



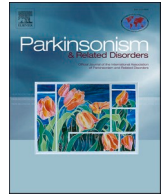
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Short communication



A French survey on the lockdown consequences of COVID-19 pandemic in Parkinson's disease. The ERCOPARK study

Margherita Fabbri^{a,b,*,1}, Clémence Leung^{a,1}, Guillaume Baille^c, Matthieu Béreau^d, Christine Brefel Courbon^{a,b,e}, Giovanni Castelnovo^f, Nicolas Carriere^g, Philippe Damier^h, Luc Defebvre^g, Anne Doe de Maindrevilleⁱ, Frederique Fluchere^j, Marie Fuzzatti^k, David Grabli^l, David Maltete^m, Vanessa Rousseau^{e,n}, Agnès Sommet A^{e,n}, Claire Thalamas^b, Claire Thiriez^o, Olivier Rascol^{a,b,e}, Fabienne Ory-Magne^{a,b}

^a Service de Neurologie, Centre Hospitalier Universitaire, Toulouse, France

^b France CHU de Toulouse, Université de Toulouse-Toulouse 3, INSERM, UMR1214 Toulouse NeuroImaging Centre "TONIC," Center of Excellence in Neurodegeneration (CoEN), NeuroToul, Centre Expert Parkinson de Toulouse, Centre d'Investigation Clinique CIC1436, NS-Park/FCRIN Network, Services de Neurologie et de Pharmacologie Clinique, UMR 1048 Institute for Cardiovascular Diseases, Toulouse, France

^c Service de Neurologie, Hôpital Delafontaine, Saint-Denis, France

^d Service de Neurologie, Centre Hospitalier Universitaire, Besançon, France

^e Service de Pharmacologie Médicale et Clinique - CHU Toulouse Université de Toulouse, France

^f Service de Neurologie, Centre Hospitalier Universitaire, NS-Park/FCRIN Network, Nîmes, France

^g Service de Neurologie, Centre Hospitalier Universitaire, NS-Park/FCRIN Network, Lille, France

^h Service de Neurologie, Centre Hospitalier Universitaire, NS-Park/FCRIN Network, Nantes, France

ⁱ Service de Neurologie, Centre Hospitalier Universitaire, NS-Park/FCRIN Network, Reims, France

^j Service de Neurologie, Centre Hospitalier Universitaire la Timone, Aix-Marseille University, NS-Park/FCRIN Network, France

^k Association France Parkinson, France

^l Service de Neurologie, Centre Hospitalier Universitaire, NS-Park/FCRIN Network, Pitié-Salpêtrière, France

^m Service de Neurologie, Centre Hospitalier Universitaire, Rouen, France; INSERM U1239, Laboratoire de Différenciation et Communication Neuronale et Neuroendocrinienne, NS-Park/FCRIN Network, Mont-Saint-Aignan, France

ⁿ Unité MeDatAS, Centre d'Investigation Clinique, Centre Hospitalier Universitaire, Toulouse, France

^o Service de Neurologie, Centre Hospitalier Universitaire, NS-Park/FCRIN Network, Caen, France

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ABSTRACT

Background: In 2020 the coronavirus disease 19 (COVID-19) pandemic imposed a total and sudden lockdown. We aimed to investigate the consequences of the first COVID-19 lockdown (mid-March – mid-April 2020) on motor and non-motor symptoms (NMS) in a cohort of French people with Parkinson's disease (PwP).

Methods: PwP were enrolled either by an on-line survey sent from the national France Parkinson association (FP) to reach the French community of PwP or as part of outpatients' telemedicine visits followed by an hospital-based Parkinson Expert Center (PEC). All patients were evaluated using the same standardized questionnaire assessing motor and NMS (including a list of most disabling, new or worsened symptoms and Patient's Global Impression-Improvement scales [PGI-I]) psycho-social queries and quality of life.

Results: 2653 PwP were included: 441 (16.6%) in the PEC group and 2122 (83.4%) in the community-based group. Physiotherapy was interrupted among 88.6% of the patients. 40.9% referred a clinical modification of their symptoms. Based on the questionnaire, pain (9.3%), rigidity (9.1%) and tremor (8.5%) were the three most frequently new or worsened reported symptoms. Based on the PGI-I, the motor symptoms were the most affected domain, followed by pain and psychic state. PwP in community-based group tended to have more frequent worsening for motor symptoms, motor complications, pain and confusion than those of the PEC group.

* Corresponding author. Service de Neurologie, Hôpital Pierre Paul Riquet, CHU de Toulouse, Centre Expert Parkinson de Toulouse, Centre d'Investigation Clinique CIC1436, NS-Park/FCRIN Network, 31059, Toulouse cedex 9, France.

E-mail address: margheritafabrimd@gmail.com (M. Fabbri).

¹ These authors contributed equally.

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Conclusions: The first COVID-19 lockdown had a negative impact on motor and NMS of PwP. Efforts should be allocated to avoid interruption of care, including physiotherapy and physical activities and implement telemedicine. .

1. Introduction

Since the Coronavirus disease 2019 (COVID-19) pandemic started, physicians questioned on whether there could be severe consequences of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection on Parkinson's disease (PD) symptoms [1] or whether people with PD (PwP) were more vulnerable to SARS-CoV-2 infection [1,2]. Concomitantly, several studies, although with inconstant results, suggested that pandemic-related lockdown, inducing social and familial isolation, could negatively affect mental and physical well-being, motor, non-motor symptoms (NMS) and quality of life (QoL) of PwP [3–5]. Additionally, the impact of COVID-19 on usual medical care could be not negligible [6].

While it is important to understand and assess the direct and indirect consequences of the COVID-19 pandemic/infection for PwP, it is also relevant to understand the direct and indirect impact of a lockdown on PwP. This is indeed a totally novel situation and the resilience capacities of PwP and conversely their dysexecutive difficulties, could constitute factors of uncertainty.

In this sense, our study aimed to investigate the consequences of the COVID -19 pandemic lockdown on motor and NMS in a large cohort of French PwP.

1.1. Patients and methods

Patients were enrolled following two recruitment strategies. First, PwP were included in ten French PD Expert centers (PEC) from the French NS-Park/FCRIN Network (Besancon, Caen, Lille, Marseille, Rouen, Nimes, Reims, Saint-Denis, Toulouse, and Paris) (PEC group). Eligibility criteria were: diagnosis of PD and having a routine follow up scheduled within the first French lockdown duration (16th March - 16th May 2020). The first COVID-related lockdown in France imposed homogeneous and full restrictions in terms of social, educational and health care activities throughout the whole country; only emergency department visits were allowed. Exclusion criteria were atypical Parkinsonism and patients already identified as demented according to the DSM-IV criteria. PEC patients' group evaluation was carried out either via telemedicine (by video-consultation or phone call) or during a classic routine follow-up consultation by a movement disorder specialist. Secondly, other PD patients were invited to participate to an online anonymous survey, available online between 20th April and 16th May 2020, by receiving an email from the France Parkinson Association (FP), i.e. the community-based group. It was specified to the patients to answer only if they had already received a diagnosis of PD, and were able to answer, and not to fulfill the questionnaire whether they had participated with their neurologist to the survey.

The national medical ethical commission approved the study (protocol number: 2020-Ao1463-36). All participants gave their informed consent prior to completing the questionnaire.

The patients were questioned about their changes occurring after the first month of the 2020 lockdown, i.e. from mid-March up to mid-April. The following data were collected: I) demographic, clinical characteristics, and medical care changes, including the interruption of physiotherapy or speech and language therapy sessions. Information about presence of clinical infectious symptoms such as cough, fever or breathing difficulties and COVID-19 diagnostic screening test (positive PCR or thorax scanner) have been also collected; II) changes in motor and NMS evaluated by a patient's Global Impression-Improvement (PGI-I) scales. PGI-I was adopted for 7 domains: general motor PD symptoms (tremor, rigidity and bradykinesia), dyskinesia, motor fluctuations,

pain, impulse control disorders (ICDs), psychic state (anxiety and depression) and confusion-hallucinations; III) Troublesome/worsened symptoms. Patients were asked to spontaneously report at most three new troublesome or worsened symptoms [7]; IV) The psycho-social repercussions of the lockdown evaluated by a numerical scale (varying between 0 [lack of fear] and 100 [maximal fear]) in three situations: a) fear of the contingency of lacking of their anti-parkinsonian treatment (fear); b) exacerbation of their feeling of frailty linked to PD (vulnerability feelings); c) the increased fear of the progression of PD with the pandemic (worrying ideas); V) QoL assessed by the Parkinson's disease questionnaire (PDQ-8).

Online and telemedicine questionnaires were identical, with the only difference that only ranges for age and disease duration were collected for the community-based group and no dose of treatment was collected for the online survey.

Our primary objective was to identify the impact COVID-19-lockdown on PD motor and NMS. The related outcomes were the three most "troublesome or worsened" symptoms, the most frequent PGI-I changed and a "several clinical aggravations", i.e. a worsening of at least 5 CGI-Is.

Our secondary objectives were: a) to assess the psychosocial impact, by means of VAS scales analysis; b) to identify any difference on COVID-19-lockdown impact between the community-based vs. PEC group.

1.2. Statistical analyses

To evaluate associated factors to "severe clinical aggravation", logistic regression models were performed. First, univariate models were built with severe clinical aggravation as response variable and one of these data: age, sex, disease duration, center (community-based vs. PEC group), presence/absence of device-aided therapies as explanatory variable (five univariate models). Then, all the explanatory variables were included in a multivariate model. No selection method was used.

To compare characteristics of PEC group vs. community-based group, Chi² test was used for qualitative variables (or Fisher's exact test as appropriate) and Wilcoxon rank-sum test for quantitative variables.

All statistical tests were two-sided and p values < 0.05 were considered statistically significant.

All analysis was performed with SAS® statistics software, version 9.4 (SAS Institute Inc., Cary, NC).

2. Results

2.1. Demographic and clinical features

We enrolled 2717 patients but 64 patients from the community-based group were excluded as they declared to have PD for at least 5 years but remained untreated.

2653 PwP were included in the analysis: 441 (16.6%) in the PEC group and 2122 (83.4%) in the community-based group. 2.8% reported infective symptoms and 0.7% had a diagnostic positive test for COVID-19 diagnosis. Patients belonging to the PEC group had a longer disease duration, were younger and were more frequently treated with a device-aided therapies if compared to the community-based group (respectively 155 [35.1%] vs. 295 [13.3%], $p < 0.0001$) (Table S1, Supplementary material).

2.2. Consequences on non-pharmacological treatments

Among the PwP who had physiotherapy (N = 2155), 89.6% were not able to continue their rehabilitation and 98.8% interrupted their speech sessions, out of the 1143 patients previously concerned.

2.3. Primary objective

2.3.1. Motor, non-motor symptoms and quality of life changes

Regarding the self-reported symptoms, 1085 patients (40.9%) indicated that they felt a modification of their PD symptoms during the lockdown (Table 1). Pain, rigidity and tremor were the most troublesome changed symptoms, reported by 9.3%, 9.1%, and 8.5% of the patients, respectively (Fig. 1, Panel A and Table 1).

Regarding PGI-I domains (Table 1; Fig. 1, Panel B), the motor one was the most frequently affected (55.8%), followed by pain (51.5%) and psychic state (46.3%).

A severe clinical aggravation was observed in 498 patients (18.8%), (Table 1).

Patients with at least five worsened PGI-I (44.2 ± 19.1) had significantly higher mean PDQ 8 scores than less aggravated patients (17.6 ± 16.5) ($p < 0.0001$ QoL; Fig. S2 panel B).

2.3.2. Variables related to clinical severe worsening

At univariate analysis, a disease duration longer than 6 years and belonging to community-based group were significantly associated to a “severe clinical worsening” (p values for disease duration: 0.0021 for 7–9 years, 0.0006 for 10–15 years and 0.0083 for > 15 years; p value for group: <0.0001). The same variables kept significance at logistic regression analysis (p values for disease duration: 0.0007 for 7–9 years, 0.0001 for 10–15 years and 0.0058 for > 15 years; p value for group: <0.0001).

2.4. Secondary objectives

2.4.1. Psychosocial repercussions

Fragility feelings related to the pandemic was the main concern (mean \pm SD: 41 ± 34.6), followed the concern about the evolution of their disease (31.6 ± 31.4), while patients were less worried about treatment lacking (20.9 ± 20.2) (Fig. S1, Panel A).

2.4.2. PEC versus community-based group

Patients belonging to the community-based group discontinued significantly more frequently physiotherapy if compared to the PEC group (9.8% vs. 6.5%, $p = 0.01$).

Regarding the self-reported symptoms, the percentage of patients without any change was significantly higher in the community-based group than in the PECs (respectively 1453 [65.7%] vs. 115 [26.1%] $p < 0.0001$) (Table 1).

Pain, anxiety, and tremor were on the top of the PEC group list, while rigidity, pain and tremor, on the top for the community-based group, with similar frequency for all the other symptoms (Table 1).

Conversely, patients in the community-based group had significantly more frequently a worsening at all the motor PGI-I scores than in the PEC group: respectively for general motor symptoms (1244 (56.2%) vs. 207 (47%)); dyskinesia (695 (31.4%) vs. 87 (19.7%)) the motor fluctuations (863 (39%) vs. 127 (28.8%)), with in both $p < 0.0001$ (Table 1). Similarly pain and confusion were significantly more frequently worsened in the community-based group than in the PEC group (respectively 1169 (52.8%) vs. 167 (37.8%) and 644 (29.1%) vs. 70 (15.8%), in both $p < 0.0001$) (Table 1).

The community-based group had a higher prevalence of “severe clinical aggravation” with 158 patients (20.7%) vs. 40 (9.1%) in the PEC group ($p < 0.0001$ Table 1).

All VAS scales for psychosocial repercussions showed a higher impact on the community-based group if compared to the PEC group (p

Table 1
Symptoms’ evolution and PGI-I worsening comparison between the Community-based group and the PEC group.

	Total N = 2653	PEC group N = 441	Community- based group N = 2212	Community- based group vs. PEC group
	N patients (%)	N patients (%)	N patients (%)	p value
Number of worsened symptoms				
1	293 (11.4)	63 (14.29)	230 (10.4)	<0.0001
2	292 (11.01)	105 (23.81)	187 (8.45)	<0.0001
3	498 (18.77)	158 (35.83)	340 (15.37)	<0.0001
No worsening	1568 (59.1)	115 (26.8)	1453 (65.6)	<0.0001
Worsened symptoms, as listed by the patients				
Pain	246 (9.2)	84 (19.5)	162 (7.3)	<0.0001
Rigidity	239 (9.0)	48 (10.8)	191 (8.6)	0.13
Tremor	223 (8.4)	66 (14.9)	157 (7.1)	<0.0001
Walking troubles	183 (6.9)	48 (10.8)	135 (6.1)	0.0003
Akinesia	181 (6.8)	46 (10.4)	135 (6.1)	0.001
Anxiety	162 (6.1)	73 (16.5)	89 (4.0)	<0.0001
Fatigue	147 (5.4)	39 (8.4)	108 (4.8)	0.0009
Balance	121 (4.5)	20 (4.5)	101 (4.5)	0.98
disturbances				
Sleep disorders	109 (4.1)	42 (9.5)	67 (3.0)	<0.0001
PGI-I				
PGI-I \geq 5_motor symptoms	1451 (55.8)	207 (46.9)	1244 (57.6)	<0.0001
PGI-I \geq 5_dyskinesia	782 (30.5)	87 (19.7)	695 (32.7)	<0.0001
PGI-I \geq 5_motor fluctuations	990 (38.6)	127 (28.8)	863 (40.7)	<0.0001
PGI-I \geq 5_Pain	1336 (51.4)	167 (37.9)	1169 (54.1)	<0.0001
PGI-I \geq 5_confusion	714 (27.3)	70 (15.9)	644 (29.6)	<0.0001
PGI-I \geq 5_ICD	305 (12)	53 (12.0)	252 (11.6)	0.82
PGI-I \geq 5_psychic state	1211 (46.3)	210 (47.6)	1001 (46.0)	0.53
Number of worsened PGI-I per patient				
Missing data	4 (0.15)	/	4 (0.15)	1
0	540 (20.4)	99 (22.5)	441 (19.9)	<0.0001
1	367 (13.8)	85 (19.3)	282 (12.8)	
2	416 (15.7)	83 (18.8)	333 (15.1)	
3	435 (16.4)	76 (17.2)	359 (16.2)	
4	393 (14.8)	58 (13.2)	335 (15.1)	
5	309 (11.65)	30 (6.8)	279 (12.6)	
6	155 (5.9)	10 (2.3)	145 (6.6)	
7	34 (1.3)	0 (0)	34 (1.5)	
At least 5 PGI-I \geq 5	493 (18.8)	40 (9.1)	458 (20.7)	<0.0001
PDQ-8				
Total score, mean (SD)	29.4 (19.7)	25.6 (17.2)	30.1 (20.0)	<0.0001
Difficulty getting around in public	25.4 (31.9)	24.1 (34.1)	25.6 (31.5)	0.04
Dressing	30.4 (31.8)	32.7 (33.7)	29.9 (31.4)	0.21
Depression	34.3 (27.3)	26.9 (28.0)	35.7 (26.9)	<0.0001
Personal relationship	37.0 (28.5)	35.7 (32.5)	37.2 (27.7)	0.16
Concentration	33.6 (28.6)	28.2 (31.1)	34.0 (28.2)	<0.0001

(continued on next page)

Table 1 (continued)

	Total N = 2653	PEC group N = 441	Community- based group N = 2212	Community- based group vs. PEC group
	N patients (%)	N patients (%)	N patients (%)	p value
Painful cramps	29.9 (29.5)	24.1 (31.2)	31.1 (29.0)	<0.0001
Embarrassed in public	19.2 (24.9)	12.0 (24.2)	20.6 (24.8)	<0.0001

Number are represented as mean (SD). PGI-I varied from 1 (best improvement) to 7 (worse aggravation), being a score ≥5, the cut-off for an aggravation). PGI-I: patient’s Global Impression-Improvement; PDQ-8: Parkinson’s disease questionnaire.

< 0.0001) (Fig. S1, Panel B).

Scores of all PDQ-8 items were significantly worse among the community-based group if compared to the PEC group (<0.0001), except for “dressing” and “personal relationship” (Table 1).

3. Discussion

The present research evaluated the impact of the first COVID-19-related lockdown on PD patients in France, in one of the largest PD cohort ever published. Our sample is representative of a national PD population, being made up of nearly 2% of the French PwP. As expected, more patients with device-aided treatments and the ones with the longest disease duration and younger age at onset, were followed in the PECs, while the less severe or the eldest patients were recruited in the community-based group.

We have sought to insight the key role of patients’ perspective by choosing easy tools to assess patients’ changes, (i.e. the spontaneous reported symptoms, the PGI-I and numeric scales) but also to compensate the lack of previous evaluation before the pandemic.

We found an impact of the lockdown on motor, NMS and QoL in at about half of the patients. Based on the patients’ perception, general parkinsonian motor symptoms and pain were the most worsened, which was consistent and reinforced with the results of the PGI-I. 45% of the patients had from mild to severe aggravation for psychic state alteration (anxiety and depression) which is unsurprisingly and probably related to

the first COVID-19 quarantine, the imposed social distancing and the abrupt onset of the lockdown and not only to the pandemic. Indeed, despite not being the focus of the study, we found a relatively low percentage of PD patients infected by the COVID-19, i.e. 0.7% which was quite similar to another cohort of parkinsonian patients surveyed during the same time frame, i.e. 0.56% [11]. The concomitant aggravation of motor symptoms, such as tremor and rigidity, particularly sensitive to stress may be related to anxiety/depression aggravation, as well as to the diffuse interruption of physiotherapy and any out-door physical activities. Indeed, it is well recognized that higher rate of physical activity positively impacts QoL, parkinsonian motor symptoms, mood, and even cognitive performance [12]. Even considering the surprisingly and previously reported resilience capacities of PD patients, able to adapt their physical activities at home, the reduction of physical activity has been already identified as the main risk factor for motor symptoms aggravation in a small cohort of PD patients during the first COVID-19 lockdown [10]. Even if a possible confusion between rigidity and pain may explain this result, particularly for the patients who participated to the on-line survey, pain was the most frequent aggravated symptoms also for the PEC group. Non-parkinsonian patients with chronic pain have shown significant aggravation during the same lockdown period [13], suggesting that it could not-being a disease-specific aggravation, quite common in chronic disease at pandemic time. However, considering the high impact of pain on PD QoL, clinicians should be aware that its aggravation could be as much important or even more severe than the one of motor symptoms during stressful situations.

It is noteworthy that more than half of the patients (59.1%) did not referred a change in their symptoms, at spontaneous symptoms reporting. However, even if considering each single PGI-I domains a worsening (PGI-I ≥5) was observed in not more than 55% of the patients (range 11.5%–54.6%), only 20.4% of them do not report any worsening at PGI-I assessment (Table 1). Discrepancies among self-reported symptoms vs. PGI-I-assessed ones could be related to the fact that for PGI-I each symptom was specified thus possibly “suggesting” the reported worsening, while for the self-reported list no domain/symptom was specified within the question. A partial stability of PD symptoms during the COVID-19 pandemic was also observed by a few previous studies [3,8,9] and multiple factors could explain this finding: a) better adherence to treatment [8,9]; b) better organization of the routine activities, including the possibility to practice physical activity using satisfactorily technology assistance, as reported in 50% of PwP, in a previous study

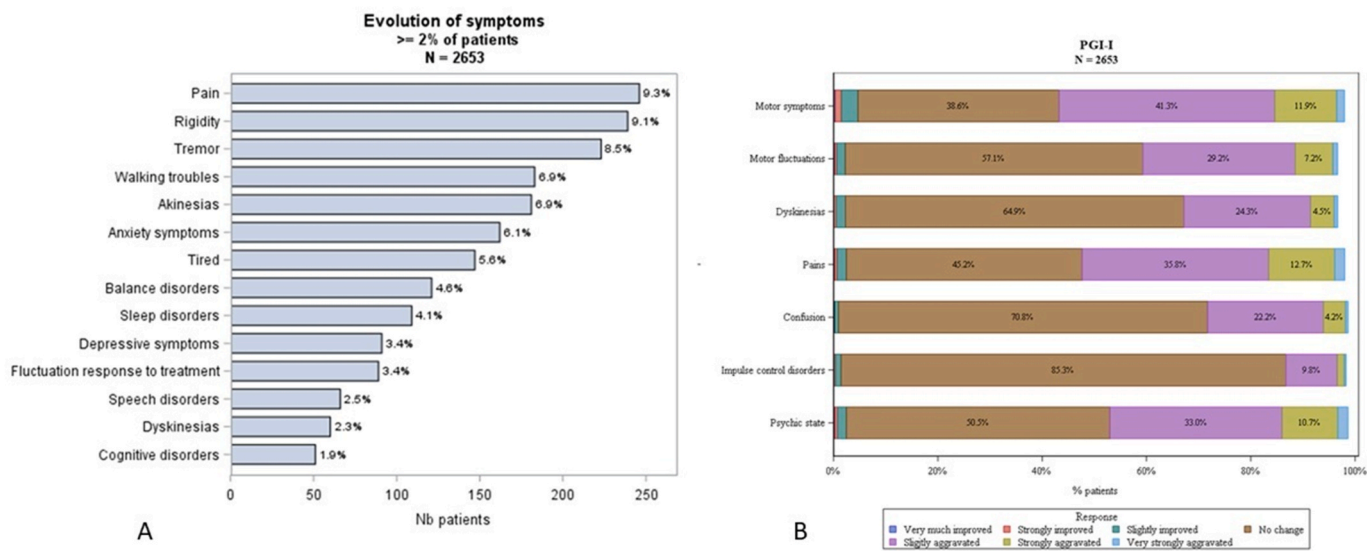


Fig. 1. Symptom’s evolution.

Panel A: Distribution of the new or worsened troublesome symptoms named by the patients. Panel B: results of the motor and non-motor PGI-I in the whole population.

(mostly true for women) [10]; c) the resilience capacity of patients, not feeling the restriction to be at home or perceiving a lower disability while staying at home because not facing “outdoor challenging situations”. Identifying patients with a stable profile is interesting, as they seemed to cope better, possibly having better self-management capacities.

The community-based group’s patients seemed to worsen less in agreement with the three spontaneous symptoms, thought a more severe aggravation was observed at the PGI-I. Although it might seem discordant, we thought that there could have been a bias induced by the neurologist while asking the patients for his/her spontaneous symptoms. However, the more severe deterioration of the community-based group, confirmed at the regression analysis, is equally reflected by worst QoL scores and higher psycho-social repercussion (Fig. S1, Panel B).

A more severe aggravation of the community-based group could be accounted to an easier access to clinics for the PEC group. However, we cannot completely exclude that some community-based patients also had a neurological visit, but likely not in an PEC. Additionally, patients who decided to fill out the online questionnaire may have been a subgroup of patients with major clinical needs or anxiety, if compared to the general PD population, with limited in-hospital evaluations while needed, because of their fear to be contaminated. Limited access to health care resources associated with restrictions of mobility and social interactions may have played a more negative role in the community-based group [14]. Changes are ongoing worldwide to implement telemedicine for urgent or even for current routine healthcare [3] as whether videoconferencing or simple phone consultations could preserve the more fragile PD patients. Identifying them and their needs to keep a continuous healthcare management is a condition needed to protect them from an expected worsening in such a crisis. On this path, the Movement Disorder Society (MDS) Telemedicine Study Group reported on a global increment of all forms of telemedicine for movement disorders due to COVID-19 pandemic across 40 countries all over the world, though not including France [15], also highlighting several concerns about regulations and reimbursement of the visits. As results of the Group work a “step-by-step” webinar to conduct a telemedicine visits for movement disorders clinicians worldwide is now available on the MDS website.

Of note our cohort include 450 PD patients having a device-aided therapies (19.6% of the whole cohort). We have not specifically investigated the difficulties in device-management of those patients during the observed month, but we are aware that those patients may require special attention during a health crisis. On this path, a triaging system has been also recently proposed with the aim to facilitate the remote management of patients with device-aided therapies during pandemic period and a development of more fine-tuning of remote kinematic measurements of motor function would be likely envisioned for those patients [16].

There are limitations mainly related to the online patient-based survey and the lack of a clinically in-person assessment that cannot guaranty us that no patients with severe cognitive decline answered the survey or that did not allow us to collect relevant clinical information, such as Hoehn and Yahr or physician-based observation for motor worsening. Equally, we cannot provide a response rate as the FP association is not able to discriminate in its files the patients from the supportive people or the caregivers. We were also not able to know if community-based patients had a follow-up visit scheduled during the lockdown period as the PEC group did. This missing information could have created an additional bias in terms of symptoms assessment. Additionally, only very few nursing-home patients were included, and the survey excluded patients with severe cognitive impairment, thus giving a not a complete representation of the whole PD population.

In conclusion, our large cohort study highlights that the COVID-19-related lockdown has exacerbated motor and NMS in about half of the included PD patients, with a more severe aggravation among the community-based group. Overall, three main implications for future

care strategies, in partly focused on France, can be drawn from our survey: 1) this pandemic crisis was an opportunity to observe the importance of the continuity of care for PD patients, suggesting the need to promptly implement and regulate the currently adopted telemedicine measures, including remote assessment of patients and remote physiotherapy/speech and language therapy sessions; 2) telemedicine is probably used in many PECs in France, but systematic data are lacking on the availability, feasibility and use of telemedicine for movement disorder patients including community-based patients in France. A state of the art of telemedicine utilization pattern would be much useful to better face another health crisis; 3) on a related note, patients’ acceptance and suggestions related to telemedicine tools should be systematically collected from PD French patients and caregivers.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.parkreldis.2021.07.013>.

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