Doctoral School of Interdisciplinary Medicine

EPIDEMIOLOGY OF PARKINSON'S DISEASE – QUALITY OF LIFE AS A CHALLENGE FOR REHABILITATION

PhD Thesis

Mária Markó-Kucsera

Supervisor:
Prof. Dr. Edit Paulik PhD

Department of Public Health
Faculty of Medicine
University of Szeged

Szeged
2020

LIST OF PUBLICATIONS

Publications related to the Thesis

I. Kucsera, M. (2012). A Parkinson-kór epidemiológiájának hatása a háziorvosi ellátásra. Medicus Universalis, 45(4), 149-151.

II. Kucsera, M., & Paulik, E. (2013). Risk of Parkinson's disease in southern great plain, Hungary. In G. Belojevic (Ed.) Proceedings of the First International Congress on Hygiene and Preventive Medicine, Belgrade, 22-24 May 2013, Serbian Medical Society, pp. 590-593.

III. Markó-Kucsera, M., Vécsei, L., & Paulik, E. (2018). Association of cardiovascular risk factors and Parkinson's disease – case-control study in South East Hungary. *Ideggyógyászati Szemle/Clinical Neuroscience*, 71(1-2), 57-62.

IV. Markó-Kucsera, M., Kullmann, L., & Paulik, E. (2018). Measuring quality of life in individuals with Parkinson's disease attending a self-help club: cross-sectional study in Hungary. International Journal of Rehabilitation Research, 41(1), 81-83.

List of citable abstracts related to the Thesis

I. Kucsera, M., & Paulik, E. (2013). Dance Therapy for Parkinson's Disease Patients. In Zs. Benkő, K. Tarkó & L. Lippai (Eds.) Leisure, health and well-being: Holistic Leisure and Health: Mid-term Conference of International Sociological Association, Research Committee on Sociology of Leisure (RC 13). Conference Abstracts, Szeged, Hungary, 18-20 September 2013, Szeged: SZTE JGYPK Alkalmazott Egészségtudományi és Egészségfejlesztési Intézet, pp. 68-69.

II. Kucsera, M., & Paulik, E. (2013). Epidemiology of Parkinson's disease. N*épegészségügy,* 91(3), 217.

III. Kucsera, M., Lad, D., & Paulik, E. (2014). Dietary habits and nutritional status of Parkinson's disease patients in Hungary. In C. Cotoraci & A. Ardelean (Eds.) 16th Danube-Kris-Mures-Tisa (DKMT) Euroregion Conference on Environment and Health: Book of Abstracts, Arad, România, 25-26 April Arad: "Vasile Goldis" University Press, p. 28.

IV. Kucsera, M., & Paulik, E. (2014). Életminőség és betegségteher, avagy élet a Parkinson-kórral. *Egészségtudomány,* 58(2), 97. Fiatal Higiénikusok Fóruma X. Pécs, Magyarország: 2014.05.14-2014.05.16.

V. Kucsera, M., & Paulik, E. (2014). The economic burden of Parkinson's disease in Hungary. *Népegészségügy,* 92(2), 122. Népegészségügyi Képző- és Kutatóhelyek Országos Egyesülete VIII. Konferenciája. Nyíregyháza, Magyarország: 2014.08.27-2014.08.29.

VI. Kucsera, M., & Paulik, E. (2016). Measuring quality of life in Parkinson's disease. *Népegészségügy,* 94(3), 163. Népegészségügyi Képző- és Kutatóhelyek Országos Egyesülete X. Jubileumi Konferencia. Debrecen, Magyarország: 2016.08.31-2016.09.02.

VII. Markó-Kucsera, M. & Paulik, E. (2017). A new opportunity in rehabilitation: self-help clubs for Parkinson's disease. In Department of Public Health Faculty of Medicine University of Szeged (Ed.) 19th Danube-Kris-Mures-Tisa (DKMT) Euroregional Conference on Environment and Health: Program and abstracts. Szeged, Magyarország, 2017.06.09-2017.06.10. p. 49.

VIII. Markó-Kucsera, M., & Paulik, E. (2017). Cardiovascular risk factors and Parkinson's disease in South-East Hungary. *Népegészségügy,* 95(2), 162. Népegészségügyi Képző- és Kutatóhelyek Országos Egyesülete XI. Konferenciája. Szeged, Magyarország: 2017.08.30-2017.09.01.

Table of Contents

List of abbreviations

ALS	Amytrophic lateral sclerosis
ANOVA	Analysis of variance
BMI	Body mass index
CBT	Cognitive behavioural therapy
CI	Confidence interval
DIY	Do It Yourself
ELEF	European Population Health Survey
EU	European Union
FINRISK	Large Finnish Population Survey on Risk Factors
GP	General practitioner
IBM SPSS	Special software platform for the statistical analysis
ICD	International Classification of Diseases
KSH	Hungarian Central Statistical Office
LDL	Low density lipoprotein
MNA	Mini NutritiJonal Assessment
MNS	Median nerve simulation
OR	Odds ratio
PD	Parkinson's disease
PDQ-39	Parkinson's Disease Questionnaire – 39
PDQOL	Parkinson's Disease Quality of Life
PDQUALIF	Parkinson's Disease Quality of Life Scale
PEPP	Patient Education Programme for Parkinson's Disease
QoL	Quality of life
RR	Relative risk
SD	Standard deviation
WHO	World Health Organisation
WPP's	World Parkinson's Program

1. Introduction

According to the current knowledge in medicine, Parkinson's disease or "paralysis agitans" is an incurable but treatable neurodegenerative disease. It is a neurological disease with slowly progressing movement disorders. James Parkinson (1755–1824) was the first to describe the disease; thus, the disease is named after him. Parkinson's disease poses a very complex problem system for researchers and clinicians, as its diagnosis is sometimes less clear, the cure is still pending, and there are many symptoms and accompanying problems in the lives of Parkinson's patients that are very challenging to live with in everyday life. In many cases, the physicians tend to focus only on physical symptoms, but in the enchantment of organ system function, it might be forgotten that patients who are mentally healthy are also challenged by a disease that they must be able to live with for several years knowing that their condition will get worse over time.

Parkinson's disease (PD) is a long-term degenerative disorder of the central nervous system. It has the second highest incidence in neurodegenerative diseases in the world, caused by the selective loss of nigrostriatal dopaminergic neurons (Komoly & Palkovits, 2018) (Figure 1). These neurons are responsible for voluntary and involuntary motor functions; thus, in their absence, the classic symptoms of PD, such as tremor, muscular rigidity, bradykinesia, and postural imbalance are manifested.

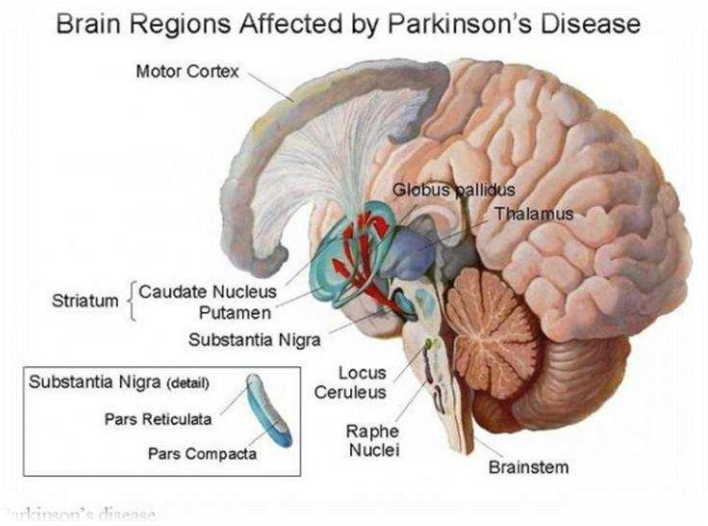

Figure 1. The pathophysiology of Parkinson's disease.

Source of figure: http://www.doctortipster.com/10054-parkinson-disease-pathophysiology-and-causes.html

The etiology of the disease is still not completely understood, but it is suspected that the pathological process of the disease is mainly due to the combination of genetic and environmental factors. Several studies have attempted to investigate the association between Parkinson's disease and environmental risk factors, such as air pollution, certain infectious diseases, or toxic harm.

The immune system may be the nexus between environmental and genetic factors; some infectious agents may be involved as triggers in the pathogenesis of PD (Caggiu et al., 2019). Toxoplasma infection as a risk factor of Parkinson's disease and Alzheimer's disease has been investigated in a meta-analysis model; there was no significant association between Toxoplasma gondii infection and PD, but there was marginally significant association between Toxoplasma infection and Alzheimer's disease (Bayani et al., 2019). Limphaibool et al. (2019) have reviewed several infectious agents as etiological factors of PD; indeed, studies from recent years have demonstrated the independent association between specific pathogens (e.g., influenza A virus, herpes simplex virus 1, Epstein-Barr virus, and varicella-zoster virus) and PD.

Various studies have investigated the effects of environmental toxic exposure on PD. The most frequently studied aspect is exposure at workplace, pesticides in agriculture, or chemical substances or permanent contact with heavy metals. Gamache et al. (2017) have found a clear correlation between exposure to pesticides and earlier onset of PD (55.1 year old vs. 59.2 year old; $p=0.003$), and former welders also have a premature onset (54.3 year old vs. 58.4 year old; $p=0.03$). The environmental factors, such as manganese, lead, and pesticides (e.g., paraquat), have been studied by Ball et al. (2019), and they conclude that individual susceptibility to environmental factors plays a large role in PD etiology.

In many cases, rural or urban life has been examined as a higher risk for PD; however, the results are contradictory. On the one hand, rural life is a predominant risk to the agricultural population considering the use of pesticides, but on the other hand, research has also shown that air pollution is a non-negligible risk for the urban population. It is also important to consider the fact that in many regions of Hungary, the average age of the population in smaller rural settlements is higher than in larger cities, and it may distort the results as the incidence and prevalence of PD significantly increase with age (Finkelstein & Jerrett, 2007; Ritz et al., 2010).

Based on the above findings, a multitude of researchers from all over the world are attempting to reveal the cause of Parkinson's disease, and thus aiding patients in being provided a more effective healing.

The signs and symptoms of PD involve progressive cardiovascular autonomic failure, orthostatic hypotension, postprandial intestinal motility and disorders, sexual dysfunction, and urinary incontinence. The disease is predominated by symptoms and signs of the autonomic nervous system, and the rate of deterioration of this system exceeds that of the motor system (Bokor, 2001).

It is a progressive disorder of the nervous system that affects movement; the symptoms start gradually, sometimes the patient has only tremor in one hand. The diagnosis is very difficult to establish because the incidence and severity of the symptoms are very diverse; tremors are common, but the process may also commonly cause stiffness or slowing of the movements.

In the early stages of PD, the patient's face may show little or no expression of their emotion, the arms may not swing until walking. These symptoms are worsening as the patient's condition progresses, and thus, the quality of life is decreasing.

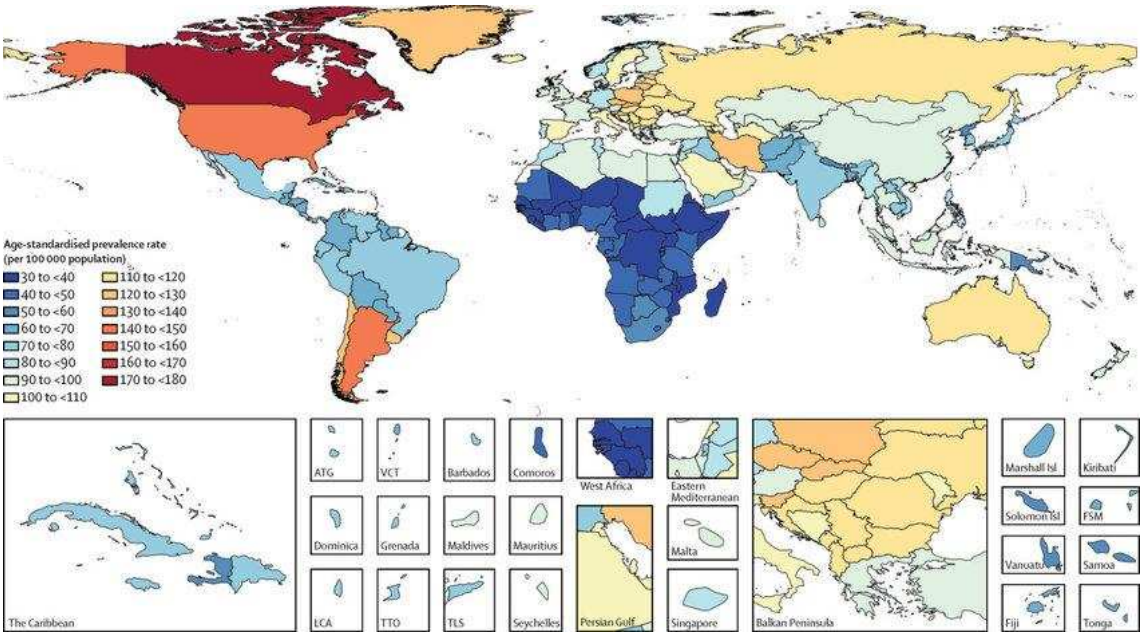

Figure 2. Age-standardized prevalence of Parkinson's disease per 100,000 population (2016)

Source of figure: Figure 1 in GBD 2016 Parkinson's Disease Collaborators (2018), p. 10

Signs and symptoms of PD can be different for everyone, but the early symptoms may be mild and go unnoticed. Symptoms often begin on one side of the patient's body and usually remain worse on that side, they might appear on both sides, but the side where they started always remains dominant in this sense.

PD is a common neurodegenerative disease in the world population (de Lau & Breteler, 2006). The incidence of PD is forecast to be doubled by 2030, primarily as a result of the ageing of the population. According to the European Brain Council Survey, 1.2 million people have been affected by PD in Europe (Figure 2). The economic and social costs of PD are sufficiently high, an estimated 13.9 billion Euros all across Europe, whereas the overall estimates of annual cost for PD, together with the cost of the treatment of the disease is 35 billion Euros (European Brain Council) (Olesen et al, 2006).

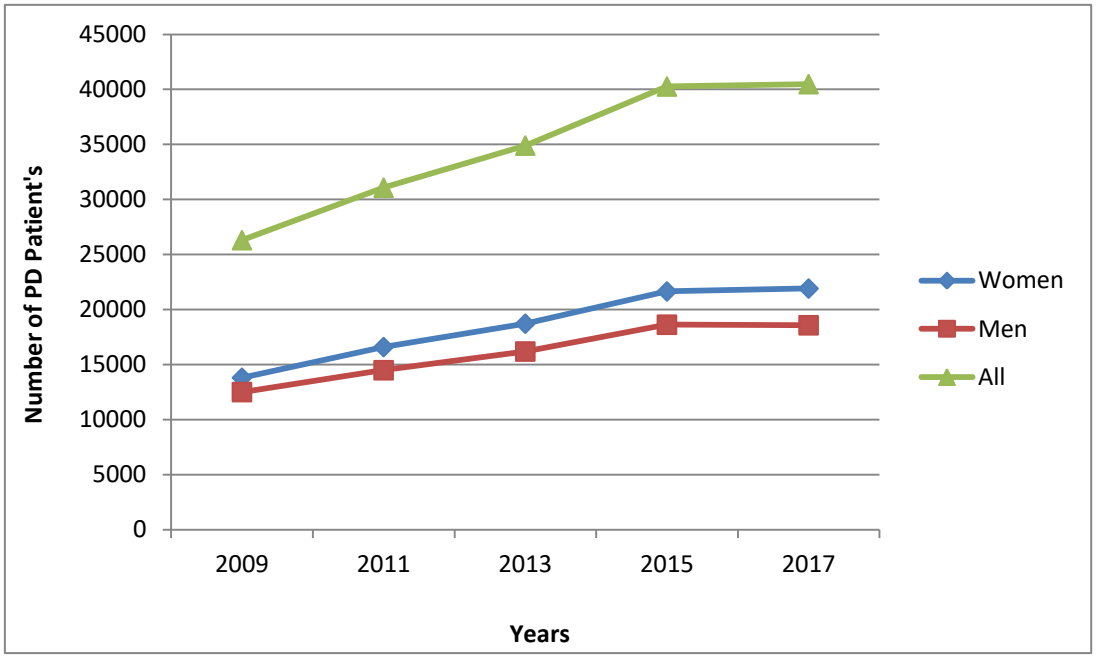

Figure 3. Parkinson's disease in Hungary (General practitioners' database)

Source: KSH, 2010-2018: Some diseases of persons aged 19 and over registered at the general practitioners' service.

In the Hungarian literature, the number of Parkinson's patients is estimated at around 20,000, but the Hungarian Centre Statistical Office data collected from general practitioners (GPs), generated from GP software highlight that this number is twice as high as it was previously estimated (Figure 3).

1.1. Classification of Parkinson's disease

Parkinsonism is classified into four main categories by the World Parkinson's Program (2016).

1. Primary Parkinsonism (idiopathic)
   - Sporadic and genetic PD
2. Secondary Parkinsonism (acquired)
   - Drug-induced: antipsychotics, such as dopamine receptors blocking drugs, antiemetics, such as metoclopramide, dopamine depleting drugs, such as reserpine, tetrabenazine, alpha-methyldopa, lithium, flunarizine, and cinnarizine
   - Infection: post-encephalitic
   - Toxins: MPTP, CO, Mn, Hg, and CS_2
   - Vascular: multi-infarct state of brain
   - Trauma: pugilistic encephalopathy
   - Hemiparkinsonism– hemiatrophy syndrome
   - Brain tumors in certain locations, such as the basal ganglia
   - Hydrocephalus
   - Hypoxia
   - Metabolic
3. Atypical Parkinsonism
   - Progressive supranuclear palsy
   - Multiple system atrophy
   - Corticobasal ganglionic degeneration
   - ALS-Parkinsonism/Dementia – complex of Guam
4. Familial neurodegenerative diseases
   - Huntington's disease
   - Wilson's disease

- Hallervorden–Spatz disease
- Olivopontocerebellar and spinocerebellar degeneration
- Familial basal ganglia calcification
- Familial Parkinsonism with peripheral neuropathy
- Neuroacanthocytosis

Proper classification is important during healing and epidemiological investigations as well.

1.2. Aim of the study

The overall aim of the study is to give a more detailed analysis of the epidemiological aspects of PD patients in Hungary.

Specific research aims:

- to analyze the clinical data and to characterize how certain risk factors/diseases (hypertension, diabetes, dyslipidemia, and obesity) affect PD in patients treated at the Neurology Department, Albert Szent-Györgyi Clinical Centre, University of Szeged;
- to measure the quality of life (QoL) of PD patients and to determine whether self-help groups may influence the quality of life and health behavior of Parkinson's patients. We consider that the concept of quality of life (QoL) is multidimensional and many factors may have an effect, such as those connected to the individual, social networks, the environment and society, but health status is also a key factor in determining how good a person's QoL is. Our study focuses on a special group of PD patients who are attending a "PD Club" in Szeged and Budapest.

Our working hypotheses were the following:

1. There is a correlation between cardiovascular diseases and PD.
2. Obesity and diabetes mellitus are significantly related to Parkinson's disease.
3. Alternative rehabilitation methods have a positive effect on the quality of life of PD patients.

2. Literature review

2.1. Epidemiology of Parkinson's disease

Currently, PD affects the life of a high number of people in Europe and in the whole world (Andlin-Sobocki et al., 2005). The European Brain Council Survey declares that 1.2 million people have been affected by PD in the study area (including the 28 EU countries as well as Iceland, Norway, and Switzerland). Because of the frequent occurrence of PD, the economic and social costs are sufficiently high, an estimated 13.9 billion Euros all across Europe (Olesen et al., 2012).

Gerlach et al. (2012) have examined 684 patients with PD in the Netherlands. They have revealed that 18% of the patients had been hospitalized at least once in the last year. The most common causes of inpatient care were traumatic injuries (24%), urinary symptoms (15%), gastrointestinal problems (15%), and diseases of cardiac origin (12%).

The prevalence of primary or idiopathic PD increases proportionally with age (Gazewood et al., 2013), and several studies analyzed the prevalence of PD from the point of age and gender differences. A systematic review and meta-analysis has examined the incidence of PD and its variation by age and gender (Hirsch et al., 2016). This study highlights that the incidence of PD has been increasing with age in both men and women. The gender analysis demonstrates that males had a higher incidence of PD in all age groups, but this difference was statistically significant in the 60 to 69 and the 70 to 79 year old patients ($p<0.05$) (Hirsch et al., 2016). A cross-sectional survey has identified sex differences in the quality of life of PD patients and highlighted the need for increased sex-specific clinical assessment and management of PD (Lubomski et al., 2014). Estrogen can act as a neuroprotective agent (Zárate et al., 2017), in females the number of children, age at menarche, and age at menopause are positively associated with a delay of PD (Frentzel et al., 2017). Smith & Dahodwala (2014) have described that estrogen and selective estrogen receptor modulators have neuroprotective role in PD.

Genetic factors are responsible for ~10–15% of all PD diseases; seven different genetic factors have been identified which are responsible for the development of familial PD: the alpha-synuclein (SNCA), glucocerebrosidase (GBA), RBR E3 ubiquitin protein ligase (PARK2), leucine-rich repeat Kinase 2 (LRRK2), vacuolar protein sorting-associated protein 35 (VPS35) parkin, phosphatase and tensin homolog-induced Kinase 1 (PINK1), and

Parkinson protein 7 (PARK7) (Verstraeten et al., 2015). Human genotypes are distinct from each other and affect individuals exposed to the same environmental factor, resulting in different diseases (Baye et al., 2011).

The coincidence of metabolic disorders and PD has also been analyzed in several studies. A relationship between diabetes and PD has been revealed by Schernhammer et al. (2011) in Denmark. The Danish population-based case-control study showed that diabetes was associated with a 36% increased risk of PD. By gender, the odds of the development of the disease was higher in women (OR=1.50) than in men (OR=1.29) (Schernhammer et al., 2011).

Jones et al. (2017) have described that PD and cardiovascular risk factors are independent risk factors for cognitive impairment. Thus, PD patients with cardiovascular risk factors may be vulnerable to impairments in executive functioning, memory, processing speed, and language. In a study of 5888 participants, 154 cases of PD were identified with ECG abnormalities (Odds Ratio: 1.45, 95% CI: 1.02–2.07, p = 0.04) or any carotid stenosis (OR: 2.40, 95% CI (1.40–4.09, p = 0.001)); the risk for the incidence of PD was higher in baseline; however, the variability in orthostasis and heart rate was not a significant predictor (Jain et al., 2012).

2.2. Parkinson's disease and risk factors

2.2.1. Vascular risk factors

Presently, several epidemiological studies search for how vascular risk factors, such as diabetes mellitus or hypercholesterolemia affect the occurrence of PD. Studies describing the relationship between diabetes and PD have shown controversial results. A large multicenter analysis in Germany shows that the metabolic control of PD patients is better than that of patients with type 2 diabetes (Scheuing et al., 2013).

Other studies have found positive association between diabetes and the risk of developing PD (Schernhammer et al., 2011; Xu et al., 2011; Kotagal et al., 2013). The Danish study mentioned above has detected a 36% increased risk of developing Parkinson's disease (OR 1.36 [95% CI 1.08–1.71]), and similarly, diabetes defined by the use of any antidiabetics was associated with a 35% increased risk for Parkinson's disease (1.35 [1.10–1.65]) (Schernhammer et al., 2011). These results have been confirmed by a biomarker analysis showing that diabetes and PD are strongly linked at the molecular level (Santiago & Potashkin, 2013).

The association between the risk of PD and hypercholesterolemia has been described by several studies, but those results are also controversial. Some studies have found an inverse relationship between hypercholesterolemia and the risk of PD (Huang et al., 2011; Cassani et al., 2013; Mounika et al., 2012). Whereas a systematic review has stated that the results are inconsistent, and further studies are needed (Hu et al., 2010). Other studies have investigated the associations between hypertension and antihypertensive drugs, and the risk of PD (Louis et al., 2009; Ritz et al., 2010; Qiu et al., 2011). Louis et al. (2009) could not identify evidence of a protective effect of antihypertensive drugs in PD, whilest Ritz et al. (2010) have suggested that there is a potential neuroprotective role of centrally acting L-type calcium channel blockers of the dihydropyridine class in PD. Qui et al. (2011) have found that high to normal blood pressure and hypertension are associated with an increased risk of PD in women, but there is no significant association identified in men.

2.2.2. Environmental contributors

Several environmental toxins have been identified playing a role in the development of PD, but the data are contradictory, and as mentioned earlier, there should be a multiplicity of factors leading to the development of genetic and environmental factors in PD. Some studies suggest that the incidence of PD may be related to occupational exposure to chemicals (Elbaz & Moisan 2016; Pezzoli & Cereda, 2013; Gamache et al., 2017).

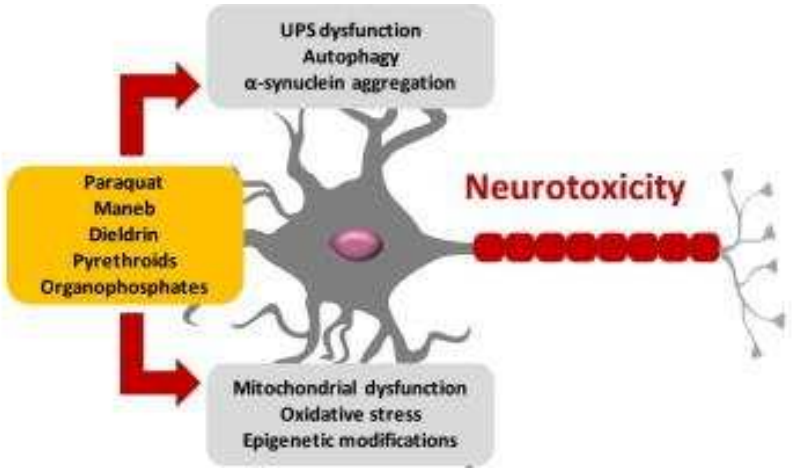

Figure 4. Pesticide exposition and neurotoxicity.

Source of figure: Graphical abstract in Baltazar et al., 2014, p. 85.

Pesticides have long been in the focus of PD risk factor sudies (including insecticides and herbicides); they are considered major disease-causing vectors all over the world in agriculture (Baltazar et al., 2014; García-García et al., 2016). Pesticides have been thoroughly studied as they are capable of influencing neurological changes in the brain, leading to the destruction of dopamine-producing neurons (Elbaz et al., 2009), which may result in the induction of PD. Commonly tested pesticides include organochlorides and organophosphates, as well as dieldrin, a well-known organochlorine pesticide that increases the risk of PD since it affects the central nervous system and causes neurotoxic damage in the dopaminergic system (Figure 4) (Kanthasamy et al., 2005). However, most of the studies have been carried out in animal models, and it should be highlighted that the correlation between human diseases is only estimated at 60% (Hartung, 2008). Regardless of this, the relationship between pesticide damage and PD should be contemplated as with all toxic harms, the duration of exposure and the dose strongly influence the output.

2.2.3. Overweight and lifestyle factors

Numerous studies have examined the relationship between dietary habits and Parkinson's disease. Several studies described the problem of malnutrition, as in many cases, difficulty in swallowing, distortion of the chewing reflex, and suffocation due to stuck of food in the pharynx require a special diet, which may be a reason why most patients suffer from weight loss and low body weight (Barichella et al., 2017; Cassani et al., 2017; Cumming et al., 2017; Shidfar et al., 2016).

In a study in China, 10 prospective studies were analyzed (Nam et al., 2018), and the results show that 5 kg/m^2 increase in BMI is not associated with PD risk, with a cumulative RR of 1.00 (95% CI: 0.89–1.12). However, an association has been found for alcohol consumption, with one-week positive association (RR: 1.13, 95% CI: 0.99–1.29). The meta-analysis performed shows no significant association between overweight ($25.00\ kg/m^2 \leq BMI \leq 29.99\ kg/m^2$), obesity ($BMI \geq 30\ kg/m^2$) or overweight ($BMI \geq 25\ kg/m^2$) and PD risk. Thus, this meta-analysis does not support the assumption that higher BMI significantly increases the risk of PD.

In PD, weight loss is a major non-motor property that is affected by severe homeostasis, a complex physiological process that will be abnormal in PD patients and lead to weight change (Sharma & Lewis, 2017). This change in weight is quite varied, while both low and high body

weight have been considered as risk factors for PD. As mentioned above, low body weight is common, but a small percentage of patients begin to gain weight. For many clinical parameters, such as older age, worsening cognitive function, the severity of the disease, and the imbalance in food intake determined by a feeling of satiety and hunger hormones can lead to weight loss. Low body weight and weight loss have a negative impact on the disease by exacerbating dyskinesia, negatively affecting the quality of life, and adversely affecting disease-related mortality. Olfactory impairment has been shown to adversely affect the maintenance of ideal body weight early in the disease. Patients with more severe loss of smell have significantly greater weight loss than patients who do not have this symptom, or only at a later stage of the disease. Losing weight in PD patients is not an esthetic problem, it has a serious impact on quality of life and disease progression, as the decline in motor function is more pronounced in the event of a physical decline that is obviously accompanied by a loss of muscle mass (Sharma & Lewis, 2017).

Studies suggest that the causes of PD are due to the complex interplay of genetic and environmental factors mentioned above, including oxidative stress, mitochondrial dysfunction, neuro-inflammatory factors, which can lead to dopaminergic effects (Mazon et al., 2017).

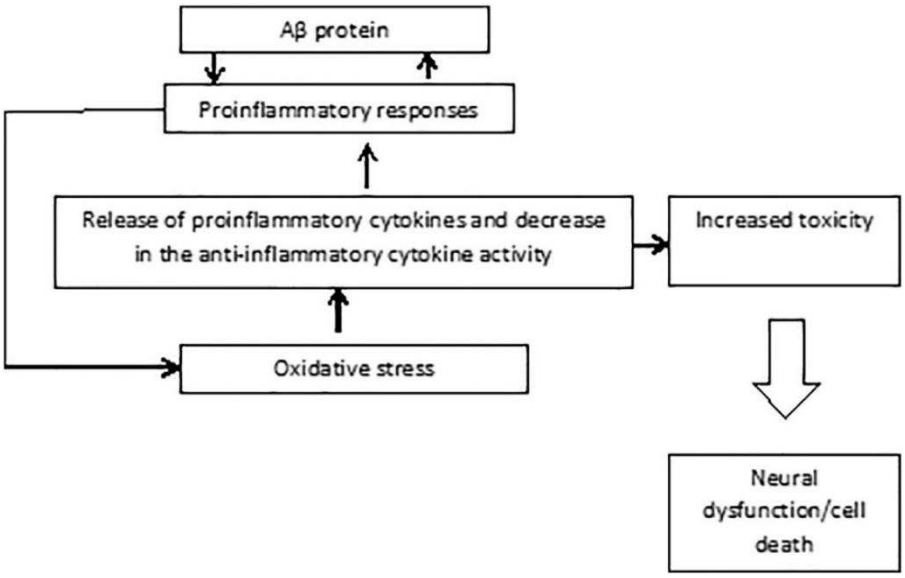

Figure 5. Oxidative stress and neural dysfunction circle.
Source: Mazon et al., 2017,
https://www.sciencedirect.com/science/article/pii/S002432051730276X?via%3Dihub

Oxidative stress is defined as an imbalance of anti- and pro-oxidative reactions in favor of the pro-oxidant. These factors interact with each other in a vicious cycle to produce an inflammatory response with oxidative stress and increased toxicity, releasing inflammatory cytokines, which have been shown to lead to nerve dysfunction and eventually to neurodegeneration (Figure 5).

There is a great deal of effort to counteract or slow down the progression of PD, since the disease cannot be cured but can only be slowed down; stress, autophagy, and DNA repair mechanisms may result in future therapeutic goals.

One study looked at how eating habits affect body weight in PD patients (Barichella et al., 2017). The study group received systematic nutritional care and counselling, and these results were compared with healthy controls. The survey was conducted by using a questionnaire of 66 dietary habits. Energy balance, constipation, levodopa (a drug used in the clinical treatment of PD) dose, and related motor complications in PD patients have also been studied. The results showed that PD patients had lower BMI, with higher food intake reported in the questionnaire than the control group. Thus, BMI was inversely related to the duration and severity of the disease and to motor complications associated with levodopa, whereas energy uptake was positively related to these variables. This study concluded that treatment should always focus on energy intake, maintain nutritional status, optimize levodopa therapy, and minimize associated motor complications.

These examples also show that monitoring the nutritional status and eating habits are extremely important in the treatment and rehabilitation of PD. Studies clearly show that malnutrition has to be addressed in the progression of the disease, as it has a decisive impact on everyday life, the severity of motor symptoms, and quality of life. Therefore, many studies focus on the importance of employing a dietician in the medical team to assist patients and their relatives. Proper patient education is essential to be aware of the principles of good nutrition and counting calories.

Some studies have been conducted on the reverse causation of smoking and PD. However, tobacco harm is not exclusively caused by cigarettes, since this group includes those who use the so-called snus, which is either chewed or consumed with a filter placed on the oral mucosa.

The inverse relationship between the use of snus and the risk of PD has been established by several studies. Benedetti et al. (2000) have reported a PD odds ratio of 0.18 (95% CI: 0.04,

0.82) for the prevalent chewing or snus use of tobacco. O'Reilly et al. (2005) have described that the current use of snus reduced the risk of PD mortality (HR = 0.24, 95% CI: 0.08, 0.75) compared to controls who had never smoked. A biological explanation for the association is also found in a study conducted by Hong et al. (2009). Nicotine and hydroquinone, the compounds in cigarette smoke, can stabilize soluble oligomeric forms of alpha-synuclein (a protein abundant in the brain).

Smoking and tobacco harm in patients with Parkinson's disease cannot simply be interpreted as risk factors as in some cardiac or vascular disorders, since all studies report an inverse proportionality. Nonetheless, it is inappropriate to label smoking as a protective factor in this disease. After all, based on the National Health Insurance Fund of Hungary Report of 2013, the prevalence of PD in Hungary is 100–200 per 100,000 inhabitants, and lung cancer, which is clearly related to smoking, remains the leading cause of cancer deaths in the same year. Thus, despite its protective effect, the goal is still to support the cessation of smoking in PD patients (Kásler et al., 2017).

In particular, the relationship between alcohol consumption and PD is unclear, and many articles describe alcohol as a protective factor, similarly to smoking. It is difficult to isolate the effect on one another because seeral studies have stated as a limitation of the research that these harmful habits are at the same time difficult to interpret. In the case of alcohol and PD patients, methodologically, the selective recall error and bias were higher. Thus, overall, no clear conclusion can be made regarding the relationship between alcohol consumption and PD, particularly in terms of harm (Bettiol et al., 2015).

2.3. Quality of life and Parkinson's disease

Finding out what quality of life is and discovering its components more and more is an important task in medicine, as the subjective quality of life of a patient is very important for the outcome of certain diseases and an excellent feedback on the success of certain therapeutic and rehabilitation procedures. If we know and are able to identify the synthesis of which elements contributes to the quality of life, then it is more likely to achieve the desired level. Quality of life and well-being are synonymous in that they express the broader meaning of welfare.

> "The WHO defines Quality of Life as an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a

> complex way by the person's physical health, psychological state, personal beliefs, social relationships and their relationship to salient features of their environment."
> (WHO, n.d.-a)

The term quality of life in the medical sense can refer to a group of patients as well as a personal report. Both self-administered and helper-completed questionnaires can be used for measuring quality of life. Basically, the self-administered format should be preferred, but if the patient is disabled for any reason, an interviewer should assist the patient. The highest level of validity should always be sought when measuring quality of life. To this end, the use of validated questionnaires developed for the given language is recommended. Perhaps the most well-known of these is the WHOQOL, developed by the WHOQOL Group with fifteen international field centers, in order to develop a culturally applicable quality of life assessment that enables its application all around the world. Continuous improvements have been made for people with HIV (WHOQOL-HIV) and 32 additional tools have been developed to assess aspects of spirituality, religiosity, and personal belief (WHOQOL-SRPB) (WHO, 2002; WHO, n.d.-a).

Investigating the quality of life of patients with Parkinson's disease is an extremely important and interesting area of science, as this disease is a constantly deteriorating condition that is currently incurable. It influences an individual's personal capacity and social relationships, and thus, his or her complete individuality. Quality of life for PD is tested by using a special set of questions developed for this patient group.

Many studies have used the validated PDQOL questionnaire to test the effectiveness of therapeutic and rehabilitation procedures. In our own research, this choice was made because, in addition to measurable parameters, the subjective feeling of social support and the quality of everyday life are very persuasive feedback in the case of a chronic neurodegenerative disease.

Individual scales have also been developed by de Boer et al. (1996). It was introduced in 1996 on the PDQOL scale, and it consists of 37 items covering four areas, such as the symptoms of PD, which include the side effects of levodopa; the "systemic" symptoms (7 items), emotional sphere (9 items), and social functions (7 items). In the test, the patients are asked about the frequency of the elements of the above-mentioned problem on a scale of 1 to 5.

Calne et al. (1996) have also developed a measurement tool called the Parkinson's Impact Scale (PIMS). A five-item scoring system (0 = no change, 1 = low effect, 2 = moderate effect,

3 = average, strong influence, and 4 = strong influence) can be used by the patients to estimate the impact of the disease on the ten spheres of life. These spheres are: 1) phenomena of positive self-esteem (self-esteem, happiness, and optimism); 2) self-esteem of negative influences (levels of stress, anxiety, or depression); 3) family relationships; 4) environment; 5) work; 6) leaving home (work, meetings, etc.); 7) leisure and recreation; 8) safety (avoiding injuries); 9) financial security; and 10) sex.

Chronologically, the most recent methodological tool is the Quality of Life Scale (PDQUALIF) developed by Welsh et al. (2003). The questionnaire consists of 33 items covering eight delicate areas: viability and improvement of life, sexuality, lifestyle, worldview (outlook), physical fitness, vitality, urinary function, and overall quality of life. The rating system consists of a five-point Likert scale from 0 to 5, (Welsh et al., 2003) and a final score from 0 to 128.

In medical research, the health-related quality of life concept, which specifically focuses on the impact of illness and the subjective well-being or satisfaction with life, has often been used (Jaracz & Kozubski, 2003). The QoL in PD is affected by the motor-syndrome, non-motor symptoms, and the treatment effects. The above-mentioned pathologies can generate very significant life deterioration in patients. One of the PD specific QoL measures was developed in 1995 (Peto et al., 1995). The 39-item Parkinson's Disease Questionnaire (PDQ-39) examines the daily living factors that influence the quality of life along eight dimensions. The PDQ-39 has been further developed on the basis of interviews with PD patients and large-scale surveys (Jenkinson et al., 1997). This questionnaire has been applied in several studies in Europe: in Estonia (Kadastik-Eerme et al., 2015), in Spain (Berganzo et al., 2016), and in the Netherlands (Marinus et al., 2008), and Yamanishi et al. (2013) have carried out a study on 117 Japanese participants with PD. The Hungarian version of PDQ-39 was adopted and validated in 2001 by Fazekas and Kullmann (2001), and the Hungarian version has been used by Tamás et al. (2014) to measure the QoL of 110 individuals with PD.

2.4. New trends in rehabilitation

For Parkinson's patients, the development of a special rehabilitation program could expand the range of multifunctional treatment options that would not only improve the quality of life of patients, but in this way, doctors, psychologists, physiotherapists, social workers, and other health professionals can improve the quality of their work. For PD patients, rehabilitation is of

paramount importance, as motor and non-motor symptoms can be alleviated with an appropriate rehabilitation plan. If international examples are taken as the basis for national care, not only the treatment could become more varied, but also the formation of professional teams involved in the development of rehabilitation could also help provide patients with more effective care.

The difficulty of initiating a proper rehabilitation process is the difficulty in dealing with PD. In many cases, due to prolonged, uncertain symptoms, the initiation of appropriate therapy may be delayed. In all cases, starting a rehabilitation program may begin after the diagnosis is established and therapy is initiated followed by the consultation with the rehabilitation team.

Patients' rehabilitation usually includes the following programs (Calleo et al., 2012):

- Increasing muscle strength and flexibility; getting up from a chair, performed during physical activity sharing attention.
- Practicing fine motor skills (handwriting), development of abilities to express thoughts (breath control, vocalization, speech, drawing, DIY, and computer use).
- Cognitive abilities (attention, imagination, memory, executive functions, and visual spatial integration) and problem solving.
- Developing and maintaining stress control, self-regulation, autonomy, and personal decision-making.

It is very difficult to start the rehabilitation process in some cases, depending on the patient's mental state, the personal struggle with the mere fact of the disease, the social support from his/her family, and the possibility of major depression. PD patients, by their nature, often struggle with depression, anxiety, and mental problems. Their treatment also has a decisive influence on the rehabilitation process, as maintaining motivation is crucial for the patient. In addition to mental health professionals, the family and self-help groups, as well as supportive patient organizations may play a huge role in this process.

In the psychotherapeutic care of Parkinson's disease, not only the patients but their relatives and friends should also be involved to achieve a higher success rate. As stated above, the disease is accompanied by reduced physical and mental performance; thus, it is difficult for the person concerned to accept this new situation and his/her illness. All these factors can put a heavy psychic burden on the environment (spouse / partner / caregiver). It is especially important to facilitate the communication between the parties. Cognitive behavioral therapy (CBT) may also be very effective. Due to the mechanism of action of CBT, there is strong

empirical evidence for better results in the treatment of mood and fear disorders. CBT is based on the regulation of emotions through thought and behavior (Cully & Teten, 2008). As is discussed above, one of the main symptoms of Parkinson's disease is depression. CBT is the most studied psychosocial treatment form of depression that is present in other neurological disorders (such as epilepsy and multiple sclerosis) and in many other diseases, indeed, it can also be adapted to treat depressive symptoms, and its implementation into the care has been suggested (Farabaugh et al., 2010, Wichowicz et al,. 2006).

Some new research examines PD patients' sense of pain associated with illness in the light of physical activity and quality of sleep. For example, Nguy et al. (2020) have pointed out that improving the sleep quality of PD patients would be of paramount importance as it affects mental well-being and the sense of daily pain.

2.4.1. Scope of education

Education is an extremely important area of rehabilitation. Both the patient and the relatives should be involved in the process. The Patient Education Program Parkinson (PEPP) is a structured, specific, and psychosocial educational process for Parkinson's patients and for their guardians. The PEPP program was developed by professionals working in the fields of neurology and psychology, seven specialists from various countries (Estonia, Finland, Germany, Italy, the Netherlands, Spain, and the United Kingdom). The program is a systematic and professional way of supporting patients and their family (in separated groups) (A'Campo 2011; Udow et al., 2017).

2.4.2. Music and dance therapy

A modern form of Parkinson's disease rehabilitation is music therapy, which involves systematic interventions promising extraordinary therapeutic benefits. It is used in hospitals, rehabilitation centers, special schools, and hospice activities. It is recommended as it improves social, psychological, intellectual, and cognitive performance. It reduces the fear, depression, anxiety of the patients, and improves being relaxed. Systematic use of music changes emotional state, motor ability, and bradykinesia, which may all contribute to improved quality of life (Raglio et al., 2015; Sihvonen et al., 2017; Leonardi et al., 2018).

Dance and conscious guided movements are among the most effective ways to counteract the effects of Parkinson's disease. This disease is less affected by the parts of the brain that control conscious, planning-related movements; thus, avoiding damaged brain circuits, as a

solution, may activate, utilize, and invite the healthy parts to perform the gesture. This instrumental feature of conscious guided movement and the rhythmic properties of music can be highly beneficial for Parkinson's patients (Westheimer et al., 2015). Keeping the brain in training is the main goal, and it might be achieved by dancing and movement. One of the tools for maintaining an active lifestyle, life affection, avoiding depression, and maintaining a positive outlook in life is proper special movement, dance, and the feeling of belonging to somewhere. Conscious movement, active participation in group relationships, and life-affection could all influence the course of the disease (de Dreu et al., 2015; McNeely et al., 2015; Allen et al., 2017, Wichowicz et al., 2006).

The above examples may support the idea that PD rehabilitation is a diverse field. We have several common tools that can help patients. Studies on the use of nintendo wii in neurorehabilitation have also been reported, with a pronounced benefit for PD patients in improving stability. These types of rehabilitation may bring some change not only to the patients' life, but they might also provide an opportunity for the family to be actively involved in the healing process (Negrini et al., 2017).

3. Materials and methods

Three main stages of the research can be distinguished (see Figure 6). In the first stage, the research was planned and prepared, in the 2nd stage we performed a case-control study based on patient documentation among the patients treated in the university hospital, and in the 3rd stage, we examined the quality of life and health behavior of patients attending the Parkinson's Club.

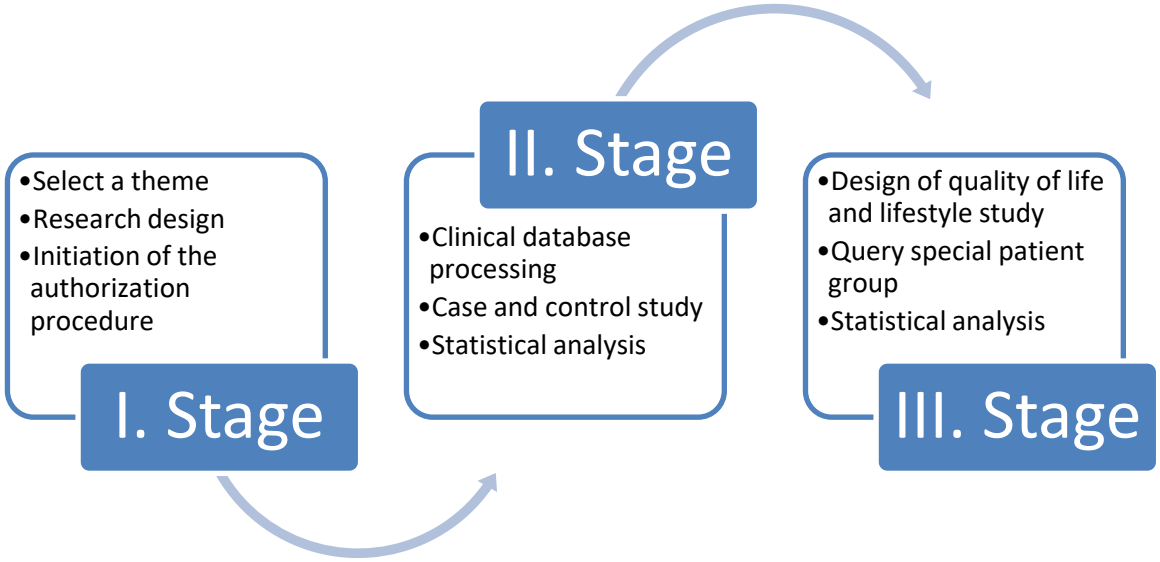

Figure 6. The main stages of the research.

3.1. Case-control study

A case-control study was conducted at the Department of Neurology, Albert Szent-Györgyi Medical Center, University of Szeged, Hungary. We collected our data from the computerized MedSolution integrated hospital information system between January 1, 2000 and January 1, 2013.

The total sample consisted of 1299 subjects who were hospitalized during the study period at the Department of Neurology, Szeged, Hungary, out of which 620 patients were identified as cases and 679 as controls. Cases included all hospitalizations in the study period if they had a diagnosis of PD (ICD-10 code: G20H0). Controls were matched to cases by age and sex, and they were selected from the patients with the diagnosis of epilepsy (ICD-10 code: G40) or

back pain (ICD-10 code: M54) at the same department. The exclusion criteria for the control group were previous diagnoses of PD or Alzheimer's disease, multiple sclerosis, myasthenia gravis, or secondary Parkinsonism.

3.1.1. Study Variables

Data on sex, age, comorbidity of dyslipidemia (ICD-10 code: E78), diabetes (ICD-10 codes: E1–E14), and hypertension (ICD-10 codes: I10–I15) of the subjects were collected from the MedSolution system. All data were registered anonymously.

3.2. Questionnaire based study

This cross-sectional study was carried out between 2013 and 2014 with the help of the Parkinson's Association "I will hold your hand" (Budapest and Szeged). The Parkinson's Clubs operating within the Delta Hungarian Parkinson's Association organize joint programs, lectures, discussions, and events for patients to discuss their problems, get answers to questions they do not dare to ask, participate in programs and rehabilitation exercises organized for them. The association expressed its support for our research, so we conducted our survey with Parkinson's patients in the auspices of the association. Data were collected by a paper-and-pencil questionnaire about socio-demographic (age, gender, and education level), lifestyle, and QoL characteristics. Participants filled in the questionnaire independently, except when having technical problems (e.g., could not hold the pen).

Altogether 150 questionnaires were allocated to the clubs, and 101 were completed. Three questionnaires were incomplete (high number of missing data), and finally, 98 persons' data were analyzed.

3.2.1. PDQ-39 questionnaire

QoL was assessed by the Hungarian version of the PDQ-39 questionnaire adapted by Fazekas and Kullmann (2001). The PDQ-39 contains 39 questions in eight dimensions (Table 1). Participants were asked to think about their health and general well-being, and to consider how often in the last month they have experienced certain events (e.g., difficulty walking). The answers were scored from 0 (never) to 4 (always), and the scores of dimensions were calculated as a scale from 0 to 100 (0=no problem at all; 100=maximum level of problem), higher scores representing worse QoL (Peto et al., 1995; Jenkinson et al., 1997).

Table 1. Dimensions of Parkinson's Disease Questionnaire (PDQ-39)

Dimension	No. of items
Mobility	10
Activities of daily living	6
Emotional well-being	6
Stigma	4
Social support	3
Cognitions	4
Communication	3
Bodily discomfort	3

Source of table: Jenkinson et al., 1997

3.2.2. Lifestyle questionnaire

Nutritional status was characterized by body mass index (BMI), which was determined by self-reported body weight and height. The BMI categories were developed in accordance with the WHO recommendation (WHO, n.d.-b). Lifestyle issues were part of the 2014 ELEF questionnaire on smoking, alcohol consumption, and dietary habits (vegetables, fruits, fat, and special diets).

3.3. Statistical analyses

Case-control study: Simple descriptive statistics were used to characterize the participants. Chi-square tests were applied to compare the basic characteristics of case and control groups. Univariate and multivariate logistic regression analyses were conducted to assess the odds of vascular risk factors (diabetes, dyslipidemia, and hypertension) in PD. All logistic models were developed for the total population, and for males and females, separately. In the regression models, we calculated the odds ratio (OR) and the 95% confidence interval (95% CI) for each predictor.

Questionnaire-based study: descriptive statistics, chi-square, and one-way ANOVA were applied. Normality was tested by one sample Kolmogorov-Smirnov test: the data of scores were not normally distributed, so one sample Wilcoxon tests were used to compare the observed and the hypothetical medians.

Statistical significance was set up at p values lower than 0.05. Statistical analyses were performed by using IBM SPSS version 24 (IBM Corporation, Armonk, New York, USA).

3.4. Ethical approval

The study protocol was approved by the Human Institutional and Regional Biomedical Research Ethics Committee, University of Szeged (Registration number: 164/2012). Participants were informed about the purpose, benefits, and risks of the study, and each participant provided written informed consent.

4. Results

4.1. Results of the case-control study

4.1.1. Patient characteristics

The mean age and gender distribution of cases (PD-patients) and controls (non-PD patients) were similar (Table 2).

Table 2. Socio-demographic characteristics of the case-control sample (N=1299).

Characteristics	Case (N=620)		Control (N=679)	
	n	%	n	%
Gender				
Male	326	52.8	373	54.9
Female	294	47.4	306	45.0
Age groups				
0–24 ys	0	0.0	0	0.0
25–34 ys	2	0.3	3	0.4
35–44 ys	3	0.48	3	0.4
45–54 ys	13	2.1	20	2.9
55–64 ys	66	10.6	79	11.6
65–74 ys	154	24.8	202	29.7
75– ys	382	61.6	372	54.7

ys: years

Diabetes mellitus was more frequent, whereas dyslipidemia was less frequent in the case group than in the control group, but no difference was found related to hypertension (Table 3).

Table 3. Biological (vascular) characteristics of the case-control sample (N=1299)

Characteristics	Case (N=620)		Control (N=679)	
	n	%	n	%
Diabetes mellitus				
Yes	222	35.8	118	17.4
No	398	64.2	561	82.6
Dyslipidemia				
Yes	50	8.1	141	20.8
No	570	91.9	538	79.2
Hypertension				
Yes	408	65.8	458	67.5
No	212	34.2	221	32.5

4.1.2. Biological (vascular) risk factors and Parkinson's disease

In the univariate logistic regression analyses (Table 4), diabetes mellitus was positively associated with PD, i.e., the odds of diabetes mellitus was significantly higher in the PD group than in the control group (OR_{total}=2.65, 95%CI: 2.05–3.43; OR_{male}=2.45, 95%CI: 1.74–3.45; OR_{female}=2.97, 95%CI: 2.01–4.40). Dyslipidemia showed a negative association: the odds were 0.62 (95%CI: 0.49–0.79) in the total population; 0.54 (95%CI: 0.38–0.75) in males and 0.71 (95%CI: 0.51–0.99) in females. In the univariate analyses, no significant associations were identified between hypertension and PD in the total population, and among males and females, respectively.

Table 4. Univariate logistic regression models of vascular factors associated with Parkinson's disease in the case-control study

Parameters	Male		Female		Total	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
DM						
Yes	2.45 (1.74–3.45)	<0.001	2.97 (2.01–4.40)	<0.001	2.65 (2.05–3.43)	<0.001
No	1.00		1.00		1.00	
Dyslipidemia						
Yes	0.54 (0.38–0.75)	<0.001	0.71 (0.51–0.99)	0.048	0.62 (0.49–0.79)	<0.001
No	1.00		1.00		1.00	
Hypertension						
Yes	1.04 (0.76–1.42)	0.809	0.79 (0.56–1.13)	0.194	0.92 (0.74–1.17)	0.530
No	1.00		1.00		1.00	

DM: diabetes mellitus; OR: odds ratio; CI: confidence interval

Age (in years) and vascular predictors were involved in the multivariate logistic regression models of the total, the male and the female populations (Table 5). The common analysis of the factors demonstrated that the odds of diabetes mellitus was higher (OR_{total}=2.86, 95%CI: 2.19–3.73; OR_{male}=2.72, 95%CI: 1.90–3.89; OR_{female}=3.24, 95%CI: 2.16–4.84), while the odds of dyslipidemia was lower (OR_{total}=0.58, 95%CI: 0.46–0.75; OR_{male}=0.48, 95%CI: 0.33–0.69; OR_{female}=0.70, 95%CI: 0.50–1.00) in PD patients than in the control group. Hypertension showed a different pattern by gender: the odds of registered hypertension was significantly lower in female PD patients (OR_{female}=0.68, 95%CI: 0.48–0.98), whereas in males, the result was not significant (OR_{male}=0.95, 95%CI: 0.69–1.32).

Table 5. Multivariate logistic regression models of vascular factors associated with Parkinson's disease in the case-control study

Parameters	Male		Female		Total	
	OR (95 % CI)	P value	OR (95 % CI)	P value	OR (95 % CI)	P value
DM						
Yes	2.72 (1.90–3.89)	<0.001	3.24 (2.16–4.84)	<0.001	2.86 (2.19–3.73)	<0.001
No	1.00		1.00			
Dyslipidemia						
Yes	0.48 (0.33–0.69)	<0.001	0.70 (0.50–1.00)	0.050	0.58 (0.46–0.75)	<0.001
No	1.00		1.00			
Hypertension						
Yes	0.95 (0.69–1.32)	0.773	0.68 (0.48–0.98)	0.039	0.82 (0.64–1.04)	0.101
No	1.00		1.00		1.00	

DM: diabetes mellitus; OR: odds ratio; CI: confidence interval

The results of our case-control study illustrated that diabetes mellitus was positively, while dyslipidemia was negatively associated with PD in males and females, whereas hypertension was negatively associated with PD only in females.

4.2. Results of the questionnaire-based study

4.2.1. Patient characteristics

Altogether 101 patients with clinically diagnosed PD were included into our study; three questionnaires were incomplete (high number of missing data); thus, finally, 98 persons' data were analyzed.

The demographic characteristics of the sample are presented in Table 6. The sex distribution showed a female dominance, and the most prevalent age-group was between 65 and 74 years. A high proportion (around 70%) of the participants were married, and half of them completed

secondary level of education, followed by college or university degree, and only a few persons had primary education level.

Table 6. Characteristics of the participants (N=98)

Characteristics	Female n (%)	Male n (%)	Total n (%)
Age groups			
25–54 ys	4 (6.8)	5 (12.8)	9 (9.2)
55–64 ys	14 (23.7)	9 (23.1)	23 (23.5)
65–74 ys	33 (55.9)	16 (41.0)	49 (50.0)
75 ys and over	8 (13.6)	9 (23.1)	17 (17.3)
Family status			
Single	2 (3.4)	2 (5.1)	4 (4.1)
Married	41 (69.5)	30 (76.9)	71 (72.4)
Divorced	6 (10.2)	6 (15.4)	12 (12.2)
Widowed	10 (16.8)	1 (2.6)	11 (11.2)
Highest educational level			
Primary school	7 (11.9)	5 (12.8)	12 (12.2)
Secondary school	33 (55.9)	23 (59.0)	56 (57.2)
College/university	19 (32.2)	11 (28.2)	30 (30.6)

ys: years

4.2.2. Quality of life and Parkinson's disease

The internal reliability of PDQ-39 was assessed by Cronbach's alpha for each dimension; high levels of internal reliability were detected in six dimensions: Cronbach's alpha was over 0.7 except the dimensions of "social support" and "bodily discomfort" (Table 7).

Table7. The structure of Parkinson's Disease Questionnaire (PDQ-39) and the internal reliability of each dimension in our sample

Dimension	No. of items	Cronbach's alpha
Mobility	10	0.946
Activities of daily living	6	0.897
Emotional well-being	6	0.890
Stigma	4	0.830
Social support	3	0.635
Cognitions	4	0.771
Communication	3	0.792
Bodily discomfort	3	0.585

The average total score of PDQ-39 was 34.29±17.82. From the eight dimensions, the highest score was found in "bodily discomfort" (42.78±22.20), whereas the lowest score was in "social support" (16.36±18.92) (Table 8).

Table 8. QOL dimensions of PD patients in our sample

Dimension	No. of cases	Mean	SD
Mobility	91	39.48	29.16
Activities of daily living	96	36.33	26.67
Emotional well-being	94	37.54	23.67
Stigma	97	35.82	26.37
Social support	83	16.36	18.92
Cognitions	96	30.01	21.39
Communication	98	28.57	25.24
Bodily discomfort	97	42.78	22.20

SD: standard deviation

Analyzing all dimensions separately (one-way analysis of variance: mean±standard deviation), gender analysis showed a significant difference only in the perception of "mobility" (males: 31.78±26.92; females: 44.28±29.70; p=0.046), age had a significant effect

on mobility (p=0.023), activities on daily living (p=0.035), and cognitions (p=0.009). No significant differences were revealed in marital status; bodily discomfort was significantly lower in the highly educated (p=0.021).

During the further analysis of our quality of life related data (see observed group), the results of the survey carried out by Tamás et al. (2014) in Hungary was used as a control (see hypothetical group); in this study, the PDQ-39 questionnaires were completed by PD patients attending routine care at the Department of Neurology, Semmelweis University, Budapest, Hungary. The characteristics of the observed and hypothetical groups are presented in Table 9.

Table 9. Sociodemographic characteristics of patients

Characteristics	Observed group n (%)	Hypothetical group* n (%)	P-value**
Age Groups			**0.006**
25–54	9 (9.2)	21 (19.1)	
55–64	23 (23.5)	37 (33.6)	
65–74	49 (50.0)	35 (31.8)	
75–	17 (17.3)	17 (15.5)	
Gender			**<0.001**
Male	39 (39.8)	70 (63.6)	
Female	59 (60.2)	38 (34.5)	
Missing data	0 (0.0)	2 (1.8)	
Marital status			**0.619**
Single	4 (4.1)	4 (3.6)	
Married or having a life partner	71 (72.4)	83 (75.5)	
Divorced	12 (12.2)	9 (8.2)	
Widow/widower	11 (11.2)	10 (9.1)	
Missing data	0 (0.0)	4 (3.6)	
Highest educational level			**0.059**
Primary school	12 (12.2)	21 (19.1)	
Secondary school	56 (57.1)	44 (40.0)	
College/university	30 (30.6)	40 (36.3)	
Missing data	0 (0.0)	5 (4.5)	

Table 10 demonstrates a comparison of the medians from our results with the previous Hungarian, i.e., hypothetical, data. In both studies, the highest score (median) was found in "bodily discomfort" (41.67 and 58.30), whereas the lowest score was found in "social support" (8.33 and 25.00). All dimensions were significantly better in patients attending the PD club ($P < 0.05$ or <0.001), especially in case of "social support".

Table 10. Comparison of PDQ-39 dimensions of patients attending PD club (observed median) with those attending routine care at the Department of Neurology (hypothetical median)

Dimensions	N	Observed median	Hypothetical median*	P value**
Mobility	91	35.00	47.50	0.014
ADL	96	31.25	50.00	<0.001
Emotional well-being	94	33.33	47.90	<0.001
Stigma	97	31.25	43.80	<0.001
Social support	83	8.33	25.00	<0.001
Cognitions	96	25.00	43.80	<0.001
Communication	98	16.67	47.10	<0.001
Bodily discomfort	97	41.67	58.30	<0.001

PDQ-39, Parkinson's Disease Questionnaire; ADL, activities of daily living

*Data from the study of Tamás et al. (2014)

**One-sample Wilcoxon test results

4.2.3. Lifestyle characteristics of PD patients

Nutritional status

The BMI data show that most patients were in the normal weight range, and much more fell in the overweight and obese categories than in the malnourished one (Figure 7).

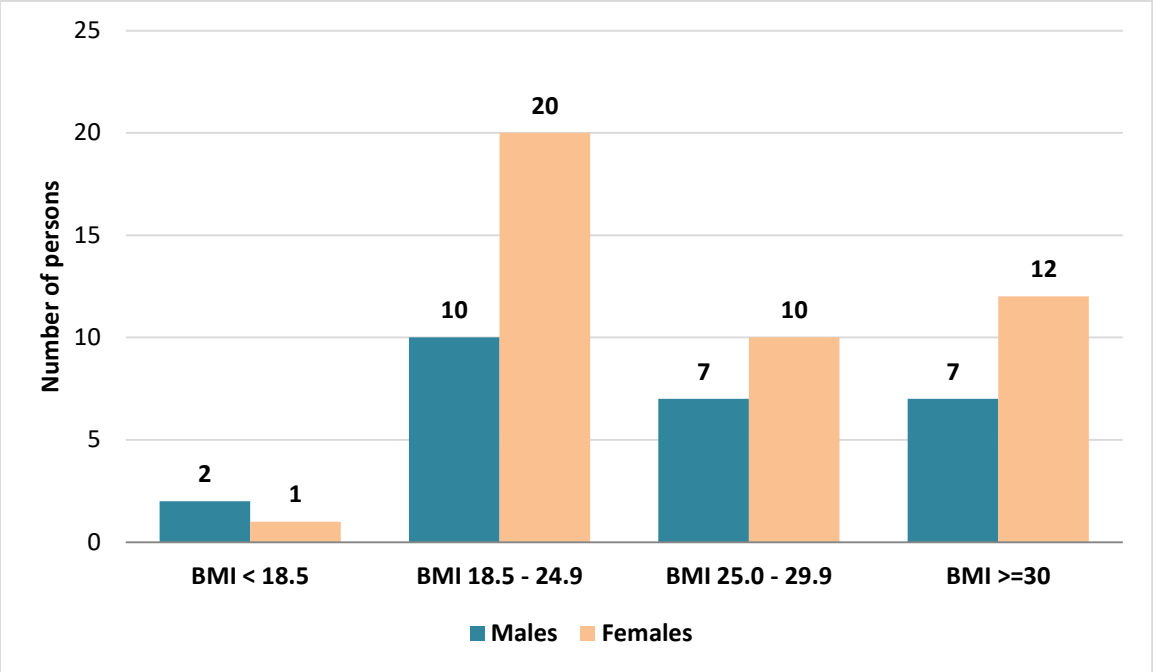

Figure 7. Body mass index (BMI) categories by gender in PD patients (n=67)

The results exhibited no significant difference between males and females (p=0.835).

In the analyzed group, 46% of the subjects consumed fruit at least once a day, and 33.7% consumed more than one time per day; the number of patients who consumed less frequently was very low, indicating that they had never consumed fruit in the sample. There was no significant difference between the genders in fruit consumption (p =0.435).

Smoking and drinking patterns

Only 4% of our sample was a daily smoker. Examination of previous smoking patterns found that 31.6% of patients had smoked in previous years (at least one year). There was no significant difference in smoking history between men and women (p =0.841).

It is noteworthy that the four individuals who have smoked to date have been doing so for more than 40 years (Figure 8).

Examining drinking patterns, we found that 44% of the sample never consumed alcohol as reported. When comparing by gender, the frequency patterns of alcohol users differ significantly by gender (p=0.041).

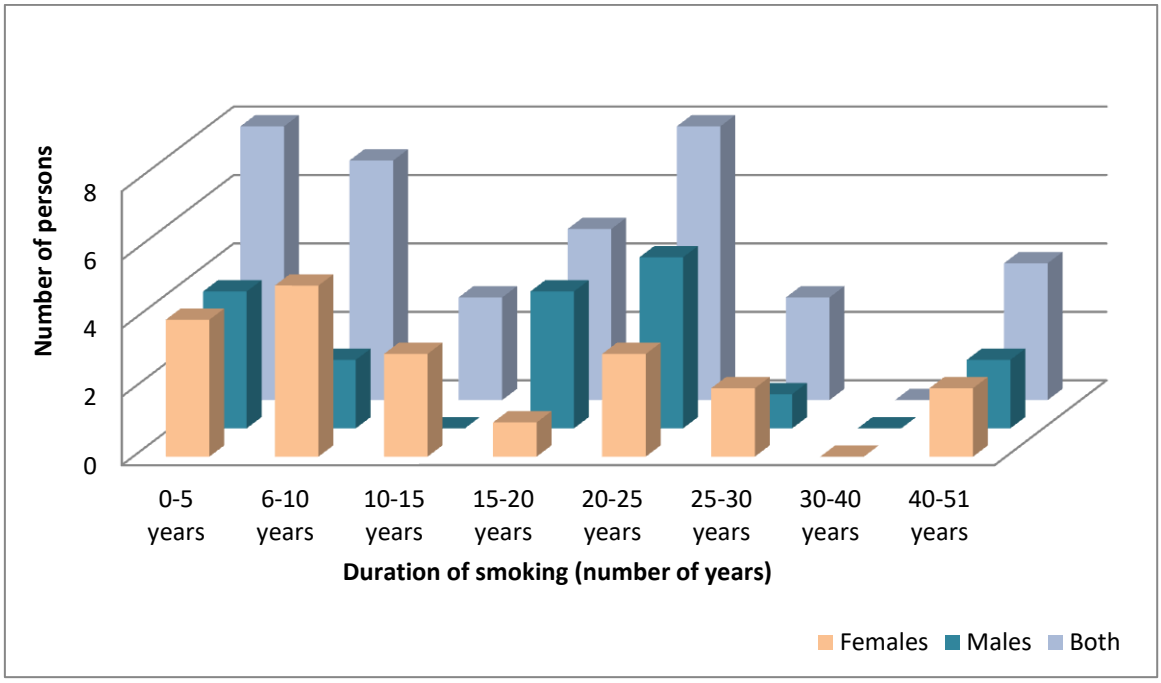

Figure 8. Number of smokers by duration of smoking and gender

Occasional alcohol drinkers have a female dominance, while regular alcohol drinkers have a male dominance. The difference between men and women is not significant (p=0.503) at the higher alcohol consumption (6 units or more) in the last year, the majority of the sample consumes large amounts of alcohol less frequently than once a month.

The alcohol consumption monitoring patterns are very important because of the increased risk of depressive disorders in PD patients.

5. Discussion

5.1. Case-control study

The results of our case-control study showed that diabetes mellitus was positively, whereas dyslipidemia was negatively associated with PD in males and females, and hypertension was negatively associated with PD only in females. The association between diabetes mellitus and PD has been described in several studies (Schernhammer et al., 2011; Konitsiotis et al., 2014, Powers et al., 2006; Lu et al., 2014). The diagnosis or the ongoing treatment of diabetes has significantly been associated with an increased risk of PD in a Danish population-based case-control study. Diabetes has been positively correlated with the severity of Parkinson's disease as well (OR=1.5) in a Greek cross-sectional study (Konitsiotis et al., 2014). Another case-control study in the USA has also found a significant relationship between PD and diabetes mellitus; the results of the study show a difference between the two genders: men with diabetes mellitus had a significantly lower risk of PD (OR=0.52) than men without diabetes, whereas the association in women was not significant (Lu et al., 2014). Nonetheless, a large meta-analysis has found negative association with future PD (OR=0.75) and diabetes mellitus (Unger et al., 1991). Our findings are in accordance with the Danish, Greek, and USA studies showing a considerable relationship between diabetes mellitus and PD.

The relationship between PD and the cause of diabetes mellitus has been discussed several times. One explanation is the inborn error of the insulin receptor expression in the substantia nigra (Unger et al., 1991), but oxidative stress and mitochondrial disorders have also been linked to the disease process.

Similarly, studies on the complex problem of elevated lipid levels and PD relationship have been published as well. A large prospective study has described that high dietary intake of cholesterol increased the risk of PD (Hu et al., 2008), while high levels of cholesterol, triglycerides, total lipids, and mean systolic and diastolic blood pressures have been less frequent in PD patients than in controls in a case-control study in Italy (Scigliano et al., 2006). The Honolulu-Asia Aging Study has also revealed an inverse association between LDL cholesterol and PD risk (Huang et al., 2008). In another prospective study, PD has not been significantly associated with hypertension, high cholesterol level, or diabetes, but it has modestly declined with the increasing blood cholesterol level (Simon et al., 2007). The association between blood pressure and the risk of PD has also been analyzed in other studies.

High blood pressure is associated with PD only in females in the National FINRISK Study; the results indicate the importance of optimal blood pressure control to reduce the risk of PD 15. The protective effect of antihypertensive medications, such as centrally acting L-type calcium channel blockers of the dihydropyridine class in PD have been described by Ritz et al. (2010). Numerous animal experiments and human observational studies have supported that a higher intake of cholesterol can reduce the risk of developing PD. The reason for this may be the increased cholesterol turnover in the brain, which promotes central nervous system repair processes, thus reducing the risk of developing PD (Dietschy & Turley, 2001).

Many studies, including our one, have found inverse causal relationship of cholesterol level and the risk of PD, which cannot be explained by lifestyle and dietary habits of the population; thus, it may be an element in the process of PD. The possible causal relationship explored in some studies suggests that certain chronic neurodegenerative disorders, such as PD, are associated with impaired cholesterol homeostasis (Vance, 2012).

In case of males, our results correlated with the previous findings related to the protective effect of abnormal lipid levels: we found negative association between dyslipidemia as a comorbidity and a risk of PD. The effect of hypertension was controversial, and it was also different by gender similarly to the findings of National FINRISK Study (Qiu et al., 2011); according to the multivariate analyses, hypertension in females is associated with a lower risk of PD, while in males no association has been found.

The strength of the present study is that prior to this study, little research had been conducted about the association between PD and some vascular risk factors in Hungary.

Our study has at least three limitations. First, the onset of PD and vascular risk factors/comorbidity is not clear because of the retrospective type of the study. Second, all diagnoses (PD, diabetes, hypertension, and dyslipidemia) were determined by the ICD codes collected from the MedSolution program of the hospital. Third, we lacked information regarding medications taken (e.g., antihypertensive drugs, statins, or antidiabetics).

5.2. Quality of Life

This study aimed to measure the QoL in individuals with PD, and the effect of attending the self-help PD club on QoL. We found that all dimensions of QoL were significantly better among those participating in the club life compared to patients being taken care of in a university hospital in Hungary.

In several international studies with the PDQ-39 questionnaire, the highest scores have been found in bodily discomfort and mobility dimensions, while the lowest in social support (Marinus et al., 2008; Žiropađa et al., 2009; Santos-Garcia & de la Fuente-Fernández, 2013; Yamanishi et al., 2013; Tamás et al., 2014; Berganzo et. al. 2016).

Our results were similar to the above-mentioned tendencies of the international and Hungarian results. The dimension of social support of our participants attending PD-club was significantly better than the results of a previous Hungarian study (Tamás et al., 2014).

Hendred and Foster (2016) have stated that participants with PD, whose QoL was measured by the WHOQOL-BREF (World Health Organization Quality of Life Scale Brief Version), had lower scores, e.g., physical limitations predicted physical domain, which was the most impaired domain in the PD group. That's why the primary element of rehabilitation in PD is physiotherapy, which increases the physical strength of the motor learning ability and reduces spasticity (Abbruzzese et al., 2016). On the other hand, the mental/psychological rehabilitation of PD is also a big challenge because of the higher risk of depression in PD patients (Blonder & Slevin, 2011). Schiavolin et al. (2017) have identified strong correlation between psychosocial difficulties and QoL in patients with PD. Simpson et al. (2014) have found that mental health measures had a high impact on health-related quality of life in people with PD, and if only physical rehabilitation is offered, then significant overall improvements on QoL are unlikely. Gill et al. (2016) have described that loneliness affected the process of inpatient rehabilitation in chronic diseases. More social support was associated with less anxiety and with less depression among elderly patients, while no positive association was revealed in younger patients; the authors have thought that social support through community clubs of PD patients might be appropriate for elderly PD patients (Saeedian et al., 2014). Loneliness and lack of social support may have a similar effect on QoL in PD patients, and the better scores among PD patients attending self-help clubs may correlate with less isolation and fewer depressive symptoms. According to our knowledge, the effect of self-help clubs on the QoL of PD patients has not yet been published; nevertheless, we found examples for the later positive impact of community-based day care on everyday life (Tollén et al., 2011).

The current study has some limitations. Primarily, the small sample size may prevent generalization of our results. Second, the cross-sectional design did not allow us to address changes in QoL; therefore, we could not completely exclude that enrolled patients had a higher QoL level also at baseline. Data collection was performed by self-administered

questionnaire and independently from health care services (during club hours); thus, the clinical parameters (e.g., Hoehn and Yahr stage) of the patients were not registered. The lack of clinical data weakens the power of comparison with the other Hungarian study sample. The variances in age and gender distribution may influence the differences between the compared studies.

5.3. Lifestyle

In contrast to the international trends, the group we examined was not characterized by malnutrition; moreover, the data of the patients typically pointed in the direction of overweight, which adapts to the domestic trends.

The study of dietary habits is crucial for Parkinson's patients as mobility difficulties due to movement problems can be exacerbated by overweight.

In many cases, patients tend to think that their obesity is purely due to genetic reasons; nonetheless, we studied their diet in details. Exercise is also an important component of achieving and maintaining ideal body weight, but due to the limitations of Parkinson's Disease it would not provide relevant information.

Numerous studies have been conducted worldwide on how Parkinson's disease affects patients' weight changes. Weight changes are influenced by many factors, since the disease affects the digestive processes; absorption is impaired, which is often accompanied by disturbances in taste and smell, and they can cause patients to lose appetite, and patients may also develop nausea and difficulty swallowing. The degree of weight loss has been studied by Cumming et al. (2017) as well. They have examined 187 Parkinson's patients and 88 atypical Parkinson's patients and compared their results with a control group of 240, who did not have any disease. Patients with Parkinson's disease and atypical parkinsonism had greater weight loss than the control group, with a 10-year odds ratio of 1.83 (95% CI 1.44–2.32). The study has also proven that weight loss was associated with a 2.23-fold increased risk of dementia and a 1.23-fold increased risk of death.

A cross-sectional study by Shidfar et al. (2016) also analyze the incidence of weight loss in PD patients. In this study, 30% of the participants (39 persons) had a normal nutritional status, and 58.5% (76 persons) were at risk of malnutrition, and 11.5% (15 persons) were already malnourished according to MNA (Mini Nutritional Assessment) ratings. Loss of muscle mass

and nutritional status, as measured by MNA score, showed significant increases with disease progression.

The results of our study were incongruent with international trends. Measured BMI values correlated with national data of ELEF 2014 survey (55% of the total population was overweight or obese); as someone over BMI 25 kg/m^2 is already overweight, so 53% of our sample was overweight or already obese (Boros et al., 2018). Thus, the trend of weight loss described in international studies could not be confirmed by our study sample; however, our study sample was in concordance with the obesity problem typical of Hungary.

Since constipation is a common problem, increased fiber intake is recommended for patients. Difficulties in swallowing and loss of appetite, as mentioned earlier, can make it more difficult, although altered consistency of food (e.g., blending) can improve compliance. Regarding the consumption of vegetables and fruits, according to the ELEF 2014 survey, 96% of the adult population consumes only half of one vegetable or fruit daily, and nearly two thirds of the population consumes them on a daily basis. Thus, the 46% daily one-fruit consumption and 33.66% daily multiple-fruit consumption measured in our study is below the national average.

Among the lifestyle factors, smoking is one of the most prominent addictive health hazards, and it is already clear that not only active smoking leads to health hazards, but it is also greatly harmed by passive smoking.

The relationship between Parkinson’s disease and smoking has been discussed in several papers, and conflicting results have emerged that smokers are less likely to have the disease (Breckenridge et al., 2016). In general, people who currently smoke and have a history of long-term smoking have a lower risk of PD than those who never smoked during their lifetime. Nicotine, a major component of tobacco products, is believed to reduce the risk of PD and play a crucial role in the regulation of striatal activity and behavior mediated by the dopaminergic system (Ma et al., 2017).

Although the support for the cessation of smoking plays an important role in PD patients as in the rest of the population, it may induce additional health problems in these patients.

6. Conclusions

Case-control study

1. Our case-control study showed considerable relationship between diabetes mellitus and PD. Diabetes mellitus was positively, while dyslipidemia was negatively associated with PD in males and females, whereas hypertension was negatively associated with PD only in females; the association between dyslipidemia and hypertension seemed to be gender-dependent.

If our starting point is that in several health policy analyses we can read that the health condition of the Hungarian population, besides the possible weaknesses of the health care system, is negatively driven by the lack of self-care, then this tendency is perfectly detectable in PD patients as well. All we have to do is to examine the nutritional status and the eating habits.

The real reason for the background of the relationship is still to be supported. Nevertheless, maintaining optimal blood sugar, blood fat, and blood pressure levels is also of paramount importance in PD patients. Because it is a chronic disease that accompanies patients for many years, comorbidities accumulated via improper lifestyle can further aggravate the condition and impair the quality of life on a daily basis.

The study of eating habits and nutritional status was induced by the correlation found in the case-control study, according to which blood sugar levels and lipid levels show different ratios in PD patients.

2. Our results showed that some risk factors of PD patients did not fit the national average, as obesity, cholesterol level, diabetes, and ischemic heart disease.

Due to the peculiarities of PD, we identified some differences. Several international studies report deteriorations in eating habits and nutritional status in PD patients. Decreased taste perception and impaired swallowing reflex function help patients become malnourished.

3. In our study, the sample did not show a decrease in BMI; moreover, the balance tipped towards overweight, as it did in the Hungarian population in general.

According to our data, the dietary patterns of PD patients were not significantly different from the unfavorable habits of the entire Hungarian population based on the national health surveys, whereas a fruit and vegetable-rich diet would be important for the whole population, especially for patients with neurodegenerative diseases.

In addition to body weight, proper nutrition is of paramount importance, in many cases with the help of health care professionals; however, it is the responsibility of the individual and the family to ensure a proper, satisfactory intake of nutrients for the affected patient. Achieving and maintaining the optimal body weight is also very important, as the instability in movement and stagnant gait is further complicated by the extra weight and the cumbersome movement that accompanies it.

Quality of life in PD

The issue of quality of life is very complex in PD patients. After all, there is a disease that is accompanied by a number of symptoms that in itself repels patients from normal social status, isolation creates a feeling of loneliness, and the majority of patients have a mental illness, such as depression, mood disorder, or panic disorder, due to decreased dopamine function. Social support, the help of the family, and support groups are inevitably important in this case.

In the case of all diseases, it may put a mental burden on the patients that they are limited in anything. In PD patients, it is an even more complex issue, as in addition to the worsening symptoms, they practically experience a situation where the intact mind is locked in a dysfunctional body with the hands and feet do not functioning as before.

These are all factors that affect quality of life. This is also particularly important in patients with PD. As the number of years of life spent in health decreases, which is not very favorable in Hungary anyway, the improvement of the quality of life in the years spent in illness is of paramount importance. Patient organizations, the social sector and mental health professionals are also called upon to advance this process. In PD patients, complete isolation can very easily develop. Loss of hope and the development of depression may further aggravate their condition.

1. Comparing our results to Hungarian and international results, we can conclude that the QoL of our patients attending the PD-club was significantly better than the results in the other Hungarian study. The members of the Szeged Parkinson Club meet once a week regularly, and a qualified physiotherapist helps them stay in shape and improve their coordination skills, and besides this, once a month, they can listen to lectures about nutrition, alternative forms of treatment, and sometimes they have the opportunity to participate in the dance therapy.

According to scientific evidence for the treatment of Parkinson's disease, PD treatment can only slow down the disease progression. A number of studies deal with the medication under which therapy can improve the physical and mental state of the participants. A significant proportion of Parkinson's patients are depressed. Therefore, a priority of physical symptoms in addition to the daily well-being and providing social support to the participants are important priorities. Several studies have addressed treatment options, such as dance therapy, which, in addition to the joy of movement for PD patients, can provide safety to be a member of a community.

2. Patient clubs provide opportunities for PD patients to learn about new procedures, to learn about new options in rehabilitation or therapy. It is also indispensable in giving patients the feeling of "I'm not alone". In many cases, the feeling of social belonging has a positive effect on quality of life and acceptance, which is essential for such an illness.
3. Although, the primary element of rehabilitation is physiotherapy in Parkinson's disease, which increases the physical strength of the motor learning ability and reduces spasticity, our results indicate that participation in club-life may provide added value to rehabilitation services of PD patients by improving mental conditions, preventing isolation, and altogether, strengthening social support.
4. Our study may be considered unique, since it was conducted among a group of persons with PD, who live an active life in a self-help club. In the light of the results, it would be worthy of support groups to include facilitating the establishment of rehabilitation options, as relevant to the subjective quality of life improves this option. Our results confirmed that the strengthening of social support of chronically ill participants can greatly contribute to the healing of them.
5. On the base of our results, we can conclude that operating patient organizations, such as the patient clubs seems to be an excellent tool of rehabilitation of PD patients /participants. Mental assistance should be made widely available as part of the therapy. There are a number of excellent efforts to bring diversity to rehabilitation procedures, and central support for this would be a huge step forward for patients. Given the dynamic growth in the number of PD patients, based on age, and that their number could even be doubled by 2040, PD patients are a very important group of the society, not only in terms of patient care, but also in terms of health economics.

7. Referencies

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ACKNOWLEDGEMENT

I would like to thank Dr. Edit Paulik, Head of Department of Public Health, for the supervision of my research, and for providing the background to it, and guiding me through my PhD work.

I wish to thank the members of the department for becoming friends from colleagues. I have learned a lot from Dr. Edina Horváth, Dr. Zsuzsanna Máté, Dr. Andrea Szabó, and Dr. Gábor Oszlánczi, you encouraged me throughout the research and thank you for your special friendship.

I would like to thank Prof. Dr. László Vécsei for arousing my interest in the topic, and then for giving me the opportunity to conduct some of my research at the Neurology Department. I am grateful to Rabi Sándorné, the leader of the Szeged Parkinson Club, for being a part of this special group. They were always welcoming and provided a huge help to me in making the investigation a reality.

Once again, I would like to thank all the colleagues of the Department of Public Health for their contribution to my professional development during my years there.

I thank my parents for the endless perseverance they bringing up me, and my precious father for always taking care of me from heaven. Special thanks to my husband for the patience and love he accompanied me in my journey.

APPENDICES

A Parkinson-kór epidemiológiájának hatása a háziorvosi ellátásra

[Dr. Kucsera Mária]

Bevezetés

James Parkinson 1817-ben elsőként írta le a róla elnevezett kórképet jellemző tünet együttest. Az elmúlt 200 év alatt számos tudományos kutatás célpontja lett a Parkinson-kór alaposabb megismerése, ám a betegség etiológiája mind a mai napig nem teljesen tisztázott (1). Több tudományos közlemény is beszámolt a genetikai és környezeti tényezők együtthatásának domináns szerepéről a Parkinson-kór kialakulásában (2–6). Az életmódi tényezők mellett, számos esetben vizsgálták a munkahelyi körülményeket is. Az utóbbi kapcsán vált ismertté, hogy bizonyos peszticidek fokozzák a Parkinson-kór előfordulásának gyakoriságát. Richardson és munkatársai a növényvédő szerek közül a p,p'-DDE-t (dichlorodiphenyldichloroethylene), illetve a β-HCH-t (hexa-kloro-ciklohexán izomer) mutatták ki nagyobb gyakorisággal a Parkinson-kóros betegek körében- a betegek 76%-ánál, míg a kontroll csoport 40%-ánál észlelték a β-HCH jelenlétét (2). Coon és munkatársai a magas ólom expozíció és a Parkinson kór előfordulása között találtak kapcsolatot: az exponáltak körében kétszer akkora volt a betegség esélye, mint a nem exponáltaknál (3). Genetikai vizsgálatok alapján hat génről jelenthető ki az egyértelmű kapcsolat a Parkinson-kór monogénes formáival (4). Familiáris halmozódás azonban csak az esetek 10%-ában igazolható, dominánsan a 40. életévüket be nem töltöttek körében (5). Idiopáthiás Parkinson-kórról abban az esetben beszélhetünk, ha a klinikai vizsgálatok során, a substantia nigrában, illetve más agytörzsi magvakban Lewy-testek mutathatók ki (6).

A Parkinson-kór diagnózisa a három alap tünet – a rigor, a nyugalmi tremor és a bradykinesis – kimutatásán alapszik. A motoros tünetek mellett többen észlelték depressziós zavarok, illetve kognitív diszfunkciók megjelenését is. A Parkinson-kór kezdeti szakaszában a felidézési nehézségek, illetve a környezeti változásokra adott késleltetett és helytelen válaszok dominálnak. Depresszió a betegek mintegy 40%-ánál áll fenn. Bouwmans és munkatársai 104 Parkinson-kóros beteget vizsgáltak depresszió és kognitív zavarok tekintetében; a minta 33,3%-ánál volt igazolható a depresszió jelenléte (7). Az anyagcsere rendellenességek és a Parkinson-kór kapcsolatát többen is elemezték. Egy dániai vizsgálat a diabétesz és a Parkinson-kór kapcsolatát tárta fel (8). A populációs alapú eset-kontroll vizsgálat eredménye szerint a diabetes 36%-os növekedést eredményezett a betegség kialakulásában. Nemek szerint a nők esélye (OR=1,50) a betegség kialakulására nagyobb volt, mint a férfiaké (1,29). Egy az Egyesült Államokban végzett epidemiológiai felmérés szerint 65 év felett a Parkinson-kór 100 000 főre vonatkoztatott prevalenciája 1588 volt a vizsgált időszakban, azaz az idősek körülbelül 1,6%-át érintette a megbetegedés. Az átlagos prevalencia a korral folyamatosan nőtt, akárcsak az incidencia, amely a 65–69 éves korosztályban 124,22, a 85 év felettieknél pedig 970,19 (9). Egy holland kutatásban a vizsgált 684 Parkinson-kóros beteg 18%-ának volt évente legalább egyszer szüksége fekvőbeteg ellátásra (10). A leggyakrabban traumás sérülések (24%), urológiai panaszok (15%), emésztőrendszeri problémák (15%) és kardiológiai ellátás (12%) kapcsán kerültek a betegek a kórházba.

Ismereteink szerint Magyarországon még nem készült hasonló felmérés, ezért nem ismert a Parkinson-kóros betegek pontos száma, és az sem, hogy az ellátásuk kapcsán milyen teher nehezedik a családorvosokra és a szakellátásra. Tekintettel a hazai adatok hiányos voltára, vizsgálatunk célja a Parkinson-kór, mint a második leggyakrabban előforduló hazai neurodegeneratív betegség előfordulási gyakoriságának felmérése, valamint háziorvosi vonatkozásainak megállapítása volt.

Vizsgált személyek és módszer

A vizsgálati csoportot a Szegedi Tudományegyetem Szent-Györgyi Albert Klinikai Központ Neurológiai Klinikáján 2000. január 1. és 2011. november 1. között Parkinson-kórral kezelt betegek alkották (BNO kód: G20H0). A felmérés az említett időszakban teljes körű volt, a fenti intervallumban 554 beteget láttak el a klinika fekvőbeteg osztályán.

Az adatgyűjtést a MedSolution integrált kórházi informatikai rendszer segítségével végeztük. A dokumentumok (kórlap, zárójelentés) elemzése során a betegek alapvető demográfiai, valamint az egyes kísérő kórképekre vonatkozó adatai kerültek rögzítésre. Az adatok feldolgozásához SPSS 19.0 szoftvert alkalmaztunk.

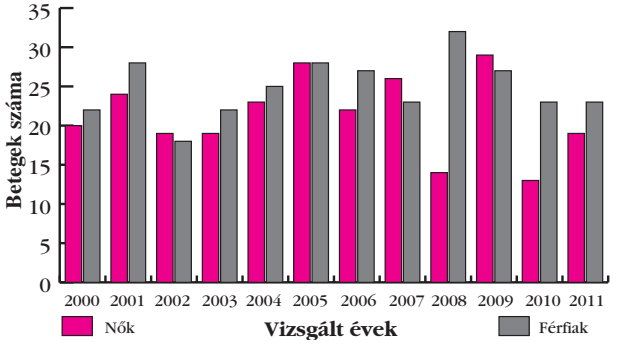
A vizsgálat elvégzését a Regionális és Intézményi Humán Orvosbiológiai Kutatásetikai Bizottság engedélyezte (Etikai engedély száma: 130/2011).

Eredmények

A tíz éves intervallum népességszámának középértékével számolva (2005) a betegség 10 éves tartamprevalenciája Csongrád megyében 1,3‰ volt. Nemek szerint jellemző volt a férfi dominancia – 297 férfinál, illetve 257 nőnél jelentkezett a kórkép.

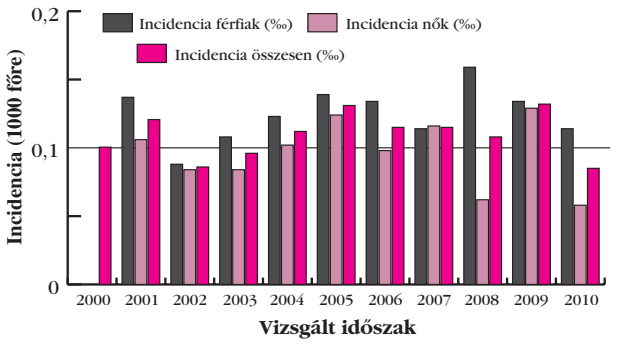
A diagnosztizált új betegek száma évenként igen eltérő értékeket mutatott *(1. ábra);* a férfi túlsúly azonban folyamatosan kimutatható volt.

1. ábra: 2000–2011 között diagnosztizált Parkinson-kóros esetek nemenkénti eloszlása (n=554)



Az évek szerinti bontásban a Parkinson-kór incidenciája 2009-ben volt a legmagasabb (0,132‰), a legalacsonyabb (0,085‰) pedig 2010-ben *(2. ábra)*. Az incidenciát nemenként lebontva is hasonló tendenciát figyelhettünk meg; a férfiak esetében a legmagasabb értéket 2008-ban (0,159‰), a nőknél pedig 2009-ben (0,129‰) találtuk.

2. ábra: A Parkinson-kór incidenciája 2000–2010 között Csongrád megye népességére vonatkoztatva



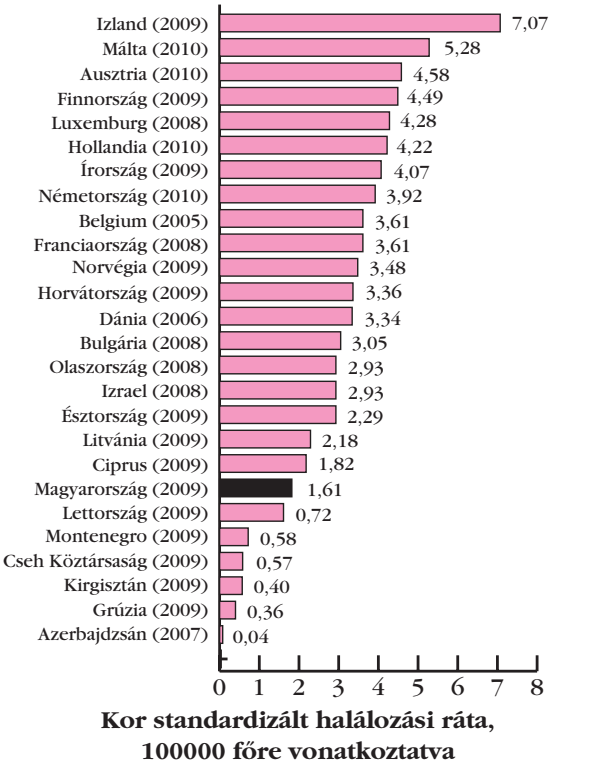
A betegek átlagéletkora 70 év volt, a nemenkénti lebontásnál szignifikáns eltérést nem találtunk (férfiak: 70,34 év, nők: 70,53 év). A diagnózis megállapításakor a legfiatalabb beteg csupán 25, a legidősebb pedig 89 éves volt.

Lakóhely szerint a Neurológiai Klinikán kezelt betegek többsége Csongrád megyéből érkezett, de az ellátás vonzáskörzetébe tartozott Bács-Kiskun és Békés megye is. A minta 76%-a (421 fő) városban, 24%-a (131 fő) községben élt, két beteg pedig külföldi lakcímmel rendelkezett.

Megbeszélés

Az Egészségügyi Világszervezet által közzétett adatok szerint jelentős különbség figyelhető meg országonként a Parkinson-kór halálozási mutatóiban *(3. ábra).* A legmagasabb arányban Máltán fordul elő a Parkinson-kór, de a szomszédos Ausztriában is igen magas ez a szám. Hazánk ezen összehasonlítás szerint a halálokként való előfordulás tekintetében az alacsony szinttel rendelkező országok között szerepel – 2009-ben a halálozások száma 260 volt, így a standardizált halálozási arányszám 1,6059‰.

3. ábra: Az Egészségügyi Világszervezet (WHO) Parkinson-kórra vonatkoztatott európai halálozási adatai. [Forrás: European Detailed Mortality Database (13)]



Az általunk vizsgált tíz éves idő intervallumban 554 beteg állt Parkinson-kór miatt kezelés alatt a szegedi Neurológiai Klinikán, eszerint a betegség Csongrád megyére vonatkoztatott prevalencia értéke 1,3 ezrelék volt. Hasonlóan hosszú időtartamot vizsgáló kutatók egészen eltérő előfordulási gyakoriságot állapítottak meg; például az Amerikai Egyesült Államokban (11). 1992 és 2006 között a Washingtoni Neurológiai Klinikán 450 beteget diagnosztizáltak ezen kórral, ami lényegesen kedvezőbb, mint a saját eredményünk, főként, ha figyelembe vesszük azt is, hogy az időszak 4 évvel hosszabb volt. Washington népessége pedig meghaladja az öt milliót, míg a teljes dél-alföldi régió lakosságszáma alig több, mint 1,3 millió (12).

A Parkinson-kór jelenleg is a második leggyakrabban elő-

forduló neurodegeneratív megbetegedés, s egyes számítások szerint 2040-re a betegek száma megduplázódhat. A European Brain Council felmérése alapján 1,2 millió embert érint a Parkinson kór a vizsgált területen (az Európai Unió 28 országa, valamint Izland, Norvégia és Svájc), ahol együttesen a betegség éves kezelési költsége 35 milliárd euró (14).

A magyar népesség elöregedése és a Parkinson-kór életkorfüggő számszerű növekedése jelentős kihívás elé állítja a beteget, a családját és az egészségügyi szereplőket is. A betegségteher jövőbeli növekedése és a folyamatos orvosi kontroll szükségessége miatt az alapellátásban tevékenykedő orvosokat is közvetlenül érinti a Parkinson-kór problematikája. A terápia célja a tünetek enyhítése mellett a betegség progressziójának lassítása. A levodopa kezelés késői mellékhatásaiként a legtöbb esetben megjelenik a motoros fluktuáció, valamint a diszkinéziák. A kór előrehaladtával nem csak a motoros funkció zavarokkal kell megküzdenie a betegnek és kezelőorvosának, de a gondolkodási funkciók is kifejezett romlásnak indulnak. Elsősorban azon exekutív funkciók leépülése figyelhető meg, amelyek felelősek a cselekvés tervezéséért és irányításáért, és az akarati elemek vezérléséért is. Csökken a memória, a problémamegoldó- és a beszédkészség is. Ha ezen állapotromlások mellé hozzátevődnek azon kutatási eredmények, amelyek szerint a Parkinson-kóros betegek körében gyakrabban fordulnak elő a diabétesz és más anyagcsere rendellenességek, továbbá jellemző a depresszió megjelenése, egyértelművé válik, hogy az alapellátást nagy kihívás elé állíthatja, ha a Parkinson-kóros betegek száma olyan drámai mértékben fog emelkedni, mint ahogy azt az előrejelzések mutatják. Ebben az esetben a családorvosokra nehezedik majd a betegek halmozódó társbetegségeinek kezelése és az esetlegesen kialakuló járásképtelenség utáni gondozás menedzselése is. A késői Parkinson-kórra jellemzőek a gyógyszerhatások megjelenése, a mozgásteljesítmény jelentős romlása, a túlmozgások és a fájdalmas izomgörcsökkel járó tartási kényszerek is. A betegség előrehaladott stádiumában tehát komoly fogyatékossághoz, rokkantsághoz vezet a kórfolyamat,melynek eredményeképpen drasztikus életminőség romlás áll be a beteg és családja életében.

Fontos, hogy a háziorvos ismerje a praxisába tartozó személyek körében a számukat, az aktuális állapotukat és annak romlását, a terápia hatékonyságát, a mindennapi életvitellel, életminőséggel kapcsolatos problémáikat, s azt hogy milyen egészségügyi segítségre, támogatásra van szükségük. Az előrejelzések szerint a betegek száma várhatóan nőni fog, emiatt a háziorvosok Parkinson-kórral kapcsolatos feladatai bővülhetnek, s erre az alapellátásnak is fel kell készülnie.

Összefoglalás

A Parkinson-kór a második leggyakrabban előforduló neurodegeneratív betegség, amelynek hazai epidemiológiai helyzete kevéssé ismert. Vizsgálatunk célja a Parkinson-kór előfordulási gyakoriságának és a kórfolyamat sajátosságainak megismerése volt a szegedi Neurológiai Klinika osztályain – 2000. január 1. és 2011. november 1. között – kezelt betegek adatai alapján. A tízéves intervallumban 554 főt (298 férfi és 256 nő) regisztráltak ezzel a kórképpel.

Eredményeink szerint a Parkinson-kór 10 éves tartamprevalenciája Csongrád megyében 1,3‰ volt a vizsgált időszakban. A betegség előfordulása enyhe férfi túlsúlyt mutatott. Az átlag életkor 70 év volt, nemenkénti lebontásnál szignifikáns eltérés nem volt igazolható (férfiak: 70,34 év, nők: 70,53 év). A betegek 76%-a városban, 18%-a községben élt.

A krónikus és progresszív kórképek, így a Parkinson-kór is elsősorban az idősebb korosztályokat érintik. Az általunk mért prevalencia érték nemzetközi összehasonlításban magasnak mondható, valamint ismeretes az is, hogy egyes kórképek (pl. diabetes mellitus) lényegesen gyakrabban fordulnak elő a Parkinson-kóros betegek körében. Nem elhanyagolható tény az sem, hogy a romló állapot mind az egyén, mind pedig a családja, környezete számára kifejezett életminőségbeli romlást eredményez, amely mellett a beteg folyamatos orvosi kontrollra szorul. Ezen szakmai tevékenység egy része a háziorvosi ellátás részét képezi, s a növekvő számú eset következtében az alapellátás részéről is fokozott odafigyelést igényel.

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RISK OF PARKINSON'S DISEASE IN SOUTHERN GREAT PLAIN, HUNGARY

Kucsera M., Paulik E.

Department of Public Health, Faculty of Medicine, University of Szeged, Hungary

INTRODUCTION

Parkinson's disease (PD) is the second in incidence order at neurodegenerative illnesses in the world. PD is due to the selective loss of nigrostrial dopaminergic neurons. These neurons are responsible for voluntary and involuntary motor function, so in their absence, the classic symptoms of PD such as tremor, muscular rigidity, bradykinesia, and postural imbalance are manifested.

Today, this disease affects a high number of people's life all over in Europe (Andlin-Sobocki et al, 2005). The European Brain Council survey declared that 1.2 million people have been affected by PD in the study area (including the 28 EU countries plus Iceland, Norway and Switzerland). Because of the frequent occurrence of PD the economic and social costs are sufficiently high, estimated 13.9 billion Euros all across Europe (Olesen et al, 2012), the overall estimates of annual cost for PD – together with the cost of disease treatment – is 35 billion Euros (Olesen et al, 2006).

Gerlach et al. (2012) examined 684 patients with PD in Netherlands. They found that 18% of patients had been hospitalized at least once in the last year. The most common causes of inpatient care were traumatic injuries (24%), urinary symptoms (15%), gastrointestinal problems (15%) and cardiac care (12%).

In Hungary, more than 20,000 patients are suffering from this disease and the disease incidence between the ages of 65 and 85 are increasing. The prevalence of primary or idiopathic PD increases proportionally with age (Gazewood et al, 2013).

The aetiology of the disease is still not completely understood, but it is suspected that the disease process is mainly due to the combination of genetic and environmental factors. The characteristic symptoms of PD are progressive cardiovascular autonomic failure, orthostatic hypotension and postprandial intestinal motility and disorders, impotence, and urinary incontinence. The autonomic symptoms of the disease predominate and deterioration of it exceeds the rate of deterioration of motor symptoms (Debreczeni et al, 2005).

The coincidence of metabolic disorders and PD were also analysed in several studies. A relationship between diabetes and PD has been revealed by Schernhammer et al. (2011) in Denmark. The Danish population-based case-control study showed that diabetes was associated with a 36% increased risk of PD. By gender the odds of the development of the disease was higher in women (OR = 1.50) than in men (1.29) (Schernhammer at al, 2011)

Taking into consideration the issues of several studies that some risk factors may influence the onset and the progression of PD, the aim of our study was to investigate the associations between the various risk factors of PD.

METHODS

This case-control study was carried out at the Neurology Department, Albert Szent-Györgyi Clinical Centre, University of Szeged, Hungary. The total sample consisted of 1299 members, of which 620 cases had been identified as PD and 679 control members. The sampling process was comprehensive in the analysed interval (1 January 2000 – 1 January 2013). The

case group of patients with PD involved those patients who were hospitalised during the study period in the Neurology Department. The diagnosis of PD (ICD code G20H0) was made on the base of the inclusion criteria of cases. The control group was also selected from the patients of the same department [ICD codes G40 (epilepsy) and M54 (back pain)]; the controls did not suffer from any neurodegenerative disease. The exclusion criteria for the control group were that if they had Parkinson- or Alzheimer's disease, multiple sclerosis, myasthenia gravis or secondary Parkinsonism.
The collection of data was based on the MedSolution integrated hospital information system. Data processing was carried out using SPSS 20 software. Chi square test, univariate and multivariate logistic regression analyses were applied. Odds ratios (OR) and 95% confidence intervals (CIs) were calculated for all variables. For all comparisons $p<0.05$ was considered significant.
The study protocol was approved by the Human Institutional and Regional Biomedical Research Ethics Committee, University of Szeged.

RESULTS

The basic demographic data are shown in Table 1. The characteristics (age, gender) of the control group were the same that of the case group.

Table 1. Demographic characteristics of the sample (N=1,299)

Characteristics		**Case (N=620)**		**Control (N=679)**	
		n	%	n	%
Gender	Male	326	52.8	373	54.9
	Female	294	47.4	306	45.0
Age groups (years)	35-59	46	7.4	52	7.6
	60-79	322	51.9	372	54.7
	80-96	252	40.6	255	37.5

The presence of diabetes was the first examined factor. Diabetes mellitus was significantly associated with PD, the adjusted OR was 2.65 (95% CI: 2.05-3.43). In all age groups, we found significantly higher odds of diabetes in the PD group, than in the control group (Figure 1).
The hyperlipidaemia (isolated hypertrigliceridaemia) was significantly associated with PD, too (OR 0.34; 95% CI: 0.24-0.47). The odds ratio (0.34) showed that the elevated lipid level may act as a protective factor in PD. No significant associations were observed between the presence of other vascular risk factors (hypertension, hypercholesterolemia) and the risk of the disease.
The odds of neurological disorders such as depression (OR: 3.03; CI 95% 1.99-4.60) and anxiety (OR: 3.90; CI 95% 1.28-11.91) were significantly higher in the PD group than in the control group.

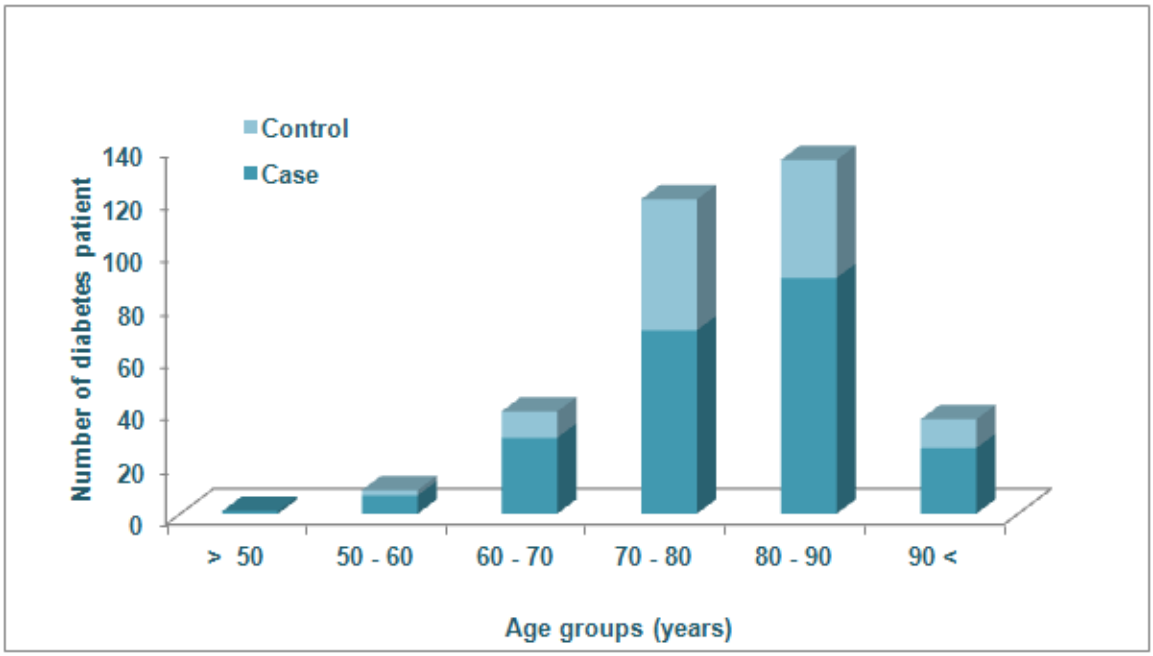

Figure 1. The occurrence of diabetes mellitus in case and control groups

CONCLUSION

PD incidence and disease burden of the society are different by countries. In the present study 620 patients with PD have been identified in the Neurology Department (Albert Szent-Györgyi Clinical Centre, University of Szeged, Hungary) in the studied period between 2000 and 2013.

In our research diabetes as a test variable was significantly associated with PD. Since the date of the onset of diabetes has not been recorded, a causal relationship between diabetes and PD cannot be stated with certainty, although, statistically, the correlation is very strong.

According to present data, the odds ratio of diabetes mellitus was nearly three times higher (2.65) in the case group than in the control group. A similar study carried out in USA has also found a higher risk of diabetes in case of PD. There1565 patients were diagnosed with PD, the risk was 40% higher among diabetic patients than among participants without diabetes (Xu at al, 2011). Several international studies have addressed the impact of hypertriglyceridaemia and/or hypercholesterinaemia on PD, therefore our study also focused on the examination of these factors. Hypertriglyceridaemia is quite striking by different in the two groups which can be seen prior analysing the two groups. This dominant relationship has been also supported by statistical analysis.

Our results show a strong relationship between the studied variables and the presence of PD. Further investigations, such as prospective studies are needed about the association between the PD and its risk factors such as diabetes mellitus and hyperlipidaemia.

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ASSOCIATION OF CARDIOVASCULAR RISK FACTORS AND PARKINSON'S DISEASE – CASE-CONTROL STUDY IN SOUTH EAST HUNGARY

Mária MARKÓ-KUCSERA[1], László VÉCSEI[2, 3], Edit PAULIK[1]

[1]Department of Public Health, Faculty of Medicine, University of Szeged, Szeged
[2]Department of Neurology, Faculty of Medicine, University of Szeged, Szeged
[3]MTA-SZTE Neuroscience Research Group, Szeged

PRINT | English | http://dx.doi.org/10.18071/isz.71.0057 | www.elitmed.hu

Aims – Parkinson's disease (PD) has the second highest incidence among neurodegenerative diseases in the world population. The study aimed to investigate the presence of some cardiovascular risk factors – dyslipidemia, diabetes, and hypertension – in PD patients and to compare their risk with non-PD population in South East Hungary.
Methods – A case-control study was conducted at the Department of Neurology, University of Szeged, Hungary. The study included 1299 subjects out of which 620 patients were identified as cases of diagnosed PD and 679 as controls. Logistic regression analyses were conducted to reveal the association of vascular risk factors with PD.
Results – In the univariate analysis, diabetes mellitus was positively associated with PD, while dyslipidemia showed negative association to it in the total population, and no significant associations were found between hypertension and PD. The multivariate logistic regression models showed that the odds of diabetes mellitus was higher (OR=2.86), while the odds of dyslipidemia was lower (OR=0.58) among PD patients than in the control group. Hypertension showed a different pattern by gender: the odds of registered hypertension was significantly lower in female PD patients (OR=0.68), whereas the result was not significant in males.
Conclusions – This is the first study that provides a comprehensive view of the cardiovascular risk factors in PD patients in Hungary and shows considerable relationship between diabetes mellitus and PD.

Keywords: *Parkinson's disease, cardiovascular risk factors, case-control study*

A PARKINSON-KÓR ÉS A CARDIOVASCULARIS RIZIKÓFAKTOROK KAPCSOLATA – ESET-KONTROLL VIZSGÁLAT A DÉL-ALFÖLDI RÉGIÓBAN

Markó-Kucsera M, MD; Vécsei L, MD, PhD; Paulik E, MD, PhD
Ideggyogy Sz 2018;71(1–2):57–62.

Bevezetés és célkitűzés – A Parkinson-kór (PD) a második leggyakrabban előforduló neurodegeneratív kórkép a világon és így hazánkban is. A vizsgálat célja egyes cardiovascularis rizikótényezők – lipidanyagcsere-zavarok, diabetes mellitus, magasvérnyomás-betegség – előfordulásának mérése volt Parkinson-kóros és attól mentes betegek körében.
Módszer – Az eset-kontroll vizsgálat a Szegedi Tudományegyetem Neurológiai Klinikáján történt. A teljes minta 1299 főből állt, amelyből 620 fő volt a diagnosztizált PD-beteg, 679 fő pedig a kontrollbeteg. A vascularis tényezők és a PD összefüggéseit logisztikus regresszióval modelleztük.
Eredmények – Az egyváltozós regressziós elemzés szerint a diabetes pozitív, a lipidanyagcsere zavarai negatív kapcsolatot mutattak a PD-vel, a magasvérnyomás-betegség esetében pedig nem igazolódott összefüggés. A többváltozós logisztikus regressziós modell megmutatta, hogy a diabetes esélyhányadosa (OR=2,86) szignifikánsan nagyobb, míg a lipidanyagcsere-zavaroké kisebb (OR=0,58) volt a PD-betegek körében, mint a kontrollcsoportban. A magas vérnyomás esélye viszont szignifikánsan kisebb (OR=0,68) volt PD esetén a nők körében, míg a férfiaknál ez nem volt megfigyelhető.
Konklúzió – Ez az első olyan hazai vizsgálat, ami a Parkinson-kórt a cardiovascularis betegségek tükrében vizsgálja, és összefüggés mutatkozott a diabetes és a PD között.

Kulcsszavak: *Parkinson-kór, cardiovascularis rizikófaktorok, eset-kontroll vizsgálat*

Correspondent: Edit PAULIK MD, PhD, Department of Public Health, Faculty of Medicine, University of Szeged; 6720 Szeged, Dóm tér 10. E-mail: paulik.edit@med.u-szeged.hu

Érkezett: 2017. november 20. Elfogadva: 2017. december 19.

Parkinson's disease (PD) is the second most common neurodegenerative disorder after Alzheimer's disease, and it affects approximately seven million people globally, and the prevalence of the disease rises parallel with the aging of the population[1]. Approximately 20 thousand people with PD

live in Hungary[2]. It is also well known that coronary artery diseases are among the leading causes of death in the world population as well as in Hungary[3].

Currently, several epidemiological studies search for how vascular risk factors such as diabetes or hypercholesterolemia affect the occurrence of PD. Studies describing the relationship between diabetes and PD have shown controversial results. A large multicenter analysis in Germany shows that the metabolic control of PD patients is better than that of patients with type 2 diabetes[4], while other studies have found positive association between diabetes and the risk of developing PD[5–7]. A large population-based case-control study in Denmark shows that those who were administered an antidiabetic drug was associated with a 35% increased risk for PD[5]. These results have been confirmed by a biomarker analysis showing that diabetes and PD are strongly linked at the molecular level[8]. The association between the risk of PD and hypercholesterolemia has been described by several studies, but those results are also controversial[9–12]. Some studies have found an inverse relationship between hypercholesterolemia and the risk of PD[9–11], while a systematic review has stated that the results are inconsistent, and further studies are needed[12]. Other studies have investigated the associations between hypertension and antihypertensive drugs, and the risk of PD[13–15]. *Louis* et al. have not found evidence of a protective effect of antihypertensive drugs in PD[13], while *Ritz* et al. have suggested that there is a potential neuroprotective role of centrally acting L-type calcium channel blockers of the dihydropyridine class in PD[14]. *Qui* et al. have found that high–normal blood pressure and hypertension are associated with an increased risk of PD in women, but there was no significant association identified in men[15].

Considering that the results of previous epidemiological studies are conflicting, the aim of our study was to investigate the prevalence of cardiovascular risk factors (diabetes mellitus, dyslipidemia, and hypertension) in PD patients and to compare their risk with non-PD population in South East Hungary.

Patients and methods

STUDY DESIGN AND PARTICIPANTS

A classical case-control study was conducted at the Department of Neurology, Albert Szent-Györgyi Health Center, University of Szeged, Hungary. We gained our data from the computerized MedSolution integrated hospital information system between January 1, 2000 and January 1, 2013.

The total sample consisted of 1299 subjects who were hospitalized during the study period at the Department of Neurology, out of which 620 patients were identified as cases and 679 as controls. Cases included all hospitalizations in the study period if they had a diagnosis of PD (ICD-10 code: G20H0). Controls were matched to cases by age and sex, and they were selected from the patients with the diagnosis of epilepsy (ICD-10 code: G40) or back pain (ICD-10 code: M54) of the same department. The exclusion criteria for the control group was previous diagnosis of Parkinson's or Alzheimer's disease, multiple sclerosis, myasthenia gravis or secondary Parkinsonism.

STUDY VARIABLES

Sex, age, comorbidity of dyslipidemia (ICD-10 code: E78), diabetes (ICD-10 codes: E1–E14), and hypertension (ICD-10 codes: I10–I15) of the subjects were collected from the MedSolution system. All data were registered anonymously.

STATISTICAL ANALYSES

Simple descriptive statistics were used to characterize the participants. Chi-square tests were applied to compare the basic characteristics of case and control groups. Univariate and multivariate logistic regression analyses were conducted to assess the odds of vascular risk factors (diabetes, dyslipidemia, and hypertension) in PD. All logistic models were developed for the total population, and for males and females, separately. In the regression models, we calculated the odds ratio (OR) and the 95% confidence interval (95% CI) for each predictor. Statistical significance was set up at p values lower than 0.05. Data analyses were performed using IBM SPSS software version 20.

ETHICS STATEMENT

The study protocol was approved by the Human Institutional and Regional Biomedical Research Ethics Committee, University of Szeged (Registration number: 164/2012).

Results

The mean age and gender distribution of cases (PD-patients) and controls (non-PD patients) were simi-

Table 1. *Baseline characteristics of participants*

Characteristics	Cases	Controls	p value*
Participants	620	679	
Age, years (mean±SD)	75.67±10.24	74.85±10.72	0.162
Female gender	294 (47.2%)	306 (45.1%)	0.390
Comorbidities			
Diabetes mellitus	222 (35.8%)	118 (17.4%)	<0.001
Dyslipidemia	160 (25.8%)	244 (35.9%)	<0.001
Hypertension	408 (65.8%)	458 (67.4%)	0.530

*Results of chi-square test

Table 2. *Univariate logistic regression models of vascular factors associated with Parkinson's disease in the case-control study*

Parameters	Univariate					
	Males		Females		Total	
	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Diabetes mellitus		<0.001		<0.001		<0.001
Yes	2.45 (1.74–3.45)		2.97 (2.01–4.40)		2.65 (2.05–3.43)	
No	1.00		1.00		1.00	
Dyslipidemia		<0.001		0.048		<0.001
Yes	0.54 (0.38–0.75)		0.71 (0.51–0.99)		0.62 (0.49–0.79)	
No	1.00		1.00		1.00	
Hypertension		0.809		0.194		0.530
Yes	1.04 (0.76–1.42)		0.79 (0.56–1.13)		0.92 (0.74–1.17)	
No	1.00		1.00		1.00	

OR: odds ratio, CI: confidence interval

lar **(Table 1)**. Diabetes mellitus was significantly more frequent, whereas dyslipidemia was less frequent in the case group than in the control group, but no difference was found related to hypertension **(Table 1)**.

In the univariate logistic regression analyses **(Table 2)**, diabetes mellitus was positively associated with PD, i.e., the odds of diabetes mellitus was significantly higher in the PD group than in the control group (OR_{total}=2.65, 95% CI: 2.05–3.43; OR_{male}=2.45, 95% CI: 1.74–3.45; OR_{female}=2.97, 95% CI: 2.01–4.40). Dyslipidemia showed negative association; the odds were 0.62 (95% CI: 0.49–0.79) in the total population, 0.54 (95% CI: 0.38–0.75) in males and 0.71 (95% CI: 0.51–0.99) in females. In the univariate analyses, no significant associations were found between hypertension and PD in the total population, and among males and females, respectively.

Age (years) and vascular predictors were involved in the multivariate logistic regression models of the total, the male and the female populations **(Table 3)**. The common analysis of the factors showed that the odds of diabetes mellitus was higher (OR_{total}=2.86, 95% CI: 2.19–3.73; OR_{male}=2.72, 95% CI: 1.90–3.89; OR_{female}=3.24, 95% CI: 2.16–4.84), while the odds of dyslipidemia was lower (OR_{total}=0.58, 95% CI: 0.46–0.75; OR_{male}=0.48, 95% CI: 0.33–0.69; OR_{female}=0.70, 95% CI: 0.50–1.00) among PD patients than in the control group. Hypertension showed a different pattern by gender: the odds of registered hypertension was significantly lower in female PD patients (OR_{female}=0.68, 95% CI: 0.48–0.98), whereas in males the result was not significant (OR_{male}=0.95, 95% CI: 0.69–1.32).

Discussion

The results of our case-control study showed that diabetes mellitus was positively, while dyslipidemia was negatively associated with PD in males and females, whereas hypertension was negatively associated with PD only in females.

The association between diabetes mellitus and PD has been described in several studies[5, 16–18]. The

Table 3. *Multivariate logistic regression models of vascular factors associated with Parkinson's disease in the case-control study*

Parameters	Multivariate					
	Males		Females		Total	
	OR (95% CI)	p value	OR (95% CI)	p value	OR (95% CI)	p value
Diabetes mellitus		<0.001		<0.001		<0.001
Yes	2.72 (1.90–3.89)		3.24 (2.16–4.84)		2.86 (2.19–3.73)	
No	1.00		1.00			
Dyslipidemia		<0.001		0.050		<0.001
Yes	0.48 (0.33–0.69)		0.70 (0.50–1.00)		0.58 (0.46–0.75)	
No	1.00		1.00			
Hypertension		0.773		0.039		0.101
Yes	0.95 (0.69–1.32)		0.68 (0.48–0.98)		0.82 (0.64–1.04)	
No	1.00		1.00		1.00	

*Adjusted for age.
OR: odds ratio, CI: confidence interval

diagnosis or the ongoing treatment of diabetes has significantly been associated with an increased risk of PD in a Danish population-based case-control study[5]. Diabetes has been positively correlated with the severity of the disease as well (OR=1.5) in a Greek cross-sectional study[16]. Another case-control study in the USA has also found a significant relationship between PD and diabetes mellitus; the results of the study show a difference between the two genders: men with diabetes mellitus had a significantly lower risk of PD (OR=0.52) than men without diabetes, whereas the association in women was not significant[17]. Nonetheless, a large meta-analysis has found negative association with future PD (OR=0.75) and diabetes mellitus[18]. Our findings are in accordance with the Danish, Greek and USA studies showing a considerable relationship between diabetes mellitus and PD.

The relationship between PD and cause of diabetes mellitus has been studied many times. One explanation is the inborn error of the insulin receptor expression in substantia nigra[19], but oxidative stress and mitochondrial disorders were linked to the disease process as well.

Similarly, studies about the complex problem of elevated lipid levels and PD relationship have been published, as well. A large prospective study has described that high dietary intake of cholesterol increased the risk of PD[20], while high levels of cholesterol, triglycerides, total lipids and mean systolic and diastolic blood pressures have been less frequent in PD patients than in controls in a case-control study in Italy[21]. The Honolulu–Asia Aging Study has also revealed an inverse association between LDL cholesterol and PD risk[22]. In another prospective study, PD has not been significantly associated with hypertension, high cholesterol level, or diabetes, but it modestly declined with the increasing blood cholesterol level[23]. The association between blood pressure and the risk of PD has also been analyzed in other studies. High blood pressure is associated with PD only in females in the National FINRISK Study; the results indicate the importance of optimal blood pressure control to reduce the risk of PD[15]. The protective effect of antihypertensive medications, such as centrally acting L-type calcium channel blockers of the dihydropyridine class in PD have been described by *Ritz* et al.[14].

Numerous animal experiments and human observational studies supported that a higher intake of cholesterol can reduce the risk of developing PD. The reason for this may be the increased cholesterol turnover in the brain, which promotes central nervous system repair processes thus reducing the risk of developing PD[24].

Many studies – including our study – have found inverse causal relationship of cholesterol level and risk of PD, which cannot be explained by lifestyle and dietary habits of the population, thus this may be an element of the process of PD. The possible causal relationship explored in some studies suggests that certain chronic neurodegenerative disorders – such as PD – are associated with impaired cholesterol homeostasis[25].

In case of males, our results correlated with the previous findings related to the protective effect of abnormal lipid levels: we found negative association between dyslipidemia as a comorbidity and a risk of PD. The effect of hypertension was contro-

versial, and it was also different by gender similarly to the findings of National FINRISK Study[15]; according to the multivariate analyses, hypertension in females is associated with a lower risk of PD, while in males no association has been found.

The strength of the present study is that prior to this study, little research had been conducted about the association between PD and some vascular risk factors in Hungary.

Our study also has at least three limitations. First, the onset of PD and vascular risk factors/comorbidity is not clear because of the retrospective type of the study. Second, all diagnoses (PD, diabetes, hypertension, and dyslipidemia) were determined by the ICD codes gained from the MedSolution program of the hospital. Third, we lacked information regarding medications taken (e.g., antihypertensive drugs, statins, antidiabetics).

This retrospective case-control study showed considerable relationship between diabetes mellitus and PD. The association between dyslipidemia and hypertension seemed to be gender-dependent. Further prospective studies are needed to confirm these findings and to characterize their role in the prevention or therapy of PD (e.g. assessment of hypertension, diabetes and dyslipidemia).

ETHICS STATEMENT

The study protocol was approved by the Human Institutional and Regional Biomedical Research Ethics Committee, University of Szeged (Registration number: 164/2012).

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Measuring quality of life in individuals with Parkinson's disease attending a self-help club: cross-sectional study in Hungary

Mária Markó-Kucsera[a], Lajos Kullmann[b] and Edit Paulik[a]

The prevalence of Parkinson's disease (PD) increases with aging. The aim of our cross-sectional study was to measure the quality of life of PD patients attending a self-help 'PD club' and to evaluate the potential positive effect of club life on quality of life. Data collection was carried out using questionnaires (PDQ-39, Hungarian version). Altogether, 101 individuals with clinically diagnosed PD were included, and finally 98 persons' data were analyzed. Among the eight dimensions, the highest score was found in 'bodily discomfort' and the lowest in 'social support'. The overall tendency of the results was similar to another Hungarian study, but the scores in all dimensions were significantly lower in our participants. These positive results seem to correlate with attending the 'PD club', indicating the potential beneficial effect of patients' organizations on promoting mental health. ***International Journal of Rehabilitation Research*** **41:81–83**

International Journal of Rehabilitation Research 2018, **41**:81–83

Keywords: Parkinson's disease, quality of life, questionnaire

[a]Department of Public Health, Faculty of Medicine, University of Szeged, Szeged and [b]Institute of Special Needs Education Methodology and Rehabilitation, Bárczi Gusztáv Faculty of Special Needs Education, Eötvös Loránd University, Budapest, Hungary

Correspondence to Mária Markó-Kucsera, MSc, Department of Public Health, Faculty of Medicine, University of Szeged, Dóm tér 10, H-6720 Szeged, Hungary
Tel: +36 62 545 119; fax: +36 62 545 120;
e-mail: kucsera.maria@med.u-szeged.hu

Received 26 June 2017 **Accepted** 2 November 2017

Introduction

The number of neurodegenerative diseases is increasing parallel with the aging of the population. After Alzheimer's disease, Parkinson's disease (PD) is the second most common neurodegenerative disorder; it affects ~10 million individuals globally, and its prevalence is increasing (de Lau and Breteler, 2006). PD typically progresses with deterioration in motor function, such as tremor or abnormal gait. Besides motor dysfunction, increasing attention is paid to the importance of emotional and mental disorders. A Norwegian research has found that 61% of PD patients had at least one psychiatric symptom, such as depression (38%) or hallucination (27%) (Wichowicz *et al.*, 2006). Blonder and Slevin (2011) have reported that 30–40% of PD patients suffer from depression. Considering the functional problems and self-help videos for PD patients, their families, and caregivers, Hammond *et al.* (2014) stated that only a few videos met standards of instructional design and that improvement in the presentation modes is needed. Therefore, besides physiotherapy, psychological and social rehabilitation is also important.

The 39-item Parkinson's Disease Questionnaire (PDQ-39) is a PD specific quality of life (QoL) test developed by Peto *et al.* (1995) and Jenkinson *et al.* (1997); it examines daily living factors influencing QoL (Marinus *et al.*, 2008; Yamanishi *et al.*, 2013; Kadastik-Eerme *et al.*, 2015; Stocchi *et al.*, 2015; Berganzo *et al.*, 2016). The Hungarian version of it was adapted and validated in 2001 by Fazekas and Kullmann (2001). Tamás *et al.* (2014) have also surveyed the QoL of 110 PD patients in Hungary.

The aim of the current study was to measure the QoL of PD patients attending a self-help 'PD club' in Hungary, and to evaluate the potential positive effect of club life on QoL by comparing our results with the previous Hungarian study (Tamás *et al.*, 2014).

Methods

This cross-sectional study was carried out on Parkinson club members in Hungary (Budapest and Szeged) in 2013–2014. Parkinson clubs working in the framework of the Delta Hungarian Parkinson Association aim to organize joint programs, lectures, discussions, and exchange of experience to improve QoL. Data were collected by a paper-and-pencil questionnaire on sociodemographic (age, sex, marital status, highest education), lifestyle, and QoL characteristics. QoL was assessed using the PDQ-39, Hungarian version. It contains 39 questions in eight dimensions (Table 1). Participants were asked about their health and general well-being, and to consider how often they experienced certain events (e.g. difficulty walking) in the previous month. The answers were scored from 0 (never) to 4 (always), and the scores of dimensions were calculated (0 = no problem at all; 100 = maximum level of problem), higher scores representing worse QoL (Peto *et al.*, 1995; Jenkinson *et al.*, 1997). Participants filled in the questionnaire independently,

0342-5282 DOI: 10.1097/MRR.0000000000000266

Table 1 Comparison of 39-item Parkinson's Disease Questionnaire dimensions of patients attending PD club (observed median) with those attending routine care at the Department of Neurology (hypothetical median)

Dimensions	*N*	Observed median	Hypothetical median[a]	*P*-value[b]
Mobility	91	35.00	47.50	0.014
ADL	96	31.25	50.00	<0.001
Emotional well-being	94	33.33	47.90	<0.001
Stigma	97	31.25	43.80	<0.001
Social support	83	8.33	25.00	<0.001
Cognitions	96	25.00	43.80	<0.001
Communications	98	16.67	47.10	<0.001
Bodily discomfort	97	41.67	58.30	<0.001

ADL, activities of daily living.
[a]Data from the study of Tamás *et al.* (2014).
[b]One-sample Wilcoxon test results.

except when having technical problems (e.g. could not hold the pen).

Altogether, 150 questionnaires were allocated to the clubs and 101 were completed. Three questionnaires were incomplete (high number of missing data), and finally, 98 persons' data were analyzed.

The results of the survey carried out by Tamás *et al.* (2014) were used as a hypothetical group; in this study, the PDQ-39 questionnaires were completed by PD patients attending routine care at the Department of Neurology, Semmelweis University, Budapest. For comparison, another option would have been the data of the validation study carried out by Fazekas and Kullmann (2001), but the sample size of this study was small, and the crude data are not available already.

Descriptive statistics, χ^2, and one-way analysis of variance were applied. Normality was tested using the one-sample Kolmogorov–Smirnov test: the data of scores were not normally distributed; thus, one-sample Wilcoxon tests were used to compare the observed and the hypothetical medians. A *P* value less than 0.05 was considered to be statistically significant. Statistical analyses were carried out using IBM SPSS, version 24 (IBM Corporation, Armonk, New York, USA).

The study protocol was approved by the Human Institutional and Regional Biomedical Research Ethics Committee, University of Szeged (registration number: 164/2012). Participants were informed about the purpose, benefits, and risks of the study, and each participant provided written informed consent.

Results

The demographic characteristics of the participants are shown in Table 2.

The internal reliability of PDQ-39 assessed by Cronbach's α was high enough (over 0.7) in six dimensions, except for 'social support' and 'bodily discomfort'.

Table 2 Sociodemographic characteristics of patients

Characteristics	Observed group [*n* (%)]	Hypothetical group [*n* (%)][a]	*P*-value[b]
Age groups			0.006
25–54	9 (9.2)	21 (19.1)	
55–64	23 (23.5)	37 (33.6)	
65–74	49 (50.0)	35 (31.8)	
75+	17 (17.3)	17 (15.5)	
Sex			<0.001
Males	39 (39.8)	70 (63.6)	
Females	59 (60.2)	38 (34.5)	
Missing data	0 (0.0)	2 (1.8)	
Marital status			0.619
Single	4 (4.1)	4 (3.6)	
Married or living together	71 (72.4)	83 (75.5)	
Divorced	12 (12.2)	9 (8.2)	
Widow/widower	11 (11.2)	10 (9.1)	
Missing data	0 (0.0)	4 (3.6)	
Highest educational level			0.059
Primary school	12 (12.2)	21 (19.1)	
Secondary school	56 (57.1)	44 (40.0)	
College/university	30 (30.6)	40 (36.3)	
Missing data	0 (0.0)	5 (4.5)	

Observed group: PD patients attending self-help PD club; hypothetical group: PD patients attending routine care at the Department of Neurology.
[a]Data from the study of Tamás *et al.* (2014).
[b]χ^2-test results.

Analyzing all dimensions separately (one-way analysis of variance), sex analysis showed a significant difference only in the perception of 'mobility' ($P=0.046$); age had a significant effect on mobility ($P=0.023$), activities on daily living ($P=0.035$), and cognitions ($P=0.009$). No significant differences were found in marital status; bodily discomfort was significantly lower in the highly educated patients ($P=0.021$).

Table 2 shows a comparison of the medians from our results with the previous Hungarian – hypothetical – data. In both studies, the highest score (median) was found in 'bodily discomfort' (41.67 and 58.30), whereas the lowest score was found in 'social support' (8.33 and 25.00). All dimensions were significantly better in patients attending the PD club ($P<0.05$ or <0.001), especially in case of 'social support'.

Discussion

This study aimed to measure the QoL in individuals with PD, and the possible effects of attending the self-help PD club. All dimensions of QoL were significantly better in individuals participating in club life compared with patients attending routine care at a university hospital.

In several international studies with the PDQ-39, the highest scores were found in bodily discomfort and mobility dimensions, whereas the lowest scores were found in social support (Marinus *et al.*, 2008; Žiropađa *et al.*, 2009; Santos-García *et al.*, 2013; Yamanishi *et al.*, 2013; Stocchi *et al.*, 2015; Berganzo *et al.*, 2016).

Our results are similar to the above-mentioned tendencies of the international and Hungarian results. The dimension of social support in participants attending the PD club was significantly better than the results of a previous Hungarian study (Tamás *et al.*, 2014).

Hendred and Foster (2016) reported that PD participant's QoL, which was measured by the World Health Organization Quality of Life Scale Brief Version (WHOQOL-BREF), was lower compared to controls in their study; for example, physical limitations predicted physical domain what was the most impaired domain in PD group. This is why the primary element of rehabilitation in PD is physiotherapy, which increases the physical strength of the motor learning ability and reduces spasticity (Abbruzzese *et al.*, 2016). However, the mental/psychological rehabilitation of PD is also a major challenge because of the higher risk of depression in PD patients (Blonder and Slevin, 2011). Schiavolin *et al.* (2017) found a strong correlation between psychosocial difficulties and QoL in patients with PD. Simpson *et al.* (2014) found that mental health measures had a high impact on health-related QoL in individuals with PD, and if only physical rehabilitation is offered then significant overall improvements on QoL are unlikely. Gill *et al.* (2016) have found that loneliness affected the process of inpatient rehabilitation in chronic diseases. More social support was associated with less anxiety and with less depression among elderly patients, whereas no positive association was found in younger patients; the authors believed that social support through community clubs of PD patients might be appropriate for elderly PD patients (Saeedian *et al.*, 2014). Loneliness and lack of social support may have similar effects on QoL in PD patients, and the better scores among PD patients attending self-help clubs may correlate with the less isolation and depressive symptoms. To our knowledge, the effect of self-help clubs on the QoL of PD patients has not been published; nevertheless, we found examples for the later positive impact of community-based day care on everyday life (Tollén *et al.*, 2011).

The current study has some limitations. Primarily, the small sample size may prevent generalization of our results. Second, the cross-sectional design did not allow us to address changes in QoL: therefore, we cannot completely exclude that enrolled patients had a higher QoL level also at baseline. Data collection was carried out by a self-administered questionnaire and independently from healthcare services (during club hours); thus, the clinical parameters (e.g. Hoehn and Yahr stage) of the patients were not registered. The lack of clinical data weakens the power of comparison with the other Hungarian study sample. The variances in age and sex distribution may influence the differences between the compared studies.

Our results indicate that participation in club life may provide added value to rehabilitation services of PD patients by improving mental conditions, preventing isolation, and altogether strengthening the social support.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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