questionnaire control group experienced a lower quality of life ($r = 0.25$) and more pain ($r = 0.29$) than the questionnaire case group, r indicating a small to medium effect size. The questionnaire control group also perceived a more negative change in general motor function ($r = 0.36$), mood ($r = 0.25$), and sleep quality ($r = 0.27$) than the questionnaire case group, r indicating a medium effect size. Although the found differences are rather small (Figure 3 and Table 3), they still represent broad worsening of nonmotor and to a lesser degree motor function. Hence, it is appropriate to take these clinical markers, just as importantly as patient perceptions, into consideration as a healthcare professional working with PD patients who have suffered from COVID-19.

However, it must be clearly stated that a final conclusion regarding these findings cannot be drawn based upon the present study. Therefore, a major benefit of this study is that it provides data that could be used in a potential metanalysis. Regarding disease mechanisms in PD, it would be interesting to explore if SARS-CoV-2 increases the risk of developing PD, as some have speculated it might [19, 33], although that would require a long-term approach as disease onset might occur years after infection. It would also be of prognostic value to study the risk of mortality in COVID-19 patients with PD compared to those without PD in greater detail.

In contrast to previous research, this study found no clear differences in any major aspects of nonmotor and motor symptoms, general health, and perception of change post-COVID-19 between PD patients who had suffered from SARS-CoV-2 infection and those that had not. Instead, we found that PD patients reported subjective improvements in the experience of pain, quality of life, and perception of change post-COVID-19 regarding general motor function, sleep quality, and mood compared to controls.

Data Availability

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Disclosure

An abstract related to this study was presented prior to publication at the 2022 International Parkinson and Movement Disorder Society (MDS) congress in Madrid [34].

Conflicts of Interest

The authors report no conflicts of interest concerning the present article. All coauthors certify that there are no relevant financial remunerations to disclose.

Authors' Contributions

GW participated in the design and execution of the study, performed the statistical analyses, and wrote the first and final drafts of the manuscript. JT and PO participated in the design and execution of the study, reviewed the statistical analyses, and reviewed the first and final drafts of the manuscript. FB, DB, ND, KG, DN, and PS participated in the study's design and reviewed the results, statistical analysis, and final manuscript drafts.

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