Published in final edited form as:

Mov Disord. 2020 February ; 35(2): 374. doi:10.1002/mds.27840.

Renal dysfunction might be a marker of cardiovascular dysautonomia in prodromal α -synucleinopathies

Jose-Alberto Palma, MD PhD¹

¹Department of Neurology, Dysautonomia Center, New York University School of Medicine, NY

We read with interest the large nationwide study by Nam and colleagues concluding that chronic renal function and proteinuria are independent risk factors for the development of Parkinson disease.¹ The authors acknowledge that the mechanism of this relationship is unknown and, based on anecdotal case reports of parkinsonism in uremic patients, they speculate that uremia caused by renal disease may trigger or accelerate basal ganglia dysfunction. An alternative explanation might be that renal dysfunction is a consequence of blood pressure abnormalities in the context of cardiovascular dysautonomia. Large population-based and multicenter prospective studies have proven that blood pressure abnormalities, in particular neurogenic orthostatic hypotension (i.e., a sustained fall of at least 20 mmHg in systolic or 10 mmHg in diastolic blood pressure when standing up), are prodromal biomarkers of central nervous system α -synucleinopathy.²

Even though Nam and colleagues adjusted their analysis for hypertension, there is no mention of the position during which the blood pressure was measured. Blood pressure dysregulation, including neurogenic orthostatic hypotension and supine hypertension (i.e., a sustained increase of at least 140 mmHg in systolic or 90 mmHg in diastolic blood pressure when lying flat, most noticeable while sleeping) are hallmark features of cardiovascular dysautonomia in patients with α -synucleinopathies. Interestingly, neurogenic orthostatic hypotension and supine hypertension coexist in approximately 50% of patients with Parkinson disease. It is increasingly recognized that high blood pressure variability, and not only fixed hypertension, predicts the development and progression of renal damage.³

In keeping with this, patients with pure autonomic failure, an α -synucleinopathy predominantly affecting peripheral autonomic nerves, have high frequency of renal dysfunction.⁴ And most patients with pure autonomic failure will end up developing a central nervous system α -synucleinopathy including Parkinson disease, dementia with Lewy bodies or multiple system atrophy.⁵

It is therefore conceivable that renal failure, rather than an independent predictor, be a surrogate marker of cardiovascular dysautonomia, a well-described feature of prodromal

Corresponding authors: Jose-Alberto Palma, MD PhD (JoseAlberto.PalmaCarazo@nyulangone.org), New York University School of Medicine, Department of Neurology, Dysautonomia Center, 530 First Ave, Suite 9Q, New York, NY 10016, USA, Tel: 212-263-7225.

AUTHORS' ROLES

J.A.P.: drafting the article and editing the manuscript for important intellectual content.

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

Parkinson disease. Dedicated studies are required to confirm this. A better understanding of the prodromal phase of the synucleinopathies will contribute to earlier diagnosis and will be key when disease-modifying treatments become available. As our knowledge increases, it is key to reexamine which diagnostic clues have the best predictive value in the prodromal phase of α -synuclein-mediated neurodegeneration.

FINANCIAL DISCLOSURES IN THE PREVIOUS 12 MONTHS

J.A.P.: Funding from the NIH, Michael J. Fox Foundation, MSA Coalition, Familial Dysautonomia Foundation, and FDA. He is the principal investigator in clinical trials funded by Theravance and Biohaven. He has been a consultant for Lundbeck, Biogen, PTC and Dr. Reddy's Laboratories; he is the managing editor of *Clinical Autonomic Research*.

Funded by: National Institutes of Health (U54NS065736) and Familial Dysautonomia Foundation

REFERENCES

1. Nam GE, Kim NH, Han K, et al. Chronic renal dysfunction, proteinuria, and risk of Parkinson's disease in the elderly. *Mov Disord* 2019.
2. Schrag A, Horsfall L, Walters K, Noyce A, Petersen I. Prediagnostic presentations of Parkinson's disease in primary care: a case-control study. *Lancet Neurol* 2015;14(1):57–64. [PubMed: 25435387]
3. Parati G, Ochoa JE, Bilo G. Blood pressure variability, cardiovascular risk, and risk for renal disease progression. *Curr Hypertens Rep* 2012;14(5):421–431. [PubMed: 22903810]
4. Garland EM, Gamboa A, Okamoto L, et al. Renal impairment of pure autonomic failure. *Hypertension* 2009;54(5):1057–1061. [PubMed: 19738158]
5. Kaufmann H, Norcliffe-Kaufmann L, Palma JA, et al. Natural history of pure autonomic failure: A United States prospective cohort. *Ann Neurol* 2017;81(2):287–297. [PubMed: 28093795]