



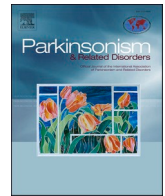
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Short communication

The changes of exercise pattern and clinical symptoms in patients with Parkinson's disease in the era of COVID-19 pandemic

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ABSTRACT

Introduction: The coronavirus disease 2019 (COVID-19) pandemic has disrupted everyday life of Parkinson's disease (PD) patients, but its clinical impact has not been illustrated. In this study, we investigated the change in physical activity and subsequently clinical symptoms of PD during the COVID-19 pandemic.

Methods: We enrolled PD patients who were able to ambulate independently and had visited our clinic at Samsung Medical Centre from December 2019 to January 2020 (baseline) and in May 2020 (follow-up during the COVID-19 crisis), and divided them into either 'the sustained exercise group' or 'the reduced exercise group'. Then, we assessed the change in the exercise and clinical features between these two groups over the study period.

Results: A total of 100 subjects were recruited. During the COVID-19 pandemic, the amount, duration and frequency of exercise were reduced. There was decrease in number of patients who do indoor-solo exercise and increase in that of patients who do not exercise. One third reported subjective worsening of both motor and non-motor features, although Unified PD Rating Scale (UPDRS) part 3 score was similar. Additionally, the reduced exercise group reported more motor and non-motor aggravation than the sustained exercise group, despite lack of significant difference in the UPDRS part 3 score.

Conclusion: The COVID-19 pandemic had a clear impact on exercise and subjective symptoms in PD patients, with reduced exercise being related to a subjective increase in both motor and non-motor symptoms of PD. Maintaining exercise should therefore be emphasized even in situations like the COVID-19 pandemic.

1. Introduction

During the worldwide COVID-19 pandemic, many countries have taken strict regulation for self-isolation, such as social distancing and lockdown of social and economic life. In Korea, the first COVID-19 was reported on January 21, 2020 and the number of daily new cases increased to 909 on February 29, 2020. The Korean government placed enhanced social distancing (staying at home and refraining from going out as much as possible) from March 22, 2020 to May 19th, 2020, and then changed to routine social distancing (<http://ncov.mohw.go.kr/en/>).

For patients with Parkinson's disease (PD), there can be two major concerns about COVID-19 pandemic. Firstly, they might be more easily infected with COVID-19 infection and suffer greater complication from the viral infection than healthy population. Second, their parkinsonian symptoms can worsen during this pandemic due to limited physical activity or emotional stress [1]. As a result of a nigrostriatal dopamine deficit, PD patients have less psychological and motor flexibility and thus less coping capacity for emotional and physical stress, and these factors can alter the amount of exercise in PD patients [2]. Considering regular exercise improves both motor and non-motor symptoms in PD patients [3,4], reduced exercise may cause worsening of parkinsonian

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symptoms. In this study, our aim was to demonstrate the clinical impact of COVID-19 pandemic on exercise pattern and clinical symptoms in PD patients.

2. Methods

2.1. Subjects and study design

This study was approved by the Institutional Review Board at our institution, and written informed consents were obtained from all participating subjects. We enrolled PD patients who visited the movement disorders clinic at the Samsung Medical Centre, Korea from May 1 to May 20, 2020. Inclusion criteria were (1) patients who were diagnosed with PD based on the clinical diagnostic criteria of the United Kingdom's Parkinson's Disease Society Brain Bank [5], (2) who had previously visited our movement disorders clinic between December 2019 to January 20, 2020, and (3) with Hoehn and Yahr stage ≤ 3 [6]. We excluded subjects who had been infected with COVID-19 to avoid the possible impact of the viral infection itself. Subjects with any of the followings were also excluded; (1) structural brain lesions including stroke or white matter changes (age-related white matter change score ≥ 2 on brain MRI) [7], (2) other known neurodegenerative diseases or psychiatric disorders requiring medications, (3) cognitive decline (Mini Mental Status Exam [MMSE] score ≤ 20 and/or below cut-off value of screening of dementia) or fulfillment of DSM-V criteria for dementia [8], (4) medical diseases including pulmonary or heart disease, head trauma, vestibulopathy, symptomatic neuropathy, or musculoskeletal problems that affected gait or exercise. We retrospectively collected baseline data from December 2019 to January 2020 (before the COVID-19 crisis) using chart reviews and prospectively followed up in May 2020 (during the COVID-19 crisis). For comparison, we looked for any change in the each patient's (1) amount of exercise; (2) pattern of exercise; (3) subjective reports of parkinsonian symptoms; (4) objective assessments of motor symptoms; and (5) prescribed medication for motor and non-motor symptoms of PD [9,10].

2.2. Clinical assessments and exercise evaluation

The motor symptoms were evaluated using the UPDRS part 3 and the Hoehn and Yahr stage based on the medication 'on' state [6], and the levodopa equivalent daily dose was calculated based on previous literature [11]. General cognition was assessed by the MMSE [8]. To determine subjective changes in PD symptoms, we asked patients whether they thought their parkinsonian symptoms had worsened with COVID-19 pandemic and if so, to choose which symptoms had aggravated from listed motor (tremors, stiffness, slowness, axial symptoms) and non-motor symptoms (fatigue, feeling stressed, feeling depressed, perceptual problems (hallucination, delusion and confusion), reduced sleep, reduced appetite, and increased aches and pains) based on revised parkinsonism from a previous study [12]. For each patient, we checked Schwab and England scale of activities of daily living (SE-ADL) which reflects patient's ability to perform daily activities [13]. Next, we collected the UPDRS part 3 scores of all subjects at baseline and follow-up visits for objective assessment of motor aggravation. We also collected data on prescribed medications for both motor and non-motor symptoms of PD to find out whether there had been clinically significant changes of symptoms causing medication adjustment [9,10].

In terms of exercise, the patients reported the primary, secondary, and tertiary exercises they performed by the name, duration, and frequency of each exercise. We used the primary exercise as the main exercise pattern and included all three exercise when we calculated the amount of exercise. Primary exercises were divided into 4 patterns: indoor-solo exercise (cycling at home, going up stairs, stretching joints), outdoor-solo exercise (active walking, cycling outdoors, hiking), exercise at sports facilities (working out at the gym, swimming, yoga, table tennis, tennis), and group exercise (tai chi, ballroom dance, group

dance, judo). We also compared the baseline duration and frequency of the primary exercise to those at follow-up. The amount of exercise was evaluated using the Korean version of the Physical Activity Scale of the Elderly (PASE) questionnaire [14]. The PASE score is divided into three parts: leisure, household chores, and work/volunteering, and we used the PASE leisure part score in this study, which includes all sports activities from light to vigorous and muscle strengthening.

Additionally, we asked all patients whether the amount of exercise was reduced due to COVID-19 pandemic. Based on their answers, we categorized our subjects into two groups: 'the sustained exercise group' and 'the reduced exercise group.' For the reduced exercise group, we enquired about the specific reason for the change in their exercise habits. To investigate the clinical impact that reduced exercise had on PD patients, we compared demographic and clinical data at baseline, and then compared the clinical symptoms from baseline to follow-up between the sustained and the reduced exercise groups.

2.3. Statistical analyses

All data are presented as the medians with interquartile range (IQR). To compare the motor symptoms, exercise characteristics, activity daily living before and after the onset of COVID-19 crisis, we performed the Wilcoxon signed rank test. Changes in exercise amount between two time periods were compared using McNemar's test, and the Bonferroni correction was performed for multiple comparisons. Demographic and clinical data between the 'sustained exercise group' and 'reduced exercise group' were compared using the Student t-test or the Mann-Whitney U test for continuous variables, and Pearson's χ^2 or Fisher's exact test for categorical variables. A p-value < 0.05 was considered significant. Statistical analysis was performed with the SPSS (version 25.0; IBM Inc., USA) software for Windows.

3. Results

3.1. Impact of COVID-19 on physical activity and parkinsonian symptoms

One hundred PD patients were enrolled in this study, and the mean follow-up duration from baseline was 4.6 ± 0.3 months. Demographic and clinical data at baseline and follow-up visits are illustrated in Table 1. After the onset of the COVID-19 pandemic, there was a significant decrease in the amount of exercise (both duration and frequency) checked by the PASE leisure part score. Likewise, number of patients who do not exercise at all increased and less number of patients were exercising at sports facilities subsequently.

Total thirty-three subjects reported subjective aggravation of parkinsonian symptoms (Table 1). Six subjects reported aggravated motor symptoms, other six subjects reported worsening of non-motor symptoms, and 21 patients reported they had deteriorated in both motor and non-motor symptoms. Slowness and tremors were the most frequently reported motor symptom aggravation. For non-motor symptom, feeling stressed, fatigue, and increased aches and pains were reported worse. SE-ADL score at follow up visit decreased significantly compared with the baseline score ($p = 0.031$). However, there was no significant difference in the UPDRS part 3 score ($p = 0.909$), and none of the subjects required adjustment of their PD medications in response to either motor or non-motor symptoms aggravation between two visits.

3.2. Comparison between the sustained exercise group and reduced activity group

Forty-five patients reported doing less amount of exercise after the onset of COVID-19 pandemic (reduced exercise group), while fifty-five patients continued to exercise as previous (sustained exercise group). Demographics and clinical information for the reduced exercise group and the sustained exercise group are summarized in Table 2. The two

Table 1
Demographics and changes of clinical symptoms and exercise pattern during COVID-19 pandemic in the patients with Parkinson's disease.

	Baseline (Dec. 2019–Jan. 2020)	Follow-up (May 2020)	p-value
Age, years	70 (62.3–76.0)		
Male, n (%)	54 (54)		
BMI, kg/m ²	24.8 (22.2–27.0)		
Disease duration, years	6.0 (4.0–10.0)		
Hoehn Yahr Stage, 1/2/3 (%)	24/35/41 (24/35/41)		
UPDRS part 3 (On state)	16.5 (11.0–22.0)	15.0 (10.0–22.0)	0.166
SE-ADL	90 (80–100)	90 (80–100)	0.031 ^{a,b}
LEDD, mg/day	466.5 (290.6–749.6)		
MMSE	28.0 (26.3–30.0)		
Education (years)	9.0 (6.0–12.0)		
Primary exercise			
Frequency, times/week	5.0 (3–7)	5.0 (2.0–7.0)	0.011 ^a
Duration, hours/session	1.0 (0.5–1.0)	0.7 (0.2–1.0)	0.003 ^a
PASE leisure part score	26.4 (9.0–38.5)	12.8 (0–27.1)	<0.001 ^a
Patterns of exercise, n (%)			
None	7 (7)	22 (22)	<0.001 ^a
Outdoor-solo	58 (58)	60 (60)	1.000
Indoor-solo	7 (7)	12 (12)	0.315
Exercise at sports facilities	23 (23)	5 (5)	<0.001 ^a
Group exercise	5 (5)	1 (1)	0.625
Subjective symptom aggravation, n (%)		33 (33)	
Motor symptoms		27 (27)	
Increased tremor		12 (12)	
Increased stiffness		7 (7)	
Increased slowness		17 (17)	
Increased axial symptoms		8 (8)	
Non-motor symptoms		27 (27)	
Excessive fatigue		6 (6)	
Feeling stressed		8 (8)	
Feeling depressed		5 (5)	
Perceptual problems ^c		0 (0)	
Reduced sleep		5 (5)	
Reduced appetite		0 (0)	
Increased aches and pains		6 (6)	

BMI, body mass index; UPDRS, Unified Parkinson's Disease Rating Scale; SE-ADL, Schwab and England activities of daily living scale; LEDD, levodopa equivalent daily dose; MMSE, mini mental status exam; PASE, physical activity scale of the elderly.

^a p-value < 0.05.
^b Mean with standard deviation of SE-ADL is 87.8 ± 13.6 for baseline, and 86.8 ± 14.4 for follow-up.
^c Perceptual problems include hallucination, delusion and confusion.

most common reasons for reduction in exercise volume were (1) that the gyms or sports facilities were closed and (2) patients' concerns about contacting the coronavirus when going out for exercise (Supplementary table). Interestingly, at the baseline visit, the PASE leisure part score was statistically higher in the reduced exercise group, meaning subjects in the reduced exercise group had been exercising greater amount before the beginning of COVID-19 pandemic. There was a significant association between reduced exercise amount and the subjective worsening of both motor and non-motor symptoms of parkinsonism between two visits, even though there was no significant change in the UPDRS part 3 score.

4. Discussion

This is the first study demonstrating how COVID-19 pandemic affects the exercise pattern and thereby clinical symptoms in PD patients. During the COVID-19 pandemic, proportion of patients who did not exercise at all increased and number of patients continuing exercise at sports facilities decreased. Nearly half of subjects in the reduced exercise

Table 2
Comparison of demographic, clinical, and exercise data between the sustained and reduced exercise groups.

	Sustained exercise group (n = 55)	Reduced exercise group (n = 45)	p-value
Age, years	69.0 (62.0–76.0)	72.0 (63.5–75.5)	0.429
BMI, kg/m ²	24.7 (22.3–26.9)	25.1 (22.1–27.6)	0.181
MMSE	29.0 (26.0–30.0)	28.0 (26.5–29.0)	0.774
Education (years)	9.0 (5.0–12.0)	9.0 (6.0–12.0)	0.791
Disease duration, years	6.0 (3.0–8.0)	6.0 (4.0–10.5)	0.695
UPDRS part 3 score			
Baseline UPDRS part 3 (On)	16.0 (12.0–22.0)	17.0 (10.5–22.0)	0.775
Δ UPDRS part 3 (On)	0 (0–0)	0 (–1.0–0)	0.581
LEDD, mg/day	449.3 (250.0–650.0)	599.5 (337.5–827.5)	0.163
SE-ADL			
Baseline SE-ADL	90 (80–100)	90 (80–100)	0.892
Δ SE-ADL	0 (0–0)	0 (0–0)	0.546 ^b
PASE leisure part score			
Baseline	24.6 (9.0–30.5)	27.1 (15.0–55.4)	0.043 ^a
Follow-up	24.6 (9.0–30.5)	9.0 (0–17.6)	0.001 ^a
Primary exercise			
frequency, times/week			
Baseline	5.0 (3.0–7.0)	5.0 (3.0–7.0)	0.959
Follow-up	5.0 (3.0–7.0)	4.0 (0–7.0)	0.058
Primary exercise			
duration, hours/session			
Baseline	1.0 (0.5–1.0)	1.0 (0.5–1.0)	0.260
Follow-up	1.0 (0.5–1.0)	0.5 (0–1.0)	0.011 ^a
Subjective			
aggravation, n (%)			
All parkinsonian symptoms	8 (14.5)	25 (55.6)	<0.001 ^a
Motor symptoms	6 (10.9)	21 (46.7)	<0.001 ^a
Non-motor symptoms	6 (10.9)	21 (46.7)	<0.001 ^a

BMI, body mass index; LEDD, levodopa equivalent daily dose; MMSE, Mini Mental Status Exam; PASE, Physical Activity Scale of the Elderly; UPDRS, Unified Parkinson's Disease Rating Scale.

^a p-value < 0.05.
^b Means with standard deviations of SE-ADL are 89.3 ± 13.0 for baseline, and 88.6 ± 13.1 for follow-up in sustained exercise group, and 86.0 ± 14.2 for baseline, and 84.7 ± 15.8 for follow-up in reduced exercise group.

group answered that they could not exercise due to the closure of sports facilities (Supplementary Table) as a result of the strict social distancing policy and a temporary shutdowns of sports facilities. In general, all the parameters evaluated for exercise quantity, such as the PASE leisure part score, and the frequency and duration of the primary exercise, were significantly reduced.

Of the 100 enrolled PD patients, nearly one-third of them reported subjective aggravation of PD symptoms, despite no difference in objective measures, suggesting the importance of physical exercise for PD patients to perceive themselves doing well. This ratio was higher (10–11%) than number reported from a previous study using telephone interviews [12]. Also, specific symptoms that had worsened also differed from existing literature. For motor aggravation, slowness was the most common symptom in this study unlike the previous study which reported tremors as the most frequent motor complaint [12]. Among non-motor symptoms, feeling stressed was most common in our study whereas other researchers found fatigue to be the most aggravated symptom [12]. These discrepancies could be due to the differences in the baseline demographics and clinical features of subjects because subjects in this study were older and had longer disease durations compared to the previous study. However, various possibilities including different cultures, lifestyles, or government policies should be also considered.

Although the patients experienced subjective worsening of parkinsonian symptoms and SE-ADL during the COVID-19 pandemic, there was no increase in the UPDRS part 3 score. Considering previous studies about the effect of regular exercise on PD [3,4], prolonged strict social

distancing could result in both the subjective and objective worsening of parkinsonism in patients with PD. However, the follow-up duration in our study (4.6 ± 0.3 months from baseline visit to follow-up visit) may not have been long enough to see an objective increase in symptoms. Another consideration is that subjective aggravation could be from non-motor aggravation. Actually, PD patients may feel more stressed about COVID-19 because the elderly with chronic diseases are particularly vulnerable. Consistently, the second most common reason not to exercise in the reduced exercise group was concerns about COVID-19 in our study (Supplementary table). Additionally, non-motor aggravation was as common as motor aggravation in our patients, and feeling stressed, fatigue, and pain were the most common non-motor symptoms reported, which could have affected subjective motor symptoms during COVID-19, even without objective aggravation of motor symptoms. Therefore, based on our results, both motor symptoms and non-motor symptoms should be carefully assessed and managed under a situation like the COVID-19 pandemic.

Additionally, the reduced exercise group had more change for subjective worsening of both motor and non-motor parkinsonian symptoms, although there was no significant difference in the UPDRS part 3 score between the two groups. It is difficult to suggest a causative relationship between reduced exercise and subjective aggravation in our study, but we would emphasize that maintaining the similar amount of exercise is important.

Our study has some limitations. First, we relied on patients' subjective evaluations about their exercise and parkinsonian symptoms, thus there could be the possibility of recall bias or the nocebo effect from COVID-19. Second, the PASE leisure part score relies on subjective patient reports, which also present the risk of reporting bias. However, the PASE is a validated measurement tool of physical activity that has been demonstrated to correlate with objective measures of aerobic capacity [15]. Third, we did not check various non-motor symptoms with specific scales, and therefore, we were unable to capture specific and more validated change for non-motor symptoms. However, we asked patients in detail to assess non-motor symptoms including direct questions about psychiatric symptoms like hallucination, which could be affected by social distancing during COVID-19. Moreover, there were no newly developed perceptual problems such as hallucination, delusion or confusion, or cognitive decline requiring additional medication or clinically meaningful during the COVID-19 pandemic. It may reflect that there were no clinically significant changes during the period, but this result should be interpreted carefully because we excluded PD patients with clinically significant cognitive impairments and psychiatric problems in the present study. Additionally, the different levels of the pandemic situation and lockdown among the countries should be also considered, because these differences could affect the changes in the motor and non-motor symptoms of PD.

In conclusion, PD patients reported a decrease in exercise during the COVID-19 pandemic. Even though there was no significant worsening of parkinsonism on objective evaluation, one third of PD patients complained of motor or non-motor aggravation of parkinsonian symptoms. Additionally, there was a significant relationship between reduced exercise and subjective worsening of PD symptoms. Therefore, the careful evaluation of both motor and non-motor symptoms and encouragement of exercise are important for PD patients in situations like the COVID-19 pandemic.

Declaration of competing interest

The authors have no conflict of interest to declare.

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None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.parkreldis.2020.09.034>.

Authors' contributions

Joomee Song: Execution, Design, Execution, Writing of the first draft. Jong Hyeon Ahn: Organization, Execution, Design, Review and Critique. Inyoung Choi: Execution. Jun Kyu Mun: Organization, Execution. Jin Whan Cho: Conception, Organization, Design, Review and Critique. Jinyoung Youn: Conception, Organization, Design, Writing of the first draft, Review and Critique.

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