



Comments

The implication of cardio-oncology on Parkinson's disease: answers begin to emerge



Parkinson's Disease (PD) is a progressive, incurable, and symptomatically devastating neurodegenerative disease.¹⁻³ PD is the second most common neurodegenerative disease affecting up to ten million people worldwide.⁴ Clinically, PD presents with tremor, rigidity, bradykinesia/akinesia, and postural instability due to the progressive loss of neurons in the Substantia Nigra pars compacta (SNpc) and extensive intracellular aggregation of α -synuclein.³⁻⁵ In addition, molecular mechanisms such as mitochondrial dysfunction, excitotoxicity, impaired autophagy, oxidative stress, and genetic mutations are implicated in the degeneration of dopaminergic neurons in PD.⁶ Available therapies for PD only affect the symptoms of the disease and mainly focus on the dopaminergic pathway.^{2,3,5,7} The most common non-motor symptoms associated with PD involve neurobehavioral complications, sensory problems, and autonomic dysfunction.⁶ Several studies have found autonomic dysfunction to be a valuable predictor of cardiovascular morbidity and mortality in PD patients.^{8,9} Despite the tremendous clinical and epidemiological relevance of these studies, Sudden Death in PD (SUDPAR), a rare but fatal event, contributes to the increased mortality in PD patients.^{2,10}

Although the authors experienced an enlightening phase in PD research in the last decade,^{2,3} data on the influence of comorbidities on morbidity and mortality in PD are still lacking. Previous studies showed that hypertension, back problems, arthritis, dementia, cataracts, diabetes mellitus type II, non-specific hyperlipidemia, depressive disorder, atrial fibrillation, and urinary incontinence were the most common comorbidities in PD patients.¹¹⁻¹³ There is also growing evidence that PD and cancer may be closely linked.^{14,15} In fact, cancer incidence increases with age, as does the incidence of PD.^{14,16} On the one hand, an increased incidence of melanoma and other skin tumors, brain cancer, thyroid, and breast cancer has been demonstrated in PD patients.^{6,17} On the other hand, other studies showed that PD is associated with a significantly reduced risk of lung cancer, genitourinary cancers, gastrointestinal cancers, and hematological cancers.^{6,17} Although these data are controversial, there is a putative link between PD and cancer that requires much caution and further studies.^{6,17} Based on all these data and the worrying situation, the authors think it is appropriate to relate PD to the multidisciplinary specialty known as cardio-oncology.¹⁸ In particular, the main goal of cardio-oncology is the prevention and treatment of cancer therapy-related cardiotoxicity to optimize cardiovascular health outcomes in cancer patients or after cancer.^{18,19} In fact, it is already recognized that some cancer treatments can lead to atrial tachyarrhythmias, ventricular arrhythmias, and bradyarrhythmias.¹⁹ Therefore, based on the authors' experience of more than a decade with the cardio-oncology program in Brazil,²⁰ it is necessary to apply this knowledge to patients with PD as well. Certainly, the authors fully agree¹⁸ that this valuable clinical convergence will enable us to identify PD patients at risk for cardiac complications and to develop precise cardioprotective strategies.

<https://doi.org/10.1016/j.clinsp.2022.100085>

Received 21 June 2022; Accepted 4 July 2022

What lessons have the authors learned overall in recent years? Firstly, with an aging population and rising life expectancy worldwide, PD is estimated to increase by more than 50% by 2030.^{2,7} Second, PD is a systemic disease with cases of premature death. SUDPAR is a rare event, but it is common in PD patients with positive family history and risk factors for cardiovascular disease. Third, several studies suggest that cancer may be associated with PD. Furthermore, as extraordinary advances in translational neuroscience have changed our understanding of PD in the last decade,² it is extremely important to integrate the concept of cardio-oncology in centers for movement disorders. In fact, as cancer survival has increased over time due to improvements in treatment, it is reasonable to expect that the significant risk of cardiovascular complications for survivors will remain high in the near future.²¹ In these lines, the authors are in agreement that new lines of research should converge the research expertise of not only cardiologists and oncologists, but potentially others, including neurologists, and those with translational research experience.²¹ Finally, all medical specialties must work together in research, education, and collaboration to ensure healthy lives of the patients in cardio-oncology.

Conflicts of interest



The authors declare no conflicts of interest.

Acknowledgments

The present studies are supported by the following grants: FAPESP (Fundação de Amparo à Pesquisa do Estado de São Paulo); CNPq (Conselho Nacional de Desenvolvimento Científico e Tecnológico) and CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior).

References

- Seo HG, Byun SJ, Oh BM, Park SJ. Ten-Year relative survival from the diagnosis of Parkinson's disease: a nationwide database study. *J Am Med Dir Assoc* 2021;22(8):1757–61.
- Scorza FA, Fiorini AC, Scorza CA, Finsterer J. Cardiac abnormalities in Parkinson's disease and Parkinsonism. *J Clin Neurosci* 2018;53:1–5.
- Poewe W, Seppi K, Tanner CM, Halliday GM, Brundin P, Volkman J, et al. Parkinson disease. *Nat Rev Dis Primers* 2017;3:17013.
- Han SA, Semilan SLA, Hong PK. Systematic review on Parkinson's Disease Medications, emphasizing on three recently approved drugs to control Parkinson's symptoms. *Int J Environ Res Public Health* 2021;19(1):364.
- Balestrino R, Schapira AHV. Parkinson disease. *Eur J Neurol* 2020;27(1):27–42.
- Leong YQ, Lee SWH, Ng KY. Cancer risk in Parkinson disease: an updated systematic review and meta-analysis. *Eur J Neurol* 2021;28(12):4219–37.
- Kalia LV, Lang AE. Parkinson's disease. *Lancet* 2015;386(9996):896–912.
- Farrell MC, Shibao CA. Morbidity and mortality in orthostatic hypotension. *Auton Neurosci* 2020;229:102717.
- Cuenca-Bermejo L, Almela P, Navarro-Zaragoza J, Fernández Villalba E, González-Cuello AM, Laorden ML, et al. Cardiac changes in Parkinson's disease: lessons from clinical and experimental evidence. *Int J Mol Sci* 2021;22(24):13488.
- Scorza FA, Almeida ACG, Scorza CA, Finsterer J. Prevention of Parkinson's disease-related sudden death. *Clinics* 2021;76:e3266.

11. Wang X, Zeng F, Jin WS, Zhu C, Wang QH, Bu XL, et al. Comorbidity burden of patients with Parkinson's disease and Parkinsonism between 2003 and 2012: a multi-centre, nationwide, retrospective study in China. *Sci Rep* 2017;7(1):1671.
12. Gil-Prieto R, Pascual-García R, San-Roman-Montero J, Martínez-Martin P, Castrodeza-Sanz J, Gil-de-Miguel A. Measuring the Burden of Hospitalization in Patients with Parkinson's Disease in Spain. *PLoS One* 2016;11(3):e0151563.
13. Pohar SL, Allyson Jones C. The burden of Parkinson disease (PD) and concomitant comorbidities. *Arch Gerontol Geriatr* 2009;49(2):317–21.
14. Zhang X, Guarín D, Mohammadzadehonorvar N, Chen X, Gao X. Parkinson's disease and cancer: a systematic review and meta-analysis of over 17 million participants. *BMJ Open* 2021;11(7):e046329.
15. Ejma M, Madetko N, Brzecka A, Guranski K, Alster P, Misiuk-Hojio M, et al. The links between Parkinson's disease and cancer. *Biomedicines* 2020;8(10):416.
16. Kendal WS. Dying with cancer: the influence of age, comorbidity, and cancer site. *Cancer* 2008;112:1354–62.
17. Li Z, Zheng Z, Ruan J, Li Z, Tzeng CM. Chronic inflammation links cancer and Parkinson's disease. *Front Aging Neurosci* 2016;8:126.
18. Wickramasinghe CD, Nguyen KL, Watson KE, Vorobiof G, Yang EH. Concepts in cardio-oncology: definitions, mechanisms, diagnosis and treatment strategies of cancer therapy-induced cardiotoxicity. *Future Oncol* 2016;12(6):855–70.
19. Fradley MG, Beckie TM, Brown SA, Cheng RK, Dent SF, Nohria A, et al. Recognition, prevention, and management of arrhythmias and autonomic disorders in cardio-oncology: a scientific statement from the American Heart Association. *Circulation*. 2021;144(3):e41–55.
20. Hajjar LA, Mathias C. Cardio-Oncology in Brazil: The Dimensions of a New Era in the care of patients. *JACC CardioOncol* 2020;2(2):340–2.
21. Adhikari BB, Shi S, Dimond EP, Shelburne N, Desvigne-Nickens P, Minasian LM. Spectrum of national institutes of health-funded research in cardio-oncology: a basic, clinical, and observational science perspective. *Heart Fail Clin* 2022;18(3):515–28.
 Fulvio A. Scorza ^{a,b,*}, Antonio-Carlos G. de Almeida^{b,c},
 Josef Finsterer ^{b,d}, Ludhmila A. Hajjar^{b,e,f}
^a *Disciplina de Neurociência, Escola Paulista de Medicina, Universidade Federal de São Paulo (UNIFESP), São Paulo, SP, Brazil*
^b *Centro de Neurociências e Saúde da Mulher “Professor Geraldo Rodrigues de Lima”, Escola Paulista de Medicina/Universidade Federal de São Paulo (EPM/UNIFESP), São Paulo, SP, Brazil*
^c *Laboratório de Neurociência Experimental e Computacional, Departamento de Engenharia de Biosistemas, Universidade Federal de São João del-Rei (UFSJ), São João del-Rei, MG, Brazil*
^d *Klinikum Landstrasse, Messerli Institute, Vienna, Austria*
^e *Instituto do Coração, Faculdade de Medicina da Universidade de São Paulo (FMUSP), São Paulo, SP, Brazil*
^f *Instituto do Câncer, Universidade de São Paulo (USP), São Paulo, SP, Brazil*
 *Corresponding author.
 E-mail address: scorza@unifesp.br (F.A. Scorza).