

## CARDIOVASCULAR COMORBIDITIES IN PARKINSON DISEASE PATIENTS

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### ABSTRACT:

*PARKINSON'S DISEASE (PD) IS THE SECOND MOST COMMON NEURODEGENERATIVE DISORDERS, AND THESE PATIENTS CAN HAVE A WIDE RANGE OF CARDIOVASCULAR COMORBIDITIES THAT INFLUENCE THE CLINICAL COURSE OF THE DISEASE<sup>2</sup>.*

*A CLINICAL, CROSS-SECTIONAL, OBSERVATIONAL STUDY HAS BEEN PERFORMED ON A GROUP OF 86 CONSECUTIVE PATIENTS WITH IDIOPATHIC PARKINSON'S DISEASE. THE PATIENTS HAVE BEEN INTERVIEWED ABOUT DISEASE DURATION, ASSOCIATED MEDICAL CONDITIONS AND CURRENT MEDICATIONS. THE MOST PREVALENT CARDIOVASCULAR COMORBIDITIES IDENTIFIED IN OUR STUDY POPULATION WERE: ARTERIAL HYPERTENSION (48.83%, 95%CI 38.27-59.39), CHRONIC CARDIAC ISCHEMIC DISEASE 40.69%, 95%CI 30.31-51.07). DATA ANALYSIS SHOWED NO STATISTICALLY SIGNIFICANT DIFFERENCE BETWEEN MALES AND FEMALES REGARDING THE PREVALENCE RATES FOR BOTH ARTERIAL HYPERTENSION (P=0.5) AND CHRONIC ISCHEMIC HEART DISEASE (P=0.5). COMPARING THE PREVALENCE VALUES IN ROMANIAN GENERAL POPULATION FOR THESE TWO IMPORTANT CARDIO-VASCULAR DISORDERS WITH OUR STUDY RESULTS LEADS TO THE CONCLUSION THAT ARTERIAL HYPERTENSION HAS BEEN FOUND NOT STATISTICALLY SIGNIFICANT MORE PREVALENT IN STUDIED ROMANIAN PARKINSONIAN PATIENTS THAN IN GENERAL POPULATION (P=0.49) AND THAT CHRONIC ISCHEMIC HEART DISEASE WERE STATISTICALLY SIGNIFICANT MORE PREVALENT IN STUDIED ROMANIAN PARKINSONIAN PATIENTS THAN IN GENERAL POPULATION (P<0.0001).*

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**KEY WORDS:** CARDIOVASCULAR, COMORBIDITIES, PARKINSON DISEASE

### INTRODUCTION

There are increasing number of reports in the scientific literatures which support a link between some of the most prevalent cardiovascular (hypertension, coronary heart disease, arrhythmias, etc ) and neurodegenerative diseases (eg Parkinson disease, Alzheimer disease). Even clinically defined by specific motor symptoms, PD includes a wide range of non-motor manifestations (cardiovascular, gastrointestinal, genito-urinary, etc) as well as various

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<sup>2</sup> McLean G, Hindle JV, Guthrie B, Stewart W. Mercer. Co-morbidity and polypharmacy in Parkinson's disease: insights from a large Scottish primary care database. BMCNeurology. (2017) 17:126 DOI 10.1186/s12883-017-0904-4

comorbidities; among the last ones, cardiovascular disorders have been most frequently reported<sup>3</sup>

Currently, supine hypertension and orthostatic hypotension are considered as manifestations of cardiovascular autonomic dysfunction in Parkinson disease<sup>4</sup>.

Two recent studies tried to clarify the controversial relation between hypertension and PD:

- a meta-analysis of seven cohort studies performed in 2018 found that hypertension history was statistically significant associated with an increased risk of clinically manifested PD (motor symptoms)<sup>5</sup>.
- a second meta-analytical study (including 9 cohort and 18 case-control studies) reported in February 2019 that hypertension might increase the risk of PD<sup>6</sup>.

This paper will present the assessed prevalence of cardiovascular comorbidities in a group of PD patients, as part of a study aimed to explore the non-motor symptoms in Parkinson's disease patients from the Southeastern Romania.

### MAIN TEXT

This clinical study (cross-sectional, observational) has been performed on a group of 86 consecutive patients with idiopathic Parkinson's disease from 5 Outpatients Clinics of Constanta, between 01 January 2017 and 31 May 2018.

The study subjects have been diagnosed as idiopathic Parkinson's disease according to the United Kingdom Brain Bank criteria<sup>7</sup>. Patients who presented atypical neurological features, suggestive for multiple system atrophy or other causes for parkinsonism have been excluded.

Sex, age, disease duration, associated medical conditions and current medications have been recorded. In order to reveal the presence of non-motor symptoms, all the patients have been assessed using the Scale for Outcomes in Parkinson's Disease for Autonomic Symptoms (SCOPA-AUT)<sup>8</sup> as a self-administered questionnaire.

The results will be presented as absolute or mean values, median values and/or percentages, together with the corresponding standard deviations, 95% confidence intervals and parametric tests for statistical relevance, using Word Excel and MedCalc applications.

Main characteristics of studied population: sex distribution (44% females and 56% males); the patients were aged 51 to 89 years; mean age = 70.63 years [SD = 9.74]; mean age

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<sup>3</sup> McLean G, Hindle JV, Guthrie B, Stewart W, Mercer. Co-morbidity and polypharmacy in Parkinson's disease: insights from a large Scottish primary care database. *BMCNeurology*. (2017) 17:126 DOI 10.1186/s12883-017-0904-4; Scorza FA, Fiorini AC, Scorza CA, Finsterer J. Cardiac abnormalities in Parkinson's disease and Parkinsonism. *J Clin Neurosci*. 2018 Jul;53:1-5. doi: 10.1016/j.jocn.2018.04.031

<sup>4</sup> Espay AJ, LeWitt PA, Hauser RA, Merola A, Masellis M, Lang AE. Neurogenic orthostatic hypotension and supine hypertension in Parkinson's disease and related synucleinopathies: prioritisation of treatment targets. *Lancet Neurol*. 2016 Aug;15(9):954-966. doi: 10.1016/S1474-4422(16)30079-5

<sup>5</sup> Hou L, Li Qiujuan, Jiang L, Qiu H, Geng C, Hong JS et al. Hypertension and Diagnosis of Parkinson's Disease: A Meta-Analysis of Cohort Studies. *Front Neurol*. 2018; 9: 162

<sup>6</sup> Chen J, Zhang C, Wu Y, Zhang D Association between Hypertension and the Risk of Parkinson's Disease: A Meta-Analysis of Analytical Studies. *Neuroepidemiology*. 2019 Feb 6;52(3-4):181-192. Doi: 10.1159/000496977. [Epub ahead of print]

<sup>7</sup> Hughes AJ, Daniel SE, Kilford L, Lees AJ. Accuracy of clinical diagnosis of idiopathic Parkinson's disease: a clinico-pathological study of 100 cases. *Journal of Neurology, Neurosurgery, and Psychiatry* 1992;55:181-184

<sup>8</sup> Visser M, Marinus J, Stiggelbout AM, Van Hilten JJ. Assessment of autonomic dysfunction in Parkinson's disease: the SCOPA-AUT. *Mov Disord* 2004; 19:1306-12

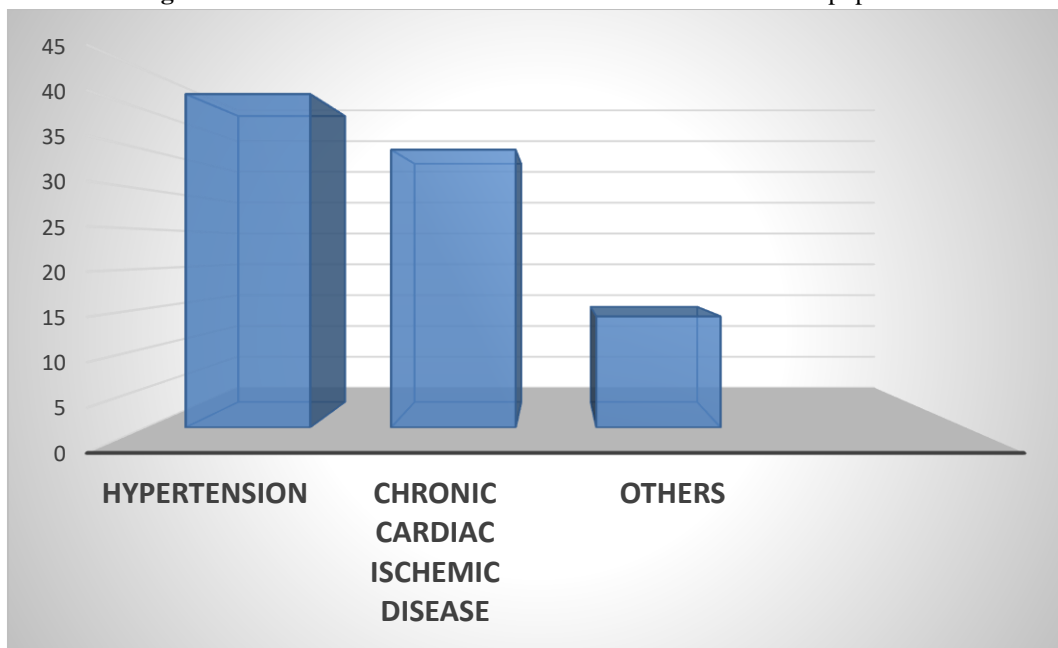
in women =71.89 years [SD 10.2]; mean age in men = 69.64 years [SD 9.35]. Median = 71 years.

Disease duration varied between 1 and 16 years in the studied group; mean 6.33 years [SD 2.98]. Mean disease duration in women was 6.25 years [SD=2.87]; mean disease duration in men was 6.35 years [SD=3.03] .

The most prevalent cardiovascular comorbidities identified in our study population were:

- arterial hypertension 42 patients (48.83%, 95%CI 38.27-59.39)
- chronic cardiac ischemic disease 35 patients – 40.69%, 95%CI 30.31-51.07)
- others: 14 patients 16.27%, 95%CI 4.47-24.07 (paroxysmal or chronic atrial fibrillation, aortic or mitral insufficiency, aortic stenosis, restrictive cardiomyopathy, cardiac failure, tachycardia, carotid endarterectomy, cardiac pacemaker, venous insufficiency).

**Figure 1:** Cardiovascular comorbidities identified in the studied population



The main cardiovascular comorbidities identified in male patients were:

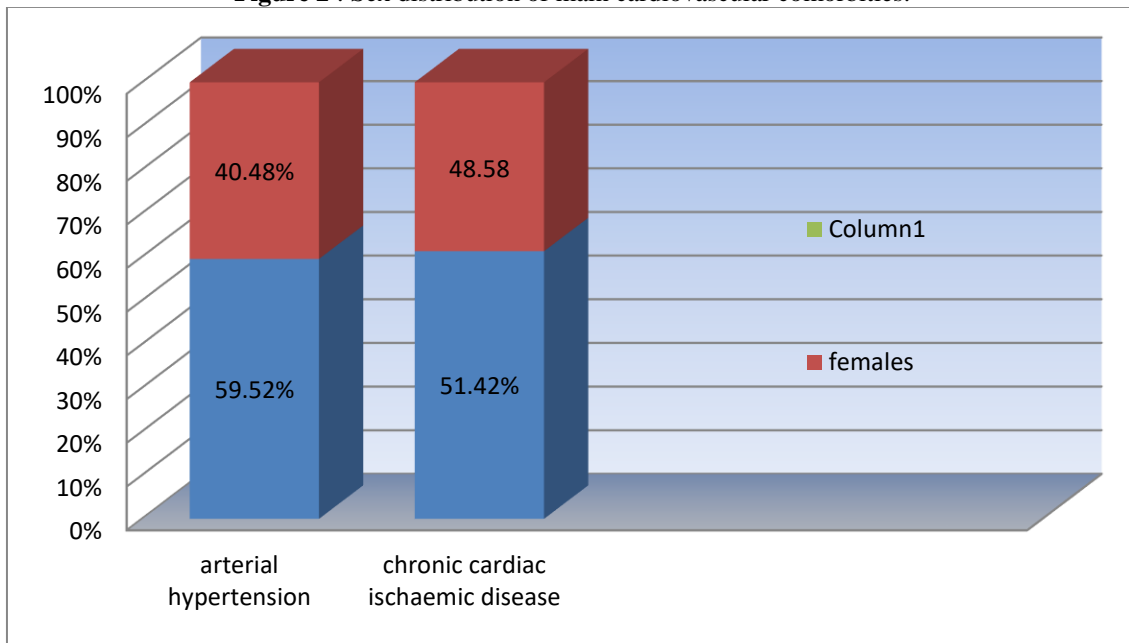
- arterial hypertension 52.08% (95%CI 37.95-66.21)
- chronic cardiac ischaemic disease 37.50% (95%CI 23.8-51.2)

The main cardiovascular comorbidities identified in female patients:

- arterial hypertension 44.73% (95%CI 28.92-60.54)
- chronic cardiac ischaemic disease 44.73% (95%CI 28.92-60.54).

Data analysis showed no statistically significant difference between males and females regarding the prevalence rates for both arterial hypertension (p=0.5) and chronic ischemic heart disease (p=0.5).

**Figure 2 :** Sex distribution of main cardiovascular comorbidities:



Reported values for hypertension prevalence in general population of Romania (according to SEPHAR III study results, assessed on a representative sample of 1970 adult subjects obtained by a multi-stratified sampling procedure) are 45.1 %<sup>9</sup>.

Chronic ischemic heart disease prevalence in general population in Romania has been estimated by CARDIO-ZONE study as 14.2% (cross-sectional study performed on 3124 adult subjects aged between 18 – 85 years, 61% female)<sup>10</sup>.

Comparing the prevalence values in Romanian general population for these two important cardio-vascular disorders with our study results leads to the conclusion that:

- arterial hypertension has been found not statistically significant more prevalent in studied Romanian parkinsonian patients than in general population ( $p=0.49$ );
- chronic ischemic heart disease were statistically significant more prevalent in studied Romanian parkinsonian patients than in general population ( $p<0.0001$ ).

A recent study conducted in the northern region of Romania, which aimed to assess the cardiovascular risk factors in 126 PD patients using laboratory tests (fasting blood glucose test, serum lipid fractions dosage), Doppler ultrasound, brain CT or MRI as well as an interview regarding the personal history of hypertension, diabetes, cerebrovascular and cardiovascular diseases, reported a prevalence of 58.73% for hypertension, with a slight predominance of female patients (65.38% vs 47.92%,  $P = 0.05$ ); carotid or vertebral atheromatosis was present in 30.95% and 22.22% of studied patients<sup>11</sup>.

<sup>9</sup> Dorobantu M, Tautu OF, Dimulescu D, Sinescu C, Gusbeth-Tatomir P, Arsenescu-Georgescu C et al. Perspectives on hypertension's prevalence, treatment and control in a high cardiovascular risk East European country: data from the SEPHAR III survey. *J Hypertens.* 2018 Mar;36(3):690-700

<sup>10</sup> Cinteza M, Pana B, Cochino E, Florescu M, Margulescu A, Florian A, Vinereanu D. Prevalence and control of cardiovascular risk factors in Romania Cardio-Zone national study. *Maedica* 2007, 2. 277-288

<sup>11</sup> Perju-Dumbravă L, Muntean ML, Muresanu DF. Cerebrovascular profile assessment in Parkinson's disease patients. *CNS Neurol Disord Drug Targets.* 2014;13(4):712-7

International studies dedicated to comorbidities prevalence rates assessment in PD reported also hypertension (41.1%) as being the most prevalent, followed by constipation (27.5%), coronary heart disease (25.1%) and painful conditions (21.7%)<sup>12</sup>.

It seems that hypertension not only increase the risk for clinically manifest PD but also have a defavourable effect on cognitive functions in the course of the disease<sup>13</sup>.

On the other hand, it has been showed that recognizing and treating earlier the cardiovascular dysfunction in PD could prevent sudden death in these patients<sup>14</sup>.

For a more appropriate therapeutic approach, some authors have even proposed that chronic comorbidities should be used for identifying PD subtypes and subsequently promoting individualized treatment for these patients (personalized medicine)<sup>15</sup>.

## **CONCLUSION**

Cardio-vascular dysfunction is quite a common condition in Parkinson's disease, very often symptomatic and leading to serious alterations of life quality in these patients.

Even further more complex studies are needed to elucidate this complex part of parkinsonian pathophysiology, the presented study revealed that the most prevalent cardiovascular comorbidities identified in the studied PD patients were arterial hypertension and chronic ardiac ischemic disease, with no statistically significant difference between males and females. Chronic ischemic heart disease were statistically significant more prevalent in studied Romanian parkinsonian patients than in general population

The continuation of the study, including more PD patients and more investigated clinical parameters, would increase the statistical significance of the results.

## **ACKNOWLEDGEMENTS**

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<sup>12</sup> McLean G, Hindle JV, Guthrie B, Stewart W, Mercer. Co-morbidity and polypharmacy in Parkinson's disease: insights from a large Scottish primary care database. *BMCNeurology*. (2017) 17:126 DOI 10.1186/s12883-017-0904-4

<sup>13</sup> Jones JD, Jacobson C, Murphy M, Price C, Okun MS, Bowers D. Influence of Hypertension on Neurocognitive Domains in Nondemented Parkinson's Disease Patients. *Parkinson's Disease*. Volume 2014, Article ID 507529, doi.org/10.1155/2014/507529

<sup>14</sup> Scorza FA, Fiorini AC, Scorza CA, Finsterer J. Cardiac abnormalities in Parkinson's disease and Parkinsonism. *J Clin Neurosci*. 2018 Jul;53:1-5. doi: 10.1016/j.jocn.2018.04.031

<sup>15</sup> Santiago JA, Bottero V, Potashkin JA. Biological and Clinical Implications of Comorbidities in Parkinson's Disease. *Front Aging Neurosci*. 2017; 9: 394. doi:10.3389/fnagi.2017.00394

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