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LETTER TO THE EDITOR

COVID-19: Implications for Sudden Death in Parkinson's Disease

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Always on the lookout for articles from the *Journal of Movement Disorders*, one in particular has attracted much attention because scientific proposals and perspectives are fascinating.[1] In brief, Bhidayasiri et al.[1] explored very precisely the risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in Parkinson's disease (PD) patients based on their susceptibility to severe disease, the impact of SARS-CoV-2 infection on PD disease severity, potential long-term sequelae, and difficulties in PD management during this outbreak. Considering the increasing awareness and recognition by neurologists about the acute and chronic consequences of SARS-CoV-2-mediated infection in PD patients,[1] we truly applaud the authors for pursuing this topic. Moreover, the possibility that the current serious pandemic of the new coronavirus disease could influence the cardiovascular system[1,2] and thereby increase the incidence of sudden death in patients with PD (SUDPAR) also deserves some reflection.

The new coronavirus (SARS-CoV-2) that hit the central Chinese city of Wuhan in late December 2019 and subsequently spread rapidly to all provinces of China and all countries worldwide has had a devastating impact on global public health.[3] SARS-CoV-2 is characterized by high contagiousness. In 85% of cases, it causes subclinical or mild disease, but compared to the flu, it more easily causes respiratory complications [e.g., severe pneumonia (ground glass opacities) and interstitial pneumonia] in 10−15% of cases. Five percent of infected patients require intensive care unit admission.[3] During these worst-case scenarios, lethality is estimated at approximately 0.7−7%.[3,4] Compared to previous coronavirus epidemics, contagiousness is higher, but mortality is decidedly lower than that observed with severe acute respiratory syndrome (SARS) infection in 2002 and Middle East respiratory syndrome (MERS) infection in 2012, both of which showed higher mortality (9.5% and 34.4%, respectively).[3,4] Furthermore, it has been suggested that for severe or critically ill patients, in addition to respiratory supportive treatment, a more careful assessment and the treatment of various affected organs are important.[4] Thus, the cardiac implications of SARS-CoV-2 infection have received special attention, and the American College of Cardiology (ACC) published a bulletin in February 2020 that highlighted the potential cardiac implications of the new coronavirus infection.[3] On these lines, it has been clearly demonstrated that the cardiovascular system is often involved in SARS-CoV-2 infection early, reflected in the release of highly sensitive troponin and natriuretic peptides (proBNP), which are all extremely prognostic, particularly in those showing continued rise, along with cytokines such as interleukin-6.[5] Moreover, inflammation in the vascular system induces diffuse microangiopathy with thrombosis.[5] Similarly, inflammation in the myocardium may also trigger myocarditis,

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Table 1. Summary of possible SUDPAR cases reported in the literature [2].

Authors	Year	Study (design)	Number of deaths/number of sudden deaths, possible causes
Rajput and Rozdilsky	1976	Necropsy	7/2 (28.5%), without specific cause
Sato et al.	2006	Cohort	131/7 (5.3%), without specific cause
Matsumoto et al.	2014	Autopsy	16/7 (43.7%), unknown, asphyxia, duodenal ulcer
Nishida et al.	2017	Clinicopathological (case report)	2/2 (100%), arrhythmogenic potential and Lewy pathology
Zhang et al.	2018	Autopsy	31/3 (9%), orthostatic hypotension, abnormal Lewy bodies

heart failure, cardiac arrhythmias, acute coronary syndrome, rapid deterioration and sudden death.[5,6] The elevation of troponin, proBNP, and inflammatory parameters could also be due to acute right heart strain secondary to interstitial pneumonia.[6]

As the coronavirus pandemic has the potential to differentially disadvantage chronically ill patients, neuroscientists have given special attention to individuals with PD in this catastrophic scenario that we are currently experiencing.[1] In this sense, although the medical team's first reaction was to limit access to clinics and neurology wards to prevent fragile PD patients from being infected, some interesting proposals regarding hospital logistics, medical procedures and treatment and telemedicine have also been discussed among various movement disorder neurologists operating in different world regions.[1] Due to the seriousness of the current situation, it would also be extremely important to discuss the possibility of premature death in PD patients.

PD is one of the most frequent age-related neurodegenerative disorders and affects millions of people globally, and epidemiological studies have demonstrated that it is accompanied by high rates of premature death compared with the general population.[2] In these circumstances, it has been clearly demonstrated that the predominant causes of death in PD are pneumonia, cerebrovascular disease, and cardiovascular diseases.[2] Additionally, it is important to emphasize that SUDPAR, although it is still considered a rare event, is increasingly discussed as a contribution to mortality in PD (Table 1).[2] Three years ago, SUDPAR was defined as unexpected death of a patient with PD without any satisfactory cause as determined by autopsy.[2] Epidemiologically, there are no studies to date that accurately evaluate the possible distribution of SUDPAR in the main research centers for movement disorders. Nevertheless, a series of studies since the 1970s that evaluated SUDPAR cases have pointed out that an average of 14% of PD patients die suddenly.[2] The effective causes of SUDPAR are not yet known.[2] However, the results of clinical and experimental studies suggest that cardiac abnormalities and autonomic dysfunction play a possible "direct" role in SUDPAR, since approximately 60% of PD patients have cardiovascular disturbances and because of frequent autonomic disturbances in PD.[2] In these lines, recent research suggests that some risk factors may be directly related to SUDPAR, such as age at onset, the duration of PD, sex, motor severity and drug treatment (polypharmacy),[2] but these potential risk factors for SUDPAR need to be further investigated in translational studies.

On the whole, we are experiencing a pandemic that is already transforming the world through economic, political, scientific, social, cultural, environmental and health aspects. Really, most of us are not prepared to deal with SARS-CoV-2 infection, especially when it is associated with critically ill patients, including individuals with PD.[7] Finally, we are fully convinced that the entire healthcare team must work together to manage complications in cases of SARS-CoV-2 infection.

Conflicts of Interest

The authors have no financial conflicts of interest.

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